Impact of the dietary polyacetylenic falcarinol and falcarindiol on inflammation and colorectal cancer: A mechanistic study in a primed rat model

Kobæk Larsen, Morten; Baatrup, Gunnar; Notabi, Martine K.; El-Houri, Rime; Pipó-Ollé, Emma ; Arnspang, Eva Christensen; Christensen, Lars Porskjær

27th UEG Week 2019

Barcelona, Spain, October 2019

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Letter of Thanks
for UEG Week 2019 Reviewers

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Dear Colleagues,

On behalf of the UEG Scientific Committee, I would like to take this opportunity to thank you most sincerely for your contribution as an abstract reviewer for the original programme of UEG Week Barcelona 2019. The abstract reviewing process is a crucial aspect, ensuring the scientific quality and relevance of UEG Week. I know just how much time and effort reviewing abstracts takes, but without your expertise we would not have achieved the excellence in the abstract-based sessions, and UEG Week would not be the top international digestive diseases meeting that it has become today.

Thank you!

We received a number of 3,421 abstracts in total for UEG Week 2019. In total, 2,443 abstracts were accepted, giving an acceptance rate of 71,5%. 366 abstracts will be delivered as oral presentations and 2,077 as posters. I am even more pleased to tell you that standards have again reached a very high level and we can expect most interesting research and great presentations. This high volume and high standard confirm that UEG Week is the most important forum at which to present your best research.

We have received 87 video cases and 358 clinical cases which were formally evaluated by the Scientific Committee for presentation in Barcelona. As in previous years, late breaking abstracts have been scored by the Scientific Committee.

The quality of reviewing this year was excellent, but if you have any further (positive or negative) comments, please do let us know! Finally, but most importantly, thanks to all investigators both within and outside Europe who have submitted their research to the meeting, and who are clearly contributing to making UEG Week Barcelona 2019 such a great success!

Herbert Tilg
Chair of the UEG Scientific Committee

Acknowledgements

(as of September 20, 2019; in alphabetical order)

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Oral Presentations
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Opening Session: Part I
08:00 – 10:00 / Hall 6

OP001 TOP-DOWN INFLIXIMAB SUPERIOR TO STEP-UP IN CHILDREN WITH MODERATE-TO-SEVERE CROHN'S DISEASE - A MULTICENTER RANDOMIZED CONTROLLED TRIAL

Jongsma M.M.E.[1], Cozijnsen M.[1], van Pieterson M.[1], de Meij T.[2], Norbuis O.[3], Groeneweg M.[4], Wolters V.[5], Wering H.[6], Hojsak I.[7], Kolho K.-L.[8], Hummel T.[9], Stapelbroek J.[10], van der Feen C.[11], Van Rheenen P.[12], Wijk M.[2], Teklenburg-Roord S.[3], Escher J.C.[1], Samsom J.[13], de Ridder L.[1]

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Introduction: In newly diagnosed paediatric Crohn's Disease (CD) patients current guidelines instruct to start exclusive enteral nutrition (EEN) or oral prednisolone in combination with immunomodulators to achieve remission. Infliximab (IFX) is proven to be highly effective in paediatric CD patients, but only used once patients are refractory, the so called step-up (SU) treatment strategy.

However, evidence is emerging IFX is more effective the sooner it is initiated. We hypothesize that initiation of IFX directly, i.e. top-down (TD) after diagnosis of moderate-to-severe CD, results in higher long term remission rate.

Aims & Methods: Aim: To compare efficacy of TD and SU treatment in newly diagnosed moderate-to-severe paediatric CD

Methods: For this international randomized controlled trial (RCT) 100 patients aged 3-17 years, with new-onset, untreated CD with weighted paediatric CD activity index (wPCDAI) > 40 were included in 12 centres. All patients were randomly assigned to TD or SU treatment. TD treatment consisted of 5 IFX (CT-P13) infusions of 5 mg/kg (0, 2, 6, 14, 22 weeks) combined with azathioprine (AZA). After 5 infusions, IFX was stopped while continuing AZA. SU treatment consisted of induction therapy with EEN or oral prednisolone (at physician and patient/parents discretion) combined with AZA as maintenance treatment. In both groups, IFX could be (re)started on predefined conditions. Primary endpoint of this study was sustained clinical remission (wPCDAI < 12.5) at week 52 without need for additional therapy or surgery. Secondary endpoints included patient rate using IFX at week 52, as well as clinical remission, endoscopic detection of mucosal healing (SES-CD < 3) and low fecal calprotectin levels (< 250 ug/g) at week 10.

Results: Three out of 100 patients didn't start with the study after randomization (n=97; TD:50 vs SU:47). There were no significant differences within the two groups at baseline. Median age was 15.0 years [IQR 11.7-16.6] in TD, and 14.2 years [IQR 12.0-16.3] in the SU group. 54% and 57% were males, and median wPCDAI was 55 [IQR 45-65] and 57.5 [IQR 47.5-67.5]) in the TD vs SU group, respectively.

For preliminary analysis of the primary endpoint data of 75/97 patients were available. At week 52, TD treatment resulted in sustained clinical remission for 18/37 [49%] of the patients compared to 5/38 [13%] of SU patients (p=0.001). After induction therapy IFX was (re)started in 13/37 [35%] TD patients compared to 27/38 [70%] SU patients within 52 weeks (p=0.001). Two patients underwent surgical resection (ileocecal resection), one in each treatment group.

At week 10, TD resulted in significant more patients in clinical remission (TD: 24/41 [59%] vs SU: 15/42 [36%], p=0.037) as well as endoscopic remission (47/97 consented to repeated endoscopy; TD: 17/28 [61%]; median SES-CD 0 [IQR 0-5] vs SU: 5/29 [17%]; median SES-CD 6 [IQR 3-15.5], p=0.001). Lastly, significantly more TD patients had a low fecal calprotectin level (n=44; TD: 9/23 [39%] vs SU: 4/21 [19%], p=0.005).

Conclusion: We are the first to compare TD IFX to SU treatment in an RCT of paediatric CD patients. Although this analysis is preliminary, TD treatment was superior to SU in achieving sustained clinical remission (wPCDAI < 12.5) without the need for additional therapy or surgery at week 52. Moreover, at week 10, significantly more TD patients were in clinical and endoscopic remission and had low calprotectin levels compared to SU patients.

Disclosure: Nothing to disclose

OP002 DEFINING THE CLONAL ORIGIN, EXPANSION RATE AND CLONAL DIVERSITY OF INTESTINAL METAPLASIA IN THE HELICOBACTER-INFECTED HUMAN STOMACH

Waddingham W.[1,2], Cross W.[3], Curtius K.[3], Metcalf G.[3], Mohammadi B.[4], Jenkinson A.[4], Dawas K.[4], Graham D.[2], Banks M.[2], Sekine S.[5], Jansen M.[6]

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Introduction: Over half the world's population is chronically infected with Helicobacter pylori, the main risk factor for gastric cancer (GC). Chronic infection provokes a mutagenic cascade involving extensive metaplastic remodelling of the gastric mucosa. Although gastric intestinal metaplasia (GIM) is an accepted pre-cursor lesion to GC, its origins, evolution and neoplastic potential remain unclear. An understanding of the stem cell dynamics and clonal diversity of GIM may allow targeted endoscopic surveillance to patients at greatest risk of progression to GC.

Aims & Methods: Our objective was to develop a quantitative understanding of the initiation, expansion, and clonal diversity of GIM in the chronically inflamed stomach. We developed a unique workflow to visualise and trace the clonal initiation and expansion of GIM in patients' tissues. Analysis of *en face* embedded gastric mucosa from cancer patients (n=12) who underwent gastrectomy reveals a mosaic patchwork of islands of GIM. Using patch size dynamics, 3D modelling, and whole exome sequencing (WES) we quantified the clonal expansion and genetic diversity of GIM. Comparison was made with normal gastric mucosa from patients undergoing sleeve gastrectomy for weight loss (n=12).

Results: Tracing the cellular origin of GIM in 3D, we demonstrate for the first time that GIM originates from a single stem cell within a single gastric gland. These metaplastic lineages expand within the gastric gland, display all cellular lines of intestinal epithelial differentiation (enterocyte, goblet cells, etc) and rapidly colonise singular glandular units. Direct quantification of the competitive advantage of these metaplastic lineages at single cell resolution shows that metaplastic stem cell lineages display biased drift. Patch size dynamics of neutral clonal markers in chronically inflamed gastric mucosa reveals a tenfold increased clonal expansion rate when compared to non-inflamed mucosa. Analysis of the patch size dynamics of GIM reveal that its clonal expansion rate is increased further by another order of magnitude. Finally, we have carried out whole exome sequencing (WES) to reconstruct the clonal phylogeny of patches of GIM and assess the mutation burden within metaplastic patches. Our analysis shows that the mutation burden of GIM is comparable to mature gastric cancer with some patches showing arm level copy number variation. Together, these data show that *H. pylori* provokes a massive adaptive radiation of metaplastic cellular clones, greatly accelerating the selection and expansion of mutant lineages.

Conclusion: This work reveals that the metaplastic phenotype confers a fitness advantage at the level of the individual stem cell. The markedly exaggerated expansion rate of GIM explains the time-dependent transfor-

mation of the gastric mucosa into a competitive field of cancer precursor lineages. Clonal genetic diversity may be a potential marker for GC progression risk in chronic gastritis patients.
Disclosure: Nothing to disclose

Opening Session: Part II
10:30-12:00 / Hall 6

OP003 THE NEUROPEPTIDE RECEPTOR ACTIVITY MODIFYING PROTEIN (RAMP)1 PROMOTES LIVER REGENERATION BY REGULATING YES-ASSOCIATED PROTEIN (YAP) ACTIVITY DURING ACUTE OR CHRONIC LIVER INJURY

Wang Y.[1], Laschinger M.[1], Holzmann G.[1], Wang B.[2], Stöß C.[3], Lu M.[1], Brugger M.[4], Knolle P.[4], Schulze S.[2], Steiger K.[5], Altmayr F.[1], Friess H.[6], Hartmann D.[2], Hüser N.[1], Holzmann B.[1]
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Introduction: The adult liver has a high capacity to regenerate after acute injury. In addition, chronic liver damage in patients with liver fibrosis triggers proliferation of residual hepatocytes and, thus, prevents liver failure. The liver is innervated by sensory nerves containing the neuropeptide calcitonin gene-related peptide (CGRP) that binds to the receptor activity-modifying protein (RAMP)1.
Aims & Methods: We aim to investigate whether the neuropeptide CGRP is able to modulate liver regeneration upon partial hepatectomy and during hepatic fibrosis. Wild type and RAMP1 deficient mice were subjected either to 70% partial hepatectomy (PH) or were injected with carbon tetrachloride (CCl4) for four weeks to induce chronic liver fibrosis. The de novo synthesis of CGRP receptor components in liver tissues of both models was determined by quantitative RT-PCR. Hepatocyte proliferation was quantified using Ki67- and BrdU-specific immunohistochemistry, and cell cycle regulatory components were analyzed by western blot and quantitative RT-PCR. Sirius Red staining was performed in order to assess collagen fibers deposition within hepatic parenchyma. Protein expression of fibrotic markers, such as α-SMA and collagen, was evaluated by western blot. Involvement of CGRP/RAMP1 in the Hippo pathway was tested by the presence of global or active YAP, as well as global and active YAP-regulators LATS1/2 and MOB1 using western blot analysis. To investigate the direct effect of CGRP signaling on hepatocytes or intact liver tissue in vitro, we stimulated primary hepatocytes or precision-cut liver slices with CGRP and analyzed YAP signaling components by detecting global and phosphory-lated YAP protein by western Blot analysis.
Results: Liver injury induced through partial hepatectomy or CCl4-injection caused a sustained upregulation of hepatic CGRP mRNA and a late increase of RAMP1 expression. During liver fibrosis absence of RAMP1 impairs collagen fibers deposition as well as expression of α-SMA and Collagen Type 1 proteins. RAMP1 deficiency severely delayed recovery of organ mass upon PH, and inhibited hepatocyte proliferation and cell cycle progression in both liver injury models. Mechanistically, expression of the Hippo pathway-regulated transcriptional coactivator YAP was decreased in livers of RAMP1-deficient mice following either partial hepatectomy or 4-weeks' CCl4 injection. RAMP1 deficiency impaired nuclear localization of YAP protein in hepatocytes and upregulation of YAP target genes in regenerating livers. Phosphorylation of YAP on Ser127 and Ser397, which promote YAP cytoplastic retention and extranuclear degradation, was found to be elevated in RAMP1-deficient livers in both models. Consistently, phosphorylation of the YAP kinases LATS1/2 as well as MOB1 was upregulated. Stimulation of primary hepatocytes or precision-cut liver slices with the neuropeptide CGRP corroborated our in vivo results in an in vitro setting and demonstrates that CGRP/RAMP1 signaling positively regulates YAP activity.
Conclusion: Our study identifies the neuropeptide CGRP signaling via its receptor RAMP1 as a previously unrecognized inducer of YAP activity in liver regeneration upon acute and chronic injury.
Disclosure: Nothing to disclose

OP004 EFFECTS OF FAECAL MICROBIOTA TRANSPLANTATION IN PATIENTS WITH IRRITABLE BOWEL SYNDROME (IBS): A RANDOMISED, DOUBLE-BLIND PLACEBO-CONTROLLED STUDY

El-Salhy M.[1], Hatlebakk J.G.[2], Gilja O.H.[3], Kristoffersen A.[4], Hausken T.[5]
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Introduction: The intestinal bacterial profile in IBS patients differs from that of the healthy subjects with a low diversity (dysbiosis) (1,2,3). Microbiota dysbiosis in IBS patients is believed to play an important role in the pathophysiology of this disorder (3). Faecal microbiota transplantation (FMT) has been tried in two double-blind placebo-controlled studies (4,5). While the first study showed improvement of the IBS symptoms, the other study did not show any effect at all. The present study was conducted to study the effect of FMT using a single donor with a favourable microbiota profile.
Aims & Methods: A randomised, double-blind placebo-controlled study was conducted, where 164 IBS patients were randomised to either placebo, 30 g transplant or 60 g transplant in ratio 1:1:1. The primary outcome was a reduction in the IBS-symptoms defined as a decrease in the IBS-SSS total score with ≥50 points 3 months after FMT. The secondary outcome was a reduction in the Dysbiosis index (DI) and a change in the intestinal bacterial profile 3 months following FMT. Abdominal symptoms, fatigue and quality of life were assessed by the IBS-SSS and Birmingham IBS symptom, fatigue Assessment Scale, IBS-Quality of Life and the Short-Form Dyspepsia index Questionnaires. Gut bacterial analysis was done using a commercially available test, GA-map Dysbiosis Test® (Genetic Analysis AS, Oslo, Norway).
Results: The response to FMT occurred in 23.6, 75.9 and 87.3% of patients received placebo, 30 g and 60 g transplant, respectively. This was accompanied by a significant improvement in fatigue and quality of life in these patients. Symptom remission (SSS≥175 points) occurred in 5.5, 35.2 and 47.3% in placebo, FMT 30 g and FMT 60 g groups, respectively. Similarly, a significant clinical improvement in fatigue (FAS≥4 points) was found in 21.8, 53.7 and 52.7% of patients received placebo, FMT30 g and FMT 60 g, respectively. The corresponding figures for the quality of life (IBS-QoL≥14 points) were 7.3, 61.1 and 58.2%. DI did not decrease significantly in patients received FMT or placebo. The intestinal bacterial profiles changed in both groups received 30 and 60 g transplant, but not in the placebo group.
Conclusion: FMT is an effective treatment for patients with IBS. A well-defined donor with normal DI and favourable specific microbial signature is essential for the success of FMT. Response to FMT increases with increased dose. There was a significant difference in the intestinal bacterial profile between responders and non-responders, which might be used to identify candidates for FMT.

References:
1. El-Salhy M and Mazzawi T: Fecal microbiota transplantation for managing irritable bowel syndrome. Expert Rev Gastroenterol Hepatol 12: 439-445, 2018.
2. Casen C, Vebo HC, Sekelja M, et al.: Deviations in human gut microbiota: a novel diagnostic test for determining dysbiosis in patients with IBS or IBD. Aliment Pharmacol Ther 42: 71-83, 2015.
3. Enck P and Mazurak N: Dysbiosis in Functional Bowel Disorders. Annals of nutrition & metabolism 72: 296-306, 2018.
4. Johnsen PH, Hilpusch F, Cavanagh JP, et al.: Faecal microbiota transplantation versus placebo for moderate-to-severe irritable bowel syndrome: a double-blind, randomised, placebo-controlled, parallel-group, single-centre trial. The lancet. Gastroenterology & hepatology 3: 17-24, 2018.
5. Halkjaer SI, Christensen AH, Lo BZS, et al.: Faecal microbiota transplantation alters gut microbiota in patients with irritable bowel syndrome: results from a randomised, double-blind placebo-controlled study. Gut 67: 2107-2115, 2018.
Disclosure: Nothing to disclose

IBD: New drugs, new risks
10:30-12:00 / A2

OP005 REAL-WORLD SAFETY OF VEDOLIZUMAB AND ANTI-TNF THERAPIES IN BIOLOGIC-NAÏVE ULCERATIVE COLITIS AND CROHN'S DISEASE PATIENTS: RESULTS FROM THE EVOLVE STUDY

Yarur A.[1], Mantzaris G.J.[2], Kopylov U.[3], Bassel M.[4], Brett N.[4], Lissoos T.[5], Lopez C.[5], Natsios A.[6], Kifnidi C.[6], Saha S.[7], Demuth D.[8], Patel H.[9], Bressler B.[10]

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Introduction: The GEMINI phase III clinical trials showed a favourable safety profile for vedolizumab (VDZ) in treating patients (pts) with moderate-to-severely active ulcerative colitis (UC) and Crohn's disease (CD), however real-world studies are needed comparing the safety of VDZ to anti-tumour necrosis factors (anti-TNF) agents.
Aims & Methods: The objective was to compare the safety of VDZ and anti-TNF agents in a real-world cohort of biologic (bio)-naïve pts with UC or CD. This was a multi-country (Canada, Greece and the United States), retrospective chart review study of bio-naïve pts (≥18 years old) with ≥ 6 months follow-up, initiating treatment (Tx) with VDZ or an anti-TNF [adalimumab, infliximab, golimumab, certolizumab pegol] between May 2014 and March 2018. Data were collected from Tx initiation to earliest of death, chart abstraction date or 6 months post-Tx discontinuation (Canada only). Serious adverse events (SAEs) and serious infections (SIs) (defined as either life threatening, requiring hospital admission, resulting in significant disability/incapacity, or recorded in the chart as an important medical event) occurring from Tx initiation up to five half-lives post-Tx discontinuation were assessed. Incidence rates (per 100 person-years [PYs]) of SAEs and SIs were estimated. A Cox proportional hazards model adjusted for baseline characteristics was used to compare incidence rates between Tx cohorts. Adjusted hazard ratios (HR) with 95% confidence intervals (CI) are reported.
Results: This study included 1,095 pts (VDZ: 598 [UC: 380; CD: 218]; anti-TNF: 497 [UC: 224; CD: 273]) from 42 sites. Compared to anti-TNF pts, the VDZ cohort were older (mean [SD] age [years]: VDZ, 47.9 [17.4]; anti-TNF, 39.6 [15.2] [p< 0.01]), were proportionately more male (male: VDZ, 56.9%; anti-TNF, 49.9% [p=0.02]) and had a longer disease duration (median [range: min-max] disease duration [years]: VDZ, 5.0 [0.04- 54.0]; anti-TNF, 2.0 [< 0.1 - 49.0] [p< 0.01]). Median (range: min-max) follow-up (months) was: VDZ, 15.3 (3.0-47.0); anti-TNF, 16.3 (3.5-51.0). Incidence rates of first occurrence (per 100 PY [95% CI]) of SAEs (VDZ: 4.6 [3.5-6.8]; anti-TNF: 10.3 [9.5-14.9]) and SIs (VDZ: 2.6 [1.9-4.4]; anti-TNF: 7.0 [5.9-10.2]) were significantly lower in VDZ versus anti-TNF pts (adjusted HR: SAE, 0.42 [0.27-0.66]; SI, 0.33 [0.18-0.58]). Similar trends were shown when data were stratified by UC and CD, separately (Table 1).

Outcome	Ulcerative Colitis			Crohn's Disease		
	Vedolizumab IR (95% CI) N=380	Anti-TNF IR (95% CI) N=224	Adjusted Hazard Ratio (95% CI)	Vedolizumab IR (95% CI) N=218	Anti-TNF IR (95% CI) N=273	Adjusted Hazard Ratio (95% CI)
Serious Adverse Events	3.8 (2.6-6.2)	11.3 (8.9-17.5)	0.34 (0.19-0.63)*	3.0 (1.8-5.0)	5.7 (3.5-9.4)	0.47 (0.22-1.02)
Serious infections	6.1 (4.1-10.5)	9.5 (7.7-14.5)	0.45 (0.23-0.89)*	1.9 (0.8-4.5)	7.9 (5.5-11.3)	0.18 (0.06-0.50)*

Data are incidence rates (95% CI) and hazard ratios (95% CI). Incidence rates are unadjusted and are per 100 person-years; hazard ratios are from adjusted Cox proportional hazards models (adjusted for baseline confounders: age, sex, disease duration, albumin, C-reactive protein, UC/CD-related hospitalisations [prior 12 months] and disease severity). Indication (UC/CD) was a covariate for the overall analysis and was not included for disease specific models. CD: Crohn's Disease; UC: Ulcerative colitis, IR: Incidence rate.

Half-lives for treatments: VDZ: 125days (18 weeks), Infliximab: 47.5 days (6.8 weeks), Infliximab-dyyb: 47.5 days (6.8 weeks), Infliximab-abda: 47.5 days (6.8 weeks), Adalimumab: 70 days (10 weeks), Adalimumab-atto: 70 days (10 weeks), Golimumab: 70 days (10 weeks), Certolizumab pegol: 70 days (10 weeks). *Significant difference between VDZ and Anti-TNF cohorts based on adjusted HRs.

[Table 1. Safety Profile of Vedolizumab and Anti-TNF Therapies in Real-World Biologic-Naïve Ulcerative Colitis and Crohn's Disease Patients]

Lastly, the proportion of pts who experienced gastrointestinal (GI) infections was significantly higher among anti-TNF versus VDZ pts (4.4% versus 1.5%, respectively, p< 0.01).
Conclusion: Bio-naïve pts treated with VDZ had a significantly lower likelihood of experiencing SAEs and SIs, including GI infections, than those treated with anti-TNF therapies. These data support a favourable safety profile of VDZ versus anti-TNF in bio-naïve inflammatory bowel disease pts in real-world clinical practice.
Disclosure: The study was funded by Takeda Pharmaceuticals Company Ltd. BB, AY, UK and GM received honoraria from Takeda Pharmaceuticals Company Ltd; MB and NB are employees of Evidera which received funding from Takeda Pharmaceuticals Company Ltd. TL, CL, AN, CK, SS, DD and HP are employees of Takeda Pharmaceuticals Company Ltd.

OP006 AN UPDATE ON THE ANALYSIS OF NON-MELANOMA SKIN CANCER IN THE TOFACITINIB ULCERATIVE COLITIS PROGRAMME

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Introduction: Tofacitinib is an oral, small molecule Janus kinase inhibitor for the treatment of ulcerative colitis (UC). We present an update on the integrated analysis of non-melanoma skin cancer (NMSC) events in the tofacitinib UC clinical programme, as of Sep 2018.
Aims & Methods: The safety of tofacitinib for the treatment of moderate to severe UC was evaluated in a randomised, placebo (PBO)-controlled induction Phase (P) 2 study (NCT00787202),[1] two induction P3 studies (NCT01465763; NCT01458951), one maintenance P3 study (NCT01458574),[2] and an ongoing open-label, long-term extension (OLE) study (NCT01470612).[3] Patients (pts) were analysed as three cohorts: Induction (P2/P3 induction studies); Maintenance (P3 maintenance study); Overall (pts receiving ≥1 dose of tofacitinib 5 or 10 mg twice daily [BID] in P2, P3 or ongoing OLE studies). For P3 studies, a blinded independent adjudication committee reviewed potential NMSC. Proportions and incidence rates (IRs; unique pts with events per 100 pt-years [PY] of exposure) for NMSC were evaluated. A Cox proportional hazards model was used for risk factor analysis. Overall Cohort data are as of Sep 2018.
Results: 1124 pts were evaluated for NMSC (P3 studies only), with 2399 PY of tofacitinib exposure and up to 6.1 years of treatment. NMSC occurred in two Induction pts receiving tofacitinib 10 mg BID. In the Maintenance Cohort, the NMSC IR for pts receiving PBO was 0.97 (one pt) and was 1.91 for tofacitinib 10 mg BID (three pts) (Table). In the Overall Cohort, the NMSC IR for tofacitinib-treated pts was 0.78 (19 pts): 0.82 for pts receiving a predominant dose (PD) of 10 mg BID (defined as an average daily dose ≥15 mg; 15 pts) and 0.67 for pts receiving a PD of 5 mg BID (an average daily dose < 15 mg; four pts). Ten pts had squamous cell carcinoma (SCC) and 12 pts had basal cell carcinoma (BCC); three pts had both SCC and BCC. No NMSC was metastatic or led to study discontinuation. Of all tofacitinib-treated pts with NMSC, seven had prior NMSC history, 18 had prior use of thiopurines and 15 had prior tumour necrosis factor inhibitor (TNFi) exposure. The Overall Cohort showed higher IRs for subgroups of pts aged ≥50 years (1.93 [95% confidence interval (CI) 1.08, 3.19]) vs 40 to < 50 years (0.74 [95% CI 0.20, 1.89]), 30 to < 40 years (0.00 [95% CI 0.00, 0.58]) and < 30 years (0.00 [95% CI 0.00, 0.77]), and for pts with prior TNFi treatment (1.23 [95% CI 0.69, 2.04]) vs those without (0.33 [95% CI 0.09, 0.84]), or prior immunosuppressant use (0.99 [95% CI 0.59, 1.57]) vs those without (0.16 [95% CI 0.00, 0.90]). Cox regression selected prior NMSC (hazard ratio [HR] 10.95; 95% CI 3.72, 32.24; p< 0.0001) and age (HR per 10-year increase 2.10; 95% CI 1.41, 3.13; p=0.0003) as significant risk factors for NMSC.
Conclusion: NMSC events were infrequent in the tofacitinib UC programme, and were more likely to occur in pts with prior NMSC and with increasing age, known risk factors for the development of NMSC.[4] NMSC IRs were similar to those reported for tofacitinib in other indications, including for tofacitinib in rheumatoid arthritis,[5] and for biologic UC treatments.[6]

All NMSC	Induction Cohort (8 weeks)		Maintenance Cohort (52 weeks)			Overall Cohort (≤6.1 years)
	Placebo (N=282)	Tofacitinib 10 mg BID (N=938)	Placebo (N=198)	Tofacitinib 5 mg BID (N=198)	Tofacitinib 10 mg BID (N=196)	Tofacitinib All (N=1157)
Age (years), mean (SD)	41.4 (14.4)	41.3 (13.8)	43.4 (14.0)	41.9 (13.7)	43.0 (14.4)	41.3 (13.9)
Exposure, PY[a]	40.39	158.37	103.20	148.77	156.80	2398.6
Pts with events, n (%)[a]	0 (0.0)	2 (0.2)	1 (0.5)	0 (0.0)	3 (1.5)	19 (1.7)[b]
IR (95% CI)[a]	0.00 (0.00, 9.13)	1.26 (0.15, 4.56)	0.97 (0.02, 5.40)	0.00 (0.00, 2.48)	1.91 (0.39, 5.59)	0.78 (0.47, 1.22)

Data are as of Sep 2018 for the Overall Cohort (OLE study database not locked)
[a]Adjudicated data do not include data from the P2 Study (A3921063; NCT00787202);
[b]Including five pts from the P3 Induction and Maintenance Cohorts
BID, twice daily; CI, confidence interval; IR, incidence rate (unique patients with events per 100 PY of exposure); N, number of patients randomised and treated; N/A, not applicable; NMSC, non-melanoma skin cancer; OLE, open-label, long-term extension; P, Phase; pts, patients; PY, patient-years

[Table. Demographics, and proportions and IRs for all NMSC events, for the Induction, Maintenance and Overall Cohorts]

References:
1. Sandborn WJ et al. N Engl J Med 2012; 367: 616-624.
2. Sandborn WJ et al. N Engl J Med 2017; 376: 1723-1736.
3. Lichtenstein GR et al. Am J Gastroenterol 2018; 113 (Suppl 1): Abstract 571.
4. Marcil I and Stern RS. Arch Dermatol 2000; 136: 1524-1530.
5. Cohen SB et al. Ann Rheum Dis 2017; 76: 1253-1262.
6. FDA Advisory Committee Meeting sNDA 203214. FDA 2018: Supplement 018 (available at www.fda.gov).

OP007 TOFACITINIB FOR THE TREATMENT OF ULCERATIVE COLITIS: ANALYSIS OF INFECTION RATES IN THE TOFACITINIB ULCERATIVE COLITIS CLINICAL PROGRAMME

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Introduction: Tofacitinib is an oral, small molecule Janus kinase inhibitor for the treatment of ulcerative colitis (UC). The safety of tofacitinib for the treatment of moderate to severe UC was evaluated in an 8-week induction Phase 2 study (NCT00787202),[1] two 8-week induction Phase 3 studies (OCTAVE Induction 1 & 2; NCT01465763 & NCT01458951) and a 52-week maintenance Phase 3 study (NCT01458574),[2] plus an ongoing, open-label, long-term extension (OLE) study (OCTAVE Open, NCT01470612).[3] Here, we present an update on infections observed in the tofacitinib UC clinical programme as of Sep 2018.[4,5]

	Induction Cohort		Maintenance Cohort			Overall Cohort		
	Placebo (N=282; 44.8 PY)	Tofacitinib 10 mg BID (N=938; 156.2 PY)	Placebo (N=198; 100.4 PY)	Tofacitinib 5 mg BID (N=198; 146.2 PY)	Tofacitinib 10 mg BID (N=196; 154.3 PY)	PD Tofacitinib 5 mg BID (N=197; 595.5 PY)	PD Tofacitinib 10 mg BID (N=960; 1808.1 PY)	Tofacitinib All (N=1157; 2403.6 PY)
AEs (all), n (%)	155 (55.0)	515 (54.9)	149 (75.3)	143 (72.2)	156 (79.6)	183 (92.9)	793 (82.6)	976 (84.4)
Infections (all), n (%), IR [95% CI][b]	43 (15.2)	196 (20.9)	48 (24.2), 58.16 [42.88, 77.12]	71 (35.9), 62.54 [48.85, 78.89]	78 (39.8), 72.82 [57.56, 90.88]	131 (66.5), 46.76 [39.10, 55.49]	498 (51.9), 53.45 [48.86, 58.35]	629 (54.4), 51.90 [47.92, 56.12]
Serious infections, n (%), IR [95% CI][b]	0 (0.0)	8 (0.9)	2 (1.0), 1.94 [0.23, 7.00]	2 (1.0), 1.35 [0.16, 4.87]	1 (0.5), 0.64 [0.02, 3.54]	8 (4.1), 1.32 [0.57, 2.61]	35 (3.6), 1.89 [1.32, 2.63]	43 (3.7), 1.75 [1.27, 2.36]
OIs, n (%), IR [95% CI][b,c,d]	0 (0.0)	3 (0.3)	1 (0.5), 0.97 [0.02, 5.42]	2 (1.0), 1.36 [0.16, 4.92]	4 (2.0), 2.60 [0.71, 6.65]	8 (4.1), 1.37 [0.59, 2.71]	20 (2.2), 1.09 [0.66, 1.68]	28 (2.5),[e] 1.16 [0.77, 1.67]
Non-herpes-zoster OIs, n (%), IR [95% CI][b,c,d]	0 (0.0)	1 (0.1)	0 (0.0), 0.00 [0.00, 3.57]	0 (0.0), 0.00 [0.00, 2.48]	0 (0.0), 0.0 [0.00, 2.35]	1 (0.5), 0.16 [0.00, 0.92]	3 (0.3), 0.16 [0.03, 0.47]	4 (0.4), 0.16 [0.04, 0.42]
Herpes zoster (all), n (%), IR [95% CI][b]	1 (0.4)	6 (0.6)	1 (0.5), 0.97 [0.02, 5.42]	3 (1.5), 2.05 [0.42, 6.00]	10 (5.1), 6.64 [3.19, 12.22]	19 (9.6), 3.62 [2.06, 5.35]	64 (6.7), 3.42 [2.78, 4.62]	83 (7.2), 3.57 [2.84, 4.43]

Data are as of Sep 2018 for the Overall Cohort (OLE study database not locked)
[a]Only patients with events occurring within 28 days after the last dose are included in this table for calculation of proportion and IR; [b]Data for the Induction Cohort are shown as n (%) due to the short duration (8 weeks) of the induction studies; [c]Infection endpoints are based on adjudicated data; adjudicated events are calculated as percentage (%), based on the number of patients in the studies in which adjudication was performed; [d]Excludes Phase 2 patients; [e]Of the 28 patients with OIs in the Overall Cohort, 24 had herpes zoster (herpes zoster OIs were either multidermatomal [2 non-adjacent or 3-6 adjacent dermatomes] or disseminated [any of: diffuse rash >6 dermatomes, encephalitis, pneumonia, other non-skin organ involvement]), 1 had cytomegalovirus infection, 1 had histoplasmosis, 1 had cytomegalovirus hepatitis and 1 had pulmonary mycosis
AE, adverse event; BID, twice daily; CI, confidence interval; IR, incidence rate (patients with events per 100 PY of exposure); N, number of patients treated in the treatment group; n, number of patients with a particular AE; OI, opportunistic infection; OLE, open-label, long-term extension; PD, predominant dose; PY, patient-years

[OP007 Table. Summary of incidence of treatment-emergent infections (all causality)[a] in the Induction, Maintenance and Overall Cohorts]

Aims & Methods: Patients who received placebo, tofacitinib 5 or 10 mg twice daily (BID) were analysed as three cohorts: Induction (Phase 2 & Phase 3 studies, N=1220), Maintenance (Phase 3, N=592) and Overall (patients in Phase 2, Phase 3 & ongoing OLE studies receiving tofacitinib 5 or 10 mg BID, N=1157). Proportions and incidence rates (IRs; patients with events per 100 patient-years [PY] of exposure, 95% CI) were evaluated for infections of special interest (including serious infections, opportunistic infections [OIs], herpes zoster and tuberculosis). OIs were based on review by an independent adjudication committee. Overall Cohort data are as of Sep 2018.

Results: In total, 1157 patients received ≥1 dose of tofacitinib 5 or 10 mg BID (83% of patients received a predominant tofacitinib dose of 10 mg BID [average daily dose ≥15 mg]), with 2403.6 PY of tofacitinib exposure (median 623 days) and up to 6.1 years of treatment. In the Overall Cohort, the infections IR (95% CI) was 51.90 (47.92, 56.12), with nasopharyngitis being the most frequently occurring infection. For serious infection events, the IR (95% CI) for all tofacitinib-treated patients in the Overall Cohort (1.75 [1.27, 2.36]) was similar to those of the Maintenance Cohort (1.35 [0.16, 4.87] for tofacitinib 5 mg BID and 0.64 [0.02, 3.54] for 10 mg BID). No serious infection events resulted in death. OIs occurred infrequently in the UC programme, with an Overall Cohort IR (95% CI) of 1.16 (0.77, 1.67). Of 28 patients with OIs, the majority were patients with herpes zoster (n=24; IR 0.99 [95% CI 0.63, 1.47]) mostly limited to skin involvement. Not all herpes zoster events were reported as OIs, with 83 patients overall with herpes zoster events (IR 3.57 [95% CI 2.84, 4.43]), of which six were classed as serious herpes zoster (IR 0.24 [95% CI 0.09, 0.53]).

Conclusion: Serious infections were infrequent in the UC clinical programme and IRs in the Overall Cohort did not suggest an increasing risk of serious infections with longer duration of tofacitinib treatment when compared with IRs of the Maintenance Cohort. OIs were rare, with the exception of herpes zoster. The incidence of serious infections was similar in the Overall Cohorts of the UC and rheumatoid arthritis programmes (including increased risk of herpes zoster)[6] and that of other UC therapies including biologics.[7]

References:

1. Sandborn WJ et al. N Engl J Med 2012; 367: 616-624.
2. Sandborn WJ et al. N Engl J Med 2017; 376: 1723-1736.
3. Lichtenstein GR et al. Am J Gastroenterol 2018; 113 (Suppl 1): Abstract 571.
4. Winthrop KL et al. J Crohns Colitis 2018; 12 (Suppl 1): Abstract P487.
5. Winthrop KL et al. Gastroenterology 2018; 154 (Suppl 1): Abstract Sa1770.
6. Cohen SB et al. Ann Rheum Dis 2017; 76: 1253-1262.
7. Shah ED et al. Inflamm Bowel Dis 2017; 23: 570-577.

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OP008 HIGH SEROCONVERSION RATE TO TRIVALENT INFLUENZA VACCINE DURING USTEKINUMAB TREATMENT IN CROHN'S DISEASE: RESULTS FROM A PROSPECTIVE COHORT STUDY

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Introduction: Influenza vaccination may be less effective in patients with inflammatory bowel disease treated with immunosuppressive therapy, especially with combined use of anti-TNFα agents and immunomodulators. However, little is known regarding the effects of anti-IL-12/23 therapy on the efficacy of vaccination. Therefore, the aim of this study was to investigate the immune response to the 2018-2019 inactivated trivalent influenza vaccine (TIV) in Crohn's disease (CD) patients treated with ustekinumab (UST) as compared to CD patients treated with adalimumab (ADA) and healthy controls (HC).

Aims & Methods: A prospective open-label study was conducted to examine the immunogenicity of the 2018/2019 inactivated TIV in adult CD patients treated with UST. Patient details, disease characteristics and vaccination history were recorded. Age and gender matched CD patients treated with ADA and healthy controls were included as control populations. Blood samples were drawn at 3 time points, T0: before vaccination, T1: 4 to 6 weeks after vaccination and T3: 3 months after vaccination. Hemagglutinin inhibition (HI) assays for all 3 influenza vaccine strains (A/Michigan/2015/H1N1; A/Singapore/2016/H3N2, B/Victoria) were performed simultaneously on all study samples.

Results: A total of 15 CD patients treated with UST, 14 CD patients treated with ADA and 20 healthy controls (HC) were included and received TIV between October and December 2018. In UST group, 4 patients received co-medication (2 MTX, 1 high-dose prednisone and 1 low-dose prednisone). In ADA group, 5 patients received co-medication (2 thiopurine and 3 low-dose prednisone). Post-vaccination seroprotection rates (HI titer ≥1:40) were high in all 3 study groups, no significant differences between study groups were observed (Table 1).

			HC	ADA	UST	P-value overall	P-value ADA vs HC	P-value UST vs HC	P-value ADA vs UST
A/H3N2	Seroprotection rate (%)	T1	100	100	100	1*	1**	1**	1**
	Seroconversion rate (%)	T1/T0	30.0	18.2	69.2	**0.023***	0.676**	**0.038****	**0.019****
	Beyer corrected MFI	T1/T0	2.15	1.86	2.31	0.121°	0.070^	0.624^	0.087^
	Beyer corrected MFI	T3/T0	1.93	1.55	2.12	**0.030°**	**0.026^**	0.396^	**0.017^**
A/H1N1	Seroprotection rate (%)	T1	100	90.9	91.7	0.280*	0.355**	0.375**	1**
	Seroconversion rate (%)	T1/T0	47.4	33.3	70.0	0.335*	0.687**	0.433**	0.179**
	Beyer corrected MFI	T1/T0	1.96	1.79	2.03	0.280°	0.451^	0.431^	0.091^
B/Victoria	Seroprotection rate (%)	T1	85.0	66.7	92.3	0.281*	0.379**	1**	0.160**
	Seroconversion rate (%)	T1	35.0	33.3	61.5	0.278*	1**	0.169**	0.238**
	Beyer corrected MFI	T1/T0	1.49	1.15	1.73	**0.022°**	0.307^	**0.043^**	**0.008^**
	Beyer corrected MFI	T3/T0	1.319	1.055	1.627	**0.021°**	0.346^	**0.036^**	**0.009^**

*[Table 1 Immune response to seasonal trivalent influenza vaccine in 3 study groups. *Fisher-F.-H. exact, **Fisher's exact, ° Kruskal-Wallis, ^Mann-Wh.U]*

Seroconversion rates (≥4-fold increase in HI titer compared to pre-vaccination) for strain A/H3N2 were significantly higher at both time points in UST group as compared to ADA group (T1; p = 0.019, T3; p = 0.015) and HC (T1; p = 0.038, T3; p = 0.029). Geometric mean titres (GMT) at T1 and T3 were lower for all strains in ADA group, as compared to UST group and HC, and

significantly lower for the A/H3N2 strain in ADA group as compared to HC (T1; p= 0.032, T3 p = 0.015). After correcting for high GMTs at baseline using Beyer's method, mean fold increase (MFI) in titers at T3 for A/H3N2 strain was significantly lower in ADA group as compared to HC (p = 0.026) and UST group (p = 0.017). MFI for the B/Victoria strain was high in UST group and significantly higher than in ADA group (T1; p = 0.008, T3; p = 0.009). Sub-analysis after exclusion of patients on combination therapy showed similar seroconversion rates.

Conclusion: Seroconversion rate to the seasonal trivalent influenza vaccination during ustekinumab treatment in CD patients is high, in contrast to the reduced rate observed for adalimumab. Patients treated with ustekinumab can be effectively vaccinated with the trivalent influenza vaccine.

Disclosure: Nothing to disclose

OP009 RISK OF IMMUNOMEDIATED ADVERSE EVENTS OR SECONDARY LOSS OF RESPONSE TO INFLIXIMAB IN ELDERLY PATIENTS WITH INFLAMMATORY BOWEL DISEASE. A COHORT STUDY OF THE ENEIDA REGISTRY

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Introduction: Infliximab is one of the most used biological drugs in inflammatory bowel disease (IBD). Immunomediated adverse events (IAE) are of the most frequent reported infliximab-related adverse events. Elderly patients have differential pharmacodynamic and pharmacokinetic characteristics.

We recently reported an increased risk of thiopurine-related AEs in this population; hence, it would be relevant to ascertain if combined treatment is adequate in this population.

Aims & Methods: Our aim was to evaluate the rate of infliximab-related IAE in elderly IBD patients. Methods: All adult patients in the ENEIDA registry (a large, prospectively maintained database of the Spanish Working Group in IBD -GETECCU) who received a first course of infliximab treatment were identified. Patients were selected in two cohorts regarding the age at the beginning of infliximab treatment: over 60 years, and between 18 and 50 years of age. The rates of IAE recorded in the ENEIDA database (infusion

reactions, delayed hypersensitivity, edema, allergy, anaphylaxis, psoriasis, lupus-like syndrome) were compared, as well as the rate of secondary loss of response (SLR).

Results: We included 939 (12%) patients who started infliximab over 60 years and 6,844 (88%) patients below 50 years. The rate of IAE (15% vs. 15%, ns) and treatment withdrawal due to IAE (13% vs. 12%, ns) was similar in both groups. Neither differences were observed according to IAE: infusion reactions (8.3% vs. 8.2%), late hypersensitivity (1.4% vs. 1.2%), paradoxical psoriasis (0.9% vs. 1.4%) and drug-induced lupus erythematosus (0.7% vs. 0.6%). Patients below 50 years were significantly more often treated with concomitant immunosuppressants (57% vs. 48.1%> 60 years, p< 0.05). In the multivariate analysis, combination with immunomosuppressants (OR 0.741; 95%CI 0.64-8.5, p< 0.05) and female sex (OR 1.8; 95%CI 1.6-2.1 p< 0.05) were the only independent predictors to develop IAE. The rate of SLR was also similar in both study groups (20% vs. 21%). Combination therapy with immunomosuppressants was the unique risk factor to develop SLR (OR 0.85; CI95% 0.73 to 0.98, p=0.021).

Conclusion: Elderly IBD patients who start treatment with infliximab have a similar risk of developing IAE and SLR than younger patients. From this point of view, elderly would benefit from combination therapy.

Disclosure: Nothing to disclose

OP010 NO SEVERE NEONATAL AND MATERNAL COMPLICATIONS IN FEMALE PATIENTS WITH INFLAMMATORY BOWEL DISEASES TREATED WITH USTEKINUMAB OR VEDOLIZUMAB DURING PREGNANCY

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Introduction: Inflammatory bowel disease (IBD) has a high incidence in population of childbearing age. Ustekinumab, a fully human monoclonal antibody targeting the p40 subunit of interleukins 12 and 23, and vedolizumab, an anti α4β7 integrin, are biologics currently used in IBD with immunosuppressant or anti TNF failure. Data concerning use and safety of these new biologics during pregnancy are scarce.

Aims & Methods: We conducted a retrospective multicenter study in the GETAID group and collected cases of women with IBD who received at least one injection of ustekinumab or vedolizumab during pregnancy or in the last 2 months before conception. The aims of the study were (1) to evaluate pregnancy and neonatal outcomes in IBD female patients exposed to ustekinumab or vedolizumab during pregnancy, and (2) to observe the impact of ustekinumab or vedolizumab withdrawal on disease activity during pregnancy and postpartum.

Results: Sixty-seven pregnancies in 62 IBD females (43 for Crohn's disease and 19 for ulcerative colitis) were reported among 19 centers of the GETAID group. Median age at conception was 29 years. Median time between introduction of ustekinumab or vedolizumab treatment and pregnancy was 12 months. Twenty-five pregnancies occurred on ustekinumab: 7 received

ustekinumab in the last 2 months before conception, 11 received 1 injection after conception, and 7 stopped ustekinumab in the 2nd trimester. Among the 25 pregnancies occurred on ustekinumab, there were 22 (88%) live births, 1 elective termination and 2 spontaneous abortions. Maternal complications were reported in 2 women (one gestational diabetes and one threat of premature labor). Fetal complications were reported in 3 pregnancies (intra uterine growth restriction). Four newborns presented a non severe neonatal complication (3 preterm deliveries, one low birth weight) and one a Tetralogy of Fallot . Forty-two pregnancies occurred on vedolizumab: 15 received vedolizumab in the last 2 months before conception, 16 received 1 injection after conception, and 11 stopped vedolizumab (6 during the 2nd trimester and 5 during the 3rd trimester). Among the 42 pregnancies occurred on vedolizumab, there were 36 (86%) live births, 1 elective termination (for Down Syndrom) and 5 (12%) spontaneous abortions. Maternal complications were reported in 5 women (one cholestasis and 4 pre-eclampsia). Fetal complications were reported in one pregnancy (intra uterine growth restriction) and 13 newborns developed a neonatal complication (6 preterm deliveries, 6 low birth weight and one congenital corpus callosum hypoplasia). Concerning IBD activity, 65% of women were in remission at conception. Among them, only 2 patients flared during pregnancy.

Conclusion: We reported in 67 pregnancies under vedolizumab or ustekinumab exposition, no severe neonatal (except a cardiac malformation) and maternal complications. However, additional prospective evaluations regarding safety concerns pregnancy outcomes in patients directly exposed to ustekinumab or vedolizumab are needed.

Disclosure: Travelling: Janssen, Biogaran Board: Ferring Speaker: Takeda

Therapeutic nutrition in IBD

10:30-12:00 / A3

OP011 HIGH PHENOLIC ACID INTAKE IS A PROTECTIVE FACTOR FROM COLORECTAL ADENOMAS AMONG EVER-SMOKERS

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Introduction: Polyphenols are a family of phytochemicals, demonstrating anti-inflammatory and antioxidant properties. High intake of phenolic acid have been linked with reduced risk of colorectal cancer (CRC) and adenoma, while smoking has been linked with a higher risk. However, the association of phenolic acids with different types of colorectal adenomas and the interaction with smoking has yet been tested.

Aims & Methods: The aims of this study were to explore the independent association between phenolic acid intake and colorectal adenomas, and to evaluate the potential interaction with smoking. This was a case-control study, among consecutive subjects aged 40-70 years, undergoing colonoscopy during 2010-2015. Cases with colorectal adenomas were compared to controls with no past or present polyps. Detailed information was gathered regarding adenoma size, histology and anatomic location, to enable the definition of non-advanced and advanced adenomas, and their location in the distal and proximal colon. Demographics, medical history, anthropometrics, smoking status, lifestyle and dietary intake was assessed. Data on the phenolic acid content in foods was obtained from the Phenol-Explorer database[1]. High phenolic acid intake was defined according to the study sample median (214.8 mg/day). Based on the questionnaires, smoking status was defined as: never-smokers and ever-smokers (past/current smokers). Smoking intensity was calculated in pack-years as: daily cigarettesXyears smoking/20. Pack years were categorized by the group median (≥19.55 pack-years).

Results: The analysis included 711 patients (cases of colorectal adenomas n=326; non-advanced adenomas n=160; advanced adenomas n=166; controls n=385). High phenolic acid intake was negatively associated with colorectal adenomas (OR=0.60, 95%CI 0.43-0.83, P=0.003), both non-advanced and advanced adenomas (OR=0.63, 0.42-0.95 vs. OR=0.56, 0.37-0.86 respectively), independently of demographic, medical and lifestyle confounders. Associations were significant with distal adenomas but not with proximal adenomas (OR=0.56, 0.37-0.84 vs. OR=0.71, 0.47-1.09 respectively). The association was modified by smoking, as high phenolic acid intake had a strong negative association with colorectal adenomas among ever-smokers but not among never-smokers (P for interaction=0.013) (Table 1). Furthermore, the association was also modified by smoking intensity, as strong inverse associations were observed between high phenolic acid intake and all types of colorectal adenomas among participants who reported high smoking intensity (≥19.55 pack years, Table 1).

Conclusion: Intake of phenolic-acids is negatively associated with colorectal adenomas, both distal and proximal, among ever-smokers. A high phenolic-acid diet should be further studied as a potential mean to reduce smoking induced oxidative stress, and prevent adenoma-carcinoma pathway.

References: 1. Neveu V, Perez-Jiménez J, Vos F, Crespy V, du Chaffaut L, Mennen L, et al. Phenol-Explorer: an online comprehensive database on polyphenol contents in foods. Database (Oxford). 2010;2010:bap024.

Disclosure: Nothing to disclose

Type of adenoma	Polyphenol intake mg/day	Never smokers		Ever smokers		Smokers of 1.1-19.54 pack years among smokers		Smokers of ≥19.55 pack years among smokers	
		n (cases/controls)	OR (95%CI), P	n (cases/controls)	OR (95%CI), P	n (cases/controls)	OR (95%CI), P	n (cases/controls)	OR (95%CI), P
Total adenomas	< 214.8 mg/day	65/87	1.00 (ref.)	122/78	1.00 (ref.)	46/38	1.00 (ref.)	76/39	1.00 (ref.)
	≥ 214.8 mg/day	70/114	0.88 (0.54-1.44) 0.625	70/105	0.42 (0.26-0.67) <0.001	41/62	0.63 (0.31-1.27) 0.202	29/41	0.33 (0.16-0.68) 0.003
Advanced adenomas	< 214.8 mg/day	35/87	1.00 (ref.)	59/78	1.00 (ref.)	17/38	1.00 (ref.)	42/39	1.00 (ref.)
	≥ 214.8 mg/day	34/114	0.95 (0.51-1.76) 0.888	38/105	0.54 (0.31-0.94) 0.029	23/62	1.26 (0.50-0.31) 0.614	15/41	0.39 (0.17-0.90) 0.028
Non-advanced adenomas	< 214.8 mg/day	30/87	1.00 (ref.)	63/78	1.00 (ref.)	28/38	1.00 (ref.)	35/39	1.00 (ref.)
	≥ 214.8 mg/day	36/114	0.88 (0.47-1.66) 0.710	31/105	0.33 (0.18-0.60) <0.001	17/62	0.40 (0.16-1.05) 0.058	14/41	0.32 (0.12-0.84) 0.021
Distal adenomas	< 214.8 mg/day	32/87	1.00 (ref.)	65/78	1.00 (ref.)	24/38	1.00 (ref.)	41/39	1.00 (ref.)
	≥ 214.8 mg/day	32/114	0.95 (0.50-1.78) 0.873	35/105	0.41 (0.23-0.72) 0.002	19/62	0.52 (0.20-1.32) 0.170	16/41	0.36 (0.15-0.85) 0.021
Proximal adenomas	< 214.8 mg/day	33/87	1.00 (ref.)	57/78	1.00 (ref.)	22/38	1.00 (ref.)	35/39	1.00 (ref.)
	≥ 214.8 mg/day	39/114	0.90 (0.48-1.66) 0.742	35/105	0.46 (0.26-0.82) 0.009	22/62	0.81 (0.34-1.93) 0.816	13/41	0.28 (0.10-0.75) 0.011

[OP011 Table. Multivariate association between high polyphenol intake and colorectal adenoma groups, according to smoking status and intensity.]

OP012 SHIFTS IN BACTERIAL COMMUNITY FUNCTION ARE ASSOCIATED WITH SHORT CHAIN FATTY ACID PATHWAYS DURING NUTRITIONAL THERAPY IN PEDIATRIC CROHN'S DISEASE PATIENTS

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Introduction: Changes in gut bacterial community structure are associated with Crohn's Disease (CD) and response to therapy. A recently completed randomized controlled trial (RCT) showed improved sustained remission with the Crohn's Disease Exclusion Diet + Partial Enteral Nutrition (CDED+PEN) as compared with Exclusive Enteral Nutrition (EEN)[1].

Aims & Methods: We examined changes in the microbiome functional network in patients reaching remission with nutritional therapy. Stool samples from 53 CD patients reaching remission after 6 weeks of dietary treatment were collected at weeks 0, 6 and 12 and whole shotgun sequence data were obtained. In total, 146 CD patient samples were combined with 26 healthy controls (previously published by Lewis et al.[2]), and characterized using HUMAnN2. Reactions, substrates and products for genes with an enzymatic commission were input into an unsupervised Bayesian analysis of community metabolism (BiomeNet). Statistical analysis of community metabolism were performed using R. Non-negative matrix factorization (NMF) and Structural topic models (STM) were used to identify patient-associated microbial metabotypes.

Results: Unsupervised analyses revealed two metabotypes. All healthy controls possessed one metabotype (M1). CD patients possessed a mixture of two metabotypes (M1 & M2), with mixtures related to time in treatment, with 48% belonging to M1 at baseline before dietary therapy. At week 6, the number of M1 samples had increased to 63% and further increased to 74% M1 at week 12 which was closer to healthy controls. Among the pathways identified within metabotypes, one differed substantially between the two metabotypes; the key reactions involve the metabolism of various sugars.

Using NMF and STM, we identified five communities; two were predominant in M1, and the other three were predominant in M2. The communities identified in M1 samples had high levels of Bacteroidetes, including *Odoribacter*, *Alistipes*, *Prevotella*, *Barnesiella* and *Bacteroides* as well as increases in Firmicute taxa *Eubacterium*, *Ruminococcus*, *Oscillibacter*, *Clostridium*, *Faecalibacterium* and *Roseburia*. The Proteobacteria were decreased in M1. M2 samples were characterized by Enterobacteriaceae.

Genes involved in butyrate formation were also associated with M1 and M2. Genes involved in the 4-aminobutyrate pathway, and crotonoyl-CoA to butyrate pathway, (p=0.03 to 0.0001) were associated with M1. M2 was associated with genes involved in the acetyl-CoA pathway as well as ato genes (p< 0.001), involved in the degradation of SCFA.

Conclusion: Diet-induced remission samples were more similar to healthy controls, having shifted away from the baseline. The functional network, associated with active disease, changes as patients progress to remission at week 6 and sustain the remission through week12. The butyrate-related change in community function is attributable to distinct shifts in bacterial species abundance. Genes significant for the M1 butyrate pathway appeared to be driven by *Bacteroides* and *Clostridium*, while genes significant for M2 butyrate pathways were driven by taxa in Enterobacteriaceae notably *Citrobacter*, *Escherichia* and *Enterobacter*.

References: 1. Levine A, Wine E, Assa A, Sigall Boneh R, Shaoul R, Kori M, Cohen S, Peleg S, Shamaly H, On A, Millman P, Abramas L, Ziv-Baran T, Grant S, Abitbol G, Dunn KA, Bielawski JP, Van Limbergen J. Crohn's Disease Exclusion Diet Plus Partial Enteral Nutrition Induces Sustained Remission in a Randomized Controlled Trial. Gastroenterology 2019 in press. 2. Lewis JD, Chen EZ, Baldassano RN, Otley AR, Griffiths AM, Lee D, Bittinger K, Bailey A, Friedman ES, Hoffmann C, Albenberg L, Sinha R,

Compher C, Gilroy E, Nessel L, Grant A, Chehoud C, Li H, Wu GD, Bushman FD. Cell Host Microbe. 2017 Aug 9;22(2):247.
Disclosure: Nothing to disclose

Modern management of oesophageal dysmotility: Can we do better?
10:30-12:00 / B2

OP013 FUNCTIONAL LUMEN IMAGING PROBE TOPOGRAPHY (FLIP) AS A SCREENING TOOL FOR ESOPHAGEAL DYSMOTILITY: COMPARISON TO HIGH-RESOLUTION MANOMETRY (HRM) IN PATIENTS WITH ESOPHAGEAL SYMPTOMS

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Introduction: High resolution manometry (HRM) is the current gold standard for the evaluation of esophageal motility. Functional lumen imaging probe topography (FLIP) is a novel approach that enables assessment of esophago-gastric junction (EGJ) distensibility and esophageal peristalsis.

Aims & Methods: Our aim was to evaluate the agreement between FLIP and HRM for esophageal motility assessment, and to assess the role of FLIP as a screening tool for dysmotility in patients undergoing endoscopy. Methods:FLIP and HRM were compared in patients who underwent both procedures. FLIP was performed with a 16 cm balloon; peristaltic response was assessed at 30-40-50-60 ml and classified as repetitive antegrade contractions (RACs), repetitive retrograde contractions (RRCs), diminished/disordered contractile response (DDCR) or absent contractility; median EGJ distensibility index (DI) was calculated at 60 ml and classified as abnormal (< 2 mm²/mmHg), indeterminate 2-3 mm²/mmHg), normal (> 3 mm²/mmHg). FLIP was considered normal if EGJ DI was normal and RACs were present without concomitant RRCs. For HRM, ten 5-ml liquid swallows were administered; Chicago classification version 3.0 was applied for manometric diagnosis. HRM diagnoses were dichotomized as normal/minor disorder (normal, ineffective esophageal motility (IEM), or fragmented peristalsis) or abnormal (achalasia, jackhammer esophagus, distal esophageal spasm (DES), EGJ outflow obstruction (EJGOO), absent contractility). Sensitivity, specificity, and positive/negative predictive values for FLIP were calculated.

Results: 75 patients were included, age 17-92, 65% women. HRM was performed a median 18 days from FLIP. HRM diagnoses: normal/minor disorder 45% (28% normal, 16% IEM, 1% fragmented) and abnormal 55% (17% absent contractility, 16% achalasia, 15 % EGJOO, 4% Jackhammer, 3% DES). FLIP diagnoses: 33% normal, 77% abnormal. In patients with normal FLIP topography, HRM diagnoses were normal/minor disorder in 58% (52% normal and 5% IEM), absent contractility 26%, jackhammer 11%, EGJOO 5%. In patients with normal FLIP, HRM never showed achalasia or DES. Normal FLIP had 80% specificity for HRM being normal or showing only minor motility disorder. When FLIP was abnormal, HRM diagnoses were achalasia 21.4%, normal 19.6%, IEM 19.6%, EGOO 17.9%, absent contractility 14.2%, distal spasm 3.6%, jackhammer 1.8%, fragmented 1.8%); FLIP had sensitivity of 80% for a major motility disorder on HRM. A normal EGJ DI by itself had a negative predictive value of 90% for normal HRM or minor motility disorder. FLIP was abnormal in 100% patients with achalasia or DES diagnosed by HRM.

Conclusion: FLIP topography performed during sedated endoscopy appears to be a good screening tool for esophageal dysmotility, with 80% specificity for normal or minor disorder on HRM, and 80% sensitivity for major disorder on HRM. With subsequent evolution and refinement of FLIP analysis, and data confirmation, a normal FLIP topography during endoscopy for evaluation of esophageal symptoms may obviate the need for manometry. Likewise, HRM is clearly indicated in patients with abnormal FLIP topography, as the likelihood of a major motility disorder on HRM is high in these patients.

Disclosure: Nothing to disclose

OP014 INEFFECTIVE ESOPHAGEAL MOTILITY WITH CONTRACTION RESERVE ON ESOPHAGEAL HIGH RESOLUTION MANOMETRY (HRM) IS ASSOCIATED WITH LOWER ACID EXPOSURE TIMES COMPARED TO ABSENT CONTRACTION RESERVE

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Introduction: Ineffective esophageal motility (IEM) is a minor motor disorder that may have reflux implications. Augmentation of esophageal body contraction on multiple rapid swallows (MRS) indicates presence of contraction reserve, which is associated with lower likelihood of late postoperative dysphagia following antireflux surgery. We hypothesized that presence of contraction reserve in IEM will be associated with reduced esophageal acid burden.

Aims & Methods: Our aim was to evaluate the interrelationship between contraction reserve on HRM and esophageal acid burden on ambulatory reflux monitoring performed off antisecretory therapy. Esophageal HRM and ambulatory reflux monitoring studies were reviewed on all patients undergoing both tests between 01/2016 and 12/2017 at a tertiary care referral center. Patients fulfilling the following three HRM motor diagnoses (using Chicago Classification 3.0 criteria) were identified: normal, ineffective esophageal motility (IEM, ≥50% ineffective swallows), and absent contractility (100% failed swallows). Single swallows (SS) and multiple rapid swallows (MRS) were analyzed using HRM software tools assessing integrated relaxation pressure (IRP, normal< 15 mmHg), distal latency (DL, normal >4.5 s), distal contractile integral (DCI, normal 450-8000 mmHg.cm.s), esophagogastric junction contractile integral (EGJ-CI, normal>39.3 mmHg.cm) and EGJ morphology. Contraction reserve required mean MRS DCI to mean SS DCI ratio >1. Total acid exposure time (AET) was abnormal if >6%; thresholds utilized for upright and supine AET were 6% and 2% respectively. Univariate analysis was performed to determine the role of contraction reserve on esophageal acid burden, and multivariate regression analyses were performed to determine predictors of abnormal total, supine and upright acid burden in the context of contraction reserve.

Results: Study criteria were fulfilled by 191 patients, 109 (57.1%) with normal HRM (53.6 ± 1.4, 70.7% F), 71 (37.2%) with IEM (52.2 ± 1.7, 72.7% F), and 11 (5.76%) with absent contractility (51.4 ± 2.5, 58.3% F). Within IEM, a higher proportion of patients without contraction reserve demonstrated upright AET >6% compared to those with contraction reserve (59.1% vs 32.7%, p=0.04); this difference was not seen with supine AET, and did not affect total AET. Contraction reserve had no impact on AET in normal HRM and absent contractility. When the IEM group was further subdivided into severe IEM (8-10 ineffective swallows, n=40) and non-severe IEM (5-7 ineffective swallows, n=31), the non-severe IEM category demonstrated significantly lower proportions with abnormal AET in the presence of contraction reserve (30.4% vs. 75.0%, p=0.03). Abnormal AET proportions in non-severe IEM with contraction reserve resembled normal HRM (p=0.96), while that in severe IEM with or without contraction reserve resembled absent contractility (p=0.39). Multivariate analysis demonstrated EGJ morphology to be an independent contributor to total AET in IEM (p=0.03). Additionally, absence of contraction reserve associated with increased total AET (p=0.01) in non-severe IEM, while EGJ morphology associated with upright AET in non-severe IEM (p=0.04), and with supine AET in severe IEM (p=0.02).

Conclusion: The presence of contraction reserve is associated with lower upright acid burden in IEM, particularly in non-severe IEM, where acid burden resembles that seen with normal HRM. In contrast, the acid burden profile of severe IEM resembles that seen with absent contractility, regardless of contraction reserve. EGJ morphology is also a contributor to acid burden in IEM.

Disclosure: Nothing to disclose

OP015 CODEINE INDUCES INCREASED RESISTANCE AT THE OESOPHAGO-GASTRIC JUNCTION IN HEALTHY VOLUNTEERS: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, CROSSOVER TRIAL

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Introduction: The adverse effects of short- and long-term use of opioids, such as codeine and morphine, on gastrointestinal transit are well known. More recently, studies showed that chronic opioid use may induce oesophageal dysfunction with symptoms similar to achalasia (eg. dysphagia) and a manometric pattern of functional oesophago-gastric junction outflow obstruction (OGJ-OO). However, little is known whether this is generalized or occurs only in susceptible subjects, and whether acute opioid administration has similar effects.

Aims & Methods: After positioning a High-Resolution impedance Manometry catheter (HRiM, Unisensor, Attikon, Switzerland), codeine (30mL codeine phosphate 10mg/5mL) or placebo (30mL glucose syrup) was infused in the proximal stomach. Forty-five minutes post-infusion, participants received different volumes (5mL and 20mL) of liquid and semi-solid boluses, classified as 0/1/2/3/4 according to the International Dysphagia Diet Standardization Initiative (IDDSI) classification and bread (2x2cm and 4x4cm). Blood samples were collected to detect slow morphine metabolizers. HRiM analysis was performed adhering to the Chicago classification v3.0 (CC v3.0) using dedicated software (Solar GI, Laborie, Canada). Additionally, pressure-flow analysis (PFA) was performed, using the online software platform swallowgateway.com for calculating the following metrics: pressure flow index (PFI), distension pressure emptying (DPE) as a measure of OGJ resistance to bolus flow, impedance ratio (IR) as measure of bolus clearance failure, distal ramp pressure (DRP) which reflects bolus pressurization and distension-contraction latency (DCL), time from nadir impedance to peak pressure.

Results: Twenty-three HV (6 men, 38±3y) completed the study. Eight participants were excluded from analysis: one due to biliary type pain, a rare side effect of codeine, one due to the presence of an OGJ-OO during placebo and six were slow metabolizers. Integrated relaxation pressure 4 seconds (IRP4) values were significantly higher after codeine (except for 4x4cm bread) and distal latency (DL) values were significant lower (except for 5mL IDDSI3). Distal contractile integral (DCI) values were similar in both conditions, except for IDDSI0 (5mL and 20mL). Based on the CC v3.0, acute infusion of codeine induced an OGJ-OO in five HV (p-value=0.042). PFI values were significantly higher after codeine infusion, for all given boluses except for 5mL IDDSI3 and bread 4x4cm. DPE was significantly increased for all boluses except for 5mL IDDSI2. The DRP was significantly increased for 5mL IDDSI0/2 and bread 4x4cm and DCL values were significantly lower for 5mL IDDSI0/3/4 and 20mL IDDSI0 in the codeine condition. No significant differences were noted for IR between placebo and codeine infusion, except for bread 2x2cm. Results are presented in Table 1.

	5mL IDDSI0 IRP4	5mL IDDSI1 DL	5mL IDDSI3 DCI	20 mL IDDSI0 PFI	5 mL IDDSI4 DPE	5mL IDDSI2 DRP	20 mL IDDSI0 DCL	5 mL IDDSI3 IR
Placebo	10 (8-14)	6.8 (6.4-7.4)	923 (621-1281)	8.1 (6.9-10.4)	21.9 (17.9-27.4)	4.7 (3-7.1)	4.2 (3.7-4.8)	0.3 (0.3-0.5)
Codeine	18 (15-21)	5.9 (5.5-6.8)	1075 (523-1568)	15.8 (10.1-42)	37.7 (31.4-47.6)	7.6 (6.5-10.6)	2.7 (2.5-3.8)	0.3 (0.3-0.5)
p-value	<0.0001*	<0.0001*	0.2339	0.009*	0.013*	0.025*	<0.0001*	0.821

[Table 1: Median (interquartile range) values of IRP4, DCI, DL, PFI, DPE, DRP, DCL and IR for codeine and placebo administration]

Conclusion: Acute administration of codeine increases bolus resistance at the OGJ in HV and is able to induce major motility disorders in a subset of subjects. These are mainly localized in the distal oesophagus as the IR data indicate no bolus clearance failure in the oesophageal body.

Disclosure: Nothing to disclose

OP016 EVALUATION OF THE HEIGHT OF THE WATER COLUMN RETAINED AFTER A RAPID DRINK CHALLENGE TEST (RDC) USING HIGH RESOLUTION IMPEDANCE MANOMETRY (HRIM) IN PATIENTS WITH ACHALASIA TREATED WITH PERORAL ENDOSCOPIC MYOTOMY (POEM)

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Introduction: High resolution impedance manometry (HRIM) allows simultaneous assessment of esophageal motility and bolus transport. Previous studies have shown that the height of the retained column after a rapid drink challenge test (RDC) correlates with the height of the barium column measured 5-min after timed barium esophagogram, with the increment of the pressurization of the esophageal body and with the intensity of dysphagia. However, evaluation of the height of the water column after treatment with POEM, which means a larger myotomy that is often associated with reflux, has not been reported.

Aims & Methods: To evaluate the effect of treatment with POEM on the height of the retained water column after a RDC, and its correlation with pressurization of the esophageal body and esophageal symptoms, in patients with achalasia.

We prospective studied 16 consecutive patients (8M, 8F, mean age 56 yr) diagnosed with achalasia and treated with POEM. In each patient, a 200-ml RDC was performed before and 2-12 months after treatment. Pressure responses, height of the retained column, number and length of reflux episodes were measured using HRIM. Symptoms were scored by the Eckardt Scale. An upper endoscopy has been performed before treatment and after treatment.

Results: Before treatment, all patients showed an obstructive pattern of pressure responses characterized by pressurization of the esophageal body (37±7 % of time with pressure >20 mmHg, pressure gradient across the EGJ 20±4 mmHg) that reverted to a non-obstructive pressure pattern after POEM in all (3±1% of time with pressure >20 mmHg, pressure gradient across the EGJ 2±2 mmHg; p< 0.05 vs before treatment for both) and that was associated to clinical improvement (Eckardt score 8.0±0,6 before vs 0.9±0,2 after POEM, p< 0.05). Treatment with POEM was associated to a reduction in the height of the water column retained immediately after the RDC, from 12±2 cm to 5±1 at 1 min after the RDC (before and after treatment respectively; p< 0.05), and this reduction correlated with the reduction of the Eckardt score (r=0.703; p=0.005). After this immediate clearance of the bolus, 6 patients had 2.5±0.5 reflux episodes of 29±18 sec duration (range 4-120sec), occurring at 81.3±13.2 sec after the end of the RDC, leading to an increment in the height of the water column measured at 5 min after the RDC (1.4±0.6 cm vs 8,5±1.3 cm after treatment; NS). The endoscopic follow up showed mild esophagitis in 7 patients that did not correlate with the presence of reflux after the RDC (p=0.622).

Conclusion: Measurement of the height of the column retained after a RDC using HRIM may objectively confirm treatment success after POEM in patients with achalasia. However, reflux of the ingested bolus occurs frequently after the RDC, and needs to be carefully considered to determine the right timing for evaluation of bolus clearance in patients treated with POEM.

References: Cho et al. Am J Gastroenterol 2014;109:829, Marin et al. Neurogastroenterol Mot 2018: e13438. DOI:10.1111/nmo.13438).

Disclosure: Nothing to disclose

OP017 A RANDOMIZED CLINICAL TRIAL ON THE THERAPEUTIC EFFECT OF TRPA1 AND TRPM8 AGONISTS ON THE SWALLOWING FUNCTION OF PATIENTS WITH OROPHARYNGEAL DYSPHAGIA

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Introduction: Oropharyngeal dysphagia (OD) is a major complain among older people, patients with neurological diseases or stroke patients. Classical treatment of OD is based on compensatory strategies that do not promote the recovery of the swallowing function. Pharyngeal sensory stimulation through transient receptor potential channel (TRP) agonists is a promising active treatment.

Aims & Methods: The main aim of this study was to assess the therapeutic effect of TRPA1 and TRPM8 agonists in improving swallowing function in OD patients. For this purpose, we designed a prospective, double-blind, randomized, interventional study (NCT02193438), in which we included 58 patients with OD caused by ageing, stroke or neurodegenerative disease. Swallowing safety and efficacy and the kinematics of the swallow response were assessed by videofluoroscopy (VFS) during the swallow of nectar boluses of a xanthan gum based thickener supplemented with a) 756.6mM cinnamaldehyde and 70mM zinc (CIN-Zn) (TRPA1 agonists), b) 1.6mM citral (CIT) (TRPA1 agonist) or c) 1.6mM citral and 1.3mM isopulegol (CIT-ISO) (TRPA1 and TRPM8 agonists). The effects on pharyngeal event-related potentials (ERP) were assessed by electroencephalography during the deglutition of two supplemented boluses with the same agonist the patients received during the VFS. The brain activation was determined with sLORETA software.

Results: Compared to control series, TRPA1 stimulation with either CIN-Zn or CIT reduced time to laryngeal vestibule closure (CIN-Zn p=0.002, CIT p=0.023) and upper esophageal sphincter opening (CIN-Zn p=0.007, CIT p=0.035). In addition, CIN-Zn reduced the penetration-aspiration scale score (p=0.009), the prevalence of penetrations (p=0.039), the latency of the P2 peak of the ERP and enhanced the brain activation of the frontal gyri and the transverse temporal gyrus. The combination of CIT-ISO had not shown any beneficial effects on swallow biomechanics or neurophysiological measures. No significant adverse events were observed.

Conclusion: TRPA1 stimulation with CIN-Zn or CIT improves swallow response which, in the case of CIN-Zn, is associated with an enhanced cortical activation, and leads to a significant improvement in swallow safety in patients with OD. These results set the basis to develop new active treatments for OD using TRPA1 agonists, moving away from compensation to the recovery of the swallowing function.

Disclosure: This study was supported by a grant from Nestlé Health Science and presented in the 8th ESSD Congress as an oral presentation.

OP018 WITHDRAWN

IBD: Basic science
10:30-12:00 / B3

OP019 TLR4-INDUCED DYSBIOSIS PROMOTES AN EXPANSION OF PROTEOBACTERIA THAT INCREASES SUSCEPTIBILITY TO TUMORIGENESIS

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Introduction: Dysbiosis in inflammatory bowel diseases (IBD) and colitis-associated cancer (CAC) is characterized by an increase in the relative abundance of facultative anaerobes (Proteobacteria). These bacteria

bloom by performing anaerobic respiration using certain substrates that are generated in the presence of reactive oxygen species (ROS). However, the interplay between the host and the microbiota that leads to dysbiosis is not fully understood. Our laboratory has shown that IBD dysplasia and colorectal adenomas overexpress toll-like receptor 4 (TLR4) in intestinal epithelial cells (IECs). Moreover, we have described that epithelial TLR4 activation increases susceptibility to CAC.

Aims & Methods: In this study, we tested the hypothesis that IECs, via TLR4 activation, provide the microbiota with ROS that can be used by Proteobacteria to outgrow obligate anaerobes. Furthermore, we aimed to determine whether TLR4-mediated susceptibility to CAC is induced by the dysbiotic microbiota.

IECs isolated from villin-TLR4 mice (which express a constitutively active form of TLR4 in IECs) and their WT littermates were analyzed for H_2O_2 production (Amplex Red) and expression of NADPH oxidase 1 (Nox1) and dual oxidase 2 (Duox2; qPCR). Colonoids from wild-type (WT), TLR4-KO, Nox1-KO, and DuoxA2-KO mice were stimulated with lipopolysaccharide (LPS) and tested for H_2O_2 production in the presence of the NADPH oxidase inhibitor, diphenyleneiodonium. Mucosa-associated microbiota (MAM) of villin-TLR4 and C57Bl/6 mice was used to colonize WT germ-free mice. After 3 weeks of engraftment, half of the MAM-engrafted mice were euthanized to verify engraftment via 16S sequencing, whereas the other half of mice underwent a chemical model of CAC by administration of azoxymethane followed by 3 cycles of 3% dextran sulfate sodium. Tumor burden and size as well as H_2O_2 production in IECs were measured at the end of the experiment.

Results: Constitutive activation of epithelial TLR4 in vilin-TLR4 mice significantly increased the production of H_2O_2, which was accompanied by a marked upregulation of Nox1, Duox2, and DuoxA2 transcripts. Similarly, LPS stimulation in WT colonoids induced the upregulation of Nox1, Duox2, and DuoxA2 and the release of H_2O_2 in a TLR4- and NADPH oxidase-dependent manner, as demonstrated by total abrogation of responses in TLR4-KO colonoids and in diphenyleneiodonium-treated WT colonoids. DuoxA2-KO colonoids showed a marked attenuation in the production of H_2O_2 upon LPS challenge, demonstrating that this NADPH oxidase drives TLR4-mediated production of H_2O_2. Villin-TLR4 MAM was characterized by an expansion in Proteobacteria that could be transmitted to WT GF recipient mice. In addition, this TLR4-induced microbiota caused an upregulation in Duox2 and DuoxA2 expression in IECs of WT germ-free recipient mice. After the chemical model of CAC, recipient mice of villin-TLR4 MAM developed more tumors of bigger size when compared to C57 MAM. Consistently, IECs isolated from non-involved areas demonstrated higher release of H_2O_2 in villin-TLR4 MAM-recipient mice, indicating that dysbiosis increases susceptibility to CAC by promoting an oxidative milieu.

Conclusion: Our findings demonstrate that TLR4 activation in IECs promotes a Duox2-mediated oxidative phenotype that facilitates the blooming of Proteobacteria in the absence of overt inflammation. Furthermore, we show that such TLR4-induced dysbiosis increased the susceptibility to CAC. These findings suggest that the intestinal epithelium plays pivotal roles in promoting dysbiosis.

Disclosure: Nothing to disclose

OP020 MYELOID CALCINEURIN IN THE CONTROL OF IMMUNE CHECKPOINT INHIBITION IN INTESTINAL TUMOR DEVELOPMENT

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Introduction: Colorectal cancer (CRC) development is based on somatic mutations in tumor suppressor genes and oncogenes. Intestinal inflammation is a risk factor for CRC but recent work has demonstrated that immunological pathways also play critical roles in the development of sporadic CRC, in the absence of clinically overt intestinal inflammation. We have previously shown that the phosphatase calcineurin and its downstream mediators of the NFAT transcription factor family are active in the intestinal epithelium and support tumor development through promotion of epithelial proliferation.

Aims & Methods: Here, we asked whether calcineurin and NFAT play similar tumor-promoting roles in myeloid cells and analyzed potential synergistic effects of epithelial and myeloid calcineurin in intestinal tumor development. We studied mice with myeloid-specific deletion (LysM-Cre) of calcineurin or NFAT in the $Apc^{Min/+}$ model of genetically-induced intestinal tumor development as well as in an orthotopic colonic CRC model associated with liver metastasis. In addition, we analyzed 1500 human CRCs.

Results: We observed barrier dysfunction at sites of intestinal adenomas, which was associated with tumor infiltration by the commensal microbiota and microbiota-dependent activation of calcineurin and NFAT in myeloid tumor-infiltrating cells. Calcineurin-NFAT signaling in myeloid cells promoted the expression of IL-6, which was associated with activation of epithelial STAT3. STAT3 in turn supported tumor cell proliferation and survival in a cell-intrinsic manner and was also associated with dramatic induction of epithelial expression of the two co-inhibitory proteins B7H3 and B7H4. Antibody-mediated blockade or epithelial deletion of these co-inhibitory proteins led to an increased CD8^{+} cytotoxic T cell response against tumor cells in mice, which was associated with protection from intestinal tumor growth as well as the development of liver metastasis, suggesting a central role of myeloid calcineurin in licensing T cell responses against intestinal tumors. Moreover, increased expression of these immune checkpoint proteins correlated with reduced CD8^{+} T cell infiltration in human CRCs and reduced CRC-associated survival.

Conclusion: Our studies reveal a novel pathway of calcineurin-dependent cross-talk between epithelial, myeloid, and T cells, which promotes tumor development through inhibition of cytotoxic T cell responses and which is potentially amenable to therapeutic targeting.

Disclosure: Nothing to disclose

OP021 SUPPLEMENTATION WITH BUTYRATE PRODUCING BACTERIA REDUCES TUMOR LOAD IN A MOUSE MODEL OF COLORECTAL CANCER

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Introduction: Colorectal cancer (CRC) is one of the most prominent cancers with increasing incidence rates, and originates at the crossroad of the microbiome and its host. Besides genetically predisposing factors, CRC is strongly influenced by the inflammatory status of the tissue, the presence of carcinogenic substances (such as microbiome metabolites), and the regulation of the host's immune response. Although the link of the intestinal microbiota to these functions is well established, the biological understanding of the modes of action is not well understood. Here, we studied how certain intestinal microbiota contributes to the prevention of CRC.

Aims & Methods: In a first approach, colitis associated tumourus were induced in wild-type (WT) and RAG2^{-/-}C57BL/6 mice via administration of three cycles of 1% dextran sodium sulfate (DSS) + azoxymethane (AOM). PBS, *Peptostreptococcus stomatis* or a mix of 4 butyrate-producing strains was supplemented via daily oral gavage on days 8-10 of each AOM/DSS cycle.

Next, we used an inflammation-independent model of CRC, where MC-38 tumour cells were injected into the cecum wall after WT mice received PBS or the mix of butyrate-producing bacteria for three consecutive days. Intestinal microbiome was analyzed in stool samples before, during and after administration of the bacteria to the mice. Colon tumour and non-tumour tissue were analyzed using RNAseq, flow cytometry and histology techniques.

Results: We found that tumour burden in the DSS/AOM model was associated with increased levels of fecal *P. stomatis*, but overall reduced levels of butyrate-producing bacteria. In DSS/AOM-treated WT mice, supplementation with *P. stomatis* significantly enhanced tumour load when compared to PBS-treated controls. In contrast, only a small fraction of WT mice treated with butyrate producers developed tumours. Supplementation with *P. stomatis* was associated with increased intestinal inflammation as assessed in endoscopy and histology after each AOM/DSS cycle compared to WT mice supplemented with butyrate producers. However, the beneficial effect of

butyrate-producing bacteria was lost in RAG2⁻/⁻ mice, indicating that T-cells are crucially involved in mediating the anti-tumour effect. As causative mechanisms, we found an increased number of IFNγ+ CD8+ cytotoxic T- cells and IFNγ+ NK cells inthe tumour tissue of WT mice supplemented with butyrate producers compared to control and *P. stomatis* groups, indicating that supplementation with butyrate producers promoted increased anti-tumour immune responses. Further, the increase in PD-L1+/PD-L2+ tumour-associated macrophages was absent in those mice.

In the cecum injection model, we found a reduction in tumour development in mice treated with butyrate producers. Interestingly, tumours from mice receiving butyrate producers had a higher amount of activated CD8+ T cells compared to controls, while in the surrounding tumour tissue there were more naïve CD8+ T cells in mice supplemented with butyrate-producing bacteria, suggesting that butyrate producers induce the infiltration and differentiation of naïve CD8+ T cells into the tumours.

Conclusion: Our results indicate that oral supplementation with selected butyrate producers protects from CRC tumour development via promoting anti-tumour T cell responses *in vivo* in inflammation-dependent and independent CRC mouse models. Our findings suggest that manipulation of the intestinal microbiota might be a promising novel approach to promote anti-cancer immune responses.

Disclosure: Nothing to disclose

OP022 HIGH-THROUGHPUT PHENOTYPIC SCREENING OF COLON CANCER STEM CELL INHIBITORS USING TUMOURSPHERES

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Introduction: Cancer stem cells (CSCs) are a subpopulation of cancer cells implied in tumour formation, metastasis and recurrence due to their long-lasting properties and chemotherapy resistance.

Aims & Methods: Here, we aimed to optimize, validate and apply a high-throughput screening (HTS) platform to identify novel molecules from large compound libraries that specifically impact on colorectal CSC phenotype.

Results: For validation of the HTS platform, HT29 human colorectal adenocarcinoma cells were plated in undifferentiated medium in ultra-low attachment conditions for sphere formation and treated with previously reported CSC-targeting agents (e.g. salinomycin; 1 μM) or traditional chemotherapeutic agents (e.g. 5-fluorouracil (5-FU), irinotecan and oxaliplatin; 1 μM) or vehicle controls. Following 7 days of incubation, the number and size of spheres were assessed, while cell viability was determined based on measurement of ATP. This screening system was tested in both 96- and 24-well plates. Classical chemotherapeutics such as 5-FU and irinotecan were not able to impact on HT29-derived spheres, while the anti-CSC agent salinomycin markedly reduced cell viability, sphere formation potential, as well as sphere size in both plate formats.

Next, we proceeded with the evaluation of the effectiveness of ~1,420 chemical compounds as potential anti-CSC agents from selected in-house and external libraries. For hit selection, a cut-off threshold > 70% of ATP depletion led to 150 hits, corresponding to ~11% hit rate for the full library, with some series particularly rich in actives. Additional compounds decreased ATP activity under 1% and have been excluded due to eventual excess of toxicity and impossibility to build a dose-response curve. To quantitatively assess hit inhibitory potency, dose-response curves were built using a 10-point concentration range of 0.03 - 16.00 μM. From those, 69 compounds showed a sigmoidal dose-response curve-fit and a half-maximal inhibitory concentration (IC$_{50}$) ≤ 2 μM. Twenty-four compounds were further selected for testing on other colorectal cancer cell lines (SW-620, HCT116), based on their structural diversity and predicted drug-like properties. Seventeen compounds displayed an IC$_{50}$ ≤ 2 μM in both cell

lines, whereby anti-CSC effect was further validated by assessing impact on tumoursphere formation. Five compounds at the IC$_{50}$ dose robustly decreased the number of HT29-, SW-620- and HCT116-derived spheres. Those hits were tested on colorectal cancer cell lines plated in adherent conditions (5,000 cells/well) and primary mouse hepatocytes (10,000 cells/well) for 72h using a 10-point concentration range of 0.01 - 243.00 μM and 1 compound was excluded for potential severe hepatotoxicity. Future work comprises *in vivo* proof-of-principle experiments, hit-to-lead medicinal chemistry and identification of precise mechanisms of action.

Conclusion: In conclusion, a novel HTS platform to test a wide range of candidate compounds to target CSCs was developed and validated, allowing the identification of potent colon cancer stem cell inhibitors.

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Disclosure: Nothing to disclose

OP023 XBP1 COORDINATES DNA DAMAGE INDUCED STEM CELL REPRESSION IN THE INTESTINAL EPITHELIUM VIA DDIT4L-DEPENDENT MTOR INHIBITION

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Introduction: Intestinal stem cells are particularly prone to the accumulation of hazardous mutations leading to malignant transformation. We have shown that RNase H2-mediated ribonucleotide excision repair (RER) preserves genomic integrity of intestinal stem cells. In the absence of RNase H2, intestinal epithelial cells generate DNA damage and induce a p53-driven suppression of the intestinal stem cell (Aden, Bartsch et al. 2019). XBP1 encodes for a transcription factor critically involved in resolving endoplasmic reticulum (ER) stress (Kaser, Lee et al. 2008). Whether Xbp1-mediated signalling is directly involved in DNA damage response mechanisms is not known.

Aims & Methods: The aim of the study is to investigate the role of XBP1 in coordinating epithelial DNA damage response and p53-driven intestinal stem cell suppression.

For this purpose, murine intestinal epithelial ModeK cells (iCtrl and i*Xbp1*) were stimulated with the DNA-damaging agent Cytarabin A (AraC) and subjected to gene expression analyses, FACS cell death assays and immunoblot analyses. We generated conditional intestinal epithelial knockout of *Xbp1*, *Rnaseh2b* and the combined DKO. Intestinal organoids of derived from *Rnaseh2b/Xbp1*fl/fl, *Xbp1*ΔIEC, *Rnaseh2b*ΔIEC and *Rnaseh2b/Xbp1*ΔIEC mice were derived used for immunoblot analyses, colony formation assays and RNA sequencing. We employed *Rnaseh2b/Xbp1*fl/fl, *Xbp1*ΔIEC, *Rnaseh2b*ΔIEC and *Rnaseh2b/Xbp1*ΔIEC mice were used for *in-vivo* basal phenotyping of young (8 week) and aged (52 week) mice as well as, acute and chronic DSS-colitis models. *Post mortem* analyses included fluorescence or IHC stainings, western blot analyses and gene expression analyses.

Results: *Xbp1*-deficiency elevates AraC-induced DNA-damage and epithelial cell death *in-vitro*. Untreated and DSS-treated *Rnaseh2b/Xbp1*ΔIEC mice exhibit display heightened amounts of DNA damage, cell death and intestinal inflammation. Compared to *H2b*ΔIEC mice, which were previously shown to exhibit a *p53*-dependent stem cell arrest that protects them from intestinal carcinogenesis, *Xbp1*-deficiency impairs stem cell arrest in *Rnaseh2b/Xbp1*ΔIEC mice, leading to epithelial hyperproliferation and spontaneous intestinal carcinogenesis. Mechanistically, RNA sequencing of intestinal organoids (*Rnaseh2b/Xbp1*fl/fl, *Rnaseh2b*ΔIEC, *Rnaseh2b/Xbp1*ΔIEC and *Rnaseh2b/p53*ΔIEC) reveals that XBP1 coordinates a *p53*-dependent induction of the DNA damage inducible transcript 4l (*Ddit4l*). *Mechanistically*, Xbp1 directs a Ddit4l- mediated mTOR-inhibition and dephosphorylation of the translation initiator 4E-BP1, leading tothereby determining suppression of epithelial proliferation. In *in-vitro* intestinal organoid growth assays we demonstrate, that pharmaceutical inhibition of the mTOR pathway by Rapamycin restores epithelial stem cell suppression in *Rnaseh2b/Xbp1*ΔIEC organoids.

Conclusion: Our data suggest a crucial role for XBP1 in directly coordinating epithelial DNA damage responses and intestinal stem cell suppression via a novel Ddit4l-mTOR dependent feedback mechanism.

References: Aden, K., K. Bartsch, J. Dahl, M. A. M. Reijns, D. Esser, R. Sheibani-Tezerji, A. Sinha, F. Wottawa, G. Ito, N. Mishra, K. Knittler, A. Burkholder, L. Welz, J. van Es, F. Tran, S. Lipinski, N. Kakavand, C. Boeger, R. Lucius, W. von Schoenfels, C. Schafmayer, L. Lenk, A. Chalaris, H. Clevers, C. Röcken, C. Kaleta, S. Rose-John, S. Schreiber, T. Kunkel, B. Rabe and P. Rosenstiel (2019). „Epithelial RNase H2 Maintains Genome Integrity and Prevents Intestinal Tumorigenesis in Mice." Gastroenterology 156(1): 145-159.e119. Kaser, A., A.-H. Lee, A. Franke, J. N. Glickman, S. Zeissig, H. Tilg, E. E. S. Nieuwenhuis, D. E. Higgins, S. Schreiber, L. H. Glimcher and R. S. Blumberg (2008). „XBP1 Links ER Stress to Intestinal Inflammation and Confers Genetic Risk for Human Inflammatory Bowel Disease." Cell 134(5): 743-756.

Disclosure: Nothing to disclose

OP024 STEM CELL DERIVED INTESTINAL ORGANOIDS AS AN ADVANCED SCREENING PLATFORM FOR POTENTIAL CLOSTRIDIUM DIFFICILE TOXIN INHIBITORS

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Introduction: The establishment of organoid culture systems represents a milestone on the route towards successful personalized medicine. Intestinal organoids dervied from human pluripotent stem cells display essential attributes of adult intestinum even composed of different tissue types. Moreover, complex organoid structures represent a highly realistic testing platform for advanced toxicity assays and subsequent evaluation of potential toxin inhibitors. Organoids can be defined as 3D structures derived either from pluripotent or organ restricted stem cells harboring the ability to mimic in vivo architecture and multi lineage differentiation of terminally differentiated tissues. The pathogeinicity of Clostridium difficile is mainly attributable to the production of the large protein toxins (C difficile toxins [Tcd]) A (TcdA) and B (TcdB) and -in few bacterial strains- the binary enterotoxin CDT.

Aims & Methods: The toxin-inhibiting effect of different potential proteins and small molecules like albumin or VER-155008 was evaluated in stem cell derived induced human intestinal organoids (iHIOs). iHIOs are derived from hair sheet keratinocyte cultures from a healthy donor. After cellular reprogramming towards induced pluripotent stem cells, intestine organoids were generated in a stepwise differentiation protocol. These organoids display basic characteristics, such as crypt-like structures and architecture of a polarized intestinal epithelium, of human intestine tissue, containing both epithelial and non-epithelial cell types. Direct effects of clostridial toxins and potential protective effects of various substances were evaluated in a standardized approach.

Results: Toxin inhibitors like VER-155008 or Albumin decreased toxin-mediated F-actin destruction, while cortical F-actin was clearly more preserved and resembled more to the structure in untreated control organoids. Moreover, a clear distribution/organization of the adhesion protein E-cadherin mainly at the cortex of cells was observed in control miniguts whereas in toxin-treated organoids E-cadherin was more diffusely distributed and clustering of E-cadherin became obvious. Toxin-inhibiting treatment led to reduced clustering while E-cadherin maintained its cortical localization comparable to control organoids.

Conclusion: iHIOs may serve as a highly advanced toxicity-screening platform with essential advantages compared to pervious single cell toxicity assays.

Disclosure: Nothing to disclose

Basic science: Neurogastroenterology
10:30-12:00 / B5

OP025 RECTAL COMPLIANCE IS AFFECTED BY ENTERIC NERVOUS SYSTEM AND INTERSTITIAL CELLS OF CAJAL IN MURINE SMOOTH MUSCLE

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Introduction: Rectal compliance, contributing to fecal storage, is different from the colonic propulsive movement. Abnormal rectal compliance is presented in many functional gastrointestinal motility disorders, such as irritable bowel syndrome, constipation and fecal incontinence.

Aims & Methods: This study aimed to explore the electromechanical characteristics of rectal compliance in the murine rectum and investigate the contribution of intrinsic inhibitory neurotransmission and interstitial cells to rectal compliance.

Male C57BL/6 mice, aged 8 weeks or more were used. For in vivo experiments, the mice were anesthetized with isoflurane, and anorectal manometry was applied to measure rectal compliance through rectum. In ex vivo experiments with using murine rectum, intra-rectal pressure was measured in organ bath. The colonic migrating motor complex (CMMC) measurements and electrophysiological microelectrode recordings for membrane potential were performed using smooth muscle strips and segments. Calcium imaging was used to measure the calcium transients in the interstitial cells and smooth muscle cells within the rectum of the mice expressing a genetically encoded calcium indicator (GCaMP). Drugs affecting inhibitory neurotransmission including L-NNA and apamin were applied.

Results: The rectal compliance was significantly decreased after in vitro intraperitoneal injection and ex vivo infusion into organ bath of L-NNA and apamin, respectively (p=0.002 *vs* 0.005; p=0.016 *vs* 0.015) (Fig 1). In ex vivo experiments, rectum did not have CMMC, and after treatment of the L-NNA or apamin in the organ bath, the rectal contractions were increased, not CMMC (6.19±3.98 *vs* 20.35 ±15.78 mN·min, p=0.031), and propagation of contractions from the distal colon increased (7.20±3.32 *vs* 29.12±20.75 mN·min, p=0.046). In membrane potential with electric field stimulation, inhibitory junction potential significantly increased after L-NNA and apamin, respectively (17±2.9 *vs* 16±1.6 mV, p=0.04; 24±2.5 *vs* 13±3.6 mV, p=0.02). In calcium transient of smooth muscle, AUC (area under the curve) in rectum was smaller than that of colon (9.36±4.57 *vs* 3.49±2.58 IU·min, p=0.03), and AUC in rectum increased after L-NNA and apamin, respectively (3.79±1.93 *vs* 9.71±4.52 IU·min, p=0.001; 3.26±1.92 *vs* 8.31±4.12 IU·min, p=0.021). In calcium transient of ICC of rectal circular muscle, AUC significantly increased after L-NNA (7.39±2.52 *vs* 10.98±3.71 IU·min, p=0.012).

Conclusion: Murine rectal compliance were identified in the study. Enteric inhibitory neurotransmissions was related to the rectal compliance. ICC could control the rectal smooth muscle activities.

Disclosure: Nothing to disclose

OP026 EVALUATION OF PLASMA M2-PYRUVATE KINASE IN DIFFERENTIATION BETWEEN FUNCTIONAL AND ORGANIC COLONIC DISORDERS

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Introduction: M2-pyruvate kinase (M2-PK) is a key regulator of tumor growth and important for tumor metabolism and can dynamically regulate aerobic glycolsis. Differentiating between functional bowel disorders, such as irritable bowel syndrome (IBS), and organic colonic disorders such as inflammatory bowel disease (IBD), colorectal polyps, and colorectal cancer (CRC) can often be difficult as they present with similar and/or overlapping clinical presentations. The investigation and procedures to differentiate between organic and functional bowel disorders often incurs consider-

able health-care costs both for patients and community health service. The selection of patients who should undergo colonoscopy and/or imaging procedures is one of the key points of the diagnostic process, which should avoid the abuse of invasive and costly tests as well as the underestimation of potentially harmful diseases.

Aims & Methods: The aim of this study is to evaluate the diagnostic value of plasma M2-pyruvate kinase level in differentiating functional colonic disorders (e.g: IBS) from organic colonic disorders(e.g: IBD, colorectal polyps and CRC).This case control study included 150 patients with different colonic disorders, 75 patients with IBS, 25 patients with ulcerative colitis (UC), 25 patients with colorectal polyp and 25 patients with CRC. We measured the plasma M2-PK using Enzyme-linked immunosorbent assay (ELIZA) in IBS patients and comparing these levels with those obtained from patients with UC, colorectal polyp and CRC.

Results: Our study revealed a highly significant increase in plasma M2-PK in patients with organic colonic disorders compared to functional group (IBS). Using Receiver operating characteristic (ROC) curve at area under curve (AUC) 0.872 and cut-off value of >3 U/ml, our overall sensitivity and specificity for organic group over the functional group were 81.94% and 83.3% respectively with 35.3% positive predictive value and 97.6% negative predictive value.

Conclusion: M2-PK is a good marker for discrimination of functional from organic colonic disorders (IBD and colorectal polyp, and CRC). Future researches including a large studies population and long-term follow-up studies is recommended.

Disclosure: Nothing to disclose

OP027 A NEW ACCURATE TEST BASED ON FAECAL MICROBIOTA TO POSITIVELY DIAGNOSE IRRITABLE BOWEL SYNDROME

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Introduction: The Irritable Bowel Syndrome (IBS) is a functional disorder affecting up to 15% of world population. Despite its high prevalence, there is not a specific diagnostic test for this syndrome. Currently, diagnosis is based on the characteristic symptoms systematized in the Rome IV criteria. Although Rome IV criteria are mandatory, they are not enough to stablish the diagnosis and the patients are not exempt from going through relevant explorations to discard some organic pathologies which share symptomatology to IBS. RAID-Dx is a non-invasive test developed to positively diagnose IBS patients based on specific faecal bacterial signature.

Aims & Methods: The aim of this work was to develop a non-invasive test to positively diagnose IBS and demonstrate its capacity. A cohort consisting on 52 IBS patients and 61 healthy subjects was used to develop a specific bacterial signature. IBS patients met Rome IV criteria and H subjects were asymptomatic, all of them went through a colonoscopy and presented no valuable macroscopic lesions in the colon. Different bacterial markers were analysed from a stool sample obtained from each subject prior to the diet-preparation for the colonoscopy. RAID-Dx was defined in a proof-of-concept with 70% of the cohort (36 IBS patients and 43 H subjects) and the obtained results were validated with the remaining 30% (16 IBS patients and 18 H subjects).

Results: In the proof-of-concept, RAID-Dx showed high sensitivity and specificity values of 91.67% and 86.05%, respectively. In addition, a Positive Predictive Value (PPV) of 84.62% and a Negative Predictive Value (NPV) of 92.50% for the diagnosis of IBS patients were also found.
In the validation of the defined bacteria signature for RAID-Dx, sensitivity increased up to 93.75% and specificity decreased until 72.22%. The PPV were also decreased (75.00%) whereas NPV was kept similar (92.86%).

Conclusion: RAID-Dx is an accurate marker to diagnose IBS with high sensitivity and specificity, which makes it a candidate to become a standard, widely accepted diagnostic method of IBS.

OP028 DELETION OF DELTA OPIOID RECEPTORS ON NOCICEPTIVE SENSORY NEURONS ABOLISHES T CELL-MEDIATED ANALGESIA WITHOUT ALTERING INTESTINAL INFLAMMATION IN MICE

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Introduction: T lymphocytes play a pivotal role in the endogenous regulation of inflammatory visceral pain. Thus, we have previously shown that the local release of enkephalins by effector CD4^{+} T lymphocytes relieves from inflammatory pain in the later phase of the Dextran Sulfate Sodium (DSS)-induced colitis model. In this model, intestinal epithelium integrity disruption leads to the translocation into the mucosa of bacteria which activate innate immune cells. This early phase of the disease results in visceral hypersensitivity. In the later phase of the disease, when the adaptive immune response against bacterial antigens took place, the migration of effector T lymphocytes within the colon normalizes the visceral sensitivity. This T-cell analgesic effect is dependent on the activation of opioid receptors expressed on nociceptor terminal endings by enkephalins locally released by mucosal effector T lymphocytes accumulating into the intestinal mucosa.

Aims & Methods: The aim of the study was to identify the receptor(s) for enkephalins (*i.e.* μ and δ opioid receptor subclasses) responsible for T cell-mediated analgesia. For this purpose, we compared colitis severity, mucosal T cell density and visceral sensitivity in both early and late phases of DSS-induced colitis in floxed (littermates) and conditional knockout mice in which each opioid receptor has been specifically deleted in $Na_v1.8^+$ sensory neurons.

Results: We show that analgesia induced by T cell-derived opioids is elicited via activation of δ but not μ opioid receptors expressed on peripheral sensory nerves. The absence of each receptor on sensory nerves did not change neither the inflammatory status nor the time-course of the adaptive immune response.

Conclusion: Endogenous regulation of inflammatory visceral pain by T cell-derived enkephalins is mediated by δ opioid receptors expressed on enteric $Na_v1.8^+$ sensory neurons

Disclosure: Nothing to disclose

OP029 INTESTINAL MICROBIOTA AS A MEDIATOR OF LUMINAL PROTEOLYTIC ACTIVITY AND ALTERED INTESTINAL PERMEABILITY IN CAMPYLOBACTER JEJUNI POST INFECTION IRRITABLE BOWEL SYNDROME

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Introduction: Up to 15% of *Campylobacter jejuni* enteritis patients may develop post-infection irritable bowel syndrome (PI-IBS). The mechanisms for PI-IBS development remain unclear. A subset of PI-IBS patients (~40%) have elevated proteolytic activity (PA) in their stool correlating with looser and more frequent bowel movements[1].

Aims & Methods: Our aim was to determine microbiota associations with PA in PI-IBS patients and microbial mediation of PA and intestinal permeability using microbiota-specific humanized mouse model. 29 PI-IBS patients (Rome III) {20 females, mean (SD) age 46.8 (16.7) yrs}, 14 PI-no-IBS controls {5 females, 50.1 (15.6) yrs} and 21 healthy volunteers (HV) {16 females, 40.6 (13.7) yrs} were recruited. Fecal PA was assessed using FITC-casein assay. Shotgun metagenomics was performed for microbiota assess-

ment. β-diversity was summarized using Unifrac and Bray-Curtis distance with significance assessed using nonparametric PERMANOVA method. Differentially abundant taxa were identified using a multivariable linear model with permutation to assess statistical significance, accounting for non-normality of abundance data. To investigate microbiome regulation of luminal PA, stool from a subset of these patients (n=6 stool/PA classification) were used to humanize 4-week old germ-free (GF) mice (ex-GF). Six weeks post humanization, fecal PA and stool frequency was measured and serum was collected after administration of creatinine, 4kDa FITC-Dextran and 70kDa Rhodamine B-Dextran to assess *in vivo* permeability.

Results: 12/29 PI-IBS {8 females}, were classified as High PA (>85th percentile of HV, >891 BAEE/mg of protein). Compared to Low PA patient stool, High PA patients had significantly decreased microbial diversity (Bray-Curtis, PERMANOVA p< 0.001). Low PA patients had an increased abundance of genus *Prevotella* and *Firmicutes* and decreased abundance of *Bacteriodes*. Humanization of mice with microbiota from Low PA stool suppressed baseline PA of GF mice while microbiota from High PA patients resulted in unchanged PA from baseline (% of baseline, Low PA 17.2 ± 30.0; High PA 100.4 ± 122.0, p< 0.05). High PA mice had increased PA at six weeks post humanization (BAEE units/mg protein, High PA 1570.9 ± 1834.3, Low PA 240.5.2 ± 374.8; p< 0.05). No difference was observed in stool frequency (pellets/hr, High PA 9.4 ± 3.0; Low PA 9.0 ± 3.6); however High PA mice had looser pellets when scored for fecal consistency (Scored 0=normal to 4=diarrhea, High PA 0.82 ± 0.49; Low PA 0.18 ± 0.33 p< 0.001. Permeability of creatinine increased only in mice humanized with High PA microbiota (mg/dL, High PA 0.81 ± 0.28); Low PA 0.58 ± 0.24; HV 0.51 ± 0.36 p< 0.05), while permeability of 4kDa FITC-Dextran increased in both Low and High PA humanized mice compared to HV humanized mice (mg/dL, High PA, 19.1 ± 14.6; Low PA 23.9 ± 23.9; HV 13.7 ± 30.3 p< 0.05). Creatinine and 4kDa FITC-Dextran permeability positively correlated with terminal PA (Spearman r=0.31 and 0.27 respectively, p< 0.05).

Conclusion: High PA PI-IBS patients have significantly decreased fecal microbial diversity. Low PA microbiota suppresses host luminal PA while High PA microbiota did not change host PA. Compared to Low PA microbiota, High PA microbiota causes increased intestinal permeability through the pore pathway. Therefore, microbiota may influence intestinal permeability in PI-IBS through modulation of proteases. *Supported by NIH K23 DK 103911.*

References: Edogawa S, Edwinson AL, Peters SA, et al. Serine proteases as luminal mediators of intestinal barrier dysfunction and symptom severity in IBS. Gut 2019:gutjnl-2018-317416.

Disclosure: Nothing to disclose

OP030 CIPROFLOXACIN TREATMENT AFFECTS THE STRUCTURE AND ACTIVITY OF ENTERIC NERVOUS SYSTEM IN MOUSE SMALL INTESTINE

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Introduction: Commensal gut microbiota ensures the functional and structural integrity of enteric nervous system (ENS) circuitries. Any change of its composition elicited by environmental factors or drugs could disrupt ENS homeostasis and determine the onset of functional bowel disorders. Ciprofloxacin is a synthetic broad-spectrum antimicrobial agent, belonging to the fluoroquinolone family, used for treating respiratory, urinary tract, gastrointestinal and abdominal infections. Ciprofloxacin usage has been associated with many adverse reactions, including neurotoxicity.

Aims & Methods: The aim of the present study was to evaluate the effect of ciprofloxacin on ENS integrity and gastrointestinal motility in young mice. Male C57Bl/6 mice (age=9±1 weeks; N=44) were orally gavaged with ciprofloxacin (50 mg/kg, suspended in 1% methylcellulose; CPX group) or vehicle (CNTR group) for 14 days. In CPX and CNTR animals we assessed:
i) gastrointestinal transit 30 minutes after intragastric administration of nonabsorbable-FITC-labeled dextran;
ii) pellet frequency, measured as changes in stool output during a 60-minute collection period;
iii) stool water content;
iv) contractile activity of isolated ileum segments, measured as changes

in isometric muscle tension following carbachol (0.001- 100 µM), KCl (60 mM), electric field stimulation (EFS, 1-40 Hz) or inhibition in non-adrenergic, non-cholinergic (NANC) conditions (EFS=10 Hz, 1 µM atropine, 1 µM guanethidine, with or without 0.1 mM L-NAME);
v) distribution of the neuronal HuC/D and glial S100β markers by confocal immunofluorescence in ileal frozen cryosections;
vi) neurochemical coding integrity, evaluated by acetylcholinesterase and NADPH-diaphorase biochemical staining in longitudinal-muscle myenteric plexus preparations (LMMPs).

Results: Ciprofloxacin treatment determined a significant reduction in the number/hour output of fecal pellets (-36±8%, N=5/group, P< 0.01) and increased stool water content (+32±9%, N=5/group, P< 0.01). Gastrointestinal transit was delayed in CPX mice compared to CNTR mice (geometric center: 8.3±0.2 vs 7.3±0.2, N=6/group, P< 0.01), respectively. In vitro contractility studies showed a significant downward shift of the concentration-response curve to carbachol in CPX group (Emax=-36±5%, N=5/group, p< 0.01) compared with CNTR group, together with a reduced KCl-induced excitatory responses (-32±8%, N=5/group, p< 0.05). Altered excitatory and inhibitory neurotransmission in CPX mice was shown by decreased EFS-elicited contractions with a significantly reduction of 10 Hz-neuronal cholinergic response (CPX=-67±11%, N=5/group, p< 0.01) and by an impaired NANC-mediated relaxation of ileal segments from CPX mice. In the ENS of CPX mice, increased HuC/D immunoreactivity and NADPH-d-positive cells (+38±2%, N=5/group, P< 0.01) in the ileum of CPX mice together with reactive gliosis, evidenced by S100β immunofluorescence distribution.

Conclusion: Ciprofloxacin-induced gut dysbiosis determines complex anomalies in ENS architecture, neurochemical coding and function leading to neuromuscular dysfunction. Such neuroglial plastic changes are highly indicative of the negative effects mediated by ciprofloxacin on the integrity of gut microbiota-ENS axis, possibly contributing to promote functional bowel disorders later in life.

Disclosure: FC, CR, GCV are employees of Alfasigma SpA. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Hot topics from Latin America
10:30-12:00 / C2

OP031 A COMPARATIVE ANALYSIS OF DIGITAL CHOLANGIOSCOPY AND PROBE-BASED CONFOCAL LASER ENDOMICROSCOPY FOR THE MALIGNANCY DETECTION IN BILE DUCT LESIONS

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Introduction: The differentiation of malignant from the benign biliary lesion is challenging in clinical practice. Peroral digital cholangioscopy (POCS) predicts malignancy through the visual impression of biliary lesions; whereas, Probe-based confocal laser endomicroscopy (pCLE) via in vivo, real-time tissue examination. Currently, both pCLE and cholangioscopy classification systems are available; however, a comparison between these classification systems remains unknown.

Aims & Methods: To compare the Paris classification criteria (pCLE) and the visual impression classification system (POCS) for the detection of malignancy in biliary lesions.

The following is a cross-sectional study. Data from patients referred for cholangioscopy and pCLE due to indeterminate biliary stricture was consecutively recorded and analyzed. The visual impression of biliary lesions during POCS were recorded following the classification system proposed by Robles-Medranda et-al. pCLE was performed using the Cellvizio CholangioFlex probe (Mauna Kea Technologies, Paris, France) during the ERCP procedure, and the pCLE findings for the diagnosis malignancy were recorded according to the Paris classification. pCLE videos were reviewed by one endoscopist, blinded to any clinical or ERCP information, and indicated which descriptive criteria (Paris classification) were observed in the videos displayed. Malignancy detection was defined following histopathology results. A video-set of 20 patients with pCLE were evaluated for interobserver agreement by two endoscopists (J.O and J.A).

Results: Forty-three patients were included; the median age was 62.2± 15.6 years; the 65.1% were female. The main reason for the evaluation was indeterminate biliary stenosis (44.18%) and suspected biliary tumor (55.8%). 67.44% of lesions were located in the proximal common bile duct. POCS visual impression detected malignancy in 76.7 % of patients, with a sensitivity, specificity, PPV, and NPV of 94%, 92%, 92%, and 94%, respectively. pCLE detected malignancy in the 79.0% of patients, with a sensitivity, specificity, PPV, and NPV of 64%, 100%, 100%, and 83%, respectively. Table 1 summarizes the overall accuracy of each pCLE criteria for malignancy prediction. A moderate interobserver agreement for pCLE criteria was obtained (K< 60).

	Sensitivity, %	Specificity, %	PPV, %	NPV, %
Tick blank band (>40 um)	85	24	37	75
Thick white band	87	40	42	83
Dark clumps	69	96	90	86
Epithelium	54	50	37	67

[Table 1. Overall accuracy for each pCLE features of malignancy.]

Conclusion: The visual impression of POCS using a classification system showed to be more sensitive than in vivo, real-time tissue examination of pCLE for the detection of malignancy in indeterminate biliary obstruction.
Disclosure: Nothing to disclose

OP032 WHOLE TRANSCRIPTIONAL ANALYSIS IDENTIFIES THE MESENTERIC ADIPOSE TISSUE OF CROHN'S DISEASE PATIENTS AS SITES OF T- AND B-CELL ACTIVATION

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Introduction: Crohn´s disease (CD) is a multifactorial disease characterized by chronic intestinal inflammation. The increased visceral adiposity near the affected intestinal area, of which mesenteric adipose tissue (MAT) is the main component, is a feature of CD. Both protective, as well as pathological, roles have been attributed to this disease-associated tissue in CD.
Aims & Methods: Our aim was to understand the contribution of MAT to CD pathophysiology by providing a molecular and cellular signature of disease-associated adipose tissue in CD patients. To do that we performed whole transcriptional analysis by RNA sequencing (RNA-seq) of MAT and ileum from CD patients with active disease (CD group, n=8) and non-IBD controls (CTR group, n=4). The biological validation of a panel of differentially expressed genes was conducted by qPCR in 26 CD patients and 17 non-IBD controls. Immunohistochemistry was also performed for validation analysis.
Results: RNA-seq identified 17 significantly regulated genes (|FC|>1.5; FDR< 0.05) in CD-MAT compared to non-IBD controls, with a marked upregulation of plasma cell genes (i.e., IGLL5, MZB1, CD79A, POU2AF1, FCRL5, JCHAIN, DERL3, SDC1, PIM2). A less strict statistical cutoff value (|FC|>1.5, nominal p£0.05) revealed a larger list of 651 genes in CD-MAT compared to controls. Ingenuity Pathway Analysis of this signature revealed a significant regulation of pathways related to T- and B-cell functionality. In contrast to MAT, transcriptional analysis of the ileum revealed a set of 849 genes significantly regulated in CD compared to non-IBD controls (|FC|>1.5; FDR< 0.05), and 2,654 genes when applying the lower cutoff (nominal p value< 0.05). Despite the differences between the MAT and ileal signatures of CD patients, we identified a subset of 204 genes significantly modulated in both tissues. This common signature included genes related to the plasma cell signature (MZB1, POU2AF1, IGLL5, JCHAIN, DERL3 and PIM2) that were significantly up-regulated both in CD-MAT and ileum. In contrast, other genes that are highly increased in CD ileum such as S100A8 and S100A9 (calprotectin), IL1B, CD14, CXCL1, CXCL8, MMP1, OSMR, all of which are related to an acute inflammatory response, were exclusively regulated in the ileal mucosa of CD disease, but not in the adjacent MAT. In

contrast, some genes encoding for lymphocyte receptors were exclusively regulated in CD-MAT, (i.e., MS4A1, CD6, CTLA4, CD3D, CD3E, IL2RG, LAG3-2, CD24, CD79A, CD5 and CD69), showing a different pattern of immune cell activation in this tissue compared to the ileum. Real-time RT-PCR in an independent patient and control cohort confirmed the significant up-regulation of CD79A, SM4A1 (CD20), CTLA4 and CD3D in CD-MAT compared to controls, with no significant differences in IL1B and S100A8. Finally, immunohistochemistry and immunofluorescence analysis confirmed the large infiltrates and localized follicular structures containing both CD3^{+} and CD20^{+} lymphocytes in CD-MAT.
Conclusion: Our study reveals the marked accumulation of lymphocytes that form disseminated aggregates, as well as well-structured lymphoid follicles, in the MAT associated with CD inflamed ileum, but not in controls. Remarkably, acute inflammatory genes highly expressed in the ileum were not markedly upregulated in the adipose tissue. Our data strongly supports the role of CD-associated MAT as a site for T- and B-cell activation and suggests that it could also act as a reservoir of memory immune responses. Whether these antigen-specific responses would be detrimental or protective will require further study.
Disclosure: Nothing to disclose

Gastric intestinal metaplasia: The premalignant stomach
10:30-12:00 / C3

OP033 RISK FACTORS FOR THE PROGRESSION OF GASTRIC INTESTINAL METAPLASIA IN A LOW RISK POPULATION: A MULTICENTER, PROSPECTIVE, COHORT STUDY

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Introduction: Gastric cancer (GC) is mostly preceded by gastric precursor lesions (GPL). The recently updated MAPS guideline for surveillance of GPL now includes the recommendation for surveillance in case of a positive family history for GC. However, the evidence for this recommendation and our tools to identify patients at risk for progression are still scarce. This study therefore aimed to investigate if risk factors such as family history, lifestyle, genetic polymorphisms, and serology at baseline are possible predictors for progression of GPL in low risk areas.
Aims & Methods: Patients with GPL were included in the PROREGAL study; a multicenter, prospective cohort study. At upper endoscopy biopsies were obtained from 12 standardised sites in the stomach and from visible lesions. These were histologically assessed according to the operative link on gastric intestinal metaplasia (OLGIM) system. At baseline, patients completed a questionnaire on family history and lifestyle factors, and fastening blood samples were taken for pepsinogen and gastrin-17. All patients underwent at least two upper endoscopies. Progression of intestinal metaplasia (IM) was defined as progression of OLGIM classification between follow-up (FU) endoscopies. Previously associated single nucleotide polymorphisms (SNPs) with *H. pylori* infection or GC were determined using polymerase chain reaction restriction fragment length polymorphism (PCR-RFLP): *NCF4* (rs4821544), *TLR1* (rs28393318), *TLR4* (rs11536889) and *ATG16L1* (rs2241880). Cox-regression was performed for analysis on risk factors. Differences in proportions for the presence of SNPs were calculated using z-test. For all tests a significance level of 0.05 was used.
Results: 308 patients (median age 61 years, IQR 17;male 48.4%) were included. Median FU was 48 months (IQR 24). During FU 116 (37.7%) patients showed progression of their OLGIM status and six patients (1.9%) developed high grade dysplasia or GC. Family history (HR 1.4; p=0.154),

smoking (HR 1.3; p=0.260), and history of Hp-infection (HR 1.1; p=0.684) were associated with non-significant risks for progression. Alcohol use (HR 0.8; p=0.428), serum levels of PG I/II (HR1.0; p=0.446) and gastrin-17 (HR 1.0; p=0.908) were not associated with an increased progression risk. The minor allele (C) on the *TLR4* (rs11536889) was negatively associated with progression (OR 0.4; p< 0.001), while the minor allele (G) in the *ATG16L1* (rs2241880) was positively associated with progression (OR 1.5; p=0.001).

Conclusion: This is the first study to assess potential risk factors for the progression of IM in a low risk area. Over one third of patients showed progression of IM during surveillance. We did not find any significant risk factors for progression. However, SNPs in *TLR4* and *ATG16L1* showed significant associations with progression of IM, suggesting that genetic risk stratification may contribute to the identification of patients eligible for surveillance.

Disclosure: Nothing to disclose

OP034 EVOLUTION OF GASTRIC PRECANCEROUS LESIONS: A LONG TERM FOLLOW-UP SINGLE CENTER STUDY IN FRANCE

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Introduction: International guidelines recommend surveillance of gastric precancerous lesions (GPL), but there are limited data on the evolution of these lesions, especially in countries of low gastric cancer incidence. Our objective was to study the evolution of GPL in France.
Aims & Methods: From the cohort of 507 patients diagnosed with GPL [atrophic gastritis (AG), or intestinal metaplasia (IM), or low grade dysplasia (LGD), or high grade dysplasia (HGD)]in our center between 2000 and 2015, the patients fulfilling the following criteria were identified:
1) at least one follow-up endoscopy performed after a minimal period of 6 months,
2) at each endoscopy, random gastric biopsies obtained, at least 3 from antrum and 2 from corpus,
3) all biopsy material available for histological review.
The biopsy specimens were retrieved from the hospital tissue bank and analysed prospectively by an expert pathologist for the presence of GPL and their extent (according to OLGA and OLGIM score). The type of IM (complete or incomplete) was also evaluated. The evolution of the lesions was assessed by comparing the initial and the final histology. Additionally, for the patients with multiples endoscopies during the follow-up, a precise evaluation of the evolution on individual level was performed.
Results: Seventy nine patients (35 men, median age 61 years), were included. At initial endoscopy, the GPL found were, by order of severity: AG in 5 patients (OLGA 1, n=4; OLGA 2, n=1), IM in 73 patients (OLGIM 1, n=39; OLGIM 2, n=28; OLGIM 3, n=6) and LGD in 1 patient. Thirty-seven patients (47%), were *H. pylori*positive by histology. Among the 73 patients with IM, 59 had IM in the antrum, 8 in the corpus, and 6 both in the antrum and in the corpus. Sixty patients had complete IM and 13 incomplete IM. The mean (±SD) follow-up period was 66 ±48 months (Min=7, Max=208), the mean (±SD) number of endoscopies per patient was 4±2 (Min= 2, Max = 14), and the total number of endoscopies performed in all patients was 341.
At final endoscopy, the GPL found were AG in 2 patients, LGD in 4 patients, HGD in 1 patient, adenocarcinoma (ADK) in 2 patients, IM in 58 patients and normal gastric mucosa (+/- superficial gastritis) in 12 patients. Six patients (7%) were *H. pylori*positive by histology.
The comparison between the initial and final endoscopy, showed stability of GPL in 56 patients (71%), progression to more severe lesion in 10 patients (13%) (from AG to IM in 4 patients, from IM to LGD in 3 patients, from IM to HGD in 1 patient, and from IM to ADK in 2 patients), and the regression in 13 patients (16%). Both patients who progressed to ADK had incomplete type of antrum IM, one OLGIM 2 and one OLGIM 3. Altogether, among 10 patients who progressed to more severe lesions, 6 (60%) had incomplete type of IM.

Among the 13 patients in whom the regression to the normal (+/-gastritis) gastric mucosa was observed, 9 had initially antrum limited OLGIM 1 complete IM and 4 had antrum limited complete OLGIM 2 IM.
Conclusion: This study shows that:
1) Most of the GPL remain stable over time,
2) Antrum-limited IM, especially of incomplete type, has the highest risk of progression to dysplasia and cancer,
3) Regression of IM is possible, especially for low grade (OLGIM 1) and for complete type.
Disclosure: Nothing to disclose

Clinical update on H.pylori management
10:30-12:00 / F3

OP035 EUROPEAN SURVEY OF *HELICOBACTER PYLORI* PRIMARY RESISTANCE TO ANTIBIOTICS - EVOLUTION OVER THE LAST 20 YEARS

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Introduction: Antibiotic resistance of *Helicobacter pylori* is the main cause of failure of most current eradication regimens. As antimicrobial susceptibility testing (AST) is not performed in all cases, it is important to have regular surveys to infer the treatments which can be used. For this purpose, European surveys were performed in 1998, 2008 and we report here the results of 2018.
Aims & Methods: Centres were recruited on a voluntary basis, one for each small country (in the range of 10 million inhabitants) and several for larger countries. The request was to include 50 adult patients who had not received previous eradication treatment.
Information collected included demographic, clinical, and endoscopic results as well as AST results (clarithromycin, levofloxacin, metronidazole, amoxicillin, tetracycline and rifampicin) performed by Etest or disk diffusion according to a standardized procedure. Control strains were also made available and a 10% random sample was sent to the coordinating centre at the end.
Results: The crude data show 1,246 *H. pylori* positive patients included in 24 centres from 19 countries (minimum: 20 cases per centre) The distribution with regard to age, gender, reason for consultation and endoscopic examination is in the range of what is usually observed for this type of patients. *H. pylori* resistance was present in 21.9% for clarithromycin, 16.6% for levofloxacin, and 38.5% for metronidazole; 30 strains were reported as resistant to amoxicillin (2.4%), 4 to tetracycline (0.3%) and 48 to rifampicin compounds (3.8%). These unusual resistance strains are now being controlled as well as a random sample of the other strains. The kit Amplidiag *H.pylori* (MobiDiag) will be used for clarithromycin and AST for the other antibiotics.
Conclusion: These results indicate a global and continuous rise in *H. pylori* primary resistance to clarithromycin but lower than in the previous decade (9.9% in 1998, 17.5% in 2008, and 21.9% in 2018), a slight increase to levofloxacin and a more important increase for metronidazole (from 33.1 to 38.5% since 2008).
Disclosure: The authors acknowledge the support of bioMérieux for providing Etests and Mobidiag for providing with PCR kits.

OP036 PAN-EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG): EXPERIENCE WITH SINGLE CAPSULE BISMUTH QUADRUPLE THERAPY IN 2,326 PATIENTS

Perez Nyssen O.[1], McNicholl A.G.[2], Perez Aisa M.&.[3], Vaira B.[4], Caldas Alvarez M.[5], Bujanda Fernández de Piérola L.[6], Castro Fernandez M.[7], Gasbarrini A.[8], Machado J.C.L.[9], Venerito M.[10], Molina Infante J.[11], Fiorini G.[12], Donday M.G.[13], Ramas M.[13], Megraud F.[14], O'Morain C.[15], Gisbert J.[16,17], Hp-EuReg Investigators, European Helicobacter and Microbiota Study Group, AEG-REDCap
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Introduction: Bismuth-quadruple therapy with a PPI, bismuth salts, tetracycline and metronidazole has resurfaced in Europe thanks to a new single-capsule formulation (Pylera®).

Aims & Methods: Our aim was to evaluate the efficacy and safety of the single-capsule bismuth-quadruple therapy (Pylera®) in the European Registry on *Helicobacter pylori* management. Patients were systematically registered at an e-CRF by AEG-REDCap. *Variables included*: Patient's demographics, previous eradication attempts, prescribed treatment, adverse events, and outcomes. Intention-to-treat and per-protocol analyses were performed. Data monitoring was performed to ensure the quality of the data

Results: So far, 30,394 patients have been included. Of these, 2,326 valid patients treated with single-capsule bismuth-quadruple therapy have been evaluated. 1,900 (81.7%) were prescribed following the technical-sheet (10 days, 3 capsules q.i.d.), the remaining where excluded. Average age was 52 years, 64% women, and 13% had peptic ulcer. Table summarizes results. The majority of cases (63%) were naïve. PPI type or dose did not influence eradication rate. 33% of cases suffered from adverse events (severe in 3%, and only 1% withdrew treatment due to adverse events). Only two serious adverse events were reported: hospitalization for diarrhea, and an allergic reaction treated with anti-histamine drugs, both solved without complications.

Conclusion: Treatment with single-capsule bismuth-quadruple therapy (Pylera®) achieves *H. pylori* eradication in approximately 90% of patients by intention-to-treat in clinical practice, both in first- and second-line, with a favorable safety profile.

	Frequency	Percent	mITT	PP
Naive (no previous treatment)	1,195	63%	92%	95%
2nd	412	22%	87%	90%
3rd	220	12%	84%	85%
mITT: Modified intention-to-treat; PP: per-protocol.				

[Prescription and eradication rates of single-capsule bismuth quadruple therapy]

Disclosure: Prof. Gisbert has served as a speaker, consultant and advisor to, or has received research funding from, Almirall, Nycomed, Astra-Zeneca, Casen Recordati, Mayoly, and Allergan. Dr McNicholl has received retributions from Allergan and MSD for training activities, and he is an advisor for Mayoly.

Pancreatic neoplasms: Improving diagnosis and outcomes

10:30-12:00 / Barcelona

OP037 ROBOTIC PANCREATODUODENECTOMY IN THE NETHERLANDS: A MULTICENTER ANALYSIS OF THE FIRST 100 PROCEDURES

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Introduction: Minimally invasive surgery is currently the gold standard for many surgical procedures. Most pancreatoduodenectomies, however, are still being performed through laparotomy. As conventional laparoscopy is limited by the rigid visual- and working axis, it might be less suited for complex procedures such as pancreatoduodenectomy. Potentially, the use of robotic technology offers a solution. The technically enhanced articulating instruments and 3D vision allow for optimal surgical dexterity, as needed during meticulous dissection and construction of the anastomoses in pancreatoduodenectomy. The aim of this study was to determine safety and feasibility of a robotic approach to pancreatoduodenectomy in the Netherlands and compare our results to recent studies reporting on the outcomes of open pancreatoduodenectomies.

Aims & Methods: This is a multicenter post hoc analysis of prospective databases from three high volume Hepato-Pancreato-Biliary (HPB) centers in the Netherlands. The first 100 patients undergoing robot-assisted pancreatoduodenectomy were included. Primary endpoint was severe complication, defined as the occurrence of one or more of the following complications: ISGPS gr. B/C postpancreatectomy hemorrhage, ISGPS gr. B/C pancreatic fistula, multiple or single organ failure, or death. Outcomes were scored during index admission. In addition, we performed a systematic review of observational, monocenter studies reporting on outcomes of > 500 open pancreatoduodenectomies, published in the past 5 years.

Results: In total, 100 consecutive patients underwent robot-assisted pancreatoduodenectomy. A total of 22 (22%) patients suffered from a severe complication. Pancreatic fistula (ISGPS gr. B/C) occurred in 19 (19%) patients and 9 (9%) patients suffered from post-pancreatectomy hemorrhage (ISGPS gr. B/C). Delayed gastric emptying (ISGPS gr. B/C) occurred in 26 (26%) patients. In 8 (8%) patients the procedure was converted to an open pancreatoduodenectomy. Seven patients (7%) underwent a relaparotomy. There was no postoperative in-hospital or 30-day mortality. The systematic review of 14 studies (n=12.708 patients) on open pancreatoduodenectomy demonstrated that complications occurred in 38% of all patients and reoperations in 7%. The weighted mean mortality was 3%.

Conclusion: These outcomes of the first 100 robot-assisted pancreatoduodenectomies demonstrate that this procedure was introduced safely in three hospitals in the Netherlands without postoperative mortality and acceptable morbidity. Clinical outcomes in this study were in line with outcomes reported in 14 recent, large, international studies on open pancreatoduodenectomies.

Disclosure: Nothing to disclose

OP038 NATIONWIDE PRACTICE AND OUTCOME OF PREOPERATIVE BILIARY DRAINAGE USING METAL OR PLASTIC STENTS IN PATIENTS WITH PANCREATIC DUCTAL ADENOCARCINOMA

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Introduction: In patients with resectable pancreatic ductal adenocarcinoma and biliary obstruction, early surgery is the preferred treatment. In patients with severe jaundice, neoadjuvant therapy, delayed surgical treatment, and acute cholangitis endoscopic biliary drainage (EBD) is often indicated. In the updated European Society of Gastrointestinal Endoscopy guidelines, self-expanding metal stents (SEMS) are strongly recommended for EBD, because of lower rates of stent dysfunction, cholangitis and endoscopic re-interventions as compared to plastic stents. We aimed to assess the implementation of SEMS use in daily clinical practice in patients with resectable pancreatic head cancer undergoing EBD and the relation between SEMS,drainage related complications and postoperative complications.
Aims & Methods: We performed a nationwide, retrospective cohort study including all patients with pancreatic ductal adenocarcinoma who underwent EBD prior to pancreatoduodenectomy in the mandatory Dutch Pancreatic Cancer Audit (January 2017 - December 2018). Patients undergoing percutaneous biliary drainage were excluded. Missing data (range 0.-10.4%) were imputed by multiple imputation techniques in which 15 dummy sets were created. Multivariable logistic regression models with adjustment for patient characteristics (sex, age, BMI, and ASA score) were performed to assess the association between type of stent and drainage-related or post-operative complications. Drainage-related complications were pancreatitis, cholangitis, perforation, bleeding, occlusion. Postoperative complications were postoperative pancreatic fistula, delayed gastric emptying, postpancreatectomy hemorrhage, bile leakage, chyle leakage, pneumonia and wound infection.
Results: In total, 585 patient, with a mean age of 68 (standard error 0.41) years, were included and 321 (55%) were male. EBD was mostly performed with plastic stents (331, 57%) compared to SEMS (254, 43%). Overall, drainage-related complications were comparable between patients with SEMS (18%) and plastic stents (19%). Cholangitis occurred less often in patients with SEMS compared to plastic stents (5% vs. 11%, p=0.029). Post-ERCP pancreatitis occurred in 9% and 8% in patients with SEMS and plastic stents, respectively. In multivariable logistic regression, adjusted for patient characteristics, SEMS was associated with lower odds of cholangitis (OR 0.394, 95% CI 0.176-0.881). Postoperative pancreatic fistula occurred less often in patients with SEMS compared to plastic stents (10% vs. 19%, p=0.011) and this effect remained after adjustment for patient characteristics in multivariable logistic regression (OR 0.568 95% CI 0.324-0.995).
Conclusion: This nationwide study shows that biliary drainage with SEMS placement is insufficiently implemented in the Netherlands despite explicit European guideline recommendations. Importantly, this nationwide study confirmed that those patients, drained with a SEMS, had a reduced rate of cholangitis and clinically relevant postoperative pancreatic fistula. Therefore, preoperative biliary drainage using SEMS should be strongly promoted and this may be facilitated and accelerated by a nationwide implementation programme.
Disclosure: Nothing to disclose

OP039 MULTICENTER RANDOMIZED CONTROLED TRIAL (RCT) COMPARING THE HISTOLOGICAL MATERIAL QUANTITY OBTAINED BY ENDOSCOPIC ULTRASOUND FINE NEEDLE BIOPSY (EUS-FNB) OF PANCREATIC MASSES WITH TWO „BIOPSY" NEEDLES: THE 20-GAUGE PROCORE® (COOK) AND THE 22-GAUGE ACQUIRE® (BOSTON SCIENTIFIC)

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Introduction: Endoscopic ultrasound-guided fine needle biopsy (EUS-FNB) has been proposed to obtain high-quality tissue samples for pancreatic tumors. We performed a multicenter randomized control trial comparing EUS-FNB with a 20-gauge Procore® needle versus a 22-gauge Acquire® needle. Our primary endpoint was the quantity of the obtained tissue, as defined by the mean cumulative length of tissue core biopsies per needle pass. The secondary aim was the tumor characterization.
Aims & Methods: Patients admitted for EUS-FNB of a pancreatic mass in 3 endoscopy units were included. One pass was performed consecutively with both needles. The order of use of the 2 needles was randomized. Histological material was studied in a blinded manner with respect to the needle, and the cumulative length of tissue core biopsies per needle pass was determined (sum of all the target tissue core lengths as measured manually with a graduated ruler under microscopy assistance, on the best cell block section). The gold standard was based on histological diagnosis, surgical resection, or more than 6 months follow-up. Assuming a 4mm difference in length of tissue core biopsies (based on a previous comparative study) [1], with a type-I error of 0.05 (2-sided) and a power of 0.9, the study required a total 60 patients.
Results: 38 men and 22 women, with a mean age of 67±9 years were included. No adverse effect was noted. Final diagnosis (based in all cases on histology for malignant tumor, and on histology and follow-up in benign pathology) was adenocarcinoma in 45 cases (75%), neuroendocrine neoplasm in 11 cases (18%), auto-immune pancreatitis in 2 cases, and others in 2 cases. Histological diagnosis was achieved in 41 out of 60 patients (68%) with the 20-gauge Procore® pass and in 53 out of 60 patients (88%) with the 22-gauge Acquire® pass (P< 0.02). The mean cumulative length of tissue core biopsies per needle pass was significantly higher with the 22-gauge Acquire® needle with 11.78±9.2mm versus 5.86±6.7mm for the 20-gauge Procore® needle (P< 0,0001).
Conclusion: Our results suggest significant differences, with a tumor characterization rate and a mean cumulative length of tissue core biopsies per needle pass significantly higher with the 22-gauge Acquire® needle than with the 20-gauge Procore®.
ClinicalTrials.gov ID: NCT03567863
References: 1- Karsenti D, Tharsis G, Zeitoun JD, et al. Comparison of 20-gauge Procore® and 22-gauge Acquire® needles for EUS-FNB of solid pancreatic masses: an observational study. Scand J Gastroenterol 2019
Disclosure: Nothing to disclose

OP040 INMEDIATE ON-SITE DIAGNOSIS OF MUCINOUS PANCREATIC LESIONS BY GLUCOMETRIC ANALYSIS OF CYSTIC FLUID OBTAINED BY ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE ASPIRATION (EUS-FNA)

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Introduction: Differential diagnosis of pancreatic cystic lesions is required for an appropriate therapeutic approach. Several markers have been evaluated in cystic fluid obtained by EUS-FNA, but they have shown limited accuracy.

Aims & Methods: Our aim was to assess the accuracy of intracystic glucose for the differential diagnosis between non-mucinous and mucinous cystic neoplasia (MCN).

Prospective, observational and analytic study of patients undergoing EUS-FNA of cystic pancreatic lesions from January to December 2018. Intracystic glucose concentration was evaluated on-site by glucometry. Additionally, fluid samples were sent to the lab for glucose and CEA quantification, and for cytological analysis. Diagnostic accuracy of glucose and CEA was evaluated by using cytology and imaging features (EUS and MRI), evaluated by two expert pancreatologists blinded to glucose and CEA levels, as gold standard.

Results: Thirty-three patients with cystic pancreatic lesions were included (mean age 73 years, range 35-88 years, 17 male). Mean size of the lesions was 37 mms (range 11-120 mms). Final diagnosis was MCN in 21 cases (18 branch duct IPMN, 1 main duct IPMN, 1 mucinous cystadenoma and 1 mucinous cystoadenocarcinoma) and non-mucinous lesions in 12 cases (4 serous cystadenomas, 2 cystic endocrine tumours, 4 walled-off necrosis, 1 pseudocyst and 1 post-surgical collection). Intracystic glucose concentration in MCN was 27.3 mg/dl (5.4-49.3) and 123.1 mg/dl (93.7-152.5) in non-mucinous lesions (p< 0.001). Intracystic glucose quantification in the lab showed an area under the ROC curve for the diagnosis of non-mucinous lesions of 0.93 (0.84-1.00). Using a cut-off point of >66 mg/dl, intracystic glucose allows diagnosing non-mucinous lesions with a sensitivity of 100% (72.0-100) and specificity of 80.0% (58.4-91.9). Intracystic glucose could be evaluated by on-site glucometry in 22 cases, showing a sensitivity of 100% and specificity of 75.0% for a cut-off of 74 mg/dl, with and area under the ROC curve of 0.85 (0.63-0.96). Compared to glucose, intracystic CEA showed an area under the ROC curve of 0.71 (0.52-0.87), sensitivity 72.2% (49.1-87.5) and specificity 81.8% (52.3-94.9) for the diagnosis of non-mucinous lesions.

Conclusion: Intracystic glucose, which can be measured on-site by glucometry, is an accurate tool for the differential diagnosis of mucinous and non-mucinous cystic pancreatic lesions.

Disclosure: Nothing to disclose

OP041 A RANDOMIZED CONTROLLED TRIAL ON THE CONTRAST ENHANCED GUIDED EUS-FNA AGAINST STANDARD EUS-FNA IN DIAGNOSING THE SOLID PANCREATIC LESIONS

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Introduction: The contrast enhanced endosonography (CH-EUS) may visualize the necrotic areas and the vessels inside the lesions. Its results combined with endosonography- fine-needle aspiration (EUS-FNA) improves the diagnosis in pancreatic solid masses. Also, CH-EUS can target EUS-FNA (CH-EUS-FNA) which might improve the diagnostic rate of EUS-FNA, but their superiority was not proved in prospective studies.

Aims & Methods: to assess if the efficiency of the targeted contrast- enhanced-EUS-FNA (CH-EUS-FNA) is superior to standard EUS-FNA in obtaining diagnosis or diagnosing malignancy in solid pancreatic masses and to evaluate whether the hypovascular aspect of the mass influences the accuracy of the diagnosis of FNA.

This randomized controlled study in one tertiar medical academic center included patients with the suspicion of pancreatic solid masses on trans-abdominal ultrasound or CT scan. Two passes with 22G standard FNA needle were done in random order by using EUS-FNA or CH-EUS-FNA and the visible core obtained was sent for pathology analysis. The final diagnosis was based on EUS-FNA or surgical specimen results and on following up data every three month by imaging methods.

Results: The study included 150 patients and two of them were lost from follow-up. There were 99 adenocarcinoma, 13 neuroendocrine tumors, 3 schwanomma, 1 GIST, 3 cholangiocarcinoma, 11 metastases, 19 benign lesions.

The EUS-FNA pass and CH-EUS FNA had the accuracy of diagnosis of 86.48% and 89.18% respectively (p=NS) and the global accuracy of the two passes was 93.2%. The rate of false negative cases did not differ between hypoenhanced or hyperenhanced lesions. No difference were seen for the results related to the location , size or tumor stage.

Conclusion: The diagnostic rate of core obtained by using 22G FNA needles with standard EUS-FNA and guided CH-EUS-FNA did not differ statistically.

Disclosure: Nothing to disclose

OP042 LIVING ON THE EDGE: LONG-TERM COMPLICATIONS, AND IMPLICATIONS FOLLOWING EUS-DIRECTED TRANSGASTRIC ERCP (EDGE): A MULTICENTER STUDY

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Introduction: Endoscopic ultrasound-directed transgastric ERCP (EDGE) is an alternative to enteroscopy- and laparoscopy-assisted ERCP in patients with RYGB anatomy. It allows for direct access via lumen-apposing metal stents (LAMS) to the excluded stomach, followed by ERCP across the gastro-gastric (GG) stent.

Although short-term results are promising with technical success in the majority of cases, the long-term outcomes are not known. Specifically, the rate of persistent GG fistula (GGF) is unknown.

Aims & Methods: To

1) determine rates of long-term adverse events (AEs) after EDGE, with a focus on rates of persistent GGF;

2) identify predictors of persistent GGF;

3) assess outcomes of endoscopic closure when persistent GGF is encountered.

This is a multicenter, retrospective study involving 12 centers between 1/2014 and 10/2018. AEs were defined according to ASGE lexicon. Persistent GGF was defined as UGI series or EGD showing evidence of fistula. Presumptive GGF was defined as weight gain of 5% of total body weight without having objective documentation of GGF. Multivariable analysis was used to determine predictors of AEs.

Results: A total of 166 patients (58yr, F 80%) underwent EDGE and had a mean follow-up of 5.7 months. EDGE was performed in a single session in 51% (n=85) of cases, and two sessions in 49% (81 patients). The excluded stomach was accessed from a transgastric location in 52% of cases and a transjejunal location in 48%. Technical success was achieved in 98% of cases (163/166) with a mean procedure time of 87 min. The LAMS was anchored in 21% of EDGE procedures (35/166; suturing 25, plastic double pigtail stents 7, hemoclips 2, and over-the-scope clip 1) with the majority (57%) done in a single session. Periprocedural AEs occurred in 28 patients (17%). Mild, moderate and severe AEs occurred in 3.1%, 11.5% and 2.4% of patients respectively. The 4 severe adverse events were managed laparoscopically.

Overall, mean LAMS dwell time was 47d. Initial fistual tract closure was performed with suturing in 31%, OTSC in 9%, and TTS clips in 4%. In 28% of patients the fistula edges were treated with APC alone without attempted closure. In 27% of patients the fistula was left entirely undisturbed following LAMS removal. GGF was identified following EDGE in 12% of those sent for objective testing (10/85). In addition, 61 (37%) patients had presumptive GGF after LAMS removal.

Following identification of GGF, 70% of patients underwent a mean of 1.2±0.8 closure attempts which at last follow-up had been successful in 71% of cases (5/7). Univariate and multivariate analyses suggested diabetes was associated with persistent GGF (OR 7.2; 1.5, 34).

Conclusion: The EDGE procedure is safe with a low risk of short-term and long-term AEs. Persistent GGF is uncommon and is independently associated with diabetes.
Disclosure: Nothing to disclose

Endoscopy: The heat in diagnosis and therapy
10:30-12:00 / Hotspot

OP043 LONG-TERM OUTCOMES AFTER ENDOSCOPIC TREATMENT FOR BARRETT'S NEOPLASIA IN 641 PATIENTS IN A CENTRALIZED CARE SETTING IN THE NETHERLANDS: RECURRENT NEOPLASIA IS RARE AND NEOSQUAMOUS BIOPSIES DO NOT CONTRIBUTE TO ITS DETECTION

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Introduction: Radiofrequency ablation (RFA), with or without endoscopic resection (ER) is the standard of care for treatment of early neoplasia in Barrett´s esophagus (BE). We aimed to report durability outcomes based on a large cohort of patients with uniform treatment and follow-up (FU) in a centralized care setting.
Aims & Methods: Endoscopic therapy for BE neoplasia in the Netherlands is centralized in 8 expert centers, where care is provided by specifically and jointly trained endoscopists and pathologists. Uniformity of treatment/FU is ensured by a joint protocol and quarterly group meetings. In an ongoing registry, prospectively collected treatment/FU data from all Dutch BE patients treated since 2008 is being registered in a uniform database. In the current study, we report on the completed data of 3 centers. Treatment indications were BE with low/high grade dysplasia (LGD/HGD) or early adenocarcinoma (EAC). Visible lesions were removed by ER, followed by RFA until complete endoscopic remission of BE and absence of intestinal metaplasia (CR-IM). FU consisted of high-resolution endoscopy and optical chromoendoscopy. From 2008 to 2015, FU endoscopy was done every 3mo in year 1, followed by yearly endoscopies in year 1-5, then every 2-3 yrs. Since 2015, FU endoscopies within the first year were abandoned. Initially, 4Q-random biopsies (Bx) were obtained from NSE and cardia (i.e. < 5mm distal from the neo-squamocolumnar junction) at every FU endoscopy. These were abandoned in 2013 and 2016 respectively.
Outcomes: Sustained CR-neoplasia (SCR-N) after CR-IM, diagnostic yield for NSE and cardia Bx.
Results: 641 patients with median BE length C2M4 and LGD (19%), HGD (32%) or EAC (49%) achieved CR-IM. Over a total FU of 2,747 person years (median 4 (IQR 2-6) yrs and 4 endoscopies per patient), 625 (98%) patients had SCR-N. The overall annual recurrence risk was 0.6%/year, with a relatively low risk in year 1 (0.1%). Based on 205 pts with FU >5yrs, there was no decrease in the recurrence risk after 5 years (0.7%/year). In total, 16 pts developed recurrent neoplasia after median 30mo (23-42). A more severe baseline histology significantly increased the recurrence risk (HR 3.1, 95%-CI 1.1-8.2). In 81% (13/16), CR-N was re-achieved after endoscopic treatment for LGD (3) HGD (4) or EAC (6), but 3 (0.5% of all pts) eventually progressed to advanced cancer (2 metastatic disease without BE, 1 submucosal cancer identified after an 18 months interval). The 3 cases were at baseline identified as highly complicated due to multifocal HGD/EAC and/or severe reflux stenosis. All recurrences were detected as visible non-flat lesions (10) or by biopsies from recurrent BE (1) or cardia (3). None of the 5,992 NSE Bx which were obtained, contributed to detection of recurrence. Abandoning NSE sampling in 2013 saved approximately 10,000 Bx in our cohort. Cardia Bx were obtained in 1,687 endoscopies with LGD (0.2%), IM

(7%) or no abnormalities (93%). In total, 69 pts (11%) had IM in a normal appearing cardia at some time point; this was reproduced in a minority and none progressed to dysplasia.
Conclusion: In a setting of centralized BE care, the 2-step approach of ER and RFA has remarkably low rates of neoplastic recurrence after CR-IM, with an annual recurrence risk comparable to the NDBE surveillance population. The vast majority of recurrences are detected at early stages that are amendable for curative endoscopic treatment. In conclusion, our data support more lenient FU intervals, especially in the first year after CR-IM, with emphasis on careful endoscopic inspection whilst NSE biopsies can be abandoned.
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OP044 CONVENTIONAL VERSUS TRACTION-ASSISTED ENDOSCOPIC SUBMUCOSAL DISSECTION FOR LARGE-SIZE ESOPHAGEAL CANCERS: A MULTICENTER, RANDOMIZED CONTROLLED TRIAL

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Introduction: Endoscopic submucosal dissection (ESD) is considered as minimum invasive treatment for large-size esophageal cancers. However, prolonged procedure time and life-threatening adverse events are a crucial matter of esophageal ESD.[1] Stable view during ESD is essential for less adverse events and more technical success. Traction-assisted ESD (TA-ESD) has the potential to maintain an adequate view during the procedures.[2]
Aims & Methods: The present study was a randomized, open-label, multicenter trial done in 7 hospitals in Japan and designed to evaluate the impact of traction assist on the efficacy and safety of ESD for esophageal neoplasms. Eligible patients were aged at least 20 years old and had endoscopically diagnosed squamous cell carcinoma or basal cell carcinoma meeting the following all conditions:
i) tumor size ≥20 mm and
ii) clinically-diagnosed intramucosal cancer (cT1a) or slightly infiltrating submucosal cancer (cT1b-SM1) according to the Japanese diagnosis and treatment guidelines for the esophagus.[3]
Enrolled patients were randomized in a 1:1 allocation ratio to receive either conventional ESD or TA-ESD via dynamic balancing using the minimization method. The primary endpoint was to ascertain if there was a difference in ESD procedure time between the two groups. The pre-defined secondary endpoints were as follows: handover to another operator; frequency of conversion from conventional ESD to TA-ESD; en bloc resection; histological assessment; and incidence of adverse events.
Results: From October 2016 to March 2019, 241 patients with large-size esophageal cancers were included in this trial and randomized. After excluding patients who did not undergo treatment (conventional ESD, three; TA-ESD, five), 233 patients were included in the analysis. ESD procedure time was significantly shorter in the TA-ESD group (60.5 vs. 44.5 minutes, P< 0.001). Six (5.2%) patients in conventional ESD were converted to TA-ESD technique to overcome technical difficulties during the procedure. Moreover, handover to another operator tended to be more frequently observed in the conventional ESD group (6.0% vs. 0.9%, P=0.066) Importantly, perforation occurred only in conventional ESD (5 cases, 4.3%), resulting in discontinuation of the procedure in one patient. Conversely, no adverse event in the TA-ESD group. En bloc resection rate and horizontal margin involvement of tumor were similar (99.1% vs. 100%, P=1.000; 10.3% vs. 6.9%, P=0.484, respectively).

Conclusion: TA-ESD significantly reduced ESD procedure time without any adverse event compared with conventional ESD and should be applied for esophageal ESD as the standard method.

	Conventional ESD	TA-ESD	P value
Total procedure time, min (range)	60.5 (18-245)	44.5 (13-156)	0.000
Conversion to TA method, n (%)	6 (5.2)	N/A	N/A
Handover to another operator, n (%)	7 (6.0)	1 (0.9)	0.066
En bloc resection, n (%)	116 (99.1)	116 (100)	1.000
Horizontal margin involvement, n (%)	12 (10.3)	8 (6.9)	0.484
Adverse events, n (%)			
Perforation	5 (4.3)	0 (0)	0.060
Delayed bleeding	0 (0)	0 (0)	1.000
Pneumonia	0 (0)	0 (0)	1.000
Mediastinitis	1 (0.9)	0 (0)	1.000

En bloc resection and adverse events were calucurated for 117 patients in the conventional ESD group including one discontinuation case after perforation. ESD, endoscopic submucosal dissection; TA, traction assisted; N/A, not available

[Clinical outcomes of conventional ESD and TA-ESD]

References: 1. Repici A, Hassan C, Carlino A, Pagano N, Zullo A, Rando G, et al. Endoscopic submucosal dissection in patients with early esophageal squamous cell carcinoma: results from a prospective Western series. Gastrointest Endosc 2010;71:715-21. 2. Yoshida M, Takizawa K, Suzuki S, Koike Y, Nonaka S, Yamasaki Y, et al. Conventional versus traction-assisted endoscopic submucosal dissection for gastric neoplasms: a multicenter, randomized controlled trial (with video). Gastrointest Endosc 2018;87:1231-40. 3. Kuwano H, Nishimura Y, Oyama T, Kato H, Kitagawa Y, Kusano M, et al. Guidelines for Diagnosis and Treatment of Carcinoma of the Esophagus April 2012 edited by the Japan Esophageal Society. Esophagus 2015;12:1-30.
Disclosure: Nothing to disclose

OP045 LINKED COLOR IMAGING FOR THE DETECTION OF GASTRIC NEOPLASM IN HIGH RISK PATIENTS: A PROSPECTIVE MULTICENTER RANDOMIZED CONTROLLED TRIAL (LCI-FIND TRIAL)

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Introduction: Gastric cancer remains one of the most common causes of cancer-related death worldwide, particularly in East Asian countries. Although the prevention and eradication of *Helicobacter pylori* infection decreased the incidence of gastric cancers, it is still high. Recently, image-enhanced endoscopy (IEE) technologies including narrow-band imaging (NBI) and blue laser imaging (BLI) have been developed. A more recently developed IEE technology, linked color imaging (LCI), enhances slight color differences in hue in the red region of the spectrum, and has been reported to be useful for the diagnosis of gastrointestinal (GI) diseases.
Aims & Methods: The aim of this study is to compare the detection rate of neoplasms in upper GI endoscopy between conventional white-light imaging (WLI) and LCI observation for high-risk patients. In this prospective multicenter randomized controlled trial (RCT), patients with a history or presence of esophageal or gastric neoplasms were enrolled in 19 Japanese institutions between November 2016 and July 2018. Patients were assigned to 2 groups; primary observation with WLI followed by LCI (WLI-LCI group) or primary LCI observation followed by WLI (LCI-WLI group). Additional detection rates of gastric neoplasms were compared between WLI-LCI and LCI-WLI groups. The characteristics of the neoplastic lesions additionally detected by each mode were also evaluated. The number of lesions detected, and endoscopic diagnosis (neoplastic or non-neoplastic) were recorded for each procedure during examination, and all lesions detected were biopsied for histopathological diagnosis. Neoplastic lesions

were defined as adenoma and adenocarcinoma. This study was approved by the institutional review board of all participating institutions and was registered with UMIN Clinical Trial Registry (UMIN000023863).
Results: A total of 1508 patients were enrolled and 1504 patients were randomly allocated to each group; 752 for WLI-LCI and 750 for LCI-WLI group. There was no significant difference in demographics including age, sex, presence/absence of surgical history, and the ratio of current and previous cancer between the two groups. In the WLI-LCI group, a total of 63 gastric neoplastic lesions were detected, which included 37 lesions detected by primary WLI and 26 lesions by secondary LCI. In the LCI-WLI group, a total of 71 gastric lesions were detected, which included 66 lesions detected by primary LCI and 5 lesions by secondary WLI. Additional detection rates of gastric neoplasm in WLI-LCI group was significantly higher than in LCI-WLI group; 41.3% vs 7.0%, p< 0.001. Additional detection rate of the patients with gastric neoplasm in WLI-LCI was also significantly higher than in LCI-WLI group; 8.0% (60/750) vs 4.8% (36/752), p< 0.05. When images of 85 gastric cancer lesions were compared between LCI and WLI, LCI showed more reddish color in 56 cancer lesions and more whitish color in 17 lesions than WLI. All 17 lesions, which were overlooked by WLI, showed enhanced color contrast in LCI image. All 10 isochromatic lesions with WLI exhibited enhanced reddish color in LCI images.
Conclusion: Our large-scale RCT strongly suggest that LCI is superior to conventional WLI for detection of gastric neoplasm during upper GI endoscopy. It is supposedly due to the characteristic color enhancement function of LCI. LCI may be a standard examination tool for the detection of gastric neoplasm for high-risk patients.
References: Ono S, Abiko S, Kato M. Linked Color imaging enhanced gastric cancer in gastric intestinal metaplasia. Dig Endosc 2017;29 :230-1.
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OP046 EFFICACY OF POLYGLYCOLIC ACID SHEETING WITH FIBRIN GLUE FOR THE TREATMENT OF PERFORATIONS RELATED TO GASTROINTESTINAL ENDOSCOPIC PROCEDURES: A MULTICENTER RETROSPECTIVE STUDY AMONG THE PGA STUDY GROUP

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Introduction: Polyglycolic acid (PGA) sheets with fibrin glue have been reported to be useful for preventing perforation and delayed bleeding after endoscopic treatment [1,2]. Although they can be useful for the closure of perforations related to gastrointestinal (GI) endoscopic procedures, no large-scale multicenter treatment outcomes have been reported yet.
Aims & Methods: This is a retrospective multicenter study conducted by the PGA study group, which is the affiliated study group of the Japanese Gastroenterological Endoscopy Society and consists of 18 institutions.

From April 2013 to March 2018, patients with perforations related to GI endoscopic procedures and endoscopically closed using PGA sheeting with fibrin glue were extracted, and were retrospectively examined. "Intraoperative perforation" was defined as a perforation through which the outside of the GI tract was visible during the endoscopic procedure, or as the case where free gas was detected outside the lumen on radiography or computed tomography (CT) just after the endoscopic procedure. Delayed perforation was defined as a perforation or symptoms appearing after the completion of the endoscopic procedure and the case where free gas was detected on radiography or CT, even though no perforation or symptoms occurred immediately after the completion of the endoscopic procedure. Perforations were filled with one or several pieces of PGA sheets followed by spraying fibrin glue using an endoscopic catheter. This procedure was sometimes repeated at 1- or 2-week intervals before closure.

Results:

Intraoperative perforation: Sixty-six cases (esophagus 6, stomach 22, duodenum 12, and colon 26) during endoscopic procedures, including 58 endoscopic submucosal dissections (ESDs), 2 endoscopic mucosal resections, 1 endoscopic submucosal resection with a ligation device, 2 endoscopic papillectomies, and 3 endoscopic balloon dilations, were detected. The median lesion and perforation diameters were 27 mm (range, 3-163 mm) and 5 mm (range, 1-30 mm), respectively. PGA sheets were filled at a median of once after perforation (range, 1-3). Nasal drainage and endoscopic clipping were performed adjunctly in 23 (35%) and 49 cases (74%) with PGA sheeting, respectively. Complete closure was attained in 60 cases (91%). The median period from the first sheeting to the diet resuming was 6 days (range, 0-23).

Delayed perforation: Twenty-four cases (esophagus 5, stomach 10, duodenum 7, and colon 2) occurred after 20 ESDs, 3 dilations, and 1 Per-Oral Endoscopic Myotomy (POEM). The median lesion and perforation sizes were 24 mm (range, 4-58) and 5 mm (range, 1-30), respectively. PGA sheets were filled at a median of once (1-4) after perforation. Nasal drainage accompanied the procedure in 12 cases (50%) and endoscopic clipping in 7 cases (29%). Complete closure was attained in all 24 cases (100%). The median period from the first sheeting to the diet resuming was 10 days (range, 1-124 days). No adverse events related to PGA sheeting occurred in all the cases.

Conclusion: PGA sheeting with fibrin glue was effective for the treatment of intraoperative or delayed perforation related to GI endoscopic treatment.

References: 1] Takimoto K, Toyonaga T, Matsuyama K. Endoscopy. 2012;44(Suppl.02):E414-E415 2] Tsuji Y, Fujishiro M, Kodashima S, et al. Gastrointest Endosc. 2015;81(4):906-912

Disclosure: Tsuji Y and Takimoto K: Lecture fees from GUNZE Medical Japan and CSL Behring

OP047 ENDOSCOPIC SUBMUCOSAL DISSECTION VS ENDOSCOPIC MUCOSAL RESECTION FOR TREATMENT OF BARRETT'S RELATED SUPERFICIAL ESOPHAGEAL NEOPLASIA: MULTICENTER RETROSPECTIVE STUDY IN THE WEST

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Introduction: The difference in long-term outcomes of endoscopic submucosal dissection (ESD) and endoscopic mucosal resection (EMR) for Barrett's related superficial neoplasia remain unclear.

Aims & Methods: We aimed to compare the rates of local and metachronous recurrence of ESD and EMR in patients with clinically staged BE-associated high-grade dysplasia (HGD) and T1a esophageal adenocarcinoma (EAC). A retrospective multicenter study was performed at six academic

hospitals in the U.S. Patients who underwent ESD with a pre-procedural diagnosis of BE-HGD or T1a EAC were included in the study. Data was collected on demographics, tumor and procedure characteristics, procedure pathology, and follow-up. The main outcome was a composite of rate of local and metachronous recurrence. Local recurrence was defined as that appearing at a similar location as previous resection and confirmed by histopathology. Flat dysplasia requiring radiofrequency ablation (RFA) was not included in the definition. Follow-up time was defined as months from initial procedure to recurrence or last follow-up visit if recurrence-free. A time-to-event analysis was performed to evaluate recurrence. A Kaplan-Meier plot was constructed, and a log-rank test was used to compare the groups. A Cox proportional hazard ratio regression analysis was performed to identify predictors of recurrence.

Results: A total of 219 patients were included. 154 underwent EMR, while 65 underwent ESD. ESD had higher en bloc (92% vs 33%, p< .0001), R0 (55% vs 31%, p=0.023) and curative resection rates (66% vs 32% , p< .0001) when compared to EMR. The 24-month local recurrence rate for EMR and ESD was 43.3% and 15%, respectively (p=.0007). Significantly more endoscopic resection procedures were required to treat recurrence after EMR compared to after ESD. EMR, piecemeal resection, positive margins, and non-curative resection were identified as predictors of recurrence on univariate analysis. EMR remained significant after multivariate analysis (Table 2).

Conclusion: This multicenter study showed that ESD results in more definitive treatment of BE-associated early neoplasia than EMR, with significant lower recurrence rates and less need for repeat endoscopic therapeutic procedures than EMR.

Disclosure: Nothing to disclose

Factor	Univariable HR 95% CI	Univariable P-value	Multivariable HR 95% CI	Multivariable P value
Technique: EMR vs ESD	3.7 [1.7-9.6]	0.0003	4.1 [1.3-18.4]	0.01
En bloc resection: Piecemeal vs en bloc	7.6 [3.9-16.5]	< .0001	1.6 [0.5-5.6]	0.42
Margins: R1 vs R0	2.6 [1.5-4.6]	0.0038	1.9 [0.9-4.4]	0.07
Lymphovascular invasion: Yes vs No	1.52 [0.4-9.3]	0.52	--	--
Differentiation: Well + moderate vs Poor	2.0 [0.8-5.4]	0.23	--	--
Curative resection: No vs Yes	6.1 [3.2-13.3]	< .0001	2.6 [0.11-8.8]	0.08

[Table. Cox proportional hazard ratio regression analysis for recurrence]

OP048 CLINICAL CHARACTERISTICS AND RISK FACTORS OF UPPER GASTROINTESTINAL CANCERS MISSED DURING ENDOSCOPY: A NATION-WIDE REGISTRY-BASED STUDY

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Introduction: Upper gastrointestinal (UGI) cancers, including esophageal, gastric and duodenal cancers, usually present at an advanced stage in the Western world, when the treatment options are limited and the prognosis is dismal. Endoscopy remains the gold standard for UGI cancer diagnosis, however, a significant proportion of these neoplasms are missed during this examination. The clinical characteristics of missed UGI cancers remain poorly understood.

Aims & Methods: This was a retrospective registry-based study done in collaboration between clinicians and data analysts from Ministry of Health in Poland aimed to characterize patients with missed UGI cancers during

endoscopy. We used National Health Fund Registry (NFZ) to identify adult patients who underwent UGI endoscopy between 2009-2015 and had a subsequent diagnosis of UGI cancer. Cancers diagnosed within 1 year after endoscopy were defined as "prevalent" cancers, those diagnosed after 1 year and within 3 years after UGI endoscopy were considered as "missed" cancers, and those diagnosed after 3 years were classified as "latent" cancers. To reduce the number of miscoding errors we included only cases of cancer confirmed at least twice in the registry on two subsequent occasions. We used Polish National Cancer Registry (KRN) for data validation. Clinical characteristics of prevalent and missed cancers where compared using t-test and chi-square test, where appropriate, with Holm-Bonferroni correction. Survival data were compared by Kaplan-Meier analysis and log-rank test.

Results: In total, we analyzed 8,040,178 UGI endoscopies [46.3% ambulatory and 53.7% secondary care] performed in 3,856,210 patients [2,178,859 females (57.7%), mean age 58.7 (±3.8) years]. After excluding cancers with a single record in the NFZ (n=11,180) and those diagnosed before the first registered endoscopy (n=10,171) we included 51,123 UGI cancers in the analysis, of which 43,388 were classified as prevalent (84.9%), 3,964 as missed (7.8%), and 3,771 as latent cancers (7.4%). NFZ data was cross-linked with KRN registry showing a 84.2% agreement. We observed a steady decline of UGI cancer incidence within the study time-frame (from 8,881 cases in 2009 to 6,231 cases in 2015), however, the proportion of missed cancers remained relatively stable oscillating between 7.3% to 8.5% in 2009-2014. Median time of missed cancer diagnosis after UGI endoscopy was 1.8 years (IQR 1.4-2.4). Gastric cancers constituted majority of missed cancers (81.4%), however, the miss-rate was highest for duodenal cancers, followed by gastric and oesophageal cancers (16.9%, 7.4% and 5.2%, respectively). When compared to prevalent cancers, patients with missed UGI cancers were more commonly female (40.9% vs 33.1%, P< .001), less commonly resided in rural areas (30.0% vs 35.1%, P=.003) and were statistically younger, however, this difference wasn't clinically significant (mean age 67.5 vs 68.1, P< .001). Missed cancers had a higher survival rate as compared to prevalent cancers cases (5-year survival: 12.6% vs 9.0%, P< .001). Within missed UGI cancers, oesophageal had the worst survival as compared to gastric and duodenal cancers [5-year survival rate: 6.9%, 13.6% and 13.0%, respectively (P< .001)].

Conclusion: Despite declining UGI cancer incidence, proportion of missed UGI cancers remain stable over time. Patients with missed UGI cancers are more commonly female, reside more often in urban areas and have a higher survival rate than prevalent cancers. Oesophageal cancers are least commonly missed, however, have the poorest survival among missed UGI cancers.

Disclosure: Nothing to disclose

OP049 LONG TERM OUTCOMES OF PER-ORAL ENDOSCOPIC MYOTOMY BEYOND 6 YEARS: A MULTICENTER STUDY OF ACHALASIA PATIENTS

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Introduction: Per-oral endoscopic myotomy (POEM) is as a safe and effective treatment for achalasia with short-term clinical response reported in over 80% of patients. However, long-term data are limited.

Aims & Methods: To (1)evaluate outcomes in achalasia patients at least 6 years post-POEM and (2)identify factors associated with clinical failure. We conducted a retrospective review of achalasia patients at 8 tertiary-care centers (2 USA, 4 Europe, 2 Asia) who underwent POEM from 2010 to 2012 with a minimum follow-up of 6 years. Response was defined by an Eckardt score of ≤3. Adverse events (AEs) were also reported and categorized by the ASGE lexicon for AEs. Univariable analysis was performed to determine factors associated with clinical failure.

Results: A total of 73 patients (46 females (63.0%); mean age 49.7 years) with at least 6 years of follow-up (type I 16, type II 15, type III 4, and un-

	Patients with available data Total; total clinical response; total clinical failure	Overall (n=73)	Clinical success (ES ≤3) n=65	Clinical failure (ES>3) n=8	p-value
Age, years (mean±SD)	73;65;8	49.7±17.4	50.6±18.0	42.4±10.1	0.07
BMI, kg/m2 (mean±SD)	37;32;5	26.5±12.4	26.3±12.6	28.3±11.6	0.73
Female, no. (%)	73;65;8	46 (63.0)	41 (63.1)	5 (62.5)	0.99
Disease Classification	73;65;8				0.005
Type 1		16 (21.9)	10 (15.4)	6 (75.0)	
Type 2		15 (20.6)	14 (21.5)	1 (12.5)	
Type 3		4 (5.5)	4 (6.2)	0 (0.0)	
Unspecified		38 (52.1)	37 (56.9)	1 (12.5)	
Any prior therapy, no. (%)	73;65;8	23 (31.5)	22 (33.9)	1 (12.5)	0.42
HRM IRP, mmHg (mean±SD)	25;21;4	32.5±14.2	32.4±15.1	33.1±9.2	0.90
Pre-poem Eckhart score, mean±SD	71;65;6	7.1±2.3	7.1±2.3	7.7±2.7	0.61
Follow up time, months, median (IQR)	50;42;8	79.5 (73.9-82.6)	76.9 (73.9-82.2)	81.6 (74.7-89.1)	0.25
72 months Eckhart score (mean±SD)	73;65;8	1.1±1.1	0.9±0.8	2.5±1.8	0.04
36 months Eckhart score (mean±SD)	61;58;3	0.9±1.1	0.8±0.8	4.3±1.2	0.03
6 months Eckhart (mean±SD)	69;63;6	0.8±1.1	0.6±0.8	3.2±1.5	0.007
Patients with adverse events, no. (%)	73;65;8	16 (21.9)	16 (24.6)	0 (0.0)	0.19
Symptomatic reflux, no. (%)	72;64;8	27 (37.5)	25 (39.1)	2 (25.0)	0.43
PPI use, no. (%)	73;65;8				0.41
Daily		23 (31.5)	22 (33.9)	1 (12.5)	
Occasionally		6 (8.2)	5 (7.7)	1 (12.5)	
Esophagitis on EGD, no. (%)	60;57;3	17 (28.3)	17 (29.8)	3 (0.0)	0.55

[OP049 Table. Clinical characteristics and outcomes in patients with clinical success versus failure.]

specified 38) were identified. Median follow-up was 79.5 months (IQR 73.9-82.6). Twenty-one (28.8%) patients had prior dilatation, 4 (5.5%) botulinum injection and 2 (2.7%) Heller myotomy. A total of 17 AEs occurred in 16 (21.9%) patients and included: 1 arrhythmia, 1 delayed bleeding, 1 esophageal leak, 3 mucosotomies, 1 subcutaneous emphysema, and 10 symptomatic capnoperitoneum (13 mild, 2 moderate, and 2 severe). Clinical success was observed in 96%(66/69), 96%(67/70), 93%(65/70), 91%(64/70), and 91%(64/70) of patients within 6, 12, 24, 36, and 48 months respectively. At 72 months, success was noted in 89%(65/73) of cases. Of 66 patients with response at 6 months, only 3 (4.5%) experienced recurrence of symptoms. Overall, mean Eckardt score decreased from 7.1±2.3 to 1.1±1.1 (p< 0.001) and 4sIRP pressure improved from 32.5±14.2 to 12.2±8.8 mmHg (p< 0.001). In univariable analysis, type I achalasia (OR 10.8, p=0.04) was associated with clinical failure. Four patients with clinical failure underwent retreatment with pneumatic dilation and clinical response was noted in 3 (75%) of these patients. Of the remaining 4 patients who did not undergo retreatment, 2 were managed conservatively and 2 were lost to follow up. After POEM, symptomatic reflux was reported by 27/72 (37.5%) patients and esophagitis was reported in 17/60 (28.3%) of patients who had post-procedure EGDs.

Conclusion: This international study reports the longest follow-up of a POEM cohort to date. POEM is safe and provides long-term symptomatic relief with sustained response in almost 90% of patients.

Disclosure: Nothing to disclose

OP050 OUTCOMES OF THE FIRST 500 PERORAL ENDOSCOPIC MYOTOMY FOR ESOPHAGEAL MOTILITY DISORDERS: OUTCOMES OF THE FIRST 500 PATIENTS WITH A MID- AND LONG-TERM FOLLOW-UP. IN A SINGLE EUROPEAN CENTER

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Introduction: Peroral endoscopic myotomy (POEM), which combines the efficacy of surgical myotomy with the benefits of an endoscopic, minimally invasive, procedure, is now considered an effective treatment for esophageal motility disorders. We report on the mid- and long-term outcomes of a large series of patients treated with POEM in a single European center.

Aims & Methods: The first 500 adult patients successfully treated in our center between May 2011 and January 2018 were retrospectively identified from a prospective database, and included in this study. Patients were treated according to the original a standard technique describe by Inoue in 2010. Demographics, clinical, procedural and follow-up data were collected and analysed.

Results: Mean age of patients was 51 years (18-85); 50.5% were male. 79.4% patients were treatment naïve; 14.4% had undergone pneumatic dilatation, 2.6% botulin toxin injection,3.6% Heller-Dor myotomy. A total of 16.6% patients had a type- I achalasia, 57.2% type- II, 13.8% type- III, 1.2% Jackhammer esophagus, 0.8% distal esophageal spasm; in 10.4% the achalasia type was not adequately classified. POEM was completed in 98% of patients. Mean symptoms duration before POEM was 24±64.1 months. Mean operative time was 62.9 minutes (19-180 minutes). Severe complications occurred in 5 patients (1%), but all were managed conservatively. A mean follow-up of 23.7 months (3-60 months) was available for 96.7% of patients. Clinical success (Eckardt score ≤3) was documented in 98% of patients, and was 96.4%, 95.6%, and 93% after 6, 24 and 36 months respectively. 13 patients with failure underwent pneumodilation with success, 4 have persisting symptoms after pneumodilation, 2 underwent surgery.

Success was 97.5% (435/424) in achalasia-patients and 81.8% (11/2) in those with spastic motility disorders (p< 0.05).

An altered esophageal pH-study was documented in 31.2% patients; esophagitis rate was 27.7% (86.9% grade A/B; 13.1% grade C/D).

At the date of the last follow-up, 10% of patients receive daily PPI for GERD.

Conclusion: Our results confirm the efficacy of POEM in a large cohort of patients, with an adequate follow-up. Benefits of POEM seem durable, with and acceptable incidence and severity of iatrogenic GERD.

Disclosure: Nothing to disclose

OP051 PERORAL ENDOSCOPIC SEPTOTOMY (POES) FOR TREATMENT OF ZENKER'S DIVERTICULUM: A PILOT STUDY

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Introduction: The definitive treatment of ZD is to transect the cricopharyngeal muscle to eliminate the septum between the diverticulum and the upper esophagus thus relieving the dysfunctional condition. In the last decade, a septotomy performed utilizing a flexible endoscope has been reported as a safe and effective alternative to both open surgery and rigid endoscopic diverticulotomy. More recently, submucosal tunneling endoscopic septum division (STESD) or Z-POEM has been developed to reduce the risk of perforation and allow a safer, more complete cricopharyngeal myotomy. However, patients with short septum (≤20mm) ZD still represent a difficult-to-treat subgroup of patients because of the anatomical limitation leading to reduced operating space for both rigid and flexible endoscopic treatments or even a STESD approach.

Aims & Methods: The aim of this pilot study is to investigate the efficacy and safety of a novel alternative third space approach, called Per-Oral Endoscopic Septotomy (POES) to treat symptomatic patients with short-septum ZD. The POES technique consisted of:
1) using a hook knife, after submucosal injection, a 15mm mucosotomy performed directly on top of the diverticular septum directed along its long axis;
2) dissection of the underlying submucosa to create an endoscopic window to directly visualize the muscular septum with continued submucosal dissection along either side of the cricopharyngeal muscle, sparing the overlying mucosa, to create two short tunnels;
3) complete myotomy of the now fully exposed cricopharnyngeal muscle fibres extended a 5-10 mm into the esophageal body;
4) closure of the mucosotomy with clips.

All patients with short-septum (≤20mm) ZD who were referred to Humanitas Research Hospital (Rozzano, Italy) for flexible endoscopic septotomy from September 2017 to present were considered for POES. Exclusion criteria consisted of previous interventions for ZD, ongoing use of anticoagulants and inability to provide informed consent.

We determined pre- and post-procedural dysphagia scores using the Dakkak and Bennett (D&B) scale (0-4). Complete or near-complete resolution of symptoms (D&B 0 or 1) was the primary endpoint. Procedure-related adverse events according to ASGE lexicon and procedure time were also recorded. Follow up was carried out by patient visits or via telephone calls by a dedicated nurse at 24 hours, 4 weeks and then regularly every month. Recurrence was defined as new onset dysphagia with a D&B score > 1 or requiring re-intervention.

Results: Sixteen patients (M/F: 11/5, mean age: 64.6±14.0) underwent POES. All procedures were performed under deep sedation with C02 insufflation. Mean size of ZD was 18.4±5.4 mm and mean pre-procedure D&B dysphagia score was 2.75±0.4. Average procedural time was 14.9±5.0 min (range: 8-26 min). No intra- or post- procedural adverse events occurred. Septal myotomy was successfully completed in all patients. There was complete or near-complete resolution of symptoms in 15 out of 16 patients (93.8%) with the D&B dysphagia score dropping from 2.75±0.4 to 0.3±0.6 (p < 0.0001). No symptomatic recurrences were reported after a mean follow up time of 8.9 ± 3.1 months (range: 6-15 months).

Conclusion: According to the preliminary results of this pilot study, third-space approach with POES provided a very safe, efficient and effective treatment for this specific difficult-to-treat group of patients with short septum ZD. Larger comparative studies with longer follow-up are needed to confirm this preliminary data.

Disclosure: Nothing to disclose

Towards microbiome targeted therapies

14:00-15:30 / A1

OP052 TOWARDS ANTI-INFLAMMATORY DIETARY RECOMMENDATIONS BASED ON THE RELATION BETWEEN FOOD AND THE GUT MICROBIOME COMPOSITION IN 1423 INDIVIDUALS

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Introduction: Gut microbiota are essential for intestinal health. As microbes thrive on dietary substrates, the question arises whether we can nourish a protective gut flora. While there is increasing interest in anti-inflammatory capacities of isolated nutrients, little is known on the association between dietary patterns or individual foods and gut microbial features. In this study, we investigated the effect of 160 dietary factors on the gut microbiome across four cohorts, comprising the general population, patients with Crohn's disease, ulcerative colitis, and irritable bowel syndrome. Connecting the diet to the gut microbiome gives us more insight into the relation between diet and intestinal disease and could guide us towards more rational dietary interventions.

Aims & Methods: For every participant one stool sample was collected along with a Food Frequency Questionnaire. To reconstruct the microbiota composition of stool samples, microbial DNA was isolated and shotgun metagenomic sequencing was performed. Unsupervised cluster analyses were performed to identify dietary patterns associated with particular microbial clusters, using hierarchical clustering. Dietary clusters were computed based on squared Euclidean distances, clusters of microbial species and pathways were based on Bray-Curtis dissimilarity. Next, linear models were conducted, adding caloric intake, age, sex, and sequencing read depth as covariates. Analyses were performed separately per cohort, followed by a meta-analysis and heterogeneity estimation. Multiple testing correction was performed on the obtained p-values and a FDR < 0.05 was defined as significance cut-off.

Results: We identified 61 individual food items associated with 123 taxa and 249 pathways (FDR< 5%) as well as 49 correlations between food patterns and microbial groups. A plant-based diet was associated with increased abundances of short chain fatty acid (SCFA) producing bacteria, as well as associated pathways of fermentation. Moreover, plant protein was associated with pathways involved in the biosynthesis of vitamins and amino acids (biotin, thiamine, L-ornithine) and degradation of sugar alcohols. While plant protein was associated with an increase in *Bifidobacteria* and a decrease in *Blautia* and *Streptococci*, the opposite was found for animal protein. Expectedly, low-fat fermented dairy correlated with an increase of *Lactococcus lactis*, *Lactobacilli* and *Bifidobacterium bifidum*, as well as pathways of peptidoglycan synthesis possessed by lactic acid bacteria. A pattern comprising plant protein, vegetables, fruits, cereals, nuts, wine and fish was associated with increased abundances of *Roseburia hominis*, *Faecalibacterium prausnitzii* and *Bifidobacteria* and carbohydrate fermenting pathways. A cluster of wine correlated with an increased abundance of the Bifidobacterium shunt, a fructose fermenting pathway. Interestingly, wine was also correlated with a decrease in clusters of potentially harmful species, namely *Bacteroides fragilis*, *Escherichia coli*, *Coprobacillus* and *Clostridium bolteae*, potentially related to a high polyphenol content.

Conclusion: We show that specific foods are associated with the abundance of gut bacteria capable of the biosynthesis of essential nutrients and carbohydrate fermentation to SCFAs, inferring that certain foods could exert mucosal protection by inducing bacteria with anti-inflammatory properties. Our work provides support of the idea that the diet represents a therapeutic strategy for intestinal diseases, through the modulation of the gut microbiome.

Disclosure: Nothing to disclose

OP053 GUT MICROBIAL CO-ABUNDANCE NETWORKS IDENTIFY FUNCTIONAL HUBS FOR INFLAMMATORY BOWEL DISEASE AND OBESITY

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Introduction: Recent studies have shown the importance of unraveling the role of the gut microbiota in human health and disease. While knowledge is increasing on abundance differences in diseases like inflammatory bowel disease (IBD) and obesity on microbial compositional level, it is also important to study the gut microbiota as an entire ecosystem. One way of doing this, is to study which microbial species and functional pathways show co-abundance networks which may also be relevant for disease.

Aims & Methods: Here, we present the largest study to date in which microbial networks are constructed from an IBD, an obesity and two general population cohorts. We collected metagenomics sequencing data of stool samples from 2,379 participants. DNA isolation was performed by using the same standardized procedures for all four cohorts. MetaPhlAn2 and HUMAnN2 tools were used to characterize the composition and functional pathways of the gut microbiota. Co-abundance of species or functional pathways were identified by using pairwise Spearman correlation. The heterogeneity Cochran's- Q test was used to analyze whether results were derived from a single cohort. A false discovery rate of < 5% was used as significance threshold to also account for multiple testing.

Results: We established co-abundance networks that revealed 1,057 species-species and 8,381 pathway-pathway co-abundance edges. Notable, 113 (10.7%) of the species edges and 4,824 (57.6%) of the pathway edges showed significant differences between the cohorts. The heme anaerobic biosynthesis pathway for example showed co-abundance with biosynthesis pathways of fatty acids in the IBD cohort. Heme is a cofactor of inducing oxidative stress and the identified fatty acids are known for their lipotoxicity. This data suggests that the gut microbiota may play an important role in inducing gut inflammation through biosynthesis of toxic fatty acids in IBD patients. Another example is the sulfur amino acids biosynthesis in the obesity cohort. This pathway has been recognized as potent modulator of lipid metabolism. This pathway was positively correlated with five carbohydrate degradation pathways in the obesity cohort, indicating that these pathways may play an important role in regulating functional dysbiosis in obesity.

Conclusion: By performing a large microbial co-abundance network comparing patients with IBD, obesity and population based subjects, we show that not only microbial abundances but also microbial co-abundance relationships are shifted in disease states. We show that the pathway networks are more different than the species networks. The obesity and IBD specific networks could point to key species or functional pathways which could potentially be used as therapeutic targets.

Disclosure: Nothing to disclose

OP054 FIRST LARGE SCALE EVALUATION OF THE SMALL INTESTINAL MICROBIOME IN PATIENTS WITH OBESITY

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Introduction: Obesity has reached epidemic proportions globally, nearly a third of the world population is now classified as overweight or obese. In 2016, the prevalence of obesity was 39.8% and affected about 93.3 million adults in US. The World Health Organization (WHO) defines overweight

and obesity as abnormal or excessive fat accumulation that presents a risk to health. In the past decade, the gut microbiome has been implicated as an important factor involved in obesity, but most of the research has focused on the stool microbiome and not the metabolically and functionally important small intestine.

Aims & Methods: In this study, we examined the small bowel microbiome in obese subjects. Subjects with normal weight (Body Mass Index (BMI) 18.5 to < 25) and subjects with obesity (BMI > 30) undergoing sole upper endoscopy were recruited. Blood was collected before the procedure. Duodenal aspirates were collected using a novel sterile aspiration catheter technique and DNA was isolated using the MagAttract PowerSoil DNA Kit. Microbiota was analyzed by 16S rRNA metagenomic sequencing. Operational Taxonomic Units clustering and taxonomic analysis were performed with CLC Microbial Genomics Module v. 2.5. The blood levels of glucagon-like peptide-1 (GLP-1) and leptin were determined by Luminex. The Wald test and Mann-Whitney test were used to determine significance between groups.

Results: 92 normal weight subjects (controls) and 45 subjects with obesity had their duodenal microbiome (DM) completely sequenced. The α-diversity indexes of subjects with obesity were similar when compared to controls (Total number, P=0.3846; Simpson's index, P=0.4938; Shannon entropy, P=0.5203). The DM of subjects with obesity and controls was predominantly colonized by taxon from Firmicutes phylum (56-60%), followed by Proteobacteria and Actinobacteria (19-21% and 7-11%). The relative abundance (RA) of the Bacteroidetes phylum represented less than 6% of the total abundance in both groups and the DM Firmicutes/Bacteroidetes ratio in subjects with obesity was also similar when compared to controls (P=0.1899). However, at the family level, the RA of the families Lactobacillaceae and Clostridiaceae, both from Firmicutes phylum, were increased when compared to controls (Fold change (FC)=11.17, P=2.73E-8; FC=16.11, P=2.96E-10 respectively). Additionally, the RA of the Neisseriaceae and Pasteurellaceae families, both from Proteobacteria phylum, were also increased in the DM of subjects with obesity when compared to controls (FC=2.05, P=0.021; FC=2.28, P=0.01, respectively). Interestingly, the RA of the Neisseriaceae family had a positive correlation with the levels of GLP-1 (Spearman r=0.193, P=0.037) and leptin (Spearman r=0.214, P=0.021). The RA of the Pasteurellaceae family also correlated with the levels of leptin (Spearman r=0.247, P=0.007). Impressively, subjects with obesity had higher circulating levels of GLP-1 and leptin when compared to controls (FC=1.14, P=0.038; FC=8.85, P< 0.0001, respectively).

Conclusion: In this first study of the small bowel microbiome, marked differences in the microbiome were seen at the family level and these differences appeared related to incretins and hormones linked to metabolism.

Disclosure: Nothing to disclose

OP055 DIMETHYL FUMARATE (DMF) INHIBITS PROLIFERATION AND MIGRATION OF HEPATOCELLULAR CARCINOMA CELLS (HCC)

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Introduction: Dimethyl fumarate (DMF) is used for treatment of psoriasis (Fumaderm®). Recently, we have shown that application of DMF induces cell death in NF-κB-dependent tumors. This data were confirmed in a mouse model. DMF application led to a reduced tumor growth and, interestingly, to a reduction of metastases formation. The inhibition of metastasis formation was NF-κB-independent. Thus, identification of the molecular mechanism inhibiting metastasis formation is a challenging aim for future. Solid tumors, like pancreas, breast or colon carcinoma, show no constitutive NF-κB activation. Interestingly, DMF also reduced the metastasis formation in these tumors. Since metastasis is the major cause of poor prognosis of HCC DMF could be an interesting new approach for a treatment of these.

Aims & Methods: Human liver tumor cell lines HepG2, Huh7 und Hep3B were treated with DMF (25 μM up to 100 μM) for up to 72 h. A luminescence based viability assay was performed. The assay measures the concentration of ATP *via* photometric quantification. The concentration of ATP is connected to the viability but also the active metabolism of cells. To maintain effects on metastasis formation a scratch assay with the cell lines HepG2, Huh7 and Hep3B were performed. The cells were treated with DMF (25 μM up to 100 μM) and cultivated for up to 48 h. Since DMF could lead to cell death cell were co-treated with 50 μM zVAD an inhibitor of apoptosis.

Migration of the cells was analyzed by microscopy. To maintain effects on proliferation HepG2 were stained with Cytopainter Cell Proliferation Staining Reagent, which stains the cytoplasm of the cells. After each cell division the dye will be divided between mother and daughter cell resulting in a reduced staining. The proliferation of the HepG2 cells was analyzed after 24 h, 48 h, 72 h and 96 h of treatment.

Results: DMF application resulted in a time- and dose-dependent reduction of the ATP-concentration in all cell lines tested. The strongest effects were observed after 72 h treatment at a concentration of 100 μM DMF. In addition, migration of Huh7 and Hep3B were inhibited time and dose-dependently. Migration of Hep3B was more effected by DMF. Inhibition of migration of Hep3B was already observed at a concentration of 25 μM DMF. At a concentration of 100 μM DMF migration of Hep3B was blocked completely. Migration of Huh7 was inhibited at a concentration of 75 μM DMF. Hence, migration of Huh7 was less effected by DMF. Migration of HepG2 could not be detected. Since the migration of the HepG2 cells could not be analyzed we switched to the measurement of the proliferation. Effects on proliferation combined with the reduction of ATP in the cells could mean that the cells will be dormant. It could be shown that the proliferation of HepG2 was also time- and dose-dependent inhibited through DMF.

Conclusion: The formation of metastases is one of the major reasons why solid tumors like HCC display a rather high mortality rate. Here, we show that DMF is capable to inhibit migration and proliferation in HCC cell lines probably caused by energy depletion. The exact mechanism which causes the inhibition of migration and proliferation still needs to be investigated. DMF is already clinical approved used for the treatment of psoriasis and shows compared to anti-cancer drugs minor side effects. Hence, DMF could be used to develop treatments against metastasis formation.

Disclosure: Nothing to disclose

OP056 DUODENAL MICROBIOME CHARACTERIZATION IN PATIENTS WITH OR WITHOUT *HELICOBACTER PYLORI* INFECTION

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Introduction: *Helicobacter pylori* a common human pathogen is a risk factor for chronic gastritis, peptic ulcer and gastric cancer. Its prevalence is higher in developing countries mainly by inadequate hygiene on food handling and preparation. *H. pylori* creates an alkaline environment on the stomach, which leads to changes in the gastric and gut microbiomes; also, *H. pylori* elicits a local immune response that could modulate gastric and duodenal microbiota. There is little information regarding the effect of *H. pylori* gastric infection on duodenal microbiota.

Aims & Methods: To conduct a culture independent metagenomic profiling of duodenal microbiome on patients with and without *H. pylori* infection, matched by age, hospital and sex.

The V3-V4 region of the 16S rRNA gene was amplified and sequenced on MiSeq Illumina platform from a total of 74 patients in 4 different hospitals in Quito, Ecuador. Patients were assessed for the presence of H. *pylori* through a biopsy obtained during an upper digestive endoscopy. From these, 34 patients had a *H. pylori* active infection on the gastric fundus, and 40 patients were negative for the bacterium. Duodenal biopsies were obtained in all patients, and additional epidemiological information was collected. Bioinformatic analysis of sequences was performed using QIIME2.

Results: Around 28 million bacterial sequences were obtained and 3,230 operational taxonomic units (OTUs) were characterized among the 74 samples. On most of the samples positive for *H. pylori* on histological observation, there was also detected *H. pylori* 16S rRNA on the culture-independent metagenomic analysis. A higher alpha diversity was encountered in the duodenum of *H. pylori* positive patients (Shannon index and observed OTUs differences between the two groups *P* < 0.01). Weighted UNIFRAC, Bray-Curtis and Jaccard beta diversity indexes also showed significant differences between groups (*P* < 0.05). Relative abundance of *Haemophilus*, *Streptococcus*, *Neisseria* and *Prevotella* spp. was higher in the *H. pylori* positive patients whilst a higher abundance of *Ralstonia* spp. was on found in negative ones.

Conclusion: Duodenal microbiomes are different between *H. pylori* positive and negative patients in terms of alpha diversity, beta diversity and relative OTUs abundance. Also, *H. pylori* infected individuals have increased abundance of *Haemophilus, Streptococcus, Neisseria* and *Prevotella* spp. in their gastric microbiome (1).

References: 1. Klymiuk, I., Bilgilier, C., Stadlmann, A., Thannesberger, J., Kastner, M. T., Högenauer, C., Steininger, C. (2017). The Human Gastric Microbiome Is Predicated upon Infection with Helicobacter pylori. Frontiers in microbiology, 8, 2508. doi:10.3389/fmicb.2017.02508

Disclosure: The current project was funded by Biocodex, USFQ and UTE, however the funders did not were involved in study design, patients recruitment, experiments, data collection and analyses, or results interpretation.

OP057 CHANGES IN DUODENAL UROGUANYLIN IMMUNOREACTIVE CELLS DENSITY CORRELATE WITH SYMPTOMS OF PATIENTS WITH DIARRHEA-PREDOMINANT IRRITABLE BOWEL SYNDROME FOLLOWING FECAL MICROBIOTA TRANSPLANTATION

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Introduction: Altered density of uroguanylin (UGN) immunoreactive (GUCA2B-positive) cells was found in the duodenum of patients with diarrhea-predominant irritable bowel syndrome (IBS-D) (1). Uroguanylin activates guanylate cyclase to regulate electrolyte and water transport in intestinal epithelia (2).

Aims & Methods: The aim was to investigate the effect of fecal microbiota transplantation (FMT) on UGN immunoreactive (GUCA2B-positive) cells density in the duodenum of IBS-D patients.

The study included 16 IBS patients according to Rome III criteria and four patients were excluded. The remaining patients (n=12, 4 females and 8 males) were divided according to the cause into post-infectious (PI, n=6) and idiopathic (n=6) IBS. They completed IBS-Symptom Severity Scoring system (IBS-SSS) questionnaire and IBS-Symptom questionnaire (IBS-SQ) before and 3 weeks after FMT. Fecal suspension (30 g fresh feces donated from patients' healthy relatives and diluted with 60 ml normal saline) was instilled via gastroscope into the duodenum. Biopsies were taken from the descending part of the duodenum before and 3 weeks after FMT. They were immunostained for UGN cells using rabbit polyclonal antibody to GUCA2B (LS-C371347, LSBio, Seattle, WA, USA) and quantified using computerized image analysis.

Fecal microbiota transplantation			
Questionnaire	Before	After	P-value
IBS-SSS	326.6±22.3	240.2±33.6	0.0009
IBS-SQ			
Total score	30.8±3.3	11.6±2.1	<0.0001
Abdominal pain	6.3±0.9	3.3±0.8	0.0012
Bloating	7.9±0.5	3.4±0.8	<0.0001
Diarrhea	6.4±0.9	1.2±0.4	<0.0001
Uroguanylin immunoreactive cells density			
Total IBS group			
Villi (cells/100 epithelial cells)	44±5.5	41±2.3	0.5
Crypts (cells/mm²)	116±8	96±3	0.049
PI-IBS			
Villi (cells/100 epithelial cells)	45.8±7.4	40.5±3.3	0.6
Crypts (cells/mm²)	108±11.8	102.5±4	0.6
Idiopathic IBS			
Villi (cells/100 epithelial cells)	42.5±8.8	40.7±3.6	0.8
Crypts (cells/mm²)	124±11	89.5±4	0.04

Paired t test. Data are presented as the mean±SEM. IBS: irritable bowel syndrome, PI: post infectious, SSS: Symptom Severity Scoring system, SQ: symptom questionnaire.

[Table 1: Symptoms scores and duodenal uroguanylin immunoreactive cells density in IBS patients before and after fecal microbiota transplantation]

Results: The total scores for IBS-SSS and IBS-SQ were significantly improved (*P*=0.0009 and < 0.0001, respectively) 3 weeks after receiving FMT. During the same period, the densities of UGN immunoreactive cells for the total group and idiopathic subgroup decreased significantly in the duodenal crypts (*P*= 0.049 and 0.04, respectively) but not in the villi (*P*= 0.5 and 0.8, respectively), as shown in Table 1. No significant changes were shown in the PI-IBS subgroups (Table 1). Using Pearson's test, UGN immunoreactive cells density in the crypts correlated positively with diarrhea (r=0.97, *P*=0.001) and negatively with bloating (r= -0.91, *P*=0.011) in the PI-IBS subgroup before FMT and positively with abdominal pain (r=0.63, *P*=0.029) in the total group of IBS patients after FMT. No correlations were found between the cells in the villi and IBS symptoms.

Conclusion: This is the first study to show the changes in the UGN immunoreactive cell densities following FMT and their correlations to IBS symptoms (pain, bloating and diarrhea). These correlations are consistent with the effects exhibited by UGN analog that is used for the treatment of IBS patients (3).

References:
1) Mazzawi T et. al. Abnormal uroguanylin immunoreactive cells density in the duodenum of patients with diarrhea-predominant irritable bowel syndrome compared to healthy control subjects. Submitted UEG Week 2019, Abstract: A-1084-0010-00312.
2) Rahbi H, Narayan H, Jones DJ, Ng LL (December 2012). „The uroguanylin system and human disease". Clinical Science. 123 (12): 659-68.
3) Miner PB, Jr., Koltun WD, Wiener GJ, De La Portilla M, Prieto B, Shailubhai K, et al. A Randomized Phase III Clinical Trial of Plecanatide, a Uroguanylin Analog, in Patients With Chronic Idiopathic Constipation. The American journal of gastroenterology. 2017;112(4):613-21.

Disclosure: Nothing to disclose

OP058 ROLE OF INTESTINAL ALKALINE PHOSPHATASE, MYOKINES AND MICROBIOME IN AMELIORATION OF EXPERIMENTAL COLITIS IN VOLUNTARY RUNNING WHEEL ACTIVITY OBESE MICE FED FAT DIET

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Introduction: Intestinal alkaline phosphatase (IAP) is an important apical brush border enzyme expressed throughout the gastrointestinal tract and secreted into both, the intestinal lumen and the bloodstream. IAP has been implicated in intestinal protection through dephosphorylating both ATP and bacterial lipopolysaccharide (LPS) released from cells during stressful conditions. The hypertrophied mesenteric white (mWAT) adipose tissue in obesity may predispose the development of colitis.

Aims & Methods: Exercise can improve colitis but the role of IAP with or without exercise in mucosal healing of colitis has been little studied. We determined the effects of daily intragastric treatment with IAP (50 - 200 U) in sixty mice fed for 6 months with high fat diet (HFD, 70% energy from fat, series A) and standard diet (SD, 10% energy from fat, series B) (Altromin, Lage, Germany) and subjected to voluntary running wheel activity on the course of trinitrobenzene sulfonic acid (TNBS) colitis. Mice (series A & B) were housed for 8 weeks in *individual running wheel cages* to measure the running distance and muscle force by grip test. Following colitis, the colonic blood flow (CBF) by Laser Doppler flowmetry, disease activity index (DAI) were determined, the plasma levels of TNF-α, IL-1β, adiponectin, leptin, TWEAK and myokines irisin, IL-6 and FNDC5 were assessed by Luminex, the expression for TNF-α, IL-1β and IL-6 mRNA was determined by qPCR and the gut microbiome was analyzed by Next-Generation Sequencing (NGS).

Results: TNBS caused a significant increase in DAI, the significant fall in the CBF, an increase in colonic tissue weight, the plasma levels, expression of IL-1β, TNF-α and IL-6 mRNA and protein (p< 0.05). In HFD mice, the running distance, muscle strength were reduced and the area of colonic damage and colonic tissue weight, the plasma IL-1β, TNF-α, TWEAK and leptin levels were significantly increased while FND5, irisin and adiponectin levels were decreased vs. SD mice. Treatment with IAP significantly

reduced DAI in SD and HFD mice, increased the skeletal muscle strenght as assessed by muscle grip test and potentiated the beneficial ameliorating effect of exercise on colitis. IAP alone or combined with exercise increased the CBF and plasma levels of myokines IL-6, FND5 and irisin while plasma levels of IL-1β, TNF-α, TWEAK and leptin was significantly diminished (p< 0.05). In HFD mice, the reduction of *Lactobacillus, Clostridium, Faecalibacterium* and an enhanced colonization by *Bacteroides, Prevotella* and *Helicobacter spp.* was detected while IAP treatment reduced *Bacteroides* and *Helicobacter* spp. and favored colonization of *Lactobacillus and Bifidobacteria spp.* compared with sedentary mice.

Conclusion: Exercise can improve the healing of experimental colitis due to release of protective myokines irisin, IL-6 and FND5 from working skeletal muscles, reduction of proinflammatory cytokines and normalization of leptin/adiponectin ratio, especially in obese mice, and 2) exogenous IAP ameliorates gut inflammation, enhances effect of exercise and favors healing of colitis due to modification of microflora and a potent enhancement in CBF. IAP may represent a novel supplementation capable of acting synergistically with moderate exercise activity in mechanism of amelioration of human IBD (grant No. K/PBO/000440).

Disclosure: Nothing to disclose

Epidemiology and treatment of IBD

14:00-15:30 / B2

OP059 INCIDENCE AND PREVALENCE OF INFLAMMATORY BOWEL DISEASE IN THE UK BETWEEN 2000 AND 2016 AND ASSOCIATED MORTALITY AND SUBSEQUENT RISK OF COLORECTAL CANCER

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Introduction: There is only limited and old data on the epidemiology of inflammatory bowel disease (IBD), including Ulcerative Colitis (UC) and Crohn's Disease (CD), in the UK. Accurate data on the IBD burden and their impact is crucial for service planning for patients. The aim of this study was to establish accurate, updated UK incidence and prevalence of IBDs and to quantify the risk of mortality and colorectal cancer in those with IBD.
Aims & Methods: Retrospective cohort studies and cross-sectional studies were carried out between 2000 and 2016 using data from the Health Improvement Network (THIN), a primary care database of 750 general practices representative of the UK population. Annual incidence rates and point prevalence among adults aged 18 years and over were calculated for CD and UC. Mortality and colorectal cancer (CRC) incidence rates were quantified using a matched cohort study design, with four controls for each UC or CD subject, matching on age, sex and general practice between 1995 and 2017. A multivariable Cox proportional hazards model was used to quantify risk of mortality adjusting for year, age-band, sex, deprivation level, Charlson comorbidity, smoking status and hypertension and a multivariable Poisson regression model was used to quantify CRC risk.
Results: 16,765 incident cases of CD and 24,410 incident cases of UC were observed among 8,767,641 subjects, totalling more than 61 million person-years at risk (py). The incidence rate (IR) of CD was 16.3 per 100,000 py. Females had a 30% higher incidence of CD than male subjects (Incidence Rate Ration 1.30 (95% CI 1.23-1.34), p< 0.001) and all age categories greater than 18-30 had a lower rate of CD incidence. Overall, CD incidence fell by 3% (0.97 (0.96-0.97), p< 0.001) over the study period, was stable in subjects under 60 years, and fell by 4% in those over 60 years (0.96 (0.95-0.97), p< 0.001). The IR of UC was 25.9 per 100,000py. Females had a 6% lower incidence of UC than males (0.94 (0.91-0.96), p< 0.001) and compared to 18-30s all older age categories had a lower rate of UC when adjusted by sex and year. Overall, UC incidence fell by 4% (0.96 (0.95-0.96), p< 0.001) between 2000 and 2016. In those aged over 60, IR fell by 6% (0.94 (0.93-0.94), p< 0.001) over the study period, but was stable

in those under 60. Point prevalence of CD increased from 218 to 414 per 100,000 population between 2000 and 2016. In 2016, prevalence was 460 and 370 for females and males respectively. UC prevalence rose from 380 to 640 per 100,000. In 2016. prevalence was 630 and 640 in females and males respectively.
CRC incidence rate in the whole THIN population was 70.6 per 100,000py (95% CI 69.6-71.5) over the study period. IR of CRC in CD was 78.4 per 100,000py (66.8-92.0). IR of CRC in UC was 133.3 per 100,000py (121.1-146.8). The adjusted incidence rate ratio (IRR) of CRC was 26% higher in CD patients than in matched controls (1.26 (1.04-1.51), p=0,014), and was 48% higher in those with UC (1.48 (1.32-1.67), p< 0.001). Among CD subjects, mortality was 41% higher (hazard ratio 1.41 (1.35-1.47), p< 0.001) and among UC subjects, mortality was 17% higher (1.17 (1.14-1.21), p< 0.001).
Conclusion: IBD prevalence in the UK is more than double that which had been previously reported. Although incidence rates of UC and CD are stable in the under 60s, there appears to have been a fall in rates of IBD in older age groups. Mortality and CRC risk was higher in both UC and CD when compared to matched controls.
Disclosure: Nothing to disclose

OP060 INFLAMMATORY BOWEL DISEASE ASSOCIATED COLORECTAL CANCER: CHARACTERISTICS AND OUTCOMES FROM AN ENGLISH POPULATION DATASET (2010 TO 2016)

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Introduction: Colorectal cancer (CRC) is an important complication of inflammatory bowel disease (IBD). Historic cohort studies have suggested that the risk of developing CRC in those with IBD (IBD-CRC) may be increasing, but contemporary, population data are lacking. There is also a paucity of information on the clinical outcomes for these cancers, including surgical outcomes, and whether there is any difference between sporadic and IBD-CRC.
Aims & Methods: This English population-based study examined the characteristics, treatments and outcomes for CRC patients with and without IBD. The CORECT-R data repository holds national, linked data on CRC diagnosis pathways, treatments and outcomes in England. Using this resource, all CRC cases between 01/01/2010 and 31/12/2016 were identified. A diagnosis of IBD (Crohn's disease or ulcerative colitis) was defined by relevant ICD-10 codes (K50-51). Study characteristics included; sex, age at diagnosis, associated comorbidity, route of diagnosis, stage of CRC, survival in days, and details of any surgical resection. Multivariable logistic regression models assessed the relationship between IBD and post-surgical outcomes and death within a year of diagnosis.
Results: There were 192,000 CRC in the study period (2,992 IBD-CRC). There was an increase in the proportion of IBD-CRC from 1,4% in 2010 to 1.9% in 2016 (p-value for trend < 0.01). IBD-CRC cases were significantly younger (median age 68 years (IQR 56-78) and 73 years (IQR 64-81) respectively), had more associated comorbidity, and more presented as an emergency. There were significantly more right-colonic, and more early (Stage I) and late (Stage IV) cancers. After a major surgical resection significantly more people with IBD were likely to be readmitted as an emergency (OR 1.30, 95% CI 1.16-1.47), have a prolonged hospital stay (≥21 days) (OR 1.47, 95% CI 1.28-1.68), and die within a year (OR 1.52, 95% CI 1.32-1.77).
Conclusion: The proportion of IBD-CRC is increasing. This is may reflect the rising incidence of IBD, but also decreasing rates of colectomy procedures leaving more people exposed to a risk of developing CRC. Outcomes for those with IBD-CRC appear worse than for sporadic CRC, and the cancers occur in younger patients. There is an urgent need to explore the diagnosis and management pathways for these individuals to try and explain the significant differences shown here.
Disclosure: Nothing to disclose

OP061 THE RISK OF FURTHER RESECTIONAL SURGERY IN THE TEN YEARS FOLLOWING A FIRST RESECTION FOR CROHN'S DISEASE IN ENGLAND

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Introduction: Most patients with Crohn's Disease (CD) will have surgery during the course of their disease[1], many of whom develop endoscopic recurrence within a year[2] and may need further surgery. This study aims to examine the proportion, timing and factors associated with further surgery following an index surgical resection.

Aims & Methods: Hospital Episode Statistics captures all patient interaction with hospitals in England. Subjects were included in the study if they had index surgical resection between 2007 and 2016 and an International Classification of Disease-10 (ICD-10) code of K51 (CD) on admission. A sub-cohort was identified whose index resection was colonic and whose ICD-10 code was K501 - this was considered a Crohn's colitis cohort. Subjects were followed for a maximum of 12-years and the primary outcome was further bowel resection. A multivariable Cox regression model assessed factors associated with further resection.

Results: 16,609 subjects with CD had a bowel resection: 53.7% female, median age 35 (IQR 26-46) years, 87.3% were white, 85.3% of subjects had no comorbidities (Charlson score of 0) and 11% of subjects were coded as having perianal disease during the study period. 70% of subjects had at least 5 years of follow-up and 19% had at least 10-years follow-up. Index surgery was performed on an emergency admission in 41.8%. The median number of annual index resections was 1,662 (IQR 1,617-1,682). 29.7% of subjects had one or more further resections during the follow-up period and 22% of these had more than two further resections. 48.7% of first further resections took place within 1-year of index surgery and 54.7% of first further operations were performed in subjects whose index surgery occurred during an emergency admission. Of those with 5 years follow-up, 26.5% had one or more further resections and in those with 10 years follow-up, 32.4% had one or more further resections. Female subjects were at lower risk of further resection (HR 0.85 (95% CI 0.80-0.90), p< 0.001), as were the older subjects 44-60 years when compared to 18-29 year olds (0.85 (0.79-0.92), p< 0.001). Those in the least deprived quintile were also at lower risk (0.90 (0.82-0.99), p=0.029), as were those whose initial resection was done on an elective basis (0.53 (0.5-0.56), p< 0.001). Perianal disease was associated with a 69% increased the risk of future resection (1.69 (1.57-1.82, p< 0.001), and a high comorbidity score was associated with a 22% increased risk (1.22 (1.03-1.44), p=0.024). Ethnicity was not associated with further resection.

In the Crohn's colitis sub-cohort, 1,933 subjects were identified. 56% female, median age 36 (IQR 26-47) years and 87% white. 33% of subjects had further resection during follow-up, 25.6% of these subjects had 2 or more further resections. Perianal disease was coded in 14.5% of this cohort. 43% of index colonic resections were performed during an emergency admission and 39.5% of these subjects had further resection. An elective admission for index resection was associated with a decreased risk of future resection in the Crohn's colitis cohort (0.68 (0.58-0.79), p< 0.001) whereas perianal disease was associated with an 85% increased risk (1.85 (1.53-2.23), p< 0.001).

Conclusion: Future resection was associated with an index resection performed during an emergency admission, perianal disease, male sex and those with greater comorbidity. Lower deprivation and older age were associated with a reduced risk of further resection. Further resectional surgery remains common in CD following index bowel resection, despite the widespread use of biologic agents.

References: 2: Frolkis AD, Lipton DS, Fiest KM, et al. Cumulative incidence of second intestinal resection in Crohn's disease: a systematic review and meta-analysis of population-based studies. Am J Gastroenterol 2014;109:1739-48. doi:10.1038/ajg.2014.297 2: Auzolle C, Nancey S, Tran-Minh M-L, et al. Male gender, active smoking and previous intestinal resection are risk factors for post-operative endoscopic recurrence in Crohn's disease: results from a prospective cohort study. Aliment Pharmacol Ther 2018;48:924-32. doi:10.1111/apt.14944

Disclosure: Nothing to disclose

OP062 COURSE OF INDOLENT CROHN'S DISEASE IN A PROSPECTIVE EUROPEAN POPULATION-BASED INCEPTION COHORT WITH FIVE YEARS FOLLOW-UP - THE EPI-IBD COHORT

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Introduction: The lack of scientific evidence regarding the efficacy of 5-aminosalicylate (5-ASA) in patients with Crohn's disease (CD) is in sharp contrast to its widespread use in clinical practice. Up to one out of three of CD patients are treated with 5-ASA at any given time during their disease course, many as monotherapy, suggesting a mild phenotype. Population-based data regarding this subgroup of patients are sparse.

Aims & Methods: The Epi-IBD cohort is a prospective population-based cohort of 1,289 unselected, uniformly diagnosed patients with IBD diagnosed from 31 centres in Europe in 2010. Clinical data were captured prospectively throughout the five-year follow-up period. Diagnosis were made according to the Copenhagen Diagnostic Criteria. Patient management was left to the discretion of the treating gastroenterologists. Patients receiving 5-ASA monotherapy or in no need of medical therapy during the first year following diagnosis were combined for the sake of analysis (Indolent cohort). The aim of the study was to investigate the course and characteristics for these patients as well as the use of 5-ASA in patients diagnosed with CD.

Results: A total of 488 (38%) patients were diagnosed with CD. Patient characteristics are shown in Table 1. Overall, 303 (62%) patients received 5-ASA at any point during follow-up for a median duration of 28 months (IQR 6-60). A total of 97 (20%) patients received either 5-ASA monotherapy (n=80, 82%) or no medical treatment (n=17, 18%) during the first year following diagnosis. These patients were older (p=0.03) and had less complicated disease behaviour (p< 0.01) compared to the other patients but were otherwise similar.

During follow-up, 4 (4%) patients in the indolent group stepped up to corticosteroids as their highest treatment step, 12 (12%) patients to immunomodulators, and 1 (1%) patient to biological therapy. Furthermore, 19 (20%) patients were hospitalized and 5 (5%) patients needed surgery. Most patients in the indolent group (n=75 [80%], 15% of the total cohort) never needed more intense therapy during follow-up. A total of 4 (5%) patients diagnosed with B1 disease behaviour progressed to B2/B3 during follow-up.

	All CD patients (n=488)	Indolent CD patients (n=97)	Other (n=391)
Age, years (IQR)	33 (23-49)	37 (27-58)	32 (23-47)
Males, n (%)	244 (50%)	47 (48%)	197 (50%)
Diagnostic delay, months (IQR)	4.2 (1.7-12.0)	3.6 (1.1-9.7)	4.3 (1.8-12.0)
Extraintestinal manifestations at diagnosis, n (%)	79 (16%)	17 (18%)	62 (16%)
Smoking at diagnosis, n (%)			
Never	183 (40%)	40 (41%)	143 (37%)
Current	171 (37%)	27 (28%)	144 (37%)
Former	103 (23%)	15 (15%)	88 (23%)
Disease behaviour, n (%)			
B1: non-stricturing, non-penetrating	347 (71%)	84 (86%)	263 (67%)
B2: stricturing	100 (21%)	11 (12%)	89 (23%)
B3: penetrating	41 (8%)	2 (2%)	39 (10%)
Perianal disease	46 (9%)	5 (5%)	41 (11%)
Disease location, n (%)			
L1: terminal ileum	128 (77%))	28 (30%)	100 (26%)
L2: colon	134 (28%)	30 (32%)	104 (27%)
L3: terminal ileum + colon	111 (23%)	21 (22%)	90 (23%)
L4: Upper GI	30 (6%)	7 (7%)	23 (6%)
L1-L3 + L4	76 (16%)	8 (9%)	68 (18%)

[Patient characteristics 2010-2015]

Conclusion: In this European population-based inception cohort of unselected CD patients, a substantial group of patients needed only mild or no treatment during follow-up and experienced a quiescent disease course. Patient stratification at baseline to prevent not only under- but also overtreatment is important. Further studies are needed to identify clinical, serological or genetic markers to identify this group of patients.
Disclosure: Nothing to disclose

OP063 EARLY SYMPTOM IMPROVEMENT WITH RISANKIZUMAB TREATMENT IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE CROHN'S DISEASE: ANALYSIS FROM A PHASE 2 STUDY

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Introduction: Risankizumab (RZB), an IL-23 p19 inhibitor, has shown safety and efficacy in inducing clinical remission in patients with Crohn's disease (CD) in a Phase 2 study.[1] Here we assessed early symptom improvement during the randomized, double-blind, placebo-controlled induction phase of the trial.
Aims & Methods: This Phase 2 study enrolled adult patients with moderate-to-severe CD with a Crohn's Disease Activity Index (CDAI) of 220-450, ulcers in the ileum and/or colon, and a Crohn's Disease Endoscopic Index of Severity (CDEIS) ≥7 (≥4 for patients with isolated ileitis) assessed by ileocolonoscopy confirmed by a blinded central reader. Patients were randomized 1:1:1 to receive intravenous RZB (200 mg or 600 mg) or placebo at Weeks 0, 4, and 8. Endpoints examined in this post hoc analysis included changes from baseline at Weeks 2, 4, 8, and 12 in CDAI, average daily stool frequency (SF) and average daily abdominal pain score (AP) for all patients with available data, and newly defined clinical remission at Week 12, based on symptom improvement, defined as SF ≤2.8 and AP ≤1, both not

worse than baseline, in patients with baseline SF ≥4 or AP ≥2. Continuous endpoints were analyzed using observed case; non-responder imputation was used for missing data of binary endpoints. Statistical comparisons of median change were based on Wilcoxon rank sum test.
Results: 121 patients were randomized in the induction phase. Baseline characteristics were similar among treatment arms.[1] Mean (SD) disease duration at baseline was 13.4 (9.4) years; 94.2% of patients received previous anti-TNF therapy. Significant improvements in CDAI and AP were observed with RZB (600 mg) versus placebo as early as Week 2 and in SF at Week 8 (Table). The proportion of patients with clinical remission based on symptom improvement was significantly higher in the 600 mg RZB group versus placebo at Week 12 (23.7% versus 6.1%; p< 0.05), supporting the previously reported superiority of RZB versus placebo for inducing CDAI remission at Week 12 (36.6% of 600 mg RZB versus 15% of placebo; p< 0.05).[1]
Conclusion: RZB induction treatment was associated with significant early improvements in clinical symptoms and disease activity in a highly refractory patient population with moderately to severely active CD.

	PBO	RZB 200 mg	RZB 600 mg
CDAI BL (median)	287.3	304.1	298.1
CDAI Median Change from BL			
Wk 2	11.0	-18.0*	-42.0***
Wk 4	7.3	-37.0*	-39.3*
Wk 8	-2.2	-38.9	-68.8**
Wk12	-33.0	-54.6	-58.8*
SF[a] BL (median)	5.9	5.9	6.3
SF[a] Median Change from BL			
Wk 2	0.0	-0.9	-0.9
Wk 4	-0.4	-1.4*	-1.3
Wk 8	-0.1	-1.2	-1.2*
Wk12	-0.4	-1.4	-1.7*
AP[a] BL (median)	5.2	5.7	5.1
AP[a] Median Change from BL			
Wk 2	0.1	-0.6	-0.8*
Wk 4	0.0	-1.3**	-0.8*
Wk 8	-0.4	-1.0	-1.2*
Wk12	-0.7	-1.5	-1.2

[a]Based on patient diaries.
*p<0.05; **p<0.01; ***p<0.001 for RZB vs PBO.
AP, abdominal pain score; CDAI, Crohn's Disease Activity Index; RZB, risankizumab; SF, stool frequency.

[Baseline values and change from baseline in median CDAI, SF, and AP over time with RZB versus placebo (as observed)]

References: 1. Feagan BG et al. Lancet 2017;389:1699-1709.
Disclosure: Brian G. Feagan: Consultant and research support from Abbott/AbbVie. William J. Sandborn: Research grants from AbbVie and others; consulting fees from AbbVie and others; and stock or stock options from BeiGene, Escalier Biosciences, Gossamer Bio, Oppilan Pharma, Precision IBD, Progenity, Ritter Pharmaceuticals, Ventyx Biosciences, and Vimalan Biosciences. Julian Panés: Consulting fees from AbbVie and others; speakers' fees from AbbVie, Janssen, MSD, Shire Pharmaceuticals, and Takeda; and research funding from AbbVie and MSD. Marc Ferrante: Advisor fees: AbbVie and others; research grants: Janssen, Pfizer, and Takeda; speakers' fees: AbbVie and others. Edouard Louis: Research grant: Takeda, Pfizer; educational grant: AbbVie, MSD, Takeda; speakers' fees: AbbVie, AstraZeneca, Ferring, MSD, Chiesi, Falk, Takeda, Hospira, Janssen, Pfizer; Advisory Board: AbbVie, Ferring, MSD, Mitsubishi Pharma, Takeda, Celltrion, Celgene, Hospira, Janssen; consultant: AbbVie. Geert R. D´Haens: Consulting and/or lecture fees from AbbVie and others; research grants from AbbVie, Janssen, Given Imaging, MSD, Dr Falk Pharma, and PhotoPill; and speaking honoraria from AbbVie, Tillotts, Tramedico, Ferring, MSD, UCB Pharma, Norgine, and Shire. Arthur Kaser: Consulting fees from Boehringer Ingelheim, Ferring, Genentech, GlaxoSmithKline, Hospira, Janssen, Pfizer, and VHsquared. Olivier Dewit: Speaker or consultancy fees from AbbVie, Ferring, Janssen, MSD, Pfizer, Takeda, Mylan, and Sandoz. Ursula Seidler: Grants from Boehringer Ingelheim, Pfizer, Janssen, Roche, Gilead, AbbVie, Takeda, Index Pharmaceuticals AB; personal fees from Janssen and Takeda. Kyung-Jo Kim: Nothing to declare. Markus F. Neurath: Reports personal fees from Boehringer Ingelheim, Index Pharmaceuticals AB, Janssen, Merck Sharp & Dohme, Pentax Europe, PPM Services, Shire, and Takeda. Wan-Ju Lee, Kristina Kligys, Xiaomei Liao, and Kori Wallace: AbbVie employees, and may own AbbVie stock and/or options. The au-

OP064 EFFICACY OF UPADACITINIB AS AN INDUCTION THERAPY IN SEVERE AND REFRACTORY ULCERATIVE COLITIS: SUB-GROUP ANALYSIS OF THE PHASE 2B STUDY U-ACHIEVE

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Introduction: An unmet need exists to find effective therapy in more severe ulcerative colitis (UC) patients, especially those who have failed multiple therapies. The efficacy and safety of upadacitinib, a selective Janus Kinase 1 inhibitor, has been assessed in an 8-week double-blind, placebo-controlled, dose-ranging, phase 2b induction study in adult patients with moderately-to-severely active UC (U-ACHIEVE).[1,2]

Aims & Methods: In U-ACHIEVE, adult patients with moderately-to-severely active UC as determined by the Adapted Mayo Score (5-9 points and centrally-read endoscopy subscore 2-3) were randomized to receive extended-release upadacitinib 7.5, 15, 30, 45 mg once daily (QD) or placebo for 8 weeks. In the current sub-analysis, the efficacy of upadacitinib in more severe and/or more refractory patient populations was assessed. Patients who at baseline had failed ≥ 2 prior biologic agents, had pancolitis, and/or an Adapted Mayo score >7, were included. Pairwise comparisons between upadacitinib doses and placebo for the primary endpoint, clinical remission per Adapted Mayo Score at Week 8 (defined as stool frequency subscore ≤1, rectal bleeding subscore =0, and endoscopic subscore ≤1) and secondary endpoints were conducted using the Fisher's Exact test and no multiplicity adjustments were applied. Non-responder imputation was utilized for missing values.

Results: At baseline, 142 (56.8% of the total study population) patients had failed ≥ 2 prior biologics, 135 (54.0%) patients had pancolitis, and 90 (36.0%) patients had an Adapted Mayo score >7. The proportions of patients achieving endoscopic improvement, clinical response per Adapted Mayo score, and clinical response per Partial Mayo score were significantly higher (nominal p-value < 0.05) with upadacitinib doses ≥30 mg QD versus the placebo group in patients who failed ≥ 2 biologics or had pancolitis at baseline (Table). Trends of higher proportions of patients achieving clinical remission per Adapted Mayo score, endoscopic improvement, clinical response per Adapted Mayo score, and clinical response per Partial Mayo score were observed with all upadacitinib groups versus placebo in all the sub-analyses.

Conclusion: In this dose-ranging induction study, upadacitinib demonstrated greater efficacy compared to placebo with dose response in the more severe and refractory population; significantly greater efficacy was demonstrated with upadacitinib at doses ≥30 mg QD for most of the endpoints evaluated.

References:
1. Sandborn, W.J., et al. Presentation #OP195. United European Gastroenterology (UEG) Week 2018.
2. Sandborn, W.J., et al. Presentation #OP14. European Crohn´s and Colitis Organisation 2019.

Endpoints, n (%)	Placebo	UPA 7.5 mg QD	UPA 15 mg QD	UPA 30 mg QD	UPA 45 mg QD
Clinical remission per Adapted Mayo Score (SFS ≤1, RBS=0, and ES ≤1) at Week 8[a]					
Biologic use ≥ 2	0/28	2/27(7.4)	2/27(7.4)	4/30(13.3)	4/30(13.3)
With pancolitis	0/27	3/25(12.0)[+]	4/24(16.7)*	3/29(10.3)	4/30(13.3)
BL Adapted Mayo score >7	0/19	1/17(5.9)	0/18	1/19(5.3)	2/17(11.8)
Endoscopic improvement (ES ≤1) at Week 8[b]					
Biologic use ≥ 2	0/28	3/27(11.1)	6/27(22.2)*	7/30(23.3)*	10/30(33.3)***
With pancolitis	0/27	5/25(20.0)*	8/24(33.3)**	7/29(24.1)*	10/30(33.3)***
BL Adapted Mayo score >7	0/19	4/17(23.5)*	3/18(16.7)	3/19(15.8)	8/17(47.1)***
Clinical response per Adapted Mayo score (decrease from baseline ≥2 points and ≥30% and in RBS ≥1 or an absolute RBS ≤1) at Week 8[b]					
Biologic use ≥ 2	2/28(7.1)	7/27(25.9)[+]	10/27(37.0)*	11/30(36.7)*	12/30(40.0)**
With pancolitis	3/27(11.1)	5/25(20.0)	9/24(37.5)*	12/29(41.4)*	13/30(43.3)**
BL Adapted Mayo score >7	4/19(21.1)	5/17(29.4)	7/18(38.9)	8/19(42.1)	10/17(58.8)*
Clinical response per Partial Mayo score (decrease from baseline ≥2 points and ≥30% and in RBS ≥1 or an absolute RBS ≤1) at Week 2[b]					
Biologic use ≥ 2	3/28(10.7)	5/27(18.5)	8/27(29.6)[+]	11/30(36.7)*	17/30(56.7)***
With pancolitis	3/27(11.1)	5/25(20.0)	9/24(37.5)*	12/29(41.4)*	18/30(60.0)***
BL Adapted Mayo score >7	3/19(15.8)	5/17(29.4)	5/18(27.8)	8/19(42.1)	11/17(64.7)**
Endoscopic remission (ES=0) at Week 8[b]					
Biologic use ≥ 2	0/28	1/27(3.7)	0/27	0/30	4/30(13.3)
With pancolitis	0/27	3/25(12.0)[+]	0/24	3/29(10.3)	2/30(6.7)
BL Adapted Mayo score >7	0/19	1/17(5.9)	0/18	2/19(10.5)	2/17(11.8)

[a]Primary Endpoint; [b]Ranked Secondary Endpoints. ***, **, *, and [+] significant at 0.001, 0.01, 0.05, and 0.1 levels, respectively.
UPA=upadacitinib; QD=once daily; SFS=stool frequency subscore; RBS=rectal bleeding subscore; ES=endoscopic subscore.
Baseline Adapted Mayo score is missing for 1 subject in upadacitinib 45 mg QD treatment group.

[OP064 Table]

Clinical perspectives on H. pylori infection
14:00-15:30 / B3

OP065 EFFICACY OF FIRST-LINE REGIMENS IN SPAIN: RESULTS FROM THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG)

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Introduction: The best empirical treatment prescribed against *Helicobacter pylori (H. pylori)* infection must be chosen following local efficacies previously observed. Therefore, updated data concerning Spanish results, obtained in daily clinical practice, is needed to meet this objective.
Aims & Methods: The aim was to analyse the efficacy of the most commonly prescribed first-line therapies in a Spanish cohort. We conducted an observational, prospective, multicenter study, carried out in 48 Spanish hospitals as part of the ´Pan-European Registry on *H. pylori* management´. The database was provided by AEG-REDCap. Gastroenterologists included data obtained in their clinical medical practice from February 2013 to January 2018. A multivariate analysis was performed considering the most efficacious therapies, and considering the sex of the patient, type of PPI (first vs. second-generation), type of PPI dose (simple vs. double), treatment duration (10 vs. 14 days), compliance and penicillin allergy.
Results: 8,581 patients naive to *H. pylori* treatment have been included so far, 61% of them being women and 4% having penicillin allergy. Median age was 51 ± 15 years. The therapies most frequently prescribed as a first-line therapy (all of them including a proton pump inhibitor, PPI) were: non-bismuth quadruple concomitant therapy (Q-NBCT, 41%), standard triple therapy containing clarithromycin and amoxicillin (T-CA, 34%), the three-in-one single capsule bismuth containing metronidazole, bismuth and tetracycline (Q-SINGLE, 9%), bismuth quadruple therapy containing clarithromycin and amoxicillin (Q-BCA, 8%), and the non-bismuth quadruple sequential therapy (Q-NBST, 3%). 5% of the remaining patients received other minority therapies. The efficacy of these therapies was analysed on a modified ITT (mITT) and PP basis. The results are shown in Table 1, divided by 10 or 14 days duration of treatment prescription. Good compliance was associated with a higher efficacy for Q-NBCT and Q-SINGLE therapies (p< 0.001). Male sex and the use of second-generation PPIs also increased efficacy rates obtained with Q-NBCT (p< 0.05). None of the variables mentioned showed efficacy increase considering Q-BCA treatment.

	Duration (days)	mITT efficacy		PP efficacy	
		N included	mITT (95% C.I.)	N included	PP (95% C.I.)
Q-NBCT	10	2,142	86% (84-87%)	2,030	89% (87-90%)
	14	1,296	91% (89-92%)	1,248	92% (90-93%)
T-CA	10	1,978	82% (80-84%)	1,871	86% (84-87%)
	14	742	81% (78-83%)	675	87% (85-90%)
Q-SINGLE	10	721	86% (83-89%)	646	95% (93-97%)
Q-BCA	14	714	89% (86-91%)	669	94% (91-95%)
Q-NBST	10	231	78% (72-83%)	189	85% (79-90%)

[Table 1: Efficacy obtained by mITT and PP with the five more common treatments used as first-line regimens.]

Conclusion: In first-line treatments, the best efficacy results were obtained with non-bismuth concomitant therapy and bismuth quadruple therapy containing clarithromycin and amoxicillin, both therapies used for 14 days, and the three-in-one single capsule, prescribed for 10 days.

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OP066 *H. PYLORI* STATUS AND OLDER AGE IS MORE RELATED TO DECREASED PEPSINOGEN LEVEL COMPARED TO DIFFERENT DIETARY FACTORS

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Introduction: Gastric cancer development is a multifactorial process influenced by *Helicobacter pylori* (*H. pylori*), genetics and environmental factors. Although there is strong evidence about the role of *H. pylori* and genetic factors in the development of gastric atrophy leading to gastric cancer, data about the influence of dietary factors on carcinogenesis remain controversial. Minimally invasive way to evaluate possible gastric epithelial atrophy is to detect level of serum Pepsinogen (Pg) I and PgII, in particular - the ratio between PgI and PgII.

Aims & Methods: To analyze whether there is an association between decreased Pg level and different dietary factors.

The study was performed within GISTAR pilot study analyzing the data of participants (aged 40 to 64) from the general population of Latvia from 2013 until 2015. Participants completed a detailed questionnaire on personal characteristics and dietary habits and those who were allocated to the Intervention Group were tested for PgI and PgII by latex-agglutination test-system (Eiken Chemical, Tokyo, Japan), and *H. pylori* IgG group antibodies by ELISA (Biohit, Finland).

Gender, age (< 50 and ≥51 years), income (< 500 € vs. ≥500€), educational level (general secondary education and lower vs. professional technical education and higher), smoking (never vs. 100 cigarettes in the last 30 days), the consumption frequency of different products and alcohol was compared between participants with normal and decreased Pg level (PgI/PgII ≤3 and PgI ≤70 ng/mL).). Statistical analyses included χ^2 test and logistic regression analysis. Factors that showed association with decreased Pg level in univariate analysis (p< 0.09) were included in multiple logistic regression model adjusting for *H. pylori* status.

Results: In total, 1725 participants (mean age 51.62, SD± 6.741) were included in the analysis. Decreased Pg level was identified in 32.4% (559/1725) of individuals; it did not differ between men and women (p=0.57) and was associated with age above 51 year (p< 0.001). In the univariate analysis decreased Pg level was inversely associated with the consumption (less than twice per month vs. more than once a week) of sour dairy products (OR 0.78; 95% CI 0.64-0.96, p=0.02), cheese and cheese products (OR 0.72; 95% CI 0.54-0.97, p=0.03) and leek (OR 0.78; 95% CI 0.63-0.97, p=0.02).

In multivariate analysis (entering variables *H. pylori* status, *age, gender, sour dairy products, cheese products, leek, 200 g vodka at a time during the last year, educational level, income, smoking*) seropositive *H. pylori* status (OR 3.40, 95% CI 2.60-4.45, p< 0.001), age above 51 years (OR 1.59, 95% CI 1.27-1.99, p< 0.001), alcohol consumption (OR 1.30, 95% CI 1.02-1.64, p=0.03) and present smoking (OR 1.44, 95% CI 1.11-1.87, p=0.007) showed a positive association with decreased pepsinogen level while an inverse association (OR 0.72, 95% CI 0.52-0.99, p=0.05) was found with higher consumption of cheese and cheese products.

Conclusion: Although a few studied dietary factors showed a significant univariate association with decreased pepsinogen level, only *H. pylori* seropositivity, advanced age, alcohol consumption and present smoking were independently linked to decreased pepsinogen level while higher consumption of cheese and cheese products showed protective effect towards decreased pepsinogen level. Thus, suggesting that the bacterium and age play more important role in the development of atrophy than different dietary factors.

Disclosure: Nothing to disclose

OP067 "TEST AND TREAT" STRATEGY WITH UREA BREATH TEST: A COST-EFFECTIVE STRATEGY FOR THE MANAGEMENT OF *HELICOBACTER PYLORI* INFECTION IN SPAIN

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Introduction: *Helicobacter pylori* (*H. pylori*) infection is a common chronic infection that is associated with upper gastrointestinal diseases. There are limited data from clinical trials comparing management strategies for patients with dyspepsia. Cost-effectiveness simulation models might help to identify optimal strategies and their cost-effectiveness.

Aims & Methods: To assess the cost-effectiveness of the *H. pylori* "Test and Treat" strategy, including the use of Urea Breath Test (UBT), *versus* symptomatic treatment and endoscopy first-line strategy, in patients with dyspepsia from the Spanish healthcare system perspective. The models compared three strategies, namely "Test and Treat" strategy including the use of UBT, „Endoscopy and Treat strategy" and „Symptomatic treatment strategy". Data were derived from the European registry of *H. pylori* management and from the literature. Advanced simulations were conducted to assess cost, effectiveness and cost-effectiveness over (1) 4 weeks-time horizon for the effectiveness endpoint „Probability of dyspepsia symptoms relief" and over (2) 10 years for two other effectiveness endpoints „Probability of gastric cancer avoided" and „Probability of peptic ulcer avoided". Probabilistic sensitivity analyses were carried out using Monte-Carlo simulations considering data distributions. Models were developed in accordance with the routine Spanish medical practices and costs.

Results: Regarding the endpoint „Probability of dyspepsia symptoms relief", „Test and Treat" was the most cost-effective strategy (883 € per success) compared to „Endoscopy and Treat" and to „Symptomatic treatment" strategies (respectively 1,628€ and 990€ per success). Regarding the endpoint „Probability of gastric cancer „, the „Test and Treat" was the most cost-effective strategy (524 € per gastric cancer avoided) compared to „Endoscopy and Treat" and „Symptomatic treatment" strategies (respectively 716€ and 696€ per gastric cancer avoided). For the endpoint „Probability of Peptic ulcer", the „Test and Treat" was also the most cost-effective strategy (421€ per peptic ulcer avoided) compared to „Endoscopy and Treat" and „Symptomatic treatment" strategies (respectively 728€ and 632€ per peptic ulcer avoided).

Conclusion: The "Test and Treat" strategy including the use of UBT is the most cost-effective medical approach for the management of dyspepsia. The results of this study should contribute to the increase of awareness about the usefulness of the "Test and Treat" strategy and concerning its beneficial impact for patients with *H. pylori*-related diseases.

OP068 LEVOFLOXACIN SEQUENTIAL THERAPY VERSUS BISMUTH QUADRUPLE THERAPY IN THE SECOND-LINE AND THIRD-LINE TREATMENT OF *HELICOBACTER PYLORI:* A MULTICENTER RANDOMIZED TRIAL

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Introduction: A recent systematic review and meta-analysis showed that the efficacy of levofloxacin triple therapy was lower than 80% in the second-line treatment for Helicobacter pylori (H. pylori). Our previous trial showed that levofloxacin sequential therapy was superior to levofloxacin triple therapy in the second-line treatment.
Aims & Methods: Therefore, we aimed tocompare the efficacy and safety of 14-day levofloxacin sequential therapy versus 10-day bismuth quadruple therapy in the second-line treatment of *H. pylori* infection. *H. pylori* infected patients who failed after one treatment were eligible in this open labeled, multicenter, randomized trial, and were randomized to receive (1) levofloxacin sequential therapy (EAML): esomeprazole 40 mg and amoxicillin 1 g for the first 7 days, followed by esomeprazole 40 mg, metronidazole 500 mg, and levofloxacin 250 mg for another 7 days (all twice daily); or (2) bismuth quadruple therapy (BQ): esomeprazole 40mg twice daily, bismuth tripotassium dicitrate 300 mg four times a day, tetracycline 500mg four times a day, and metronidazole 500mg three times a day, for 10 days. The primary end point was the eradication rate in the second-line treatment according to intention to treat (ITT) analysis. The minimum inhibitory concentrations were determined by agar dilution test.
Results: A total of 560 patients have been recruited and results were available for analysis in 533 patients up to April 2019. The demographic characteristics and antibiotic resistance rates were similar across the two treatment groups. The eradication rate in the second line treatment were 88.3% (235/266) and 88.4% (236/267) in the levofloxacin sequential therapy and bismuth quadruple therapy groups, respectively (p=1.000) in the ITT analysis. The eradication rates were 89.7% (235/262) and 92.9% (236/254) in the levofloxacin sequential therapy and bismuth quadruple therapy according to PP analyses, respectively (p=0.195). The efficacy of levofloxacin sequential therapy, but not bismuth quadruple therapy, appeared to be affected by levofloxacin resistance. The frequency of any adverse effects was higher in patients treated with bismuth quadruple therapy than levofloxacin sequential therapy (76.4% vs. 44.1%, p< 0.001).
Conclusion: Levofloxacin sequential therapy and bismuth quadruple therapy are similarly effective in the second-line treatment for *H. pylori* infection. (Trial registration number: NCT NCT03148366).

References: 1. Chen PY, Wu MS, Chen CY, et al. Systematic review with meta-analysis: the efficacy of levofloxacin triple therapy as the first- or second-line treatments of Helicobacter pylori infection. Aliment Pharmacol Ther 2016;44:427-37. 2. Liou JM, Bair MJ, Chen CC, et al. Levofloxacin sequential therapy versus levofloxacin triple therapy in the second line treatment of Helicobacter pylori: A randomized trial. Am J Gastroenterol 2016; 111:381-7.
Disclosure: Nothing to disclose

OP069 GASTRIC MICROBIOME ASSOCIATED WITH PROGRESSION OF GASTRIC INFLAMMATION, ATROPHY AND INTESTINAL METAPLASIA AFTER *HELICOBACTER PYLORI* ERADICATION

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Introduction: Infection with *Helicobacter pylori* is associated with gastric inflammation and increases the risks for precancerous gastric atrophy (GA) and intestinal metaplasia (IM). Evidences however abound that these risks persist in some patients after *H. pylori* eradication.
Aims & Methods: We aimed to identify non-*H. pylori* gastric microbes that are associated with inflammation, GA and IM post-treatment of *H. pylori* infection. Five hundred and eighty-seven H. pylori positive subjects residing in Yantai county of Shandong Province, China. A total of 295 received one-week course omeprazole, amoxicillin and clarithromycin (OAC) while 292 received placebo. Subjects underwent endoscopy with biopsy at baseline and after one year. Severity of inflammation, GA and IM was graded according to the updated Sydney classification. Progression and regression were defined as worsening or improvement, respectively, of inflammation, GA or IM scores after one year.
Analysis of 16S rRNA sequences was performed on a total of 404 gastric biopsy samples, comprising of 102 pairs before and after successful H. pylori eradication by OAC treatment estimatedby negative rapid urease test and histology, and 100 pairs before and after placebo. Multiple linear regression, discriminant and microbial network analyses were used to identify microbes associated with inflammation, GA and IM.
Results: Analysis of microbial sequences confirmed the eradication of *H. pylori* in OAC treated group (0.013 ±0.0018) compared to placebo group (0.67 ±0.028) (P< 0.00001). Principal component analysis revealed distinct microbial clusters and proliferation of a wide variety of bacterial species, reflected by marked increase in bacterial diversity (P< 0.00001) after *H. pylori* eradication (Figure 1).
Much less microbial co-occurrence was observed after H. pylori eradication, while microbial interactions remained largely unchanged before and after placebo treatment. In addition, without *H. pylori* re-infection, gastric inflammation persisted in 16%, GA emerged in 33% and IM emerged in 17% of patients one year following *H. pylori* eradication.
A distinct cluster of oral bacterial genera comprising *Peptostreptococcus*, *Streptococcus*, *Parvimonas*, *Prevotella* and *Porphyromonas* were observed to be associated with persistent or progressive GA and IM (P< 0.05) after *H. pylori* eradication. *Streptococcus anginosus* (P=0.012, R=0.3) and *Ralstonia* (P=0.02, R=0.25) were positively correlated with inflammation scores and increased in patients with persistent inflammation, suggesting their involvement in gastric inflammation in the absence of *H. pylori*.
Two probiotic bacterial species namely *Roseburia inulinivorans* (P=0.027) and *Lactobacillus salivarius* (P=0.04) were enriched in subjects whose gastric inflammation regressed following *H. pylori* eradication.
Conclusion: Oral bacterial genera *Peptostreptococcus*, *Streptococcus*, *Parvimonas*, *Prevotella* and *Porphyromonas* are associated with the progression of gastric inflammation, GA and IM following anti-*H. pylori* therapy. Treatment targeting these bacteria may be prescribed to patients to reduce the risk of developing into gastric cancer.
Disclosure: Nothing to disclose

OP070 TIME LATENCIES OF RETREATMENT FOR *HELICOBACTER PYLORI* AND RISK OF UPPER GASTROINTESTINAL BLEEDING IN PATIENTS WHO FAILED INITIAL ERADICATION THERAPY

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Introduction: Delays in primary eradication of *H. pylori* (HP) in patients newly diagnosed with peptic ulcer could result in higher risk of ulcer complications.
However, it remains unknown whether delays in retreatment of patients who failed initial HP eradication therapy would affect subsequent risk of upper gastrointestinal bleeding (UGIB).

Aims & Methods: We determined the risk of UGIB in patients who required retreatment for HP after failure of initial eradication therapy according to time latencies of retreatment. All HP-infected patients who had received the first course of clarithromycin-containing triple therapy for HP between 2003 and 2012 were identified from the territory-wide electronic health database of the Hong Kong Hospital Authority.

We excluded patients with prior GI cancers, surgical resection of the GI tract, bleeding tendency and esophageal varices. The primary outcome was hospitalization for non-variceal UGIB after the first HP therapy. The follow-up period commenced from 60 days of the first HP therapy until the occurrence of UGIB, death or the end of the study (30 Jun 2016). Patients were divided into different groups according to time latencies between initial and final HP eradication (< 3, 3-12 and >12 month). Those who did not require retreatment were included as reference. Covariates included baseline demographics, concurrent medical illnesses and medication uses. Time-dependent Cox proportional hazards model was used to adjust for confounders, in which all medications were included as time-varying variables. Sensitivity analyses were performed with propensity score (PS) matching in a ratio of 1:5 and excluding patients with baseline peptic ulcer or UGIB.

Results: 70,518 patients were included in this analysis (7,761 in the retreatment group and 62,757 in the reference group). The median follow-up was 7.75 years (interquartile range 5.3-10.4 years). The crude incidence rate of UGIB was 6.62 per 1000 person-year (95% CI 6.01-7.28) in the retreatment group and 3.25 (95% CI 3.09-3.41) in the reference group. Compared to the reference group, patients who received retreatment have a higher risk of UGIB (adjusted hazards ratios [aHR] 1.90, 95% confidence intervals [CI] 1.70-2.12; PS matching analysis HR 1.91, 95% CI 1.71-2.15). There was a progressive increase in risk of UGIB with longer latency intervals of retreatment (Table; aHR for < 3m: 1.17, 95% CI 0.98-1.40; 3-12m: 1.88, 95% CI 1.48-2.39; >12m: 3.42 95% CI 2.92-3.99). Similar results were obtained with PS matching or after excluding patients with baseline peptic ulcer/GIB (HR 2.01; 95% CI 1.72-2.36).

Conclusion: Patients who failed initial HP eradication had a 1.9-fold increase in UGIB risk, which progressively increased with the time latencies of retreatment. Early retreatment within 3-month should be considered to minimize the risks of subsequent UGIB after failed HP eradication.

Disclosure: Nothing to disclose.

	Crude HR (95% CI)	Adjusted HR (95% CI)	PS matching HR (95%CI)
No retreatment		1.00 (reference)	
All retreatment groups	2.10 (1.84-2.28)	1.90 (1.70-2.12)	1.91 (1.71-2.15)
<3 month	1.67 (1.40-1.98)	1.17 (0.98-1.40)	1.57 (1.31-1.87)
3-12 month	1.86 (1.47-2.35)	1.88 (1.48-2.39)	1.74 (1.37-2.21)
>12 month	2.56 (2.21-2.97)	3.42 (2.92-3.99)	2.39 (2.05-2.78)

[Risk of UGIB with different latency intervals between the first and last HP eradication therapies]

Hepatology from bench to bedside
14:00-15:30 / B5

OP071 GENETIC STUDIES OF MRI LIVER IRON CONTENT IDENTIFIES LOCI REGULATING HEPCIDIN AND YIELD INSIGHTS INTO ITS LINK WITH HEPATIC AND EXTRAHEPATIC DISEASES

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Introduction: Background and aims: Excess liver iron content is common, however its genetic background and link to hepatic and extrahepatic disease risk is unknown. We aimed to identify genetic variants influencing liver iron content and use genetics to understand its link to other traits and diseases.

Aims & Methods: First, we performed a genome-wide association study (GWAS) in 8,289 individuals in UK Biobank with MRI quantified liver iron, and validated our findings in an independent cohort (n=1,513 from IMI DIRECT). Second, we used Mendelian randomisation to test the causal effects of 29 predominantly metabolic traits on liver iron content. Third, we tested phenome-wide associations between liver iron variants and 770 anthropometric traits and diseases.

Results: We identified three independent genetic variants (rs1800562 (C282Y) and rs1799945 (H63D) in *HFE* and rs855791 (V736A) in *TMPRSS6*) associated with liver iron content that reached the GWAS significance threshold (p< 5×10^{-8}). The two *HFE* variants account for ~85% of all cases of hereditary haemochromatosis. Mendelian randomisation analysis provided evidence that higher central obesity plays a causal role in increased liver iron content.

Phenome-wide association analysis demonstrated shared aetiopathogenic mechanisms for elevated liver iron, high blood pressure, cirrhosis, malignancies, neuropsychiatric and rheumatological conditions, while also highlighting inverse associations with anaemias, lipidaemias and ischaemic heart disease.

Conclusion: Our study provides genetic evidence that mechanisms underlying higher liver iron content are likely systemic rather than organ specific, that higher central obesity is causally associated with higher liver iron, and that liver iron shares common aetiology with multiple metabolic and non-metabolic diseases.

Disclosure: Conflict of Interest statement: M.K and R.B. are employees and shareholders of Perspectum Diagnostics. H.W. and S.N. are shareholders in Perspectum Diagnostics. No other potential conflicts of interest relevant to this article were reported.

OP072 PORTAL ENDOTHELIAL DAMAGE IN CIRRHOSIS

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Introduction: Cirrhotic patients show a systemic heparin-like effect at thromboelastometric tracing during infection or bleeding. Endotoxemia, shear stress and inflammation may lead to endothelial damage and subsequent release of endogenous heparinoids by disruption of glycocalyx. The endothelium of portal vein could be persistently damaged by portal

hypertension, and this could correlate with the high incidence of portal vein thrombosis in cirrhosis. Data regarding heparin-like effect in the portal venous system are lacking.

Aims & Methods: We consecutively enrolled adult cirrhotic patients undergoing liver transplantation (LT) or transjugular-intrahepatic-portosystemic-shunt(TIPS). Rotational-thrombelastometry(ROTEM) along with evaluation of endothelial dysfunction by quantification of circulating endothelial-microparticles (MP), and endotoxemia (LPS) were performed on citrated peripheral and portal venous blood samples of all enrolled patients.

Results: Forty-one cirrhotics (16 LT and 25 TIPS) were enrolled. ROTEM-analysis showed similar coagulative-assets in portal blood of cirrhotic patients compared to their own peripheral blood. However, we highlighted the presence of a heparin-like effect in portal blood by heparinase addition to native test (median α angle NATEM 51° (46-57) vs HEPTEM median 57° (50-59), p=0.05; median CT NATEM 678sec (576-785) vs HEPTEM 596sec (560-651), p=0.026), which was not detected in peripheral blood (median angle α NATEM 53° (48-58) vs HEPTEM 53° (46-63), p=0.9; median CT NATEM 782sec (560-832) vs HEPTEM 623sec (536-741), p=0.2). Additionally, an increased concentration of endothelial-MP (CD62E-MP median 1607MP/µL (680-1885) vs 1391MP/µL (651-2031), p=0.09) and endotoxemia (LPS median 182.95pg/mL (149-300) vs 160.25pg/mL (103-243), p=0.005) were detected.

Conclusion: The detected heparin-like effect, supported by the increased levels of endotoxemia and the MP-asset could be indirect hematic signs of a higher local endothelial damage in cirrhotics portal vein, caused by portal hypertension. Portal site-specific endothelial damage could hamper its antithrombotic properties and may be an important local risk factor in the pathogenesis of PVT along with the already documented venous stasis.

Disclosure: Nothing to disclose

OP073 THE EFFECT OF *ESCHERICHIA COLI* NF73 ON LIVER TRIGLYCERIDE IN NON-ALCOHOLIC FATTY LIVER DISEASE MICE AND THE POTENTIAL MOLECULAR MECHANISM

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Introduction: In our previous research, we isolated *Escherichia coli* pathogens NF73 (patent application NO. 201610591293.4) from the intestinal mucosa of a non-alcoholic steatohepatitis (NASH) patient, and demonstrated that *Escherichia coli* NF73 increased hepatic damage in high fat diet (HFD) induced non-alcoholic fatty liver disease(NAFLD) mice. In this study, we aimed to investigate the effect of *Escherichia coli* NF73 upon hepatic triglyceride metabolism and the potential molecular mechanism.

Aims & Methods: All male C57BL/6J mice (6 weeks of age) were randomly divided into normal group and flora-deficient group, and were fed with HFD for 16 weeks. In the 8[th]week, mice in flora-deficient group were treated with a cocktail of broad-spectrum antibiotics (including ampicillin, vancomycin, neomycin and metronidazole) in drinking water for 2 weeks to diminish the intestinal bacteria, while the normal group received sterile tap water. After 10 weeks, both groups were further divided as HFD group, *Escherichia coli* NF73 group and *Escherichia coli* MG1655 group, treated intragastrically by Luria-Bertani (LB) medium, 1*10[8]cfu *Esherichia coli* NF73, 1*10[8]cfu *Esherichia coli* MG1655 (control bacteria) every day, respectively. Hepatic lipid depositions were detected by HE and oil red O staining. Lipid synthesis related protein expressions were determined by Western Blot.

Results: *Escherichia coli* NF73 administration induced more severe hepatic steatosis in normal and flora-deficient mice. Notably, *Escherichia coli* NF73-treated mice had higher triglyceride level, and more significant liver lipid deposition than mice in *Escherichia coli* MG1655 and HFD control groups. It was found that *Escherichia coli* NF73 increased liver triglyceride levels by upregulating SREBP-1c expression and transcriptional activity of genes involved in hepatic fatty acid synthesis (FASN, ACC). Meanwhile, *Escherichia coli* NF73 enhanced the expression of PI3K, p-AKT, mTOR and p-mTOR. The results indicated that *Escherichia coli* NF73 promoted hepatic triglyceride accumulation via upregulating SREBP-1c expression through the PI3K-AKT-mTOR pathway.

Conclusion: Triglyceride accumulation induced by *Escherichia coli* NF73 plays a key role in the pathological process of hepatic damage. Therefore, intestinal mucosal-adherent *Escherichia coli* NF73 might be a critical trigger in the progression of NAFLD to NASH.

Disclosure: Nothing to disclose

OP074 NOVEL CLINICAL AND GENETIC RISK FACTORS FOR EARLY POST-OPERATIVE THROMBOSIS IN LIVER TRANSPLANTATION

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Introduction: Post-operative thrombosis (PT) is one of the leading causes of graft loss and mortality after liver transplantation (LT), and is associated with a plethora of donor, recipient and transplant-related risk factors. While clinical risk factors can largely be accounted for, better knowledge of genetic risk factors for PT is essential for developing targeted strategies to improve graft survival.

Aims & Methods: A post-hoc analysis of a prospective cohort (*www.trialregister.nl – Trial NL6334*) of LT recipients between 1993-2017 was performed. Upon availability, donor and recipient DNA were genotyped with the Illumina Global Screening Array. Risk factors for early PT (< 90 days) were analyzed in univariate and multivariate logistic regression models. To study genetic risk factors for PT, we performed genome-wide association (GWA) analysis.

Results: A total of 1099 recipients underwent 1337 LT procedures. Only primary adult LT (748 [55.9%]) were included in subsequent analyses. Multivariate regression analyses demonstrated that smoking status of the donor (OR=2.505 [1.288-4.871]; P=0.007), and nonalcoholic steatohepatitis (NASH) in the recipient (OR=2.343 [1.057-5.193]; P=0.036) were independent clinical risk factors for early PT. Using GWA analysis with donor genotypes, we identified 42 genetic loci associated with increased risk of PT at a suggestive genome-wide significance threshold (P< 5x10^{-05}). One of these variants (rs1336472 [P=1.2x10^{-05} OR=1.84]), in a locus harboring the *AK4* gene, has been reported as a risk variant for venous thromboembolism, outside the context of LT.

Conclusion: We identified donor smoking status and NASH in the recipient as novel clinical risk factors for early PT. Moreover, we observed that genetic variation within the donor influences risk for early PT. These preliminary results warrant further investigation into the contribution of donor genetic risk factors for early PT.

Disclosure: Nothing to disclose

OP075 ANALYSIS OF GASTROINTESTINAL SYMPTOMS, DIAGNOSTIC PATTERNS, AND PROVIDER PERSPECTIVE OF ACUTE HEPATIC PORPHYRIA AMONG EU-5 COUNTRIES

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Introduction: Acute hepatic porphyria (AHP) is a family of rare genetic diseases, the most common being acute intermittent porphyria (AIP). AHP results from enzyme deficiencies involved in haem synthesis, leading to accumulation of neurotoxic haem intermediates, aminolaevulinic acid (ALA) and porphobilinogen (PBG), causing potentially life-threatening attacks and chronic symptoms. Patients afflicted by AHP often remain without a proper diagnosis for up to 15 years due to lack of awareness and testing. First-line diagnostic biochemical tests include measuring spot urinary ALA and PBG as both are elevated in the majority of AHP patients.

Aims & Methods: The study aimed to describe gastroenterologists' experience diagnosing AHP and characterize patients from the United Kingdom,

France, Italy, Germany, and Spain (EU-5).EU-5 physicians (n=100) who actively managed AHP patients (with and without recurrent attacks) in the preceding year were recruited from 9/2017-10/2017 to complete an online survey collecting information on demographics, familiarity with AHP and diagnostic tests, perspective on symptoms important to diagnosis, referral patterns, and treatment preferences. Physicians also completed a chart review of 304 patients and reported anonymized data on demographics, medical history, attacks and symptoms. Data was analysed using descriptive statistics.

Results: Physicians practiced a mean of 19 years, 65% worked in academic settings, and 19% were gastroenterologists. Gastrointestinal symptoms leading to AHP diagnosis included abdominal pain (88%), vomiting (63%), fatigue (55%), nausea (54%), weight loss (43%), and constipation (37%). Patients were aged 40 years (mean), female (52%), with AIP (83%). AHP diagnostic tests gastroenterologists considered informative for diagnosis included urinary PBG (59) and ALA (71%); however, several non-specific tests were also commonly considered informative of AHP. For most patients (68%), diagnoses were assessed as uncertain (41%) or incorrect (27%). Misdiagnoses included non-specific abdominal pain (49%), irritable bowel syndrome (47%), Crohn's disease (28%), diverticulitis (26%), appendicitis (21%), lead poisoning (19%), and gastroesophageal reflux disease (GERD) (19%). Patients had a mean of 1.9 attacks and 1.1 hospitalizations in the past year. Chronic symptoms included pain (60%), weakness (59%), fatigue (57%), anxiety (50%), nausea/vomiting (49%), constipation (39%), diarrhea (36%).

Conclusion: This study highlights the challenges diagnosing AHP due to non-specificity of symptoms and limited understanding of diagnostic procedures. Due to the frequent presentation of gastrointestinal symptoms, AHP should be included in gastroenterologists' differential diagnosis of patients presenting with non-specific abdominal pain. Among patients diagnosed with AHP, both acute attacks and chronic symptoms were reported, implicating both in the disease.

Disclosure: Joseph Salameh, Sarah Murray, and John Ko are full time employees and stock holders in Alnylam Pharmaceuticals. Stephen Meninger and Nicole Lyn are contractors for Alnylam Pharmaceuticals. Chitra Karki, Katherine Krautwurst, and Renata Mustafina are full time employees of Ipsos LLC.

OP076 THE MANAGEMENT OF BILIARY STRICTURE IN IGG4-RELATED SCLEROSING CHOLANGITIS

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Introduction: Although endoscopic biliary drainage (EBD) and corticosteroid (CS) therapy are important for the treatment of biliary stricture in IgG4-related sclerosing cholangitis (ISC), clinical evidences about short and long-term prognosis and the risk of biliary tract complications in ISC are still insufficient. This research aimed to elucidate the appropriate way to manage biliary stricture in ISC.

Aims & Methods: The study enrolled ISC patients diagnosed in our hospital or its affiliated institutes from January 2007 to December 2017. We reviewed medical records of ISC patients, such as clinical characteristics, and the way of treatment with EBD and/or CS. The appropriate duration of EBD for preventing detachment of a biliary stent was assessed. We verified the safety of treatment with CS alone without EBD for patients with obstructive jaundice. We also compared the rate of biliary tract complications between groups treated with and without EBD.

Results: A total of 70 ISC patients with the mean age of 66.9 years were enrolled. The median follow-up period was 64.5 months. Autoimmune pancreatitis was concurrent in 98.4% and extrapancreatic biliary stricture was seen in 21.9%. 64 patients (91.4%) were treated with CS and 24 (34.3%) underwent EBD. Scheduled EBD removal after clinical remission of ISC by CS treatment was carried out in 11 patients (45.8%). 9 (81.8%) of 11 patients underwent EBD removal within a month after CS initiation, all of which were safely carried out without early recurrence of obstructive

jaundice or biliary tract infection. EBD detachment during CS treatment was seen in 11 patients (45.8%) and was likely to occur from 2-3 weeks after CS initiation. 7 patients who had obstructive jaundice with serum total bilirubin levels more than 3.0 mg/dL were treated with CS alone without EBD and all of them achieved clinical improvement free from biliary tract infection. All the 3 patients who developed bile duct stones were treated with EBD. The development of bile duct cancer in ISC patients did not occur during follow-up.

Conclusion: EBD removal should be carried out within 2-3 weeks after CS initiation to prevent EBD detachment in ISC patients who achieved clinical remission by CS treatment. Obstructive jaundice due to biliary stricture can safely be treated with CS alone without EBD. We should be careful about the long-term management of ISC since bile duct stones are likely to occur in patients treated with EBD.

Disclosure: Nothing to disclose

Update in cholangiocarcinoma
14:00-15:30 / E1

OP077 ENDOTHERAPY IN PATIENTS WITH PRIMARY SCLEROSING CHOLANGITIS: OVER 30 YEARS' EXPERIENCE

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Introduction: Primary Sclerosing Cholangitis (PSC) is a chronic cholestatic liver disease characterized by inflammation and periductal fibrosis of the intrahepatic and/or extrahepatic bile ducts. Endoscopic dilation of symptomatic dominant biliary strictures is a temporary therapeutic option in these patients frequently candidate to liver transplantation. Our experience over a 30-years period is reported.

Aims & Methods: Between March 1984 and April 2019, 73 patients with PSC (46 Males, mean age 46 ± 18 years) were identified from a prospectively collected database. Indications for endoscopic drainage were the presence of symptomatic "dominant" biliary strictures located at the common bile duct or main hepatic confluence. Strictures were dilated with balloon and/or temporary plastic stents insertion. Brush cytology of dominant strictures was performed in patients with new onset or worsening strictures. When MRC was not routinely available, abdominal US and/or CT-Scan were performed before ERCP.

Results: Indications for ERCP were: cholangitis (n=28, 38.3%), anicteric cholestasis and pruritus (n=18, 24.6%) and jaundice (n=27, 36.9%). Bile ducts morphology was assessed by MRC in 51 cases (69%) before ERCP.
A total of 161 ERCPs were performed in 73 pts [mean 4.3 (range 1-13)]. Results are summarized in table I.
One patient (0.6%) developed severe post-ERCP pancreatitis that resolved after surgical treatment.
Cholangitis recurrence requiring re-treatment occurred after a mean of 28.2 months after stents removal and 16.6 months after balloon dilation.
Brush cytology was performed in 42 patients (57.5%): 4 patients (5.4 %) resulted positive for high grade dysplasia, 1 patient (1.3 %) for carcinoma.
A mean follow-up of 7.4 years (range 0.2-21.7) is available in 46 patients (63%): 29 patients (63%) had no further episodes of cholangitis, 7 (15.2%) underwent OLT, 3 (6.5%) died for cholangiocarcinoma, 6 (13%) died for unrelated other disease, 1 (2.2%) had an incidental finding during laparoscopic cholecystectomy of gallbladder cancer and is still alive.

Conclusion: According to our experience endotherapy of dominant biliary strictures secondary to PSC is effective in the long term-follow-up and can delay liver transplantation. Early diagnosis of cholangiocarcinoma in PSC is still an unsolved issue.

Disclosure: Nothing to disclose

	N	%
ERCP failure	2	1.24
Site of "dominant" biliary strictures		
Common bile duct	51	31.6
Hilum / intrahepatic ducts	67	41.6
Common bile duct + hilum	31	19.2
No dominant strictures / presence of common bile duct stones	10	6.2
Therapeutic procedures		
Balloon dilation (diameter 4-10 mm)	71	44.1
Single plastic stent	15	9.3
Multiple plastic stents (range 2 - 7)	19	10.6
Naso-biliary drains	131	81.3

[Table I. Results from 161 ERCPs in 73 patients with Primary Sclerosing Cholangitis.]

OP078 THE ROLE OF "ROSE" FOR ERCP-GUIDED BRUSHING ON INDETERMINATE BILIARY STRICTURES: EXPERIENCE OF A REFERRAL CENTER

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Introduction: Endoscopic Retrograde CholangioPancreatography (ERCP), although nowadays used only for therapeutic purposes, still has a prominent diagnostic role in patients with indeterminate biliary strictures and no evidence of mass lesion at EUS or CT scan. The use of biliary stricture brushing is a safe, easy, cheap and fast way to acquire cytological specimen from the determination of the etiology, but the sensitivity can be as low as 50%. Rapid On-Site Evaluation (ROSE) of the sample has been used for years in referral centers for the determination of the adequacy of EUS-guided FNA cytological specimens, improving its sensitivity and specificity. Nevertheless, there are currently no studies evaluating its role for ERCP brushing.
Aims & Methods: The aim of this study was to assess the diagnostic yield of ERCP brushing of indeterminate biliary strictures when supported by ROSE.
We conducted a retrospective single center study enrolling consecutive patients undergoing ERCP and brush cytology supported by ROSE for indeterminate biliary strictures, including patients from January 1st 2010 to May 31st 2018. Data recorded included patient's characteristics, clinical/radiological and EUS features, ERCP features including stricture features, number of passages performed with the brush, final cytology or histology when biopsy was performed as an adjunct, use of cholangioscopy or confocal laser endomicroscopy, final diagnosis after surgery or follow-up when the patient would not undergo a resection. The diagnostic yield of ERCP-guided brushing with ROSE was then calculated.
Results: 96 patients underwent ERCP for indeterminate biliary stenosis, with 50% being males, mean age 68.1 years, 80% having an extrahepatic biliary stricture. 90 patients underwent brushing with ROSE and were included in the analysis, with 86.7% of patients having an adequate sample at ROSE. The preliminary diagnostic yield calculated showed a sensitivity of 80%, a specificity of 82%, an accuracy of 81%, a positive predictive value of 92% and a negative predictive value of 61%.

Conclusion: The availability of ROSE in patients undergoing ERCP with indeterminate biliary stricture without a mass lesion increases the diagnostic yield of brushing, decreasing the need of further procedures, such as cholangioscopy and confocal laser endomicroscopy and can, therefore, decrease costs and increase safety.
Disclosure: Nothing to disclose

Brave new world: Neurons vs. neuronal network
14:00-15:30 / Barcelona

OP079 APPLICATION OF CONVOLUTIONAL NEURAL NETWORK IN THE DIAGNOSIS OF THE INVASION DEPTH OF GASTRIC CANCER BASED ON CONVENTIONAL ENDOSCOPY

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Introduction: According to guidelines, endoscopic resection should only be performed for patients whose early gastric cancer invasion depth is within the mucosa or submucosa of the stomach regardless of lymph node involvement. The accurate prediction of invasion depth based on endoscopic images is crucial for screening patients for endoscopic resection. The recent findings suggest that the deep learning of endoscopic images by convolutional neural networks (CNN) can have clinical applications. In particular, we suspected that a CNN might be effective in determining the invasion depth of gastric cancer and thus could be used to screen patients for endoscopic resection. To evaluate the ability of a CNN to determine gastric cancer invasion depth, we constructed a convolutional neural network computer-aided detection (CNN-CAD) system based on endoscopic images to determine invasion depth and screen patients for endoscopic resection.
Aims & Methods: We constructed a convolutional neural network computer-aided detection (CNN-CAD) system based on endoscopic images to determine invasion depth and screen patients for endoscopic resection. Endoscopic images of gastric cancer tumors were obtained from the Endoscopy Center of Zhongshan Hospital. An artificial intelligence-based CNN-CAD system was developed through transfer learning leveraging a state-of-the-art pretrained CNN architecture, ResNet50. A total of 790 images served as a development dataset and another 203 images as a test dataset. We used the CNN-CAD system to determine the invasion depth of gastric cancer and evaluated the system's classification accuracy by calculating its sensitivity, specificity, and area under the receiver operating characteristic curve.
Results: The area under the receiver operating characteristic curve for the CNN-CAD system was .94 (95% confidence interval [CI], .90-.97). At a threshold value of .5, sensitivity was 76.47%, and specificity was 95.56%. Overall accuracy was 89.16%. Positive and negative predictive values were 89.66% and 88.97%, respectively. The CNN-CAD system achieved significantly higher accuracy (by 17.25%; 95% CI, 11.63-22.59) and specificity (by 32.21%; 95% CI, 26.78-37.44) than human endoscopists.
Conclusion: We constructed a CNN-CAD system to determine the invasion depth of gastric cancer with high accuracy and specificity. This system distinguished early gastric cancer from deeper submucosal invasion and minimized overestimation of invasion depth, which could reduce unnecessary gastrectomy.
Disclosure: Nothing to disclose

OP080 NEURAL NETWORK SYSTEM FOR IDENTIFYING UPPER-GASTROINTESTINAL ORGANS IN ENDOSCOPIC IMAGES

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Introduction: Neural networks(NNs) is the mathematical model which imitates principle of action of human's neuron in the brain. Recently, NNs is used for classifying images in various fields of medicine, for example, skin cancer classification, diabetic retinopathy, and gastro-intestinal endoscopies. Image recognition using NNs has been applied for the automated detection of gastric cancer during gastrointestinal endoscopies.
Aims & Methods: While developing NNs system, it is necessary to conduct data cleansing and classify several endoscopic images to form a training dataset, which is time-consuming. Therefore, this study aims to develop an automated system for classifying the upper-gastrointestinal organs in large sets of endoscopic images captured under various imaging conditions. For this purpose, we have developed a ten-layer NNs system. The NNs architecture comprises a 1530-dimensional input layer followed by nine fully connected affine layers with batch normalization to facilitate training and a rectified linear unit for activation. The color histogram (255 × 3) and the spatial gradient histogram(255 × 3) obtained by Scharr edge filtering were utilized as the input layer. The training dataset comprised 52,390 anonymized images collected from patients with gastric cancer who underwent upper-gastrointestinal endoscopies in our institution during 2017/01/01 to 2017/12/31.
A total of 35,537 cleansed upper-gastrointestinal endoscopic images (i.e., the training data) were manually classified as white-light (WL) stomach (15,075), WL esophagus (1,573), WL duodenum (1,673), WL stomach with local indigo carmine (IC) (5,823), WL esophagus with IC (379), narrow band (NB) imaging stomach (7,194), and NB imaging esophagus (2,309). These datasets were selected by the following criteria. 1)they must include a visually identifiable each organs, esophagus, stomach, and duodenum without excessive blur. 2)the area of halation(blackout) must be less than 50% of the effective pixels. 3)no treatment devices should be visible with the exception of old clips. 3)there must not be any therapeutic findings, such as markings, infusions, mucosal excisions, and massive hemorrhages. After the NNs were trained using the training dataset, the system performance was evaluated by the testing dataset, which was another set of 27,862 images, to classify the images into these eight categories. To evaluate the performance of the proposed system, we used the MNIST database 28×28-pixels images of hand-written digits from 0 to 9 as a benchmark, which is separated into a training dataset of 60,000 examples and a testing dataset of 10,000 examples.
Results: The accuracy of the classification system in the training and testing data were found to be 0.988 and 0.961, respectively. The accuracy of the system in the training and testing data when applied to the MNIST database reached 0.999 and 0.982, respectively.
Conclusion: Thus, it was concluded that the proposed system is effective for identifying the upper-gastrointestinal organs in endoscopic images. This system can be utilized as an organ identifier to aid the process of data cleansing in the development of an automated lesion-detection system.
Disclosure: Nothing to disclose

OP081 APPLICATION OF ARTIFICIAL INTELLIGENCE USING A CONVOLUTIONAL NEURAL NETWORK FOR DIAGNOSIS OF EARLY GASTRIC CANCER BY MAGNIFYING ENDOSCOPY WITH NARROW-BAND IMAGING

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Introduction: As many reports have indicated the usefulness of magnifying endoscopy with narrow-band imaging (ME-NBI) for diagnosing gastric cancer, the magnifying endoscopy simple diagnostic algorithm for early gastric cancer (MESDA-G) has been proposed as a new uniform diagnostic system for gastric cancer by means of ME-NBI in Japan. However, although ME-NBI is thought to have made a huge contribution to clinical practice, acquiring skill at ME-NBI diagnosis using MESDA-G requires substantial effort. Recently, there has been remarkable progress in artificial intelligence (AI) using deep learning and convolutional neural networks (CNNs) in various medical fields for diagnostic imaging. However, no reports have assessed the usefulness of AI using CNNs for diagnosis of early gastric cancer (EGC) by ME-NBI.
Aims & Methods: We aimed to develop an AI-assisted diagnostic system of EGC using ME-NBI images and evaluate the diagnostic accuracy of the AI system in diagnosing EGC. From the 745 lesions of EGC resected by endoscopic procedures at our hospital between April 2013 and March 2018, 5,227 ME-NBI images using the water immersion technique at the maximum magnification that had sufficient quality to permit diagnosis by MESDA-G were collected. ME-NBI images of gastric adenocarcinoma of fundic gland type and diffuse-type EGC were excluded, since the diagnostic yield was unclear in MESDA-G. Additionally, 2,592 ME-NBI images of non-cancerous mucosa or non-cancerous lesions that were obtained under the same conditions were collected. A CNN-based diagnostic system was pre-trained and fine-tuned on a dataset of 5,574 ME-NBI images (3,797 EGCs, 1,777 non-cancerous mucosa or lesions). To evaluate the diagnostic accuracy, a separate test data set of 2,245 ME-NBI images (1430 EGCs, 815 non-cancerous mucosa or lesions) was applied to the constructed CNN.
Results: The CNN required 60 s to analyze 2,245 test images. The overall accuracy, sensitivity, specificity, positive predictive value and negative predictive value of the CNN were 98.7%, 98%, 100%, 100% and 96.6%, respectively. All missed images of EGCs were superficially depressed and intestinal-type intramucosal cancers that were difficult to distinguish from gastritis even by experienced endoscopists.
Conclusion: The constructed CNN system for diagnosis of EGC could process many stored ME-NBI images in a short period of time and had clinically high diagnostic ability. A more advanced system will be developed by adding the EGC images of cases that could not be diagnosed by MESDA-G and images of a wide variety of non-cancerous mucosa and non-cancerous lesions. This AI-assisted diagnostic system of EGC using ME-NBI images may be able to reduce the burden of endoscopists.
References: Hirasawa T et al. Application of artificial intelligence using a convolutional neural network for detecting gastric cancer in endoscopic images. Gastric Cancer. 2018. Shichijo S et al. Application of convolutional neural networks for evaluating Helicobacter pylori infection status on the basis of endoscopic images. Scand J Gastroenterol. 2019
Disclosure: Nothing to disclose

OP082 ARTIFICIAL INTELLIGENCE FOR REAL-TIME POLYP LOCALISATION IN COLONOSCOPY WITHDRAWAL VIDEOS

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Introduction: There is considerable variation in polyp detection rates during colonoscopy. Missed adenomas may contribute to interval colorectal cancers. Artificial intelligence (AI) can potentially improve ADR. Previous work has focussed on still images and selected video sequences which may be subject to bias and lack clinical utility. This pilot work assesses whether a convolutional neural network (CNN) developed using still images and short video sequences from a multicentre dataset using different processors generalises effectively to locate polyps in new video dataset consisting of complete colonoscopy withdrawals (caecum to rectum).

Aims & Methods: Our group previously developed a CNN using 4664 polyp test frames from the MICCAI 2015 polyp detection challenge dataset. Here, we created a second dataset using 17 complete colonoscopy withdrawal videos, previously unseen by the CNN, containing 83 unique polyps consisting of 83,716 frames (14,634 polyp and 69,082 non-polyp) using Olympus EVIS LUCERA CV290(SL) processors and colonoscopes. White light frames were manually annotated by drawing bounding boxes around polyps. Polyp size, morphology, histopathology and location was recorded for each polyp sequence (Table 1). Low quality frames (blurred/indistinguishable image) were excluded. Half the procedures were randomly selected to create a testing set consisting of 24,596 frames (4,804 polyp and 19,792 non-polyp). A true positive was scored if the computer-generated prediction overlapped with the bounding box. A false positive indicated a non-overlapping location (more than one can occur per frame).

Results: The CNN operated at real-time video-rate achieving a sensitivity of 91.6% and positive predictive value 75.3% in the MICCAI challenge test set consisting of 196 high definition still images from 44 polyps. When the MICCAI trained CNN was tested on our previously unseen colonoscopy procedures, it achieved a sensitivity of 76.6% and specificity of 78.9%. This CNN was fine-tuned by using polyp positive frames from our training dataset. This improved sensitivity to 84.5% and specificity to 92.5%.

Conclusion: Whilst the CNN achieved excellent results on the public still image dataset, it is more challenging to generalise results to complete colonoscopy withdrawals. Fine-tuning using our dataset led to improved performance. Furthermore, our procedures were performed by expert endoscopists, including a significant proportion of right sided flat elevated and subtle sessile serrated lesions which were not evaluated in recently published test sets. AI development should include complete colonoscopy withdrawals to reflect true clinical practice and focus specifically on identifying challenging polyps that may be overlooked by colonoscopists.

Disclosure: Nothing to disclose

Lesions (n)	83
Mean size (mm)	5.4
Morphology (Paris Classification)	
Protruded (Ip/Isp/Is)	35
Flat elevated/Flat (IIa/IIb)	48
Location	
Right Colon	58
Left Colon	20
Rectum	5
Pathology	
High Grade Dysplasia Tubular Adenoma	1
Low Grade Dysplasia Tubular Adenoma	61
Sessile Serrated Lesion	14
Hyperplastic Polyp	7

[Polyp Details (Complete Colonoscopy Video Dataset)]

OP083 THE REAL-TIME DETECTION AND DIFFERENTIAL DIAGNOSIS OF COLORECTAL POLYPS IN COLONOSCOPY WITH AN ARTIFICIAL INTELLIGENCE ALGORITHM; A PROSPECTIVE OBSERVATIONAL STUDY

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Introduction: For supporting detection and diagnosis of colorectal polyps in real time by artificial intelligence (AI) technology, we have developed AI-aided endoscopic diagnosis system (AAE). This system has been developed using Convolutional Neural Network, one of deep learning approaches. We have already reported its polyp detectability and differential diagnostic accuracy in retrospective studies using stored still images. The aims of this study were to validate whether the AAE could detect colorectal polyps which were detected by endoscopists as the gold standard, and to evaluate differential diagnostic accuracy of AAE in real time under a clinical setting.

Aims & Methods: AAE analyzes all image frames during a colonoscopy on GPU workstation, and a box-shaped alert is presented on the lesion area in real-time. When the endoscopist presses the freeze button at the target polyp in white light imaging (WLI), the differential diagnosis between neoplastic and non-neoplastic is made by AAE. In order to prepare the training data of AAE, 69,285 images were collected from 4,147 colonoscopy case underwent in Jikei University hospital since April 2014 to December 2018. All training data was annotated by enclosing lesion area on each image with a bounding box. Following the development of the algorithm, a prospective observational study was conducted at Jikei university hospital in January 2019. The patients who underwent colonoscopy were enrolled. Patients with known IBD were excluded. In this study, results of detection and differential diagnosis by AAE were displayed on a monitor separated from the main monitor used by endoscopists. When an endoscopist detect a polyp, polyp information (size, morphologic type, location and the time to detect a polyp) were informed to research assistants and recorded. We evaluated the success rate of polyp detection during colonoscopy by reviewing videos at the recorded time to detect a polyp. Successful polyp detection with AAE was defined when a polyp detected by endoscopists as gold standard could be detected by AAE within 2 seconds from the initial appearance of a polyp on a video frame. Furthermore, the differential diagnostic accuracy between neoplastic and non-neoplastic by AAE was analyzed only for the polyp removed endoscopically. The differential diagnosis of AAE was made by freezing the video image when an endoscopist judged that highly-quality closeup images would be obtained without blur.

Results: Thirty patients (with 102 polyps) were analyzed. AAE succeeded to detect 95 polyps (93.1%) in 102 polyps within 2 sec from their initial appearance, of which 62 polyps (65.2%) were diminutive polyps of 5 mm or less. The median detection time was 0.4 seconds (range 0.1 - 20.2 seconds). AAE was able to predict differential diagnosis in 58 polyps (41 neoplasm and 17 non-neoplasm) of 81 polyps (63 neoplasm and 18 non-neoplasm) endoscopically resected (71.6%). When 23 polyps in which AAE could not predict differential diagnosis were treated as misdiagnosed polyps, differential diagnostic accuracy between neoplastic and non-neoplastic was sensitivity 58.7% /specificity 77.8% /positive predict value 90.2% /negative predict value 35.0% /accuracy 63.0% in overall 81 polyps. In diagnosable 58 polyps, it was sensitivity 90.2% /specificity 82.4% /positive predict value 92.5% /negative predict value 77.8% /accuracy 86.8%, respectively.

Conclusion: This preliminary study demonstrated that the polyp detectability of AAE and differential diagnostic accuracy between neoplastic and non-neoplastic polyp were comparable to endoscopists in a real-time clinical setting.

Disclosure: Nothing to disclose

OP084 ARTIFICIAL INTELLIGENCE FOR DETECTING DIMINUTIVE COLON POLYPS BASED ON AUTOMATIC COLLECTING SYSTEM FOR DAILY ANNOTATED DATASETS FROM THE COMMERCIALLY AVAILABLE ENDOSCOPY REPORTING SYSTEM

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Introduction: Recently, artificial intelligence (AI) has been shown the remarkable progress in image recognition. The application of AI system for the endoscopic images are expected to be the favorable assistance. The recent AI progressions are primarily are based on the availability of large-scale annotated datasets. In general, the dataset of high-quality annotated endoscopic images are retrospectively made by endoscopic specialist with much effort. In Japan, endoscopists make reports including selected key images with localized annotation at diagnosis in daily practice. Collecting system for daily annotated datasets from the endoscopy reporting systems enables continuous accumulation of high-quality annotated endoscopic dataset.

Aims & Methods: The aim of this study is to assess the validity of using daily annotated endoscopic images in constructed reporting system for prototype AI model for diminutive polyp detection. We constructed automatic collecting system for daily annotated datasets from the endoscopy reporting system (NEXUS, FUJIFILM medical Co.) with Japan Endoscopy Database (JED) project conducted by Japan Gastroenterological Endoscopy Society (JGES). By the keyword of diagnostic information, we automatically extracted annotated endoscopic images of diminutive colon polyps which diagnosed between March 2018 and September 2018. To verify the collecting system, we have created the AI model for detecting diminutive colon polyp from the collected dataset and additional collected normal colon dataset. The detection model was made by RetinaNet network architecture, which is one of the latest deep learning algorithm for object detection.

Results: We automatically collected 47391 endoscopic images of 745 colonoscopy and extracted 1356 key images of diminutive colon polyps with localized annotation which added at diagnosis. Additionally, we collected 700 images of normal colon. To validate the quality of dataset for making AI model, we used 1056 datasets of colon polyps and 400 images of normal colon for training and used 300 datasets of colon polyps and 300 images of normal colon for validation. The sensitivity, specificity, and accuracy of our trained colon polyp detector for 300 polyp images and 300 normal images was 95.0%, 97.7%, and 96.3%.

Conclusion: This automatic collecting system for daily annotated datasets enabled creating high-performance detector for diminutive colon polyps with reducing much efforts of endoscopic specialists. This scheme leads to continuous extensive information collection infrastructure for making endoscopic AI diagnostic system.

Disclosure: Nothing to disclose

Barrett's oesophagus
16:00-17:30 / Hall 6

OP085 DEEP LEARNING SYSTEM DETECTS BARRETT'S ESOPHAGUS NEOPLASIA WITH HIGH ACCURACY IN A MULTI-STEP TRAINING AND EXTERNAL VALIDATION STUDY

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Introduction: Early neoplasia in Barrett's esophagus (BE) is often difficult to detect endoscopically. Computer aided detection (CAD) systems might be able to assist endoscopists in real-time recognition of BE neoplasia. Recently, CAD *deep learning techniques* have shown promising results in other fields.

Aims & Methods: The aim of this study was to develop a deep learning CAD system for endoscopic recognition of BE neoplasia using multi-step training followed by internal- and external validation.

The CAD system was pre-trained via a novel approach, for which we created a unique dataset of 494,364 labelled images of broad endoscopic variety, named *GastroNet*. The system was further trained and refined by datasets 2 and 3. Dataset 2 consisted of *retrospectively* collected WLE overview images of BE neoplasia (n=690) and non-dysplastic BE (NDBE; n=557). Dataset 3 consisted of *prospectively* collected overview images of BE neoplasia (n=129) and NDBE (n=168). The CAD system was constructed using a fully residual, hybrid ResNet-UNet model using transfer- and ensemble learning. The system was first internally validated on dataset 3, using 4-fold cross validation methodology.

Finally, a fourth dataset was created for external validation. This dataset consisted of 40 *prospectively* collected WLE overview images of BE neoplasia and 40 WLE NDBE images from 80 patients not included in dataset 1-3. In dataset 2-4, all NDBE images were reviewed by experts for absence of neoplasia. All neoplastic images were delineated by multiple experts, where the area with ≥1 delineation served as ground truth for training- and validation.

Outcome parameters: 1) Correct classification of images (neoplastic/NDBE); 2) Correct delineation of neoplastic lesions (i.e. CAD's delineation within experts delineation: delineation score); 3) Correct positioning of preferred biopsy location within experts delineation (red flag indication score).

Results: Accuracy, sensitivity, and specificity for classification of all images in internal validation were 88%, 88% and 89%, respectively. In the external validation these values were 88%, 93%, and 83%, respectively. The CAD-delineation overlapped with the expert ground truth in all correctly classified neoplastic cases in the external validation set, and red-flagged this area in 97%.

Conclusion: We developed a deep learning CAD system for primary detection of BE neoplasia, using multi-level validation. The system detected neoplasia with high accuracy and near-perfect delineation- and red-flag performance. These performance parameters indicate that our CAD system is ready for real-time, image-based testing in clinical practice.

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H. Neuhaus: Boston Scientific, CDx Diagnostics, Cook Medical, Demcom, Erbe, Falk Foundation, Fujifilm, Medtronic, Olympus (consulting, advisory, speaking fees); Boston Scientific, CDx Diagnostics, Demcom, Erbe, Fujifilm, Olympus, Pentax Medical (research support) R. Bisschops: Fujifilm (research support, consulting fees, speakers fees) E.J. Schoon: None declared P.H. de With: None declared J.J. Bergman: Fujifilm, NinePoint Medical (research support); Fujifilm (speaking fees)

OP086 HIGH ACCURACY AND EFFECTIVENESS WITH DEEP NEURAL NETWORKS AND ARTIFICIAL INTELLIGENCE IN DETECTION OF EARLY ESOPHAGEAL NEOPLASIA IN BARRETT'S ESOPHAGUS

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Introduction: The most widely used approach for surveillance of Barrett's esophagus (BE) is oesophagogastroduodenoscopy. However, the visual detection of early esophageal neoplasia (high grade dysplasia and T1 cancer) in BE with white light and virtual chromoendoscopy is still difficult.
Aims & Methods: The aim of this study is to assess if a convolutional neural artificial intelligence network can aid in the recognition of early esophageal neoplasia in BE.
Over 800 images from 65 patients were retrospectively collected of histology-proven early esophageal neoplasia in BE containing high grade dysplasia or T1 cancer (Dysplasia Group). Within each image, the area of neoplasia was masked using image annotation software by two experts in BE imaging. Over 800 control images were collected of either histology-proven or confocal endomicroscopy-proven BE without high grade dysplasia (Non -Dysplastic Group).
A training set with ~1200 images split 50/50 Dysplasia/Non-Dysplasia was used to train the algorithm. We used a convolutional neural network (CNN) and hybrid algorithm design including Inception blocks to deepen the neural net and maximize efficiency and accuracy. The algorithm was pre-trained on ImageNet and then fine-tuned with the goal to provide the correct binary classification: "Dysplastic" (1) or "Non-dysplastic" (0). Adam optimizer performed stochastic optimization of a binary cross-entropy loss function to produce a probability value between 0 and 1. A set 458 images unique of the training set was used for algorithm validation.
We additionally developed an object detection algorithm which drew localization boxes in real-time around regions classified as dysplasia. Testing was performed for near-focus images, non-near focus (far) images, white light and NBI images.
Results: The CNN analyzed 458 test images (225 dysplasia/233 non-dysplasia) and correctly detected early neoplasia in BE cases with sensitivity of 95.6% and specificity of 91.8% (Fig.1). The accuracy was 93.7% and the AUC was 0.94 (Fig.3). With regards to the object detection algorithm for all images in the validation set, the system was able to achieve a mean-average-precision (mAP) of 0.7533 at an intersection over union (IOU) of 0.3, Sensitivity 96.7% and Specificity 87.6% (Fig 2). For NBI images only, a mAP 0.802 was achieved and mAP 0.819 with Near-focus images only.
Conclusion: Our AI model was able to detect early esophageal neoplasia in Barrett's Esophagus images with 93.7% accuracy. In addition, the object detection algorithm was able to draw a localization box around the areas of dysplasia with high precision. This system appears promising and an algorithm of this kind may aid endoscopists detect dysplastic lesions more effectively. Real-time live video validation of the algorithm is currently underway.
Disclosure: Jason Samarasena and William Karnes (Co-founders of DocBot)

What's hot in eosinophilic oesophagitis
16:00–17:30 / B2

OP087 DIFFERENCES IN IMPLEMENTATION OF GUIDELINES ON DIAGNOSIS AND TREATMENT OF EOSINOPHILIC ESOPHAGITIS (EOE): AN OVERVIEW OF CURRENT PEDIATRIC AND ADULT GI PRACTICE IN EUROPE

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Introduction: Guidelines for diagnosis and treatment of Eosinophilic Esophagitis (EoE) have changed markedly over the last decade. An international survey, conducted by the ESPGHAN EGID Group, aimed to analyze differences in current practice of European Pediatric (PG) and Adult Gastroenterologists (AG) in their management of EoE, and to assess self-reported adherence to guidelines.
Aims & Methods: Gastroenterologists treating children and/or adults in 13 European countries and the United Arab Emirates were contacted and asked to complete a multiple-choice questionnaire to gauge physician demographics, EoE diagnosis and management strategies.
Results: Of the 1232 gastroenterologists who completed the questionnaire, 465 were PG and 697 were AG. In contrast to current guidelines on EoE diagnosis, only 41% of gastroenterologists (22% AG vs. 68% PG, p< 0.01) reported taking biopsies in patients with symptoms of esophageal dysfunction but without macroscopic endoscopic abnormalities; 92% (97% PG vs. 88% AG, p< 0.01) reported to take biopsies when dysphagia was the specific symptom; 81% (86.2% PG vs. 77% AG, p< 0.01) sampled multiple esophageal sites when suspecting EoE. High dose PPI administration (68.1% PG vs. 72.4% AG) followed by elimination diets (31.6% and 27.3% respectively) were the most common first line treatments. Following failure of initial PPI treatment, the majority of both PG and AG opted for oral topical steroids (56.4% PG vs. 86.9% AG, p< 0.01), however PG utilize food elimination diets as second line treatment significantly more often than AG (43.5% PG vs. 13.3% AG, p< 0.01). Geographic practice differences were noted, for example the highest use of high dose PPI as first line treatment was reported in Spain while, of elimination diets, in the United Arab Emirates. Although proven unreliable, 24.1% of prescribed food elimination diets were reported to be based on specific allergy testing (32.8% PG vs. 16.3% AG, p< 0.01) and up to 83% refer their patients for allergic assessment after diagnosis of EoE.
After initiating therapy, the majority reported monitoring therapeutic response endoscopically (86.3% PG vs. 69.7% AG, p< 0.01). German PG universally reported endoscopic follow-up while Dutch gastroenterologists were least likely to follow this approach. A greater proportion of PG

than AG indicated that had read at least one recent international guideline (89% PG vs. 56% AG), but both PG and AG alike recognize the potential benefit of national guidelines concerning the diagnosis and treatment of EoE (86% PG vs. 85% AG).

Conclusion: The general practice of pediatric and adult gastroenterologists differs and diverges from international guidelines on diagnosis as well as treatment of EoE. Geographic practice variations are apparent. Although the majority indicated awareness of recent practice standards, strategies to improve the implementation of current guidelines are urgently needed.

Disclosure: Nothing to disclose

OP088 ENDOSCOPIC AND HISTOLOGIC DIFFERENCES BETWEEN PPI-RESPONSIVE AND NON-RESPONSIVE EOSINOPHILIC ESOPHAGITIS IN CHILDREN POPULATION: A TERTIARY CENTER EXPERIENCE

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Introduction: Eosinophilic esophagitis (EoE) is defined as histological features of 15 or more eosinophils per high power resolution (hpf) without other causes of esophageal eosinophilia. Endoscopic and/or histological differences between PPI responders and non-responders were never clearly defined. PPI-responder eosinophilic esophagitis (PPI-REE) patients are defined those patients presenting clinical and histological features of EoE but with a resolution of eosinophilic infiltrate after a treatment of high dose PPI for eight weeks. Aim of this study is to evaluate if endoscopic, histological or constitutional feature may be specific of PPI responder and non responder patients in a pediatric population.

Aims & Methods: Non consecutive patients in children population with confirmed eosinophilic esophagitis were screened. All patients have undergone an initial upper GI endoscopy with esophageal biopsy and have had a definite diagnosis of eosinophilic esophagitis (eosinophilic infiltration ≥15 per hpf at the esophageal biopsy).

All patients received high dose (1mg/kg) of PPI therapy for eight weeks without changing the current diet. At the end of PPI treatment a second endoscopic look with bioptic sampling was performed to evaluate the response to PPI treatment and to assign each patients to PPI responder or non responder group. Endoscopic features (stenosis, longitudinal stripes, trachealized esophagus, white spots) and histologic findings (absolute number of eosinophils per hpf) at first endoscopy were evaluated and compared between PPI- responder and non responder group . History of food allergies and/or atopic diseases were also recorded.

Results: Of the 64 patients screened for the analysis, 6 patients were excluded because were lost during follow up and/or they did not show at the second look endoscopy. Therefore, 58 patients were included in the final analysis (mean age 10,5 years old; male: 35, female: 23). 37 patients were classified as PPI non-responder (male:21, female:16; average age: 11,1 years old) and 21 patients as PPI responder (male:14, female:7; average age: 9,5 years old). Differences between the 2 groups are shown in Table 1. [Table 1]

Endoscopic characteristics	Non responder (n. 37)		Responder (n. 21)		p-value
Stenosis	n 4	10.8 %	n 1	4.7 %	0.39
Longitudinal stripes	n 20	54.1 %	n 9	42.8 %	0.29
White spot	n 17	45.9 %	n 8	38.1 %	0.38
Trachealized esophagus	n 13	35.1 %	n 1	4.7 %	0.008
Normal mucosa	n 1	2.7 %	n 5	23.8 %	0.02
Histological findings					
15-50 eos/hpf	n 8	21.6 %	n 10	47.6 %	0.04
50-99 eos/hpf	n 12	32.5 %	n 5	23.8 %	0.35
>100 eos/hpf	n 17	45.9 %	n 5	23,8 %	0.007

[Table 1]

No differences were observed in terms of concomitant food allergies between non-responder and responder group: n= 18 (cow's milk protein: 8; egg: 7 ; fish: 5; cereals: 1) vs n=7 (cow's milk protein:2; egg: 3; fish: 2), respectively (p= 0,19). No differences were observed in terms of concomitant atopic diseases between non-responder and responder group: 22 patients (asthma: 3; rhinoconjunctivitis: 3; atopic dermatitis: 1) vs 15 patients (asthma: 7 ; rhinoconjunctivitis: 7; atopic dermatitis: 2), respectively (p= 0,26).

Conclusion: Trachealized esophagus,and a higher number of eosinophils on biopsy sample at the index endoscopy are more prevalent in PPI not responders and might be used to predict a lack of response to PPI and to guide the treatment. Conversely, a normal mucosa and a lower number of eosinophils on biopsy sample at the index endoscopy predict a response to PPI treatment.

Disclosure: Nothing to disclose

OP089 BUDESONIDE ORODISPERSIBLE TABLETS ARE SUPERIOR TO MAINTAIN COMBINED CLINICAL AND HISTOLOGICAL REMISSION IN ADULT PATIENTS WITH EOSINOPHILIC ESOPHAGITIS: RESULTS FROM THE 48-WEEKS, DOUBLE-BLIND, PLACEBO-CONTROLLED PIVOTAL EOS-2 TRIAL

Straumann A.[1,2], Lucendo A.J.[3], Miehlke S.[4], Vieth M.[5], Schlag C.[6], Biedermann L.[7], Santander Vaquero C.[8,9], Ciriza de Los Rios C.[10], Hartmann D.[11], Madisch A.[12], Hruz P.[13], Hayat J.[14], von Arnim U.[15], Bredenoord A.J.[16], Schubert S.[17], Müller R.[18], Greinwald R.[19], Schoepfer A.[20], Attwood S.[21], on Behalf of the International EOS-2 Study Group
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Introduction: In the recent EOS-1 trial, a 6-week therapy with a novel budesonide orodispersible tablet (BOT), with a unique mode of delivery and esophageal targeting, given twice daily (1mg BID) induced clinico-histological remission in 57% of adult patients with active eosinophilic esophagitis (EoE), with 93.2% achieving histological remission (1).

Aims & Methods: This maintenance study assessed the efficacy and safety of two doses of BOT vs placebo for maintaining EoE in clinico-histological remission over 48 weeks. In total, 204 patients being in clinico-histological remission at baseline were randomized (1:1:1) to a 48-weeks treatment with BOT 1 mg BID, BOT 0.5 mg BID or placebo.

Primary endpoint: Proportion of patients in clinico-histological remission after 48 weeks of double-blinded treatment, defined as fulfilling all of the following criteria:

- Absence of clinical relapse (as defined by dysphagia or odynophagia [7-day recall period] severity ≥4 points, confirmed by ≥4 points on at least 1 day during the subsequent week on the respective 010 NRS for dysphagia or odynophagia [24-hours recall period]),
- Lack of histological relapse (defined as a peak of ≥48 eos/mm² hpf [corresponding to peak of ≥15 eos/hpf] at the end of treatment (EOT) and derived from six biopsies (2 from each esophageal third),
- Absence of food impaction requiring endoscopic intervention,
- No need of dilation,
- No premature withdrawal for any reason.

Secondary _a priori_ ordered endpoints (confirmatory tested):
- Individual components of the primary endpoint,
- Proportion of patients in clinical remission at week 48/EOT defined by EEsAI-PRO ≤20,
- Proportion of patients being at week 48/EOT in clinical (NRS [7-day recall period] for dysphagia and odynophagia ‚0') AND endoscopic (EREFS scores: fixed rings ‚≤1'; exudates, furrows, and edema: all ‚0'), AND histological remission (< 15 eos/hpf).

Further main secondary efficacy endpoints (exploratory) contained clinical, endoscopic, and histological endpoints.

Results: Both BOT dosing groups were significantly superior over placebo in maintaining EoE in clinico-histological remission, with no significant differences between the budesonide groups in the standard efficacy criteria (Table 1; 1.-4. endpoints). However, the higher dose was more efficacious for achieving and maintaining clinical and endoscopic and histological remission (Table 1; 5. endpoint).

All further secondary endpoints confirmed the findings of the primary endpoint. Our study confirmed the well-known safety profile of topical budesonide for the first time also over a long-term administration period in a randomized double-blind trial. There were no differences in the baseline morning cortisol levels over 1 year between patients receiving BOT and placebo. Suspected symptomatic candidiasis were reported in only 12% and 16% of patients in the high and low dose, respectively, all cases easily to be treated.

		BOT 1mg BID (n=68)	BOT 0.5mg BID (n=68)	Placebo BID (n=68)
	Primary confirmatory endpoint: Number (%) patients in clinico-histological remission after 48 weeks of treatment	51 (75.0%) P<0.0001*	50 (73.5%) P<0.0001*	3 (4.4%)
1)	Secondary a priori ordered confirmatory endpoints: Number (%) patients with histological relapse, defined as a peak of ≥48 eos/mm² hpf at wk48/EOT	7 (10.3%) P<0.0001*	9 (13.2%) P<0.0001*	61 (89.7%)
2)	Mean [95%CI] change from baseline to wk48/EOT in peak eos/mm2 hpf	21 [5; 37] P<0.0001**	38 [10; 65] P<0.0001**	262 [208; 316]
3)	Number (%) patients with clinical relapse, or food impaction requiring endoscopic intervention, or dilation during 48 weeks	5 (7.4%) P<0.0001*	7 (10.3%) P<0.0001*	41 (60.3%)
4)	Number (%) patients in clinical remission at wk48/EOT defined by EEsAI-PRO ≤ 20	50 (73.5%) P<0.0001*	49 (72.1%) P<0.0001*	14 (20.6%)
5)	Number (%) of patients in clinical AND endoscopic AND histological remission at week48/EOT	36 (52.9%) P<0.0001*	27 (39.7%) P<0.0001*	0 (0%)
	Secondary exploratory endpoints: Number (%) patients with deep histological remission defined as a peak of '0' eos/mm2 hpf at wk48/EOT	54 (79.4%) P<0.0001*	52 (76.5%) P<0.0001*	1 (1.5%)

P-values (test for superiority vs placebo); 1-sided with Bonferroni adjusted α=0.0125
*normal approximation test; ** Wilcoxon rank sum test

[Table 1: Efficacy endpoints]

Conclusion: Both, BOT 1mg BID and BOT 0.5mg BID were safe and highly superior vs placebo in maintaining EoE patients in clinico-histological remission over 48 weeks. 90% of patients had a histological relapse when on placebo for 1 year.
References: (1) Lucendo AJ, et al. Gastroenterology 2019, DOI:https://doi.org/10.1053/j. gastro.2019.03.025
Disclosure: Mueller R & Greinwald R are employees of Dr. Falk Pharma GmbH

OP090 COMPARISON OF FIRST- AND SECOND-LINE THERAPEUTIC OPTIONS AND THEIR EFFECTIVENESS RATES IN EUROPEAN PATIENTS WITH EOSINOPHILIC ESOPHAGITIS: RESULTS FROM THE _EOE CONNECT_ REGISTRY

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Introduction: Eosinophilic oesophagitis (EoE) is a chronic immune-mediated inflammatory disorder of the oesophagus in response to a non-IgE-mediated food allergy. Although avoiding specific food triggers constitutes the only therapy that targets the cause of the disease, the limitations of dietary therapy in clinical practice promoted the use of anti-inflammatory drugs, mainly swallowed topic steroids and proton-pump inhibitors (PPIs).
Aims & Methods: This study aims to analyse criteria for selecting a second line therapy for EoE patients, by a searching within the _EoE CONNECT_ database (a prospectively maintained registry of EoE patients from EUREOS) in order to improve our current knowledge about how EoE patients are managed in real world practice. Demographic and clinical variables were considered to seek on determinant factors. First and second-line therapies were analysed. Frequency tables were generated for each treatment modality while contingency tables were analysed by chi-square test using GraphPad software.
Results: First-line treatment data from 493 patients and second-line treatment data from 303 patients recruited at 9 hospitals in Spain and 1 more in Italy were analysed. PPIs overall constituted the preferred first-line option for EoE, followed by topic steroids and dietary interventions. When they failed, dietary interventions (mainly empiric elimination diets) were the most common second-line options used for non-responders to PPIs (51.9%), topic steroids (43.2%) or other previous dietary approaches (32.1%). Among PPIs, omeprazole was the most frequently prescribed drug in both first and second treatment lines (51.6% and 57.8%, respectively).
As for topical steroids, fluticasone was the only drug used as a first-line therapy, while budesonide was used in 31.4% of patients as a second-line steroid treatment. As for dietary intervention, empiric elimination diets were the preferred alternative, with six-food and two-food elimination diets being the most commonly used as first-line (42.9%) and second-line (43.6%) therapies, respectively.
Topic steroids provided the highest effectiveness in terms of clinical and histological responses in both lines of treatment. Except for dietary therapies, second-line treatments were overall more effective than first-line ones. Endoscopic dilation was used in a minority of patients, most commonly as a second-line therapy.
Among the variables analysed, three of them were identified as significant determinants for the choice of a first-line treatment: age (p< 0.001), EoE phenotype (p< 0.05) and hospital of origin (p< 0.001). Regarding second-line therapies, differences in treatment were found also for EoE phenotype, recruiting hospitals and previous therapy (all p< 0.001).
Conclusion: Most EoE patients were initially treated with PPIs, with no responders having a two-food elimination diet as second-line therapy. Patients' age and EoE phenotype determined the choice of a first-line therapeutic option, while phenotype and previous treatment affected the selected of second-line therapy. Preferred treatment in both lines was also dependant on the referral hospital.
Disclosure: Nothing to disclose

Type of treatment	First-line treatment			Second-line treatment		
	Use (%)	Failure to achieve clinical response (%)	Failure to achieve histological response (%)	Use (%)	Failure to achieve clinical response (%)	Failure to achieve histological response (%)
PPIs	76.5	28.3	45.9	29.4	15.6	30.6
Topic steroids	10.5	14.6	21.7	16.8	3.2	13.8
Dietary interventions	7.5	18.2	50.0	48.2	28.3	50.9
Dilation	1.6	8.3	nd	5.3	0.0	nd
Other	3.9	nd	nd	0.3	nd	nd

[Table 1]

OP091 A NOVEL ORAL BUDESONIDE FORMULATION IS HIGHLY EFFECTIVE FOR INDUCTION OF REMISSION IN PATIENTS WITH ACTIVE EOSINOPHILIC ESOPHAGITIS: RESULTS FROM THE 6-WEEKS OPEN-LABEL TREATMENT PHASE OF EOS-2 TRIAL

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Introduction: In the recent EOS-1 trial, a 6-week therapy with a novel budesonide orodispersible tablet (BOT), with a unique mode of delivery and esophageal targeting, given twice daily (1mg BID) induced clinico-histological remission in 57% of adult patients with active eosinophilic esophagitis (EoE), with 93.2% achieving histological remission (1).

Aims & Methods: We report here the efficacy of a 6-week open-label induction (OLI) treatment with BOT 1mg BID in a large prospectively treated cohort of EoE patients, which was used as a feeding arm for the further double blind (DB) maintenance phase of the EOS-2 trial.

In total, 181 patients with clinical and histological active EoE were treated in the 6-week OLI phase. The major endpoint and basis for later random-ization into the DB maintenance phase was clinico-histological remission, i.e. achieving clinical remission (≤2 points on numerical rating scales (0-10 points) each for dysphagia and odynophagia on each of the 7 days prior to end-of-treatment) and histological remission (peak eosinophil count <16 eos/mm² hpf). Further study endpoints included clinical, histological re-mission rates and change in peak eosinophil counts, beside other second-ary efficacy endpoints.

Results: Clinico-histological remission of EoE was achieved in 69.6% (126/181) of patients after 6 weeks of therapy. Compared to baseline, BOT 1mg BID achieved all assessed clinical, endoscopic or histological end-points (Table 1).

Conclusion: A 6-week open-label treatment with BOT 1mg BID was highly effective in bringing clinico-histological active EoE into remission. These findings were similar and confirm in a larger number of active EoE pa-tients the results obtained under DB treatment with BOT 1mg BID in the EOS-1 study (n=88, amongst these 59 having received verum) (1).

References: (1) Lucendo AJ, et al. Gastroenterology 2019, DOI:https://doi.org/10.1053/j. gastro.2019.03.025

Disclosure: Mueller R and Greinwald R are empoyees of Dr. Falk Pharma GmbH

Number (%) patients in clinico-histological remission at wk 6 (LOCF)	126 (69.6%)
Number (%) patients in histological remission (peak <16 eos/mm2 hpf) at wk 6 (LOCF)	163 (90.1%)
Number (%) patients in deep histological remission (‚0' eos/mm2 hpf) at wk 6 (LOCF)	153 (84.5%)
Mean [95% CI] change in peak eos/mm2 hpf	-283 [-323; -243]
Number (%) patients in clinical remission (dysphagia and odynophagia each ≤2 points on 0-10 points NRS) at wk 6 (LOCF)	136 (75.1)
Mean (SD) total modified EREFS score (0-9) at wk 0 / wk 6 (LOCF)	4 (1.6) n=181 / 1 (1.3) n=176
Number (%) patients with all modified EREFS features graded as ‚0' at wk 0 / wk 6 (LOCF)	1 (0.6%) / 72 (39.8%)
Number (%) patients with endoscopist's overall assessment of ‚no signs of EoE' at wk 0 / wk 6 (LOCF)	-- (0%) / 101 (55.8%)

eos, eosinophils; EREFS; Endoscopic activity score; hpf, high power field; LOCF, last observation carried forward; NRS, numerical rating scale

[Open-label induction phase (n=181 patients)]

OP092 A NOVEL BUDESONIDE ORODISPERSIBLE TABLET FORMULATION IS HIGHLY EFFECTIVE TO MAINTAIN ENDOSCOPIC INFLAMMATORY REMISSION AND EVEN COMPLETE ENDOSCOPIC REMISSION IN ADULT PATIENTS WITH EOSINOPHILIC ESOPHAGITIS: RESULTS FROM THE 48-WEEKS, DOUBLE-BLIND, PLACEBO-CONTROLLED PIVOTAL EOS-2 TRIAL

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Introduction: In the recent EOS-1 trial, a 6-week therapy with a novel budesonide orodispersible tablet (BOT), with a unique mode of delivery and esophageal targeting, given twice daily (1mg BID) induced endoscopic inflammatory remission in 59% of adult patients with active eosinophilic esophagitis (EoE) versus 0% under placebo (1).

Aims & Methods: This maintenance study also assessed the efficacy of two doses of BOT vs placebo for maintaining EoE in endoscopic inflammatory remission and in complete endoscopic remission over 48 weeks.

In total, 204 patients being in clinico-histological remission at baseline were randomized (1:1:1) to a 48-weeks treatment with BOT 1 mg BID, BOT 0.5 mg BID or placebo.

Endoscopic assessment by using the validated modified EREFS score (2) was performed at baseline and end of treatment (EOT). Endoscopic in-

flammatory remission was defined as previously suggested by Greuter et al. (3): i.e., modified EREFS subscores: fixed rings = ´Grade 0: none´ or ´Grade 1: mild´, exudates = ´Grade 0: none´, furrows = ´Grade 0: absent´, and edema = ´Grade 0: absent´. Additional EREFS subscores were also assessed. Complete endoscopic remission was defined as all modified EREFS features graded as '0'.

Results: see Table:

	BOT 1mg BID (n=68)	BOT 0.5mg BID (n=68)	Placebo BID (n=68)
Number (%) patients in endoscopic inflammatory remission at baseline	48 (70.6%)	45 (66.2%)	47 (69.1%)
Number (%) patients in endoscopic inflammatory remission at wk48/EOT	51 (75.0%) p<0.0001	49 (72.1%) p<0.0001	4 (5.9%)
Number (%) of patients maintaining endoscopic inflammatory remission from Baseline to wk48/EOT	38 (79.2%) n=48 p<0.0001	32 (71.1%) n=45 p<0.0001	4 (8.5%) n=47
Number (%) of patients in complete endoscopic remission at baseline	34 (50.0%)	34 (50.0%)	35 (51.5%)
Number (%) of patients in complete endoscopic remission at wk48/EOT	39 (57.4%) p<0.0001	36 (52.9%) p<0.0001	4 (5.9%)
Number (%) of patients with no fixed rings present at baseline	42 (61.8%)	39 (57.4%)	42 (61.8%)
Number (%) of patients with no fixed rings present at wk48/EOT	47 (69.1%) p=0.0010	43 (63.2%) p=0.0098	27 (39.7%
P-values (exploratory test for superiority vs placebo; 1-sided Fisher exact test			

[Endoscopic efficacy endpoints]

Conclusion: Both BOT dosing groups were significantly superior over placebo in maintaining EoE in endoscopic inflammatory remission and even in complete endoscopic remission. Moreover, both BOT groups were able to delay or even revert fibrotic remodeling as indicated by improvement in fibrotic signs such as fixed rings. 20% of patients on placebo developed new fixed rings, compared to none on maintenance BOT.

References: (1) Lucendo AJ, et al. Gastroenterology 2019 (accepted for presentation as poster of distinction at DDW 2019) (2) Hirano I, et al. Gut. 2013;62:489-95. (3) Greuter T, et al. Am J Gastroenterol. 2017;112:1527-35.

Disclosure: Mueller R & Greinwald R are employees of Dr. Falk Pharma GmbH

Pathogenesis of H. pylori infection
16:00-17:30 / B3

OP093 RE-DIFFERENTIATION OF GASTRIC CARCINOMA AFTER SUCCESSFUL *HELICOBACTER PYLORI* ERADICATION THERAPY

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Introduction: Gastric cancer may develop after successful eradication of *Helicobacter pylori*,although the incidence is lower than in non-eradicated individuals. We previously reported that the appearance of characteristic epithelium with low-grade atypia (ELA) on the surface of gastric cancer after *H. pylori*eradication. However, whether ELA originates from cancer after re-differentiation or from the non-cancerous surrounding mucosa is unknown.
Aims & Methods: We isolated ELA regions from 10 early gastric cancer patients and analyzed the nucleotide sequences for 90 oncogenes and 35 fusion oncogenes, comparing them with counterpart cancer tissue, normal gastric mucosa, and blood cell-derived DNA. Somatic mutations in each tissue were identified by comparing them with the sequences from whole blood-derived DNA.
Results: Gene alterations were observed in nine of the ten patients, and up to 42 and 70 somatic mutations were seen in cancer and ELA samples, respectively. Common mutations shared between cancer and ELA tissues

were found in eight of these nine patients. In contrast, common mutations between non-cancer mucosa and ELA was only detected in one patient, who also had common mutation between cancer and ELA. ELA-specific nucleotide substitutions were seen in seven patients. In contrast, cancer-specific substitutions were only found in two patients. 18 out of 19 amino acid substitutions present in cancer tissue were also identified in ELA. These results suggest that ELA originated from cancer tissue and accumulated further nucleotide substitutions.
Conclusion: Differential diagnosis of ELA and normal mucosa should be carefully performed to prevent misdiagnosis of ELA as normal mucosa with atypia.
Disclosure: Nothing to disclose

OP094 RECIPROCAL EXPRESSION OF 8-OHDG AND DNA REPAIR PROTEINS IN THE PROGRESSION OF*HELICOBACTER PYLORI* ASSOCIATED GASTRIC CANCER

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Introduction: Role of *Helicobacter pylori* in the establishment and progression of gastric cancer is still not well understood. It was hypothesized in this study to determine any possible role of *H. pylori* in the enhanced expression of reactive oxygen species which may result in the accumulation of DNA damages and escape from DNA repair enzymes activity, ultimately lead to the establishment and progression of gastric cancer.
Aims & Methods: Gastric tissues from dyspeptic patients (n=300), normal individuals (n=100) and gastric cancer patients (n=100) were analyzed immunohistochemically for PMS2 and ERCC1 expression in comparison with the presence or absence of *H. pylori* infection and 8-OHdG occurrence.
Results: Regression analysis of 8-OHdG, PMS2 and ERCC1 expressions showed the reciprocal relation between 8-OHdG and PMS2 (r=-0.964) / ERCC1 (r=-0.967). Statistical analyses including mean rank determination, mean comparisons and spearman coefficient analysis, of PMS2 and ERCC1 expression in gastric tissues collected from dyspeptic and gastric cancer patients also confirmed the reciprocal relation observed between expression of these proteins and *cagA -ve/cagA +ve H. pylori* infection. Intestinal type gastric cancer were highly deficient for both proteins, which may suggest the presence of critical role of *cagA +ve H. pylori* in transforming gastritis into precancerous lesions and then into intestinal type gastric cancer by causing impairment in NER and MMR systems.
Conclusion: Findings of this study can suggest the possible involvement of *cagA +ve H. pylori* in enhanced expression of 8-OHdG and decreased expression of PMS2 and ERCC1, resulting in the progression of intestinal type gastric cancer.
Disclosure: Nothing to disclose

OP095 CD44V9-POSITIVE CANCER STEM CELL IS DEVELOPED FROM CAPZA1 OVER-EXPRESSING CELL INDUCED BY OXIDATIVE STRESS

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Introduction: It is known that CD44 variant 9 (CD44v9) is a splicing variant of cancer stem cell marker and CD44v9 expression is strongly associated with the recurrence of early gastric cancer (*Br. J. Cancer* 109:379-386, 2013). However, the mechanism of CD44v9 expression in *H. pylori*-infected gastric mucosa has not been clarified. Although translocated *Helicobacter pylori*-derived CagA is usually degraded by autophagy, it specifically accumulates in CD44v9-positive cancer stem cells (*Cell Host Microbe* 12:764-777, 2012).
We recently reported that CAPZA1 functions as a negative regulator of the autophagy, and thereby translocated CagA accumulates in CAPZA1-over-

expressing cells (*Autophagy* 15:242-258, 2019). The present study was conducted to examine the generating mechanisms of CAPZA1-overexpressing cells that lead to the production of CD44v9-positive cancer stem cells.

Aims & Methods: CAPZA1 expression levels in gastric mucosa were evaluated using *H. pylori*-infected Mongolian gerbils. Lipid peroxidation and protein carbonylation in the *H. pylori*-infected mucosa were evaluated on the basis of malondialdehyde and protein carbonyl levels, respectively. Expression mechanisms of CAPZA1 were examined by western blotting and chromatin immunoprecipitation. CD44v9 expressions were evaluated by western blotting and immunohistochemistry.

Results: In CAPZA1-overexpressing cells infected with *H. pylori*, CD44v9 expression was enhanced due to accumulation of CagA oncoprotein. CD44v9-expressing cells were detected among cells strongly stained for CAPZA1 in *H. pylori*-infected gastric mucosa of Mongolian gerbils and human gastric cancer tissues. Moreover, CAPZA1-overexpressing cells infected with *H. pylori* exhibited enhanced expression of Sal-like protein 4 (SALL4) and Krüppel-like factor 5 (KLF5), which encode reprogramming factors. Our findings show that CD44v9-expressing cancer stem cells arise from CAPZA1-overexpressing cells following CagA accumulation. We subsequently examined the induction mechanisms of CAPZA1 expression. The levels of CAPZA1 expression in the gastric mucosa of *H. pylori*-infected Mongolian gerbils were significantly higher than that in uninfected gastric mucosa. In *H. pylori*-infected gastric mucosa, a significant linear correlation was observed between CAPZA1 expression and lipid peroxidation (r = 0.614, p < 0,005). CAPZA1 expressions in AGS cells were increased in the dose-dependent manner by the treatment with H_2O_2 or Di-*tert*-butyl peroxide. Such increased expression of CAPZA1 was abolished by treatment with N-Acetyl-L-cysteine. These results show that CAPZA1 expression is enhanced by oxidative stress stimulus.

Conclusion: CAPZA1-overexpressing cells behave as progenitor cells for CD44v9-positive cancer stem cells. Oxidative stress in *H. pylori*-infected gastric mucosa could increase CAPZA1 expression.

Disclosure: Nothing to disclose

OP096 THE CANDIDATES OF THE AMINO-ACID POLYMORPHISM IN N-TERMINAL REGION OF EAST ASIAN CAGA RELATING TO THE PATHOGENIC FUNCTION OF CAGA

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Introduction: The cytotoxin-associated gene A (CagA) is generally accepted to be the most important virulence factor of *Helicobacter pylori* and increases the risk of developing gastric cancer. Especially, infection of *H. pylori* with East Asian CagA which includes EPIYA-D segment in C-terminal region significantly increases the risk of the incidence of gastric cancer than the other type of CagA. Though there are many studies analyzing the amino acid polymorphism of East Asian CagA in C-terminal region surrounding EPIYA motif, much less works about the amino-acid polymorphism in N-terminal region relating to the high virulence of East Asian CagA have been done.

Aims & Methods: The aim of this study is to detect the amino acid polymorphisms in N-terminal region of East Asian CagA which will result in the strong pathogenesis of East Asian CagA *in sillico*. First, our previous whole-genome sequencing (WGS) data of *H. pylori* deposited in DNA Data Bank of Japan (DDBJ) were downloaded. After sequence reads of 40 *H. pylori* strains being mapped to reference using CLC Genomics Workbench, 40 *H. pylori* strains were classified by the EPIYA segment type and divided into two groups, East Asia group including 37 strains and the other group including 3 strains. Specific single nucleotide variants (SNVs) and amino acid changes (AACs) in East Asia group were detected with the tool of Fisher Exact test.

Next, possible influence of the specific AACs existing in N-terminal region of East Asian CagA on the functions of CagA were evaluated with *in silico* simulation model. The tertiary structure of mutant CagA reflecting the specific AACs was made by SWISS-MODEL server using crystal model of CagA (Protein Data Bank (PDB)-ID:4DVY). The docking simulations of CagA with phosphatidylserine (PS) were performed by Swiss-Dock. The docking simulations of CagA with α5β1 integrin were performed by ClusPro. The energy of each docked model, ΔG (kcal/mol) and total energy (kJ/mol) respectively, was calculated and analyzed by Wilcoxon test using JMP 10.

Results: Four high frequent AACs in N-terminal region of East Asian CagA were detected in our previous 40 *H. pylori* sequence data and the two AACs (V356A, Y677F) out of four were demonstrated the reproducible specificity using validation dataset (20 strains of East Asian CagA vs 20 strains of the others) obtained from National Center for Biotechnology Information (NCBI).

After the mutant tertiary structure of CagA reflecting these two specific AACs being made by SWISS-MODEL server, the docking simulations of CagA with PS were performed. As a result, there is no significant difference of ΔG between control CagA and mutant CagA. On the other hand, in docking simulation of CagA with α5β1 integrin, the total energy of complex of mutant CagA with α5β1 integrin was significantly lower than that of control CagA (*p* < 0.01).

This result indicates that the complex of mutant CagA with α5β1 integrin is more stable than that of control. Therefore, these two AACs significantly increase the binding affinity of CagA to α5β1 integrin and may contribute to the high virulence of East Asian CagA.

Conclusion: Two novel AACs which can be the candidates relating to the pathogenicity of CagA were detected in N-terminal region of East Asian CagA.

Disclosure: Nothing to disclose

OP097 *HELICOBACTER PYLORI* INFECTION INHIBITS NOTCH SIGNALLING IN GASTRIC EPITHELIAL CELLS AND THE GASTRIC MUCOSA

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Introduction: *Helicobacter pylori* infects approximately 4.4 billion people worldwide and poses a major health burden due to its association with chronic gastritis, ulcers, gastric cancer and mucosa-associated lymphoid tissue lymphoma. Disease progression is correlated with host and bacterial factors. Increasing *H. pylori* antibiotic resistance has led to a decrease in eradication success using current therapies. A deeper understanding of host-pathogen interaction is vital to uncover alternative therapeutic strategies. The Notch pathway is highly conserved and central to numerous biological processes including cell differentiation, proliferation and survival. Notch signalling is essential for normal function of gastric epithelial cells (1) and dysregulation is associated with inflammatory conditions and gastric cancer (2). The role of Notch signalling in *H. pylori* pathogenesis is not fully understood.

Aims & Methods: The aim of the study was to monitor expression of Notch signalling pathway components during *H. pylori* infection and assess the role of the virulence factors CagA and VacA. AGS gastric epithelial cells were infected with *H. pylori* 60190 or isogenic CagA and VacA mutant strains. Cells were lysed at 0, 3 and 6 hours post-infection and total RNA was isolated. RNA was also isolated from antral biopsies of *H. pylori*-infected and uninfected patients. Patients were classified as infected if 2 of 3 test results (rapid urease test, histology, culture) were positive. Expression of Notch pathway genes was measured using reverse transcription quantitative PCR. Changes in expression were evaluated using the comparative CT method. Results were normalised to GAPDH levels, and expressed relative to uninfected cells. IL-8 was measured as a positive control. The Student's T-test and Mann-Whitney U-test were used to compare gene expression in cell culture samples and biopsies, respectively. A P value of < 0.05 was considered significant.

Results: *H. pylori* 60190 infection led to a significant increase in IL-8 mRNA expression in AGS cells, together with a significant decrease in the production of several Notch pathway components, including Notch receptors; 1 and 3, Notch ligands; Jagged 1, Jagged 2 and Delta-like 1, as well as Notch target genes Hes1 and Hey1. A similar level of reduction was also observed following infection with *H. pylori* 60190 lacking functional CagA or VacA. In all, biopsy samples from 25 *H. pylori*-infected and 17 uninfected patients were analysed (mean age 50.8 ± 12.9 versus 49.8 ± 17.5 years, respectively; P=0.82). Histology findings reported chronic gastritis in all of the *H. pylori*-infected patients. A significant decrease in the median expression levels of Notch 4 (46%; P=0.02), Jagged 2 (39%; P=0.01), Hes1 (38%; P=0.02) and Hey1 (45%; P=0.03) was observed in the gastric mucosa of *H. pylori*-infected patients compared to uninfected controls.

Conclusion: *H. pylori* infection inhibits Notch signalling in gastric epithelial cells, independent of the CagA and VacA virulence factors. Decreased Notch signalling was also observed in the gastric mucosa of infected patients. Further experiments will be necessary to fully elucidate the role of decreased Notch signalling in *H. pylori* pathogenesis.

References: 1. Kim T-H, Shivdasani RA. Notch signaling in stomach epithelial stem cell homeostasis. Journal of Experimental Medicine. 2011;208(4):677-88. 2. Wu X, Liu W, Tang D, Xiao H, Wu Z, Chen C, et al. Prognostic values of four Notch receptor mRNA expression in gastric cancer. J Scientific reports. 2016;6:28044.

Disclosure: Nothing to disclose

OP098 HELICOBACTER PYLORI INFECTION ANTAGONIZES THE PROCESS FROM INFLAMMATION TO COLITIS ASSOCIATED COLON CANCER BY REGULATING TH17/TREG BALANCE

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Introduction: Large epidemiological studies and meta-analyses have demonstrated an inverse association between Helicobacter pylori (H.pylori) infection and the risk of developing inflammatory bowel diseases (IBD). Our previous study has demonstrated H.pylori infection can modulate Th17/Treg balance to protect against colitis. Colitis associated colon cancer (CAC) is one of the most common cause of death in IBD patients. Compared with hereditary and sporadic colon cancer, the pathogenic mechanisms of CAC involve the crosstalk among tumor cells, tumor stromal cells and immune cells. The differentiation balance between Th17 and Treg cells palys significant role in the CAC. Thus, we speculate H.pylori infection might ameoliorate the severity of CAC by regulating Th17/Treg balance.
Aims & Methods: The aim of this work was to investigate whether H.pylori infection may influence the severity of CAC in a mouse model of early colorectal carcinogenesis by modulating Th17/Treg balance. C57BL/6 mice received azoxymethane (AOM) i.p. at a dose of 10 mg/kg body weight to induce dysplasia and then received 4 cycles of 2% DSS, each separated by 14 days of regular water. All mice were sacrificed 90 days after the first AOM injection to perform histology, flow cytometry analysis and immunohistochemistry of colonic mucosa. The tumor number and tumor load were counted for each group. Immunohistochemical staining for BrdU was performed to evaluate the proliferative activity of colonic epithelial cells. Flow cytometry was used to determine the percentage of Th17, IL10+Treg, IL17+Treg and tumor associated macrophages (TAM) in colon. The m-RNA expression of Th17 and Treg associated cytokines (IL6, IL10, IL17A, IL23, TGFβ).
Results: AOM/DSS treatment resulted in the formation of colon tumors in both H.pylori infected and non-infected mice. Compared with non-infected group, H.pylori infected mice exhibited less tumor number and tumor load (7.83±2.64 vs 5.00±1.51, P< 0.05 and 18.68±4.56 vs 9.04±3.40, P< 0.05). In accordance, BrdU staining revealed significantly decreased proliferative activity in both tumor and peri-tumor tissues (44.62±4.38 vs 27.65±3.24, P< 0.05 and 10.69±1.42 vs 4.45±1.24, P< 0.05). Flow cytometry study revealed lower Th17 and IL17+Treg cells percentage in the colon of H.pylori infected group mice, showing an inhibited Th17 cell differentiation by H.pylori infection (3.52±0.32 vs 1.16±0.20, P< 0.05 and 0.30±0.02 vs 0.22±0.02, P< 0.05). In turn, H.pylori infected mice exhibited higher IL10+Treg cells percentage in colon (0.42±0.02% vs 0.58±0.03%, P< 0.05), which might involve in the protective mechanism against colon cancer. In addition, we found that H.pylori infected group also presented lower TAM percentage in colon tissues (21.81±1.06 vs 13.46±0.42, P< 0.05). Accordingly, Th17 cells associated cytokines (IL17, IL6 and IL23) decreased in infected group, whereas Treg cells associated cytokines (IL10 and TGFβ) increased significantly.
Conclusion: Our data demonstrated that H.pylori infection might antagonize the process from colitis to CAC in CAC mouse model. This effect is likely mediated via regulating Th17/Treg balance by modulating TAM in colon cancer.
Disclosure: All authors have declared no conflicts of interest.

IBD: Health care and patient-reported outcomes
16:00-17:30 / B5

OP099 THE EXPERIENCE OF INFLAMMATORY BOWEL DISEASE PATIENTS WITH HEALTHCARE: A SURVEY OF 2011 PATIENTS FROM THE GETAID

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Introduction: Patient experience with healthcare is positively associated with clinical effectiveness and patient safety in a wide range of diseases. Inflammatory bowel diseases (IBD) are chronic and disabling conditions involving the gastrointestinal tract. Besides, the quality of information given by the physician to patients and the development of shared decision processes may be helpful to improve confidence and adherence in IBD management. The aim of this study was to assess experience of patients with IBD on their disease, their treatment and the relationship with their physician.
Aims & Methods: We performed a nationwide cross-sectional survey in 42 tertiary centers in France and Belgium affiliated to the GETAID from November 26th to December 2nd 2019, on consecutive outpatients with IBD. A standardized self-administered anonymous questionnaire was completed by each patient. The recorded data included patients, IBD and treatment characteristics combined with multiple-choice questions and 10-point Likert scales regarding patient global assessment of clinical remission, daily life IBD burden, treatment adherence, information on IBD, doctor-patient relationship, overall satisfaction, patient-self management, concerns about their treatment, knowledge on biosimilars and alternative management.
Results: A total of 2011 outpatients with IBD responded to the survey (930 men; median age 40.0 (29.0-52.0) years; median IBD duration 10.5 (4.5-18.5) years; 67.8% of patients with Crohn's disease). Most of the patients were treated with biological agents (63.9%) or immunomodulator (8.5%). Patient global assessment of clinical remission was noted in 49.9% and daily life IBD burden score was 5.2 ± 2.9. Assessment of doctor-patient relationship considering IBD and IBD treatment knowledge and doctor-patient relationship was good ranging from 7.4 to 8.3 (table 1) associated with a high adherence to treatment (9.1 ± 2.2).
Alternative sources of information about ongoing treatment and IBD was mainly obtained from internet in 62.9% and 79.8%, respectively, and from general practitioner in 54.3% and 61.4%. Indeed, patients with IBD reported consulting their general practitioner 2.6 ± 3.9 times a year in addition to their gastroenterologist. Lost working days were frequent in 71.2% of patients accounting for 0.8 working day loss per years. Complementary medicine was used by 28.2% of patients including 19.4% on a regular basis. Knowledge about biosimilars was poor (20.4%) and associated with a low acceptance rate (21.4%).
Main concerns about IBD treatment were the fear of adverse events (47.4%) and lack and/or loss of efficacy (32.9%), while the absence of any concerns was observed in 24.4%. Claim for prospective access to complementary and alternative healthcare professionals were noticed in 89.2% including dietician (24.9%), sports coach (22.0%), psychotherapist (14.6%), sexologist (9.4%) and social worker (8.5%).

	Total (n=536)	No treatment (n=138)	5-ASA (n=113)	Immuno-modulator (n=112)	Anti-TNF (n=112)	Vedoli-zumab (n=29)	Ustekinumab (n=16)
Crohn´s disease, n(%)	286 (53)	83 (60)	12 (11)	66 (59)	91 (71)	19 (66)	15 (94)
Disease duration, median years (IQR)	11 (5-20)	12 (6-21)	10 (4-20)	11 (5-20)	12 (6-20)	14 (5-20)	11 (7-15)
Disease activity, n (%)	122 (23)	28 (20)	17 (15)	28 (25)	32 (25)	7 (24)	10 (63)
Perianal disease, n (%)	32 (11)	10 (12)	2 (2)	5 (8)	10 (11)	2 (10)	3 (20)
Prior bowel resection, n (%)	143 (27)	57 (41)	3 (3)	26 (23)	40 (31)	7 (24)	10 (63)
Severe absenteeism, n (%)	36 (7)	8 (6)	2 (2)	3 (3)	13 (10)	4 (14)	6 (38)
Severe presenteeism, n (%)	85 (16)	23 (17)	6 (5)	16 (14)	29 (23)	6 (21)	5 (31)
Severe overall WP loss, n (%)	115 (22)	30 (22)	8 (7)	20 (18)	38 (30)	9 (32)	10 (63)

[Table 1. Baseline characteristics]

Conclusion: In this large IBD cohort, 7%, 16% and 22% of patients had severe absenteeism, presenteeism and overall WP loss. Major risk factors for WP loss were perianal disease and disease activity, resulting in high indirect costs. Patients using ustekinumab had the highest yearly indirect costs, patients on 5-ASA the lowest, which is most likely related to the number of patients with disease activity and perianal disease within these groups. A substantial proportion of indirect costs are related to presenteeism.
Disclosure: This work was sponsored by dr. Falk Pharma Benelux B.V.

OP101 PATIENT AND PHYSICIAN ASSESSMENT OF DISEASE BURDEN IN PATIENTS WITH EARLY UC: 2-YEAR DATA FROM ICONIC

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Introduction: ICONIC is the largest prospective, multi-country, observational study assessing disease burden in adults with ulcerative colitis (UC) under routine care over a 2-year period. The study assessed quality of life and disease burden using standard Inflammatory Bowel Disease (IBD) patient reported outcome measures as well as a visual measure of disease-associated suffering, Pictorial Representation of Illness & Self-Measure (PRISM). The final analysis of the study is presented.
Aims & Methods: Adult patients with early UC (diagnosed ≤36 months) were enrolled irrespective of disease severity or treatment. Patient visits occurred every 6 months (+/- 3months) for 2 years. The primary objective was to evaluate PRISM as a tool to assess disease-associated suffering in patients with UC. Lower PRISM scores represent a greater suffering associated with illness. The correlation between patient and physician perception of disease was also assessed. Patient self-assessments included PRISM, Patient Health Questionnaire-9 (PHQ-9), Short IBD Questionnaire (SIBDQ), and patient-modified Simple Clinical Colitis Activity Index (P-SCCAI). Physician assessments included clinical parameters, PRISM, and SCCAI. Data are presented as-observed. Mean differences between patient and physician measures, and differences between the 2-year and first visits were calculated using Wilcoxon signed-rank test. Correlation between PRISM and SIBDQ, PHQ-9, and SCCAI were performed using Spearman correlation.
Results: A total of 1806 patients were enrolled and fulfilled the selection criteria; 53.8% female, mean (SD) age 38.5 (14.6) years; 336 (18.6%) discontinued the study. At the 2-year visit, data were available for 1265 pa-

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Knowledge about IBD	7.4 ± 1.2
Sufficient information about ongoing treatment	8.1 ± 2.1
Overall satisfaction about ongoing treatment	7.6 ± 2.5
Adherence to ongoing treatment	9.1 ± 2.2
Overall satisfaction on doctor-patient relationship	8.3 ± 2.2

[Table 1]

Conclusion: In 2011 outpatients with IBD followed-up in tertiary care centres, we observed a high level of satisfaction, adherence and knowledge about IBD and IBD treatment. However, we highlight several fields that still need improvement: knowledge and acceptance of biosimilars, access to complementary and alternative healthcare professionals, loss of work productivity and concerns about effectiveness and safety of IBD treatment.
Disclosure: This study was funded by Abbvie

OP100 WORK PRODUCTIVITY LOSS IS A MAJOR COST DRIVER IN IBD PATIENTS: THE WORK-IBD STUDY

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Introduction: Inflammatory bowel disease (IBD) negatively impacts work productivity (WP). Most studies focus on absence from work (absenteeism), while on the job productivity loss (presenteeism) is present in more than 30% of patients. Indirect costs, defined as expenses incurred from WP loss due to IBD, have not been thoroughly studied in economic evaluations.
Aims & Methods: The aim of the WORK-IBD study was to determine predictors for WP loss and estimate corresponding indirect costs. Crohn's disease (CD) and ulcerative colitis (UC) patients that attended the outpatient clinic of four hospitals between May 1st and August 31st 2017 were invited. WP loss was measured using the Work Productivity and Activity Impairment questionnaire, disease activity using the patient-reported Harvey Bradshaw Index or Simple Clinical Colitis Activity Index. Severe absenteeism, presenteeism and overall WP loss were defined as ≥ 50% work time missed, ≥ 50% on the job productivity loss, and ≥ 50% overall work impairment (absenteeism plus presenteeism) in the previous week, respectively. Annual indirect costs were calculated based on hourly wage data from Statistics Netherlands (CBS) 2017, percentages WP loss, contract hours per week and 47 weeks worked annually.
Results: In total, 1590 IBD patients were invited, 768 (48%) responded (119 not eligible, 86 declined) and 536 were included (58% female, 53% CD) with a median age and disease duration of 45 (33-53) and 11 (5-20) years (table 1). Severe absenteeism, presenteeism and overall WP loss was reported by 36 (7%), 85 (16%) and 115 (22%) of patients, respectively. Eight (7%) patients using mesalamine (5-ASA), 20 (18%) using immunomodulators, 26 (30%) on anti-TNF monotherapy, 12 (29%) on combination therapy, 9 (32%) on vedolizumab, 10 (63%) on ustekinumab and 30 (22%) without maintenance treatment reported severe overall WP loss. Risk factors for severe WP loss were disease activity (OR 6.6, 95% CI 3.6-12.1) and perianal disease (OR 3.7, 95% CI 1.5-8.7), whereas 5-ASA treatment was associated with a lower risk (OR 0.2, 95% CI 0.0-0.8). Median costs per patient for absenteeism, presenteeism and overall WP loss were €0 (0-0), €0 (0-8430) and €1905 (0-10537), respectively. Median costs due to overall WP loss were €0 (0-6734) for patients using 5-ASA, €1143 (0-8767) for immunomodulators, €3810 (0-14875) for anti-TNF monotherapy, €3049 (0-16859) for combination therapy, €5603 (0-15771) for vedolizumab, €10350 (3049-28201) for ustekinumab and €762 (0-9146) for patients without treatment. Costs were higher for patients with disease activity and perianal disease (€13,338 vs 0, p< 0.001 and €14363 vs 2382, p=0.001).

tients. The most common reasons for discontinuation were did not attend routine visit and lost to follow-up. At baseline, 37.0% and 12.9% of patients were assessed by the physician to have moderate or severe disease, respectively. At the 2-year visit, the physician assessments were 13.4% of patients with moderate disease and 2.5% with severe disease. Mean ± SD patient-reported PRISM score and P-SCCAI were significantly different than the physician measures, with patients reporting a higher disease burden than that perceived by the physician (patient PRISM: 5.1 ± 2.5 and physician PRISM: 5.6 ± 2.4; p< 0.0001; P-SCCAI: 2.5 ± 2.8 and SCCAI: 1.3 ± 2.1; p< 0.0001; Table). A high correlation was observed between patient and physician PRISM scores and between P-SCCAI and SCCAI. Mean ± SD scores for PHQ-9 and SIBDQ were 4.2 ± 4.6 and 55.7 ± 11.6, respectively. Patient PRISM scores were moderately correlated with SIBDQ, PHQ-9, and P-SCCAI (Table).

Significant differences in mean ± SD scores between the 2-year visit and the first visit were observed for all measures (PHQ-9: -1.8 ± 5.5; P-SCCAI: -1.6 ± 4.0; SCCAI: -1.5 ± 3.2, SIBDQ: 6.8 ± 13.9; patient PRISM: 1.2 ± 3.0; physician PRISM: 1.3 ± 2.9; p< 0.0001 for all measures).

	SIBDQ	PHQ-9	PRISM (physician)	P-SCCAI (patient)
PRISM (patient), r (p-value)	0.56 (0.0001)	-0.43 (<0.0001)	0.63 (<0.0001)	-0.50 (<0.0001)
SCCAI (physician), r (p-value)	Not determined	Not determined	-0.48 (<0.0001)	0.67 (<0.0001)

PRISM=Pictorial Representation of Illness & Self- Measure, SCCAI=Simple Clinical Colitis Activity Index; SIBDQ=Short Inflammatory Bowel Disease Questionnaire, PHQ-9=Patient Health Questionnaire-9.

[Table. Spearman correlation coefficients between selected instruments at the final visit.]

Conclusion: PRISM may be a valuable tool to assess disease burden in patients recently diagnosed with UC. Although patient and physician measures of disease related suffering and disease severity were strongly correlated, the perception of UC-related burden significantly differed between physician- and patient- assessments. These discrepancies between patient and physician ratings warrant further investigation.

Disclosure:

OP102 THERE IS MORE THAN PHARMACOLOGY: COMPREHENSIVE LIFESTYLE-MODIFICATION IN PATIENTS WITH ULCERATIVE COLITIS: A RANDOMIZED CONTROLLED TRIAL

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Introduction: The chronic impairment of health related quality of life (HrQoL) is of high relevance in patients with ulcerative colitis (UC). Many patients perceive a treatment regime solely based on drug therapy as limited. A standardised multimodal lifestyle-modification program including modules in mind-body medicine, naturopathic self-help strategies, herbal treatments and dietary counseling shows promising first evidence to lower the burden of disease and increase patients HrQoL.

Aims & Methods: Ninety-seven patients with ulcerative colitis in clinical remission and impaired HrQoL were randomly assigned to a 10 week comprehensive lifestyle-modification program or a control group that received a single workshop of intense training in naturopathic self-help strategies (Table 1).

	Lifestyle-modification (n = 47)	Control (n = 50)
Age years	50.28 ± 11.90 (18 - 74)	45.54 ± 12.49 (19-71)
Female n (%)	34 (72.3)	35 (70)
Weight	72.79 ± 14.90 (52-100)	70.24 ± 16.86 (49.6 - 150)
Anamnestic pattern n (%)		
Proctitis	14 (29.8)	15 (30)
Left-sided colitis	17 (36.2)	15 (30)
Pancolitis	13 (27.7)	17 (34)
Missing	3 (6.4)	3 (6)
Time since diagnosis years	18.04 ± 12.00 (2 - 46)	14.76 ± 10.99 (1 - 43)
Smokers n (%)	2 (4.3)	3 (6)
Married n (%)	33 (70.2)	39 (78)
Blood parameters		
Leucocytes	6.40 ± 1.70	6.73 ± 4.38
Thrombocytes	272.26 ± 81.69	269.98 ± 72.68
Blood sedimentation rate	9.17 ± 10.55	9.54 ± 11.99
C-reactive protein	.36 ± .67	.29 ± .58

[Table 1. Sociodemographic and clinical characteristics at baseline.]

Patients were randomized using stratified block randomization (Strata: sex, azathioprine and biologics). Primary outcome was disease-specific total HrQoL at week 12 (Inflammatory Bowel Disease Questionnaire; IBDQ). Secondary outcomes included IBDQ sub-scores, generic HrQoL (SF-36), disease activity (Rachmilewitz clinical activity index, fecal lactoferrin, and fecal calprotectin), microbiome, and safety. In 31 patients additional endoscopy with histology was performed pre and post intervention.

Results: In both groups, a relevant increase in HrQoL (>16 in the IBDQ) at week 12 was achieved. In the Intention-to-treat analysis, the intervention group showed significantly higher improvement on the IBDQ subscale Bowel Symptoms (p=.045) and the SF36 mental health index (p=.002). In the Per Protocol (PP) analysis (pts who attended ≤50% of the intervention and screening failures were excluded), 37 patients in the intervention group and 43 patients in the self-care group were analyzed. Within the PP analysis, the LSM group showed a significant higher response in the IBDQ global score (p=.034; mean IBDQ=172.8) as well as the IBDQ systemic subscore (p=.034) and the IBDQ emotional subscore (p=.004) indicating a

higher HrQoL. No significant group difference was shown regarding endoscopy (*p*=.451) and histology (*p*=.406), disease activity (CAI *p*=.239), fecal Lactoferrin (*p*=.648) or fecal Calprotectin (*p*=.751). In addition, there was no significant difference in the fecal microbiota.

Conclusion: UC patients benefit from defined non-pharmacological treatment modules. A comprehensive lifestyle-modification program improves quality of life in patients with ulcerative colitis, while no effects were shown on disease activity in this group of patients in clinical remission. The results suggest that patients have to attend more than 50% of the training sessions of the 10 week lifestyle-modification program. Trial registration: Clinicaltrials.gov (NCT02721823).

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OP103 RESPONDER DEFINITIONS FOR THE CROHN'S DISEASE PATIENT-REPORTED OUTCOMES SIGNS AND SYMPTOMS (CD-PRO/SS) TOOL USING PATIENTS WITH CROHN'S DISEASE TREATED WITH ETROLIZUMAB

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Introduction: Clinically relevant patient-reported outcome (PRO) tools are important for evaluating treatment efficacy. Available PRO instruments used in Crohn's disease (CD) have limitations in evaluating the full extent of disease components, appropriately quantifying clinical symptoms, and adequately capturing the patient perspective. The Crohn's Disease Patient-Reported Outcomes Signs and Symptoms (CD-PRO/SS) is the first CD PRO tool developed with input from health authorities, patients, and clinical experts.[1] In April 2019, the EMA released a letter supporting use of the CD-PRO/SS as an end point in IBD clinical trials.[2] Here, we propose responder definitions for the CD-PRO/SS using data from patients with moderate-to-severe CD treated with etrolizumab in BERGAMOT (NCT02394028).

Aims & Methods: In BERGAMOT (Phase 3 trial), aTNF-naive and aTNF-experienced patients with CD were treated with etrolizumab 105 mg, 210 mg, or placebo SC every 4 weeks during a 14-week induction phase. Cohort 1 (blinded) and cohort 2 (open-label) were analysed independently, encompassing all treatments. Data reported are from the pooled analysis. The CD-PRO/SS consists of 2 separately scored scales: a 3-item functional domain and a 3-item bowel domain. The domain score is equal to the sum of the item scores, which were calculated as an average of ≥ 4 out of 7 days before every induction visit. Mininum clinically important differences (MCID) were calculated using distributional- and anchor-based methods on a reduction of ≥ 16 points in the Inflammatory Bowel Disease Questionnaire, ≥ 70 points in the Crohn's Disease Activity Index (CDAI), and ≥ 100 points in the CDAI at week 14.

Results: As of September 2018, the CD-PRO/SS scores from patients with non-missing data (67.4% aTNF-experienced; cohort 1 n=215; cohort 2 n=264) were pooled for analysis (**Table**). Based on a reduction of ≥ 70 CDAI and ≥ 100 CDAI, the MCID from anchor-based method were 2.5 and 2.7, respectively, for the functional domain and 3.1 for the bowel domain regardless of treatment arm. Preliminary responder definitions for the CD-PRO/SS were a reduction ≥ 2.5 for the functional domain and ≥ 3.0 for the bowel domain that were determined through triangulation. Using these cutoffs, 45% of patients were responders based on the functional domain and 41% of patients were responders based on the bowel domain.

Conclusion: The proposed responder definitions determined from 479 patients show that a clinically meaningful response on the CD-PRO/SS are a reduction of ≥ 2.5 in the functional domain or ≥ 3.0 in the bowel domain. These definitions for the CD-PRO/SS will be confirmed in the ongoing etrolizumab Phase 3 CD studies for use in both clinical trials and practice to assess a clinically meaningful improvement.

	Functional Domain (0-12)	Bowel Domain (0-16)
Baseline		
N	479	479
Mean (SD)	6.41 (2.13)	8.23 (2.56)
Median	6.43	8.43
Min, max	1.43, 11.43	1, 13
Week 14		
N	421	421
Mean (SD)	4.21 (2.35)	5.83 (3.07)
Median	4.14	5.85
Min, max	0, 11.43	0.43, 13.75
Change from Baseline at Week 14		
N	334	334
Mean (SD)	-2.28 (2.55)	-2.45 (2.89)
Median	-2.08	-2.28
Min, max	-9.86, 6.01	-10.43, 4.72

CD-PRO/SS, Crohn's Disease Patient-Reported Outcomes Signs and Symptoms; SD, standard deviation.

[Table. Baseline, Week 14, and Change from Baseline in CD-PRO/SS Scores by Domain]

References: 1. Higgins PDR et al. J Patient Rep Outcomes. 2018;2:24. 2. European Medicines Agency (EMA). Letter of Support for the development of Patient-Reported Outcomes tools for use as an endpoint in Inflammatory Bowel Disease (IBD) clinical trials. April 2019.

Disclosure: PDR Higgins has nothing to disclose. K DeBusk is employee of and shareholder in Genentech/Roche and employee of Bristol-Myers Squibb (outside submitted work). R Jacob, A Hassanali, Z Sharafali, and A Matsui are employees of Genentech. YS Oh is employee of and shareholder in Genentech/Roche.

OP104 IMPACT OF BIOLOGIC TREATMENT OF ULCERATIVE COLITIS ON HEALTHCARE RESOURCE UTILIZATION IN US PATIENTS

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Introduction: This study compared healthcare resource utilization (HCRU) among Ulcerative Colitis (UC) patients currently receiving biologics and UC patients not currently receiving biologics.

Aims & Methods: Adult (18+ years) patients with ≥1 UC diagnosis code (ICD-9: 556.x; ICD-10:K51.x) from January 1, 2017 to December 31, 2017 were included in this retrospective analysis of medical and pharmacy claims data from the IBM Marketscan Commercial, Medicaid, and Medicare-Supplemental Claims database. Patients with a Crohn's Disease diagnosis were excluded from this study. Subgroups analyses were conducted to compare UC patients prescribed biologics and UC patients not prescribed biologics during 2017. A two-sample t-test was conducted to compare continuous variables and chi-squared tests were used to compare categorical variables.

Results: A total of 62,146 UC patients were included in this analysis; 7,705 patients (12.4%) were prescribed a biologic and 54,441 (87.6%) were not prescribed a biologic. Biologic users were more likely to be male (50.6% vs. 45.6%; p<0.0001) and younger (mean age: 42.94 vs. 49.88 years; p<0.0001) when compared to patients not prescribed a biologic. Biologic users were more likely to be prescribed immunomodulators (24.2% vs. 7.9%; p<0.0001), 5-ASAs (50.7% vs. 48.5%; p=0.0004), corticosteroids (47.7% vs. 29.5%; p<0.0001), and opioids (41.5% vs. 40.0%; p=0.0132). Biologic users were also more likely to have gastroenterologist visits (76.9% vs. 62.0%; p<0.0001), however patients not prescribed biologics were more likely to have ER visits (28.4% vs. 25.6%; p<0.0001) and inpatient hospital visits (13.6% vs. 15.8%; p<0.0001).

Conclusion: Medication use was higher among UC biologic users, however UC patients not prescribed biologics had higher HCRU.

Disclosure: Nothing to disclose

Management of patients with portal hypertension

16:00-17:30 / C3

OP105 SELECTIVE ACTIVATION OF STAT1-DEPENDENT APOPTOSIS IN HEPATIC STELLATE CELLS BY RILPIVIRINE AS A NEW THERAPEUTIC OPTION FOR LIVER FIBROSIS

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Introduction: Liver fibrosis is a common clinical outcome of all chronic liver diseases. Its current incidence is achieving pandemic dimensions and the lack of effective therapeutic options represent a major health problem worldwide. Among the wide range of signaling pathways that contribute to the progression of this pathology, JAK-STAT1 and JAK-STAT3 have been recently proposed as interesting therapeutic targets since they play a key role in the regulation of cell proliferation and cell death in both parenchymal and non-parenchymal cells. Rilpivirine (RPV) is a widely used antiretroviral drug that not only is considered safe in chronic treatments but also has been associated with an improvement in the lipid profile and glycemic control of HIV-infected patients after switching from other antiretroviral regimens.
Aims & Methods: We aimed to study the role of RPV in the progression of chronic liver damage as well as the involvement of JAK-STAT1 and JAK-STAT3 signaling pathways in this process, especially focusing on its actions on hepatic stellate cells (HSC) and hepatocytes.
To do this, a nutritional model of nonalcoholic fatty liver disease (NAFLD) and a CCl_4-induced liver fibrosis model (both in C57BL/6 mice) were used; RPV was daily administered at clinical doses. Human cell lines of hepatocytes (Hep3B) and HSC (LX-2), as well as primary human HSC (hHSC) were also treated with RPV. Standard molecular biology and histology techniques were used to assess the progression of liver damage and the activation of STATs. Gene silencing and conditioned medium experiments were carried out to evaluate the implication of STAT1 and STAT3 as well as the crosstalk between different cell types in response to RPV.
Results: RPV significantly reduced hepatic inflammation and fibrosis *in vivo*, and produced an increase of STAT3 activation in hepatocytes and of STAT1 in HSC. These effects were accompanied by augmented numbers of proliferating hepatocytes and apoptotic HSC. *In vitro*, RPV did not directly alter the viability or STAT3 activation in hepatocytes, but it did induce a clear pro-apoptotic effect in LX-2 cells, together with a decrease in STAT3 and collagen 1 protein expression, and an increase in STAT1 activation. Interestingly, this selective cytotoxic effect completely disappeared when STAT1 was silenced. In addition, STAT3 was activated in hepatocytes incubated with conditioned medium from apoptotic LX-2 cells. All these results were reproduced in hHSC.
Conclusion: The hepatoprotective effect of RPV is directly mediated by the selective STAT1-dependent induction of apoptosis in HSC. Additionally, RPV activates STAT3 in hepatocytes, increasing its proliferation and favoring liver regeneration. These effects could be of great clinical relevance in the development of new effective therapies for liver diseases with a fibrotic component.
Disclosure: Nothing to disclose

OP106 EUS-GUIDED PORTAL PRESSURE GRADIENT MEASUREMENT SAFELY PERFORMED WITH EUS-GUIDED LIVER BIOPSY: ENDOHEPATOLOGY IN PRACTICE

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Introduction: The portal pressure gradient (PPG) is useful to predict the development of complications of portal hypertension (PH). Recently, we showed the feasibility and safety of a simple novel technique for Endoscopic ultrasound (EUS) guided PPG measurement (PPGM) in a pilot study. EUS-guided liver biopsy (EUS-LB) has been shown to be a safe and effective alternative to percutaneously or Interventional Radiology performed liver biopsy for the diagnosis of liver disease.
Aims & Methods: We aimed to assess feasibility and safety of concomitant EUS-guided PPGM with EUS-LB in a single session. Secondarily, we aimed to evaluate the correlation between PPG and clinical markers of PH in an expanded clinical series.
This was a retrospective study of EUS-PPGM at single tertiary endoscopy center that enrolled 51 consecutive patients suspected of liver cirrhosis between February 2014 and October 2017.
Results: Technical success rate of EUS-PPGM was 100% without any severe adverse events. PPG ranged from 0 to 27.3 mm Hg. There was excellent correlation between PPG and clinical parameters of PH including the presence of clinical features of cirrhosis (11.26 vs 3.14 mmHg, p < 0.001), varices (14.94 vs 4.09 mmHg, p < 0.001), portal hypertensive gastropathy (14.37 vs 5.23 mmHg, p < 0.001), and thrombocytopenia (10.91 vs 4.81 mmHg, p = 0.0027). Platelet count also had a moderate negative correlation with PPG (R = -0.579). EUS-guided liver biopsies were performed in 35 patients (68.6%). All biopsies were deemed adequate for achieving histologic diagnosis by our pathologists. There were no early or late major adverse events.
Conclusion: EUS-guided PPG measurement using a 25-gauge needle and compact manometer correlates well with clinical markers of portal hypertension and appears safe in this study with an expanded selection of patients. EUS-LB can be performed safely at the same session as EUS-PPGM further adding value to the endoscopic evaluation of the patient with liver disease.
Disclosure: Presented at DDW

Expanding the horizons for early colonic cancer

16:00-17:30 / F2

OP107 COVERT CANCER IN COLONIC POLYPS: SIZE DOES MAKE A DIFFERENCE!

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Introduction: Colorectal polyps with overt endoscopic features of invasive cancer are referred for surgery. However, polyps without overt features might still harbour cancer. We aim to identify incidence of such covert cancers in colorectal polyps to see if the 'resect and discard' strategy could be extended beyond diminutive polyps.
Aims & Methods: We analysed outcomes of all patients who underwent screening colonoscopy between January 2007 to December 2018 and were found to have polyps. Data was prospectively collected on an online endoscopy reporting system and pathology reporting system. A using multinomial logistic regression.
Results: A total of 15906 polyps were removed at colonoscopy over the specified period. Mean size was 7.3 mm (range: 1 to 120 mm) with 82.5% polyps being < 10mm in size. 86.6% of all polyps were non pedunculated and 56.3% polyps were located in the left colon and rectum. The size, site, morphology and histology of these polyps is shown in table 1.
A histopathological diagnosis of polyp cancer was made in 104 /15906 polyps (0.65%). 94/104 polyp cancers (90.25%) were associated with non pedunculated morphology [OR 1.45, 95%CI 0.75-2.78 p=0.005].

No cancer was found in polyps < 5mm in size. However, the cancer incidence was 4/2365 (0.17%) in polyps 6-10mm [OR 1.10 95% CI 1.09-1.12, p<0.001], 58/1793 (3.25%) in polyps 10-30mm and 42/973 (4.30%) in polyps > 30mm in size. Risk of developing in cancer in polyps >10mm was significantly higher than in polyps 6-10 mm [OR 21.1 95% CI 7.9-58, p< 0.001]. 89 cancers were found in the left colon and rectum compared with 15 cancers in the right colon (85.5% vs 14.5%) [OR 1.98, 95%CI 0.9-3.1 p=0.007]. All 4 cancers found in the 6-10mm category were non-pedunculated polyps in left colon.

Size	Proportion %	Morphology %		Location %		Dysplasia %			
		Pedunculated	Non pedunculated	Right Colon	Left Colon	None	LGD	HGD	Cancer
< 5mm (N= 10775)	67.74	3.7	96.3	50.3	49.7	34.0	65.40	0.60	0.0
6-10mm (N= 2365)	14.87	31.75	68.25	30.8	69.2	21.33	74.44	4.06	0.17
10-30mm (N=1793)	11.27	46.9	53.1	31.0	69.0	12,20	68.89	15.67	3.25
>30mm (N= 973)	6.12	14.08	85.92	24.0	76.0	10.10	69.50	16.10	4.30

[Table 1]

Conclusion: We have demonstrated that the prevalence of covert cancer in colorectal lesions < 5mm is negligible and that of polyps 6-10 mm is very low (0.17%). All these cancers were in non-pedunculated polyps in left colon.This means that the 'resect and discard' strategy could be extended to 6-10 mm polyps in right colon and potentially to pedunculated polyps in left colon.
Cancer risk, however, increased more than 20 fold in polyps between 1-3 cm (3.25%) and 25 fold in polyps > 3 cm (4.3%). This calls for careful resection (preferably en-bloc) and retrieval of these polyps to obtain all prognostic information.
Disclosure: Nothing to disclose

OP108 APPLICATION OF ARTIFICIAL INTELLIGENCE AND DEEP LEARNING ALGORITHM IN THE PREDICTION OF ADVANCED HISTOLOGY OF COLORECTAL ADENOMAS

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Introduction: Recognition of high grade dysplasia or intramucosal malignancy in colorectal polyps is of critical importance before polypectomy to ensure that the optimal operative endoscopic method is selected for the removal. This is currently mainly based on expert opinions. Therefore, we developed an artificial intelligence-based decision support system (AI-DSS) that can differentiate between low- and high-grade dysplasia or intramucosal neoplasia in adenomatous polyps.
Aims & Methods: In the present study our aim was to analyze the effectiveness and accuracy of an AI-DSS in the prediction of advanced histology. We took still images from videos (colonoscopy containing colorectal adenomas with low- and high-grade dysplasia). We enrolled 1033 HD images of a total of 91 polyps (85 patients, 57.45% male, 56.4 average age), and we set up and trained a deep learning model with these images. The images went trough a pre-process algorithm, images of malignancies (invasive cancer), and low-quality images were excluded from both the train and test sets. Using the Gradient-weighted Class Activation Mapping (Grad-CAM) technique, the software can visually explain via a „heatmap" which areas on the image contained key information for the decision.
Results: We trained the neural network with 480 images of 55 polyps with a histological diagnosis of low-grade dysplasia and 457 images of 41 polyps with high-grade dysplasia. 119 images of 17 polyps (7 with low-grade and 5 with high-grade dysplasia + 2 with intramucosal carcinoma) were used for the test set. The test group had more images of each polyp, the

program analysed all images, and the final conclusion regarding the polyp was based on the averaged results. Then the results of the AI-DSS were compared to the final histology. Thus, we achieved 82.35% accuracy with 81.82% sensitivity, 83.33% specificity, 90% PPV, 71.43% NPV.
Conclusion: AI-DSS is able to predict the advanced histology of the polyp and differentiate between adenomas with low- and high-grade dysplasia with high accuracy. This software can support everyday clinical decisions and even the training of endoscopists. Due to the nature of deep learning neural networks, accuracy of the software could be further increased with a higher number of polyp images. The software does not require medical expertise.
Disclosure: Nothing to disclose

OP109 ENDOSCOPIC SUBMUCOSAL DISSECTION FOR COLORECTAL MALIGNANT POLYPS. RESULTS OF A PROSPECTIVE MULTICENTER WESTERN COHORT

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Introduction: Endoscopic submucosal dissection (ESD) allows en bloc resection of early gastrointestinal tumours regardless of size, with an en bloc resection rate in colon around 91.7%[1], thus allowing an adequate histological examination. This is important in the resection of malignant polyps (those who invade the submucosal layer) as they carry a risk for LNM, that can be stratified in high or low risk according to the histological features.
Aims & Methods: Our aim was to describe the feasibility, technical success, en bloc resection rate and complications of ESD for colorectal malignant polyps in a western cohort.
We analyzed all the cases of colorectal ESD performed in polyps with histology showing submucosal or deeper invasion (at least pT1), that were recruited in 19 centers between January 2016 and January 2019 in a prospective Spanish study.
Stata software was used for statistical analysis. Categorical data were expressed as frequencies and percentages. Comparative data according to location was analyzed. Categorical data was compared using Pearson´s chi-squared test, and cuantitative data was compared with T student test.
Results: From a total of 851 colorectal ESDs, 58 (6.8 %) cases with submucosal or deeper invasion were evaluated.
Mean age of patients was 68 years old, being male 72%. ASA score was I-II in 39 patients, III in 18 and IV in 1.
The lesions were located in rectum n=21 (36%), sigmoid n=10 (17%), descending colon n=8 (13.7%), splenic flexure=2 (3.4%), transverse colon n=4 (7%), hepatic flexure n=3 (5%), ascending colon n=7 (12%), and cecum n=3 (5%).
Complete resection of the lesion was achieved in 48 cases (82.7%). The en bloc resection rate was 70.7% (n= 41). When comparing the results of ESD for malignant polyps according to location, the en bloc resection rate was

higher in the rectosigmoid compared to the rest of the colon (83.9% vs 55.5% respectively, p=0.02).

There were 10 (17%) aborted procedures due to technical reasons (2/10), perforation (2/10) or muscle retracting sign (6/10).

The mean size of the resection was 38.3mm x 30.7mm (CI 95% 33.9-42.7 for major axis, and 26.1-35.2 for minor axis).

Submucosal fibrosis was absent (F0) in 18 cases, it was mild (F1, white web-like structure in the submucosa) in 17 cases and there was severe fibrosis (F2, "white submucosa") in 23 cases (39.66%).

There were 6 (10%) intraprocedural bleeding, 3 (5%) delayed bleeding, 10 (17%) intraprocedural perforations and 2 (3.4%) delayed perforations.

There were a total of 30 (51.7%) surgeries: 19 (63% of surgeries) due to high risk histologic features, 10 for aborted ESD (mainly due to muscle retracting sign as discussed before), and 1 for delayed perforation.

There were 2 pT2 and 1 pT3 cases diagnosed after surgery due to aborted ESD.

LNM were positive in 6 cases (5 pT1N1 and 1 pT2N1).

Regarding the need for surgery, it was much lower after ESD in the rectum than in the colon, with 8 surgeries (38%) in rectum vs 22 surgeries (59%) in colon, p= 0.03.

Conclusion: ESD for malignant polyps in the distal colon (sigmoid and rectum) shows better results compared to more proximal locations.

In a Western population, the *en bloc* resection rate for malignant polyps proximal to sigmoid location is lower than expected for colorectal ESD according to current literature.

LST Granular	G. Nodular Mixed =18 G. Homogeneous = 2
LST NonGranular	NG Pseudodepressed=15 NG Flat = 4
0-Is	13
0-Ip	1
0-IIc or 0-IIc component	4
0-IIb	1

[Morphology of the lesions]

References: Fujiya M, Tanaka 1, Dokoshi T, et al. Efficacy and adverse events of EMR and endoscopic submucosal dissection for the treatment of colon neoplasms: a meta-analysis of studies comparing EMR and endoscopic submucosal dissection. Gastrointest Endosc 2015;81:583-95

Disclosure: Nothing to disclose

OP110 ENDOSCOPIC FULL-THICKNESS RESECTION IS FEASIBLE FOR T1 COLORECTAL CANCERS - A DUTCH NATIONWIDE PROSPECTIVE COHORT STUDY

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Introduction: For T1 colorectal cancer (CRC), endoscopic resection is an attractive alternative for surgical resection due to substantially lower morbidity and mortality. However, conventional polypectomy for T1 CRC often leads to suboptimal histologic risk assessment and colonic ESD is challenging. Exact risk stratification with certainty about resection margin status and the presence of histologic risk factors for lymph node metastasis (LNM) is crucial for further decision making. Allowing transmural resection, endoscopic full-thickness resection (eFTR) could potentially serve as a valid diagnostic and therapeutic primary treatment option for T1 CRCs as well as completion treatment after previous incomplete resection of low-risk T1 CRCs.

Aims & Methods: The aim of this study was to determine the technical success, clinical success and safety of eFTR for T1 CRCs. In our prospective multicenter cohort of all eFTR procedures performed between September 2015 and April 2019 in 21 Dutch hospitals, we evaluated all T1 related procedures. This included primary treatment for lesions with optical diagnosis of T1 CRC and secondary treatment after previous (potentially) incomplete resection of T1 CRC. To determine technical success, we studied the number of macroscopic complete (no macroscopic evidence of residual lesion judged by the endoscopist) *en bloc* resections. Other outcomes were clinical success (R0 resection with tumor-free lateral and deep resection margins and possibility of discrimination between high-risk versus low-risk T1 CRCs) and adverse events. A lesion was defined as high-risk if one of the following risk factors was present: poor differentiation, lymphatic or vascular invasion, deep submucosal invasion (≥1000 μm) or incomplete resection (R1/Rx resection).

Results: We included 247 procedures. Indications for eFTR were primary resection for suspected T1 CRCs (n=81) and re-resection after previous incomplete resection of T1 CRCs (n=166). Technical success of all procedures was achieved in 85.4% (n=211/247). No histopathology was obtained in 6.1% (n=15/247), because the lesion either could not be reached or retracted into the cap. In the remaining 232 cases amenable to eFTR, R0 resection rate was 88.8% (n=206/232). Final histopathology confirmed residual adenocarcinoma in 33.2% (n=77/232). Subgroup analysis showed adenocarcinoma in 85.5% (n=65/76) after primary resection and in 7.7% (n=12/156) after previous incomplete resection. Discrimination between high-risk versus low-risk T1 CRC was achieved in 97.4% (n=75/77). Low-risk T1 CRC was identified in 22.1% (n=17/77) and high-risk T1 CRC in 75.3% (n=58/77). In 46.6% (27/58) of the high risk cases, deep submucosal invasion was identified as the only risk factor for LNM. Additional surgery was performed in 41.4% (n=24/58) of the high risk cases, of which 87.5% (n=21/24) had no residual cancer or LNM. Endoscopic surveillance strategy

was initiated in 46.6% (n=27/58). The overall adverse event rate was 8.5% (n=21/247), with emergency surgery in 2.4% (n=6/247) for 2 immediate and 4 delayed perforations.

Conclusion: eFTR is a feasible and safe treatment for T1 CRCs, both as primary treatment and secondary treatment after previous incomplete resection. eFTR delivers optimal histology for risk assessment and leads to R0 resection rate in 88.8% overall, avoiding surgery in most cases. Further studies focussing on long term outcomes need to clarify the role of eFTR for scars after previous incomplete resection and as a primary treatment method for deep submucosal invasive T1 CRC.

Disclosure: Nothing to disclose

OP111 LONG-TERM OUTCOMES IN 944 T1 COLORECTAL CANCER AFTER ENDOSCOPIC AND SUGICAL RESECTION

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Introduction: Lymph node metastasis (LNM) occurs in 6-12% of patients with T1 colorectal cancer (T1-CRC). In some studies, the depth of submucosal invasion, histological type, lymphovascular invasion, and tumor budding have been reported as risk factors for nodal metastasis, and the remainders were classified into high-risk group. Recent studies reported that invasion depth only has no clinical impact to LNM of CRC. pT1b CRCs have a good prognosis if treated along guidelines. However, the high rate of recurrence has been reported in rectal pT1b CRCs when they were followed it up without additional surgical resection (SR). Therefore we aim to examine the recurrence rate and clinicopathological features associated with invasive recurrence after endoscopic resection for T1 CRC, in particular in rectum.

Aims & Methods: A total of 944 patients with T1 CRCs treated by endoscopic resection (ER) or SR from January 2000 to April 2018 at our unit were analyzed retrospectively. The exclusion criteria were as follows; 1) patients with FAP, HNPCC, or IBD, 2) patients with active malignant diseases in any other organs, 3) patients with synchronous or metachronous advanced colorectal cancer, 4) patients with T1a-CRCs treated by primary SR and 5) follow up periods. We evaluated the invasive recurrence rate and clinicopathological features of 883 T1-CRCs.

Results: A total of 883 patients were involved according to criteria of this study (median follow-up period: 76 months). Of 883 patients, 246 patients underwent ER alone, 60 of 246 patients were followed-up without additional SR. 251 patients underwent ER+SR, and 386 patients underwent primary SR. 246 patients in ER alone were divided into 186 patients in ER-L (Low risk) and 60 patients in ER-H (High risk). 637 patients in SR (ER+SR and primary SR) were divided into 281 patients in SR-L (Low risk) and 356 patients in SR-H (High risk). In ER alone, 2 patients were cancer death. The outcomes of ER-L and ER-H were that 0% vs 8.3% (5 of 60 patients) in recurrence rate (RR). ER-H was tended to be higher in recurrence than ER-L. In 5 patients with recurrence in ER-H, tumor location were all rectum. In 637 patients in ER+SR and primary SR, Synchronous LNM occurred in 10.5%. The outcomes of SR-L and SR-H were that 3.9% (11 of 280 patients) vs 15.7% (56 of 357 patients). SR-H was tended to be higher in Synchronous LNM than SR-L, and a sub-analysis showed that primary treatment and lymph invasion and vascular invasion were equivalent to the risk factors of Synchronous LNM (p< 0.01). In SR, 4 patients were cancer death. The outcomes of SR-L and SR-H were that 0% vs 2.2% (8 of 357 patients) in RR. Synchronous LNM was the only factor that contributed significantly to increase recurrence in SR (p< 0.01).

Conclusion: pT1b CRCs have a good prognosis if treated along guidelines. The invasive recurrences for T1 CRC in our study was 1.5% overall. Our results suggested that a risk factor of recurrences in ER alone was only rectum. Therefore surgery should be considered in addition to ER regardless of the risk factors in pT1b rectal CRCs. We didn't experience recurrence in SR-L, but experienced 8 recurrences (2.2%) in SR-H. So careful follow-up is required even in high-risk group undergoing surgery that included lymph node dissection.

Disclosure: Nothing to disclose

OP112 FULL-THICKNESS RESECTION BY USING LAPAROSCOPY ENDOSCOPY COOPERATIVE SURGERY (LECS) TO OVERCOME THE LIMITATIONS OF ENDOSCOPIC RESECTION FOR COLORECTAL NEOPLASMS

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Introduction: We established a new procedure, laparoscopy endoscopy cooperative surgery (LECS) applied with endoscopic submucosal dissection (ESD) technique to overcome the limitations of endoscopic resection for colorectal tumors. In this report, we clarify the feasibility of performing a safe full-thickness resection with an adequate surgical margin by LECS procedure.

Aims & Methods: We performed full-thickness resection for 18 colorectal tumors in 18 patients (male: female 11:7; mean age, 65.8 years) by LECS. The clinicopathological outcomes of these 18 cases and the feasibility of full-thickness resection were evaluated retrospectively.

The indications for LECS were as follows: 1) intramucosal cancer and adenoma (Vienna Classification; Category 3, 4) accompanied by severe fibrosis in the submucosal layer (tumor recurrence after endoscopic or surgical resection), 2) intramucosal cancer and adenoma involving the diverticulum or appendix, and 3) intraluminal or intramural growth-type submucosal tumors.

Results: We successfully performed full-thickness resection using LECS in 18 cases (intramucosal cancer [n=6], adenoma [n=10], schwannoma [n=1], and gastro-intestinal stromal tumor [GIST] [n=1]. The mean tumor size was 22.2mm (range, 8-41mm). LECS was successfully performed in 18 all cases without conversion to open surgery; the R0 rate was 100%. The indications for LECS were as follows: involvement of the appendix (n=7), tumor accompanied by severe fibrosis (n=5), involvement of a diverticulum (n=3), submucosal tumor (n=2), and poor endoscopic operability (n=1). We experienced no adverse events (*e.g.*, grade 3 or more of Clavien-Dindo classification), and the mean hospital stay was 6.4(range, 4 to 12) days. All patients who were followed for ≥6 months (mean, 37.3 months; range, 11-80 months) showed no residual/local recurrence. Thus, the use of the ESD technique in LECS, can achieve a safe oncological margin in cases involving colorectal tumors.

Conclusion: LECS was a safe, feasible, minimally-invasive procedure that achieved the full-thickness resection of colorectal tumors and which showed excellent clinical outcomes.

References: [1] Fukunaga Y, Tamegai Y, Chino A, et al: New technique of en bloc resection of colorectal tumor using laparoscopy and endoscopy cooperatively (laparoscopy and endoscopy cooperative surgery - colorectal). Dis Colon Rectum 2014; 57, 2: 267-271 [2] Tamegai Y, Fukunaga Y, Suzuki S, et al: Laparoscopic and endoscopic surgery (LECS) to overcome the limitations of endoscopic resection for colorectal tumors. Endoscopy Int open 2018; 06: E1477-E1485

Disclosure: Nothing to disclose

Perianal fistula in Crohn's disease
16:00-17:30 / F3

OP113 STEP-UP FECAL MICROBIOTA TRANSPLANTATION: TARGETING COMPLAINTS IN CROHN'S DISEASE

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Introduction: The benefits of fecal microbiota transplantation (FMT) in Crohn's disease (CD) is unclear.

Aims & Methods: This real-world study aims to evaluate FMT's potential therapeutic targets in CD. FMT for CD as a registered trial (NCT01793831) was performed from October 2012 to December 2017. Clinical response was assessed at 1 month and 3 months after step-up FMT. We defined seven major complaints and recorded them as 1 (yes) or 0 (no) in the long-term follow up for each patient, which include abdominal pain, diarrhea,

hematochezia, fever, steroid-dependence, enterocutaneous fistula, active perianal fistula. Step-up FMT strategy includes: step 1: single FMT; step 2: ≥ 2 FMTs; step 3: FMT(s) followed by immunosuppressant or enteral nutrition. Potential predictors for non-response to FMT were analyzed.

Results: Totally 174 patients completed follow-up. Median follow-up was 28 (IQR 12-47) months. 74.7% (130/174) and 67.2% (117/174) of patients achieved clinical response at one month and three months after FMT. The total complaint score decreased significantly at 3, 6, 12, 24, 36 months after FMT. 71.9% (100/139), 68.3% (95/139), 64% (89/139), 56.5% (65/115), and 52.2% (47/90) of patients had abdominal pain improvement at 3, 6, 12, 24, 36 months after FMT, respectively. 61.4% (89/145), 57.9% (84/145), 53.8% (78/145), 44.4% (52/117), 42.2% (38/90) of patients had diarrhea improvement at 3, 6, 12, 24, 36 months after FMT, respectively. 55% (11/20) of steroid-dependent patients were able to discontinue steroids after FMT. Disease duration > 2 years (p = 0.011) was associated with poor response to FMT.

Conclusion: Step-up FMT strategy could be an effective therapeutic option for CD-related complaints.

Disclosure: Nothing to disclose

OP114 PERIANAL LESIONS IN CROHN'S DISEASE AT DIAGNOSIS: ANALYSIS OF EPIMAD REGISTRY FROM 2007 TO 2012 IN A POPULATION BASED-STUDY

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Introduction: Perianal lesions (PL) affect up to 26% of Crohn´s disease (CD) patients in the first two decades after diagnosis and are associated with poor outcomes.[1] Data concerning evaluation and clinical management of PL at diagnosis are limited.[2,3]

Aims & Methods: To perform a population based-study to characterise CD patients presenting with PL at diagnosis and describe their initial diagnosis and assoicated therapeutic management.

All CD patients diagnosed between 2007 and 2012 were extracted from a French multi-centre prospective registry (EPIMAD Registry).[4] PL were defined as the presence of fistula or abscess at CD diagnosis. For all patients with PL at diagnosis, complementary data were collected via a standardised questionnaire through examination of gastroenterologist and surgeon records by a university proctologist. The following variables were described: clinical examination, perianal resonance imaging (magnetic resonance imaging [MRI]), echo-endoscopy, examination under general anesthesia (GA) and medical and/or surgical management within the first three months after CD diagnosis. Associated factors with PL at CD diagnosis were identified using a multivariate logistic regression.

Results: Among the 2,906 patients with CD diagnosed between 2007 to 2012, 116 (4%) had PL at CD diagnosis. Forty-four percent of patients were women, the median age at diagnosis was 25 years (IQR: 19-39) and 51 (45%) patients had a previous history of PL. Ileocolonic CD (L3) was predominant in 51 patients (47%); one patient (1%) had only perianal involvement and 51% of patients presented rectal lesions. Patients could present one or more PL: 81% had fistula (including 12 rectovaginal fistulas) and 58% had abscess; one patient (1%) had anal stenosis. An examination under GA was performed in 50% of patients, MRI in 34% of patients and an echo-endoscopy in 1 case. For initial therapeutic management of CD: 63% of patients received antibiotics, 42% 5-ASA and 47% steroids. Twenty-seven percent of patients received azathioprine, 29% anti-TNF therapy (87% infliximab) and 13 (12%) patients received combination therapy. Surgery was performed in 64 patients (57%) with 41 abscess drainages, 25 seton drainages, 16 fistulotomy and 2 diverting ileostomy. Multivariate logistic regression analysis found that male sex (p = 0.006), an absence of abdominal pain (p = 0.003) and colonic location (p = 0.02) were significantly associated with the presence of PL at CD diagnosis.

Conclusion: In this large population-based study, the proportion of patients with PL at CD diagnosis was 4%. Male sex, absence of abdominal pain, and colonic location were associated with the presence of PL at CD diagnosis. Surgery was performed in over half of the cases. An immuno-

suppressant, anti-TNF or combination therapy was respectively prescribed for 27%, 29% and 12% of cases, reflecting the current approach for treating CD patients with PL. Further exploration of treatment options after CD diagnosis is warranted.

References: 1. Schwartz DA, Loftus EV Jr, Tremaine WJ, et al. Gastroenterology 2002;122: 875-880. 2. Gomollón F, Dignass, A, Annese V, et al. J Crohns Colitis 2016;11: 3-25. 3. Gottgens KW, Jeuring SF, Sturkenboom R, et al. Eur J Gastroenterol Hepatol 2017;29: 595-601. 4. EPIMAD (2019) Retrieved from http://epimad.chru-lille.fr/historique/index.html. (Last accessed: April 2019).

Disclosure: P. Wils has received lecture fees from Takeda and Ferring and travel expenses from Janssen, Hospira, and Biogaran A. Leroyer has no financial disclosures or potential conflicts of interest to disclose M. Fumery has no financial disclosures or potential conflicts of interest to disclose A. Fernandez Nistal is an employee of Takeda D. Bojic is an employee of Takeda R. D´Ambrosio is an employee of Takeda H. Sarter as no financial disclosures or potential conflicts of interest to disclose G. Savoye has received lecture fees from MSD, Janssen, Takeda, Pfizer, Tillots and Mayoly and travel support from Takeda and Ferring Pharmaceutical C. Gower-Rousseau has no financial disclosures or potential conflicts of interest to disclose B. Pariente has received consulting fees from AbbVie, MSD, Takeda, Janssen, Lilly, Pfizer, and Biogaran and lecture fees: Abbvie, MSD, Takeda, Janssen, and Ferring

Shifting paradigms in oesophageal cancer management
16:00-17:30 / Barcelona

OP115 THE DETECTION OF ESOPHAGEAL SQUAMOUS CELL CARCINOMA IN ENDOSCOPIC MOVIES BY THE ARTIFICIAL INTELLIGENCE USING CONVOLUTIONAL NEURAL NETWORKS

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Introduction: Esophageal cancer is the eighth most common cancer worldwide, and the sixth cause of death. When esophageal cancer is diagnosed in advanced stage, it will require highly invasive treatments and its prognosis will be poor, thus it is important to detect in early stage. In recent years, artificial intelligence (AI) using deep learning has made remarkable progress in various medical fields, and we had reported the great ability of artificial intelligence to detect esophageal cancer including squamous cell carcinoma (SCC) and adenocarcinoma in still pictures.

Aims & Methods: We demonstrated the diagnostic ability of AI to detect superficial esophageal SCC in movies.

We retrospectively collected 8428 training still images of esophageal cancer that was histologically proven to be SCC or adenocarcinoma, including 6026 white light imaging (WLI) and 2402 narrow band imaging (NBI), from Cancer Institute Hospital, Tokyo, Japan from 2014 to 2017. These images were used to develop deep learning through a convolutional neural networks (CNNs) to detect esophageal cancer.

Then we prepared 80 test movies of 40 patients both in WLI and in NBI, including 20 patients with 22 superficial esophageal SCC and 20 patients with no esophageal cancer to evaluate the accuracy of AI diagnosis. All cases of esophageal cancer were confirmed to have no other cancer using WLI, NBI, iodine staining, and follow-up endoscopy after the treatment.

In the movies, we inserted endoscopy from cervical esophagus to esophagogastric junction in the speed of 2cm /sec. AI diagnosed SCC when the lesions were detected for 0.06 sec.

Results: The AI correctly diagnosed 81.8% (18/22) of esophageal cancers both in WLI and in NBI. Of them, 45.4% (10/22) of cancers were diagnosed with WLI and 77.2% (17/22) with NBI. In contrast, the AI misdiagnosed 31 non-cancerous lesions, which caused low positive predictive value (PPV) (36.7%). However, these sensitivity and PPV in movies were not so different from in still pictures (sensitivity 98%, positive predictive value 54%). The misdiagnosed lesions included scars of endoscopic resection (3 lesion), esophagogastric junction (7 lesions), shadows of esophageal lumen (15 lesions). Inflammation of esophageal mucosa (6 lesions). This can be

corrected by deep learning about each normal structure and benign lesion, which will surely reduce false positives and improve the PPV significantly. Furthermore, because endoscopists will never think esophagogastric junction or shadows of esophageal lumen as cancer, considering the practical use of this system, this PPV is not so high but acceptable.

The missed cancers were less than 1 cm in size or in background inflammation. It was very difficult to detect these lesions with WLI or NBI even by experienced endoscopist in the movies, because of their speed and indistinguishable lesions.

Conclusion: AI could detect superficial esophageal SCC in movies with high sensitivity, same as in still pictures. This system would well support endoscopists in real time during endoscopic examinations in the near future.

Disclosure: Nothing to disclose

OP116 WITHDRAWN

OP117 CLINICAL EFFICACY OF THE ESOPHAGEAL TRIAMCINOLONE ACETONIDE-FILLING METHOD: A NOVEL STENOSIS-PREVENTIVE PROCEDURE AFTER EXTENSIVE ESOPHAGEAL ENDOSCOPIC SUBMUCOSAL DISSECTION

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Introduction: Endoscopic submucosal dissection (ESD) for extensive esophageal carcinomas causes severe esophageal stenosis requiring endoscopic balloon dilation (EBD), but a standard prophylactic treatment has not been established. As a novel procedure for the local steroid administration, we developed the esophageal Triamcinolone Acetonide (TA)-filling method. This method fills the esophagus with a saline solution containing 80 mg TA for a certain time to infiltrate the drug evenly into extensively resected surface [1].

Aims & Methods: The aim of this study is to analyze the clinical efficacy and safety of the esophageal TA-filling for stenosis-prevention after extensive esophageal ESD. We enrolled a total of 44 consecutive patients with esophageal cancer requiring subcircumferential ESD, which is three quarters of the circumference or more horizontal resection but not circumferential. They had no previous treatment for the lesions, such as endoscopic resection or radiation therapy. Esophageal TA-filling was performed the day after ESD and one week later, and follow-up endoscopy was performed every 2 weeks until complete re-epithelialization. We treated severe stenosis preventing endoscope passage with EBD and additional TA-filling, and mild stenosis allowing endoscope passage with additional TA-filling only.

Primary endpoint was the incidence of severe stenosis, which is reportedly 66% to 75% after subcircumferential ESD without any preventive procedure [2-4]. Setting the clinically meaningful preventive effect to 30% incidence reduction, we determined lower boundary of the target incidence value at 40%. Secondary endpoints were total number of EBDs, execution rate of additional TA-filling, time to initial stenosis and complete re-epithelialization without stenosis, dysphagia score, and adverse events. Dysphagia score was estimated based on 5 grades: each grade of 0, 1, 2, 3, and 4 denoted the ability to eat a normal diet, some solid foods, only semisolid foods, liquids only, and nothing, respectively [5]. The horizontal resection range of ESD was divided into three grades (grade 1; ≥9/12 and < 10/12, grade 2; ≥10/12 and < 11/12, grade 3; ≥11/12 but not circumferential), and analyzed statistically for correlation with the endpoints.

Results: All lesions in 44 enrolled patients were resected en bloc. The horizontal resection grade was grade 1 in 19 patients, grade 2 in 14, and grade 3 in 11. All patients concretely followed the study protocol. The median size of the lesions and the resected specimens was 38 (22-70) mm and 52 (32-85) mm, respectively.

The incidence of severe stenosis was 6.8% (3/44; 1.4%-18.6%), which was sufficiently lower than target incidence value, showing a statistically acceptable stenosis-preventive effect. EBD was performed median 2 (1-3) times in these 3 patients. 10 patients demonstrated mild stenosis. Time to initial stenosis was median 3 (3-5) weeks, and rate of additional TA-filling was 29.5% (13/44); 5.2% (1/19) for grade 1 resection, 28.5% (4/14) for grade 2, and 63.6% (7/11) for grade 3 (P< .05). Median time to complete

re-epithelialization was 6 weeks (range, 5-14). Dysphagia score deteriorated to 1 to 2 in 31.8% (8/44), but showed a final score of 0 after complete re-epithelialization in 93.1% (41/44). No severe adverse events occurred.

Conclusion: The esophageal TA-filling method is highly effective for preventing severe stenosis after subcircumferential esophageal ESD, and the procedure is simple, feasible, and safe. However, grade 2 or higher resection has a high risk for stenosis.

References: 1. Shibagaki K, Ishimura N, Oshima N, et al. Esophageal triamcinolone acetonide-filling method: a novel procedure to prevent stenosis after extensive esophageal endoscopic submucosal dissection (with videos). Gastrointest Endosc 2018;87:380-89. 2. Katada C, MutoM, Manabe T, et al. Esophageal stenosis after endoscopic mucosal resection of superficial esophageal lesions. Gastrointest Endosc 2003;57:165-9. 3. Hashimoto S, Kobayashi M, Takeuchi M et al. The efficacy of endoscopic triamcinolone injection for the prevention of esophageal stricture after endoscopic submucosal dissection. Gastrointest Endosc 2011;74:1389-93. 4. Hanaoka N, Ishihara R, Takeuchi Y, et al. Intralesional steroid injection to prevent stricture after endoscopic submucosal dissection for esophageal cancer: a controlled prospective study. Endoscopy. 2012;44:1007-11. 5. Knyrim K, Wagner HJ, Bethge N. A controlled trial of an expansile metal stent for palliation of esophageal obstruction due to inoperable cancer. N Engl J Med 1993;329:1302-7.

Disclosure: Nothing to disclose

OP118 COMPARABLE LONG-TERM OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION AND ESOPHAGECTOMY FOR EARLY ESOPHAGEAL SQUAMOUS CELL NEOPLASIA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Endoscopic submucosal dissection (ESD) has become treatment of choice for superficial esophageal squamous cell neoplasia (ESCN) owing to the minimal invasiveness and high rate of complete resection. However, it is not clear whether ESD has similar long-term outcome compared to esophagectomy.

Aims & Methods: This study is aimed to evaluate the long-term outcomes of ESD with comparison of that to esophagectomy in patients with superficial ESCN. Comprehensive literature search and review were conducted using PubMed, Cochrane Library, and ProQuest databases through January 2019. The inclusion criteria were studies having > 20 cases and reporting survival data longer than 3 years with ESD for superficial ESCN. The exclusion criteria were those with incomplete data, or inability to extract data from mixture results with adenocarcinoma or other treatment modality. All extracted data were present and analyzed either with the original format or following appropriate calculation. The primary outcomes were overall survival, disease free survival and disease specific survival at 3 and 5 years. Secondary outcomes included adverse events, R0 resection, locoregional recurrence and distal metastasis. Meta-analyses were performed with hazard ratio (HR) for survival analysis and odds ratio (OR) for other variables using appropriate models and expressed with 95% confidence interval (CI).

Results: Total 21 eligible retrospective studies and 3796 patients were included. Among these, 5 studies compared ESD and esophagectomy and the others only reported the outcome with endoscopic treatment. For all the cases of ESD, the distribution of tumor invasion depth was 52.0% for m1-m2, 43.2% for m3-sm1 and 4.7% sm2 or deeper; however, up to 35.6% of cases had discrepancy between clinical and pathological stage. The mean R0 resection rate was 92%, and proportion of lesions exceeding 50% and 75% of circumference were 36.5% and 8.6%. The local recurrence, metachronous recurrence and nodal/distal metastasis rate of ESD were 1.8%, 8.5%, and 3.3% respectively. Severe complication of ESD included perforation (3.4%) and stricture (9.5%), although endoscopic treatment was successful in most cases, the median sessions of balloon dilatation ranged from 2-8 and more procedures were necessary for cervical lesions.

Overall survival and cancer specific survival at 5-year were 88% and 99%. In terms of the comparison between ESD and esophagectomy, there were no difference in the 5-year overall survival (HR = 0.66, 95% CI 0.39 - 1.11) and recurrence free survival (HR = 1.52, 95% CI = 0.74 - 3.09). Despite the similar perioperative mortality rate in both groups, the adverse events were remarkably lower in ESD group (19.8% vs. 44.0%, OR = 0.29, 95% CI = 0.19 - 0.43).

Conclusion: For superficial ESCN, ESD is highly effective with less morbidity than esophagectomy. It should be considered as the first line treatment in centers with expertise.

	Yamauchi (2017)	Yuan (2018)	Min (2018)	Takeuchi (2018)	Zhang (2018)
Case Number	ESD = 54, OP = 51	ESD = 69, OP = 47	ESD = 120, OP = 120	ESD = 73, OP = 54	ESD = 322, OP = 274
Lesion size (Median, mm)	Not recorded	ESD = 45.9, OP = 52.1	ESD = 17, OP = 16.4	ESD = 20, OP = 32	ESD = 26, OP = 20
Lesions > 3/4 circumference	Not recorded	ESD = 18, OP = 23	Not recorded	ESD = 13, OP = 22	Not recorded
R0 resection (%)	Not recorded	ESD 92.7%, OP = Not recorded	Not recorded	ESD 78.1%, OP 88.9%	ESD 91.9%, OP 98.2%
Adverse events (%)	ESD 29.6%, OP = 49.1%	ESD 43.4%, OP = 72.3%	ESD 18.5%, OP = 55.5%	ESD 10.9%, OP = 38.8%	ESD 15.8%, OP = 31.3%
M1-M2 invasion	Not recorded	ESD = 52, OP = 24	ESD = 64, OP = 63	ESD = 10, OP = 7	ESD = 107, OP = 24
M3-Sm1 invasion	Not recorded	ESD = 17, OP = 23	ESD = 35, OP = 37	ESD = 41, OP = 18	ESD = 215, OP = 250
Sm2 or deeper	Not recorded	ESD = 0, OP = 0	ESD = 21, OP = 20	ESD = 22, OP = 29	ESD = 0, OP = 0
Lymphovascular invasion	Not recorded	ESD = 1, OP = 0	ESD = 16, OP = 9	ESD = 17, OP = 31	ESD = 11, OP = 36

[Baseline characteristics in studies comparing the outcomes of ESD and esophagectomy]

References: 1.Ono et al. Gastrointestinal endoscopy. 2009;70(5):860-6. 2.Takahashi et al. Gastrointestinal endoscopy. 2010;72(2):255-64 3.Toyonaga et al. Surgical endoscopy. 2013;27(3):1000-8. 4.Joo et al. Gut and liver. 2014;8(6):612-8. 5.Nakagawa et al. American journal of gastroenterology. 2014;109(3):348-56. 6.Ikeda et al. Internal medicine. 2015;54(22):2803-13. 7.Kim et al. Gut and liver. 2015;9(4):470-7. 8.Probst et al. Endoscopy. 2015;47(2):113-21. 9. Tsujii et al. Endoscopy. 2015;47(9):775-83. 10.Park et al. The Korean journal of internal medicine. 2016;31(6):1064-72. 11.Park et al. Clinical endoscopy. 2016;49(2):168-75. 12.Lizuka et al. Endoscopy international open. 2017;5(8):E736-e41. 13.Nagami et al. Digestive and liver disease 2017;49(4):427-33. 14.Yamauchi et al. UEG 2017 Spain. 2017;5(5 Supplement 1):A361. 15.Baisi et al. Surgical endoscopy. 2018, Epub ahead of print. 16.Berger et al. Endoscopy. 2019 Apr;51(4):298-306. 17.Furue et al. Surgical endoscopy. 2018, Epub ahead of print. 18.Min et al. Gastrointestinal endoscopy. 2018;88(4):624-33. 19.Qi et al. Endoscopy. 2018;50(9):839-45. 20.Takeuchi et al. Gastrointestinal endoscopy. 2018;88(3):456-65. 21.Zhang et al. Clinical gastroenterology and hepatology. 2019;17(1):73-81.e3.
Disclosure: Nothing to disclose

OP119 LASTING SYMPTOMS AFTER ESOPHAGEAL RESECTION (LASER) – EUROPEAN MULTI-CENTER CROSS-SECTIONAL STUDY

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Introduction: Long-term functional outcomes and the associations to health-related quality of life (HRQOL) after esophagectomy is largely unknown.
Aims & Methods: This multi-center European study aimed to identify the most prevalent symptoms, and those with the greatest impact upon HRQOL among patients surviving more than one-year after esophagectomy for cancer, and to develop a clinically relevant tool.
Twenty European centers participated in the study. Patients who underwent esophagectomy for esophageal cancer between 2010 and 2015, and were disease-free at least one year postoperatively were invited to complete the LASER questionnaire, EORTC-QLQ30 and OG25. LASER questionnaire items that were associated with a poor HRQOL as identified by EORTC-QLQC30 and OG25 were identified by multivariable linear and logistic regression analysis and combined to form a tool, which was tested using receiver operating characteristics curve analysis.
Results: A total of 876 of 1081 invited patients responded to the questionnaire, giving a response rate of 81%. Of these, 66.9% stated in the last 6 months they had had symptoms associated with their esophagectomy and 52.4% of patients had sought medical treatment for their symptoms. Ongoing weight loss was reported by 10.4% of patients while 32.4% was struggling to maintain their body weight, and 18.8% of patients required supplemental oral nutrition. Only 13.8% of patients returned to work with the same activities as before.
Three LASER symptoms in multivariate analysis were correlated with poor HRQOL; pain on scars on chest (Odds ratio (OR) 1.27; 95% CI 0.97-1.65), low mood (OR 1.42; 95% CI 1.15-1.77) and reduced energy or activity tolerance (OR 1.37; 95% CI 1.18-1.59). The areas under the curves for the development and validation datasets were 0.81±0.02 and 0.82±0.09 respectively.
Conclusion: The three key symptoms identified in this study should be further validated, and could be used in clinical practice to identify patients who require increased long-term term support in survivorship.
Disclosure: Nothing to disclose

OP120 ENDOSCOPIC THERAPY REPLACES SURGERY FOR CLINICAL T1 OESOPHAGEAL CANCER IN THE NETHERLANDS: A NATIONWIDE POPULATION-BASED STUDY

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Introduction: Oesophageal cancer is the eight most common cancer worldwide and the sixth leading cause of cancer related mortality. The incidence of oesophageal cancer increases worldwide. Recent studies showed comparable survival after endoscopically or surgically treated oesophageal cancer in the United States and Asia. Survival after endoscopic resection or surgery of oesophageal cancer has not been investigated in a Dutch population.
Aims & Methods: This study will provide insight into the treatment and survival for patients with clinical T1 oesophageal and cardia cancer over a fifteen-year period between 2000 and 2014 in the Netherlands. Data were obtained from the nationwide population-based Netherlands Cancer Registry (NCR). All patients diagnosed with clinical in situ and T1 oesophageal or cardia cancer without lymph node or distance metastasis during the study period were extracted from the NCR. Primary outcome parameters were the trends in treatment modalities over time and relative survival of each treatment regime.
Results: A total of 1822 patients were diagnosed with a clinical in situ or T1 oesophageal or cardia cancer in the Netherlands between January 2000 and December 2014. Patients with metastatic disease (n=285) and/or unknown lymph node metastasis (n=513) were excluded. In total of 1020 patients were included. Almost half of the patients receive endoscopic therapy (44.9%), around a third underwent surgery (35.1%) and twenty per cent underwent other treatment (12.3%) or no treatment et al (7.7%). Patients who underwent surgery were significantly younger than patients treated with endoscopic therapy (median 64 years vs. 67 years; p < 0.0001). There were significantly more oesophagus carcinoma resected with endoscopic therapy compared to cardia carcinoma (96.1% vs. 79.6%; p < 0.0001) and the group with endoscopic therapy significantly had a clinical in situ tumour more often (p< 0.0001). The proportion of patients who received endoscopic treatment increased from 2.5% in 2000 to 64.1% in 2014. During the same period the proportion of patients who received surgery decreased from 57.5 to 17.1%.
The 5-year relative survival of all patients with clinical in situ or T1 oesophageal or cardia cancer was 70%. The 5-year relative survival after endoscopic therapy was 85% and after surgery 78%. Relative excess risk analyses showed significant difference in survival between patients in the endoscopic therapy group and patients in the surgery group after adjustment for age, sex, clinical TNM classification, morphology and tumour location (RER 1.80; CI interval 1.20-2.70; p< 0.001). In subgroup analysis, the 5-year relative survival of all patients with T1 oesophageal or cardia cancer was 66%. The 5-year relative survival after endoscopic therapy was 81%, after surgery 73%. Relative excess risk analyses for the subgroup T1 oesophageal or cardia cancer showed significant difference in survival between patients in the endoscopic therapy group and patients in the surgery group after adjustment for age, sex, clinical TNM classification, morphology and tumour location (RER 1.71; CI interval 1.14-2.55; p< 0.01).
Conclusion: Our results demonstrate an increase in endoscopic resections and a decrease of surgical treatment for in situ and T1 oesophageal/cardia cancer between 2000-2014 in the Netherlands. The relative 5-years survival after endoscopic treatment is high (85%) and significantly higher when compared to surgery (78%) which is different from previous studies.
Disclosure: Nothing to disclose

Different faces of microbiota along the digestive tract
08:30-10:00 / A1

OP121 COMPOSITION AND FUNCTION OF GUT MICROBIOTA AFFECTS THE RESPONSE RATE AND SURVIVAL OF MELANOMA PATIENTS TREATED WITH IMMUNE CHECKPOINT INHIBITORS

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Introduction: Immune checkpoint inhibitors (ICIs) have demonstrated strong clinical benefit in patients with irresectable cutaneous melanoma, with now an increased 1-year survival of up to 70%. Approximately 40% of patients, however, do not respond to ICI therapy, while 25% of patients develop serious adverse events. Previous studies in animal models and small-scale human studies identified a link between composition of gut microbiota and response to ICI therapy, but these studies showed low concordance and did not take into account common confounders such as patient sex, age, BMI as well as medications that alter composition of gut microbiom.
Aims & Methods: The aim of this study was to assess the effect of composition and function of gut microbiota on the response rate and survival of ICI-treated melanoma patients, while taking into account known factors that influence the composition of gut microbiome.
This study employed a strictly protocolized collection procedure to obtain high-quality fresh-frozen stool samples from 25 patients with metastatic melanoma before the start of ICI therapy. Twelve of these patients went on to respond to ICI therapy. Metagenomic shotgun sequencing was used to obtain a high-resolution profile of the gut microbiome composition and biochemical pathways encoded in the microbiome. Composition (192 bacterial taxa) and function (260 pathways) of microbiota were tested for association with ICI response, overall survival, and progression-free survival using multivariate associations with linear models (implemented in MaAsLin toolkit). These models included known factors that influence gut microbiota: age, sex, BMI, tumor M-stage (AJCC version 8), LDH-level (> 250 U/L vs. < 250 U/L), previous anti-melanoma therapy, type of therapy (anti-PD1 or anti-PD-1/anti-CTLA-4 combination), antibiotic use (yes/no), proton pump inhibitor use (yes/no) and colitis during ICI therapy (yes/no, any grade).
Results: We observed no differences in alpha-diversity and bacterial prevalence between responders and non-responders (p-value > 0.05). Multivariate analysis identified 68 taxa and 17 microbial pathways that showed differential abundance between responders and non-responders (FDR < 0.05), including previously reported associations with *Veillonella parvula, Bacteroides thetaiotaomicron, Akkermansia muciniphila, Escherichia coli* and *Actinomyces odontolyticus*. In addition, multiple taxa were associated with overall or progress-free survival, including *Streptococcus parasanguinis* (Overall survival HR: 6.9), Peptostreptococcaceae Family (Overall survival HR: 0.11, Progression-free survival HR: 0.18) and *B. massiliensis* (Progression-free survival HR: 3.79).
Conclusion: This study shows that composition and function of the gut microbiom influences the response to immune checkpoint inhibitors (ICIs) in patients with cutaneous melanoma. This suggests that manipulation of gut microbiota might be viable strategy to improve the response to ICIs.
Disclosure: Nothing to disclose

OP122 THE EFFECTS OF F. PRAUSNITZII ON CANDIDA ALBICANS GROWTH AND PATHOGENICITY AND RELATED MECHANISMS

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Introduction: Inflammatory bowel disease (IBD), including ulcerative colitis (UC) and crohn´s disease (CD). The pathogenesis of the disease is complex. It is believed that genetic, environmental, intestinal microbes and immune factors are involved in the occurrence and development of IBD, especially the intestinal flora disorder has become a research hotspot in recent years. The reduction of Faecalibacterium prausnitzii (F. prausnitzi) and the increase of the opportunistic pathogen Candida albicans are one of the important features of intestinal flora disorder in patients with IBD. Many studies have shown that Faecalibacterium prausnitzii and its supernatant can improve intestinal inflammation, regulate dysbacteriosis, maintain the homeostasis of the intestinal microenvironment, etc. Intestinal bacteria and fungi influence each other in many ways.Therefore, exploring the interactions between intestinal bacteria and fungi and its role in the development of IBD is of great significance to understand the intestinal micro-ecological environment.
Aims & Methods: F. prausnitzii and its supernatant were co-cultured with Candida albicans in vitro to observe the effects of F. prausnitzii and its supernatant on Candida albicans growth, hyphal and hydrolytic enzyme production capacities. To investigate whether F. prausnitzii and its supernatant can inhibit the growth and reproduction of Candida albicans by stimulating the expression of inflammasomes (NLRP6) and antimicrobial peptides (LL-37/BD-2/BD-3) and tight junction proteins(ZO-1, occludin) in intestinal epithelial cell.
Results:
1. It was found that the amount of C.albicans with F. prausnitzii and its supernatant co-cultured were significantly decreased compared with the control group by plate counting method.
2. It was found that the expressions of Hyphae-Specific Genes (BCR1, CDC24b, ECE1, HGC1, HWP1 and EFG1) and production of hyphal phase CA were inhibited and hydrolytic enzyme production capacities (Ep, Sap, and Ha)were dcreased when F. prausnitzii and its supernatant were co-cultured with CA.
3. Western blot analysis showed that F. prausnitzii and its supernatant may inhibit the growth of CA by stimulating IEC secretion of NLRP6, ASC, IL-1β/IL-18 and antibacterial peptides BD-2 and BD-3, but caspase-1 and LL-37 had no significant effect.
4. Western blot analysis showed that F. prausnitzii and its supernatant may enhance the intestinal mucosal barrier function by promoting the expression of IEC tight junction protein (occludin, zo-1).
Conclusion: F. prausnitzii and its supernatant have inhibitory effects on CA. The direct effects are as follows: inhibiting CA growth and reproduction, inhibiting the expression of CA Hyphae-Specific Genes (BCR1, CDC24b, ECE1, HGC1, HWP1 and EFG1), reducing production of hyphal phase CA, reducing the production of CA hydrolytic enzyme production capacities (Ep, Sap, and Ha). The indirect effect is by stimulating the expression of NLRP6, ASC, IL-1β/IL-18, BD-2, BD-3 and the tight junction proteins occludin and ZO-1 in IEC to inhibition the growth of CA.
Disclosure: Nothing to disclose

OP123 ALTERATIONS IN FUNGAL MICROBIOTA AFTER CHOLECYSTECTOMY IN PATIENTS

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Introduction: Fungal microbiota of the gastrointestinal tract is affected by many factors, such as pH, diet. After cholecystectomy, the gut physico-chemical environment changes, and the fungal microbiota may change accordingly. Notably, few reports focused on gut fungal microbiota after cholecystectomy. Therefore, we tended to investigate the differences and composition characteristics of gut fungal microbiota in patients after cholecystectomy.
Aims & Methods: We called on 104 people for this study, including 52 healthy controls (HC) and 52 post-cholecystectomy (PC) patients. 9 of the 52 PC patients accompanied with precancerous lesions and colorectal cancer (preCA_CRC). Fecal samples of all patients were collected for internal transcribed spacer (ITS) 3-4 rDNA amplicons sequencing to profile the overall structure of the fecal fungal microbiota. Based on the Operational Taxonomic Units (OTUs), fungal composition and the correlation analysis with environmental factors were analyzed, respectively.
Results: Fungal richness in PC patients was similar to the one in HC, but the composition was quite different. The abundance of exogenous pathogens *Alternaria*, *Aspergillus* and opportunistic pathogen *Candida* increased significantly; while *Malassezia*, *Vanrija* and protective genus *Ganoderma* had a remarkable reduction in PC patients. *Indicspecies* analysis showed that *Candida glabrata* and *Aspergillus unassigned* were characteristic species of PC patients, and *Candida albicans* was a characteristic species of HC. Previous studies suggested that *Candida glabrata* displayed more virulence factors, triggering host cell damage. The intraspecific competition of *Candida* may play an important role, and *Candida albicans* may suppress the growth of *Candida glabrata* in HC. About 10 kinds of indexes were collected as environmental factors for correlation analysis with fungal composition. As a result, we found that the duration after cholecystectomy was an independent factor, which mainly affected the composition of the fungal microbiota. Addtionally, according to the presence or absence of precancerous lesions and CRC, we divided PC patients into preCA_CRC and nonCA. We found that preCA_CRC patients had lower fungal richness than the nonCA patients with statistical difference. In addition, most species were reduced in abundance, such as *Pleosporales unassigned*, *Sordariales unassigned* and *Gibberella zeae*.
Conclusion: Our study showed a specific gut fungal composition in PC patients. The duration after cholecystectomy was an important environmental factor which affected fungal microbiota. It was suggested that the duration after cholecystectomy may be associated with the risk of relative diseases. The abundance of *Candida glabrata* may be associated with clinical long-term outcome in patients after cholecystectomy.
Disclosure: Nothing to disclose

OP124 NEXT-GENERATION SEQUENCING OF FAECAL MICROBIOTA IN ULCERATIVE COLITIS PATIENTS TOGETHER WITH CONSANGUINEOUS AND NON-CONSANGUINEOUS RELATIVES

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Introduction: The gut microbiota has been recognized as a relevant fingerprint to predict the development of inflammatory bowel disease (IBD) like ulcerative colitis (UC). Accordingly, inter-individual variation in the gut microbial community may reflect inter-individual variation in the risk of developing IBD or other diseases.
Further recently, the Next-Generation Sequencing (NGS) has been validated for determining bacterial species in faecal samples. Essentially, NGS is a molecular biology sequencing technique for the precise identification and assessment of bacterial species.

Aims & Methods: This study was to analyse faecal bacteria and establish a biomarker of disease activity in ulcerative colitis (UC) patients. The subjects were 82 patients with UC together with 61 healthy relatives as controls. Twenty-five patients had active UC (group I) and 57 had quiescent UC; 29 with mild inflammation in the large intestine (group II), and 28 without inflammation (group III). The patients' relatives were consanguineous (group IV, n=33), and non-consanguineous (group V, n=28). Faecal bacteria between groups I to V were compared by the t-test. The Discriminant Score (Ds) for each subject together with the quantity and the diversity of each bacterial variant which had significant difference were calculated. The Discriminant analysis in all five groups was done for Species. We calculated the Discriminant Score (Ds) in each case.

Results: We obtained 1011 varieties of bacteria as Phyla, Class, Order, Family, Genera and Species. 648 bacteria that were not considered important were excluded. The t-statistic was done on 363 bacteria between groups I to V. Significant difference was calculated in 18 Species, 10 Genera, and 4 Families. The Discriminant analysis was done on these 18 Species from all groups. The Ds value showed an increasing tendency in this order: group I < group II < group III < group IV < group V. Significant difference was calculated for group I vs group II, vs group III, vs group IV, and vs group V (P< 0.01); group V vs group I, vs group II, vs group III (P< 0.01), indicating a strong association between gut microbial species and the development of UC.

The diversity of Bacteroides Genus was higher in group V, but the quantities of Bacteroides Genus and the Bacteroides fragilis were higher in group I. Further, in group I, the amount of Bacteroides fragilis was increased, but the diversity of Bacteroides Genus was decreased, while in group V, the opposite result was observed. It's very interesting, and the balance can be key point between Bacteroides fragilis and the diversity of Bacteroides in UC activity. Considering Genus, Anaerococcus, Finegoldia and Peptoniphilus were dramatically increased in group I compared with group V. All these bacteria belong to Clostridiales Family XI. Incertae Sedis.

Conclusion: In this study, we compared 363 bacteria between active UC patient (groups I) to control (group V), significant difference was calculated in 18 Species, 10 Genera, and 4 Families. To our knowledge, this is the first report on so many bacteria being related to UC activity. Additionally, the Ds related to UC, or otherwise absence of UC in the five groups. Potentially, Ds might be a clinically relevant biomarker of disease activity in UC. This is the first application of the NGS and the Ds to the study of microbiota in UC patients, consanguineous and non-consanguineous relatives. Moreover we could obtain a lot of interesting results the quantity and the diversity of the bacteria, especially Bacteroides. Clinical trial No: UMIN000017103

Disclosure: Nothing to disclose

OP125 STRAIN LEVEL ANALYSIS OF *KLEBSIELLA PNEUMONIA* SHOWS ASSOCIATION WITH INFLAMMATORY BOWEL DISEASE AND DISEASE SEVERITY

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Introduction: *Klebsiella pneumoniae* (KP) is a bacterium mainly found in the human oral cavity, but also inhabiting human skin and gut. While it is primarily associated with bacterial inflammation of the lung recent research has identified that KP-strains can cause ulcerative colitis (UC) -like pathology in germ-free mice. The prevalence and abundance of KP in IBD patients has not been studied in detail, and it is unknown if strain composition of KP differs between healthy individuals and IBD patients. It is also unclear which specific KP strains are associated to clinical characteristics of IBD such as disease severity and location.

Aims & Methods: Aim of this study was to identify if KP is associated with inflammatory bowel disease in humans, and to identify IBD-specific strains of KP.

The study utilised whole metagenome sequencing to study the gut microbiota of 447 IBD patients (291 Crohn's disease cases and 156 cases with ulcerative colitis) and 933 population-based controls. Species-level composition of metagenomes was determined by aligning metagenomic reads to a database of unique marker genes, while KP strains were identified and quantified using reference-based approaches utilising genomes of 276 KP strains and 10,484 other bacterial species. Prevalence, relative abundance, and diversity of KP were tested against IBD-related clinical phenotypes, while unsupervised clustering and dimensionality-reduction approaches were used to study strain composition.

Results: Prevalence and relative abundance of KP were found to be significantly increased (p-value < 1.0×10^{-4}) in the gut of IBD patients (prevalence ≈ 10%) when compared to the general population (prevalence ≈ 2%), with a trend of increased prevalence of KP in more severe cases of UC (pancolitis, severe colitis, and patients who underwent colonic resection). Strain identification was considered if the relative abundance of a specific strain was above 10% of the total KP content in the sample. In total, 54 strains of KP were identified and quantified, of which 33 were found only in IBD patients (18 in UC, 6 in CD and 9 in both CD and UC patients). Our results also show concordance with previous in-vitro studies: Two KP strains previously described to cause UC-like pathology and strong immune response in mice (strains KP-700603 and KP-2H7) were found to be specific to gut of UC patients in our cohorts.

Conclusion: We demonstrate the increase in prevalence of KP in the gut microbiome of IBD patients, and show that certain strains of KP are specific to IBD patients. Thus, KP may be involved in IBD and has a potential to be exploited as novel target for alleviating the severity of the disease.

Disclosure: This study was partially funded by Takeda Pharmaceuticals Inc., United states.

OP126 RISK OF GASTRIC CANCER AFTER *HELICOBACTER PYLORI* ERADICATION IN DIABETES MELLITUS PATIENTS: A TERRITORY-WIDE STUDY WITH PROPENSITY SCORE ANALYSIS

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Introduction: Whether diabetes mellitus (DM) increases gastric cancer (GC) risk remains controversial in prior studies due to inadequate adjustment for important risk factors including *Helicobacter pylori* (HP) infection, glycemic control, concomitant medication usage and cancer sites.

Aims & Methods: We aimed to investigate whether type II diabetes mellitus (DM) increased GC risk in patients after HP treatment.

This was a territory-wide cohort study of patients aged ≥45 years who had received clarithromycin-based triple therapy for HP between 2003 and 2012. Data were retrieved from the public electronic health database. Observation started from HP therapy to GC diagnosis, death or end of study (December 2015). Exclusion criteria included type I DM, GC diagnosed within first year of HP therapy, prior GC or gastrectomy, and failure of HP eradication. The adjusted hazard ratio (aHR) of GC with DM was calculated by Cox model with propensity score regression adjustment for 20 covariates (age, sex, smoking, alcoholism, past history of gastric and duodenal ulcers, other comorbidities [atrial fibrillation, ischemic heart disease, congestive heart failure, chronic renal failure, cirrhosis, stroke, hypertension and obesity] and medications [aspirin, non-steroidal anti-inflammatory drugs (NSAIDs), cyclooxygenase-2 (COX-2) inhibitors, and proton pump inhibitors (PPIs)]).

Results: Of 46,460 eligible patients, 6,900 (14.9%) had DM. During a median follow-up of 7.1 years (IQR:4.8-9.8) with 337,313 person-years, 153 (0.33%) developed GC at a median age of 72.4 years (IQR:63.8- 82.6). There were 31 (20.3%) cardia cancers and 88 (57.5%) non-cardia cancers, while the remaining 34 (22.2%) cases did not have site specified. DM was associated with an increased GC risk (adjusted HR:1.67; 95% CI:1.08-2.58). This association was biased towards null if concomitant medication usage was not adjusted (adjusted HR:1.30; 95% CI:0.85-1.99), with the most influential effect from statins (**Table**). On the other hand, HR increased to 1.92 (95% CI:1.28-2.90) without adjusting for comorbidities. Stratified analysis shows the risk was increased for cardia cancer only (aHR:3.40, 95% CI:1.45-7.97), in those with suboptimal DM control (time-weighted average HbA1c ≥6.0%; aHR:1.68, 95% CI: 1.07-2.63) and metformin non-users (aHR 2.59, 95% CI 1.41-4.74).

Conclusion: Type II DM was associated with an increased GC risk among HP-eradicated patients, in particular cardia GC and those with suboptimal DM control. Inadequate adjustment for concomitant medications and comorbidities could potentially bias the results in previous studies.

Disclosure: Nothing to disclose

	No. of patients without DM and GC	No. of patients with DM and GC	HR	95% CI	p-value
All variables adjusted for	39,560 (GC = 117)	6,900 (GC=36)	1.67	1.08 - 2.58	0.021
Statins not adjusted for	39,560 (GC = 117)	6,900 (GC=36)	1.43	0.93 - 2.19	0.101
Statins and aspirin not adjusted for	39,560 (GC = 117)	6,900 (GC=36)	1.32	0.86 - 2.02	0.203
All drugs not adjusted for	39,560 (GC = 117)	6,900 (GC=36)	1.30	0.85 - 1.99	0.234
Comorbidities not adjusted for	39,560 (GC = 117)	6,900 (GC=36)	1.92	1.28 - 2.90	0.002
Subgroup analysis					
Metformin use					
Yes	39,560 (GC=117)	6,379 (GC=32)	1.28	0.74 - 2.20	0.378
No	39,560 (GC=117)	521 (GC=4)	2.59	1.42 - 4.74	0.002
Time-weighted average HbA1c level					
HbA1c ≥ 6.0%	39,560 (GC=117)	6,379 (GC=32)	1.68	1.07 - 2.63	0.025
HbA1c < 6.0%	39,560 (GC=117)	521 (GC=4)	1.99	0.71 - 5.54	0.188
Cancer site*					
Cardia	39,462 (GC=19)	6,876 (GC=12)	3.40	1.45 - 7.97	0.005
Non-cardia	39,513 (GC=70)	6,882 (GC=18)	1.53	0.84 - 2.78	0.161
Non-carida + unspecified site	39,541 (GC=98)	6,888 (GC=24)	1.33	0.80 - 2.23	0.271

DM, diabetes mellitus; GC, gastric cancer; HR, hazard ratio; 95% CI, 95% confidence interval; NSAIDs, non-steroidal anti-inflammatory drugs; COX-2, cyclooxygenase-2; PPIs, proton pump inhibitors; HbA1c, hemoglobin A1c * total cancer cases = 153 (non-cardia: 88, cardia: 31, unspecified: 34)

[Association between diabetes mellitus and gastric cancer (propensity score regression adjustment)]

OP127 VALIDATION OF SCORING SYSTEMS FOR DIFFERENTIATING INTESTINAL TUBERCULOSIS FROM CROHN'S DISEASE UTILIZING CLINICAL, ENDOSCOPIC AND PATHOLOGICAL FINDINGS: A MULTICENTER STUDY FROM THAILAND AND HONG KONG

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Introduction: Differentiating between Intestinal tuberculosis (ITB) and Crohn's disease (CD) is a diagnostic challenging in TB-endemic areas. Several models have been developed to distinguish these two diseases; however, no studies have externally validate these scores using data from the same cohort.

Aims & Methods: To validate existing scoring systems which used clinical, endoscopic and pathological findings in differentiating ITB from CD based on data from the same cohort.

We retrospectively collected data from patients newly diagnosed ITB and CD in 5 referral-centers in Thailand and Hong Kong. Clinical data was reviewed from medical records. Endoscopic and pathological findings were reviewed by endoscopists and pathologist blinded to the diagnosis. The data was applied to published scoring systems including score from Lee *et al* (Endoscopy 2006;38:592-7), Makharia *et al* (Am J Gastroenterol 2010;105:642-51), Jung *et al* (Am J Gastroenterol 2016;111:1156-64) and Limsrivilai *et al* (Am J Gastroenterol 2017;112:415-27). The performance of each score was evaluated with the area under the receiver operating characteristic curve (AuROC) and were compared to each other using the DeLong test.

Results: Of the 590 patients assessed, 163 patients had ITB, and 427 patients had CD. The mean age was 51.8 years in ITB and 36.6 years in CD (p<0.01). Fifty-four percent in ITB and 61% in CD were male (p=0.49). Applying the data to Lee's score which used only endoscopic findings, 149 patients (27%) obtained the score of zero in which the score could not conclude the diagnosis. In the remaining 394 patients, the sensitivity, specificity, and accuracy of the score for the diagnosis of ITB was 96%, 47%, and 61.2%, respectively. The AuROC was 0.713. By including clinical presentation, Jung's score and Limsrivilai's score were validated. The AuROC was 0.850 and 0.858, respectively. The difference between these two scores was not significantly different (p=0.75), but both performed superiorly than endoscopic score (p<0.01). By including pathological findings, Makharia's score and Limsrivilai's score were validated. The AuROC based on the data of 82 patients with available pathology review was 0.628 and 0.900, respectively. The difference was significant (p<0.01). The summary of each model performance in each cohort was shown in Table 1.

Conclusion: In a multi-center study across two different TB endemic areas, scoring systems which combined more potential parameters and diagnostic modalities performed better in differentiating ITB from CD. Further prospective studies to validate the model including more diagnostic modalities such as computed tomography enterography or serological tests are warranted.

Disclosure: Nothing to disclose

Authors	Country	Thai n=242 (137 CD, 105 ITB)	Hong Kong n=348 (290 CD, 58 ITB)	Thai & Hong Kong n=590 (427 CD, 163 ITB)	Scores
Lee, Endoscopy 2006;38:592-7	South Korea	For Dx of ITB (242 pt, TB prevalence 43%) Sen 96% Spec 32% Accuracy 61.3% PPV 54% NPV 89% (48 pt inconclusive)	For Dx of TB (301 pt, TB prevalence 13%) Sen 96% Spec 56% Accuracy 61% PPV 25% NPV 99% (101 pt inconclusive)	For Dx of ITB (543 pt, TB prevalence 29%) Sen 96% Spec 47% Accuracy 61.2% PPV 43% NPV 96% (149 pt inconclusive)	8 parameters of endoscopic findings +1 for 4 findings favoring CD (Longitudinal ulcer, cobblestone, aphthous, anorectal lesions) -1 for 4 finding favoring ITB (Transverse ulcer, patulous IC, pseudopolyps, < 4 segmental involvement) Sum of score: > 0 = CD, < 0 = ITB, 0 = inconclusive
Area under area under the ROC curve					
Makharia GK*, Am J Gastroenterol 2010;105:642-51	India	0.628 (0.511 - 0.746) (44 CD and 38 ITB)	0.708 (0.630 - 0.787) (180 CD, 35 ITB)	0.671 (0.605 - 0.737) (224 CD and 73 ITB)	- 2.5 × involvement of sigmoid colon - 2.1 × blood in stool + 2.3 × weight loss - 2.1 × focally enhanced colitis + 7
Jung Y, Am J Gastroenterol 2016;111:1156-64	South Korea	0.810 (0.757 - 0.863) (135 CD, 105 ITB)	0.857 (0.793 - 0.921) (205 CD, 38 ITB)	0.850 (0.815 - 0.886) (340 CD, 143 ITB)	1/[1+e-(-4.423+0.037×age+2.226×sex-2.203×diarrhea+2.345×tran_ring-1.911×longitudinal-2.123×sigmoid+5.606×pul_tbc)]
Limsrivilai, Am J Gastroenterol 2017;112:415-27 (Score from meta-analysis of each significant finding, please go to bit.ly/ITBvsCD)					
Clinical		0.741 (0.678 - 0.804)	0.766 (0.701 - 0.831)	0.766 (0.723 - 0.809)	
Endoscopy		0.769 (0.712 - 0.826)	0.735 (0.671 - 0.800)	0.786 (0.748 - 0.824)	
Clinical and endoscopy		0.833 (0.783 - 0.883)	0.849 (0.793 - 0.904)	0.858 (0.825 - 0.892)	
Clinical, endoscopy, and pathology*		0.853 (0.806 - 0.900)	0.814 (0.752 - 0.876)	0.861 (0.828 - 0.894)	

[OP127 Table 1]

Primum non nocere: Making ERCP safer

08:30-10:00 / B2

OP128 ADDING INTRAVENOUS SOMATOSTATIN TO RECTAL NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) IN PREVENTION OF POST – ENDOSCOPIC RETROGRADE CHOLANGIO PANCREATOGRAPHY (ERCP) PANCREATITIS IN HIGH RISK PATIENTS

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Introduction: Endoscopic Retrograde CholangioPancreatography (ERCP) is used frequently for treatment of pancreatobiliary diseases. Pancreatitis is one of most frequent complication of ERCP. Pharmacologic measures have been studied for preventing this complication. Somatostatin use has been proposed by previous studies but with inconclusive results.

Aims & Methods: Regarding the prevalence and importance of pancreatitis after Endoscopic Retrograde Cholangio Pancreatography (ERCP), present study was conducted to evaluate the effect of adding intravenous somatostatin to indomethacin on the incidence of pancreatitis after ERCPIn this clinical trial study, 240 patients with primary diagnosis of pancreatobiliary disorders with high risk features of post RCP pancreatitis (patient related, operator dependent or procedure dependent) who were referred to the main academic hospital of Golestan province, Northeast of Iran for diagnostic and therapeutic ERCP during March 2018 to February 2019 were included. They were randomly divided into 2 groups to receive either intravenous somatostatin plus rectal indomethacin (group A, N=120) or rectal indomethacin plus normal salin (group B, N=120).

Serum amylase was evaluated 2 and 18 hours after ERCP and the length of hospitalization or complications had been recorded. Independent t-test was used to compare means and Chi-2 test was used to compare qualitative variables.

Results: Amounts of dye injection, duration and time of cannulation were not significant different between two groups (p>0.05). Significant difference was noted between the two groups in amylases after 2 hours (147.66 vs 198.88 U/L) and 18 hours (124.14 vs 166.55 U/L). Results showed 4.2% pancreatitis in group A and 15% in group B (p = 0.004).

Conclusion: It can be concluded that the administration of somatostatin during and after ERCP could significantly decrease the risk of pancreatitis and hyperamylasemia between the two groups.

Disclosure: Nothing to disclose

OP129 INDIRECT TREATMENT COMPARISON OF USTEKINUMAB VERSUS OTHER ADVANCED THERAPIES IN MODERATE TO SEVERE ULCERATIVE COLITIS AFTER 1 YEAR

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Introduction: Indirect evidence on the relative efficacy of ustekinumab in moderate to severe ulcerative colitis (UC) to other therapies is needed to better inform decision-makers. An indirect treatment comparison (ITC) was performed to compare the 1-year efficacy of therapies in non-biologic failure and biologic failure UC patients.

Aims & Methods: Randomised controlled trials reporting induction and maintenance clinical efficacy of anti-tumour necrosis factors (infliximab [IFX], adalimumab [ADA], golimumab [GOL]), vedolizumab (VDZ), tofacitinib (TOF) or ustekinumab (UST) were identified by a systematic literature review through MEDLINE, MEDLINE IN PROCESS, Embase and Cochrane up to the 28th March 2019. Analyses were conducted for clinical response (decrease in baseline total Mayo score ≥30% and ≥3 points, decrease in rectal bleeding subscore ≥1, or rectal bleeding subscore 0 or 1) and clinical remission (total Mayo score ≤2 points, no individual subscore >1 [definitions with rectal bleeding subscore of 0 were also included]) in each population. Due trial design differences, comparisons of maintenance data alone would be biased. To mimic an ITT-based approach, maintenance data from trials with re-randomised response designs were re-calculated to correspond to treat-through arms including responders at induction and non-induction responders. UST efficacy was calculated for patients starting on the ~6 mg/kg IV regimen. For trials with only short-term placebo (PBO) rates or missing data for PBO non-responders, end of 1-year placebo-to-placebo rates were externally imputed. Bayesian ITCs were conducted to obtain posterior distribution probabilities for UST to perform better than its comparators by population. In the non-biologic failure population, maintenance doses were pooled as no dose-response was apparent.

Results: Six trials were included in the non-biologic failure population ITC [1,2,3,4,5,6], and four included in the biologic failure ITC [1,2,3,4]. Imputed rates for the PBO responders and non-responders in the non-biologic failure group were derived from multiple trials and were consistent. UST given as a 1-year regimen showed higher probabilities of both clinical response and remission versus all treatments in the non-biologic failure group, with Bayesian probabilities of UST being better than active therapies ranging between 91% (VDZ) to 100% (ADA) doses for response and 82% (VDZ) to 99% (ADA) for remission, respectively. In the biologic failure group, the probabilities of UST being better than each active treatment were all higher than 80% for response with the exception of TOF with 10mg in maintenance, and remission was similar between the therapies.

Conclusion: Results of the 1-year ITC indicate a higher likelihood of response and remission on UST in non-biologic failure population versus comparators, especially versus anti-TNFs. In biologic failure patients, results were more uncertain due to smaller sample sizes and data limitations, though a higher likelihood of response to UST versus most comparators was observed.

Treatments sequence (induction - maintenance)	Clinical response Median OR [95% CrI] Pr UST ~6mg/kg - UST 90mg pooled (Q8W and Q12W) vs.	Clinical remission Median OR [95% CrI] Pr UST ~6mg/kg - UST 90mg pooled (Q8W and Q12W) vs.
VDZ 300mg - VDZ 300mg pooled (Q4W and Q8W)	1.93 [0.75 ; 4.82] 91.45%	1.47 [0.65 ; 3.34] 82.34%
IFX pooled - IFX pooled (5mg/kg and 10mg/kg)	2.62 [1.22 ; 5.60] 99.31%	1.89 [0.83 ; 4.30] 93.52%
GOL 200/100mg - GOL pooled (50mg Q4W and 100mg Q4W)	3.76 [1.90 ; 7.57] 99.99%	1.99 [0.93 ; 4.26] 96.27%
ADA 160/80/40mg - ADA 40mg EOW	4.76 [2.25 ; 10.16] 100%	2.43 [1.10 ; 5.41] 98.55%
TOF 10mg - TOF pooled (5mg and 10mg)	2.27 [1.06 ; 4.86] 98.21%	1.51 [0.64 ; 3.52] 83.00%
PBO - PBO	8.70 [5.03 ; 15.40] 100%	5.11 [2.83 ; 9.51] 100%

QXW: every X weeks, EOW: every other week, Pr: probability for ustekinumab to perform better than the comparator

[Table 1 ITC results in the non-biologic failure population]

References: [1]Janssen. A Phase 3, Randomized, Double-blind, Placebo-controlled, Parallel-group, Multicenter Study to Evaluate the Safety and Efficacy of Ustekinumab Induction and Maintenance Therapy in Subjects with Moderately to Severely Active Ulcerative Colitis (44-Week Clinical Study Report). Research & Development (2018). [2]Feagan BG, Rubin DT, Danese S, Vermeire S, Abhyankar B, Sankoh S, James A and Smyth M. Efficacy of vedolizumab induction and maintenance therapy in patients with ulcerative colitis, regardless of prior exposure to tumor necrosis factor antagonists. Clinical Gastroenterology and Hepatology. 201;15:229-239. [3]Sandborn WJ, Van Assche G, Reinisch W, Colombel JF, D´Haens G, Wolf DC, et al. Adalimumab induces and maintains clinical remission in patients with moderate-to-severe ulcerative colitis. Gastroenterology. 2012;142(2):257-65. [4]Sandborn WJ, Su C, Sands BE, D'Haens GR, Vermeire S, Schreiber S, et al. Tofacitinib as induction and maintenance therapy for ulcerative colitis. New England Journal of Medicine. 2017;376(18):1723-36. [5]Rutgeerts P, Sandborn WJ, Feagan BG, Reinisch W, Olson A, Johanns J, et al. Infliximab for induction and maintenance therapy for ulcerative colitis. New England Journal of Medicine. 2005;353(23):2462-76. [6]Sandborn WJ, Feagan BG, Marano C, Zhang H, Strauss R, Johanns J, et al. Subcutaneous golimumab induces clinical response and remission in patients with moderate-to-severe ulcerative colitis. Gastroenterology. 2014;146(1):85-95.

Disclosure: Margaux Welty, Laura Mesana, Amie Padhiar, and Maud Pacou are consultants for Janssen Pharmaceutica NV Dominik Naessens, Suzy van Sanden, and Joris Diels are all employees of Janssen Pharmaceutica NV

OP130 META-ANALYSIS OF RANDOMIZED TRIALS OF POST-ERCP PANCREATITIS AFTER EARLY AND LATE NEEDLE-KNIFE SPHINCTEROTOMY IN DIFFICULT BILIARY CANNULATION

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Introduction: Needle-knife sphincterotomy (NKS) and prolonged cannulation attempts are both considered as risk factors for post-ERCP pancreatitis (PEP). Previous meta-analyses compared the effect of early precut versus persistent cannulation attempts on PEP.

Aims & Methods: Our aim was to analyze the effect of early versus late NKS on PEP in difficult biliary cannulation. MEDLINE/PubMed, EMBASE were searched. Only randomized controlled trials (RCT) containing data of early (< 10 minutes of cannulation attempts and/or < 5 inadverent pancreatic duct cannulation) and late (additional 10 minutes of attempts) NKS were selected and analyzed.

A subgroup of patients where cannulation attempts were prolonged but NKS was not needed served as the prolonged cannulation group. Pooled estimates of PEP were analyzed using odds (OR) and risk ratios (RR), and number needed to treat (NNT) was calculated.

Results: 6 RCTs were found, but only 3 RCTs were included in the meta-analysis (3 excluded: 2 used prophylactic pancreatic stenting which could alter the effect of NKS; and only moderate and severe PEP were analyzed in 1 RCT). NKS was used early in 310 and late in 220 patients. In 216 patients prolonged standard cannulation was used. PEP occurred in 14/310 (4.06%) vs. 29/220 (12.23%) vs. 14/216 (9.47%) patients.

The cannulation success rates were 272/310 (86%) in early NKS vs. 187/220 (80.7%) in late NKS groups. Regarding PEP, our meta-analysis showed a significantly increased risk, when NKS was used late compared to early (OR=3.21 (95% CI: 1.65-6.23; p=0.0006); RR=2.92 (95% CI: 1.57-5.39; p=0.0006); NNT=11.54). When NKS is applied late after prolonged cannulation attempts, it further increases the risk of PEP compared to prolonged cannulation only (OR=2.19 (95% CI: 1.12-4.27; p=0.0214); RR=2.03 (95% CI: 1.11-3.74; p=0,0225); NNT=14.9).

Conclusion: Early, but not late precut NKS is safe in difficult biliary cannulation when used by experts. The incidence of PEP of early NKS is half compared to prolonged cannulation and third compared to late NKS. We suggest using early precut sphincterotomy in difficult biliary cannulation and/or using other preventive methods (eg. prophylactic pancreatic stents or rectal indomethacin) to lower PEP rates.

Disclosure: Nothing to disclose

OP131 IS THERE A DIFFERENCE IN THE INCIDENCE AND CHARACTERISTICS OF POST-ERCP PANCREATITIS BETWEEN EMERGENCY AND ELECTIVE ERCP?: A PROSPECTIVE MULTICENTER STUDY

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Introduction: Post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis (PEP) is a potentially serious complication. Risk factors for PEP after elective ERCP have been reported. ERCP is often performed urgently, but the difference in the risk factors for PEP between elective and emergency ERCP remains unclear.

Aims & Methods: We aimed to identify the incidence of and risk factors for PEP in emergency ERCP. We performed a prospective study of 3914 patients undergoing diagnostic and therapeutic ERCP at five Japanese institutions between April 2015 and May 2017. The exclusion criteria were as follows: active pancreatitis, choledochojejunostomy, inability to approach a papilla, and inspection only of the pancreatic duct (PD). In this study, emergency ERCP was defined as unscheduled inspections performed within and beyond regular working hours. A diagnosis of PEP was made when two of the following three conditions were met: (1) serum amylase levels greater than three times the upper limit of the normal range at each institution, (2) persistent abdominal pain for more than 24 h, and (3) evidence of pancreatitis on computed tomography. In the first study, we compared the incidence and characteristics of PEP between emergency and elective ERCP. In the second study, we determined the predictive risk factors for PEP in emergency ERCP using univariate and multivariate analyses.

Results: In total, 3,410 patients were enrolled in this study. < Study 1> PEP developed in 44 of 800 (5.5%) cases and 190 of 2,418 (7.9%) cases in the emergency and elective groups, respectively. No significant difference was noted in the incidence of PEP between the two groups (odds ratio [OR], 0.73; 95% confidence interval [CI], 0.52-1.03; P = 0.07). Endoscopic sphincterotomy, pre-cutting, stone removal, endoscopic papillary balloon dilatation (EPBD), and intraductal ultrasound were more frequently performed in the elective group than in the emergency group (P < 0.001); while biliary stent placement was significantly more common in the latter group (P < 0.001) . In addition, a considerably longer procedure time (40.2min. vs 30.8min.;P < 0.001) and higher number of endoscopists with more than 5 years of experience (P = 0.02) were noted in the elective group than in the emergency group. < Study 2> The multivariate analysis showed that the following factors increased the risk for PEP in emergency ERCP: contrast medium injection into the PD (OR, 2.56; 95% CI, 1.30-5.03; P = 0.005), more than four cannulation attempts (OR, 5.72; 95% CI, 2.61-12.50; P < 0.0001), and EPBD (OR, 9.24; 95% CI, 2.13-40.10; P < 0.0001).

Conclusion: No significant difference was noted in the incidence of PEP between emergency and elective ERCP. For noninvasive methods, a procedure time less than 30 minutes is acceptable even for a trainee with less than 5 years of experience during the emergency ERCP. The contrast medium injection into the PD necessitates close monitoring, particularly when more than four cannulation attempts are required; furthermore, surgeons should refrain from performing EPBD in emergency ERCP.

Disclosure: Nothing to disclose

OP132 A NOVEL SINGLE-USE DUODENOSCOPE HAD COMPARABLE PERFORMANCE RATINGS TO REUSABLE DUODENOSCOPES IN A RANDOMIZED BENCH STUDY

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Introduction: Multidrug-resistant (MDR) infectious outbreaks are a major global concern.[1] Duodenoscope contamination during reuse and reprocessing is one of many potential nosocomial sources of patient-to-patient transmission of pathogenic MDR organisms. Duodenoscope reprocessing guidelines are evolving and impose a significant economic burden to hospitals. In addition, guideline adherence alone cannot prevent duodenoscope contamination because the current cleaning paradigm for duodenoscopes is ineffective.[2] In this context, single-use duodenoscopes could offer benefits. No single-use duodenoscope is currently available in gastroenterology clinical practice. Similar performance to reusable duodenoscopes is a prerequisite to considering further investigation of a single-use duodenoscope for endoscopic retrograde cholangiopancreatography (ERCP).

Aims & Methods: The aim of this study was for 6 expert ERCP endoscopists to compare performance characteristic ratings of a novel single-use duodenoscope to those of 3 marketed reusable duodenoscopes.

Beginning in March 2017, 9 laboratory animal studies were conducted to develop a single-use duodenoscope intended to bring a familiar design with a minimal learning curve. Prototype revisions based on physician feedback led to the first-generation single-use duodenoscope used in the current study. Also based on physician feedback, a handmade, fully synthetic ERCP anatomical bench model was developed for use in ERCP simulation testing.

In January 2019, a bench study with randomized block design was conducted in which the 6 endoscopists rated the performance of the single-use EXALT Model D duodenoscope (Boston Scientific, Marlborough, USA) and 3 reusable duodenoscopes (Q180V (Olympus, Japan), ED-3470TK (Pentax, Japan), ED-530XT (Fujifilm, Japan) to complete 4 simulated ERCP tasks: guidewire locking (single-use and one reusable duodenoscope only), plastic stenting, metal stenting, and basket sweeping. Each task was performed once with each duodenoscope model. Task completion rates and times, and subjective performance ratings on a scale of 1 (worst) to 10 (best) were compared among duodenoscopes using non-parametric tests with adjustment for multiple comparisons.

Results: Task completion rates were 100% for all 4 duodenoscopes. Median task completion time ranged from 1.5 to 8.0 minutes per task. Overall performance (Table) and tip control (medians 9.0-10.0, P=0.77 among all 4 duodenoscopes) were rated similarly among the duodenoscopes tested.

Task Number	EXALT Model D	Q180V	ED-3470TK	ED-530XT	P value
1	9.0 (8.0-10.0)	9.0 (8.0-10.0)	--	--	1.00
2	8.5 (8.0-9.0)	10.0 (8.0-10.0)	9.0 (8.0-10.0)	9.0 (8.0-10.0)	0.14
3	8.5 (8.0-9.0)	9.5 (8.0-10.0)	8.0 (8.0-9.0)	9.5 (8.0-10.0)	0.11
4	8.5 (8.0-10.0)	9.0 (8.0-10.0)	9.0 (8.0-10.0)	9.0 (8.0-10.0)	0.74

[Table: Median ratings (range) for overall performance]

The 2 duodenoscopes capable of guidewire locking both received median ratings of 10 for that function (P=0.14 for difference in subtask ratings). Among all 4 duodenoscopes, navigation/pushability was rated lower for the single-use duodenoscope (medians 8.0, 10.0, 9,0, 9.0 respectively, P<0.01). Image quality was rated lower for one of the reusable duodenoscopes (ED-3470TK) (medians 8.0, 9.0, 9.0, 9.0 respectively, P< 0.01) compared to the other duodenoscopes tested.

Conclusion: In a comparative bench study including 4 simulated ERCP tasks, performance ratings were similar for the new single-use duodenoscope and 3 brands of reusable duodenoscopes. A multicenter clinical study of the safety, feasibility and efficacy of the new single-use duodenoscope is warranted.

References: 1. Cassini A, Hogberg LD, Plachouras D, et al. Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: a population-level modelling analysis. Lancet Infect Dis 2019;19:56-66. 2. Hutfless SM, Kalloo AN. Commentary on the 2016 Multi-Society Task Force Endoscope Reprocessing Guidelines. Gastroenterology 2017;152:494-6.

Disclosure: ASR: consulting fees and research funding from Boston Scientific Corporation; MJB: consulting and speaker fees and investigator-initiated grants from Boston Scientific Corporation, Cook Medical, Pentax Medical and 3M, and consultant fees from Mylan; RK: research support from Boston Scientific Corporation; BTP: consultant/investigator relationship with Boston Scientific Corporation, consultant fees from Olympus America, Advanced Steriliz Products and GI Medical; DKP: consultant fees from Boston Scientific Corporation, Olympus, Fuji and Nine Point Medical; DVS: consulting/research relationship with Boston Scientific Corporation, consultant fees from Olympus; AS: research funding from Boston Scientific Corporation and Olympus; DM: consultant fees from Boston Scientific Corporation; JP, JI, MR and GPT are full-time employees of Boston Scientific Corporation; VRM: consulting fees and research funding from Boston Scientific Corporation.

OP133 ERCP IN BABIES: LOW RISK OF POST-ERCP-PANCREATITIS – RESULTS FROM A EUROPEAN MULTICENTER SURVEY

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Introduction: ERCP is rarely performed in newborns, and the risk of post-ERCP-pancreatitis (PEP) has not been defined in this age group. We therefore performed a European multicenter analysis of PEP rates and risk factors in children ≤1-year-old.

Aims & Methods: Based on a sample size estimation, 135 consecutive ERCPs in 126 children ≤1-year-old were evaluated from five European centers. All ERCP and clinical reports were reviewed manually for PEP and associated risk factors. All ERCPs were performed by endoscopists with high ERCP expertise.

Results: No PEP was observed (0/126, 0.0%, CI 0-2.9%) despite formal presence of multiple risk factors and despite lack of PEP prophylaxis (except one patient having received a pancreatic duct stent). The PEP rate was significantly lower than the PEP rate expected in adults with similar risk factors.

Conclusion: : ERCP in ≤1-year-old children is safe in terms of PEP. The PEP risk is significantly lower in children ≤1-year-old than in adults, therefore no PEP prophylaxis seems to be needed in young children. Risk factors from adults may not apply to children under 1 year. Reluctance to perform diagnostic ERCP in suspected biliary anomalies should not be based on presumed PEP risk.

Disclosure: Nothing to disclose

New impulses in management of gastroparesis

08:30-10:00 / B3

OP134 THYMIDINE PHOSPHORYLASE ABNORMALITIES AND GASTROINTESTINAL VASCULAR CHANGES IN GENETIC AND SPORADIC FORMS OF SEVERE DYSMOTILITY

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Introduction: Mitochondrial neurogastrointestinal encephalomyopathy (MNGIE) is an extremely rare autosomal recessive disease caused by thymidine phosphorylase (TP) enzyme defect. Normally, TP converts the nucleosides thymidine and deoxyuridine into respective nucleotides. In MNGIE these nucleosides accumulate in most tissues and induce toxic effects leading to mitochondrial DNA (mtDNA) abnormalities. MNGIE patients show severe gastrointestinal (GI) dysmotility and neurological impairment, resulting in a poor quality of life and fatal outcome. Although permanent tissue replacement of TP (via either liver or hematopoietic cell transplantation) is the best way to stably revert the biochemical imbalance, transplanted patients do not recover the poor BMI and may dye for GI massive bleeding. The liver transplant follow-up suggests that the phenotype directly linked to the accumulation of nucleosides seems to be reversible, while other mechanisms underlying non-reversible GI damage may occur. During the conversion of nucleosides TP produces 2-deoxy-D-ribose-1-phosphate (dRP) that has been demonstrated to be the chemotactic agent inducing endothelial progenitor cells to form/repair blood vessels.

In MNGIE patients the conversion does not take place. In order to exert its effect dRP has to be locally released, hence vascular changes may occur in the GI tract of MNGIE patients.

Aims & Methods: This study was designed to explore the enteric submucosal microvasculature in the jejunal of MNGIE patients in comparison with asymptomatic GI controls (CTR) and non-MNGIE patients with well characterized severe dismotility (SD) and normal TP activity.

Jejunal full thickness biopsies were collected from n=4 MNGIE (4M, 24-32 yrs); n=10 CTR (7M, 30-73 yrs) and n=21 SD (9M; 16-75). Formalin fixed-paraffin embedded tissue sections were stained with orcein to identify, measure and count blood vessels. Vessels were subdivided in 4 classes: >300 µm (large); 300-101 µm (medium); 100-51 µm (small) and < 50 µm (very small). Snap frozen tissue was used to quantify TP protein expression.

Results: MNGIE patients showed two times more submucosal vessels/mm^2 ($P< 0.05$) vs. CTR, while SD showed only a non significant trend to increase. In contrast the area of submucosa occupied by vascular tissue was about half in MNGIE ($P< 0.01$) and SD ($P< 0.001$) vs. CTR. The percentage of the small vessels (< 50 µm) in CTR was very low ~19%, whereas drastically increased in SD (43%; $P< 0.001$) and MNGIE (54%; $P< 0.01$). Conversely, the percentage of higher diameter vessels (>300 µm) in CTR was ~15 % and in SD and MNGIE patients decreased up to 7% and 5% ($P< 0.01$ and $P< 0.05$), respectively. Medium vessels (300-101 µm) represented the 40% of vessels in CTR and decreased to 25% and 17% in SD and MNGIE patients ($P< 0.001$ and $P< 0.01$). The TP amount showed a significant decrease in the jejunum of SD patients ($P< 0.0001$).

Conclusion: Our results indicate that, compared to CTR, MNGIE and SD vasculature showed quantitative abnormalities likely related to the absence/ lower TP conversion. This study addressed the abnormal vascularization in the small intestine of genetic (MNGIE) and sporadic SD as a possible contributory mechanism underlying gut dysfunction in these severe conditions.

Disclosure: Nothing to disclose

OP135 DIAGNOSTIC YIELD OF SYMPTOM SEVERITY, VISCERAL SENSORY TESTING, SMALL INTESTINAL, BACTERIAL LOAD AND GASTRIC EMPTYING FOR THE DIAGNOSIS OF FUNCTIONAL GASTROINTESTINAL DISORDERS

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Introduction: Patients presenting with functional gastrointestinal disorders (FGIDs) frequently report debilitating symptoms which may be more severe than symptoms experienced by patients with organic intestinal disease. While presence or absence (i.e. symptom pattern) is generally used to categorise patients with FGIDs, the role of symptom intensity to categorise and diagnose patients has not been tested. In addition, alterations of gastrointestinal sensory function, altered motility and bacterial dysbiosis are considered to play key roles in FGID pathophysiology.

Aims & Methods: In this study we aimed to explore the diagnostic yield of severity of self-reported GI symptoms, visceral sensory testing, qPCR to quantify small intestinal mucosal bacterial load and gastric emptying in differentiating functional from organic GI disease. We recruited 284 patients (150 female, 95 patients with FGID (68 functional dyspepsia (FD)/IBS overlap, 21 FD, 3 IBS), 118 organic disease (43 Crohn's disease, 48 ulcerative colitis (UC), 16 UC/primary sclerosing cholangiopathy (PSC), 4 PSC alone, 9 other) and 71 patients with a positive stool occult blood test without structural lesions). After informed consent, type and severity of GI symptoms were recorded using a standardized valid questionnaire (SAGIS). Patients underwent a nutrient challenge test and the cumulative symptom response to a standardised test meal (Ensure, 600 cc) were recorded. In addition, gastric emptying of a solid test meal was measured utilising ^{13}C-octanoic breath testing. During endoscopy, mucosal tissue samples were

collected utilising the Brisbane Aseptic Biopsy Forceps (MTW, Germany) to avoid the luminal and working channel contamination of tissue, and total DNA was extracted. Tissue bacterial density was normalised to human DNA by qPCR using Bacteria-Domain 16S rRNA gene- and beta-actin gene-specific primers, respectively. Based upon on all available clinical data, patients were categorised as FGID or non-FGID. The FGID and non-FGID groups were compared utilising non parametric testing, and Spearman correlation to determine the relationships between disease category and the respective variables. In addition, Receiver Operator Curves (ROC) for the variables that were significantly different for FGID and non-FGID provided areas under the curve for comparison.

Results: SAGIS symptom scores, the symptom response to the nutrient challenge, and the tissue bacterial load were all significantly greater (all $P< 0.005$) in FGID patients as compared to non FGID patients (Table 1).

	SAGIS-score	Nutrient challenge score	Bacterial load, ratio	Gastric emptying, t-lag (min)
Non-FGID	10.8 (±12.9)	204 (±190)	0.04 (±0.11)	116.0 (±37.3)
FGID	30.6 (±15.1)#	458 (±399)*	0.20 (±0.5)#	115.8 (±29.3)

#$P< 0.001$, *$P< 0.005$

[Table 1. GI symptom severity, symptom response to nutrient challenge, bacterial load (ratio of 16s RNA:β actin) and t-lag gastric emptying]

There was no difference with regard to gastric emptying. SAGIS score (r=0.62, $P< 0.001$), nutrient challenge score (r=0.41, $p< 0.001$) and bacterial load (r=0.342, $p< 0.001$) were linked to FGID, whereas gastric emptying was not (r=0.024, $p>0.8$). For the total SAGIS score the AUC was .892 (95% CI 0.83-0.954), for the nutrient challenge score 0.74 (95%CI .64-0.83), bacterial load (0.71 (95%CI 0.61-0.80).

Conclusion: In patients referred to a tertiary setting for assessment and treatment, self-reported symptom severity, response to a standardised nutrient challenge and small intestinal bacterial load but not gastric emptying rate differentiate patients with functional and non-functional symptoms. Further studies need to explore the utility of these simple tests to better tailor diagnostic and therapeutic interventions for patients presenting with chronic unexplained GI symptoms.

Disclosure: Nothing to disclose

OP136 EFFECT OF RIKKUNSHITO ON GASTROINTESTINAL MOTILITY AND UPPER GASTROINTESTINAL SYMPTOMS - THE FIRST STUDY IN A BELGIAN FUNCTIONAL DYSPEPSIA POPULATION

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Introduction: Functional dyspepsia (FD) is a common chronic gastrointestinal (GI) disorder. Rikkunshito, a traditional Japanese Kampo medicine, has shown efficacy in improving FD symptoms in controlled trials in Japan. Its putative benefit for European patients has never been investigated. Further, its exact mechanism of action is incompletely elucidated.

Aims & Methods: This study aimed to examine the effect of rikkunshito on gastric motility and GI symptom perception in FD patients with postprandial distress syndrome (PDS) subtype in a randomized, placebo-controlled, cross-over study. After a 2-week run-in period, during which adequate symptom intensity was confirmed, patients were treated with rikkunshito (2.5g t.i.d.) and matching placebo for 4 weeks, separated by a 4-week washout period. Symptom severity was assessed by the Leuven Postprandial Distress Scale (LPDS) diary throughout the study. At baseline and at the end of both treatment arms, intragastric pressure (IGP) was assessed using high-resolution manometry after an overnight fast. Thirty minutes after study medication intake, a liquid meal was infused intragastrically at a constant speed (60 mL/min) until full satiation. IGP measurement continued until 2 hours after the liquid meal. GI symptoms were scored on a 100mm visual analogue scale every 10 minutes. At baseline, before and after each treatment period, the PAGI-SYM (patient assessment GI symp-

toms), VSI (visceral sensitivity index) and SF-NDI (short form Nepean dyspepsia index) questionnaires were completed. Data were analyzed using mixed models.

Results: Thirty-four patients were randomized in the study, of which 11 dropped-out, resulting in 23 fully evaluable patients (33±14 y, 22.7±3.22 kg/m²). The IGP was numerically, although not significantly, lower after rikkunshito compared to both baseline and placebo (mean difference: 1.51 mmHg, $p < 0.221$; 2.19mmHg, $p=0.132$, respectively). No significant differences were found in gastric accommodation, nutrient volume tolerance and symptoms assessed during IGP measurements. An exploratory subgroup analysis, comparing patients on PPI (7 patients) and off PPI (16 patients), showed that the numerical difference in IGP was driven by the patients who were not on PPI treatment. However, no significant difference was observed between both subgroups. Early satiation, bloating and epigastric pain, scored on the LPDS diary, decreased after rikkunshito compared to baseline ($p< 0.025$ for all). However, comparable symptom improvement occurred after placebo ($p< 0.045$ for all; NS between groups). Exploratory subgroup analysis on overall LPDS symptom scores revealed significant improvement after rikkunshito for the patients off PPI ($p=0.021$) and after placebo for the patients on PPI ($p=0.006$). Total PAGI-SYM scores were equally improved after rikkunshito and placebo compared to baseline ($p< 0.001$ and $p< 0.001$, respectively; NS between groups). Placebo, but not rikkunshito, significantly improved frequency, severity and bothersomeness of SF-NDI scores compared to baseline ($p< 0.008$ for all). No significant changes in VSI scores occurred. No adverse reactions occurred.

Conclusion: Rikkunshito did not alter gastric accommodation and nutrient volume tolerance. Treatment with rikkunshito improved upper GI symptoms in FD patients but a similarly high placebo effect was observed using the LPDS diary, PAGI-SYM and SF-NDI. Rikkunshito was safe and well tolerated. Exploratory analyses indicate potentially better responses in patients who are not on concomitant PPI treatment.

Disclosure: Nothing to disclose

OP137 TRADIPITANT, A NOVEL NK-1 RECEPTOR ANTAGONIST, SIGNIFICANTLY IMPROVED NAUSEA AND OTHER SYMPTOMS OF GASTROPARESIS IN A PHASE II TRIAL

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Introduction: A phase II multicenter, randomized, double-blind, placebo-controlled trial with gastroparesis subjects demonstrating delayed gastric emptying and moderate to severe nausea were randomized to receive oral 85mg tradipitant bid or placebo (1:1) for four weeks. Of the 152 patients, 60% of patients had idiopathic and 40% had diabetic gastroparesis.

Aims & Methods: The primary outcome was change in average nausea score from baseline, measured using the 5-point Gastroparesis Core Symptom Daily Diary (GCSDD). Overall gastroparesis symptoms were evaluated using the Gastroparesis Cardinal Symptom Index (GCSI), and Patient Assessment of Gastrointestinal Disorders Symptom Severity Index (PAGI-SYM).

Results: A statistically significant and clinically meaningful improvement in nausea and overall gastroparesis symptoms was observed in patients on tradipitant. Subjects receiving tradipitant had a significant decrease in their average nausea score compared to placebo with LS mean difference (95% CI) of −0.53 (−0.92, −0.13, p=0.0099) as well as a significant increase in nausea free days (28.8% increase on tradipitant compared to 15.0% increase on placebo, p=0.0160). A clinically meaningful response of 1-point or more improvement on the GCSI total score was observed in 46.0% of patients on tradipitant compared to 24.2% of patients on placebo.

Conclusion: Tradipitant treatment resulted in statistically and clinically meaningful improvements in nausea and overall gastroparesis symptoms. Tradipitant was well tolerated with comparable rates of adverse events between tradipitant and placebo groups. These robust efficacy results suggest tradipitant has the potential to become a first line pharmacological treatment for gastroparesis.

Disclosure: All authors are employees of Vanda Pharmaceuticals, Inc.

OP138 EFFICACY OF VELUSETRAG TREATMENT IN PATIENTS WITH IDIOPATHIC GASTROPARESIS: SUBGROUP ANALYSIS OF A PHASE 2B STUDY

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Introduction: Velusetrag (VEL) is a highly selective oral 5-hydroxytryptamine receptor type 4 agonist with demonstrated prokinetic effects throughout the gastrointestinal tract. A phase 2b trial evaluated VEL efficacy and safety in patients with idiopathic or diabetic gastroparesis; this subanalysis assessed effects of VEL vs placebo on symptoms and gastric emptying in only patients with idiopathic gastroparesis.

Aims & Methods: Patients with baseline 24-hour Gastroparesis Cardinal Symptoms Index (GCSI-24H) 7-day mean composite score ≥2.5 and delayed gastric emptying based on scintigraphy (GES) or gastric emptying breath test were randomized, stratified by gastroparesis type, to receive oral VEL 5, 15, or 30 mg, or placebo, once daily in the morning, in parallel for 12 weeks and followed for another 2 weeks. Symptoms were assessed daily using the GCSI-24H, a daily version of the GCSI including nausea/vomiting, postprandial fullness/early satiety, and bloating subscales. Gastric emptying was evaluated at day 28 by the same test used for screening. The primary efficacy outcome was change from baseline to week 4 in 7-day mean GCSI-24H composite score in patients receiving each dose of VEL vs placebo. Key secondary outcomes included change from baseline to day 28 in gastric emptying assessed by GES in patients receiving VEL vs placebo, and safety and tolerability of VEL in patients with idiopathic gastroparesis.

Results: Of 228 randomized patients who received study drug and had evaluable efficacy data, 112 had idiopathic gastroparesis: 29 patients received VEL 5 mg, 24 received VEL 15 mg, 31 received VEL 30 mg, and 28 received placebo. The majority of patients were female (85%); mean age was 45.4 (range, 19-73) years, and mean baseline GCSI-24H total score was 3.1 (standard deviation, 0.51) points (n=111). GES was assessed in 58 patients.

Change from baseline GCSI-24H composite score at weeks 4 and 12 showed an inverse dose response, with larger treatment effects vs placebo for VEL 5 mg vs 15 or 30 mg. In patients receiving VEL 5 mg, GCSI-24H composite score decreased from baseline significantly at week 4 (treatment difference [95% confidence interval (CI)], −0.6 [−1.08, −0.05] points; nominal p=0.03) and numerically at week 12 (treatment difference [95% CI], −0.6 [−1.19, 0.00] points; nominal p=0.05]) relative to placebo. All GCSI-24H symptom subscale scores in patients receiving VEL 5 mg vs placebo decreased from baseline in week 1 of treatment, stabilized or decreased through week 6, and were stable through week 12. No tachyphylaxis was observed. Gastric emptying assessed by GES improved from baseline to day 28 in 9/13 patients receiving VEL 5 mg, 13/13 receiving VEL 15 mg, and 16/16 receiving VEL 30 mg vs 6/16 patients receiving placebo. Gastric emptying normalized (< 10% GES hour 4 retention) in all patients receiving VEL 15 mg and 81% receiving VEL 30 mg vs 0% receiving VEL 5 mg or placebo.

VEL was generally well tolerated. The most common adverse events (AEs) across all treatment arms were diarrhea, nausea, and headache. Numerically greater proportions of patients receiving VEL 5, 15, or 30 mg vs placebo had diarrhea (13.8%, 30.8%, and 19.4%, respectively, vs 7.4%) and nausea (6.9%, 7.7%, and 19.4%, respectively, vs 3.7%).

Conclusion: VEL treatment for 12 weeks reduced gastroparesis symptoms, with greatest effect for the 5-mg dose; demonstrated gastroprokinetic activity at all doses; and was well tolerated in patients with idiopathic gastroparesis. Future phase 3 studies will further evaluate VEL efficacy in this population.

Disclosure: TLA is a consultant to Theravance Biopharma, Inc.; an investigator for Vanda, Allergan, Anylam, Censa, and Theravance Biopharma R&D, Inc.; a reviewer for Up To Date; an Editor of MedStudy, Neuromodulation, and Wikistim; and a founder of ADEPT-GI. BK reports grant funding from AstraZeneca; Evidera; Gelesis, Inc.; Genzyme; GSK; Medtronic; Takeda; Theravance Biopharma R&D, Inc.; and Vanda; and personal fees from Actavis Pharma, Inc.; AstraZeneca; Biogen; Entrega; Forest Pharma-

ceuticals; Gelesis, Inc.; Genzyme; GLG; GSK; Ironwood Pharmaceuticals; Medtronic; Takeda; and Theravance Biopharma R&D, Inc. TE reports nothing to disclose. DC, KZ, and CNB are former employees of Theravance Biopharma US, Inc. RT, MG, GCV, and CR are employees of Alfasigma S.p.A. DDN is an employee of Theravance Biopharma US, Inc., and shareholder of Theravance Biopharma, Inc. RM reports grant funding from Allergan Pharma; Medtronic Corp.; Takeda Pharma; Vanda Pharma; Theravance Biopharma R&D, Inc.; and Evoke Pharma; and personal fees from Salix Pharma.

OP139 GASTRIC PERORAL ENDOSCOPIC MYOTOMY (G-POEM) FOR THE TREATMENT OF REFRACTORY GASTROPARESIS: RESULTS FROM THE FIRST INTERNATIONAL PROSPECTIVE TRIAL

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Introduction: Gastric per-oral endoscopic myotomy (GPOEM) was first reported in 2013 for the treatment of gastroparesis. Early data suggested efficacy of the procedure; however, data from prospective multicenter studies are currently lacking.
Aims & Methods: The aim of this study is to prospectively evaluate the efficacy and safety of G-POEM in patients with gastroparesis refractory to conventional medical treatment. This is a multicenter study involving 6 tertiary centers (5 US, 1 South America) between 11/2015 and 11/2018. Adult patients with refractory gastroparesis, defined as failing prior conventional medical therapy, and confirmed by gastric emptying study (GES).The primary outcome was clinical success, defined as at least one score decrease in total Gastroparesis Cardinal Symptom Index (GCSI) with more than a 25% decrease in at least 2 sub-scales. Secondary outcomes were quality of life based on Short Form 36 (SF-36) and improvement of gastric motility assessed by GES. Data were collected before the procedure and 1 month, 3 months, 6 months, and 12 months after the procedure. GES was performed before and after G-POEM.
Results: A total of 73 patients with refractory gastroparesis (51 female [70 %]; median age 44yr) underwent G-POEM during the study period. The most common etiologies were idiopathic 29 (39.7 %), post-surgical 26 (35.6 %), and diabetes 18 (24.7 %). All procedures were technically successful. Clinical success was achieved in 57.9 % and 36.8% of patients at 6 and 12 months, respectively. Repeated measures ANOVA showed that the mean GCSI score and nausea/vomiting and bloating subscores improved significantly over follow-up intervals (table 1).

GCSI subscales, mean ± SD	Preprocedural	1 month after procedure	3 months after procedure	6 months after procedure	12 months after procedure	p-value
Nausea/ vomiting	2.69 ± 1.29	1.44 ± 1.32	1.22 ± 1.4	1.54 ± 1.21	1.72 ± 1.48	0.17
Early satiety	2.76 ± 1.19	1.21 ± 1.14	1.12 ± 1.25	1.47 ± 1.12	1.67 ± 1.17	**0.04**
Bloating	3.65 ± 1.44	1.98 ± 1.72	1.58 ± 1.68	2.2 ± 1.7	2.06 ± 1.57	0.06
Total	2.96 ± 1.05	1.57 ± 1.14	1.39 ± 1.23	1.62 ± 1.14	1.84 ± 1.12	**0.015**

[Improvement of GCSI and its sub-scales, after G-POEM]

Quality of life generally improved after G-POEM. Subscales with significant improvement were Physical functioning (p=0.043), social functioning (0.024), and health change (0.005); however, the improvement of bodily

pain, role limitations due to physical health and emotional problems, energy/fatigue, emotional well-being, and general health were not statistically significant (p>0.05). Comparison of GES results before and after G-POEM showed that gastric emptying rate normalized in 55% of patients and the mean 4-hr gastric retention percentage decreased significantly from 39.4 ± 20.4 to 18.3 ± 24.8 (p< 0.001). A total of 4 AEs occurred: 3 capnoperitoneum and 1 mucosotomy, all rated as mild according to the ASGE lexicon. The 3 capnoperitoneum cases were treated by needle decompression, while the inadvertent mucosotomy was successfully treated by stent deployment.
Conclusion: With high technical success rate, limited adverse events, and high clinical efficacy, G-POEM appears to be a feasible and promising therapeutic intervention for management of refractory gastroparesis.
Disclosure: Nothing to disclose

Advances in endoscopy and faecal testing for IBD and cancer
08:30-10:00 / B5

OP140 LOCATION BUT NOT SEVERITY OF ENDOSCOPIC LESIONS AT BASELINE INFLUENCES ENDOSCOPIC HEALING RATES IN CROHN'S DISEASE PATIENTS TREATED WITH INFLIXIMAB: A POST-HOC ANALYSIS OF THE TAILORIX TRIAL

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Introduction: Whether severity and location of endoscopic lesions may influence the likelihood of endoscopic healing in Crohn's disease patients treated with anti-TNF is poorly known. We assessed rates of endoscopic healing in CD patients responding to infliximab (IFX) in combination with an immunomodulator at the end of the induction period and at one year according to baseline endoscopic findings (severity of lesions and their location).
Aims & Methods: We conducted a post-hoc analysis of the endoscopic data prospectively collected in the TAILORIX study, a randomized trial investigating treatment with IFX based on biomarkers and therapeutic drug monitoring in biologic-naïve patients with an active luminal CD (1). All patients had endoscopic ulcerations at inclusion. Ileo-colonoscopies were performed at week 0, 12 and week 54. Endoscopic healing was defined as absence of ulcers, complete endoscopic remission as either CDEIS< 3 or SES-CD< 3, and endoscopic response as >50% decrease in CDEIS or SES-CD scores. Individual segments (ileum, right colon, transverse colon, left colon and rectum) were centrally read and scored separately for healing and response.
Results: Of the 122 patients included in the trial, the 75 patients who received IFX until week 54 and underwent ileocolonoscopy at week 0, 12 and week 54 could be analysed (median (interquartile range) disease duration: 6 (1-67) months), corresponding to 234 diseased segments (ileum n=47, right colon n=46, transverse colon n=46, left colon n=54, rectum n=41) at baseline. Thirty-five patients with early discontinuation of IFX during the study and 12 with missing ileocolonoscopy at week 12 or 54 were excluded. Overall at weeks 12 and 54, 32 (43%) and 54 (72%) patients displayed endoscopic healing, 54 (72%) and 64 (85%) complete endoscopic remission and 63 (84%) and 69 (92%) endoscopic response, respectively. The severity of endoscopic lesions at inclusion did not affect endoscopic outcomes: endoscopic healing rates at weeks 12 and 54 were similar among patients with deep ulcerations at baseline and those with only superficial ulcerations (20/50 (40%) *vs.*12/25 (48%), p=0.68 and 35/50 (70%) *vs.*19/25 (76%), respectively, p=0.79), as well as complete en-

doscopic remission rates (35/50 (70%) *vs.*19/25 (76%), p=0.79 and 43/50 (86%) *vs.*21/25 (84%), respectively, p=1.00) and endoscopic response rates (44/50 (88%) *vs.*19/25 (76%), p=0.32 and 46/50 (92%) *vs.*23/25 (92%), respectively, p=1.00). The location of endoscopic lesions affected endoscopic outcomes: disappearance of deep ulcerations was lower in the ileum than in the colon both at weeks 12 (18/23 (78%) *vs.*57/57 (100%), p < 0.01) and 54 (20/23 (87%) *vs.*57/57 (100%), p=0.02). Consistently, a segmental CDEIS< 3 was less frequent in the ileum than in the colon at weeks 12 and 54 (51% *vs.*80%, p< 0.01 and 70% *vs.*94%, p< 0.01, respectively). No difference was observed between disappearance rates of colonic and rectal deep ulcerations (p=0.17). No difference of segmental remission rates was observed between colonic and rectal lesions at weeks 12 and 54 (80% *vs.*68%, p=0.10 and 94% *vs.*90%, p=0.42, respectively).

Conclusion: In biologic-naive CD patients treated with IFX combo therapy during one year, severity of endoscopic lesions at baseline does not influence healing rates at short- and long-term. Healing rate was lower for ileal than for colonic lesions.

References: 1. D'Haens G, Vermeire S, Lambrecht G, Baert F, Bossuyt P, Pariente B, et al. Increasing Infliximab Dose Based on Symptoms, Biomarkers, and Serum Drug Concentrations Does Not Increase Clinical, Endoscopic, and Corticosteroid-Free Remission in Patients With Active Luminal Crohn's Disease. Gastroenterology. 2018 Apr;154(5):1343-1351.e1.

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OP141 ASSESSING MUCOSAL BARRIER FUNCTION IN VIVO WITH CONFOCAL LASER ENDOMICROSCOPY CAN PREDICT MAJOR CLINICAL EVENTS IN IBD PATIENTS WITH HIGH SENSITIVITY

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Introduction: Probe-based confocal laser endomicroscopy (pCLE) enables *in vivo* microscopic imaging during ongoing endoscopy. Further, pCLE enables visualization of mucosal barrier dysfunction (MBD) in patients with inflammatory bowel diseases (IBD). With this, pCLE is the only technology allowing functional imaging within the GI tract in IBD patients.

Aims & Methods: Here we evaluated whether assessment of MBD by pCLE can accurately predict major clinical events (MCE) in IBD patients. IBD patients in clinical and endoscopic remission were prospectively enrolled. pCLE was performed initially and subsequently patients were followed-up for at least 12 months. During follow-up major clinical events (MCE= IBD-related hospitalization, need for surgery, need for initiation of systemic corticosteroids, immunosuppressants or biologics, escalation of existing biologic therapy) were recorded.

Results: 60 patients were prospectively included (37 Crohn's disease [CD], 23 ulcerative colitis [UC]) with a median age of 38 years (range 19-68). CLE-scoring showed strong correlation with histopathology (r≥0.75, p≤0.05) with an almost perfect interobserver agreement of pCLE findings among different readers (Kappa >0.8). MBD as assessed with pCLE in the terminal ileum showed 100% sensitivity (95% CI, 77-100), 75% specificity (95% CI, 47-92) and 88% accuracy in CD patients and 83.3% sensitivity (95% CI, 50.8-97.1), 81.8% specificity (95% CI, 47.8-96.8) and 82.6% accuracy in UC patients for predicting MCEs during the 12 month follow-up. In those patients with MBD in the colon, sensitivity, specificity and accuracy for predicting MCEs with pCLE were 91.7% (95% CI, 59.8-99.6), 72.8% (95% CI, 39.3-92.7) and 82.6%, respectively.

Conclusion: By assessing MBD *in vivo*, pCLE allows to predict MCE in IBD patients in clinical end endoscopic remission with very high sensitivity. Therefore, pCLE can be used to effectively time and personalize anti-inflammatory treatment in IBD patients.

Disclosure: Nothing to disclose

OP142 CROHN´S DISEASE LESIONS DETECTION BY SMALL-BOWEL CAPSULE ENDOSCOPY: AN AUTOMATIC DEEP LEARNING METHOD

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Introduction: Detection of abnormalities in small-bowel capsule endoscopy (SBCE) is challenging and time consuming. Although Crohn´s disease (CD) is one of the main indications to perform SBCE, at the era of deep learning, few efficient computer-aided detection methods have been established.

We aimed to develop an artificial intelligence system based on deep learning to automatically detect CD lesions in SBCE.

Aims & Methods: An attention based-deep convolutional neural network (ACNN) system has been trained, using two databases, CrohnIPI and a public national database, CAD-CAP. The CrohnIPI database encompassed images extracted from Pillcam® SB2 and SB3 videos of patients with a known or suspected CD, in whom a SBCE was performed between 2013 and 2018 in our department. Pathologic frames have been annotated as follow: aphtoid ulceration, ulceration between 3 and 10mm, ulceration over 10mm, stenosis, erythema and edema. Lesions were not localized or delineated into the image. Pathologic and normal images were not selected in regard of their cleanliness or lighting. The CAD-CAP public database was used for the Gastrointestinal Image ANAlysis deep-learning challenge in 2018. It contains normal, vascular and inflammatory frames.

The whole original CrohnIPI's images were randomly split into three groups: 70% for the training phase, 10% for the validation phase and 20% for the test phase. The training phase was performed 10-times with random split of data to get a robust 10 folds cross-validation. CAD-CAP's images were split into the same three groups as follow: 80%, 20% and 10%. For this database, no cross-validation was done. We assessed our ACNN performance by calculating accuracy, sensitivity and specificity for each database using an independent dataset from the one used for training.

Results: The CrohnIPI database was composed of 1628 normal frames and 1590 containing CD lesions, acquired from 63 videos of 54 patients. The pathologic dataset contained 1281 ulcerations, 419 erythema, 64 stenosis and 428 edemas. Note that one frame could contain several lesions. The CAD-CAP database contained 600 images of each type (normal, vascular and inflammatory). Our classifier reached 90.85% accuracy, 91.47% specificity and 90.22% sensitivity on our own dataset, CrohnIPI. The accuracy, specificity and sensitivity for the CAD-CAP database were respectively 99.67%, 100% and 98.97%.

Conclusion: We developed a new system based on a CNN to automatically detect CD lesions in images obtained from SBCE. The AI system showed a better performance on a selected frames national database. The promising performance of this ACNN paves the way for a complete computer-aided diagnosis system that could support physician´s clinical practice. Future work is aiming to train our ACNN on entire videos and developing an application that could permits a collaborative annotation.

Disclosure: Nothing to disclose

OP143 A PATIENT SELF-MADE ONE STEP QUICK FAECAL TEST IMPROVES DIAGNOSTIC ACCURACY FOR DETECTING ENDOSCOPIC ACTIVITY COMPARED WITH FAECAL CALPROTECTIN ALONE IN INFLAMMATORY BOWEL DISEASE PATIENTS

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Introduction: Faecal Calprotectin (FC) has a good correlation with inflammatory activity in Inflammatory Bowel disease (IBD). Faecal occult blood test (FOBT) has demonstrated effectiveness detecting colorectal cancer or precancerous lesions in screening programs, but it's value for monitoring

IBD activity is less well established. Other faecal biomarkers, including faecal lactoferrin or faecal transferrin, are less used in clinical practice. Quick faecal tests, performed by patients at home or in the outpatients clinic, may be a useful strategy to monitor closely the disease activity.

Aims & Methods: To evaluate the diagnostic accuracy for detecting inflammatory colorectal mucosal activity of a one-step combo card faecal test for the simultaneous semi-qualitative detection of human haemoglobin (hHb), human transferrin (hTf), human calprotectin (hCp) and human lactoferrin (hLf) in samples of IBD patients.

Methods: Consecutive IBD patients referred for colonoscopy according to our center protocol, who complete colonic examinations and returned stool samples, were prospectively recruited. Certest FOB+Transferrin+Ca lprotectin+Lactoferrin® (Certest Biotec S.L, Zaragoza, Spain), a coloured chromatographic inmmunoassay for the simultaneous semi-qualitative detection of hHb, hTf, hCp and hLf, was performed.

Endocoscopic activity was defined using endoscopic MAYO score in Ulcerative Colitis (UC), and SES-CD score for Crohn's Disease (CD).Clinical activity was evaluated by MAYO partial score in UC and Harvey-Bradshaw Index in CD. Laboratory data (C reactive protein, albumin, white blood cell count) were collected.

Positive and negative predictive values (PPV, NPV), sensitivity and specificity and area under ROC curve (AUROC) for each marker and for the different combinations for the detection of endoscopic activity were calculated.

Results: 106 patients (56,6% female, median age 52 years, IQR 42-61) were finally included. 54 (50,9%) with UC and 52 (49,1%) with CD. Median time since diagnosis was 14 years (IQR 9-20). 24 (22.6%) patients report clinical activity, while endoscopic activity was detected in 42 patients (39.6%). No significant difference was observed in C reactive protein mean levels according to the presence of endoscopic activity.

Diagnostic accuracy for hHb, hCp, hTf, hLf and its combination are summarized in Table 1.

AUROC were 0.62 (95% CI: 0.5-0.73) for C reactive protein and 0.83 (95% CI: 0.75-0.91) for the combination of the 4 biomarkers.

Test	Negative test	Positive test	PPV	NPV	Sensitivity	Specificity
hCp	23	83	49.3%	95.6%	97.6%	34.3%
hHb	73	33	75.8%	76.7%	59.5%	87.5%
hTf	79	27	70.4%	70.8%	45.2%	84.9%
hLf	78	28	82.1%	75.6%	54.7%	92.1%
All negative	19	87	48.3%	100%	100%	29.7%
All positive	93	13	100%	68%	30.9%	100%

[Table 1.]

Conclusion: FC alone is a good biomarker to rule out endoscopic activity in IBD, but with a low PPV. The one step quick simultaneous determination of 4 faecal biomarkers with the same kit improves the accuracy of FC alone for detecting patients with high risk of endoscopic activity.

Disclosure: Nothing to disclosure

OP144 LONG-TERM OUTCOMES FOLLOWING ENDOSCOPIC RESECTION OF NEOPLASTIC LESIONS IN ULCERATIVE COLITIS: A LARGE SINGLE-CENTRE RETROSPECTIVE STUDY

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Introduction: Patients with ulcerative colitis (UC) are enrolled into surveillance programs for the early detection of precursor dysplasia and colorectal cancer (CRC). The SCENIC[1] consensus recommends endoscopic resection of amenable dysplastic lesions; however, long-term patient outcomes, particularly for larger and/or non-polypoid lesions, remains poorly defined.

Aims & Methods: We conducted a retrospective observational study at St. Mark's Hospital to identify all patients with Montreal classification E2 & E3 UC who underwent endoscopic resection of dysplastic & serrated le-

sions arising within the extent of inflammation, between 01 January 2005 and 30 June 2016. Patients with incomplete endoscopic resection at index endoscopy, no follow-up endoscopy/colectomy, and those with other CRC-predisposing conditions (e.g. polyposis) were excluded. Patients were followed up until the date of colectomy, or the last endoscopy up to 31 December 2018. Survival analyses were performed using Kaplan-Meier estimation and Cox proportional hazards models.

Results: 236 patients met the inclusion criteria, with a median patient age of 64 years (range 28-88) and median 23 year duration (range 1 - 57) of diagnosed UC, at index endoscopy. CRC was found in the endoscopy resection specimens of 7 patients; 5 underwent colectomy in the following 18 months, with the other two remaining CRC-free and on active monitoring. For the remaining 229 patients, the median patient follow-up time of post-resection was 5.2 years, with a median 4 follow-up endoscopies per patient. There was a median 12.2 months until first follow-up endoscopy for patients with their largest lesion < 10mm, and median 6.2 months until first follow-up endoscpy for those with lesion(s) >=10mm. 22% of patients underwent resection of multiple lesions at their first procedure. Of the 1,259 total endoscopies, only 2 resulted in complications requiring hospitalisation (post-polypectomy bleeding).

In these 229 patients, the risks of first dysplasia recurrence at 1 and 5 years were 27.4% and 59.2% respectively. Colectomy risks at 1 and 5 years were 3.5% and 8.3% respectively in patients with the largest index lesion is < 10mm (n=142), and 8.0% and 26.4% respectively for patients with lesion(s) >10mm (n=87, log-rank p< 0.001). In all but 1 patient who required surgery for UC severity, colectomies were performed either for neoplastic progression to CRC, or for endoscopically unresectable dysplasia. CRC was detected in 45% of colectomy specimens (17/38).

Multivariate Cox proportional hazards analysis demonstrates that lesion size >=10mm (HR = 2.16 [1.06 - 4.4, 95% CI]) and non-polypoid shape (HR = 3.2 [1.51 - 6.4, 95% CI]) were significant predictors of future colectomy (model log-rank p=0.02). Covariates for the presence of multifocal dysplasia, high grade dysplasia, pseudopolyposis, patient age, IBD duration, PSC and serration were statistically insignificant. Of note, patients with LGD resected by endoscopic submucosal dissection (n=15) and piecemeal EMR (n=40) had similar risk of future colectomy (p=0.94).

Conclusion: With over 1,272 patient-years of data, this is the largest study of endoscopic resection in IBD, and the first to correlate resection outcomes with clinical & endoscopic characteristics. While endoscopic dysplasia resection is safe and effective, over 25% of patients with lesions larger than 10mm ultimately required a colectomy within 5 years despite ostensibly complete dysplasia resection at index endoscopy, highlighting the importance of long-term surveillance and counseling these patients, who face the ongoing possibility of surgery.

References: Laine L, Kaltenbach T, Barkun A et al. SCENIC international consensus statement on surveillance and management of dysplasia in inflammatory bowel disease. Gastroenterology. 2015 Mar; 148(3):639-651

Disclosure: Nothing to disclose

OP145 PROGRESSIVE REDUCTION OF COLORECTAL CANCER INCIDENCE AND MORTALITY IN THE CZECH REPUBLIC: EFFECT OF SUBSTANTIAL TARGET POPULATION COVERAGE BY EXAMINATIONS?

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Introduction: The organized non-population based National Colorectal Cancer (CRC) Screening Program in the Czech Republic was running since year 2000. In January 2014, the transition to population-based setting has been implemented. Currently, the annual immunochemical fecal occult blood test (FIT) is offered at the age 50 - 54, followed by FIT+ colonscopy, if positive. In age of 55, there is a choice of either FIT biennially or screening colonoscopy in 10 years interval. Besides these preventive colonoscopies, adenomas and colorectal cancers might be found out and

treated with diagnostic colonoscopy. Between years 2000 and 2015, significant reduction of the CRC incidence (18.4 %) and mortality (32.4 %) was observed.

Aims & Methods: Estimation of the overall coverage of the screening target population (aged 50+) in the Czech Republic by available tests: FIT, screening colonoscopy or diagnostic colonoscopy. The analysis was performed using the newly available database (National Registry of Reimbursed Health Services), which contains individual data on reimbursed healthcare in the Czech Republic. Overall coverage was assessed over a three-year period 2015-2017.

Results: The CRC screening target population consists of 4,056,641 individuals. The FITs were performed in 1,758,596 individuals (43.4 %), screening colonoscopies in 36,387 individuals (0.9 %) and diagnostic colonoscopies in 268,701 individuals (6.6 %). The overall target population coverage in the Czech Republic reached 50.9 % (women 52.0 %, men 49.5 %), highest in the age group of 65 - 69 years. The coverage is heterogenous among the regions (44.6 - 58.2 %), lowest in the capital city.

Conclusion: The overall target population coverage of CRC screening and diagnostic tests (50.9 %) has reached the recommended level according to the European guidelines (45-60 %). The most common examination is FIT, but significant part of screening target population (6.6.%) has been examined with diagnostic colonoscopy. The high number of preventive and diagnostic colonoscopies might be the reason for the observed CRC incidence and mortality reduction in the Czech Republic.

Disclosure: Nothing to disclose

Randomised controlled trials in IBD I

08:30-10:00 / C2

OP146 MUCOSAL MOLECULAR SIGNATURES DIFFER BETWEEN ULCERATIVE COLITIS PATIENTS WITH OR WITHOUT RESPONSE TO VEDOLIZUMAB THERAPY

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Introduction: The anti-integrin monoclonal antibody vedolizumab has been successfully incorporated in the treatment algorithms for moderate to severe ulcerative colitis. A substantial percentage of patients, however, do not respond to this agent and fail to achieve sustained clinical remission. The identification of mucosal or systemic molecular biomarkers that could predict response to vedolizumab is urgently needed to facilitate better patient selection.

Aims & Methods: In a prospective study we aimed to identify mucosal molecular signatures with predictive value for response to vedolizumab in patients with ulcerative colitis. To accomplish our aim, mucosal biopsies were obtained at baseline, i.e. before commencement of vedolizumab, from pre-defined involved areas during lower GI endoscopy.
Total RNA was extracted and the mRNA expression for several inflammatory mediators were examined with an RT² Profiler PCR Array Gene Expression array (Qiagen). Baseline transcriptomic profiles were compared between patients who were subsequently responders to scheduled vedolizumab treatment until week 54 and patients who failed to respond to vedolizumab. A significant difference was considered when there was a

>2-fold increase or decrease in expression and a P value of < 0.05 for the comparison between the 2 groups.

Results: To compare baseline transcriptomic profiles, overall, we assessed 10 patients who continued vedolizumab treatment and were in clinical remission at week 54 and 10 patients who failed treatment with vedolizumab. Mucosal mRNA signatures at baseline differed between the two groups of patients. In particular, we identified eight genes that were significantly upregulated at baseline in non-responders (CD40LG, CXCL10, LTB, IL-23A, CXCL9, SELE, CEBPB, CXCL5) and 9 genes that were significantly downregulated (CXCL6, CCL4, CCL5, NR3C1, TNFSF14, CCL24, CCL2, CD14, CSF1). The top two mostly differentiated genes between the two groups were CD40LG (37-fold increase in non-responders, P= 0.000961) and CXCL6 (20-fold decrease in non-responders, P= 0.0035).

Conclusion: Using a targeted transcriptomic profiling approach we were able to identify, at baseline, several differentially expressed inflammatory mediators in the colonic mucosa of patients with ulcerative colitis who were responders or non-responders after 54 weeks of vedolizumab therapy. If these results are replicated in larger cohorts they could provide reliable predictive biomarkers for better pre-treatment stratification of patients and for optimization of their clinical response to vedolizumab.

Disclosure: This study has been funded by an IISR from Takeda to G.B.

OP147 ANTI-INFLAMMATORY GUT MICROBIAL PATHWAYS ARE DECREASED DURING CROHN'S DISEASE EXACERBATIONS

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Introduction: Crohn's disease (CD) is a chronic inflammatory disorder of the gastrointestinal tract characterized by alternating periods of exacerbation and remission. We hypothesized that changes in the gut microbiome are associated with CD exacerbations, and therefore aimed to correlate multiple gut microbiome features to CD disease activity.

Aims & Methods: Fecal microbiome data generated using whole-genome metagenomic shotgun sequencing of 196 CD patients were of obtained from the 1000IBD cohort (one sample per patient). Patient disease activity status at time of sampling was determined by re-assessing clinical records three years after fecal sample production. Fecal samples were designated as taken 'in an exacerbation' or 'in remission'. Samples taken 'in remission' were further categorized as 'before the next exacerbation' or 'after the last exacerbation', based on the exacerbation closest in time to the fecal production date. CD activity was correlated with gut microbial composition and predicted functional pathways via logistic regressions using MaAsLin software.

Results: In total, 105 bacterial pathways were decreased during CD exacerbation (FDR< 0.1) in comparison to the gut microbiome of patients both before and after an exacerbation. Most of these decreased pathways exert anti-inflammatory properties facilitating the biosynthesis and fermentation of various amino acids (tryptophan, methionine and arginine), vitamins (riboflavin and thiamine) and short-chain fatty acids (SCFAs).

Conclusion: CD exacerbations are associated with a decrease in microbial genes involved in the biosynthesis of the anti-inflammatory mediators riboflavin, thiamine and folate and SCFAs, suggesting that increasing intestinal abundances of these mediators might provide new treatment opportunities. These results were generated using bioinformatic analyses of cross-sectional data and need to be replicated using time-series and wet lab experiments.

Disclosure: Nothing to disclose

OP148 EARLY HISTOLOGIC IMPROVEMENT DEMONSTRATED WITH ORAL OZANIMOD IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE CROHN'S DISEASE IN THE STEPSTONE TRIAL

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Introduction: Ozanimod, an oral immunomodulator that selectively targets $S1P_1$ and $S1P_5$, has demonstrated efficacy and safety in ulcerative colitis (UC) (Sandborn *NEJM* 2016) and is being evaluated in active Crohn's Disease (CD). The aim of the STEPSTONE study was to examine histologic, endoscopic, and clinical outcomes, and safety of ozanimod in adults with CD.

Aims & Methods: STEPSTONE was an open-label uncontrolled phase 2 multicenter trial of ozanimod for 12 weeks, followed by an extension period. Patients with active CD (Crohn's Disease Activity Index [CDAI] score 220-450, total simple endoscopic score for CD [SES-CD] ≥6 [or in isolated ileum disease SES-CD ≥4]) received ozanimod 1 mg daily. Ileo-colonic endoscopic biopsies (perpendicular to the mucosal surface at the edge of the largest ulcer or in the most severely affected area in segments without ulcers) were obtained from the terminal ileum and 4 colonic segments at baseline and Weeks 12 and 52 for assessment of histologic change. A post hoc analysis of histology data through week 12 are reported here, based on a 02-Oct-2017 interim data cut. The Robarts Histopathology Index (RHI) is a validated, reproducible, and responsive index that incorporates four histological descriptors (severity of chronic inflammatory infiltrate, the number of lamina propria neutrophils, the number of neutrophils in the epithelium, and the severity of erosions or ulceration), each of which is objectively graded from 0 to 3 (Mosli *Gut* 2017).

Results: Sixty-nine patients were enrolled. At baseline, mean age was 38 years, mean SES-CD was 13, mean CDAI score was 321, and mean RHI was 16.3. Mean CD duration since diagnosis was 9 years, with 54% of patients having had prior exposure to biologic therapy (i.e., anti-TNF-α, vedolizumab). Table 1 presents the mean change in RHI for paired segments from baseline to Week 12 in the overall study population and in subgroups of patients with or without prior exposure to biologic therapy and by segment. Through 12 weeks, most non-serious and serious adverse events appeared to be related to underlying moderate to severe CD. No new safety signals were identified.

Conclusion: Results of the STEPSTONE trial demonstrated early histologic improvements among patients with moderately to severely active CD who were treated for 12 weeks with ozanimod. These improvements were seen in the patients with and without prior biologic exposure and across all segments.

Study Group	N (ITT N=69)	Mean (Standard Deviation)
Overall Population	52	-4.5 (9.48)
Biologic Exposure		
Prior Biologic Exposure	30	-4.0 (8.59)
Biologic Naïve	22	-5.1 (10.75)
Segment (analysis includes patients with baseline segment scores of >3)		
Ileum	30	-5.3 (8.58)
Rectum	26	-8.2 (10.59)
Left Colon	24	-8.1 (11.38)
Right Colon	19	-4.5 (12.63)
Transverse Colon	17	-2.3 (9.29)

[Table 1: Change from Baseline in Robarts Histopathology Index (RHI) Score at Week 12 - Observed Cases, Intent-to-Treat Population]

References: Sandborn WJ, Feagan BG, Wolf DC, et al. Ozanimod induction and maintenance treatment for ulcerative colitis. N Engl J Med. 2016;374(18):1754-1762. Mosli MH, Feagan BG, Zou G, et al. Development and validation of a histological index for UC. Gut. 2017;66(1):50-58.
Disclosure: Brian G. Feagan: AbbVie, Actogenix, Albireo, Amgen, Astra-Zeneca, Avaxia Biologics, Baxter, Biogen Idec, Boehringer Ingelheim, BMS, Calypso, Celgene, Elan, EnGene, Ferring Pharma, Roche/Genentech, GiCare, Gilead, Given Imaging, GSK, Ironwood, Janssen, Johnson & Johnson, Lexicon, Lilly, Merck, Millennium, Nektar, Novo Nordisk, Pfizer, Prometheus, Protagonist, Celgene, Sanofi, UCB - consultant; Robarts Clinical Trials - director. Geert D'Haens: AbbVie, Ablynx, Amakem, AM Pharma, Avaxia, Biogen, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Celltrion, Cosmo, Covidien/Medtronic, Ferring, Dr. Falk Pharma, EnGene, Galapagos, Genentech/Roche, Gilead, GlaxoSmithKline, Hospira, Immunic, Johnson & Johnson, Lycera, Medimetriks, Millennium/Takeda, Mitsubishi Pharma, Merck Sharp & Dohme, Mundipharma, Novo Nordisk, Otsuka, Pfizer, Prometheus Laboratories/Nestle, Protagonist, Receptos, Robarts Clinical Trials, Salix, Sandoz, SetPoint, Shire, Teva, Tigenix, Tillotts, TopiVert, Versant, Vifor - consultant; AbbVie, Biogen, Ferring, Johnson & Johnson, Merck Sharp & Dohme, Mundipharma, Norgine, Pfizer, Shire, Millennium/Takeda, Tillotts, Vifor - speaker; Robarts Clinical Trials - director; EnGene - shareholder. Keith Usiskin: Celgene - employment/shareholder. Jerry Liu: Celgene - employment/shareholder. Rish K. Pai: none to disclose.

OP149 HISTOLOGIC REMISSION AND MUCOSAL HEALING IN A PHASE 2 STUDY OF MIRIKIZUMAB IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS

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Introduction: Interleukin (IL)-23 is a key cytokine in inflammatory bowel disease pathogenesis. Mirikizumab (miri), a p19-directed IL-23 antibody, demonstrated efficacy and was well-tolerated during 12 weeks of induction followed by an additional 40 weeks of maintenance treatment in a phase 2 randomized clinical trial (NCT02589665) in patients with ulcerative colitis (UC). The histologic results at Week 12 induction and Week 52 maintenance are presented here.

	Induction Treatment Groups			
	Placebo (N=63)	Mirikizumab 50 mg EB IV Q4W (N=63)	Mirikizumab 200 mg EB IV Q4W (N=62)	Mirikizumab 600 mg IV Q4W (N=61)
Mean (SD) unless otherwise specified	Baseline Characteristics			
Age, years	42.62 (13.47)	41.83 (14.06)	43.35 (14.75)	42.44 (13.71)
Male, n (%)	36 (57.1)	38 (60.3)	37 (59.7)	38 (62.3)
Disease duration, years	9.5 (9.6)	8.2 (7.2)	9.0 (9.0)	6.0 (5.7)
Previous biologic use, n (%)	40 (63.5)	39 (61.9)	40 (64.5)	38 (62.3)
	Mayo Score, n (%)			
6-8	27 (42.9)	24 (38.7)	27 (44.3)	26 (42.6)
9-12	36 (57.1)	38 (61.3)	34 (55.7)	35 (57.4)
	Induction Period, Study Week 12			
Histologic remission, n (%)	11 (17.5)	9 (14.3)	28 (45.2)	21 (34.4)
% Difference vs PBO (95% CI)	---	-3.2 (-15.9, 9.6)	27.7 (12.2, 43.2)	17.0 (1.8, 32.1)
	Maintenance Treatment Groups			
	Mirikizumab 200 mg SC Q4W (N=47)		Mirikizumab 200 mg SC Q12W (N=46)	
	Maintenance Period, Study Week 52			
Histologic remission[a], n (%)	31 (66.0)		17 (37.0)	
Durable histologic remission[b], n (%)	20 (42.6)		9 (19.6)	
Mucosal healing[c], n (%)	23 (48.9)		11 (23.9)	

[a]Histologic remission: Geboes histologic subscores of 0 for neutrophils in lamina propria, neutrophils in epithelium, and erosion or ulceration parameters.
[b]Durable histologic remission: histologic remission at both Week 12 and 52.
[c]Mucosal healing: Histologic remission + endoscopic improvement (Mayo endoscopic subscore=0 or 1).

[Table 1.]

Aims & Methods: Patients were randomized 1:1:1:1 to receive intravenous placebo (PBO), miri 50mg or 200mg with possibility of exposure-based dose increases, or fixed miri 600mg every 4 weeks (Q4W), with efficacy assessment at Week 12. Patients who achieved clinical response to miri at Week 12 were re-randomized 1:1 to a double-blind maintenance treatment with miri 200mg subcutaneously (SC) Q4W or every 12 weeks (Q12W), and were treated through Week 52. Endoscopy was performed at Weeks 0, 12, and 52, with biopsy of the sigmoid colon obtained at the most affected area lying at least 30 cm from the anal verge. Glass slide sections of the biopsies, stained with hematoxylin and eosin for histologic evaluation, were digitized and centrally read by one of two gastrointestinal pathologists with scoring performed using the Geboes Score. Histologic remission was defined as Geboes histologic subscores of 0 for neutrophils in lamina propria, neutrophils in epithelium, and erosion or ulceration parameters.

Results: Greater proportions of patients who received 200 or 600mg of miri achieved histologic remission at 12 Weeks compared to PBO (PBO: 17.5% [95% CI: 8.1-26.8]; miri 50mg: 14.3% [95% CI: 5.6-22.9]; 200mg: 45.2% [95% CI: 32.8-57.5]; 600mg: 34.4% [95% CI: 22.5-46.3]. Of the patients who continued onto the maintenance period, 66.0% and 37.0% of patients in miri 200mg Q4W and Q12W groups, respectively, achieved histologic remission at Week 52. Moreover, 42.6% (Q4W) and 19.6% (Q12W) of patients had durable histologic remission throughout the maintenance period, and 48.9% (Q4W) and 23.9% (Q12W) achieved mucosal healing (histologic remission plus endoscopic improvement).

Conclusion: Patients treated with miri achieved and sustained histologic remission over 52 weeks of treatment. These are the first histologic data with an IL-23 p19 targeted antibody in patients with UC.

Disclosure: Study was funded by Eli Lilly and Company.

OP150 HISTOLOGIC IMPROVEMENT WITH VEDOLIZUMAB VS ADALIMUMAB IN ULCERATIVE COLITIS: RESULTS FROM VARSITY

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Introduction: Histologic remission is associated with superior long-term clinical outcomes in ulcerative colitis (UC). VARSITY, the first head-to-head comparison of biologic agents in UC (NCT02497469; EudraCT 2015-000939-33), showed superior clinical remission and endoscopic improvement at Week 52 with vedolizumab (VDZ), a gut-selective, humanised, $\alpha_4\beta_7$ integrin monoclonal antibody, vs adalimumab (ADA), a systemic, human,

anti-tumour necrosis factor (anti-TNF) monoclonal antibody.[1] Both VDZ and ADA were generally safe and well-tolerated.[1] This analysis compared histologic improvements with VDZ vs ADA in VARSITY.

Aims & Methods: Patients with moderately to severely active UC were randomised 1:1 to active VDZ intravenous (IV) infusions (300 mg)/placebo subcutaneous (SC) injections or placebo IV/active ADA SC (160/80/40 mg). Prespecified histologic exploratory endpoints included histologic remission (Geboes score < 2 or Robarts Histopathology Index [RHI] score < 3) and minimal histologic disease activity (Geboes score < 3.2 or RHI score < 5) at Week 14 and Week 52. Histologic remission was also assessed based on previous anti-TNF use.

Results: A total of 769 patients received ≥1 dose of VDZ (n=383) or ADA (n=386). Median (range) duration of exposure was 477 (127, 630) days for VDZ and 420 (71, 454) days for ADA. Mean (standard deviation) baseline histologic disease activity was similar between groups (Geboes: VDZ, 15.0 [4.92]; ADA, 15.1 [5.03]; RHI: VDZ, 19.5 [8.74]; ADA, 19.6 [8.89]). Histologic remission induced by VDZ at Week 52 was greater than with ADA in the overall (Geboes or RHI), anti-TNF naïve (Geboes or RHI), and anti-TNF failure (RHI only) groups (Table). Histologic remission at Week 14 favoured VDZ over ADA, with larger differentiation when using RHI (Table). VDZ also outperformed ADA in achieving minimal histologic disease activity at Weeks 14 and 52 (Table).

Conclusion: VARSITY showed that use of VDZ, compared with ADA, achieved higher rates of histologic remission and minimal histologic disease activity at Weeks 14 and 52 in patients with moderately to severely active UC. These data support the use of VDZ over ADA in UC.

References: 1. Schreiber S, et al. J Crohns Colitis. 2019;13(suppl 1):S612-S613. Abstract OP34.

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Parameter	Adalimumab SC 160/80/40 mg (n=386) Histologic Remission (Geboes Score <2), n (%)	Vedolizumab IV 300 mg (n=383)	Difference (95% CI)	P value	Adalimumab SC 160/80/40 mg (n=386) Histologic Remission (RHI Score <3), n (%)	Vedolizumab IV 300 mg (n=383)	Difference (95% CI)	P value
Overall, Wk 14	12 (3.1)	19 (5.0)	1.8 (-0.9 to 4.6)[a]	0.1944	62 (16.1)	98 (25.6)	9.5 (3.8 to 15.2)[a]	0.0011
Anti-TNF naïve, Wk 14	12 (3.9)	16 (5.3)	1.3 (-2.0 to 4.7)[b]	0.4348	58 (19.0)	82 (27.0)	8.0 (1.3 to 14.6)[b]	0.0198
Anti-TNF failure, Wk 14	0	3 (3.8)	3.8 (-11.9 to 19.5)[b]	0.1180	4 (4.9)	16 (20.3)	15.3 (0.1 to 30.6)[b]	0.0038
Overall, Wk 52	12 (3.1)	40 (10.4)	7.3 (3.8 to 10.8)[a]	<0.0001	77 (19.9)	144 (37.6)	17.6 (11.3 to 23.8)[a]	<0.0001
Anti-TNF naïve, Wk 52	11 (3.6)	40 (13.2)	9.6 (5.2 to 13.9)[b]	<0.0001	69 (22.6)	121 (39.8)	17.2 (9.9 to 24.4)[b]	<0.0001
Anti-TNF failure, Wk 52	1 (1.2)	0	-1.2 (-16.9 to 14.5)[b]	1.0000	8 (9.9)	23 (29.1)	19.0 (7.1 to 31.0)[b]	0.0022
Parameter	Minimal Histologic Disease Activity (Geboes Score <3.2), n (%)				Minimal Histologic Disease Activity (RHI Score <5), n (%)			
Overall, Wk 14	49 (12.7)	81 (21.1)	8.4 (3.2 to 13.6)[a]	0.0017	94 (24.4)	143 (37.3)	12.9 (6.5 to 19.4)[a]	<0.0001
Overall, Wk 52	53 (13.7)	128 (33.4)	19.6 (13.8 to 25.5)[a]	<0.0001	99 (25.6)	162 (42.3)	16.6 (10.0 to 23.1)[a]	<0.0001

[OP150 Table. Histologic Remission and Minimal Histologic Disease Activity]

[a]Adjusted treatment difference and nominal P value: based on the Cochran-Mantel-Haenszel method, stratified by concomitant use of oral corticosteroids (Yes/No) and prior use of anti-TNF therapy (Yes/No); vedolizumab versus adalimumab.

[b]Adjusted treatment difference and nominal P value: based on the Cochran-Mantel-Haenszel method, stratified by concomitant use of oral corticosteroids (Yes/No) or the Fisher´s exact method if the numerator is ≤5; vedolizumab versus adalimumab.

CI, confidence interval; IV, intravenous; RHI, Robarts Histopathology Index; SC, subcutaneous; TNF, tumour necrosis factor-alpha.

OP151 LONG-TERM MUCOSAL HEALING, CLINICAL RESPONSE AND CLINICAL REMISSION IN PATIENTS WITH ULCERATIVE COLITIS TREATED WITH THE ANTI-MUCOSAL ADDRESSIN CELL ADHESION MOLECULE-1 (MADCAM-1) ANTIBODY ONTAMALIMAB (SHP647): RESULTS FROM THE OPEN-LABEL EXTENSION STUDY TURANDOT II

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Introduction: Ontamalimab (SHP647), a human monoclonal IgG$_2$ antibody, targets endothelium expressed mucosal addressin cell adhesion molecule-1 (MAdCAM-1), to reduce lymphocyte homing to the gastrointestinal (GI) tract. In the TURANDOT II trial, ontamalimab was well-tolerated and clinical benefit was seen up to 144 wks in patients with ulcerative colitis (UC). This abstract reports long-term mucosal healing, response and remission in a subset of patients in TURANDOT II.

Aims & Methods: TURANDOT II (NCT01771809) is a phase 2, 2-part open-label (OL) extension study of ontamalimab in patients with moderate-to-severe UC who received placebo or ontamalimab 7.5, 22.5, 75 or 225mg subcutaneously (sc) in the feeder study (TURANDOT). At TURANDOT II baseline (TURANDOT wk 12), patients were randomized to ontamalimab 75 or 225mg sc every 4 wks for 72 wks (OL1). Dose escalation from 75 to 225mg was permitted between wks 8 and 72 in cases of clinical exacerbation or no response. In OL2, patients received 75mg every 4 wks for 72 wks. Endoscopies were carried out at wk 16 for all patients, and a subset of patients undergoing routine cancer surveillance underwent at least one follow-up endoscopy between wks 40 and 72 of OL1: all endoscopies were centrally-read. Mucosal healing (Mayo endoscopy subscore ≤1), clinical remission (total Mayo score ≤2, no subscore >1) and clinical response (≥3-point decrease in total Mayo score from TURANDOT baseline, ≥30% change; ≥1-point decrease in or ≤1 rectal bleed absolute score) were measured.

Results: Of 330 patients in TURANDOT II, 101 had follow-up endoscopies (Table 1), 25.7% (n = 26) of whom had mucosal healing at TURANDOT II baseline. At week 16, 43.6% of patients (n = 44) had mucosal healing, and 75% of these patients (n = 33) maintained mucosal healing up to week 40-72. Of the 65 responders in TURANDOT, 37 (56.9%) had mucosal healing at both wk 16 and at wk 40-72. Of 36 non-responders, 19.4% (n = 7) and 25% (n = 9) achieved mucosal healing at wk 16 and wk 40-72, respectively. Of the responders, 89.2% (n = 58) maintained response and 41.5% (n = 27) were in remission at wk 16; at wk 40-72, 81.5% (n = 53) maintained response and 50.8% (n = 33) were in remission. Of non-responders, 61.1% (n = 22) achieved response and 13.9% (n = 5) achieved remission by wk

16; by wk 40-72, 47.2% (n = 17) had responded and 22.2% (n = 8) were in remission. Overall, the mean Mayo endoscopic subscore of 2 (SD, 0.1) was maintained from baseline to wk 40-72.

	Ontamalimab overall (n = 101)
Mean (SD) Age, years	39.2 (12.5)
Sex, n (%) male	62 (61.4)
Anti-TNF naïve, n (%)	51 (50.5)
Mean time since UC diagnosis, years	7.89 (6.8)
Number (%) of patients in clinical remission	17 (16.8)
Mean (SD) total Mayo score	5.1 (2.7)
Mean (SD) partial Mayo score	3.1 (2.1)
Mean (SD) concentration of hsCRP (mg/dL) (n = 98)	0.7 (1.1)
Mean (SD) concentration of fecal calprotectin (µg/g) (n = 90)	1746 (2950)

[Table 1. Patient demographics and characteristics at TURANDOT II baseline.]

Conclusion: Mucosal healing, response and remission persisted in a subset of patients who continued ontamalimab treatment up to 72 wks and underwent surveillance endoscopies between wks 40 and 72. These findings support study of ontamalimab in on-going phase 3 trials.

Optimising treatment strategies in pancreatitis and pancreatic cancer

08:30-10:00 / E1

OP152 DOUBLE PIGTAIL PLASTIC STENTS ARE CHEAPER AND AS EFFECTIVE AS LUMEN APPOSING METAL STENT FOR THE ENDOSCOPIC DRAINAGE OF WALLED-OFF NECROSIS: A CASE CONTROL STUDY

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Introduction: The presence of infected walled off necrosis (WON) increases morbidity and mortality in severe acute pancreatitis. In the last years, endoscopic drainage has gained increased attention as part of step-up approach, through the creation of a controlled fistula between the upper gastrointestinal tract and the pancreatic necrotic collection. The patency of fistula is allowed by endoscopic stenting and, for this purpose, double pigtail plastic stents have been traditionally used. In the last years lumen apposing metal stents (LAMS) have been proposed. By harboring a wider diameter, they are supposed to allow better necrotic tissue clearance through the execution of multiple sessions of endoscopic necrosectomy. Despite a substantial higher initial cost, a non-unequivocally demonstrated safety and a still unclear effectiveness, lumen apposing metal stents have progressively gained wide spread in clinical practice. Few and mostly heterogeneous studies have compared double pigtail plastic stents and lumen apposing metal stents in terms of short and long-term outcomes. Most of previous studies lacked methodological rigorous designs and have either considered mixed cohorts of patients (WON plus pseudocyst), or have retrospectively investigated extremely inhomogeneous cohorts of patients with WON.

Aims & Methods: To compare short and long-term outcomes of plastic double pigtail versus lumen-apposing metal stents for the endoscopic drainage of infected walled-off necrosis. Single-center, 1:1 case-control study. Patients who have undergone drainage of infected or highly suspected infected pancreatic necrosis through lumen-apposing metal stents (cases) or double pigtail plastic stents (controls) were compared. Controls date up to 2016, when our center used exclusively double pigtail stents; cases date from 2016 onwards, when endoscopic necrosectomies were performed exclusively using lumen-apposing metal stents.

Results: 15 cases and 15 matched controls were enrolled at Karolinska University Hospital, Stockholm, Sweden, between 2011 and 2017. Cases and controls were homogeneous in terms of etiology and clinical characteristics. 93.0% of cases and 86.7% of controls were clinically successful, without any signifcant differences in rates of infection, bleeding and stent migration (respectively 13.3% vs 21.4%; p=0.65; 13.3% vs 0%; p=0.48; 13.3% vs 7.1%; p=1.00), nor of the need for additional percutaneous or surgical treatments (33.3% vs 13.3%; p=0.39). Cases however display a significantly prolonged mean hospital stay (90.2 days vs 18.5 days; p< 0.01) and a higher mean number of endoscopic procedures per patient (1.5 vs 4.8; p< 0.01).

Conclusion: We find that double pigtail stents are not inferior to lumen-apposing metal stents in the treatment of pancreatic WON, and are thus to be favored as a cheaper yet equally effective strategy.

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OP153 PRO-ACTIVE PERCUTANEOUS CATHETER DRAINAGE OF NECROTIC PANCREATIC COLLECTIONS: A LARGE SINGLE CENTER EXPERIENCE

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Introduction: A pro-active protocol that involves frequent catheter upsizing and insertions has been shown to improve the clinical success of percutaneous catheter drainage (PCD). However, there are a limited number of studies with small sample size.

Aims & Methods: In this large cohort, we aim to compare the outcomes of pro-active protocol in patients with acute pancreatitis (AP) and necrotic collections with a published PCD data.
Consecutive patients with AP who underwent PCD with a pro-active protocol between January 2018 and January 2019 were included. The pro-active protocol was defined as PCD of all the drainable collections after an indication of drainage was identified. This was followed by frequent upsizing with the aim to drain the entire collections including both the liquid and the necrotic component. The outcomes were compared with patients from a retrospective published cohort who underwent PCD between January 2011 and December 2017. Outcome measures included need for surgery, mortality, intensive care unit (ICU) stay, hospital stay and complications.

Results: 110 patients underwent PCD with a pro-active protocol. Their outcome was compared with that of 375 patients who had undergone PCD between 2011 and 2017. There was no significant difference in the age, gender, and etiology of AP between the two groups. A fewer number of patients in the pro-active group required ICU admission (34.5 % vs. 61%, $p< 0.001$). Patients in the pro-active PCD group had a significantly reduced length of hospital stay, and ICU stay (27.45±14.2 vs. 36.59±22.49 days; $p=0.001$ and 4.12 ± 8.5 vs. 11.5± 13.6 days; $p< 0.001$ respectively). However, there was no significant difference in terms of mortality and need for surgical intervention between the two groups ($p=0.558$ and 0.153 respectively). The rate of complications was also comparable.

Conclusion: Pro-active PCD protocol results in reduced length of hospital stay, and ICU stay and can reduce hospitalization costs.

Disclosure: Nothing to disclose

OP154 SUPERIORITY OF ENDOSCOPIC INTERVENTIONS OVER MINIMALLY INVASIVE SURGERY FOR INFECTED NECROTIZING PANCREATITIS: A META-ANALYSIS OF RANDOMIZED TRIALS

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Introduction: Infected necrotizing pancreatitis is a highly morbid disease managed either by minimally invasive surgery or endoscopy-based treatment approaches. This meta-analysis was conducted to compare clinical outcomes between patients treated using either approach.

Aims & Methods: MEDLINE and EMBASE were searched to identify all randomized trials that compared minimally invasive surgery and endoscopy-based interventions for the treatment of infected necrotizing pancreatitis. The main outcome measure was to compare rates of complications or death during 6-months of follow-up.

Results: Three studies (184 patients; Bakker OJ et al. PENGUIN trial, JAMA 2012; van Brunschot S et al. TENSION trial, Lancet 2018; Bang JY et al. MISER trial, Gastroenterology 2018) met inclusion criteria (Table). While there was no significant difference in mortality (14.5 vs. 16.1%, risk ratio (RR) 1.02, p=0.96), complications of new onset multiple organ failure (5.2 vs. 19.7%, RR=0.34, p=0.045), enterocutaneous fistula/perforation (3.6 vs. 17.9%, RR=0.34, p=0.034) and pancreatic fistula (4.2 vs. 38.2%, RR=0.13, p< 0.001) were significantly lower for endoscopy compared to minimally invasive surgical treatment approaches. Also, the length of hospital stay was

significantly shorter for endoscopy as compared to surgery (standardized mean difference (SMD) -0.41, p=0.01). There was no significant difference in intrabdominal bleeding (6.2 vs. 12.3%, RR=0.60, p=0.58), new onset diabetes (22.1 vs. 27.3%, RR=0.78, p=0.38) or pancreatic exocrine insufficiency (39.5 vs. 57.8%, RR=0.99, p=0.96) between the cohorts.

Conclusion: An endoscopic treatment approach, as compared to minimally invasive surgery, significantly reduces complications in patients with infected necrotizing pancreatitis.

Outcome measure	Number of patients (n)		Pooled estimate: mean % (95% CI)		Pooled risk ratio (95% CI)	p-value
	Endo-scopy	Surgery	Endoscopy	Surgery		
Major complications or death	95	89	25.8 (7.9 - 49.7)	50.8 (33.5 - 68.0)	0.46 (0.17 - 1.27)	0.136
Major complications or death (inc. pancreatic fistula in all studies)	95	89	26.4 (7.5 - 51.7)	57.0 (38.7 - 74.4)	0.44 (0.19 - 1.01)	0.053
Death	95	89	14.5 (8.3 - 22.1)	16.1 (5.0 - 31.8)	1.02 (0.42 - 2.51)	0.963
New onset Multiple organ failure	95	89	5.2 (1.7 - 10.4)	19.7 (6.1 - 38.7)	0.34 (0.12 - 0.98)	0.045
Enterocutaneous fistula/perforation	95	89	3.6 (0.2 - 11.2)	17.9 (10.8 - 26.3)	0.34 (0.13 - 0.92)	0.034
Pancreatic fistula	86	83	4.2 (0.4 - 11.8)	38.2 (19.9 - 58.5)	0.13 (0.04 - 0.37)	<0.001
Intraabdominal bleeding	95	89	6.2 (0.2 - 27.0)	12.3 (3.5 - 25.4)	0.60 (0.10 - 3.59)	0.575
Endocrine pancreatic insufficiency	85	79	22.1 (14.1 - 31.3)	27.3 (18.0 - 37.7)	0.78 (0.45 - 1.36)	0.380
Exocrine pancreatic insufficiency	85	79	39.5 (3.7 - 84.5)	57.8 (17.8 - 92.5)	0.99 (0.66 - 1.48)	0.962
Length of hospital stay (days)	85	79	-	-	SMD -0.41 (-0.71 to -0.095)	0.010

[Table. Summary of pooled outcome measures and risk ratios]

Disclosure: Ji Young Bang and Shyam Varadarajulu are Consultants for Boston Scientific Corp. and Olympus American Inc.

OP155 TIMING OF PANCREATODUODENECTOMY AFTER BILIARY DRAINAGE IN PATIENTS WITH PERIAMPULLARY CANCER IN THE NETHERLANDS

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Introduction: Obstructive jaundice is a frequent symptom in patients with periampullary cancer. Preoperative biliary drainage (PBD) is indicated in patients with cholangitis, severe jaundice (serum bilirubin > 250 μmol/L), intended neoadjuvant chemotherapy and with extended waiting time for definitive surgical treatment due to logistic reasons. Several studies suggest to delay surgery until 4-8 weeks after PBD to allow for recovery of the liver and immune function but consensus is lacking. The aim of this study is to investigate the relation between time from PBD to pancreatoduodenectomy and (major) postoperative outcomes in patients who underwent resection for periampullary cancer.

Aims & Methods: Anonymized data from patients who underwent pancreatoduodenectomy after PBD for periampullary cancer (i.e. pancreatic ductal adenocarcinoma, distal cholangiocarcinoma, ampullary cancer) between Jan 2017 and Dec 2018 were extracted from the mandatory, nationwide, Dutch Pancreatic Cancer Audit. Patients who underwent (radio) chemotherapy prior to pancreatoduodenectomy were excluded from the analysis. Patients were stratified by time from PBD to surgery into group: A; short (< 4 weeks), B; intermediate (4 - 8 weeks), and C; long (> 8 weeks). The primary outcome was the rate of major postoperative complications, defined as any complication classified as Clavien-Dindo grade ≥3 within 30 days after pancreatoduodenectomy. Secondary outcomes were the rate of PBD-related complications and overall complications. PBD-related complications were pancreatitis, cholangitis, perforation, bleeding, stent occlusion or exchange. Overall complications included PBD-related complications and major postoperative complications. A logistic regression analysis was performed, adjusted for age, gender, body mass index, ASA-score, texture of the pancreas and diameter of the pancreatic duct, to assess the association between time from PBD to pancreatectomy and major postoperative complications.

Results: In total, 539 patients were included after PBD prior to pancreatoduodenectomy, group A 221 (41%), group B 251 (47%), and group C 67 (12%) patients, respectively. The median time between PBD and surgery was 56 days (range 5 - 555 days). The rate of PBD-related complications was 15%, with similar outcomes in the three patient groups (group A 13% vs. group B 16% vs. group C 16%; P = 0.697). Major postoperative complication (Clavien Dindo ≥ 3) rate was 26% and did not differ between the three groups (group A 25% vs. group B 25% vs. group C 38%; P = 0.096). The 30-day mortality rate was 2.2%. The overall complication rate was 69% , with similar outcomes in the three patient groups (group A 67% vs. group B 71% vs. group C 70%; P = 0.574). In the multivariable analysis, the duration of preoperative biliary drainage was not associated with a greater risk of major postoperative complications.

Conclusion: The risk for major postoperative complications after pancreatoduodenectomy is not influenced by the interval between preoperative biliary drainage and the surgical procedure.

Disclosure: Nothing to disclose

OP156 TREATMENT AND SURVIVAL OF LOCALLY ADVANCED PANCREATIC CANCER: A PROSPECTIVE MULTICENTER COHORT

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Introduction: About 30-40% of patients with pancreatic cancer present with locally advanced pancreatic cancer (LAPC). Clinical outcomes are mostly described in highly selected patient cohorts.

Aims & Methods: This study aims to give an overview of treatment and survival within an unselected, consecutive cohort of patients with LAPC. Prospective multicenter study including consecutive patients with LAPC according to Dutch Pancreatic Cancer Group (DPCG) criteria between 04/2015-12/2017 from 14 centers. The decision to start treatment was based on the advice of the multidisciplinary team meeting followed by patient consultation of a medical oncologist. Restaging of CT-scans was performed by a nationwide expert panel after two months of systemic treatment. The panel evaluated response according to RECIST criteria, resectability and eligibility for clinical trials.

Results: In total, 422 patients were included, of whom 325 (77%) started chemotherapy, 84 (20%) received best supportive care (BSC) and 13 (3%) started other primary treatments. Most patients started FOLFIRINOX (n=252, 60%), 32 patients (8%) were treated with gemcitabine plus nab-paclitaxel and 41 (10%) with gemcitabine monotherapy. 309 patients were restaged of whom 33 (11%) had a partial response, 221 (72%) had stable disease and 55 (18%) had progressive disease. A total of 34/422 patients (8%) underwent a resection. Median overall survival (mOS) in all patients was 10 months (95%CI 9-11) In patients treated with FOLFIRINOX, nab-paclitaxel plus gemcitabine or gemcitabine monotherapy, mOS was 14 (95%CI 12-16), 9 (95%CI 7-11), and 9 months (95%CI 8-10) respectively. Resected patients had a mOS of 23 months (95%CI 12-34).

Conclusion: In a large prospective multicenter cohort of LAPC, median overall survival was 10 months, 60% received FOLFIRINOX treatment and 8% were eligible for a resection after neoadjuvant chemotherapy with promising survival. Since treatment allocation bias cannot be excluded future randomized studies are needed.

Disclosure: Nothing to disclose

OP157 PAMPAC TRIAL: OCCURRENCE OF PAIN AND QUALITY OF PAIN MANAGEMENT IN PATIENTS WITH PANCREATIC CANCER

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Introduction: Pancreatic ductal adenocarcinoma (PDAC) is associated with moderate to severe cancer-related pain in most patients, as it has a high rate of neural invasion. Despite WHO management guidelines for pain management, more than 50% of cancer patients worldwide still experience pain. One-third of these patients don't receive an adequate pain treatment. This data indicates that there is a need for more investigations in this field. Especially for patients with PDACan adequate pain therapy is essential to maintain the quality of life as they are often in a palliative situation with very limited life expectancy.

Therefore we conducted this study to investigate the occurrence of pain and the quality of pain management in patients with PDAC.

Aims & Methods: A multi-center, prospective, cross-sectional study with the aim to evaluate the quality of care in patients with PDAC. The level of pain and the impact of pain on functioning was assessed by the brief pain inventory. Additionally insufficient pain treatment (undertreatment) and possible determinants (e.g. patient characteristics, disease characteristics, tumour therapy) were registered. Undertreatment was defined as a negative PMI (pain management index), which is a score constructed upon the patients level of worst pain substracted from the most potent level of analgesic drug therapy. To investigate the impact of e.g. changes in tumor therapy or disease progression on pain and pain therapy we conducted an follow up after a minimum of 4 weeks.

Results: We recruited 128 patients with histologically proven PDAC. 44% of the patients were female and the mean age was 68 yrs. 77 patients (60%) were questioned while hospitalised and 51 patients (40%) in the outpatient department or private practice. 50 patients (39%) had resectable pancreatic cancer, whereas 22 patients (17%) had locally advanced disease (LAPC) and 56 patients (44%) metastatic disease (mPDAC). A total of 79 patients suffered from pain regularly (62%). 90% of these patients showed an impaired quality of life. Patients in an more advanced disease stage (LAPC, mPDAC) suffered more frequently from pain (77%) than patients with resectable disease (38%). Most common locations of pain were the epigastric area (72%), the lumbar region (34%) and the lower abdomen (22%). 30 patients (38%) showed an insufficient pain treatment (undertreatment). Interestingly, undertreatment was more frequent in resectable disease (58%) than in LAPC (41%) or mPDAC (21%). Furthermore patients with high performance status (ECOG 0: 55%; ECOG 1: 37%) showed a higher rate of undertreatment than patients with a low performance status (ECOG 2: 18%, ECOG 3: 25%). Until now 60 patients (47%) have completed the follow up after a median of 2,2 months. The proportion of patients with pain has not changed markedly (57%), but untertreatment was less frequent (18%) compared to the first interview.

Conclusion: The preliminary results of this ongoing study confirm that there is a high percentage of patients with PDAC suffering from pain. Despite comprehensive pain management guidelines we can show that the amount of patients affected from undertreatment is still very high. Furthermore, our data indicates that especially patients in an early disease stage and with high performance status will need a better pain management in the future.

When the study will have collected more patient data, we'll might be able to identify other determinants of undertreatment and thereby help to improve the pain management in PDAC patients.

Disclosure: Nothing to disclose

Novel therapeutic approaches in microscopic colitis and c. difficile

08:30-10:00 / Barcelona

OP158 MICROBIOTA RESTORATION THERAPEUTIC CANDIDATES FOR PREVENTING RECURRENT *CLOSTRIDIUM DIFFICILE* INFECTIONS: SIMILAR 6-MONTH OUTCOMES FOR ENEMA-ADMINISTERED RBX2660 AND ORAL CAPSULE-ADMINISTERED RBX7455

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Introduction: Recurrent *Clostridium difficile* infections (rCDI) are a public health threat and linked to intestinal microbiome disruption. In response to the need for a standardized, FDA-approved treatment, numerous microbiota-based drugs are being evaluated to restore a healthier microbiome and reduce recurrence. Herein we compare data from clinical trials of RBX2660 and RBX7455, two dosage forms of an investigational standardized, stabilized microbiome restoration therapeutic currently under study for potential FDA approval.

Aims & Methods: This comparison includes a large multicenter, open-label Phase 2 trial of RBX2660 (administered by enema; n=149) and a single-center, open-label Phase 1 investigator-sponsored trial of RBX7455 (administered by room-temperature-stable oral capsules in 3 dosing regimens; n=30). Both trials had similar participant populations. The RBX2660 trial included multi-recurrent CDI participants while the RBX7455 trial included first- and multi-recurrent CDI participants (n=17 and 13, respectively). For both trials, primary efficacy was defined as absence of recurrent CDI at 8 weeks after the last study treatment. Safety and durability were further assessed at 6 months. Microbiome restoration was assessed by shallow-shotgun sequencing of pre- and post-treatment stool samples and product samples, followed by calculation of a previously reported prototype Microbiome Health Index (MHI) that expresses collective changes in taxonomic composition.

Results: Primary efficacy was 80% for RBX2660 and 90% for RBX7455. Among primary treatment responders in the RBX2660 trial evaluable at 6 months (n=109), 97% were CDI occurrence-free at 6 months. All primary responders in the RBX7455 trial remained CDI occurrence-free at 6 months. Reported safety was similar between the studies. In addition, mcrobiome changes were similar between the studies, characterized by a predominance of *Gammaproteobacteria/Bacilli*-class bacteria before treatment and

predominance of *Bacteroidia/Clostridia*-class bacteria after treatment. The change in compositional microbiome as expressed via the MHI from before to after treatment was statistically significant for both studies.

Conclusion: Two clinical studies confirm similar safety, durable efficacy, and microbiome restoration for RBX2660 and RBX7455 microbiota restoration therapies. These 6-month outcomes suggest that microbiome restoration for preventing rCDI can be comparably effective via enema or oral administration routes. Since the manufacture of both products is standardized and adheres to quality control specifications, these results represent an important advance towards FDA-approved microbiome therapeutics. Ongoing placebo-controlled studies will expand upon these data.

Disclosure: This analysis was funded by Rebiotix Inc., Roseville, MN, USA.

OP159 CURE OF RECURRENT *CLOSTRIDIUM DIFFICILE* INFECTION WITH A MIX OF 12 GUT BACTERIA, FAECAL MICROBIOTA TRANSPLANTATION OR ORAL VANCOMYCIN: RESULTS FROM AN OPEN-LABEL MULTICENTRE RANDOMISED CONTROLLED TRIAL

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Introduction: Faecal microbiota transplantation (FMT), i.e. transfer of stool from a healthy donor to a recipient, is an effective treatment for recurrent *Clostridium difficile* infection (rCDI)[1,2] but there are concerns on safety and long-term risks. Using a mix of specified microorganisms instead of donor stool could be a solution. Rectal bacteriotherapy (RBT) using a mix of 12 well-characterised gut bacteria has a reported efficacy for rCDI at 64-88 % in case series but has not been evaluated in a randomised controlled trial (RCT).[3-5]

Aims & Methods: An open-label multicentre RCT compared the efficacy of FMT, RBT and oral vancomycin for rCDI. We hypothesized that FMT and RBT were *superior* to vancomycin and that RBT was *non-inferior* to FMT (non-inferiority margin: 5% difference in cure rate).

All consecutive patients with a positive test for *Clostridium difficile* (CD) were screened for eligibility May 2017 - March 2019 at two centres covering eastern Denmark, including primary care. Patients with rCDI, defined as diarrhoea and a positive CD-test after at least one treatment course for CDI, were eligible. Patients with life expectancy <3 months, other GI infections or GI-disease with diarrhoea, concomitant antibiotic use or severe immune deficiency were excluded.

Patients were stratified according to number of recurrences (first vs. multiple recurrences) and randomly allocated 1:1:1 to FMT, RBT or vancomycin by computer-generated stratified block randomisation. The FMT and RBT groups were pre-treated with vancomycin for 7-14 days. Both FMT and RBT was applied rectally. FMT was applied once but, if needed, repeated twice within two weeks. RBT was applied on three consecutive days. Patients in the vancomycin-group received 14 days of vancomycin, but for patients with multiple recurrences, this was continued with tapering for additional five weeks.

The primary outcome was clinical cure, defined as absence of CDI during 90 days of follow-up. We planned an interim analysis of the primary outcome after 90 participants. Treatments were compared with Mantel-Haentzel odds ratios (95 % CI) and χ²-tests with adjustment for stratification in the superiority analysis. Non-inferiority was evaluated with the difference in cure rates (95 % CI).

Results: Cure rates for FMT, RBT and vancomycin in the interim-analysis (n=90) are shown in Table 1.

FMT, 1-3 infusions (n = 31)	RBT (n = 29)	Vancomycin (n = 30)
22 (71 %), (52 - 86 %)	16 (55 %), (36 - 74 %)	13 (43 %), (25 - 63 %)

[Table 1 - Clinical cure at 90 days (Intention-to-treat analysis): n (%), (95% CI)]

Patients receiving 1-3 infusions of FMT had a higher cure rate than patients receiving only vancomycin (OR 3.2 (1.1; 9.2), p = 0.05) with a NNT of 3.5. The cure rate for one infusion of FMT was 48 % (30 - 67 %) and 68 % (49 - 83 %) for 1-2 infusions.

We found no difference between the efficacy of RBT and vancomycin (OR 1.6 (0.6; 4.5)) or FMT and RBT in a superiority-analysis (OR 2.1 (0.7; 6.4)), but could not show non-inferiority between FMT and RBT either (difference in cure rate: 15.8 % (-43 %; 12 %)).

Recruitment for the RCT was terminated after the interim-analysis for logistic reasons.

Conclusion: Rectally applied faecal microbiota transplantation was superior to oral vancomycin in treating recurrent *Clostridium difficile* infection, but multiple infusions were often needed. The effect of rectal bacteriotherapy with 12 gut bacteria appeared similar to both faecal microbiota transplantation and vancomycin, but the study had insufficient power for non-inferiority analysis. Rectal bacteriotherapy could be a safe alternative in treating recurrent *Clostridium difficile* infection, but further RCTs are needed.

References: 1. van Nood E, Vrieze A, Nieuwdorp M, et al. Duodenal infusion of donor feces for recurrent Clostridium difficile. N Engl J Med. 2013;368(5):407-415. doi:10.1056/NEJMoa1205037 2. Cammarota G, Masucci L, Ianiro G, et al. Randomised clinical trial: faecal microbiota transplantation by colonoscopy vs. vancomycin for the treatment of recurrent Clostridium difficile infection. Aliment Pharmacol Ther. 2015;41(9):835-843. doi:10.1111/apt.13144 3. Tvede M, Rask-Madsen J. Bacteriotherapy for chronic relapsing Clostridium difficile diarrhoea in six patients. Lancet. 1989;1(8648):1156-1160. doi:10.1016/S0140-6736(89)92749-9 4. Tvede M, Tinggaard M, Helms M. Rectal bacteriotherapy for recurrent Clostridium difficile-associated diarrhoea: results from a case series of 55 patients in Denmark 2000-2012. Clin Microbiol Infect. 2015;21(1):48-53. doi:10.1016/j.cmi.2014.07.003 5. Emanuelsson F, Claesson BEB, Ljungström L, Tvede M, Ung K-A. Faecal microbiota transplantation and bacteriotherapy for recurrent Clostridium difficile infection: A retrospective evaluation of 31 patients. Scand J Infect Dis. 2014;46(2):89-97. doi:10.3109/00365548.2013.858181

Disclosure: Michael Tvede owns MT MicroSearch, that manufactures the bacteria mix for RBT. All other authors have nothing to disclose.

OP160 RIDINILAZOLE REDUCES RECURRENCE OF *CLOSTRIDIUM DIFFICILE* INFECTION WITH MINIMAL IMPACT ON THE GUT MICROBIOTA

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Introduction: Recurrence of *Clostridium difficile* infection (rCDI) is a particular concern with significant impacts on patient welfare and healthcare resources. Ridinilazole (RDZ) is a novel targeted spectrum antibiotic under investigation to treat CDI and reduce rCDI. Here translation of *in vitro* data to clinical trial data is reviewed.

Aims & Methods: Susceptibility testing was performed to CLSI standards with vancomycin (VAN), metronidazole (MTZ) and fidaxomicin (FDX) as comparators. The Phase 2 clinical trial was a double-blind, randomised, study of 100 patients assigned 1:1 to 10 days RDZ 200 mg BID or VAN 125 mg QID treatment. Primary endpoint was sustained clinical response (SCR), defined as cure at end of therapy (EOT) and no rCDI for the next 30 days. Primary analysis population was the modified intent-to-treat (MITT); all randomised subjects with a diagnosis confirmed by presence of free toxin. Relative effects of RDZ and VAN on the gut microbiota was examined by sequencing 16S rDNA amplicons from stool collected at baseline, days 5, 10, 25 and end of study. Bioinformatic analyses were performed in QIIME.

Results: Across 4 studies RDZ *C. difficile* (N=439) MIC range was 0.015-0.5μg/mL with no major differences by ribotype or resistance phenotype. RDZ and FDX were less active against Gram negative anaerobes, especially *B. fragilis* group, than VAN and MTZ. RDZ had limited activity against Gram positive anaerobes. The Phase 2 clinical study exceeded its primary endpoint (MITT), with RDZ shown to be superior on SCR to VAN with rates of 66.7% and 42.4%, respectively. Superiority on SCR was driven by a reduction in rCDI for RDZ (14.3%) compared with VAN (34.8%). Microbiota analysis showed at RDZ EOT that significant relative abundancy reductions were limited to 2 Firmicute families including Peptostreptococcaceae (includes *C. difficile*). In contrast VAN at EOT resulted in significant losses

(often to below detection) in 4 Firmicutes families: Peptostreptococcaceae, Ruminococcaceae, Erysipelothrichaceae and Lachnospiraceae. A 70% drop in Actinobacteria, and greater than 3 log decrease in Bacteroidetes, abundance were also observed. These changes were associated with a 25-fold increase in Proteobacteria abundance, in particular Enterobacteriaceae.

Conclusion: These data demonstrate targeted *C. difficile* activity with RDZ both *in vitro* and in CDI patients. Preservation of the microbiome likely contributed to the low rate of recurrence, and superior efficacy on SCR, compared to vancomycin. Further clinical development is warranted.

Disclosure: E. Duperchy, R. Vickers and D. Roblin: Summit Therapeutics´ Employees; Hold stock options; M. Wilcox: Consultant Summit Therapeutics; J. Freeman: Research Contractor Summit Therapeutics.

OP161 MOLECULAR CLASSIFICATION OF COLLAGENOUS COLITIS BY WHOLE-GENOME SEQUENCING

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Introduction: Collagenous colitis (CC) is a common, inflammatory bowel disease that deteriorates the patients' quality of life due to chronic watery diarrhoea. Treatment with the locally active glucocorticoid budesonide is effective in inducing clinical remission. However, how budesonide restores water homeostasis in the gut is unknown. To address this question, we performed genome-wide RNA sequencing (RNAseq) analysis on mucosal samples from different CC patient populations.

Aims & Methods: We collected colonic biopsy samples from healthy controls and CC patients with active disease. Additionally, we obtained matched samples from budesonide-responsive patients (clinical remission) under treatment with budesonide (9mg/d for 8 weeks), as well as biopsies from budesonide-refractory patients (n=9 patients/group). Ulcerative colitis (UC) samples were included as a separate control. Total RNA was isolated for library construction and RNA sequencing (RNAseq). Whole genome expression data was processed using the R statistical software, and analysed by principal component analysis (PCA), linear models with least square regression, and empirical Bayes moderates t statistics. Results were corrected using the Benjamini-Hochberg FDR method, with an adjusted *p* value < 0.05 considered to be statistically significant. Gene ontology (GO) analysis was performed in Cytoscape, using the ClueGO and CluePedia packages.

Results: Unsupervised PCA of all samples identified three principal components which separated sample groups into distinct clusters of gene expression, explaining 31% of the transcriptional variation. One of the components (8% of the variation) clearly demarcated UC samples from healthy controls and CC. Remarkably, mucosal samples from budesonide-refractory patients exhibited a discrete RNA expression profile that was distinct from all other groups. Moreover, PCA of budesonide-responsive persons revealed two principal components (24% of the variation) that separated these sample groups.

Subsequent analysis of differentially regulated genes showed that the expression of 395 genes was altered in patients with active CC patients compared to healthy controls, and that these were evenly split into 201 up- and 194 down-regulated genes. GO analysis of these genes indicated that up-regulated genes were mainly involved in immune response, whereas metabolic pathway genes were down-regulated. In samples from budesonide-treated patients, 75 genes were differentially regulated compared to controls. These genes were found to regulate glycogen metabolism and mineral absorption. A paired comparison of the matched active CC patients and budesonide-treated patients showed a dysregulation of 337 genes. A GO analysis of these genes were dominated by categories covering carboxylic acid transmembrane transport, protein ubiquitination and immune response. Finally, genes dysregulated in refractory CC were mostly associated with the transport of secretory proteins.

Conclusion: Our analyses suggest that collagenous colitis is a transcriptionally homogeneous disease that can be characterised by means of differential gene expression. We were able to identify unique gene expression profiles that describe patient sub-populations, also with regard to their treatment response. Interestingly, transcriptome analysis indicates that budesonide-refractory CC may be a discrete disease entity, which may explain the lack of treatment response. Further study of the transcriptional landscape of CC may reveal pathogenic mechanisms and therapeutic vulnerabilities for this common, debilitating inflammatory bowel disease.

Disclosure: CEH and AM have received an unrestricted research grant from Ferring Pharmaceuticals (Switzerland). The remaining authors do not have any conflicts of interest.

OP162 CRITICAL ROLE OF AQUAPORIN 8 IN COLLAGENOUS COLITIS

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Introduction: Collagenous colitis (CC) patients experience chronic watery diarrhoea that effectively can be treated by budesonide, a locally acting glucocorticoid. The diarrhoeal mechanism in CC is unclear, as well as budesonide's mode of action. We hypothesize that aquaporin (AQP) water channels are critical in the development of watery diarrhoea in CC; hence, they are highly important proteins in CC pathogenesis that could be targeted by new drugs.

Aims & Methods: Colonic biopsy samples from controls (n=27), active CC patients (n=26), matched CC patients under treatment with budesonide (9mg for 8 weeks; n=18), and refractory CC patients (active disease despite 6mg budesonide for more than 12 weeks; n=15) were collected at the local university hospital, and either preserved in AllProtect for subsequent gene analyses or embedded in paraffin. Total RNA was isolated for analysis of the AQP genetic expression profiles (AQPs 0-12) by quantitative polymerase chain reaction (qPCR); whereas paraffin embedded samples were used for fluorescent staining of AQP8 and subsequent analysis by confocal microscopy. AQP8 protein levels in the apical membrane of colonic epithelial cells were determined by computer-assisted image analysis using ImageJ. Non-parametric Mann-Whitney (for unpaired samples) or Wilcoxon (for paired samples) statistical tests with Monte Carlo algorithm were used to analyze the results in SPSS.

Results: Gene expression of AQPs 8 and 11 was significantly downregulated in all CC patient sets when compared to control samples. In patients that achieved clinical remission under budesonide treatment, AQP 8 and 11 levels were increased compared to their corresponding pre-treatment samples. In contrast, budesonide-refractory patients had similar AQP gene expression levels as non-matched patients with active CC. The gene expression of the remaining AQPs (AQP0-7, AQP10, and AQP12) did not significantly change in any group.

Protein levels of AQP8 were further studied by confocal microscopy in the apical side of intestinal epithelia of all CC patient groups. As with gene expression, AQP8 protein levels were significantly decreased in active CC patients. Budesonide treatment increased AQP8 protein in the mucosa, albeit not to the same level as in the control group. Curiously, budesonide-refractory CC patients had similar AQP8 protein levels as controls.

Conclusion: Aquaporin 8 is significantly downregulated in active CC. Both AQP8 gene and protein expression are partially restored after treatment with budesonide, which is sufficient to achieve clinical remission. In budesonide-refractory patients, AQP8 gene expression is decreased, while its protein levels do not change when compared to controls. Therefore, we conclude that AQP8 has a critical role in active CC leading to malabsorption of water in the colon which could represent a novel diarrhoeal pathomechanism.

Disclosure: CEH and AM have received an unrestricted research grant from Ferring Pharmaceuticals (Switzerland).

OP163 EFFICACY AND SAFETY OF ANTI-TNFα THERAPY IN BUDESONIDE REFRACTORY, DEPENDENT OR INTOLERANT MICROSCOPIC COLITIS: A FRENCH REGISTRY

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Introduction: Currently, budesonide is the best documented treatment for microscopic colitis (MC); however, relapses, even after maintenance therapy, remain high, and some patients become intolerant or refractory. Tumor necrosis factor (TNF) α antagonists have revolutionized the management of inflammatory bowel diseases (IBD) and may represent an interesting option in refractory MC patients. The aim of the study was to evaluate the efficacy and safety of anti-TNFα in refractory MC in France.

Aims & Methods: Budesonide refractory, intolerant or dependent MC patients treated with anti-TNFα agents (infliximab (IFX), adalimumab (ADA)) in the French Groupe d'étude thérapeutique des affections inflammatoires du tube digestif (GETAID) centers were included in the registry. The data was collected from october 2018 to february 2019. Clinical remission was defined by strictly less three daily bowel movements, and clinical response by an improvement in stool frequency ≥ 50%.

Results: Fourteen patients were included, 7 received IFX and 7 received ADA. Maintenance therapy was prescribed in 13/14 patients with a median duration of 10 months. Clinical remission without steroids at week 12 was reached in 5/14 patients (35.7%): 5/7 (71.4%) in the IFX group and 0/7 in the ADA group. Clinical response at week 12 was reached in 6/7 patients in the IFX group and 3/7 patients in the ADA group. Clinical response at week 52 was obtained in 7/14 (50%) patients. A 36.4% and 68.1% reduction rate was observed in mean daily stools at weeks 12 and 52, respectively. Histological response, evaluated in nine patients, was complete in 11.1% and partial in 44.4%. All patients in clinical remission at week 12 achieved histological response; conversely, none of the patients in clinical failure at week 12 had histological response. The only patient who achieved clinical and histological remission was on combination therapy with IFX and azathioprine. Five patients were switched to another anti-TNFα in second-line therapy and two subsequently reached clinical remission. Two patients received vedolizumab for loss of response, it was successful in one. All treatment lines confounded, seven patients (50%) and eight patients (57.1%) were in clinical remission at week 12 and 52, respectively. Six adverse events have been reported, including a serious one (anaphylactoid reaction with anti-IFX antibodies).

Conclusion: To date, this is the biggest case series evaluating the efficacy and safety of anti-TNFα in refractory MC. Anti-TNFα therapies appear to be effective and could represent a suitable option in highly refractory MC patients.

Disclosure: Nothing to disclose

Randomised controlled trials in IBD II
10:30-12:00 / A3

OP164 EFFICACY OF UPADACITINIB AS AN INDUCTION THERAPY FOR PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS, WITH OR WITHOUT PREVIOUS TREATMENT FAILURE OF BIOLOGIC THERAPY: DATA FROM THE DOSE-RANGING PHASE 2B STUDY *U-ACHIEVE*

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Introduction: Upadacitinib (UPA), a Janus kinase 1 (JAK1) selective inhibitor, shows promise as a future treatment option for ulcerative colitis (UC). Initial data analyses from an 8-week, double-blind, placebo (PBO)-controlled, dose-ranging, Phase 2b induction study in patients with moder-

Treatment groups		Clinical Remission per Adapted Mayo Score[a]	Endoscopic Improv[b]	Endoscopic Remission[c]	Clinical Response per Adapted Mayo Score[d]	Histologic Improv[e]	Clinical Response per Partial Mayo Score[f]
				Week 8			Week 2
		Primary endpoint			Secondary endpoints		
All, n (%)	Placebo n=46	0	1 (2.2)	0	6 (13.0)	3 (6.5)	7 (15.2)
	UPA 7.5 mg QD n=47	4 (8.5)	7 (14.9)*	3 (6.4)	14 (29.8)*	15 (31.9)**	11 (23.4)
	UPA 15 mg QD n=49	7 (14.3)*	15 (30.6)***	2 (4.1)	22 (44.9)***	25 (51.0)***	18 (36.7)*
	UPA 30 mg QD n=52	7 (13.5)*	14 (26.9)***	5 (9.6)*	23 (44.2)***	23 (44.2)***	19 (36.5)*
	UPA 45 mg QD n=56	11 (19.6)**	20 (35.7)***	10 (17.9)**	28 (50.0)***	27 (48.2)***	31 (55.4)***
Bio-IR, n (%)	Placebo n=34	0	0	0	2 (5.9)	3 (8.8)	5 (14.7)
	UPA 7.5 mg QD n=34	2 (5.9)	3 (8.8)	1 (2.9)	8 (23.5)	7 (20.6)	6 (17.6)
	UPA 15 mg QD n=36	3 (8.3)	9 (25.0)**	0	13 (36.1)**	15 (41.7)**	11 (30.6)
	UPA 30 mg QD n=40	4 (10.0)	8 (20.0)**	1 (2.5)	13 (32.5)**	15 (37.5)**	15 (37.5)**
	UPA 45 mg QD n=42	5 (11.9)	11 (26.2)***	5 (11.9)	17 (40.5)***	20 (47.6)***	22 (52.4)***
Non-Bio-IR, n (%)	Placebo n=12	0	1 (8.3)	0	4 (33.3)	0	2 (16.7)
	UPA 7.5 mg QD n=13	2 (15.4)	4 (30.8)	2 (15.4)	6 (46.2)	8 (61.5)**	5 (38.5)
	UPA 15 mg QD n=13	4 (30.8)	6 (46.2)	2 (15.4)	9 (69.2)	10 (76.9)***	7 (53.8)
	UPA 30 mg QD n=12	3 (25.0)	6 (50.0)	4 (33.3)	10 (83.3)*	8 (66.7)**	5 (41.7)
	UPA 45 mg QD n=14	6 (42.9)*	9 (64.3)**	5 (35.7)*	11 (78.6)*	7 (50.0)**	9 (64.3)*

Intent-to-treat population, non-responder imputation aSFS ≤1, RBS = 0, endoscopic score ≤1. bEndoscopic subscore ≤1. cEndoscopic subscore = 0. dDecrease from BL ≥2 points and ≥30%, plus RBS decrease ≥1 or absolute RBS ≤1. eDecrease from BL in Geboes score. fMayo score excluding endoscopic subscore; defined as decrease from BL in the Partial Mayo Score ≥2 points and ≥30% from BL, plus decrease in RBS ≥1 or absolute RBS ≤1. Improv, Improvement; RBS, rectal bleeding subscore; SFS, stool frequency subscore ***, **, *statistically significant at 0.001, 0.01, and 0.05 levels, respectively, for UPA versus PBO

[OP164 Table: Clinical efficacy in the overall patient population and in Bio-IR and non-Bio-IR patients]

ately to severely active UC suggest that UPA is generally well tolerated with significantly greater efficacy compared with PBO.[1] In this subgroup analysis, efficacy was assessed in patients who either had an inadequate response, loss of response, or intolerance to biologic therapies (Bio-IR), or were non-Bio-IR.

Aims & Methods: Adult patients with moderately to severely active UC (Adapted Mayo Score [Mayo score without Physician Global Assessment] 5-9 points) and centrally read Mayo Endoscopy Subscore ([MES] 2-3) were randomized to receive extended-release UPA 7.5, 15, 30, 45 mg, or PBO once daily (QD) for 8 weeks. Patients were stratified by previous biologic use, baseline (BL) corticosteroid use, and BL Adapted Mayo Score (≤7/>7). Efficacy measures (defined in Table) were the primary endpoint of Clinical Remission per Adapted Mayo Score at Week 8, and secondary endpoints were Endoscopic Improvement, Endoscopic Remission, Clinical Response (CR) per Adapted Mayo Score, Histologic Improvement (all Week 8), and CR per Partial Mayo Score (Week 2). Pairwise comparisons between UPA doses and PBO for efficacy endpoints were conducted using the Cochran-Mantel-Haenszel test stratified by randomization factors. Non-responder imputations were utilized for missing values.

Results: A total of 250 patients were randomized with a mean (SD) age of 42.3 (14.2) years and a disease duration of 8.2 (2.5) years. At BL, 74.4% were Bio-IR, 36% had an Adapted Mayo Score >7, and 79% had a MES of 3. At Week 8, a UPA dose-response relationship was observed for all efficacy endpoints in the overall population, and in each of the two subpopulations. The highest efficacy rates were observed with UPA 45 mg QD treatment for the majority of the endpoints, which were all significant for the non-Bio-IR group analyses and in the majority of the Bio-IR group analyses. While the non-Bio-IR subpopulation was small, efficacy rates were numerically higher than in the Bio-IR subpopulation. Adverse events leading to discontinuation were similar across the overall UPA groups, and numerically higher in the PBO group.[1]

Conclusion: Upadacitinib showed a dose response in Bio-IR and non-Bio-IR patients with moderately to severely active UC, with numerically greater efficacy in the non-Bio-IR population. Patient numbers were small in both groups and the findings need to be confirmed in larger Phase 3 studies.

References: 1. Sandborn WJ, et al. UEGW 2018, #OP195

Disclosure: The authors and AbbVie scientists designed the study, and analyzed and interpreted the data. AbbVie funded the research and provided writing support.

OP165 EARLY CLINICAL RESPONSE AND REMISSION WITH VEDOLIZUMAB VERSUS ADALIMUMAB IN ULCERATIVE COLITIS: RESULTS FROM VARSITY

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Introduction: VARSITY is the first head-to-head trial comparing the efficacy and safety of 2 biologic therapies, vedolizumab (VDZ) and adalimumab (ADA), in patients with moderately to severely active ulcerative colitis (UC). We previously reported significantly higher rates of clinical remission (31.3% vs 22.5%; p=0.0061) and endoscopic improvement (39.7% vs 27.7%; p=0.0005) at Week 52 with VDZ vs ADA.[1] Here we report data on early response and remission within the first 14 weeks, as well as durable clinical remission.

Aims & Methods: VARSITY was a phase 3b, randomised, double-blind, double-dummy, active-controlled study (NCT02497469; EudraCT 2015-000939-33). As predefined, exploratory endpoints, we examined early clinical response and remission, along with the durability of remission. Clinical response was defined as reduction in complete Mayo score of ≥3 points and ≥30% (or partial Mayo score reduction of ≥2 points and ≥25% from baseline if sigmoidoscopy was not performed), with a decrease in rectal bleeding subscore of ≥1 point or absolute rectal bleeding subscore of ≤1 point. Clinical remission was defined as complete Mayo score of ≤2 (or partial Mayo score ≤2 points if sigmoidoscopy was not performed) and

no individual subscore >1 point. Patients who were in clinical remission at Week 14 and Week 52 were considered as having achieved durable clinical remission.

Results: A total of 769 patients received ≥1 dose of VDZ (n=383) or ADA (n=386). Baseline characteristics were comparable between the 2 groups. A trend for separation in clinical response started to emerge at Week 6 favouring VDZ vs ADA. Clinical response at Week 14 favoured VDZ vs ADA (257 [67.1%] vs 177 [45.9%]; treatment difference 21.2%). A greater number of patients achieved clinical remission at Week 14 on VDZ vs ADA (102 [26.6%] vs 82 [21.2%]; treatment difference 5.3%). Patients on VDZ achieved higher rates of durable clinical remission (70 [18.3%] vs 46 [11.9%]); laboratory results correlated with these findings. Post-hoc analyses showed a larger mean (standard deviation) change of C-reactive protein (CRP) from baseline to Week 14 (-32.88 [155.77] nmol/L VDZ vs -3.35 [260.82] nmol/L ADA) and to Week 52 (-50.87 [174.76] nmol/L VDZ vs -37.21 [169.17] nmol/L ADA) in favour of VDZ. Greater mean declines in faecal calprotectin (FCP) levels were seen in patients on VDZ compared to ADA (Week 14: -1,551.3 [6,236.70] mg/kg VDZ vs -1,167.6 [4,647.67] mg/kg ADA; Week 52: -2,187.3 [7,440.42] mg/kg VDZ vs -1,846.6 [4,560.55] mg/kg ADA).

Conclusion: Patients on VDZ had numerically higher rates of both clinical response and clinical remission by Week 14 compared with ADA. Those patients on VDZ also achieved higher rates of durable clinical remission compared with ADA. CRP and FCP results correlated with these findings. These data on early clinical response and clinical remission, as well as durable remission, further support the use of VDZ over ADA in patients with moderately to severely active UC.

References: 1. Schreiber S, et al. J Crohns Colitis. 2019;13(suppl 1):S612-S613. Abstract OP34.

Disclosure: Silvio Danese: Lecture fee(s): AbbVie, Ferring, Hospira, Johnson and Johnson, Merck, MSD, Takeda, Mundipharma, Pfizer Inc, Tigenix, UCB Pharma, Vifor, Biogen, Celgene, Allergan, Celltrion, Sandoz, Boehringer Ingelheim; Consultancy: AbbVie, Ferring, Hospira, Johnson and Johnson, Merck, MSD, Takeda, Mundipharma, Pfizer Inc, Tigenix, UCB Pharma, Vifor, Biogen, Celgene, Allergan, Celltrion, Sandoz, Boehringer Ingelheim ; Edward V. Loftus Jr.:EVL has received financial support for research from: AbbVie, Takeda, Janssen, UCB, Amgen, Pfizer, Genentech, Celgene, Receptos, Gilead, MedImmune, Seres Therapeutics, and Robarts Clinical Trials; and has served as a consultant for AbbVie, Takeda, Janssen, UCB, Amgen, Pfizer, Eli Lilly, Celltrion Healthcare, Allergan, Bristol-Myers Squibb, Celgene, Gilead, Genentech, and Boehringer Ingelheim. Jean-Frederic Colombel: Consultancy/advisory board membership: AbbVie, Amgen, Boehringer Ingelheim, Celgene Corporation, Celltrion, Enterome, Ferring, Genentech, Janssen Pharmaceuticals, Medimmune, Merck & Co., Pfizer, Protagonist, Second Genome, Seres, Takeda, Theradiag; Speaker: AbbVie, Ferring, Takeda, Shire; Research support: AbbVie, Genentech, Takeda; Stock options: Intestinal Biotech Development, Genfit.; Laurent Peyrin-Biroulet: LPB has received consulting fees from Merck, AbbVie, Janssen, Genentech, Mitsubishi, Ferring, Norgine, Tillots, Vifor, Therakos, Pharmacosmos, Pilège, BMS, UCB-pharma, Hospira, Celltrion, Takeda, Biogaran, Boehringer Ingelheim, Lilly, Pfizer, HAC-Pharma, Index Pharmaceuticals, Amgen, and Sandoz; Lecture fees from Merck, AbbVie, Takeda, Janssen, Takeda, Ferring, Norgine, Tillots, Vifor, Therakos, Mitsubishi, and HAC-Pharma; Brihad Abhyankar :Former employee of Takeda; Jingjing Chen: Employee of Takeda; Raquel Rogers: Employee of Takeda; Richard A. Lirio: Employee of Takeda; Jeffrey D. Bornstein: Employee of Takeda; Stefan Schreiber: On-spot consultancy fees from AbbVie, Celltrion, Janssen, Merck, Pfizer, Roche, and Takeda; Bruce E. Sands: Consulting fees from 4D Pharma, Abbvie, Allergan Sales, Amgen, Arena Pharmaceuticals, Boehringer Ingelheim, Capella Biosciences, Celgene, EnGene, Ferring, Gilead, Janssen, Lilly, Lyndra, MedImmune, Oppilan Pharma, Otsuka, Palatin Technologies, Pfizer, Progenity, Rheos Medicines, Seres Therapeutics, Synergy Pharmaceuticals, Takeda, Target PharmaSolutions, Theravance Biopharma R&D, TiGenix, Vivelix Pharmaceuticals, and WebMD; research funding from Celgene, Pfizer, Takeda, Janssen.

OP166 EFFICACY AND SAFETY OF MIRIKIZUMAB (LY3074828) IN A PHASE 2 STUDY OF PATIENTS WITH CROHN'S DISEASE

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Introduction: Mirikizumab (Miri; interleukin [IL]-23p19 antibody) is a humanized, immunoglobulin G4 monoclonal antibody specifically targeting the p19 subunit of the IL23 cytokine. Prior studies have shown Miri to have efficacy in psoriasis and ulcerative colitis. We assessed safety and efficacy of Miri with a Phase 2, multicenter, randomized, parallel-arm, double-blind, placebo (PBO)-controlled trial (NCT02891226) in patients with moderate-to-severely active Crohn's disease (CD).

Aims & Methods: At baseline, subjects (N=191) were randomized with a 2:1:1:2 allocation across 4 treatment arms (200, 600, 1000mg Miri, and PBO, administered intravenously (IV) at Weeks 0, 4, and 8). The primary objective was to evaluate superiority of Miri to PBO in inducing endoscopic response, defined as 50% reduction from baseline in Simple Endoscopic Score for Crohn´s disease (SES-CD), at Week 12. Secondary objectives included clinical remission by Patient-Reported Outcomes (PRO remission), endoscopic remission, and safety, with Crohn´s Disease Activity Index (CDAI) assessed as an exploratory endpoint. Treatment comparisons of the primary endpoint and other efficacy variables were conducted using a logistic regression analysis with treatment, geographic region, and prior biologic CD therapy use included in the model, with a 2-sided alpha level of 0.10 considered significant.

Results: Baseline characteristics were similar among treatment groups. At Week 12, endoscopic response rates were significantly greater for all Miri groups compared to PBO, with 25.8% (8/31[95%CI: 10.4-41.2], p=0.079), 37.5% (12/32[95% CI: 20.7-54.3], p=0.003), and 43.8% (28/64[95%CI: 31.6-55.9], p< 0.001) patients in the 200, 600, and 1000mg groups, respectively, achieving endoscopic response compared to 10.9% (7/64[95%CI: 3.3-18.6]) of PBO patients. Endoscopic remission was achieved in 15.6 and 20.3% of patients treated with 600 and 1000mg Miri (p=0.032 and p=0.009, respectively; 200mg p=0.241), versus 1.6% of PBO. Likewise, PRO remission rates were greater in 200, 600, and 1000mg Miri groups (12.9% [4/31], p=0.346; 28.1% [9/32], p=0.005 and 21.9% [14/64], p=0.025, respectively), versus 6.3% PBO. CDAI response was greater in all Miri groups (200mg: 48.4%, p=0.015; 600mg: 56.3%, p=0.001; 1000mg: 42.2%, p=0.026) versus 23.4% of PBO and CDAI remission rates greater in the 600 and 1000mg Miri groups (200mg: 16.1%, p=0.321; 600mg: 40.6%, p< 0.001; 1000mg: 26.6%, p=0.013) versus 9.4% of PBO. The frequencies of serious adverse events (SAEs) and treatment-emergent adverse events (TEAEs) across treatment groups (SAEs: 0-9.4%, TEAEs: 58.1-65.6%) were similar to PBO (SAEs: 10.9%, TEAEs: 70.3%) and consistent with the previous safety profile.

Conclusion: These data affirm the efficacy of Miri in the induction of statistically significant and clinically meaningful improvements in clinical and endoscopic outcomes. Sustained efficacy and safety are being evaluated in the maintenance phase of this study.

OP167 COMPARISON OF VEDOLIZUMAB AND INFLIXIMAB EFFICACY IN ULCERATIVE COLITIS AFTER FAILURE OF A FIRST SUBCUTANEOUS ANTI-TNF AGENT: A MULTICENTRE COHORT STUDY

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Introduction: Few data are available so far to select the best therapeutic option after failure of a first subcutaneous anti-TNF agent in ulcerative colitis (UC). The objective of the present study was to compare the efficacy of infliximab (IFX) and vedolizumab (VDZ) in UC patients who stopped a first subcutaneous anti-TNF agent.

Aims & Methods: Consecutive UC patients who started IFX or VDZ from February 2009 to November 2018 in 12 French referral centres after receiving at least one injection of adalimumab or golimumab have been included in a retrospective study. Inclusion corresponded to the first administration of IFX or VDZ. Outcomes were rate of clinical remission (defined as a partial Mayo score - PMS - ≤ 1) at week 14, survival without treatment discontinuation, and survival without any UC-related event (treatment discontinuation, colectomy, acute severe UC or hospitalization). Predictors of clinical remission at week 14 were determined by multivariate analysis logistic regression.

Results: Among the 225 patients included [133 (59%) male; median age: 41; InterQuartileRange: 27-55) years; median PMS was 6/9 (5-8)], 154 (68%) received IFX and 71 (32%) VDZ after failure of a first subcutaneous anti-TNF agent. At inclusion, patients treated with IFX were significantly more often men, having more recent UC and more primary non-response to the first anti-TNF (116 (77%) in the IFX group, 44 (62%) in the VDZ group), were more often admitted for the current flare, received more combotherapy and had a higher median PMS [6 (5-8)] as compared to those treated with VDZ [5.5 (3-7)]. At week 14, 40 (26%) patients treated with IFX were in clinical remission as compared to 35 (49%) patients treated with VDZ (p< 0.01; odds ratio (OR): 2.77; 95%-confidence interval (95%CI): 1.54; 4.99). After adjustment on baseline characteristics, the difference between both drugs was nearly significant (OR 2.12; 95%CI: 0.95-4.80; p=0.07). With a median follow-up duration of 115 (55-165) months, survival rates without treatment discontinuation at 1 year and 3 years were 86% and 69% for patients receiving IFX, and 97% and 91% for those receiving VDZ (p< 0.01). Survival rates without UC-related event at 1 year and 3 years were 85% and 67% with IFX and 93% and 87% with VDZ (p< 0.01).

Conclusion: After failure of a first subcutaneous anti-TNF agent, patients treated with VDZ achieved more clinical remission at week 14 and less UC-related events – including treatment discontinuation, colectomy, acute severe UC and hospitalization – than those treated with IFX. Such results have to be confirmed by head-to-head trials.

Disclosure: Nothing to disclose

OP168 ADALIMUMAB FOR PATIENTS WITH CROHN'S DISEASE COMPLICATED BY INTRA-ABDOMINAL ABSCESS: A MULTICENTRE PROSPECTIVE, OBSERVATIONAL COHORT STUDY

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Introduction: Management of intra-abdominal abscess complicating Crohn's disease (CD) is challenging. Surgery with delayed intestinal resection is often recommended in this situation.

Aims & Methods: The aim of this study was to estimate the success rate of adalimumab (ADA) in patients with CD complicated by intra-abdominal abscess, after complete resolution of sepsis and abscess, and to identify predictive factors of success.

We performed a multicentre, prospective, observational cohort study in patients with CD complicated by intra-abdominal abscess. Patients previously treated with an anti-TNF at the time of abscess occurrence, and patients with post-operative abscesses were not eligible. Patients with complete resolution of sepsis and abscess confirmed by MR enterography (MRE) at baseline were included and received 160 mg of ADA at W0, 80 mg at W2, and then 40 mg every 2 weeks. The primary endpoint was ADA success at W24 defined as no steroids use after the 12th week following inclusion, no intestinal resection, no abscess recurrence and no clinical relapse (CDAI > 220 or HBI > 4 and CRP > 10 mg/L at two consecutive visits). Baseline factors associated with ADA success were identified using the logistic regression model.

Results: From April 2013 to December 2017, 190 patients from 27 GETAID centers were screened. Seventy-three patients were excluded, and 117 were analysed for the primary endpoint. Median age at inclusion was 28 years (inter-quartile range [IQR]:24-36), 58 (50%) patients were male and 39 (35%) were active smokers. Median disease duration before abscess occurrence was 2.4 (0-58.7) months. Thirty-three (28%) patients had been previously exposed to thiopurines. Small bowel CD was responsible for intra-abdominal abscess in 101 (86%) patients. The median size of abscess was 25 (18-40) mm. MRE at baseline showed a visible fistula tract in 67 (58%) patients. Eleven (9%) patients had a percutaneous drainage of the abscess and 114 (97%) patients received antibiotics for a median duration of 21.5 (8-31) days. Fifty-nine (50%) patients had an exclusive enteral nutrition, 12 (10%) an exclusive parenteral nutrition and 28 (24%) oral feeding. Median CRP and albumin level at inclusion after abscess resolution

were 5 (2-9) mg/L and 39 (36-43) mg/L, respectively. At W24, 83/117 (71%) patients achieved ADA success. Ten (9%) patients underwent an intestinal resection. At least one serious adverse event was reported in 40 patients, with relapse of intra-abdominal abscess in 10 patients, other infections in 7 patients, and gastrointestinal disorders including CD worsening in 27 patients. No death was reported. In multivariate analysis, predictive factors of ADA success were a mural high signal intensity on T2-weighted MRE (Odds ratio[OR]=2.92; 95% Confidence interval [CI]:1.06-7.99; p=0.04), active smoking (OR=0.37; 95%CI: 0.14-1.00; p=0.05) and CRP level at ADA initiation (OR=0.98; 95%CI: 0.96-1.00; p=0.11).

Conclusion: In this prospective cohort of CD patients complicated by intra-abdominal abscess, ADA success was observed in 71% of cases at W24. During this period, 9% of cases had an abscess recurrence and 9% needed an intestinal resection. No death was reported. Non-smoking status, low CRP level and active signs of inflammation on MRE at ADA initiation were associated with ADA success at W24.

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OP169 IMPACT OF RESPONSE AND INFLAMMATORY BURDEN AT START OF MAINTENANCE THERAPY ON CLINICAL EFFICACY OF USTEKINUMAB DOSING REGIMEN IN UC: WEEK 44 RESULTS FROM UNIFI

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Introduction: The UNIFI maintenance study was a Phase 3, double-blind, placebo-controlled, randomized-withdrawal study in pts with moderate to severely active ulcerative colitis (UC) who failed conventional or biologic therapy and were in clinical response 8 weeks after receiving a single ustekinumab (UST) IV induction dose. In this study, patients were randomized to placebo, UST 90 mg SC q8w or q12w.

Aims & Methods: To examine the relative efficacy of the UST 90 mg SC q8w or q12w maintenance regimens, subgroup analyses were performed for clinical outcomes of clinical remission, symptomatic remission, and endoscopic improvement at Week 44 for patients who did and did not achieve these endpoints at the start of maintenance. Additionally, analyses of clinical remission and endoscopic improvement at Week 44 based on pre-specified cut-points of the concentrations of inflammatory biomarkers (CRP [≤3 mg/L, >3 mg/L] and fecal calprotectin [≤250 mg/kg, >250 mg/kg]) at maintenance baseline were conducted.

Results: For patients who had achieved clinical remission, symptomatic remission, or endoscopic improvement at maintenance baseline, efficacy of UST q8w and UST q12w regimens for the respective endpoint at Week 44 was similar (Table 1). By contrast, for patients who did not achieve clinical or symptomatic remission or endoscopic improvement at maintenance baseline, UST q8w demonstrated greater efficacy than UST q12w for that endpoint at Week 44.

Patients with low inflammatory burden marked by CRP ≤3 mg/L at maintenance baseline achieved similar efficacy at Week 44 with UST q8w and q12w dosing regimens as measured by clinical remission and endoscopic improvement (Table 1). By contrast, patients with high inflammatory burden, marked by CRP>3 mg/L at maintenance baseline, achieved greater

efficacy at Week 44 with UST q8w versus q12w dosing over the endpoints. Generally similar trends were seen in patients with fecal calprotectin measurements for low (≤ 250 mg/kg) and high (>250 mg/kg) inflammatory burden at maintenance baseline.

Conclusion: Among patients with a clinically meaningful response to a single IV induction dose of UST, maintenance treatment with UST q8w or q12w demonstrated similar efficacy at Week 44. By contrast, the efficacy of UST q8w at Week 44 was greater than the q12w regimen for patients with higher inflammatory burden or who did not achieve clinical or symptomatic remission or endoscopic improvement at week 8. These data suggest that multiple clinical measures can help inform the decision on the most appropriate maintenance dosing regimen for UST in the treatment of patients with UC.

Endpoint	Patients attaining outcome at maintenance baseline			Patients not attaining outcome at maintenance baseline		
	Placebo SC[a]	UST 90 mg q12w	UST 90 mg q8w	Placebo SC[a]	UST 90 mg q12w	UST 90 mg q8w
Clinical remission[b]	37.8% (17/45)	70.0% (28/40) *	65.8% (25/38) *	19.2% (25/130)	28.8% (38/132)	37.7% (52/138) *
Symptomatic remission[c]	51.6% (63/122)	73.0% (89/122) *	73.1% (87/119) *	30.2% (16/53)	36.0% (18/50)	56.1% (32/57) *
Endoscopic improvement[d]	35.2% (25/71)	60.3% (41/68) *	64.9% (37/57) *	24.0% (25/104)	32.7% (34/104)	44.5% (53/119) *
	Subjects with CRP ≤3 mg/L at maintenance baseline			Subjects with CRP >3 mg/L at maintenance baseline		
Endpoint	Placebo SC[a]	UST 90 mg q12w	UST 90 mg q8w	Placebo SC[a]	UST 90 mg q12w	UST 90 mg q8w
Primary efficacy analysis set	111	121	111	60	49	65
Clinical remission at Week 44[b]	29 (25.4%)	53 (43.8%)*	50 (45.0%)*	13 (21.7%)	12 (24.5%)	27 (41.5%)*
Endoscopic improvement at Week 44[d]	33 (28.9%)	57 (47.1%)*	59 (53.2%)*	17 (28.3%)	16 (32.7%)	31 (47.7%)*

a: Patients who were in clinical response to ustekinumab IV induction dosing and were randomized to placebo SC on entry into this maintenance study
b: A Mayo score ≤2 points, with no individual subscore >1.
c: Mayo stool frequency subscore of 0 or 1 and a rectal bleeding subscore of 0.
d: A Mayo endoscopy subscore of 0 or 1.
* Nominal p-value < 0.05.

[Table 1. Clinical Outcomes at Week 44 by Maintenance Baseline Status for the Outcome]

Disclosure: Drs. Panaccione, Peyrin-Biroulet, Danese, Leong, Arasaradnam, Rowbotham, Abreu, and Sands are all investigators for Janssen Research & Development, LLC Drs. Marano,O'Brien, Szapary, Zhang, Johanns are all employees of Janssen Research & Development, LLC.

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10:30-12:00 / B3

OP170 INFLUENCE OF EARLY CHOLECYSTECTOMY TIMING FOR ACUTE CHOLECYSTITIS ON SHORT TERM SURGICAL MORBIDITY AND MORTALITY: A NSQIP DATABASE ANALYSIS

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Introduction: There is growing evidence that supports early cholecystectomy is associated with better outcomes. Nonetheless, the exact timing of early cholecystectomy is still yet to be determined.
Aims & Methods: To elucidate the optimal timing of early cholecystectomy and determine the outcomes of patient undergoing early versus delayed same admission cholecystectomy in patients with acute cholecystitis. We studied all patients undergoing open or laparoscopic cholecystectomy

from the National Surgery Quality Improvement Program (NSQIP) participant use data specific file 2014-2016. NSQIP includes prospective validated 30-day outcomes and anonymized data for patients undergoing major surgery in more than 500 hospitals. The primary outcome in this study was short term surgical morbidity and mortality. The patients were divided into 4 groups, those who underwent surgery at days 0, 1, 2, 3+ for AC. We used the chi square test or Fisher's exact (when one or more cells had an expected frequency lower than 5) to compare categorical variables between groups 0 and groups 1,2 and 3+ respectively. We used the independent t-test for continuous variables. We performed multivariate logistic regression to evaluate the association between the timing of surgery after admission and 30-days postoperative outcomes. We included confounders into the models based on both clinical and statistical significance.
Results: A total of 21,392 patients were included. Laparoscopic approach was used in 86% of cases. Patients who performed their operation at 3+ were significantly older and had worse baseline clinical status prior to operation. The overall morbidity (including wound infection, cardiac and respiratory complications, urinary infections, thromboembolism and sepsis) occurred in 1439 patients (6.82%), while 1-month rebleeding and mortality occurred in 457 (2.1%) and 185 (0.9%) patients. On univariate analysis, all morbidity events and mortality increased significantly with increased surgery timing from admission (Table 1).

	Adjusted ORs (95% CI)						
	Days from hospital admission to operation				p-value		
	0 (n=8906)	1 (n=6952)	2 (n=2605)	3+ (n=2929)	1 vs 0	2 vs 0	3+ vs 0
Mortality	Reference	0.99 (0.62 - 1.56)	1.38 (0.83 - 2.30)	1.57 (1.01 - 2.44)	0.96	0.21	0.05
Composite Morbidity	Reference	0.79 (0.68 - 0.93)	0.81 (0.66 - 0.99)	0.99 (0.82 - 1.19)	0.004	0.04	0.89
Bleeding	Reference	1.14 (0.86 - 1.49)	1.41 (1.03 - 1.94)	1.83 (1.39 - 2.43)	0.36	0.03	<0.0001
Return to OR	Reference	0.86 (0.66 - 1.13)	0.76 (0.53 - 1.09)	1.07 (0.79 - 1.45)	0.28	0.14	0.67

[Adjusted 30-day outcomes]

Compared to patients who underwent surgery at day 0, and after adjusting for confounders (table 1), patients who underwent surgery at day 1 and day 2 had a significantly slightly lower composite morbidity. No significant difference among the four groups in the need for reoperation was noted. The bleeding rate was significantly higher in patients who were operated at day 2, and was highly significant in the 3+ group. Patients who underwent surgery at day 3+ had a significantly higher mortality rate.
Conclusion: Early cholecystectomy performed after 72 hours from admission was associated with higher mortality and rebleeding. Our results support the "golden 72 hours window "for surgery in AC.
Disclosure: Nothing to disclose

OP171 A NEW ENDOSCOPIC TRANSPAPILLARY GALLBLADDER DRAINAGE COMBINED WITH INTRADUCTAL ULTRASONOGRAPHY FOR PATIENTS WITH ACUTE CHOLECYSTITIS

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Introduction: Endoscopic transpapillary gallbladder drainage (ETGBD) is a useful drainage technique for acute cholecystitis, although this method is technically difficult.
Aims & Methods: When ETGBD is combined with intraductal ultrasonography (IDUS), the orifice of the cystic duct (CD) in the common bile duct is more easily detected, and the CD is more easily cannulated. The aim of the present study is to evaluate the efficacy and feasibility of ETGBD with IDUS compared to ETGBD alone.
A hundred patients with acute cholecystitis requiring ETGBD were recruited between January 2015 and December 2017. The first consecutive 50 out of 100 patients were treated by ETGBD without IDUS, and the following consecutive 50 patients were treated by ETGBD with IDUS. The primary outcome was technical success rate.

Results: The technical success rate of ETGBD with IDUS was significantly higher than that of ETGBD without IDUS (92.0% [46/50] vs 72.0% [36/50], P= 0.014). There was no significant difference between the procedure lengths of both groups (74.0 minutes [10-140] vs 65.6 minutes [14-215], p = .219). Complication rates of ETGBD with IDUS were significantly higher than those of ETGBD without IDUS (6.0% vs 0% P< .001); however, IDUS technique-related complications such as pancreatitis were found in only one case.

Conclusion: ETGBD with IDUS may be one of the best therapeutic methods for patients with acute cholecystitis.

Disclosure: Nothing to disclose

OP172 ENDOSCOPIC ULTRASOUND VS ENDOSCOPIC TRANS-PAPILLARY VS PERCUTANEOUS GALLBLADDER DRAINAGE IN HIGH-RISK ACUTE CHOLECYSTITIS PATIENTS: A SYSTEMATIC REVIEW AND COMPARATIVE META-ANALYSIS

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Introduction: Endoscopic transpapillary gallbladder drainage (ETGBD) and endoscopic ultrasound guided gallbladder drainage (EUSGBD) are alternative to percutaneous gallbladder drainage (PCGBD) in the management of acute cholecystitis unfit for surgery. Data comparing these modalities are limited and have reported conflicting results.

Aims & Methods: We searched multiple databases from inception through December2018 to identify studies that reported on ETGBD, EUSGBD, and PCGBD in the management of acute cholecystitis high risk for surgery. Our goals were to compare the pooled rates of technical success, clinical success, adverse events, and disease recurrence.

Results: 13 studies (815 patients), 12 studies (506 patients), and 8 studies (1484 patients) were treated by ETGBD, EUSGBD, and PCGBD respectively. Baseline patient characteristics were comparable between the groups. Age ranged from 65 to 85 years with 61% males. The pooled technical and clinical successes of EUSGBD was statistically superior to ETGBD [95.9% (95% CI 91-98.1, I²=6.4) vs 80.3% (95% CI 67.4-89, I²=68), p=0.001; 96.7% (95% CI 94.1-98.1, I²=0) vs 88.6% (95% CI 84.3-91.8, I²=42.3), p=0.001; respectively]. Bleeding and perforation was statistically more with EUSGBD [3.8% (95% CI 2.3-6.2, I²=0) vs 1.6% (95% CI 0.7-3.2, I²=0), p=0.03; 4.4% (95% CI 2.8-6.9, I²=0) vs 1.7% (95% CI 0.9-3.4, I²=0), p=0.004; respectively], whereas pancreatitis was statistically more with ETGBD [6.4% (95% CI 4.1-9.8, I²=27.3 vs 0, p=0.001]. Pooled clinical success of EUSGBD was statistically superior to PCGBD [96.7% (95% CI 94.1-98.1, I²=0) vs 90% (95% CI 85.7-93.1, I²=37.6), p=0.001], whereas the pooled rate of technical success was comparable (Table).Pooled rate of disease recurrence was comparable between the groups (Table).

(95% CI, I2)	Technical success	Clinical Success	Adverse events	Recurrence
ETGBD	80.3% (67.4-89, 68)	88.6% (84.3-91.8, 42.3)	9.8% (5.3-17.2, 40.7)	3.6% (1.9-6.6, 17.1)
EUSGBD	95.9% (91-98.1, 6.4)	96.7% (94.1-98.1, 0)	12.1% (6.9-20.2, 7.9)	4.5% (2.7-7.4, 0)
PCGBD	94.7% (85.7-98.1, 95.3)	90% (85.7-93.1, 37.6)	18.4% (9.9-31.5, 93.7)	7.5% (4.7-11.6, 48.6)
p-value of statistical significance				
ETGBD vs EUSGBD	0.001	0.001	0.69	0.66
ETGBD vs PCGBD	0.03	0.53	0.2	0.1
EUSGBD vs PCGBD	0.91	0.001	0.37	0.1

ETGBD: endoscopic transpapillary gallbladder drainage, EUSGBD: endoscopic ultrasound guided gallbladder drainage, PCGBD: percutaneous gallbladder drainage

[Summary of pooled results]

Conclusion: EUSGBD demonstrates superior clinical success when compared to ETGBD and/ or PCGBD in the treatment of acute cholecystitis in surgically unfit patients. Based on our analysis, EUSGBD should be considered the first line approach for treating patients with acute cholecystitis who are high risk for surgery and preferable be done in high volume centers due to significant but rare adverse events.

Disclosure: Nothing to disclose

OP173 EVALUATIONS OF SEVERITY ASSESSMENT FOR ACUTE CHOLECYSTITIS : JAPAN-TAIWAN COLLABORATIVE MULTICENTER STUDY FOR ACUTE CHOLECYSTITIS

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Introduction: Acute cholecystitis is a disease frequently encountered in daily practice presenting with right hypochondrial pain as the main symptom. Tokyo Guidelines 2013 (TG13) have already been recognized as the severity assessment criteria to be recommended in today's medical care for acute cholecystitis all over the world. Severe acute cholecystitis was defined as acute cholecystitis accompanying organ dysfunctions directly related to poor prognosis. Exactly acute cholecystitis is basically not a disease with a high mortality. However, it was thought that guidelines should make it clear that adequate management with appropriate use of severity assessment criteria for acute cholecystitis does lead to improved patients' prognosis.

Aims & Methods: The aim for this study was validation of the clinical impact of TG13 severity assessment criteria for acute cholecystitis. The study was designed as Japan-Taiwan collaborative multicenter retrospective study of acute cholecystitis from 2011 to 2013. Based on the data, we investigated the TG13 severity assessment criteria by analyzing the correlations between grade and prognosis, surgical procedures, and histopathology, in addition between the numbers of organ dysfunctions and mortality.

Results: A total of 5,459 patients in 154 Japanese and Taiwanese institutions were included in our study. Of the 5,459 patients, 4,716 were from Japan and 743 from Taiwan. With exclusion criteria of missing data, 1,099 patients were excluded and a final total of 4,360 patients were included for this study. A Study revealed that 30-day overall mortality rate was 1.1% for Grade I, 0.8% for Grade II, 5.4% for Grade III. The 90-day mortality rate was 1.0% for Grade I, 0.8% for Grade II, 5.6% for Grade III. The mortality rate for Grade III was significantly higher than lower grades (P < 0.001). The relationship between the numbers of organ dysfunctions and 30-day mortality was investigated, the greater the numbers of organ dysfunction, the higher the mortality rate (P < 0.001). However, the mortality rate varied depending on the number of organ dysfunction (3.1-25%). Especially neurological dysfunction and Respiratory dysfunction were considered as a significant poor prognostic factor on 30-day mortality (P < 0.001). With respect to the surgical procedures, laparoscopic cholecystectomy was significantly selected for Grade I patients (P < 0.001), and the higher the grade, the more likely open cholecystectomy was performed (P < 0.001). Pathological findings research revealed that Gangrenous cholecystitis and Chronic cholecystitis were significantly diagnosed with higher grade of TG13 severity assessment (P < 0.001).

Conclusion: This international multicenter investigation between Japan and Taiwan revealed that severe acute cholecystitis judged by TG13 severity assessment criteria were exactly worse conditions with organ dysfunctions and it would have possible to be poor prognosis. As a result, it would be better performance for the management of acute cholecystitis with using TG13 severity assessment criteria on emergency room and after admission. TG13 for AC would be providing great impact in actual clinical practice.

References: Takada, et al. TG13: Updated Tokyo Guidelines for the management of acute cholangitis and cholecystitis. J Hepatobiliary Pancreat Sci. 2013 Jan;20(1):1-7. Yokoe, et al. TG13 diagnostic criteria and severity grading of acute cholecystitis (with videos).J Hepatobiliary Pancreat Sci. 2013 Jan;20(1):35-46.

Disclosure: Nothing to disclose

OP174 IS SELECTIVE HISTOPATHOLOGIC EXAMINATION OF THE GALLBLADDER PERMISSIBLE?

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Introduction: Necessity of routine histopathologic examination of gallbladders has been debated for the past decades. Implementation of a selective histopathologic policy is hampered by fear of missing small carcinoma in macroscopically normal gallbladders. We wanted to investigate how gallbladder cancer was detected and identified. We aimed to identify GBC in macroscopically normal gallbladders and to what extend these malignancies might have had clinical consequences.

Aims & Methods: Using the Dutch Cancer Registry all patients were reviewed with diagnosis of gallbladder cancer between 2004 and 2015 in the South region of the Netherlands, a population of 2.3 million people. We identified all patients that had unexpected malignancies operated for benign gallstone disease. Based on clinical and pathological report we determined whether malignancies were macroscopically suspected or detected by microscopy only. In patients with GBC only detected by histopathology tumour stage and clinical consequence were summarized.

Results: A total of 205 malignancies of the gallbladder were identified. In 75 patients there was no suspicion of gallbladder cancer prior to surgery. Of these 37, the surgeon described a tumour in the operation report. In 38 there was no mention of abnormalities in the operation report. 8 gallbladders would probably been send for histopathologic examination based on difficulties during surgery (e.g. conversion or excessive gallbladder emphysema) or clinical indication (e.g. Mirizi syndrome). Pathologic examination identified macroscopic abnormalities in 23 cases. In the remaining 7 specimens there were no macroscopic abnormalities and samples were taken at random. None of these patients received additional treatment. In the same time period histological gallbladder examination occurred in 31902.

Conclusion: We present one of the largest single study cohort of histopathologic gallbladder examination and relation to gallbladder cancer. The major part of the invasive gallbladder cancers showed macroscopic abnormalities peroperatively. Over a decade, in a population of 2.3 million people, histology alone resulted in a change of treatment plan in just one patient. Therefore, selective histopathology seems a feasible policy and would reduce costs and pathological workload.

Disclosure: Nothing to disclose

OP175 THE APPLICATION OF INDOCYANINE GREEN-FLUORESCENCE IMAGING DURING ROBOTIC LIVER RESECTION: A CASE-MATCHED STUDY

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Introduction: The ICG-fluorescence properties are progressively gaining momentum in the HPB surgery. However, the exact impact of ICG application on surgical outcomes is yet to be established.

Aims & Methods: Twenty-five patients who underwent ICG-fluorescence guided robotic liver resection were case matched in a 1:1 ratio to a cohort who underwent standard robotic liver resection.

Results: In the ICG group six additional lesions not diagnosed by preoperative workup and intraoperative ultrasound were identified and resected. Four of the lesions proved to be malignant. Despite the similar operative time (288 vs 272 min, p= 0.778), the risk of postoperative bile leakage (0% vs 12%, p= 0.023), R1 resection (0% vs 16%, p= 0.019) and readmission (p= 0.023) was reduced in the ICG group compared with the no-ICG group.

Conclusion: The ICG-fluorescence is a real time navigation tool which enable surgeons to enhance visualization of anatomical structures and over-

come the disadvantages of minimally invasive liver resection. The procedure is not time-consuming and its applications can reduce the postoperative complication rate in robotic liver surgery.
Disclosure: Nothing to disclose

Basic science: The intestinal epithelium and IBD
10:30-12:00 / B5

OP176 THE EFFECT OF ULCERATIVE COLITIS RELATED CIRCRNA CIRC-SOD2 ON INTESTINAL EPITHELIAL BARRIER

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Introduction: To explore the dysregulated circRNAs and mRNAs profiles in inflamed ulcerative colitis (UC) colorectal mucosa and identify the crucial circRNAs associated with UC. To clarify the roles and potential mechanisms of the key circRNA involved in intestinal epithelial barrier.
Aims & Methods:
1. CircRNAs microarray and mRNAs microarray were used to determine the differences of circRNAs and mRNAs between 5 paired inflamed UC colorectal tissues and normal colorectal tissues;
2. To predict the functions and involved pathways of dysregulated circRNAs and mRNAs with bioinformatics tools and identify the critical circRNA;
3. Quantitative real-time polymerase chain reaction (qRT-PCR) was applied to examine the expression of candidate circRNAs in extended UC colorectal tissues and colon epithelial cell models;
4. Fluorescence in Situ Hybridization(FISH) was performed to confirm the cellular location in UC tissues;
5. Construct overexpressed circ-SOD2 vector and transfected into Caco2 cells to object the influences of circ-SOD2 in intestinal epithelial barrier;
6. Detect epithelial barrier related proteins such as CLDN-8, ZO-1 and occludins with Western Blotting after circ-SOD2 vector transfected;
7. Build a network included circRNAs, microRNAs and mRNAs to predict the potential role mechanisms of circ-SOD2 in intestinal epithelial barrier.
Results:
1. The microarray assays indicated that 110 upregulated and 152 downregulated circRNAs and 1004 upregulated, 865 downregulated in mRNAs;
2. The functional analysis of differentially expressed circRNAs derived parental genes found that these parental genes were involved in HIF1-α, Rap1 signaling pathway and cellular adhesion;
3. Multiple dysregulated circRNAs were validated in UC with qRT-PCR and hsa_circ_0004662 derived from SOD2 gene was upregulated significantly (named as circ-SOD2) and related to the severity of UC;
4. circ-SOD2 mostly located in colon epithelial and increased after the treatment of inflammation factors in vitro;
5. The overexpression of circ-SOD2 in Caco2 cells led to TEER decreased, FITC-dextran permeability improved, microvillus and tight junction reduced;
6. Overexpressed circ-SOD2 in Caco2 cells caused that epithelial related protein CLDN-8 was decreased;
7. The potential mechanism of the role of circ-SOD2 in intestinal epithelial barrier was that circ-SOD2 harbored some microRNAs such as hsa-miR-424-5p, hsa-miR-497-5p, hsa-miR-935, hsa-miR-16-5p, hsa-miR-152-3p to control the downstream mRNAs.
Conclusion: The profile of circRNAs and mRNAs in inflamed UC colorectal tissues changed significantly, among them, circ-SOD2 had an obvious decrease. Additionally, the overexpression of circ-SOD2 caused the injury of intestinal epithelial barrier and its possible mechanisms were that circ-SOD2 regulated the expression of CLDN-8 directly or bound microRNAs to control target mRNAs indirectly.
Disclosure: Nothing to disclose

OP177 GPX4 RESTRICTS ENVIRONMENTALLY-INDUCED COLITIS

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Introduction: Glutathione Peroxidase 4 (GPX4) is an antioxidative enzyme, which particularly reduces lipid peroxides and is the key regulator of a novel cell death pathway called ferroptosis which is characterised by uncontrolled lipid peroxidation (LPO) [1,2]. A recent study demonstrated that deletion of GPX4 in myeloid cells of mice, leads to increased susceptibility to chemical induction of colitis [3]. However, the role of intestinal epithelial GPX4 in intestinal homeostasis remains unclear.

Aims & Methods: We aimed to study a role for epithelial GPX4 in the control of intestinal homeostasis.

We crossed *Gpx4^{fl/fl}* mice with *Villin-Cre+* mice to obtain *Gpx4[fl/wt] VillinCre+* (*Gpx4[+/-IEC]*) mice that lack one allele of *Gpx4* specifically in intestinal epithelial cells. In these mice colitis was induced with three percent dextran sodium sulfate (DSS) in drinking water for five consecutive days followed by three days of tap water. Mice were dissected three days after withdrawal of DSS. Disease severity was assessed by comparing the colon length and the histology score.

Results: *Gpx4[+/-IEC]* mice had significantly reduced colon lengths after DSS-colitis compared to wild type littermates, indicative for severe colitis. This finding was corroborated by histopathological evaluation, which showed that mice lacking one allele of GPX4 exhibited more severe inflammation in their colons after colitis induction with DSS.

Conclusion: Intestinal epithelial GPX4, a central antioxidative enzyme in cells, protects mice against inflammation in the large intestine. So far, the mechanisms how GPX4 interacts with inflammatory pathways remain unknown, but it presents a promising target for future anti-inflammatory therapies.

References: 1 Dixon SJ, Lemberg KM, Lamprecht MR, Skouta R, Zaitsev EM, Gleason CE, et al. Ferroptosis: an iron-dependent form of nonapoptotic cell death. Cell 2012;149:1060-72. 2 Stockwell BR, Friedmann Angeli JP, Bayir H, Bush AI, Conrad M, Dixon SJ, et al. Ferroptosis: A Regulated Cell Death Nexus Linking Metabolism, Redox Biology, and Disease. Cell 2017;171:273-85. 3 Canli Ö, Nicolas AM, Gupta J, Finkelmeier F,Goncharova O, Pesic M, et al. Myeloid Cell-Derived Reactive Oxyben Species Induce Epithelial Mutagenesis, Cancer Cell 2017; 32(6):869-883

Disclosure: Nothing to disclose

OP178 BACTERIA INDUCE THE RELEASE OF PROALGESIC LIPIDS BY EPITHELIAL CELLS

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Introduction: Irritable bowel syndrome is the most common functional intestinal disorder. It is characterized by visceral hypersensitivity and an altered gut transit that are associated with a gut microbiota dysbiosis. Among the studied pronociceptive mediators, host and bacterial lipid compounds have been described as major regulators of visceral hypersensitivity.

Aims & Methods: The aim of our study was to identify the role of the host and bacterial lipids interplay on visceral hypersensitivity. To differentiate bacterial and host lipids, *Escherichia coli* were cultivated in a minimal medium with ^{13}C- glucose as unique source of carbon, leading to the production of ^{13}C-labelled bacterial lipids. Bacterial lipid extracts were added at the apical side of polarized intestinal epithelial cells (caco2) cultured in transwell. Twenty four hours after treatment, quantification by high-resolution mass spectrometry of the ^{13}C-labelled lipids from the bacteria and the unlabeled lipids from the epithelial cells in the basolateral compartment allowed us to determine epithelial and bacterial lipids that could potentially be in contact with nerve endings. Lipid quantification by liquid chromatography coupled to tandem mass spectrometry was performed in the colon of germ free and conventional mice. We then assessed the ability of the epithelial and bacterial lipids found in the basolateral compartment to increase intracellular calcium concentration in primary culture of mouse sensory neurons.

Results: Amongst the uniformly ^{13}C-labelled bacterial lipids, we identified long chain fatty acids, from 10 to 18 carbons, hydroxylated on the 3rd carbon with or without a double bound, and aminolipids in the bacterial culture. Twenty four hours after treatment by bacterial lipids at the apical side of the transwells, we quantified an increase of the concentration of bacterial C10-3OH, C12AsnOH and C14AsnOH as well as epithelial 9,10-Di-HOME and 12,13-DiHOME in the basolateral compartment. Similar results were obtained when the bacterial lipids were unlabeled, meaning that these results were not due to the labelling. We found a significantly lower concentration of 9,10- and 12,13-DiHOME in the colon of germ-free mice, strengthening the link between the microbiota and the host production of those lipids. Bacterial lipids and 12,13-DiHOME did not activate sensory neurons. In contrast, the 9,10-DiHOME induced calcium flux in sensory neurons. This effect was inhibited by a pretreatment of the neurons with a TRPV1 antagonist (AMG9810).

Conclusion: Our study show that bacterial lipids induce the release of potentially proalgesic lipids by epithelial cells. Lipid metabolism could be the link between dysbiosis and visceral pain in IBS.

Disclosure: Nothing to disclose

OP179 CONTRIBUTION OF FULL FIELD OPTICAL COHERENCE TOMOGRAPHY (FF-OCT) FOR THE STUDY OF THE DIGESTIVE EPITHELIAL BARRIER IN PATIENTS WITH SPINA BIFIDA

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Introduction: Full Field Optical Coherence Tomography (FF-OCT) is an ex vivo imaging technique, with micrometric resolution, usually reserved for imaging biological environments (1) (2). It allows rapid acquisition of ex vivo tissue images on a cellular scale, and therefore represents an attractive approach for analysis of human samples such as endoscopic biopsies. Adult patients with Spina Bifida (SB) often have digestive disorders (3) whose pathophysiology is poorly known and remains to be explored. The objective of this study was to evaluate the feasibility and relevance of FF-OCT in the study of the morphology of the intestinal epithelial barrier from colonic biopsies of patients with SB.

Aims & Methods: FF-OCT analyses were performed on fixed colonic biopsies of SB patients and healthy volunteers (HV), collected during a short colonoscopy. Biopsies were scanned using the Light-CT scanner (LLTech, Paris, France). This device allows to produce contrast images in grayscale (axial resolution 1µm, frequency 75Hz), with the possibility of making a mosaic in order to obtain a maximum examination field of 25mm. The analyse depth is adjustable, with a maximum depth of several millimeters and the possibility of performing a three-dimensional reconstruction of the specimen. 2 biopsies per patient/HV were analyzed. The different morphological criteria studied in FF-OCT were: the average density of the connective tissue, the number of crypts, the average area of the crypts, the total area of the crypts, the average roundness of the crypts, the average circularity of the crypts and the average of the major axis/small axis of the crypts. These data were compared with each other by a Student t-test. A standard histological analysis was also performed.

Results: Data from 36 adult SB and 16 HV patients were analyzed. Among SB patients: 26 (72%) had abdominal pain, 6 (17%) faecal incontinence, the average number of stools was 3/week. The appearance of the mucosa was macroscopically healthy in endoscopy and the standard anatomo-pathological study found no abnormalities. The connective tissue density in FF-OCT was significantly decreased in Spina Bifida patients: p < 0.0001.

No significant differences were found concerning, per section, the number of crypt p = 0.4210, the average crypt area p = 0.2332, the total crypt area p = 0.2391, the average crypt roundness p = 0.7906, the average crypt circularity p = 0.09 and the average major/small crypt axis measurement mean p = 0.3463.

Conclusion: Morphological abnormalities of the intestinal epithelial barrier could be detected by FF-OCT in adult Spina Bifida patients. This innovative technique allows the precise quantitative study of specific histological parameters and therefore provides additional information to the classical anatomopathological study.

References: 1- Beaurepaire E, Boccara AC, Lebec M, Blanchot L, Saint-Jalmes H. Full-field optical coherence microscopy. Opt Lett. 1998; 23: 244-246 2- Dubois A, Vabre L, Boccara AC, Beaurepaire E. High-resolution full-field optical coherence tomography with a Linnik microscope. Appl Opt. 2002; 41: 805-812. 3- Brochard C, Peyronnet B, Dariel A, Ménard H, Manunta A, Ropert A, Neunlist M, Bouguen G, Siproudhis L.Bowel Dysfunction Related to Spina Bifida: Keep It Simple. Dis Colon Rectum. 2017 Nov;60(11):1209-1214.

Disclosure: Nothing to disclose

OP180 MIR-124A MEDIATES THE IMPAIRMENT OF INTESTINAL EPITHELIAL INTEGRITY BY TARGETING ARYL HYDROCARBON RECEPTOR IN CROHN'S DISEASE

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Introduction: Aryl hydrocarbon receptor [AHR] is a transcription factor, which induced by various ligands. AHR palsys a important role in the immune response. Meanwhile, activation of AHR can attenuate epithelial barrier dysfunction. The expression level of AHR is downregulated and miR-124a is upregulated in Crohn's Disease [CD]. How to modulate the AHR expression during the development of CD has yet to be thoroughly expounded.

Aims & Methods: The expression levels of miRNA and AHR protein were determined in Caco-2 monolayers and inflamed colon from patients with CD by RT-PCR and western blot analysis. Combining miRNA target prediction softwares, we verified microRNAs that targeted AHR. Trans-epithelial electrical resistance [TEER] and fluorescein isothiocyanate [FITC]-dextran were used to assess the permeability of the Caco-2 cell monolayers. The wild type [WT], miR-124a-Nju and AHR knockout mice were induced colitis using TNBS enema. Colitis mice using anti-miR-124a to inhibit miR-124a expression. We evaluated the intestinal inflammation and determined miR-124a, AHR and tight junction [TJ] proteins levels in mice of different treated groups.

Results: miRNA profiles of colon samples from CD patients were different with normal controls. There was an negative correlation between miR-124a and AHR protein levels in inflamed colon tissues from active CD patients. In vitro studies [Caco2 monolayers] revealed that: the downregulated AHR and TJ proteins were induced by TNF-α or miR-124 mimic. Meanwhile, TNF-α or miR-124a mimic induced-hyperpermeability via overexpression of the miR-124a, which was abrogated by miR-124a inhibitor. In vivo studies [colitis model mice] demonstrated that: miR-124-1-Nju and AHR^{-/-} mice using TNBS enema had more severe intestinal inflammation than WT colitis mice. MiR-124-1-Nju and AHR^{-/-} mice experienced severely intestinal barrier dysfunction, which was ameliorated after administrating anti-miR-124a in miR-124a-Nju mice but not in AHR^{-/-} mice.

Conclusion: This study suggested that miR-124a can cause intestinal barrier dysfunction and induce intestinal inflammation via supressing AHR. Furthermore, we will explicate the exact molecular mechanisms for CD.

Disclosure: Nothing to disclose

OP181 ACTIVE EPITHELIAL SERINE PROTEASES ARE PRODUCED BY INTESTINAL EPITHELIUM TO CONTROL MUCOSAL BIOFILMS

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Introduction: Proteolytic homeostasis is observed at the surface of intestinal mucosa and is known to be disrupted in diseases (inflammatory bowel disease, infection or irritable bowel syndrome)(1-3). Here, we investigated how mucosal proteolytic homeostasis might control microbial biofilms present at the intestinal epithelium surface.

Aims & Methods: Our aim was to determine if epithelial proteases could control microbial biofilm composition, and structure.

We measured proteolytic activity and protease expression at mucosal surfaces in mouse and human tissues, and in monolayers of human epithelial cell lines. We studied the biophysical structure, biomass and microbial composition of biofilms at mucosal surfaces, or grown on synthetic solid surfaces. For the latest, we used cultured mucosa-associated microbiota from 4 healthy human colon biopsies. Mucosal proteolytic activity was modulated by the use of selective protease inhibitors in vivo and in vitro. Finally, N-terminomics/TAILS approaches were used to identify protease cleavages in human complex microbial biofilms.

Results: We report that healthy human and mouse colon epithelium are a major source of active serine proteases, released in the lumen. Using germ-free animals, we demonstrated that mucosal serine proteases were directly regulated by the presence of commensal microbiota. Specific inhibition of luminal serine protease activity caused macro-, microscopic damage and transcriptomic alterations of genes involved in host-microbiota interactions. Further, luminal serine protease inhibition impaired the spatial segregation of microbiota biofilms, allowing bacteria to invade the mucus layer and to translocate across the epithelium, but had no obvious effect on microbiota composition. Epithelial proteases cleaved the biofilm matrix of reconstituted mucosa-associated human microbiota, and can alter in a concentration-dependent manner the biofilm biomass.

Conclusion: We demonstrate a previously unknown physiological role for epithelial proteases that constrains biofilms at mucosal surfaces. Our discovery points to an important role for proteolytic homeostasis at the intestinal mucosal surface with regards to biofilm organization and invasive behavior.

References: 1- Motta JP et al. Sci. Trans. Med. 2012 2- Motta JP et al. Gastroenterology 2011 3- Denadai-Souza A. et al. Sci. Rep. 2018

Disclosure: Nothing to disclose

Colonic ESD: Does size matter?
10:30-12:00 / C2

OP182 BRIDGE FORMATION METHOD IN COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSSECTION

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Introduction: Colorectal endoscopic submucosal dissection(ESD) is becoming an established procedure, difficult cases still exist. As effective traction for approaching to submucosal layer can reduce difficulty of ESD proce-

dure, the normal mucosa on both lateral sides of lesion is used for natural traction. it is called the Bridge Formation Method (BFM). We present the procedure of BFM and comparison of treatment results of BFM group and non-BFM group in our hospital.

Aims & Methods: From January 2009 to December 2018, colorectal ESD was performed in 1577 lesions consecutively at our hospital. There were 867 cases for the BFM group and 710 cases for the non-BFM group. Flush Knife(FUJIFILM) and Distal attachment(Olympus) were used as the main devices. The procedure is as follows:
1) Make a mucosal incision on the anal side of lesion,
2) Advance submucosal dissection without mucosal incison of both lateral sides,
3) Make a mucosal incision on oral side of lesion and finish almost submucosal dissection,
4) Open the tunnel and bridge will be completed,
5) At last make a mucosal incision on both lateral sides.
The difference from the normal tunnel method is that almost submucosal dissection under the tumor is completed before mucosal incision on both lateral sides of lesion.

Results: In comparison with BFM group and non-BFM group, Average tumor size[27.0 ± 19.5 mm vs 25.0 ± 13.5 mm, P=0.017], morphology 0-Is, 0-IIc, laterally spreading tumor-granular(LST-G), laterally spreading tumor-non granular(LST-NG) [3.6%, 1.1%, 30.9%, 64.5% vs 1.7%, 0.3%, 50.7%, 47.3%, P=0.000], localization [colon: rectum, 84.1%:15.9% vs 85.4%:14.6%, P=0.528], submucosal(SM) invasion≥1000μm [13.5%, 117/867 vs 3.9%, 28/710, P = 0.000], en block resection rate [99.6%, 864/867 vs 97.6%,693/710, P=0.000], R0 resection rate [98.2%, 851/867 vs 97.0%, 689/710, P=0.181], average dissection speed [28.5 ± 17.2mm²/ min vs 24.9 ± 18.3 mm²/ min, P < 0.001], perforation rate [1.4%, 12/867 vs 1.8%, 13/710, P=0.546], post-bleeding rate [1.4%, 12/867 vs 0.8%, 6/710, P = 0.351].
In BFM group, average tumor size was significantly larger than non-BFM group, and the ratio of LST-NG was higher.
There was no significant difference in the localization of the lesions. The rate of SM massive invasion and en block resection rate were significantly higher in BFM group. R0 resection rate was higher in the BFM group but there was no statistically significant difference. Average dissection speed was significantly faster in the BFM group, and there was no significant difference in perforation rate and post-bleeding rate.
The results in the BFM group that the ratio of LST-NG is high and the high SM massive invasion rate suggests the degree of fibrosis in submucosal layer is high, so treatment difficulty is high. Despite under these conditions, the average dissection speed in the BFM group was significantly faster, and the en block resection rate was significantly higher.

Conclusion: The results suggests the usefulness of BFM is to leave the normal mucosa on both lateral sides of lesion for using the natural traction to the last of ESD. BFM enables stable manipulation under the lesion without using dedicated traction device, and dissection at an appropriate depth will be easier. Therefore, BFM is versatile method appropriate from normal lesions to difficult lesions.

Disclosure: Nothing to disclose

OP183 ROUTINE USE OF THE POCKET-CREATION METHOD FOR ENDOSCOPIC SUBMUCOSAL DISSECTION OF COLORECTAL LESIONS: A MULTICENTER RANDOMIZED CONTROLLED TRIAL

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Introduction: Endoscopic submucosal dissection (ESD) of colorectal lesions can be difficult due to submucosal fibrosis, a thin muscularis or a poorly-controlled colonoscope. To overcome these obstacles, the pocket-creation method (PCM) was developed and may be an ideal strategy for resecting all types of colorectal lesions.

However, there are no randomized clinical trials to date assessing the efficacy of the PCM for ESD of routine colorectal lesions compared with the conventional method (CM).
Aims & Methods: This study was designed as a randomized controlled parallel clinical trial in three tertiary-care hospitals. Patients with colorectal neoplasms ≥20mm were enrolled and randomly allocated to PCM or CM. Patients were excluded if lesions were suspicious for deep (≥1mm) submucosal invasion; spread to the ileocecal valve, appendiceal orifice or diverticulum; recurrent lesions after endoscopic resection; inflammatory bowel disease or familial adenomatous polyposis; and/or a bleeding tendency. Randomization was conducted to minimize differences in lesion morphology, location (colon or rectum), and institution. The primary endpoint was ESD completion rate. "Completion" was defined as achieving an en-bloc resection within 3 hours, without changing the assigned strategy. Procedures were not complete with interruption of the ESD procedure for ≥10 minutes, severe injury to the muscularis, or perforation/penetration. Secondary endpoints were en-bloc resection rate, cutting time, dissection speed and adverse events.
Results: A total of 121 patients were enrolled and randomly allocated to CM or PCM. Seven patients were excluded after randomization, and 59 patients for PCM and 55 patients for CM finally included. Patient demographics and lesion characteristics showed no significant differences between the two groups. The completion rate was significantly higher in the PCM group compared to the CM group (93% [55/59] vs. 73% [40/55]; *P*=.01). In contrast, en-bloc resection rates, cutting time and dissection speed were not significantly different comparing the two groups. Analysis of subgroups showed the PCM was better for colon lesions (P = .003), lesions 30 mm or larger (P = .03), lateral spreading tumor granular type or protruded morphology (P = .009), treatment in institution A (P = .001) and non-expert endoscopists (P = .003).The incidence of adverse events was similar in the two groups (delayed bleeding one in each group, and perforation one in the CM group). All adverse events were treated successfully with endoscopy.
Conclusion: The resection completion rate using the PCM is significantly higher than the CM. The PCM is useful for routine ESD of colorectal lesions, not only for difficult lesions.

	PCM Group (n=59)	CM Group (n=55)
Male/female Male (%) Female (%)	34 (58%) 25 (42%)	33 (60%) 22 (40%)
Median age (range, years)	70 (41-92)	68 (42-86)
Location- Cecum, Ascending, Transverse, Descending, Sigmoid, Rectum	8 (14%), 19 (33%), 9 (15%), 2 (3%), 10 (17%), 11 (19%)	9 (16%), 16 (29%), 9 (16%), 1 (2%), 8 (15%), 12 (22%)
Morphology- LST-G, Protruded, LST-NG	31 (53%), 3 (5%), 25 (42%)	28 (51%), 6 (11%), 21(38%)
Median estimated tumor size (range, mm)	30 (18-75)	30 (20-80)
Operator- Expert, Non-expert	27 (46%), 32 (54%)	28 (51%), 27 (55%)
Institution- A, B, C	27 (46%), 19 (32%), 13 (22%)	24 (44%), 14 (25%), 17 (31%)

[Baseline data of the treatment groups]

Disclosure: Dr. Yamamoto has patents for the double-balloon endoscope produced by Fujifilm Corp. He also serves as a consultant for and has received honoraria, grants, and royalties from Fujifilm Corp. All other authors disclosed no financial relationships relevant to this publication.

OP184 COLONIC ESD WITH DOUBLE-CLIP TRACTION: A REVOLUTION COMING FROM EUROPE!

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Introduction: ESD in the colon is more challenging technically than other locations.

This difficulty explain poor results of colonic RSD (except rectal cases) outside of japan with a low R0 resection rate, a high perforation rate and a long procedure time. Due to these bad results most European experts promotes piece-meal EMR instead of ESD for the endoscopic treatment of large benign colonic lesions.

Recently we presented our new systematic strategy for colonic ESD by countertraction by clips and rubber band that considerably facilitates the procedure. Here, we report a large prospective case series of colon ESD using this strategy.

Aims & Methods: Prospective consecutive sudy of all colonic ESD performed prospectively two experts centers from April 2017 (First Colonic ESD with clips and rubber band) to April 2019. Since the first case of colonic ESD with clips and rubber band in April 2017, all cases of colonic ESD were performed using this strategy.

Primary Endpoint: Monobloc, R0 and curative resection rate.

Secondary Endpoints: Perforation rate, risk factors in multivariate analysis of Perforation, R0 resection and Optimal ESD (defined by R0 resection without perforation and faster than 20mm²/min).

Results: 618 colorectal ESD were performed in the study period. Rectal cases (180) were excluded. About the 438 remaining colonic cases, appendiceal lesions, recurrent or partial resection lesions, dysplasia on IBD lesions and lesions invading diverticula were excluded. Finally 374 cases were included in the study performed by 4 operators in to experts centers. Lesions were SMSA 4 in 82% of cases with a mean size of 55 mm. Mean duration procedure was 67 min with a min speed of resection at 38,7 mm²/min. 63% of the lesions were located above the splenic flexure.

Primary Endpoint: Monobloc, R0 and curative resection rate were respectively 96%, 83% and 81%.

Secondary Endpoint:

- Perforation rate was 4,6%.

-predictive factors of optimal ESD were one operator (OR 3,9; p< 0,0001) and no F2 fibrosis (OR 4,3 p=0,0003), and ESD performed in 2018 à 2019 (OR 7; p=0,0004) in multivariate analysis.

- predictive factors of non R0 resection were presence of perforation (OR 0,32; p=0,05) and intense fibrosis (OR 0,30; p= 0,008).

- predictive factors of perforation were intense fibrosis (OR 18,4; p=0,03) and big size of the lesion (OR 1,037; p< 0,0001) in multivariate analysis.

Conclusion: Systematic countertraction using a double clip and rubber band facilitates colon ESD. Speed of ESD is twice as reported by recent Japanese teams using Pocket creation Method whereas oncologic results are similar. This strategy should become the standard for colon ESD and help to widespread colonic ESD. Our results feeds the debate between piece-meal EMR and ESD for the treatment of large colonic superficial lesions.

Disclosure: Nothing to disclose

OP185 IS THE SMSA SCORE ACCURATE ENOUGH TO PREOPERATIVELY PREDICT SUBOPTIMAL CLINICAL OUTCOMES IN COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION (CR-ESD)? A MULTICENTER SPANISH PROSPECTIVE STUDY

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Introduction: The SMSA (size, morphology, site, access) polyp scoring system is a method for stratifying the difficulty of polypectomy. It was developed by an expert consensus using the Delphi method.

Aims & Methods:

1. To assess the ability of SMSA to predict CR-ESD suboptimal clinical outcomes (SCOs): excessive duration of the procedure and percentages of piecemeal resections, aborted procedures and complications.

2. To develop a new preoperative model to predict those SCOs and compare its performance with that of the SMSA.

Consecutive patients were enrolled in a prospective multicenter Spanish CR-ESD registry since January 2016 to October 2018. We analyzed 585 cases in 19 hospitals. The overall ability of the scores to discriminate between those who developed SCOs and those who did not was assessed by the area under the ROC curve.

Results: Overall, 221 cases (38%) developed any of the predefined SCOs. There were 13 aborted procedures (2.2%), 92 piecemeal resections (16.1%), 86 intraprocedural perforations (14.7%), 19 delayed perforations (3.4%) and 37 delayed bleedings (6.6%). There were 40 SMSA2 (6.8%), 189 SMSA3 (32.3%) and 356 SMSA4 (60.8%) lesions. Surprisingly, SMSA2 lesions were significantly associated with piecemeal resections (SMSA2 vs SMSA3/4: 27.5% vs. 14.8%; OR= 0.5; CI95%: 0.2-0.9; p= 0.04). Statistically significant differences were observed between intraprocedural perforations and SMSA3/4 lesions (SMSA2 vs. SMSA3/4: 2.5% vs. 15.6%; OR= 7.2; IC95%: 1.01-53.1; p= 0.02). We did not observe statistically significant association between higher SMSA scores and duration of the procedure > 240 min., aborted procedures or delayed complications. The AUROC of the SMSA score >= 3 was 0.51 (CI95%: 0.46-0.55). Thus, an alternative logistic regression model was designed. It included significant variables that were associated with the predefined outcomes in the univariate analysis: case load < 10 lesions: OR=4.5 (CI95%: 1.5-13.2; p= 0.007), poor manoeuvrability, OR=1.6 (CI95%: 1.1-2.2; p= 0.007), size > 30 mm, OR=1.5 (CI95%: 1.01-2.2; p= 0.02), LST-G mixed type with a nodule > 10 mm, OR=2.8 (CI95%: 1.1-7.1; p= 0.03) and previous endoscopic electrosurgical treatment, OR=2.2

(CI95%: 1.06-4.6; p= 0.03). The AUROC for this multivariate model was 0.61 (CI95%: 0.57-0.66). The difference between both AUROCs was statistically significant (p< 0.00001).

Conclusion: The SMSA score was useless to predict CR-ESD SCOs. A new score based on a multivariate logistic regression model showed a slightly better discrimination ability to predict these suboptimal events.

Variable	Yes (n= 221)	No (n=364)	Univariate OR (CI 95%)	p	Multivariate OR (CI 95%)	p
Size > 3 cm	151 (68.3)	219 (60.2)	1.43 (1.01-2.0)	0.04	1.55 (1.08-2.24)	0.02
LST-G mixed type nodule > 10 mm	13 (6)	8 (2.2)	2.78 (1.13-6.8)	0.02	2.83 (1.13-7.07)	0.03
Previous electrosurgery	18 (8.1)	15 (4.1)	2.06 (1.02-4.2)	0.04	2.21 (1.06-4.62)	0.03
Poor manoeuvrability	122 (55.2)	163 (4.8)	1.52 (1.08-2.1)	0.01	1.60 (1.13-2.25)	0.008
Case load < 10	12 (5.4)	5 (1.4)	4.12 (1.43-11.8)	0.005	4.48 (1.51-13.2)	0.007

[Suboptimal clinical outcomes. Univariate and multivariate analysis]

Disclosure: Nothing to disclose

OP186 ENDOSCOPIC CLIPPING CLOSURE FOR PREVENTING POST-ESD COAGULATION SYNDROME AND PERFORATION (CLIPEC STUDY): A MULTICENTER, SINGLE-BLIND, RANDOMISED CONTROLLED TRIAL

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Introduction: Endoscopic submucosal dissection (ESD) has been widely applied as an endoscopic treatment for superficial colorectal neoplasms, however some complications occasionally occur after ESD, including delayed perforation and post-ESD coagulation syndrome (PECS). The PECS reveals abdominal pain, inflammation and fever without perforation after ESD, but the exact cause and epidemiology of PECS remain unknown. We thus conducted a randomized controlled trial (CliPEC study) to assess usefulness of endoscopic clipping closure for prevention of PECS and delayed perforation.

Aims & Methods: CliPEC study is a multicenter, single-blind randomized controlled trial. Patients who will receive ESD for superficial colorectal neoplasms were prospectively enrolled, and randomly allocated to ESD followed by endoscopic clipping closure (the closure group) and non-closure (the non-closure group), stratifying by institution and tumor size. According to pre-planned protocol, this study was analyzed for full analysis set: patients who could not endoscopically resect tumor and develop to perforation during ESD were excluded from this analysis. All participants routinely received computed tomography (CT) scan and blood examination on day 1 after ESD and pain severity was assessed on day 1-3 after ESD using visual analogue scale (VAS). PECS was defined as VAS ≥30mm, a raise of VAS ≥20mm from baseline, BT ≥37.5ºC or WBC ≥10,000/µl after ESD. Delayed perforation was defined as PECS accompanied with peri-luminal air (minor) or intra-abdominal free air (major).

Primary endpoint of this study was the rate of PECS and delayed perforation. Pre-planned sample size was 320 patients by estimating that clipping closure decrease the rate of PECS and delayed perforation from 15% to

5% with overall 2-sided-α and β errors of 0.05 and 0.20, and allowing an approximate 10% dropout rate. According to O'Brien Fleming type α spending rule, 2 sided α levels of 0.0056 and 0.044 were defined for the interim and final analysis, respectively.
(University Hospital Medical Network Clinical Trials Registry, Number: UMIN000027031)

Results: At the planned interim analysis with a half of study enrollment, this trial was terminated by recommendation of the independent data and safety monitoring committee because conditional power with superiority of closure to non-closure (0.12%) was less than pre-planned futility limit of 20% in the interim analysis.

In total, 181 patients were enrolled from April 2017 to August 2018 at 10 Japanese institutions, and 155 patients after exclusion (2: protocol violation for criteria, 3: consent withdrawal, 9: perforation during ESD, 12: no-completion of ESD) were finally analyzed including 71 patients in the closure group and 84 patients in the non-closure group. Patient and tumor characteristics were well balanced between 2 groups. The rate of PECS and delayed perforation was 23.9% (PECS: 19.7%, delayed perforation: 4.2%) in the closure group and 15.5% (PECS: 11.9%, delayed perforation: 3.6%) in the non-closure group, respectively (*P*=0.184). All cases with delayed perforation were within minor criteria, and all patients with PECS and delayed perforation were conservatively improved without emergency surgery. Interestingly, 15.5% (13/84) in the non-colure group and 9.9% (7/71) in the closure group revealed simple extra-luminal air without any symptoms after ESD.

Conclusion: Endoscopic clipping closure could not reduce the incidence of PECS and delayed perforation after colorectal ESD. Colorectal ESD has been safely managed in a clinical practice.

Disclosure: Nothing to disclose

OP187 COVERT CARCINOMA AMONG RECTAL ESD SPECIMEN IS HIGH: A EUROPEAN TERTIARY CENTER PROSPECTIVELY COLLECTED EXPERIENCE

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Introduction: Endoscopic resection (ER) represents the treatment of choice for superficial rectal lesions. Careful assessment of the lesions is crucial for decision making in order to optimize outcomes for the patient. Endoscopic submucosal dissection (ESD) is becoming increasingly common in Western countries and is currently proposed by the European Society of Gastrointestinal Endoscopy (ESGE) for the resection of large lesions due to the risk of harbouring a superficial invasive cancer

The rate of covert SMIC (unpredicted submucosal invasive cancer found on the specimen) has been described among endoscopic mucosal resection (EMR) specimen but is poorly known for rectal ESD in Europe.

Aims & Methods: In the current study, we aim to evaluate the rate of covert carcinoma among ESD specimen. Furthermore, we assess the efficacy and safety of this treatment approach in one European academic tertiary center.

Clinical and technical data from Erasme Hospital (Brussels) was systematically and prospectively collected from June 2015 to March 2019. Covert carcinoma is defined as no suspicion of cancer in the rectal lesion based on pit pattern analysis and pre-ESD biopsies if available. Complete resection (R0) is defined as no carcinoma and no adenoma on the margins. Curative resection is defined as en bloc R0 resection of a superficial lesion, well-differentiated adenocarcinoma (G1/G2), sm1 (≤1mm submucosal invasion, with no lymphovascular invasion, as defined by the ESGE). Procedure-associated complications and recurrence rate were also assessed.

Results: Fifty-seven patients, mostly men (57.9%), with a mean age of 67 [30-85] years underwent ESD for a superficial rectal lesion. Most of the lesions were laterally spreading tumors (64.9%), large buldging polyps representing 28.1%, mostly located in the upper rectum (> 5 cm from the

anal margin: 61.4%), with a mean size of 49 [10-130] mm. Endoscopic characterization revealed mainly Paris 0-Is-IIa lesions (58%). Mean duration of the procedure was 136 [41-480] minutes.

En bloc resection was achieved in 98.2% of patients and R0 resection in 58.9%. Histopathological examination displayed (31.6%, 18/57) adenocarcinomas comprising 50% (9/18) pTis tumors, 39% (7/18) pT1sm2/sm3 and 11% (2/18) T2 lesions. Curative oncological resection was obtained in 44.4% (8/18) of patients with carcinoma. All the pTis and 3 of the pT1sm2/sm3 were not suspected to be carcinoma at the first evaluation giving a covert carcinoma rate of 21% (12/57) and a covert SMIC rate of 5% (3/57).

Three out of 4 patients proposed for complementary surgery underwent a surgical treatment and the histopathological examination showed no residual tumor on the specimen nor on lymphadenopathies.

Altogether, 95% of the patients had no complication needing an intervention: 2 presented delayed bleeding managed endoscopically and one patient presented stenosis that was calibrated after one balloon dilation.

A 6 months endoscopy follow-up was obtained in 22 patients disclosing a free-recurrence rate of 100%, in favor of coagulation artefacts on the specimen seeing the 58% R0 (no adenoma on margins) rate.

Conclusion: ESD for superficial rectal lesions is showing favorable results in terms of efficacy and safety. A 21% rate of covert carcinoma among rectal large polyps underline the added value of using ESD compared to piece-meal resections.

Disclosure: Nothing to disclose

Lower GI diseases 4.0: Integrating modern approaches into daily practice
10:30-12:00 / C3

OP188 THE IBD-DISK PROVIDES A DETAILED DISEASE ACTIVITY AND DISABILITY ASSESSMENT IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: THE IBD-DISK VALIDATION AND PERFORMANCE STUDY

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Introduction: Various instruments have been developed to assess inflammatory bowel disease (IBD)-related disability, but these tools are often time consuming and difficult to use in an outpatient setting. The IBD Disk is a fast and self-administered 10-item visual instrument developed to overcome these limitations[1]. Data on the correlation of the IBD disk with standard activity indices are lacking.

Aims & Methods: The aim of this study was to validate the performance of the IBD Disk in clinical practice and to correlate the IBD disk with standard clinical activity indices in IBD.

We prospectively evaluated consecutive patients with IBD in an outpatient setting between April 1th 2018 and December 31th 2018. All patients completed the questionnaire of the IBD disk (10 items scored from 0 to 10). In addition, the stool frequency and abdominal pain patient reported outcome (PRO-2) of the Clinical Disease Activity Index were assessed for patients with Crohn's disease (CD), whereas the Simple Clinical Colitis Activity Index (SCCAI) was used for patients with ulcerative colitis (UC) and IBD unspecified (IBD-U). All questionnaires were recorded by an e-health pre-assessment digital tool before the actual clinical visit. Correlation analysis between the scores was performed using Pearson's product-moment correlation coefficient.

Results: Two hundred fifty two evaluations were performed amongst 146 patients (83 CD, 59 UC, 4 IBD-U). In patients with CD, the median PRO-2 score was 4.7 (IQR: 1.6-10). Amongst the separate IBD-disk items, the 'lack of energy'-item had the highest mean score: 4.8 (SD: 3.1), whereas the 'negative impact on interpersonal relations'-item had the lowest score: 2.1 (SD: 3).

There was a significant moderate correlation between the PRO-2 and the cumulative score of all IBD disk items (r=0.53), abdominal pain (r=0.56), regulating defecation (r=0.59), interpersonal relations (0.41) and education/work (r=0.48) (all p< 0.0001). The correlation with the other items were weak to very weak (r< 0.4). In patients with UC or IBD-U, the median

SSCAI was 4 (IQR: 2-5). Amongst the separate IBD-disk items 'the lack of energy'-item had the highest mean score: 5.3 (SD: 3), whereas the 'sexual dysfunction'-item had the lowest score: 2.4 (SD: 2.6). There was a significant strong correlation between SCCAI and the cumulative score of all IBD disk items (r=0.68), regulating defecation (r=0.60), interpersonal relations specifically (0.61) and lack of energy (r=0.62) (all p< 0.0001). The correlation with the other items were moderate to weak (r< 0.6).

Conclusion: This is the first study prospectively validating the use of the IBD-disk in a large cohort. Correlation with disease activity was strong in UC and moderate in CD. Since lack of energy was the dominant item of the IBD disk and an overall weak correlation between the standard activity indices and psychosocial items, the IBD-disk provides a more detailed and holistic evaluation of the patient with IBD.

References: 1. Ghosh S, Louis E, Beaugerie L, et al. Development of the IBD Disk: A Visual Self-administered Tool for Assessing Disability in Inflammatory Bowel Diseases. Inflamm Bowel Dis 2017;23:333-340.

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OP189 CT-SCOUT™ PLATFORM, THE DIGITAL SOLUTION TO BOOST PATIENT RECRUITMENT IN INFLAMMATORY BOWEL DISEASE CLINICAL TRIALS: A MULTICENTER PROSPECTIVE OBSERVATIONAL COMPARATIVE STUDY INVOLVING 134 SITES AND 644 PATIENTS IN 6 COUNTRIES

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Introduction: The main issue to validating new molecules in the field of IBD is insufficient patient enrollment into clinical trials, resulting in premature trials termination and cost increase. CT-SCOUT™ platform is a web-based solution built by the GETAID to help clinicians to pre-screen potential candidates at their site and facilitating the coordination of the research team. It is customized per site giving access to all academic and selected industrial trials in active recruitment period.

Aims & Methods: The aim of the current assessment was to evaluate the added value of CT-SCOUT™ platform in patient enrollment in industrial IBD clinical trials. We conducted a prospective, multicenter, open-label, observational study in equipped sites in France and in non-equipped sites in different countries participating to two phase 3 trials evaluating the efficacy and safety of etrolizumab in ulcerative colitis (UC, Hickory) and in Crohn's disease (CD, Bergamot) participants previously exposed or naïve to anti-TNF. Patients' recruitment in the 21 sites in France equipped with CT-SCOUT™ at the time of studies launch was compared to the 113 sites non-equipped with the app located in 4 European countries [Belgium (n=14), Germany (n=41), Spain (n=19), United Kingdom (n=26)] and in Israel (n=13). The primary endpoint was the mean patient randomization rate per site for both studies. Secondary endpoints included mean number of patients screened and randomized in Hickory, Bergamot and in both studies. Patients who signed study informed consent (screened) and those finally randomized were compared in sites equipped and non-equipped with CT-SCOUT™ using one-way ANOVA followed by post-hoc Tukey test and Mann-Whitney test.

Results: During the observational period of 27 months (Sept 2015 - Dec 2018), 644 and 289 patients were screened and randomized in 134 sites in Hickory and Bergamot trials, respectively. There were 307 and 149 patients in 78 sites for Hickory, and 337 and 140 patients for Bergamot in 102 sites. The mean numbers of included and randomized patients were significantly higher in equipped centers compared to non-equipped centers in both pooled and separate analysis (Table 1).

The mean number of patients randomized in Hickory in CT-SCOUT™ sites has been increased by 4.04 folds as compared to non-equipped sites (p< 0.001). The mean number of patients randomized in Bergamot in CT-SCOUT™ sites has been increased by 1.88 folds as compared to non-equipped sites (p=0.009).

Conclusion: This is the first multicentric international study to demonstrate a dramatic increase in patient recruitment in IBD clinical trials, with randomization rates twice to four times higher during Crohn's disease and ulcerative colitis in sites equipped with the app versus those non-equipped. CT-SCOUT™ appears to be a promising and easy-to-use digital solution to the global issue of patient enrollment in clinical trials in reducing clinical trial duration, and allowing new drug candidates to be available to patients earlier.

	French sites equipped with CT-SCOUTTM	Sites from other countries non-equipped with CT-SCOUTTM	p
Screened in both studies (UC + CD)	7.55	3.05	p<0.001
Randomized in both studies (UC + CD)	3.79	1.28	p<0.001
Screened in Hickory (UC)	9.17	3.14	p<0.001
Randomized in Hickory (UC)	5.17	1.28	p<0.001
Screened in Bergamot (CD)	5.94	2.95	p=0.003
Randomized in Bergamot (CD)	2.41	1.28	p=0.003

[Table 1]

References: 1 Use of digital technology to boost patient recruitment in inflammatory bowel disease clinical trials. J Crohns Colitis, 2017; 1027 (doi: 10.1093/ecco-jcc/jjx002.177)
Disclosure: Nothing to disclose

Holistic management of IBD patients
10:30-12:00 / E1

OP190 EPIGENETIC PROFILING OF BLOOD FROM PATIENTS WITH PRIMARY SCLEROSING CHOLANGITIS AND ULCERATIVE COLITIS COMPARED TO PATIENTS WITH ULCERATIVE COLITIS AND HEALTHY CONTROLS

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Introduction: The aetiology of primary sclerosing cholangitis (PSC) is unknown. The concurrence of PSC and inflammatory bowel disease (IBD) has led to various hypotheses linking these two disease entities, e.g. the aberrant gut-lymphocyte homing in IBD contributing to PSC. This mechanism may be due to genetic predisposition of the host and/or epigenetic changes in circulating lymphocytes. Epigenetic changes in blood cells have been described in the context of IBD: the DNA methylome of patients with ulcerative colitis (UC) differs from patients with Crohn's disease (CD) and healthy controls (HC) (1).

Aims & Methods: We hypothesized that the peripheral blood DNA methylome of patients with concurrent PSC and UC is distinct from that of UC patients without PSC and healthy controls.

DNA was isolated from peripheral blood samples from 18 PSC-UC and 17 UC patients, as well as 12 healthy controls. Only male patients were selected, and groups were matched for age (mean age 41, 40 and 40 years for PSC-UC, UC and HC, respectively), UC duration (15 and 11 years for PSC-UC and UC patients, respectively) and medication use (all PSC-UC and UC patients used Mesalazine, 50% used Thiopurins and none used biologicals). After bisulfite conversion, DNA methylation was determined using the Illumina HumanMethylation Infinium BeadChip (850K) EPIC microarray. Additionally, in a hypothesis driven approach, changes in genes associated with PSC from previous genome wide association studies (GWAS) as well as genes involved in lymphocyte trafficking were assessed (2, 3).

Results: In a non-biased approach, no significantly differentially methylated positions (DMPs) or regions (DMRs) were identified when comparing PSC-UC with UC or HC. Principal component analysis revealed no clear separation or clustering of the different groups, and no statistically significant differences were found when comparing PSC-UC with UC or PSC-UC with HC.

In a hypothesis driven analysis, 52 genes associated with PSC, identified from previous studies, were specifically analysed. We observed that two genes, BACH2 and ASAP2, were significantly differentially methylated in PSC-UC compared to UC patients. In addition, comparison of PSC-UC with healthy controls showed that the genes FOXP1, UBASH3A, BACH2, DDIT4, CD28, TNFAIP6, SOCS3 and ITGB1 were differentially methylated, although effect sizes were limited (< 20%).

Conclusion: We observed only limited differences in the genome-wide DNA methylomes that were associated with the presence of PSC. We conclude that the total peripheral blood methylome does not discriminate PSC-UC from UC alone. The differential methylation of BACH2, a gene that plays a role in regulating memory T-lymphocyte differentiation, is of interest in the context of mistargeted lymphocyte homing in PSC, and could be an interesting target for further studies.

References: (1) McDermott E, Ryan EJ, Tosetto M, Gibson D, Burrage J, Keegan D, et al. DNA Methylation Profiling in Inflammatory Bowel Disease Provides New Insights into Disease Pathogenesis. J Crohns Colitis. 2016;10(1):77-86. (2) Chung BK, Hirschfield GM. Immunogenetics in primary sclerosing cholangitis. Current opinion in gastroenterology. 2017;33(2):93-8. (3) Aoki CA, Dawson K, Kenny TP, Gershwin ME, Bowlus CL. Gene expression by PBMC in primary sclerosing cholangitis: evidence for dysregulation of immune mediated genes. Clin Dev Immunol. 2006;13(2-4):265-71.
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OP191 IMMUNOGENICITY OF USTEKINUMAB IN PATIENTS WITH CROHN'S DISEASE: RESULTS FROM THE IM-UNITI STUDY

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Introduction: Patients (pts) with moderately to severely active Crohn's disease (CD) who completed induction treatment with IV ustekinumab (UST) were eligible for a study of maintenance treatment with SC UST or placebo (PBO). Previous analyses of randomized pts who did not undergo dose adjustment in the maintenance study showed that rates of antibody formation were higher for those who received a single IV UST induction dose and SC PBO maintenance (4.9%) than those who received IV UST induction and SC UST maintenance (2.9% and 2.0% for q12w and q8w groups, respectively). The aim of this analysis was to further characterize pts who had antibodies to UST in the maintenance study, including randomized and nonrandomized pts.

Aims & Methods: In the induction trials (UNITI-1, n=741; UNITI-2, n=628), pts were randomly assigned to a single dose of IV PBO or UST (130 mg or ~6 mg/kg). Pts who responded to UST induction were randomly assigned to SC PBO or UST 90mg (q12w or q8w) at Wk 0 of the maintenance study (IM-UNITI) (n=397). Randomized pts who lost response between Wks 8 and 32 were eligible for dose adjustment to UST 90mg q8w. Nonrandomized pts (n=884) received SC UST q12w or UST q8w. Blood samples drawn at baseline and Wk 6 in the induction trial and Wks 12, 24, 36, and 44 in the maintenance trial were evaluated for antibodies to UST using a validated, drug-tolerant electrochemiluminescence immunoassay. Analysis set included all pts who were treated in the maintenance study, received ≥1 dose of UST induction or maintenance, and had ≥1 sample evaluable for antibodies from induction Wk 6 through maintenance Wk 44.

Results: Of the 914 pts who received UST in the induction trials, 2(0.2%) were positive for antibodies through Wk 8. Of the 1,154 pts who were treated in the maintenance study, received UST in the induction or maintenance study, and had samples that were appropriate for antibody testing, 27(2.3%) had antibodies detected through Wk 44. Among the 27 pts who were positive for antibodies, 7 had at least one sample with high titers (>1:800), 7 had positive samples at ≥3 visits including Wk 44, and 7 were receiving immunomodulators at baseline (Table). No pts had infusion or injection-site reactions at the visit they were positive for antibodies. Among pts who were receiving UST maintenance, median trough UST serum concentrations at the visits of the positive antibody results were 0.18 and 0.72 µg/mL for pts whose highest antibody titers were >1:800 and ≤1:800, respectively.

Conclusion: Antibodies to UST were uncommon in pts with CD who received induction and maintenance treatment with UST. When antibodies did occur, they were usually transient and low titer.

	Nonresponders to IV Induction			
	Responders to UST IV induction →PBO[a]	Placebo IV and UST maintenance →q12w[b]	UST IV and UST maintenance →q8w[c]	Total
Analysis set[d]	396	284	474	1,154
Patients positive for antibodies to UST, n (%)[e]	14 (3.5%)	4 (1.4%)	9 (1.9%)	27 (2.3%)
Before any UST dose	1	1	0	2
1 visit then negative	8	0	2	10
Wk 44 only	1	1	0	2
Safety follow-up visit only	0	0	1	1
2 visits then negative	3	1	0	4
Wks 36 and 44 only	0	1	0	1
≥3 visits including Wk 44	1	0	6	7
Received immunomodulators at baseline	4	1	2	7
Total number of positive antibody test results, n	23	6	29	58
Patients with highest antibody titer >1:800, n (%)	2	2	3	7

a Includes patients who were in clinical response to ustekinumab IV induction and were randomized in the maintenance study to ustekinumab or placebo.
b Includes patients who did not respond to IV placebo induction, were not randomized in the maintenance study, received ustekinumab 130 mg IV at Week 0 of the maintenance study, achieved clinical response at Week 8, and initiated ustekinumab 90 mg SC q12w.
c Includes patients who did not respond to IV ustekinumab induction, were not randomized in the maintenance study, received ustekinumab 90 mg SC at Week 0 of the maintenance study, achieved clinical response at Week 8, and initiated ustekinumab 90 mg SC q8w.
d Patients who were treated in the maintenance study, received ≥1 dose of ustekinumab in either the induction or maintenance studies, and had ≥1 samples that were evaluable for antibodies from induction Week 6 through maintenance Week 44.
e Patients who had at least 1 positive sample at any time from induction Week 6 through maintenance Week 44.

[Summary of antibody to ustekinumab status through Wk 44 of the maintenance study for pts who were treated with ustekinumab induction or maintenance]

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OP192 EFFECT OF ANTI-TNF-α TREATMENT IN PRIMARY SCLEROSING CHOLANGITIS

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Introduction: Few patients with primary sclerosing cholangitis and inflammatory bowel disease (PSC-IBD) are exposed to anti-TNF-α drugs due to the often mild nature of the IBD. This study assessed the effect of anti-TNF-α drugs on liver function and their efficacy in treating IBD in in PSC-IBD patients. The effect of anti-TNF-α drugs in liver transplant (LTx) PSC-IBD was also considered.

Aims & Methods: A retrospective analysis of 141 PSC-IBD patients receiving anti-TNF-α at 20 sites across Europe and North America was carried out via the International PSC Study Group (IPSCSG). Eighty-nine (63%) were male, 84 (60%) had UC, 52 (37%) had CD and 5 (4%) had indeterminate colitis; 110 (78%) received infliximab (IFX) and 31 (22%) adalimumab (ADA). Effects on alkaline phosphatase (ALP), IBD activity (response defined endoscopically or where endoscopic data were lacking clinical response as determined by physician assessment, or calprotectin < 250 µg/g or ≥30% drop in calprotectin; remission defined as endoscopic healing, or where endoscopic data were lacking, as clinical remission as determined by physician assessment), PSC related symptoms, and adverse events were recorded. Linear regression analyses were carried out to identify significant predictors of ALP during anti-TNF-α treatment.

Results: Lever biochemistry was available for 90 patients during the first 4 months of treatment of which 67 (74%) received IFX and 23 (26%) ADA. There was no significant difference in the proportion of patients with raised ALP at baseline between IFX (n=40, 60%) and ADA (n=13, 57%, p=0.50[CH1]). Patients treated with IFX experienced a median 4% reduction (IQR -25 to +19%, n=67) in ALP compared with median 15% (IQR -29 to -4%, n=23) reduction for ADA, (p=0.035). This difference was also apparent at 12 months, although non-significant (IFX median 2% reduction in

ALP (IQR -20 to +32%, n=56), ADA median 20% reduction (IQR -32 to +9%, p= 0.084, n=16)). In regression analysis normal ALP at baseline (p < 0.01), treatment with ADA (p=0.090) and European site (p=0.083) were found to be predictive of lower ALP, (F(3,61)=18.86, p< 0.001) R^2= 0.47. IBD-response rate to anti-TNF-α treatment was 48% and the remission rate was 23%. There was no difference between IFX and ADA in the frequency of PSC symptoms after drug exposure. Ten additional patients who underwent LTx prior to anti-TNF-α were analysed: neither ALP nor bilirubin changed significantly during the study, however the small numbers precluded comparison of IFX and ADA. The proportion of post-LTx patients whose IBD responded to anti-TNF-α was not significantly different compared with non-LTx patients, (p=0.69). Data regarding the eventual reasons for anti-TNF-α discontinuation were available for 72 patients who were exposed to anti-TNF-α for a median of 415 days (IQR 176-1735). The most common reasons for anti-TNF-α discontinuation were primary IBD non-response (30%) and adverse event (32%). Reasons for stopping anti-TNF-α were also similar between LTx and non-LTx patients.

Conclusion: Serum ALP improved during treatment with ADA but not IFX in PSC-IBD patients, indicating possible advantages for ADA in treating PSC patients with IBD. There is no obvious explanation for this difference between the two anti-TNF-α agents. However, overall IBD-response rates to anti-TNF-α appeared to be lower than in the absence of PSC. Post-LTx patients had similar IBD-response rates to anti-TNF-α drugs and similar adverse events compared with non-LTx patients.

Disclosure: Nothing to disclose

OP193 IDENTIFICATION OF RISK FACTORS ASSOCIATED WITH LOSS OF RESPONSE TO USTEKINUMAB IN CROHN'S DISEASE

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Introduction: Ustekinumab (UST) therapy induced and maintained response and remission in patients with moderate-to-severe Crohn's disease (CD) in induction, maintenance, and 2-year extension trials in the IM-UNITI program. Secondary loss of response (LoR) was observed in some patients during follow-up. This post-hoc analysis aims to characterize and identify potential predictors of LoR through 2 years of UST (Wk 96).

Aims & Methods: The analysis included initial responders (IR) to UST IV at Wk 8 who were randomized to 90 mg SC UST q8w or q12w maintenance therapy and delayed responders (DR: responders at Wk 16 after not achieving clinical response at Wk 8; subsequently received UST q8w). LoR was defined as CDAI score ≥220 and a ≥100-point increase in CDAI score from Wk 8 or 16. Discontinuation due to lack of efficacy was also considered LoR, while patients who discontinued for other reasons were excluded from the analysis. Baseline (BL), Wk 8, and Wk 16 variables were described for LoR and no LoR patients. Univariate and multivariate logistic regression modeling was conducted on BL and Wk 8/16 variables.

Results: This analysis included 473 patients, of whom 191 (40.4%) met criteria for LoR through Wk 96: 36.6% among IR randomized to UST q8w, 37.6% among IR randomized to UST q12w, and 43.8% among DR on q8w dosing. Patients with LoR versus patients without LoR during follow-up had higher mean CDAI scores at BL and at Wk 8 (321.6 [SD 60.6]and 227.8 [SD 108.3] vs 305.7 [61.6] and 184.5 [90.75] and higher FeCal at Wk 8 (622.5 [SD 1065.5] vs 446.7 [SD 671.2]). In addition, LoR was more frequent among patients with previous anti-TNF exposure (72.2%) and no use of 5-ASA (71.2%). Univariate analysis identified higher CDAI at induction and maintenance BL, lower delta CDAI after induction, Wk 8 FeCal levels, previous

anti-TNF exposure and previous TNF failure as factors associated with increased risk for LoR (Table 1). Serum UST levels and concomitant IMM use were not identified as potential predictors of LoR. At multivariate analysis, only CDAI at maintenance baseline (OR: 1.42; 1.14-1.77), and previous TNF failure (OR: 2.05; 1.15-3.65) remained significant predictors of LOR.

Conclusion: Throughout 2 years of follow up, secondary LoR occurred in ~40% of initial or delayed responders to UST. Patients with higher CDAI at maintenance BL, and history of previous anti-TNF failure were found to be at increased risk for LoR. UST levels were not helpful as potential predictors of LoR and concomitant use of IMM did not reduce the risk of LoR during UST therapy.

Predictors of LoR (vs no LoR) by Univariate Logistic Regression Model

	OR	95% CI	p-value
Induction baseline CDAI (per 100-points)	1.52	1.13, 2.05	0.0063
Maintenance baseline CDAI (per 100-points)	1.56	1.28, 1.88	<0.0001
Delta CDAI induction/ Maintenance (per 100-points)	1.40	1.13, 1.72	0.0016
FeCal levels at Week 8 (per 100 mg/kg)	1.03	1.00, 1.05	0.040
Previous TNF exposure	2.13	1.44, 3.16	0.0002
Previous TNF failure	2.46	1.69, 3.58	<0.0001

Predictors of LoR (vs no LoR) by Multivariate Logistic Regression Model

	OR	95% CI	p-value
Maintenance baseline CDAI score (per 100-points)	1.42	1.14, 1.77	0.0021
Previous TNF exposure	1.06	0.58, 1.94	n.s.
Previous TNF failure	2.46	1.15, 3.65	0.015

[Table 1: Predictors of LoR (vs no LoR): univariate and multivariate logistic regression models]

Disclosure: Drs. Hanauer, Sands, Feagan, Targan, de Villiers, Rutgeerts, Colombel, and Ghosh are all investigators for Janssen Research & Development, LLC Dr. Laliman is a consultant to Janssen Research & Development, LLC Drs. Oortwijn and van Kruchten are employees with Janssen Biologics BV Drs. Izanec and Gasink are employees of Janssen Scientific Affairs, LLC Drs Adedokun and Gao are employees of Janssen Research & Development, LLC Dr. Sloan is an employee of Janssen Global Services, LLC

OP194 SERUM METABOLOMIC FINGERPRINT OF ULCERATIVE COLITIS (UC) PATIENTS WITH PRIMARY SCLEROSING CHOLANGITIS (PSC) CAN DISCRIMINATE THEM FROM UC PATIENTS WITHOUT PSC

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Introduction: Primary sclerosing cholangitis (PSC) is a chronic, cholestatic, idiopathic liver disease that can progress to end-stage liver disease, cirrhosis and cholangiocarcinoma. It is strongly associated with inflammatory bowel disease, especially ulcerative colitis (UC). It is still unknown why some UC patients develop PSC or why UC patients with PSC are at higher risk of colorectal cancer development.

Aims & Methods: In the present study, we aimed to compare the serum metabolomic profiles of UC patients with PSC to UC patients without PSC in order to explore the underlying pathophysiological mechanisms and to identify PSC-related biomarkers. Fasting serum samples were collected from a group of adult UC patients with confirmed diagnosis of PSC and a group of UC patients without PSC who were matched for different demographic and clinical characteristics. Metabolomic assessment was done using nuclear magnetic resonance (NMR) spectroscopy and direct infusion/liquid chromatography tandem mass spectrometry (DI-LC MS/MS).

Results: Forty-nine UC patients were recruited (24 with PSC and 25 without PSC). Their mean age was 42.9±15.6 years and 62% of them were men. Forty-seven (94%) patients had a history of pan-colitis and 20% of them were on biologic medications. Fifty-three and 129 metabolites were identified and quantified using NMR and DI-LC MS/MS, respectively. In the multivariate analysis using partial least squares discriminant analysis,

serum metabolome of UC patients with PSC were significantly distinctive from those without PSC. Increased 2-oxoglutaric acid, ethanol, alpha-ketoglutaric acid, phosphatidylcholines and decreased alpha-aminobutyric acid, malonic acid, and glutamine were among the most important metabolic changes in UC patients with PSC that could differentiate them from patients without PSC.

Conclusion: This is the first study indicating that metabolomic profiling in UC patients can discriminate between patients with and without PSC. The discriminatory metabolites are involved in host cellular energy metabolism, as well as amino acid and fatty acid metabolism and are likely involved in PSC pathogenesis and its complications in UC.

Disclosure: Nothing to disclose

OP195 ORAL FERRIC MALTOL VERSUS INTRAVENOUS FERRIC CARBOXYMALTOSE FOR THE TREATMENT OF IRON-DEFICIENCY ANAEMIA IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A MULTICENTRE PHASE 3B, OPEN-LABEL RANDOMISED CONTROLLED TRIAL

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Introduction: Iron-deficiency anaemia (IDA) is a serious complication of inflammatory bowel disease (IBD), resulting from inflammation, chronic mucosal blood loss and iron malabsorption. Treatment of IDA involves iron-replacement therapy, often with oral agents; however, use of standard oral ferrous iron (Fe^{2+}) compounds may be limited by poor iron bioavailability and adverse events, in which case patients require intravenous (IV) iron. Ferric maltol (FM), a chemically stable complex of ferric iron (Fe^{3+}) and maltol, provides another oral option formulated to improve absorption and reduce adverse events. FM is effective and well tolerated in patients with IBD (Gasche et al. *Inflamm Bowel Dis* 2015;21:579-588) but no head-to-head studies between FM and IV iron have been done.

Aims & Methods:

Objectives: To compare the efficacy and safety of oral FM and IV iron (ferric carboxymaltose [FCM]) in the treatment of IDA in patients with IBD.

Methods: This prospective, multicentre, phase 3b, open-label randomised controlled trial (EudraCT 2015-002496-26) included patients aged ≥18 years with confirmed IBD and IDA (haemoglobin [Hb] 8.0-11.0 g/dL for women, 8.0-12.0 g/dL for men AND either ferritin < 30 ng/mL or ferritin <100 ng/mL with transferrin saturation < 20%). Patients were randomised to 12 weeks of oral FM 30 mg twice daily or IV FCM administered according to standard prescribing information. Treatment could continue for up to 52 weeks. Efficacy was assessed in all randomised patients (intention-to-treat [ITT] population) and in patients without serious protocol deviations (per-protocol population; PP). The primary endpoint was Hb responder rate defined as the proportion of patients achieving either a 2 g/dL increase in Hb or normalisation of Hb (women ≥12 g/dL; men ≥13 g/dL) at Week 12, with a noninferiority limit set to 20% in either the ITT or the PP population.

Results: Mean ± SD treatment exposure was 30.2 ± 17.94 weeks for FM and 15.5 ± 15.60 weeks for FCM. The PP population included 178 patients (FM n=86; FCM n=92). At 12 weeks, the PP responder rate was 74% with FM and 84% with FCM; the difference was therefore well within the 20% non-inferiority limit (p=0.023; Table). In the safety population (FM n=127; FCM n=120), 118 patients had treatment-emergent adverse events (FM n=75, 59%; FCM n=43, 36%), of which 15 were severe (FM n=11; FCM n=4). For FM, most cases were gastrointestinal (n=40, 31%). For FCM, most cases were infections/infestations (n=22, 18%). No serious adverse events related to study treatment were reported. Fourteen patients discontinued because of adverse events (FM n=13; FCM n=1).

Conclusion: This first comparative trial shows noninferiority of oral FM versus IV FCM in improving Hb after 12 weeks of treatment. Both treatments were well tolerated, with safety profiles as expected from previous studies. FM may therefore be an appropriate alternative to IV iron for treatment of IDA in IBD, even in patients in whom other oral iron therapy is not an option.

Disclosure: Nothing to disclose

	IV FCM (n=92)	Oral FM (n=86)	Difference (FM-FCM)	
			%*	Risk difference (95% CI)
Mean ± SD Hb at baseline, g/dL	10.11 ± 1.077	10.02 ± 0.997		
Mean ± SD Hb at Week 12, g/dL	13.12 ± 1.456	12.68 ± 1.544		
LSM (95% CI) difference (baseline to Week 12), g/dL	3.02 (2.71-3.32)	2.69 (2.37-3.01)		-0.32 (-0.76 to 0.11), p=0.142
Hb responder rate at Week 12, n (%)	77 (84)	64 (74)	10	-0.1 (-0.2 to 0.0), p_{noninf}=0.023
≥2 g/dL increase in Hb at Week 12, n (%)	70 (76)	59 (69)	7	-0.1 (-0.2 to 0.0), p_{noninf}=0.027
Hb normalisation at Week 12, n (%)	72 (78)	52 (60)	18	-0.2 (-0.3 to -0.0), p_{noninf}=0.338

*Noninferiority limit set at 20%. CI, confidence interval; FCM, ferric carboxymaltose; FM, ferric maltol; Hb, haemoglobin; IV, intravenous; LSM, least-squares mean; p_{noninf}, p value for noninferiority; SD, standard deviation.

[Haemoglobin endpoints at 12 weeks (per-protocol population)]

Tackling the NAFLD/NASH epidemics
10:30-12:00 / F2

OP196 POSITIVE RESULTS FROM REGENERATE: A PHASE 3 INTERNATIONAL, RANDOMIZED, PLACEBO-CONTROLLED STUDY EVALUATING OBETICHOLIC ACID TREATMENT FOR NONALCOHOLIC STEATOHEPATITIS

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Introduction: Obeticholic acid (OCA), an FXR agonist, improved both fibrosis and histologic features of nonalcoholic steatohepatitis (NASH) in the Ph2 FLINT study.

Aims & Methods: : This Month 18 pre-specified interim analysis of the on-going Ph3 REGENERATE study evaluated the effect of OCA on liver histology in patients with biopsy-confirmed NASH. Patients with NASH and fibrosis stages F2-3 (ITT), and an exploratory group of F1 patients with metabolic syndrome, were randomized to placebo, OCA 10 mg, or OCA 25 mg QD. Primary endpoints were fibrosis improvement (≥1 stage) with no worsening of NASH, or NASH resolution with no worsening of liver fibrosis per liver biopsy. The safety population included all randomized and dosed patients (F1-3, N=1968). Clinical outcomes will be evaluated at the end-of-study.
Results: The ITT population included 931 patients (placebo [n=311], OCA 10 mg [n=312] or OCA 25 mg [n=308]), comprised of 44% F2 and 56% F3. Baseline characteristics were well-balanced across groups. Results in Table. The primary fibrosis endpoint was met by 11.9% placebo, 17.6% OCA 10 mg (p=0.0446 vs placebo), and 23.1% OCA 25 mg (p=0.0002 vs placebo) patients (ITT). The primary NASH endpoint was not statistically significant (ITT). More patients on OCA 25 mg showed improvements in hepatocellular ballooning (p=0.0011 vs placebo) and lobular inflammation (p=0.0322 vs placebo). Dose-dependent reductions in ALT, AST and GGT were observed. Pruritus was the most common AE (19% placebo, 28% OCA 10 mg, 51% OCA 25 mg) and was predominantly mild to moderate in severity (severe pruritus: < 1% placebo, < 1% OCA 10 mg, 5% OCA 25 mg). More OCA 25 mg patients discontinued due to pruritus (< 1% placebo, < 1% OCA 10 mg, 9% OCA 25 mg; protocol mandated discontinuation of treatment with severe pruritus). SAEs occurred in 11% placebo, 11% OCA 10 mg and 14% OCA 25 mg patients. Increases in LDLc with OCA were observed by Week 4, but approached baseline by Month 18 (OCA 25 mg: LS mean change Wk4 +22.6 mg/dL, M18 +4.0 mg/dL). Cardiovascular SAEs were similar across groups (2% placebo, 1% OCA 10 mg, 2% OCA 25 mg). Cholelithiasis or cholecystitis were reported in 1% placebo, 1% OCA 10 mg and 3% OCA 25 mg patients. Hepatic disorder SAEs were uncommon but occurred more frequently in OCA 25 mg patients (< 1%). Three deaths occurred; none were considered treatment-related (placebo n=2; OCA 25 mg n=1).

Primary: ITT Population (F2 + F3)	Placebo (n=311)	OCA 10 mg (n=312)	OCA 25 mg (n=308)
Fibrosis improvement + no worsening of NASH	11.9%	17.6% (p=0.0446)	23.1% (p=0.0002)
NASH resolution + no worsening of fibrosis	8.0%	11.2% (p=0.1814)	11.7% (p=0.1268)
Improvement in hepatocellular ballooning	23.2%	27.2% (p=0.2423)	35.1% (p=0.0011)
Improvement in lobular inflammation	35.7%	39.1% (p=0.3380)	44.2% (p=0.0322)
Overall study discontinuations (ITT): 16% Placebo, 17% OCA 10 mg, 15% OCA 25 mg			

[REGENERATE Table]

Conclusion: Treatment with OCA 25 mg improved liver fibrosis, key histologic features of steatohepatitis and liver biochemistry, demonstrating consistent efficacy with an overall AE profile similar to previous studies.
Disclosure: Nothing to disclose

OP197 MOUSE AND HUMAN ADULT LIVER - DERIVED BIPOTENT DUCTAL ORGANOIDS FUNCTIONALLY RECAPITULATE LIVER STEATOSIS

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Introduction: Recently both mouse and human adult liver - derived bipotent ductal organoids (consisting of adult ductal stem cells) have been described and shown capable of differentiation from the biliary state to the hepatic state. Although such hepatically differentiated organoids have been shown to accumulate lipids in the presence of fatty acids, the molecular pathways regulating lipid metabolism in organoids are not known. To determine if adult liver-derived organoids can be a useful experimental model for mouse and human liver steatosis we set out to functionally characterize the metabolic pathways governing lipid accumulation in mouse and human organoids and compare them to known steatotic pathways including the Trib1 deficient genetic mouse model of steatosis. The Trib1

-/- mouse model is likely relevant for at least a subset of steatotic patients because several GWAS studies strongly correlate Trib1 down - regulating mutations with high plasma LDL levels, high plasma triglyceride levels, coronary artery disease and steatotic liver disease. Indeed, Trib1's suspected role in metabolic syndrome has been functionally proven by Trib1 liver specific ko mouse models which also show that Trib1 acts at least in part through upregulation of the liver specific transcription factor C/EBPalpha which in turn causes metabolic syndrome (Bauer et al 2015 J Clin Invest 125:3809-18). It has also been convincingly demonstrated that HepG2 liver cancer cells feature strongly reduced levels of C/EBPalpha which in turn induces over expression of the transcriptional co-activator YAP, the main effector of the Hippo pathway, through direct physical interaction of C/EBPalpha with YAP (Wang et al 2013, Mol Cell 2:221-225).
Aims & Methods: Using Trib1-/- mouse liver - derived bipotent ductal organoids, we present here evidence that Trib1 deficiency - mediated upregulation of C/EBPalpha may in turn further down regulate normal - already low - YAP activity in hepatically differentiated organoids. YAP is the main effector of the evolutionary conserved Hippo pathway that regulates liver size, regeneration and some aspects of liver pathogenesis.
Results: We show that almost complete absence of YAP leads to a deficiency of the hepatically differentiated organoids to dedifferentiate back to proliferating ductal organoids, consistent with the well documented block of liver regeneration caused by low YAP activity levels. Most importantly, experimentally induced downregulation of YAP in hepatically differentiated normal organoids phenocopies the lipid droplet accumulation and reduced uptake of LDL seen in Trib1-deficient hepatic organoids. Consistent with this, drugs that upregulate YAP activity partially rescue Trib1 deficiency - mediated lipid accumulation and low LDL uptake. To our knowledge this is the first time YAP activity has been implicated in the regulation of steatosis.
Importantly, we present evidence that YAP activating drugs, which can also alleviate liver fibrosis in mice, can partially rescue experimentally induced steatosis in human organoids. Further, we show that liver - derived organoids from NASH patients, but not normal donors, spontaneously recapitulate lipid accumulation in the absence of experimental steatotic stimulus.
Conclusion: We conclude that normal and steatotic human liver- derived organoids can be used to study important aspects of patient steatosis, and may be useful in future patient specific screens for antisteatotic drugs.
Disclosure: Nothing to disclose

IBS treatment
10:30-12:00 / Barcelona

OP198 CONSEQUENCES OF CHANGING TO THE ROME IV DIAGNOSTIC CRITERIA FOR IRRITABLE BOWEL SYNDROME AMONG PEOPLE LIVING WITH THE CONDITION

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Introduction: Irritable bowel syndrome (IBS) is a common condition with a prevalence in the community of 10%. The diagnosis is made using symptom-based diagnostic criteria. There are few studies examining implications of applying the Rome IV criteria for IBS, in preference to the previous gold standard, the Rome III criteria. We conducted a cross-sectional survey of over 1000 individuals who self-identified as having IBS in order to examine this issue.
Aims & Methods: We collected complete demographic, symptom, mood, and psychological health data from 1375 adults who self-identified as having IBS, but who were not recruited from a referral population. We applied both the Rome III and the Rome IV criteria simultaneously to examine what proportion met each of these diagnostic criteria for IBS. We measured the level of agreement between the Rome III and Rome IV criteria, and assessed for presence of an alternative functional bowel disorder in individuals who no longer met diagnostic criteria for IBS with the more restrictive Rome IV criteria. Finally, we compared characteristics of individuals who met only Rome III criteria with those who met Rome IV criteria.

Results: In total, 1080 (78.9%) of 1368 individuals with IBS met the Rome III criteria. In contrast, only 811 (59.1%) of 1373 individuals with IBS met the Rome IV criteria. Agreement between the criteria was only moderate (Kappa = 0.50). The reasons for not meeting the Rome IV criteria for IBS among those meeting the Rome III criteria are shown in Table 1.

	Reported abdominal discomfort, rather than abdominal pain (%)	Reported abdominal pain, but not at the required frequency (%)	Other reasons (%)
Met Rome III criteria, but not Rome IV criteria, for IBS (n = 286)	26 (9.1)	253 (88.5)	7 (2.4)
Rome IV functional constipation (n = 33)	3 (9.1)	29 (87.9)	1 (3.3)
Rome IV functional diarrhea (n = 118)	9 (7.6)	108 (91.5)	1 (0.8)
Rome IV functional abdominal bloating (n = 68)	6 (8.8)	61 (89.7)	1 (1.5)
Rome IV unspecified functional bowel disorder (n = 67)	8 (11.9)	55 (82.1)	4 (6.0)

[Table1: Reasons for not meeting the Rome IV criteria for IBS among those meeting the Rome III criteria]

Among those who no longer had IBS according to the Rome IV criteria, 33 (11.5%) met Rome IV criteria for functional constipation, 118 (41.3%) functional diarrhoea, 68 (23.8%) functional abdominal bloating or distension, and 67 (23.4%) an unspecified functional bowel disorder. Individuals with Rome IV-defined IBS had more severe symptoms, and higher levels of mood disorder and poor psychological health, compared with those who only met the Rome III criteria for IBS (P < 0.001).

Conclusion: Changing from the Rome III criteria to Rome IV IBS has substantial implications, both for individuals who believe they suffer from IBS, and for the spectrum of disease severity seen. Understanding the impact of these changes on clinical trials of novel agents in IBS will be important. Of those individuals with Rome III IBS who did not meet the Rome IV criteria for IBS, only 11.5% were reclassified into another functional bowel disorder where licensed and evidence-based therapies are available, namely functional constipation. In contrast, the treatment of people with functional diarrhoea, functional bloating, and unspecified functional bowel disorder relies on off-label therapies with only anecdotal evidence for their efficacy. Alternatively, these individuals could still be treated as if they have IBS. If use of the Rome IV criteria for IBS makes these conditions more prevalent, this highlights the need for rigorous randomised controlled trials (RCTs) of neuromodulators, probiotics, anti-diarrheals, and other agents in these disorders.

Disclosure: Nothing to disclose

OP199 OPTIMAL DELIVERY OF CARE FOR FUNCTIONAL GASTRO-INTESTINAL DISORDERS: RANDOMISED CONTROLLED TRIAL OF STANDARD GASTROENTEROLOGIST VERSUS MULTI-DISCIPLINARY CARE (THE MANTRA STUDY)

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Introduction: Functional gastrointestinal disorders (FGIDs) are common and costly to treat. Only a minority of patients are symptomatically improved with standard gastroenterologist care[1]. Many patients have psychological morbidity, yet despite psychological, behavioural and dietary therapies being well validated in these conditions, gastroenterology services do not provide them as part of integrated routine care.

Aims & Methods: We aimed to determine whether standard or multidisciplinary care provides the best clinical outcome for patients with a FGID. In a single hospital setting consecutive new referrals of patients with a Rome IV criteria-defined FGID were randomised 1:2 to a standard care gastroenterology specialist (SC) or multi-disciplinary (MD) clinic, the latter comprising gastroenterologists, dieticians, gut-hypnotherapists, psychiatrists and behavioural ("biofeedback") therapists situated in the same clinic simultaneously. At the MD clinic all patients initially saw a gastroenterologist and were then referred to allied clinicians as felt appropriate. Outcomes were assessed at clinic discharge or at 9 months. The primary outcome was global symptom improvement: "slightly better" (4/5) or "much better" (5/5) on a 5-point Likert scale. Secondary outcomes included gut symptoms (Gastro-Intestinal Symptom Severity Index (GISSI), condition-specific symptom scores [IBS: Irritable Bowel Severity Scoring System (IBS-SSS), functional dyspepsia: Nepean Dyspepsia Index (NDI)], psychological well-being (Hospital Anxiety and Depression Scale - HADS), and Quality of Life (Euro-QOL: EQ-5D).

Results:

Patient disposition: 188 patients (mean age 39, 63% female) were randomised, of whom 144 (46 SC and 98 MD) had sufficient outcome data and form the basis of this modified intention to treat analysis. 59% had IBS, 27% functional dyspepsia, the remainder other FGIDs. In the MD clinic, 61 patients (62%) saw at least one allied clinician. Median clinic visits were 2 in SC and 6 in MD (p< 0.01), and time to discharge 226 and 179 days, respectively (p=NS).

Outcome: The primary outcome was achieved in 57% versus 84%, respectively (p< 0.01). Patients scoring "much better" was 28% versus 51% (p=0.01).

Conditions: ≥50 point decrease in IBS-SSS in IBS patients: 38% v 66% (P=0.02), and ≥ 50% decrease in NDI in functional dyspepsia patients 27% v 46% (P=0.47).

Symptoms: Whole group ≥50% drop in GISSI sub-scores was 20% v 38% for reflux, 26% v 44% for nausea and vomiting, 17% v 42% for constipation, 22% v 43% for diarrhoea (all P< 0.04), but not significantly different for abdominal discomfort or dyspepsia. HADS score decreased from baseline to discharge in MD but not SC: SC 14.4 vs 13.7 (p=0.28) v MD 14.5 vs 11.5 (P< 0.01); HADS at discharge 13.7 v 11.5 (P=0.09), respectively. Baseline v discharge EQ-5D quality of life: SC 70 vs 70 (P=0.17) v MD (67 vs 75 (P< 0.01); EQ-5D at discharge 70 v 75 (P< 0.01).

Conclusion: In this randomised, controlled trial multi-disciplinary care was significantly superior to standard gastroenterologist-only care in patients with a functional gastro-intestinal disorder. Multi-disciplinary care based in a single clinic provided superior improvement in global symptoms, specific conditions, specific symptoms, psychological well-being, and quality of life. Superior outcomes were achieved over a shorter time, but with more clinic visits. The pragmatic study design that included all referrals supports the generalisability to gastroenterological practice. Consideration should be given to providing routine multi-disciplinary care for these conditions.

References: 1. Basnayake, C. , Kamm, M. A., Salzberg, M. , Stanley, A. , Khera, A. , Burrell, K. , Wilson O'Brien, A. , Hebbard, G. and Thompson, A. J. (2019), Outcome of hospital outpatient treatment of functional gastrointestinal disorders. Intern Med J, 49: 225-231. doi:10.1111/imj.14067

Disclosure: Nothing to disclose

OP200 PELVIC FLOOR BIOFEEDBACK IS EFFECTIVE TREATMENT FOR BLOATING IN FUNCTIONAL GASTROINTESTINAL DISORDERS WITH OUTLET DYSFUNCTION

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Introduction: It has been suggested that biofeedback may improve bloating in constipation due to dyssynergic defecation (DD) (1). However, data on different functional gastrointestinal disorders (FGID) are lacking.

Aims & Methods: Aim of our study was to evaluate the efficacy of pelvic floor biofeedback for severe bloating unresponsive to diet advise in FGID patients.

Materials and methods: Sixty-nine consecutive FGID patients consulting for bloating as main complaint were considered for the study. Four refused and were excluded. All the 65 remaining patients reported bloating as not improved by NICE diet advise augmented by lactose abstinence accord-

ing to a 5 point likert scale (range worse-major improvement/cure) and rated symptom severity VAS score >24 on a 100-mm scale. All 65 subjects underwent electromyography (EMG) testing of pelvic floor muscle function on straining by a surface EMG anal plug and rectal balloon expulsion test (BET) with a 16F Foley catheter inflated with 50 ml of tepid water. BET was considered failed if the balloon could not be evacuated within two minutes (2). A biofeedback protocol previously used for constipation due to DD was provided in all patients by a registered nurse who was unaware of the physiology results (3). Primary study aims were a) subjective report of fair-major improvement from baseline, b) >50% reduction of bloating VAS score from baseline. Secondary aim was achievement of successful BET. Dropouts (4 patients total, 2 BET failure) were included in the analysis with the last observation carried forward. Clinical and physiology follow-up visits were scheduled at 1-3-6 months post-treatment.

Results: All sixty-five patients (56 Female, mean age 41 years) completed the biofeedback protocol and attended the first follow-up visit. Most of the patients were affected by functional bloating (43.5%) or constipation predominat irritable bowel syndrome (27.5%), according to Rome III Criteria. DD was diagnosed in 32 patients (59%) (failed BET, EMG evidence of paradoxical contraction of the pelvic floor muscles on straining), 4 patients (6.3%) were discordant (failed BET, EMG evidence of pelvic floor muscle relaxation on straining), while the remaining 29 patient (43.8%) showed normal defecation pattern. As a whole, 35/65 patients (53.8%) met both primary aims at 1-3-6 month follow-up (McNemar non parametric test, p< 0.0001). According to BET results, 30/36 (83.3%) patients who failed BET at baseline evaluation met both primary aims at 1-3-6 month follow-up intervals compared with 5/29 (17.2%) patients with successful BET (chi square p< 0.001). A strong correlation between adequate relief and a >50% reduction of VAS bloating score was observed (r=1.00). In the failed BET group, 30/36 (83.3%) patients learned to evacuate the balloon within two minutes at all follow-up intervals (Friedman test for non-parametric data p>0.001), while no physiology modifications was observed in the successful BET group from baseline evaluation.

Conclusion: Pelvic floor biofeedback aimed to improve defecation effort is effective treatment for severe bloating in FGID with comorbid outlet dysfunction. Dyssynergic defecation may present without prevalent obstructed defecation and/or constipation symptoms.

References: 1) Baker J, et al. Abdominal Symptoms Are Common and Benefit from Biofeedback Therapy in Patients with Dyssynergic Defecation. Clinical and Translational Gastroenterology 2015; 6, e105; 2) Chiarioni G, et al. Validation of the balloon evacuation test: reproducibility and agreement with findings from anorectal manometry and electromyography. Clin Gastroenterol Hepatol 2014;12:2049-54. 3) Chiarioni G, et al. Biofeedback is superior to laxatives for normal transit constipation due to pelvic floor dyssynergia. Gastroenterology 2006;130:657-664.

Disclosure: Chiarioni G is a Member of the Anorectal Committe of the Rome Foundation. No COI to be disclosed for all of the remaining Authors

OP201 HUMAN MILK OLIGOSACCHARIDES IMPROVE ALL THE CENTRAL SYMPTOMS OF IRRITABLE BOWEL SYNDROME: A MULTI-CENTER, OPEN LABEL TRIAL

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Introduction: Altered gut microbiota is increasingly seen as a potential factor in irritable bowel syndrome (IBS) pathophysiology. Human milk oligosaccharides (HMOs) have been shown in healthy adults to increase the abundance of bifidobacteria[1], which are reported to be depleted in IBS[2]. HMOs may also have beneficial impact on gut motility and visceral pain[3].

Aims & Methods: We aimed to assess the potential for HMOs to support normal bowel habits and improve other bowel symptoms of IBS. A multi-center, open label trial was conducted in clinical patients with IBS (Rome IV criteria plus physician diagnosis) at 17 sites across the United States. The subjects took 5 grams of the HMOs 2'fucosyllactose (2'FL) and lacto-N-neotetraose (LNnT) in a 4:1 mix daily by mouth for 12 weeks. Bowel habits, IBS symptoms and quality of life were assessed at baseline and every 4 weeks during the intervention. Results were analyzed with Intention-to-Treat (ITT) methodology (last observation carried forward for non-completers), using repeated measures Analysis of Variance.

Results: A total of 317 subjects (70.7% females; mean age 44.0 years, range 18-93 years) received the study product; 136 with constipation predominant, 85 with diarrhea predominant, 95 with mixed, and 1 with unspecified IBS. The full twelve week intervention was completed by 245 subjects. In the ITT analyses, the subjects showed a significant reduction in total percentage of abnormal bowel movements (Bristol Stool Form Scale types 1, 2, 6, or 7) from baseline to 12 weeks (means and 95% CI: 89.8% [88.1%-91.5%] vs. 54.9% [51.4%-58.4%]) as well as substantial reductions in overall IBS Symptom Severity Score (327 [317-337] vs. 128 [117-139]), abdominal pain severity (62.5 [60.1-64.9] vs. 25.4 [22.6-28.2] and bloating severity (56.8 [53.8-59.8] vs. 23.2 [20.5-25.8]), and improvement in health-related quality of life (IBS-QOL scores: 50.4 [48.0-52.8] vs. 74.6 [72.3-76.9]): p< 0.0001 for all changes. The degree of therapeutic response was similar in all IBS subtypes, and most of the symptom improvement occurred in the first 4 weeks of intervention (see Table 1). Younger age was predictive of greater improvement in stool consistency and abdominal pain severity. The study product tested was well tolerated by most patients. The only common side effects were mild GI symptoms such as abdominal discomfort, distension and flatulence.

Conclusion: Our findings suggest that oral supplementation with 2'FL and LNnT HMOs can provide nutritional support that significantly reduces abnormal stool consistency, abdominal pain and bloating and improves health-related quality of life in IBS sufferers of all subtypes. However, the results from this open label trial need to be followed up by a randomized controlled trial.

Percentage of abnormal bowel movements in the past 4 weeks measured by Bristol Stool Form Scale			
	Overall (n=317)	IBS-C (n=136)	IBS-D (n=85)	IBS-M (n=95)
Baseline	88.0 [86.4-89.7]	84.9 [82.4-87.5]	87.5 [84.0-91.1]	93.1 [90.3-95.8]
Week 4	59.2* [56.5-62.0]	55.5* [51.3-59.8]	54.6* [49.3-59.9]	68.2* [63.7-72.8]
Week 8	56.5* [53.5-59.5]	53.5* [49.1-57.8]	56.2* [50.4-62.1]	61.3* [55.3-67.3]
Week 12	56.3* [53.2-59.4]	49.3* [44.8-53.8]	60.0* [54.4-65.6]	62.8* [56.8-68.9]
Total IBS Symptom Severity Score			
	Overall (n=317)	IBS-C (n=136)	IBS-D (n=85)	IBS-M (n=95)
Baseline	323 [314-332]	316 [302-329]	322 [305-339]	332 [314-349]
Week 4	178* [167-188]	164* [148-180]	181* [163-198]	195* [174-215]
Week 8	150* [140-161]	136* [121-151]	155* [136-174]	165* [142-188]
Week 12	144* [133-155]	118* [103-134]	155* [138-172]	170* [146-193]

significantly different from baseline at p<0.0001.

[Table 1. Changes in abnormal bowel movement percentage and IBS Symptom Severity Score (IBS-SSS) throughout the trial (ITT analyses; means [95% CI])]

References: [1] Elison, E., et al., Oral supplementation of healthy adults with 2´-O-fucosyllactose and lacto-N-neotetraose is well tolerated and shifts the intestinal microbiota. Br J Nutr, 2016. 116(8): p. 1356-1368. [2] Rajilić-Stojanović, M., et al., Intestinal microbiota and diet in IBS: causes, consequences, or epiphenomena? The American Journal of Gastroenterology, 2015. 110(2): p. 278-287. [3] Bienenstock, J., et al., Fucosylated but not sialylated milk oligosaccharides diminish colon motor contractions. PLoS One, 2013. 8(10): p. e76236.

Disclosure: Dorthe Seitzberg, Ingvild Dybdrodt Amundsen and Bruce McConnell are employed at Glycom A/S, Denmark, which funded this trial. Olafur Palsson, Anne Peery and Magnus Simren received research support from Glycom A/S related to the trial.

OP202 THE EFFICACY OF LACTIBIANE IKI (*BIFIDOBACTERIUM LACTIS LA 304, LACTOBACILLUS SALIVARIUS LA 302, LACTOBACILLUS ACIDOPHILUS LA 201*) IN REDUCING ABDOMINAL SYMPTOMS AND INFLAMMATORY BIOMARKERS IN ACUTE UNCOMPLICATED DIVERTICULATIS

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Introduction: Diverticular Disease (DD) is the most frequent abnormality in the digestive tract mainly in developed countries.

Most of people suffering from DD are asymptomatic, while 20% experience abdominal symptoms and eventually complications, episodes of diverticulitis or bleeding.

Acute Uncomplicated Diverticulitis (AUD) is defined as the inflammation of a colon diverticulum, often involving colic wall and pericolic fat. Conventional treatment of AUD includes antibiotic therapy, usually Ciprofloxacin and Metronidazole, fasting and fluid therapy.

Although several studies have been performed aimed at evaluating the clinical efficacy of probiotics in AUD, no definitive results have been achieved yet.

Aim of our pilot study is to test the efficacy of *Bifidobacterium Lactis LA 304, Lactobacillus Salivarius LA 302, Lactobacillus Acidophilus LA 201* (Lactibiane IKI, Biocure), in association with conventional antibiotics in treating AUD compared to conventional antibiotic therapy.

Aims & Methods: We enrolled 84 (25M/59F mean age 61,5 +- 11,5 years) consecutive patients who came to the Emergency Department of Foundation Policlinico A. Gemelli Hospital with a diagnosis of AUD. All patients performed routine blood test, dosage of C-Reactive Protein value and they were then randomly divided into two groups.

Group A (42 patients, 10M/32F mean age 32,23 +- 10,3 years) was treated with ciprofloxacin 400mg twice a day and metronidazole 500mg three times a day for one week, with a supplementation of Lactibiane IKI twice a day for 10 days.

Group B (42 patients, 15M/27F mean age 59,01 +- 11,3 years) was treated with ciprofloxacin 400mg twice a day and metronidazole 500mg three times a day for one week.

All patients filled a daily Visual Analog Scale (VAS) for abdominal pain, with a range value from 0 (asymptomatic) to 10, and C-RP value was determined on admission and at discharge.

Primary outcome of the study is the reduction of abdominal pain and inflammatory markers (C-RP) in the group treated with Lactibiane IKI supplementation.

Results: All patients completed the study. No side effect were observed.

As regards the VAS values: between day 1 and 3, group A decreased 4.07 points of vas scale, group B decreased 2.79 points of vas scale (p=0,0002); between day 1 and 5 group A decreased 6.3 points of vas scale, group B decreased 4.85 points of vas scale (p< 0,0001); between day 1 and 7 group A decreased 7.26 points of vas scale, group B decreased 6.1 points of vas scale (p < 0,0001); between day 1 and 10 group A decreased 7.8 points of vas scale, group B decreased 7.2 points of vas scale (p=0,048).

Regarding C-RP value, the mean decrease between the admittance value and after 72h was 49 mg/l for group A and 21,8 mg/l for group B (p=0,006). Finally, group A has a mean of 88,8 +- 17 hours (3,7 days) of hospitalization in BOU, meanwhile group B has a mean of 101 +- 20 hours (4,2 days) (p< 0,05).

Conclusion: Our study showed that the supplementation with Lactibiane IKI in the standard AUD therapy significantly reduce abdominal pain and inflammatory markers compared to control group.

These interesting results could be due to its anti-inflammatory activity, already well documented in the IBD therapy. Larger studies are needed to validate its use in the clinical practice.

Disclosure: Nothing to disclose

OP203 THE EFFECTS OF HUMAN MILK OLIGOSACCHARIDES ON BIFIDOBACTERIA AND GASTROINTESTINAL SYMPTOMS IN IRRITABLE BOWEL SYNDROME PATIENTS: A PARALLEL, DOUBLE BLIND, RANDOMIZED, PLACEBO-CONTROLLED TRIAL

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Introduction: Gut microbiota alterations seem to be a relevant factor in the pathophysiology of irritable bowel syndrome (IBS). Therefore, modulating the gut microbiota by using prebiotics, such as human milk oligosaccharides (HMO), might influence gastrointestinal (GI) symptoms through their effect on specific gut bacteria. However, the safety and tolerance of HMO have not been assessed in IBS patients. Thus, we aimed to determine the dose of a HMO mix of 2'-O-Fucosyllactose (2'FL) and Lacto-N-neotetraose (LNnT) that increased fecal bifidobacteria abundance in IBS patients without aggravating overall GI symptoms.

Aims & Methods: We performed a parallel, double-blind, randomized, placebo-controlled trial in an IBS patient cohort diagnosed according to the Rome IV criteria. We studied the effects of 5g and 10g doses of 4:1 mix of 2'FL and LNnT (2'FL/LNnT) compared to placebo (powdered glucose) after 4 weeks of oral intake, followed by a 4 weeks wash-out period. Gastrointestinal Symptom Rating Scale-IBS (GSRS-IBS) and fecal samples were collected at baseline, at the end of intervention and the washout period. Fecal bifidobacteria abundance was analyzed by the GA-map™ platform technology. Non-parametric analysis were performed between and within intervention groups.

Results: We included 61 IBS patients, (41 women; median age 45 (19 - 73) years); 27 IBS with diarrhea, 14 IBS with constipation and 20 mixed IBS. During the intervention phase, two patients, one from the placebo group and one from the 10g group, discontinued prematurely (after 2 weeks of intervention) due to worsening symptoms.

As can be seen in table 1, the bifidobacteria abundance differed between the groups after the intervention period, with higher abundance in the 10g group compared with the other intervention groups (p< 0.05). Within-group comparisons demonstrated a significant increase in bifidobacteria abundance in the 10g group at the end of the intervention period compared to baseline (p=0.018).

	Placebo (n=21)		5g 2´FL/LNnT (n=20)		10g 2´FL/LNnT (n=20)		#p-value
	Baseline	Week 4	Baseline	Week 4	Baseline	Week 4	
Log bifidoacteria abundance*	3.77 (± 1.48)	3.78 (±1.62)	4.81 (± 0.89)	4.86 (± 0.99)	4.21 (± 1.34)	5.03 (± 1.00)	< 0.05
GSRS-IBS scores*							
Total score	49.76 (± 10.04)	41.71 (± 10.43)	45.15 (± 7.99)	43.06 (± 13.43)	52.55 (± 8.41)	48.42 (± 11.65)	ns
Constipation score	6.05 (± 3.47)	5.24 (± 2.84)	3.70 (± 2.45)	4.33 (± 3.43)	5.35 (± 4.17)	4.68 (± 3.33)	ns
Abdominal pain score	8.57 (± 1.99)	7.76 (± 2.17)	8.10 (± 2.71)	7.06 (± 3.39)	9.20 (± 1.64)	8.53 (± 2.61)	ns
Bloating score	14.00 (± 3.54)	11.94 (± 3.99)	12.35 (± 4.00)	11.61 (± 4.54)	15.10 (± 3.02)	14.16 (± 4.07)	ns
Diarrhea score	15.52 (± 4.39)	11.94 (±4.17)	15.35 (± 4.78)	14.83 (±4.97)	17.20 (± 5.21)	15.95 (± 6.92)	ns
Satiety score	5.62 (± 3.41)	4.82 (± 3.43)	5.65 (± 2.81)	5.22 (± 2.69)	5.70 (± 3.34)	5.11 (± 2.71)	ns

*Data shown as mean (±sd). #p-values reflecting comparisons between the three groups (placebo, 5g and 10g 2´FL/LNnT) after the intervention (week 4), relative to baseline.

[Table 1. Fecal bifidobacteria abundance and gastrointestinal symptom severity (GSRS-IBS scores) at baseline and after the intervention (week 4).]

However, after the 4 weeks washout period no difference between the groups was detected. Overall GI symptom severity (GSRS-IBS total score) or individual GI symptoms did not differ between the groups after the treatment (ns, non-significant). However, tendencies towards improvements of GI symptom severity within the groups were observed at the end of the intervention (week 4). The 10g group showed a trend towards reduction in overall GI symptom severity (GSRS-IBS total score) compared to baseline (p=0.076), whereas the placebo group showed reduction of overall GI symptom severity, bloating and diarrhea at the end of the intervention (p< 0.05 for these comparisons). No symptom deterioration was seen in any of the groups.

Conclusion: In conclusion, 10g HMO dose of 2'FL/LNnT mix is able to induce the growth of the beneficial bacteria *Bifidobacterium* in patients with IBS without aggravating gastrointestinal symptoms. This approach may be worthwhile to restore IBS gut microbiota towards a healthy profile.

Disclosure: Nothing to disclose

Lower GI on fire
10:30-12:00 / Hotspot

OP204 MARKERS OF SYSTEMIC INFLAMMATION IN PRECLINICAL ULCERATIVE COLITIS

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Introduction: Data on the preclinical stage of ulcerative colitis (UC) are sparse. At diagnosis, UC often shows a modest increase in systemic inflammatory markers like C-reactive protein (CRP). However, a subclinical inflammation with elevated levels of CRP and interleukin-6 (IL6) in serum have been observed several years before diagnosis [1]. First-degree relatives, including healthy twin siblings, also display elevated levels of some inflammatory markers as a consequence of shared genetic and environmental risk factors [2]. It is reasonable to believe that the preclinical inflammation, reflecting early pathogenic mechanisms, ultimately leads to a diagnosis of UC.

Aims & Methods: We aimed to deeper examine the systemic preclinical inflammation in UC using a comprehensive set of protein markers. Cases with UC were identified at clinical follow-up of a prospectively collected population-based cohort of healthy individuals from northern Sweden. Plasma samples from cases and controls were subjected to proximity extension assay for relative quantification of 92 protein markers of inflammation. Results were validated in an inception cohort of treatment naïve, newly diagnosed patients with UC (n=101) *vs.* healthy controls (n=50). In addition, to examine the impact of shared genetic and environmental factors, a cohort of healthy mono- and dizygotic twin siblings of twins with UC (n=41) and matched healthy controls (n=37) were explored.

Results: Pre-diagnostic plasma samples from 72 cases who later in life developed UC and 140 controls, matched for gender, age, year of health survey and area of residence, were identified (table 1). Six proteins were significantly upregulated (p< 0.05) in pre-diagnostic UC compared to matched healthy controls. A receiver-operating curve based prediction model using the six protein markers combined with sex, age, smoking status and time to diagnose was set up for validation. The model discriminated newly diagnosed, treatment naïve UC cases from healthy controls (AUC=0.96; CI 0.93-0.98). An AUC of 0.73 (CI 0.62-0.84) was observed when the model was applied to healthy twin siblings *vs.* healthy controls and four out of six proteins were upregulated similarly as in the pre-diagnostic samples. The relative levels of the six proteins showed an intermediate upregulation in pre-diagnostic samples and samples from healthy twin siblings compared to samples at diagnosis of UC. Only one protein showed a significant correlation with time to diagnosis in the pre-diagnostic samples. Using pathway analysis, the six protein upregulations pointed towards subclinical inflammation in UC being caused by dysregulation of four immune pathways.

Conclusion: This is the first comprehensive characterisation of preclinical systemic inflammation in UC. Inflammatory proteins were upregulated several years prior to diagnosis of UC and to some extent these alterations were also seen in healthy twin siblings of UC patients. Characterisation of the preclinical stage of UC could pave the way for identification of predictive biomarkers and preventive strategies.

	Ulcerative colitis n=72	Controls n=140
BMI (IQR)	25.0 (23.2-27.5)	25.5 (23.1-27.8)
Sex; male (%)	34 (47.2)	64 (45,7)
Smoking status, current (%)	22 (30.6)	22 (30.6)
Median (range) age at sample (years)	50 (30-70)	50 (30-70)
Median (range) age at diagnosis (years)	54 (31-75)	
Disease extent (%)		
Proctitis (E1)	16 (22.2)	
Left-sided colitis (E2)	28 (38.9)	
Extensive colitis (E3)	28 (38.9)	

[Table 1. Clinical and demographic characteristics (before diagnose >1 year).]

References: 1. Lochhead P, Khalili H, Ananthakrishnan AN, Richter JM, Chan AT. Association Between Circulating Levels of C-Reactive Protein and Interleukin-6 and Risk of Inflammatory Bowel Disease. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association. 2016;14(6):818-24 e6. PubMed PMID: 26844874 2. Zhulina Y, Hahn-Stromberg V, Shamikh A, Peterson CG, Gustavsson A, Nyhlin N, et al. Subclinical inflammation with increased neutrophil activity in healthy twin siblings reflect environmental influence in the pathogenesis of inflammatory bowel disease. Inflammatory bowel diseases. 2013;19(8):1725-31. PubMed PMID: 23669399.
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OP205 OVERALL AND CAUSE-SPECIFIC MORTALITY IN MICROSCOPIC COLITIS: A DANISH NATIONWIDE MATCHED COHORT STUDY

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Introduction: Microscopic colitis (MC) is a chronic inflammatory disease characterized by watery diarrhea and characteristic histological findings in the setting of a normal macroscopic appearance of the colonic mucosa. The etiology is assumedly multifactorial and smoking is a known risk factor.

The disease course in MC is generally considered benign. However, the long-term natural history remains largely unknown and the risk of death in these patients has not been systematically evaluated.

Aims & Methods: Using Danish nationwide registry information, we aimed to investigate the overall and cause-specific mortality in a large consecutive and unselected cohort of patients with MC.

All patients with an incident diagnosis of MC from 2001-2017 were identified from the national pathology and patient registry. Patients were subcategorized according to subtype of MC, lymphocytic colitis (LC) and collagenous colitis (CC).

Overall and cause-specific mortality in patients with MC was compared with that of an age and sex matched cohort from the general population (controls) in a variable 1:10 ratio. The relative risk of death was analyzed with Cox regression models, estimating both crude and comorbidity-ad-

justed hazard ratios (HRs) with 95% confidence intervals (CIs). Analyses were stratified according to sex, age at diagnosis and subtype of MC.

Results: A total of 14.024 patients with MC of whom 42% had LC were identified. The mean age at diagnosis was 63.6 years for patients with LC and 67.0 years for CC and patients were predominantly female (64.4% of LC patients and 74.4% of CC patients).

During follow up, 3047 patients with MC died compared to 26.395 in the control group, unraveling a 25% significantly increased risk of death (HR 1.25; 95% CI, 1.20-1.30) in crude analyses. The mortality was attenuated in analyses adjusted for comorbidity, however, the relative risk remained significantly augmented (HR 1.08; 95% CI, 1.04-1.13). Stratifying according to MC subtype, crude analyses showed a significantly increased risk of death in both patients with LC (HR 1.30; 95% CI, 1.22-1.39) and CC (HR 1.21; 95% CI, 1.16-1.27). Again, the risk of death, although reduced, remained significant increased, in comorbidity-adjusted analyses (HR$_{LC}$ 1.13; 95% CI, 1.06-1.20 and HR$_{CC}$ 1.06; 95% CI, 1.00-1.11).

Compared to matched controls, patients with MC were more likely to die due to infections, diabetes, ischemic heart diseases and chronic lung diseases.

Conclusion: In an unselected large nationwide cohort of MC patients, the risk of death was significantly increased compared to the background population. The increased mortality was largely, but not entirely, associated to an increased burden of comorbidities and patients with MC were more likely to die from smoking-related diseases.

The increased mortality associated with a diagnosis of MC, as observed in our study, is however unexpected and needs to be confirmed in other large cohorts.

Disclosure: Nothing to disclose

OP206 NOVEL NOMOGRAMS TO PREDICT LYMPH NODE METASTASIS AND LIVER METASTASIS IN PATIENTS WITH EARLY COLON CARCINOMA

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Introduction: The poor prognosis and frequent recurrence of colon carcinoma might be related to lymph node metastasis (LNM) and distant metastasis. Advanced colon carcinoma (stage III or IV) is diagnosed when LNM or distant metastasis occurs, regardless of the pathologic T (pT) classification. Studies have indicated that 27.3% of patients diagnosed with colon carcinoma develop liver metastasis (LIM) during the course of their disease. We attempted to develop and validate nomograms to predict LNM and LIM in patients with early colon carcinoma (pT1+pT2) .

Aims & Methods: A total of 32,819 patients who underwent surgery between 2004 and 2015 for pT1 or pT2 colon carcinoma were enrolled in the study and divided into a training set (n=21880) in an earlier period and a validation set (n=10939). Univariable and multivariable analysis were used to identify independent risk factors predictive of LNM and LIM in the SEER discovery set. All variables were screened using the forward stepwise selection method in a multivariate binary logistic regression model. Calibration curves were plotted to validate the accuracy and reliability of the nomograms by the Hosmer-Lemeshow test. The predictive performance of the nomograms was measured by a receiver operating characteristic (ROC) curve. The predictive accuracy and clinical values of the nomograms were measured by decision curve analysis (DCA) by calculating the net benefits at each risk threshold probability. The predictive nomograms were further validated in the internal testing set.

Results: LNM was present in 3111 of 21880 patients (14.2%) and 30 of 10939 patients (14.5%) in the training and testing sets, respectively. LIM occurred in 1.5% of patients in the training set and 1.2% of patients in the testing set. In the correlation analysis, five variables, namely, histological grade, T classification, tumor size, serum CEA level and overall survival, were significantly correlated (P< 0.001) with LNM and LIM in both the training and testing sets. Based on the independent risk factors identified in the multivariate regression analysis, two nomograms were developed to predict the possibility of LNM (marital status, histological grade, histological type, T classification, tumor size and serum CEA level) and LIM (age, histological grade, tumor size, serum CEA level and N classification). The calibration curves showed perfect agreement between nomogram predictions and actual observations. DCAs indicated the clinical usefulness of the prediction

nomograms and threshold probabilities of 0-0.3 for LNM or 0-0.2 for LIM were the most beneficial for predicting LNM and LIM with our nomograms. Receiver operating characteristic curves indicated good discrimination in the training set (area under the curve [AUC] = 0.667, 95% CI=0.661-0.673) and the testing set (AUC=0.658, 95% CI=0.649-0.667) for the LNM nomogram and encouraging performance in the training set (AUC=0.766, 95% CI=0.760-0.771) and the testing set (AUC=0.825, 95% CI=0.818-0.832) for the LIM nomogram.

Conclusion: In conclusion, based on the clinical risk factors identified in a large population-based cohort, we established the first practical nomograms that can objectively and accurately predict individualized risk of LNM and LIM. Moreover, the internal cohort validation results demonstrate that the two nomograms perform well and have high accuracy and reliability. Our nomograms were demonstrated to be clinically useful in DCAs, and they should therefore help clinicians to improve individual treatment, make clinical decisions and guide follow-up management strategies for patients with early colon carcinoma.

Disclosure: Nothing to disclose

OP207 LPA-INDUCED GPR35 SIGNALLING IN MACROPHAGES RESULTED IN ALTERED CYTOKINE EXPRESSION AND MODULATION OF COLITIS

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Introduction: Host- or bacterial-derived metabolites orchestrate immune responses in inflammatory bowel diseases through G protein-coupled receptors. Genome-wide association studies indicated that polymorphisms in GPR35 are associated with an increased risk of ulcerative colitis (UC) and primary sclerosing cholangitis (1). The chemokine CXCL17, the tryptophan metabolite kynurenic acid (KNA) and the phospholipid derivative lysophosphatidic acid (LPA) have been suggested as potential ligands (2). GPR35 also interacts with the sodium potassium pump to ensure electrochemical gradients in epithelial cells (3). The endogenous ligand and cell type in which GPR35 signaling modulate intestinal inflammation is rather unexplored.

Aims & Methods: To investigate GPR35 in macrophages the mouse lines GPR35tdTomato, GPR35Ko and GPR35$^{\Delta CX3CR1}$, in which tamoxifen injection silences GPR35 expression in CX3CR1$^+$macrophages have been created. Potential ligands were screened in *Gpr35.2*-deficient zebrafish.

Results: *In situ* hybridization of *Gpr35.2* in zebrafish 120 hours post fertilization revealed restricted *Gpr35.2*expression in the intestine. *Ex vivo* imaging of GPR35tdTomato / CX3CR1-GFP double reporter animals showed GPR35 expression by intestinal epithelial cells and CX3CR1+ macrophages. Flow cytometry confirmed that monocytes but not B cells, T cells and innate lymphoid cells express GPR35. During the development of monocytes into gut macrophages GPR35 expression is down-regulated, which can be discriminated in GPR35-positive and -negative macrophages with higher *Tnf, Il1b*and *Il23*expression by GPR35-positive macrophages. *Gpr35* expression is regulated by the microbiota as antibiotic-treated zebrafish and mice as well as germ-free mice have reduced GPR35 expression. Conversely, TNBS-colitis in zebrafish, DSS-colitis in mice induced GPR35 expression in macrophages, and increased numbers of GPR35-positive macrophages were present in inflamed regions of UC patients. Potential agonistic ligands of GPR35, were screened with a Chinese Hamster Ovary (CHO)-K1 GPR35 Gi cell line, that stably overexpressed human GPR35 coupled to an inhibitory G protein which inhibits forskolin-induced cAMP accumulation in response to GPR35 agonists. LPA and CXCL17 but not KYNA inhibited forskolin-induced cAMP production, and the potential candidate LPA was further tested in *Gpr35.2*-deficient zebrafish. As macrophages express other lysophophospatic acid receptors bone marrow-derived macrophages from GPR35Ko mice were stimulated with GPR35. LPA induced *tnf,Il1b*and *Il1a* production in macrophages and induced macrophage migration in a GPR35-dependent manner. Increased expression of autotaxin, which converts lysophosphatidylcholine into LPA, was observed in zebrafish and mice undergoing intestinal inflammation. In agreement with the potential activation of GPR35 during colitis, GPR35-deficient mice have increased DSS-colitis severity. The deletion of GPR35 in CX3CR1+ macrophages in-

dicated that GPR35 signaling in macrophages is critical for the increased severity of DSS colitis. GPR35 deletion in macrophages resulted in reduced *tnf* production by macrophages. As TNF regulates *CYP11A1* and *CYP11B1* expression required for extraadrenal corticosterone synthesis, the silencing of GPR35 in macrophages was associated with reduced intestinal *CYP11A1* and *CYP11B1* expression.

Conclusion: LPA-induced GPR35-signalling in macrophages modulates cytokine responses and colitis. The depletion of GPR35 in macrophages resulted in increased DSS colitis severity associated with reduced *CYP11A1* and *CYP11B1* expression involved in extraadrenal corticosterone synthesis.

References: 1. Ellinghaus, D et al. Hepatology. 2013; 58(3):1074-83 2. Milligan G. Br J Pharmacol. 2018;175(13):2543-2553. 3. Schneditz, G et al. Sci Signal. 2019;12(562)

Disclosure: Nothing to disclose

OP208 EFFICACY AND SAFETY OF UPADACITINIB AS AN INDUCTION THERAPY FOR PATIENTS WITH MODERATELY-TO-SEVERELY ACTIVE ULCERATIVE COLITIS: COMBINED RESULTS FROM 382 SUBJECTS IN THE PHASE 2B STUDY U-ACHIEVE

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Introduction: The efficacy and safety of upadacitinib (UPA), an oral Janus Kinase 1-selective inhibitor, were assessed in an 8-week double-blind, placebo-controlled, dose-ranging phase 2b induction study (part 1) in patients with moderately-to-severely active ulcerative colitis (UC) who had inadequate response, loss of response, or intolerance to corticosteroids, immunosuppressives, or biologic therapies.[1,2] During the analysis of part 1, additional patients were enrolled in part 2 to avoid interrupting the study activities and to provide a sufficient number of clinical responders for the maintenance portion of the study.

Aims & Methods: We present the efficacy and safety of the combined results of part 1 and part 2 of U-ACHIEVE.

Adult patients with moderately-to-severely active UC (Adapted Mayo Score 5-9 points and centrally-read endoscopy subscore 2-3) were randomised in a 1:1:1:1:1 ratio to receive extended-release UPA 7.5, 15, 30, 45mg once daily (QD) or placebo for 8 weeks (N=250). In part 2, an additional 132 patients were randomised to UPA 30 or 45mg QD with 1:1 allocation for 8 weeks. Pairwise comparisons between UPA doses and placebo for the primary endpoint of clinical remission per Adapted Mayo Score at Week 8 (defined as stool frequency subscore ≤1, rectal bleeding subscore =0, and endoscopic subscore ≤1) and ranked secondary endpoints were conducted using the Cochran-Mantel-Haenszel test stratified by previous biologic use, baseline corticosteroid use, and baseline Adapted Mayo score. No multiplicity adjustments were applied. Non-responder imputation was utilized for missing values in 13% of patients. Treatment emergent adverse events (AEs) were reported from first dose of study drug to up to 30 days after last dose.

Results: A total of 382 patients were randomised with a mean (SD) age of 42.7 (14.3) years and a disease duration of 8.4 (7.4) years. The primary endpoint of clinical remission, and secondary endpoints of endoscopic improvement, clinical response per Adapted Mayo score, clinical response per Partial Mayo score, endoscopic remission, and histologic improvement were significantly higher with UPA doses ≥30mg QD compared to placebo (Table). Incidences of AEs and AEs leading to discontinuation were similar across UPA groups, and numerically higher in the placebo group. Rates of serious AEs were 10.9%, 0%, 4.1%, 4.3% and 4.9% for placebo and UPA 7.5, 15, 30, and 45mg QD, respectively. Serious infections occurred in patients receiving placebo (4.3%, n=2), 15mg QD (2.0%, n=1), 30mg QD (0.9%, n=1), and 45mg QD (1.6%, n=2). One case of herpes zoster and one case of pulmonary embolism (PE)/deep vein thrombosis (DVT) with UPA 45mg QD were reported. The case of PE/DVT was reported 26 days after study drug discontinuation due to UC worsening and hospitalization. No deaths were reported.

Endpoints, n (%)	Placebo N=46	UPA 7.5 mg QD N=47	UPA 15 mg QD N=49	UPA 30 mg QD N=117	UPA 45 mg QD N=123
Clinical remission per Adapted Mayo Score (SFS ≤1, RBS=0, and ES ≤1) at Week 8[a]	0	4(8.5)	7(14.3)*	25(21.4)***	22(17.9)**
Endoscopic Improvement (ES ≤1) at Week 8[b]	1(2.2)	7(14.9)*	15(30.6)***	40(34.2)***	42(34.1)***
Clinical response per Adapted Mayo score (decrease from baseline ≥2 points and ≥30% and in RBS ≥1 or an absolute RBS ≤1) at Week 8[b]	6(13.0)	13(27.7)+	22(44.9)***	63(53.8)***	65(52.8)***
Clinical response per Partial Mayo score (decrease from baseline ≥2 points and ≥30% and in RBS ≥1 or an absolute RBS ≤1) at Week 2[b]	7(15.2)	11(23.4)	18(36.7)*	52(44.4)***	63(51.2)***
Endoscopic remission (ES=0) at Week 8[b]	0	3(6.4)+	2(4.1)	19(16.2)**	20(16.3)**
Histologic improvement (any decrease from baseline in Geboes score) at Week 8[b]	3(6.5)	16(34.0)**	25(51.0)***	55(47.0)***	62(50.4)***

[a]Primary Endpoint; [b]Ranked Secondary Endpoints

***, **, *, and + significant at 0.001, 0.01, 0.05, and 0.1 levels, respectively compared with placebo

UPA=upadacitinib; QD=once daily; SFS=stool frequency subscore; RBS=rectal bleeding subscore; ES=endoscopic subscore

[Table]

Conclusion: In this combined analysis, primary and ranked secondary endpoints consistently met statistical significance with UPA doses ≥ 30mg QD compared with placebo in patients with moderately-to-severely active UC. These results are consistent with the part 1 intention-to-treat analysis.[1,2] UPA was well-tolerated, and no new safety signals were identified compared to previous studies of UPA.[3]

References:

1. Sandborn, W.J., et al. Presentation #OP195. United European Gastroenterology (UEG) Week 2018.

2. Sandborn, W.J., et al. Presentation #OP14. European Crohn´s and Colitis Organisation 2019.

3. Burmester et al., Lancet 2018; 391(10139):2503-12.

OP209 PROMINENCE OF ILEAL MUCOSA ASSOCIATED MICROBIOTA TO PREDICT POST-OPERATIVE ENDOSCOPIC RECURRENCE IN CROHN´S DISEASE

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Introduction: Following ileal resection for Crohn's disease (CD), recurrence is very frequent. Although several clinical risk factors of recurrence have been identified, predicting relapse remains challenging. Performing an ileocolonoscopy within the first year after surgery is currently recommended to assess endoscopic recurrence and adjust the treatment.

Aims & Methods: We took advantage of a large prospective multicentric cohort to investigate the role of the ileal mucosa-associated microbiota in post-operative endoscopic recurrence. This is a prospective study performed in 9 centers of the REMIND group, collecting clinical and biological data at time of surgery and of endoscopy (performed at 6 months). Ileal mucosa-associated microbiota was analyzed by 16S sequencing (MiSeq, Illumina) at the time of surgery and/or of endoscopic evaluation in 201 patients (288 samples in total) prospectively recruited in France. The obtained sequences (rarefied to 5000 read/sample) were analyzed using the Qiime pipeline to assess composition, alpha and beta diversity. Linear discriminant analysis effect size (LEfSe) pipeline was used to identify bacterial taxa differentially represented. We used logistic regression and Random Forest to evaluate the role of the gut microbiota at the time of surgery to predict endoscopic recurrence (defined by a Rutgeerts score >i1).

Results: Among the 201 patients included: 98 (49%) were male, mean age at surgery was 35 years (SD 12), 66 patients (33%) were active smoker at time of surgery, 39 patients (19%) had a previous resection, and 47 patients (23%) had perianal lesions. Indication for surgery was stricturing disease (116), penetrating disease (71). After surgery, 48 patients received thiopurines, and 68 patients received anti-TNF therapy. The microbiota was composed of bacteria from the Firmicutes, Proteobacteria, Bacteroidetes, Actinobacteria and Fusobacteria phyla. As expected, antibiotics treatment within one month before surgery had a dramatic impact on microbiota composition (Anosim, p < 0.0001) and diversity (Shannon index mean 4.3 ± 0.1 vs 3.7 ± 0.2, p=0.006). Ileal mucosa-associated microbiota exhibits profound changes following surgery in CD. Compared to non-recurrence setting, endoscopic recurrence was associated with strong changes in ileal mucosa-associated microbiota that were highly reminiscent of those observed generally in ileal CD compared to healthy subjects with a reduction in alpha diversity, increase in several members of the Proteobacteria phylum and decrease in several members of the Lachnospiraceae and the Ruminococcaceae families within the Firmicutes phylum. At the time of surgery, we identified several bacterial taxa associated with endoscopic recurrence and that can better predict relapse than usual clinical risk factors (ROC Curve, Area under the curve, AUC: 97.1% [93.8%-100%] and 81.0% [60.8%-100%] in the whole population and in the validation set respectively).

Conclusion: Surgery has an important impact on ileal-mucosa associated microbiota. Post-operative endoscopic recurrence is associated with changes in microbiota composition and alpha diversity. The gut microbiota has the potential to predict post-operative evolution and recurrence.

Disclosure: This study has been supported by grants from MSD France, Association François Aupetit, the Helmsley Charitable Trust and INSERM

OP210 MULTICENTER PROSPECTIVE RANDOMIZED STUDY TO COMPARE ENDOSCOPIC TREATMENT OF STRICTURES IN CROHN´S DISEASE: SELF-EXPANDING METAL STENTS VS ENDOSCOPIC BALLOON DILATION. PROTDILAT STUDY

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Introduction: Endoscopic Balloon Dilation (EBD) is the established endoscopic treatment for short strictures in Crohn´s Disease (CD). Self-expanding metallic stents (SEMS) have been used for the treatment of refractory strictures with good results in patients that failed to dilation.

Hypothesis: Endoscopic treatment of strictures in CD by placing a SEMS is more effective than EBD.

Aims & Methods: Objectives:
1)To compare the efficacy and safety of endoscopic treatment (SEMS vs EBD) in CD patients with stenosis;
2) To perform a comparative cost study.

Methods: Randomized, prospective, multicenter clinical trial of patients with CD and obstructive symptoms with stenosis < 10 cm and refractory to medical treatment. We exclude patients with stenosis previously treated with SEMS and/or EBD in the previous year and with stenosis no accessible to colonoscopy. The main outcome was to determine the efficacy of the endoscopic treatment defined by the percentage of patients free of a new therapeutic intervention (EBD, SEMS or surgery) due to symptomatic recurrence at one year of follow-up. Those who failed the endoscopic primary treatment were crossed over to the other endoscopic option. A direct cost study was done.

Results: A total of 99 patients from 19 Spanish hospitals were randomized, 19 were excluded because they did not fulfil the inclusion criteria. Eighty patients, 39 women, with a median age of 45 (IQR: 38-54.7) were finally included. The primary treatment was 39 SEMS and 41 EBD for ITT analysis. In 42.5% of the cases the stenosis was in the anastomosis site whereas in 57.5% were de novo strictures. The median length of the strictures was 3.4 cm (IQR: 2-5.5). No differences related to demographic, disease, treatment and stenosis characteristics were found between the two groups. The success rate of EBD and SEMS was 80.5% and 51.3%, respectively (Adjusted OR, 3.5; 95% CI, 1.3-9.6; p=0.016). In a subanalysis of patients with strictures >3 cm differences between the 2 endoscopic procedures disappeared (EDB: 66.7% vs SEMS: 63.6%). In multivariate analysis of patients with EBD, the only variable associated with the success was the length of the stricture (OR, 1.05; 95% CI, 1.01-1.10; p=0.038). A 6.3% adverse events were reported without differences between the two treatments. Only 3 complications were related to endoscopic procedure (1 perforation in each therapy arm, 1 mild self-limited hemorrhage in EBD group). The average

cost for EBD patient was 802.83 euros (average 1.3 dilations) and for SEMS patients was 1827.06 euros (cost analysis of first 55 randomized patients). A total of 20 patients were crossed over to the other endoscopic option; 13 patients completed the follow-up (10 SEMS and 3 EBD initial failure crossed over to EBD and SEMS respectively) with a final success of 10/10 in rescue EBD treatment and 1/3 in rescue SEMS treatment.

Conclusion: The EDB is more effective than SEMS for CD strictures, with a good safety profile of both treatments. In addition, EBD is a more cost-effective than SEMS. The length of the stricture is the only factor related to EBD success. The clinical scenario in which SEMS could be useful is strictures >3 cm. ClinicalTrials.gov NCT 02395354.

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OP211 RIFAMYCIN SV-MMX® FOR ACUTE UNCOMPLICATED DIVERTICULITIS? RESULTS OF INNOVATIVE ANTIBIOTIC THERAPY FROM A PROSPECTIVE DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

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Introduction: Traditionally, guidelines recommended bowel rest and an up to 10-day treatment regime with a broad-spectrum antibiotic in acute uncomplicated diverticulitis (AUD). Recent studies have questioned this common strategy. However, placebo-controlled studies are lacking, and if effective, the duration of treatment is unclear. We conducted a double-blind trial, studying therapeutic benefits of the novel broad-spectrum, poorly absorbed antibiotic Rifamycin SV multi-matrix (MMX®) in comparison to placebo.

Aims & Methods: The aim was to compare efficacy and safety of two doses of Rifamycin SV-MMX® versus placebo (PLC) in the oral treatment of AUD. This was an exploratory, double-blind, double-dummy, randomized multi-center trial, with three treatment groups: (I) Rifamycin SV-MMX® 400mg BID (RIF800), (II) Rifamycin SV-MMX® 600mg TID (RIF1800) and (III) placebo (PLC). Out-patients with AUD proven by cross-sectional imaging and biomarkers were randomly assigned to one of the three treatment groups for a 10-day oral treatment. The primary endpoint was treatment success (required absence of fever, left lower quadrant pain, CRP improvement and absence of complications) at day 10. Key secondary endpoint was complete treatment success (required a normalization of CRP in addition) at days 0, 3, 7 and 10.

Results: A total of 201 patients qualified for the full analysis set (FAS). Main baseline characteristics were: 60% female, mean age 58.6 years, mean BMI 29.1 kg/m², mean CRP 40.5 mg/l and intensity of abdominal left lower quadrant pain of 5.6 cm (on a 10 cm visual analogue scale). The proportion of patients with treatment success at day 10 was numerically higher in the RIF800 group (62.2%) than in the PLC group (47.5%) (p=0.06) (Table 1). In a subgroup of patients with > 3 days of symptoms prior to start of the therapy both Rifamycin groups reached higher complete treatment success rates at day 10 compared to placebo, which was statistically significant for the RIF800 group (Table 1). In addition, both Rifamycin groups achieved statistically significant higher complete treatment success rates at day 3 compared to placebo (p< 0.05) (Table 1). It is to be noted that none of the placebo treated patients had complete treatment success at day 3. No unexpected side effects occurred and the rate of adverse events did not differ among groups.

	Number (%) of patients		
	RIF800 (n=82)	RIF1800 (n=79)	Placebo (n=40)
Treatment Success at day 10	51/82 (62.2%) / p=0.06	39/79 (49.4%) / p=0.42	19/40 (47.5%)
Complete Treatment Success at day 10 for subgroup with >3 days of symptoms	16/30 (53.3%) / p=0.01	16/42 (38.1%) / p=0.08	1/12 (8.3%)
Complete Treatment Success at day 3	9/82 (11%) / p=0.03	10/79 (12.7%) / p=0.02	0/40 (0%)

[Table 1: Results from clinical efficacy endpoints (FAS)]

Conclusion: Overall, antibiotic treatment with Rifamycin SV-MMX® trended to demonstrate therapeutic superiority over placebo in acute uncomplicated diverticulitis. It was faster than placebo in achieving complete treatment success, with most pronounced effect already at day 3. The subgroup of patients with more than 3 days of symptoms of AUD benefitted most from the Rifamycin treatment. The preferred dosis of Rifamycin seems to be 400mg BID. Rifamycin SV-MMX® was safe and well tolerated.

Disclosure: The following authors have financial relationship with a commercial interest: Wolfgang Kruis received lecture fees and travel costs by Dr. Falk Pharma GmbH. Roland Greinwald and Tanju Nacak received salary (employment) by Dr. Falk Pharma GmbH.

OP212 PRECLINICAL AND CLINICAL EFFICACY OF OLORINAB, A PERIPHERALLY RESTRICTED, HIGHLY SELECTIVE FULL AGONIST OF THE CANNABINOID TYPE 2 RECEPTOR FOR THE MANAGEMENT OF VISCERAL PAIN IN INFLAMMATORY BOWEL DISEASE

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Introduction: Abdominal pain is common in patients with inflammatory bowel diseases (IBDs), including Crohn's disease (CD), and available treatments often fail to relieve this pain. Cannabinoid receptors can modulate visceral pain; however, clinical development of non-selective agonists is limited by unwanted psychoactive effects. Olorinab is a highly selective full agonist of the cannabinoid type 2 receptor (CB_2) and showed low blood-brain barrier penetration in rodents. Reported here, preclinical evaluation assessed whether olorinab reduced visceral hypersensitivity in a rat model of IBD (colitis), and a randomized, open-label, multi-centre, phase 2a study evaluated olorinab in patients with quiescent CD experiencing abdominal pain.

Aims & Methods: In preclinical study, colitis was induced using 12 mg 2,4,6-trinitrobenzene sulfonic acid (TNBS) in 35% ethanol in rats, applied rectally. Vehicle or olorinab (3 or 30 mg/kg) was given twice daily for 5 days in control or colitis rats beginning 1 day after TNBS. Visceral mechano-sensitivity was measured *in vivo* as visceromotor responses (VMR) to colorectal distension (CRD; distension pressures 0-80 mm Hg). Colonic nociceptor firing was measured *ex vivo*.

In the phase 2a study, subjects aged 18-66 years with quiescent CD (simple endoscopic score-CD < 10 or faecal calprotectin < 500 µg/g) experiencing abdominal pain, defined as weekly average abdominal pain score (AAPS) ≥4 on a scale of 0 (no pain) to 10 (worst possible), were randomly assigned 1:1 to 25 or 100 mg oral olorinab 3 times a day (TID) for up to 8 weeks. Primary objectives were safety and tolerability. Efficacy endpoints included change in AAPS from baseline week (BL) to weeks 4 and 8, change in AAPS from pre-dose to 1.5 hours post-dose, and proportion of clinical responders (≥30% reduction in weekly AAPS from BL).

Results: Visceral hypersensitivity was observed in vehicle-treated colitis rats with higher VMR to CRD vs healthy controls ($P< 0.05$ at 20 mm Hg; $P< 0.01$ at 40-80 mm Hg). Colitis rats treated with olorinab had lower VMR to CRD vs their vehicle-treated counterparts ($P< 0.001$, N=9/group). Control rats treated with olorinab did not show altered VMR to CRD ($P>0.05$, N=8-11/group). Olorinab reduced colonic nociceptor hypersensitivity in a concentration-dependent manner via CB_2.

In the phase 2a study (N=14), AAPS significantly improved at weeks 4 and 8 from BL. Change in AAPS from BL to the time of peak concentration

(1.5 hours post-dose) during week 8 was -4.6 on an 11-point scale (N=11; $P< 0.001$). The proportion of clinical responders was 85% (11/13) at week 4 and 100% (11/11) at week 8 among evaluable subjects. Adverse events (AEs) occurred in 4/6 (67%) and 6/8 (75%) subjects who received 25 mg and 100 mg TID, respectively, and were generally mild to moderate with limited duration. AEs in ≥2 subjects included drug hypersensitivity, pain in extremity, and hypomagnesaemia; 2 serious AEs (pneumonia, worsening interstitial pneumonia) occurred in 1 subject and were not considered treatment related. There were no discontinuations due to AEs, and no clinically significant changes in vital signs or laboratory results were observed.

Conclusion: Olorinab, a highly selective full agonist of CB_2, showed preclinical efficacy in reducing visceral hypersensitivity in a rat model of IBD. Olorinab-treated subjects with quiescent CD experiencing abdominal pain had an improvement in AAPS without psychoactive effects in phase 2a. These preclinical and clinical results support further clinical development of olorinab for the treatment of abdominal pain.

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Paradigm shifts in IBD treatment
14:00-15:30 / B2

OP213 TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, IN THE TREATMENT OF ULCERATIVE COLITIS: AN INTERIM ANALYSIS OF AN OPEN-LABEL, LONG-TERM EXTENSION STUDY WITH UP TO 5.5 YEARS OF TREATMENT

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Introduction: Tofacitinib is an oral, small molecule Janus kinase inhibitor for the treatment of ulcerative colitis (UC). Tofacitinib safety and efficacy were demonstrated in patients (pts) with moderate to severe UC in 3 Phase 3, randomised, placebo-controlled studies,[1] and are being further evaluated in an ongoing open-label long-term extension (OLE) study.[2]

Aims & Methods: We present an update (as of Sep 2018) on previously presented safety and efficacy data[2] from the ongoing OLE study (NCT01470612; database not locked) in pts who completed or demonstrated treatment failure in OCTAVE Sustain (NCT01458574) or were non-responders in OCTAVE Induction 1/2 (NCT01465763/NCT01458951). Eligibility was determined per Week (Wk)8 data from OCTAVE Induction 1/2, or Wk52 (for completers) or early-termination data from OCTAVE Sustain. Pts in remission (total Mayo score ≤2, no individual subscore >1, rectal bleeding subscore 0) at Wk52 of OCTAVE Sustain (per central read) were assigned tofacitinib 5 mg twice daily (BID) in the OLE study; all others were assigned 10 mg BID. At Month 2, all pts underwent endoscopy, and induction non-responders were mandated to withdraw if they did not show clinical response. Incidence rates (IRs) for adverse events (AEs) of special interest were calculated as the number of unique pts with events per 100 pt-years (PY). Efficacy endpoints were derived from Mayo score per local read, with non-responder imputation for missing data at all visits but last observation carried forward after a pt advanced to the next study (NRI-LOCF).

Results: Of 944 pts who received ≥1 dose of study drug (for up to 5.5 years), 175 (18.5%) received tofacitinib 5 mg BID and 769 (81.5%) received tofacitinib 10 mg BID (total PY exposure 454 and 1550, respectively). In total, 337 (35.7%) pts discontinued due to insufficient clinical response, and 78 (8.3%) discontinued due to AEs excl. worsening UC. AEs, serious AEs and severe AEs occurred in 764 (80.9%), 162 (17.2%) and 109 (11.5%) pts, respectively (Table). The most frequent AE classes were infections and infestations (52.1%) and gastrointestinal disorders (43.3%). The most frequent AEs were nasopharyngitis (20.3%), worsening UC (19.5%) and increased blood creatine phosphokinase (10.8%). IRs (95% confidence interval) in

the 'Tofacitinib All' group were: serious infections 1.61 (1.10, 2.27); herpes zoster (all) 3.35 (2.58, 4.27); major adverse cardiovascular events 0.15 (0.03, 0.44); malignancies excl. non-melanoma skin cancer (NMSC) 0.85 (0.50, 1.36); and NMSC 0.81 (0.46, 1.32), with no clustering of malignancy type; IRs by dose are shown in the Table. No new safety risks were identified. At Month 36 (NRI-LOCF) in the 5 and 10 mg BID groups, respectively, 55.9% and 32.2% of pts were in remission, 62.5% and 35.8% had mucosal healing, and 65.8% and 38.9% showed clinical response.

Conclusion: In pts with moderate to severe UC in the OLE study with up to 5.5 years of treatment, no new safety risks emerged vs those observed in earlier analyses of the OLE study[2] or with tofacitinib in rheumatoid arthritis. Efficacy data from the OLE study continue to support long-term efficacy with tofacitinib 5 or 10 mg BID up to 36 months beyond Wk52 of OCTAVE Sustain.

	Tofacitinib 5 mg BID (N=175; 454 PY)		Tofacitinib 10 mg BID (N=769; 1550 PY)		Tofacitinib All (N=944; 2004 PY)	
	n (%)	IR (95% CI)	n (%)	IR (95% CI)	n (%)	IR (95% CI)
Serious infections[a]	6 (3.4)[b]	1.33 (0.49, 2.89)	26 (3.4)[c]	1.69 (1.10, 2.48)	32 (3.4)	1.61 (1.10, 2.27)
Herpes zoster (all)[a]	11 (6.3)	2.49 (1.24, 4.45)	53 (6.9)[d]	3.61 (2.70, 4.72)	64 (6.8)	3.35 (2.58, 4.27)
MACE[e,f]	2 (1.1)[g]	0.44 (0.05, 1.59)	1 (0.1)[h]	0.06 (0.00, 0.36)	3 (0.3)	0.15 (0.03, 0.44)
Malignancies excluding NMSC[e,f]	5 (2.9)[i]	1.11 (0.36, 2.58)	12 (1.6)[j]	0.78 (0.40, 1.35)	17 (1.8)	0.85 (0.50, 1.36)
NMSC[e,f]	5 (2.9)	1.12 (0.36, 2.61)	11 (1.4)	0.72 (0.36, 1.29)	16 (1.7)	0.81 (0.46, 1.32)

Data are as of Sep 2018, database not locked
IRs were calculated as the number of unique patients with events per 100 PY
[a]Events that occurred >28 days after the last dose of study drug were excluded for calculation of proportion and IR; [b]Three events were reported as severe (number of events): appendicitis (1), gastroenteritis norovirus (1), necrotising fasciitis (1); [c]Thirteen events were reported as severe (number of events): appendicitis (3), arthritis bacterial (1), atypical pneumonia (1), herpes zoster (2), herpes zoster meningitis (1), mastoiditis (1), meningitis viral (1), osteomyelitis (1), sinusitis (1), wound infection (1); [d]Four events were reported as severe; [e]All events, including those outside the 28-day risk period, were included for calculation of proportion and IR; [f]Adjudicated events; [g]MACE (number of events): acute myocardial infarction (1), cerebellar haemorrhage (1); [h]An event of cerebrovascular accident; [i]Malignancy (number of events): breast cancer (2), cervical dysplasia (1), diffuse large B-cell lymphoma (1), pulmonary mass (1); [j]Malignancy (number of events): acute myeloid leukaemia (1), adenocarcinoma of colon (2), cervical dysplasia (1), cholangiocarcinoma (1), cutaneous leiomyosarcoma (1), Epstein-Barr virus-associated lymphoma (1), essential thrombocythaemia (1), hepatic angiosarcoma (1), invasive ductal breast carcinoma (1), malignant melanoma (1), renal cell carcinoma (1)
AE, adverse event; BID, twice daily; CI, confidence interval; IR, incidence rate; MACE, major adverse cardiovascular events; N, number of patients who received ≥1 dose of study drug; n, number of patients with the specified event within the given category; NMSC, non-melanoma skin cancer; OLE, open-label, long-term extension; PY, patient-years

[Table. Proportions and IRs of AEs of special interest in the OLE study]

References: 1. Sandborn WJ et al. N Engl J Med 2017;376:1723-1736.
2. Lichtenstein GR et al. Am J Gastroenterol 2018; 113 (Suppl 1): Abstract 571.
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OP214 INTERLEUKIN-6 TRANS-SIGNALLING INHIBITION WITH OLAMKICEPT (SGP130FC) IN ACTIVE IBD RESULTS IN EARLY UNIQUE MOLECULAR SIGNATURES PREDICTING CLINICAL REMISSION AND DIFFERENTIATING FROM REMISSION INDUCTION BY VEDOLIZUMAB OR INFLIXIMAB

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Introduction: The cytokine interleukin-6 (IL-6) regulates many important immunological processes. Many IL-6-mediated effects are attributed to classic IL-6 signalling, *i.e.*, binding of IL-6 to a membrane receptor complex consisting of the specific IL-6 receptor (IL-6R) expressed mainly on hepatocytes and leukocytes and the ubiquitously expressed signal-transducing co-receptor gp130.In contrast, chronic inflammation is mediated by trans-signalling, in which a complex of circulating soluble IL-6R isoforms (sIL-6R) together with IL-6 can engage virtually every body cell by binding to the ubiquitous gp130 co-receptor. The fusion protein olamkicept (sgp-130Fc, FE 999301, ola) is a cytokine trap that selectively neutralizes IL-6/sIL-6R complexes and hence intercepts trans-signalling.

Aims & Methods: The aim of this study was to i) identify early molecular response patterns in Ola treated IBD patients and ii) to compare these with response patterns from Infliximab or Vedolizumab treated patients in order to identify ola-specific signatures of clinical response.

Samples were obtained from a multi-centre, open-label, Phase IIa, exploratory proof-of-concept trial administering ola over 12 weeks by intravenous infusion in patients with active IBD. 16 patients with IBD (CD=7, UC=9) received 600 mg ola every 2 weeks from week 0 to a maximum of 12 weeks. For multi-modal molecular assessment, blood, stool, and biopsies from the sigmoid colon were collected twice before (screening, week 0) and at several time points (+4 h, +24 h, 2 weeks, 6 weeks, and 14 weeks) after ola infusion. Phosphorylation of STAT3 was assessed in colonic biopsies by immunohistochemistry and with an in vitro PBMC stimulation assay to investigate target engagement. Integrated omics analysis was based on RNA sequencing (blood, sigmoid colon) and 16s rRNA/DNA (stool) data sets. Ola-induced mucosal transcriptome signatures were compared with mucosal transcriptome signatures from anti-TNFa(infliximab, IFX, n=12) and anti-a4b7 integrin (vedolizumab, VDZ, n=18) treated patients undergoing the same protocol to identify drug-specific signatures of clinical remission.

Results: RNAseq analysis revealed compartment-specific transcriptomal response (blood vs. sigmoid colon) to ola exposure. Ola induced pronounced downregulation of inflammation-associated transcripts starting at +4 h after initial drug infusion in PBMCs coinciding with inhibition of *in vitro*pSTAT3 phosphorylation induced by stimulation with a IL-6/sIL-6R fusion protein (hyper-IL6). Importantly, mucosal STAT3 phosphorylation and expression of inflammatory transcripts in the intestinal mucosa showed significant downregulation at week 2 timepoint, being highly predictive of later clinical and endoscopic remission. By comparing ola-induced transcriptomal signatures associated with clinical remission with mucosal signatures in remission induced by IFX- (n=12) or VDZ- (n=18), we could define common as well as olamkicept-specific mucosal transcriptional signature of clinical remission.

Conclusion: The study demonstrates the utility of molecular response mapping in early drug development by comprehensive multi-omics assessments using mucosal biopsies and peripheral blood samples. In-depth molecular analysis of IL-6 trans-signalling inhibition in humans represents a novel therapeutic principle for the management of IBD. The delineation of drug-specific remission signatures in the intestinal mucosa may early identify patient populations with differential response to specific anti-cytokine classes of drugs.

Disclosure: Nothing to disclose

OP215 MAINTENANCE OF REMISSION AMONG PATIENTS WITH INFLAMMATORY BOWEL DISEASE AFTER VEDOLIZUMAB IS STOPPED: A MULTICENTER COHORT STUDY FROM THE GETAID

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Introduction: It is unclear whether vedolizumab therapy can be discontinued in patients with inflammatory bowel disease (IBD) after achieving clinical remission. The aim of this study was to assess the risk of relapse after vedolizumab therapy was discontinued in patients with IBD.

Aims & Methods: We performed a retrospective observational study, collecting data from 21 tertiary centers in France affiliated to the GETAID from January 2017 to April 2019, on consecutive patients with IBD treated with vedolizumab in clinical remission for at least 3 months who discontinued vedolizumab therapy. Disease activity was assessed using the Harvey-Bradshaw Index for Crohn's disease (CD) and the partial Mayo Clinic score for ulcerative coliits (UC). Relapse was defined as partial Mayo Clinic score ≥ 3 and/or a stool frequency or rectal bleeding subscores of >1 for UC and Harvey-Bradshaw index >4 for CD and the initiation of second line therapy. Relapse-free survival was studied with Kaplan-Meier method, log-rank test and Cox regression model. Patients were censured when vedolizumab was reintroduced despite persistence of clinical remission.

Results: 95 patients (24 male; median age: 32.5 [IQR 27.3-42.4] years; 58 with CD) were included in the present study. Before discontinuation, the median duration of vedolizumab therapy was 17.5 [10.6-25.4] months. Patients discontinued vedolizumab therapy for pregnancy in 37 cases (38.9%), adverse events in 26 (27.4%), by their own choice in 24 (25.3%) and reimbursement issue in 8 (8.4%). At baseline, Harvey-Bradshaw index and partial Mayo Clinic score was 1.7 ± 1.4 and 0.9 ± 1.1, respectively. Only 6 (6%) were still treated with immunomodulator when they discontinued vedolizumab therapy. After a median follow-up period of 11.2 (5.8-17.7) months, 61 of the 95 patients experienced a relapse. Four patients were retreated with vedolizumab after pregnancy in three cases and ovarian cyst work up in one, with a mean delay of 0.7 ± 0.5 years. The probabilities of relapse-free survival were 83%, 59% and 36% at 6, 12 and 18 months, respectively. The multivariate analysis demonstrated that patients with CRP level < 5 at the time of vedolizumab discontinuation (OR = 0.56, CI95%[0.33-0.95], p = 0.03) and patients who discontinued vedolizumab by their own choice (OR = 0.41, CI95%[0.21-0.80], p = 0.009) were less likely to experience relapse. Among the 61 relapsers, vedolizumab was re-introduced in 24 cases permitting to re-induce steroid-free clinical remission after 14 weeks in 71%. After a median follow-up of 11.0 [5.4-13.3] months, 15 (62.5%) patients were still in clinical remission on vedolizumab therapy.

Conclusion: Almost two thirds of patients with IBD who discontinued vedolizumab therapy while achieving clinical remission experienced a relapse within 1 year after discontinuation of vedolizumab. Normal CRP level

(< 5 mg/L) and patients' choice rather than pregnancy, adverse events and reimbursement issues was associated with a lower probability of relapse. After re-introduction of vedolizumab therapy, more than two thirds of patients achieved steroid-free clinical remission after 14 weeks.
Disclosure: Nothing to disclose

OP216 HIGH VERSUS STANDARD ADALIMUMAB INDUCTION DOSING REGIMENS IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS: RESULTS FROM THE SERENE-UC INDUCTION STUDY

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Introduction: Adalimumab (ADA) is effective and well tolerated in inducing and maintaining clinical remission in adult patients (pts) with ulcerative colitis (UC).[1-3] We report results from the 8 wks induction period of SERENE-UC (NCT02065622), comparing two ADA dosing regimens: a higher induction dosing regimen (HIR) and a standard induction dosing regimen (SIR).
Aims & Methods: SERENE-UC is a Phase 3, double-blind, randomized multicenter study of higher versus standard ADA dosing regimens for induction and maintenance therapy in adult pts with moderately to severely active UC. Pts were randomized 3:2 to receive either the HIR (160 mg at Wks 0, 1, 2, and 3, followed by 40 mg at Wks 4 and 6) or the SIR (160 mg at Wk 0 and 80 mg at Wk 2, followed by 40 mg at Wks 4 and 6) of ADA.
At randomization, pts were stratified by baseline corticosteroid use and previous infliximab (IFX) use. All pts who entered the study on oral corticosteroids were mandated to begin steroid taper at Wk 4.
The primary efficacy endpoint for the induction study was the proportion of patients in the intent to treat population achieving clinical remission, defined as full Mayo Score ≤2 with no subscore >1, at Wk 8. The endoscopic component of the Mayo Score was scored via a central reading protocol. ADA trough serum concentrations were measured at Wks 2, 4, and 8. Exposure-response (ER) modelling was performed using NONMEM 7.3 for the overall population and the ER relationship (ERR) was compared with the ULTRA 2 study.[3] Non-responder imputation was used for missing values. Safety assessment included collection of adverse events (AEs), vital signs, and laboratory data.
Results: In total, 852 pts were randomized, 512 and 340 into the HIR and the SIR, respectively. Baseline demographics were generally balanced across the two treatment groups; overall, mean UC disease duration was 7.2 (7.1) years, 87.1% of pts were biologic-naïve (12.9% had prior IFX experience with initial response and subsequent inadequate response or intolerance), and 58.7% of pts were receiving corticosteroids. There was no significant difference in clinical remission rate at Week 8 between the HIR and SIR (13.3% vs 10.9%, respectively; p=0.273).
The Table displays results for secondary efficacy endpoints. ADA trough concentrations were higher in the HIR versus the SIR (mean [SD] = 39.2 [20.7] and 10.8 [5.2] μg/mL at Wk 4 and 19.3 [9.5] and 8.0 [4.9] μg/mL at Wk 8, respectively) and the levels for the SIR were comparable to those previously reported in ULTRA 2. Higher ADA concentrations were associated with higher clinical remission rate; however, modeling results indicated shallower ERR in this study compared with ULTRA 2. The observed safety

profile was similar between the HIR and SIR groups, including AEs of special interest (< 1% across both groups).
Conclusion: In SERENE-UC, there was no additional benefit of the HIR at Wk 8 beyond the approved SIR. Both induction dosing regimens of ADA demonstrated similar clinical and endoscopic efficacy. Both dosing regimens were generally safe and well tolerated. The maintenance portion of the study is ongoing.

Endpoints (Wk 8), n (%)	Adalimumab HIR (n=512)	Adalimumab SIR (n=340)	p-value
1. Endoscopic improvement[a] (endoscopic subscore of 0 or 1)	159 (31.1)	92 (27.1)	0.182
2. Fecal calprotectin < 150 mg/kg	115 (22.5)	67 (19.8)	0.283
3. IBDQ response (increase of IBDQ ≥ 16 from BL)	342 (66.8)	207 (60.9)	0.063
4. Clinical response per full Mayo Score[a,b]	241 (47.1)	136 (40.0)	0.034*
5. Endoscopic remission[a] (endoscopic subscore of 0)	67 (13.1)	34 (10.0)	0.162

*Nominal p-value < 0.05. [a]Endoscopy scored via a central reading protocol. [b]Clinical response per full Mayo Score: Decrease from baseline in the full Mayo Score ≥ 3 points and ≥ 30% from baseline, plus a decrease in RBS ≥ 1 or an absolute RBS ≤ 1. BL, baseline; HIR, higher induction dosing regimen; IBDQ, Inflammatory Bowel Disease Questionnaire; RBS, rectal bleeding score; SIR, standard induction dosing regimen

[Ranked secondary efficacy endpoints]

References: 1. Reinisch W et al. Gut 2011;60:780-7. 2. Reinisch W et al. Inflamm Bowel Dis 2013;19:1700-9. 3. Sandborn WJ et al. Gastroenterology 2012;142:257-65.

OP217 VEDOLIZUMAB EFFICACY, SAFETY AND PHARMACOKINETICS WITH REDUCED FREQUENCY OF DOSING FROM EVERY 4 TO EVERY 8 WEEKS IN PATIENTS WITH ULCERATIVE COLITIS AND CROHN'S DISEASE

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Introduction: Ulcerative colitis (UC) and Crohn's disease (CD) are chronic diseases generally requiring long-term maintenance therapy. Vedolizumab (VDZ) is a humanised monoclonal antibody targeting $\alpha_4\beta_7$ integrin to reduce lymphocyte migration to the gut. VDZ was effective and well tolerated with 8-wk (Q8W) and 4-wk dosing (Q4W) in CD and UC in the GEMINI Phase 3 studies and with Q4W dosing in the GEMINI long-term safety (LTS) study. After GEMINI LTS, an extended access program (XAP) with Q8W dosing was initiated. Data from patients (pts) who reduced VDZ dosing from Q4W to Q8W are limited. From the XAP pharmacokinetics (PK) substudy, we report clinical efficacy, PK, and safety for pts who reduced VDZ frequency from Q4W to Q8W.

Aims & Methods: VDZ XAP (NCT02743806) is a prospective, open-label, multinational, interventional study to provide pts access to VDZ and monitor safety. Eligible pts were on VDZ 300mg IV Q4W during GEMINI LTS with continued clinical benefit. In XAP, VDZ frequency was reduced to 300mg IV Q8W and pts were followed for 56 wk; return to Q4W dosing was allowed based on physician's assessment of pt clinical status and Medical Monitor approval. Blood samples for PK analyses were obtained at enrolment (last Q4W dosing visit) and wks 8, 16, and 56; serum VDZ was measured using a validated ELISA. Clinical remission was defined as Harvey-Bradshaw Index (HBI) ≤4 for pts with CD and partial Mayo score ≤2 with no subscore >1 for pts with UC. Clinical response after restarting Q4W dosing was defined as decreased HBI of ≥3 from XAP baseline, or decreased partial Mayo score of ≥2 and ≥25% from baseline with a decrease of ≥1 point in rectal bleeding subscore (RBS) from baseline or an RBS of ≤1 point.

Results: A total of 167 pts (88 CD, 79 UC) enrolled in the XAP-PK substudy. Overall, pts had a median of 6.5 y (range, 4.4-10.0) of prior VDZ use; 69% of pts were anti-TNF naïve at VDZ initiation in prior studies. Of pts with CD and UC, 91% and 92%, respectively, completed the 56-wk substudy, with 86% and 90% remaining on Q8W dosing. Rates of clinical remission and corticosteroid (CS)-free clinical remission in pts remaining on Q8W were stable through wk 56 (Table). Four pts with CD and 2 pts with UC returned to Q4W dosing; 3 of 4 CD pts regained clinical response. Pts remaining on Q8W VDZ through wk 56 had low CRP levels that were stable over time; 2.2 mg/L and 1.7 mg/L at baseline and wk 56 for CD pts and 2.2 mg/L and 1.2 mg/L for UC pts. Median trough VDZ was 43.6 µg/mL at baseline and 10.4 µg/mL at wk 56 in pts with CD and 42.4 µg/mL and 13.3 µg/mL in pts with UC. Adverse events (AEs) related to VDZ were infrequent; no new or serious AEs related to VDZ were reported.

	Baseline		Week 8		Week 16		Week 56	
	CD	UC	CD	UC	CD	UC	CD	UC
Clinical remission, %	84.0	95.8	84.2	91.5	83.8	91.2	82.7	94.4
CS-free remission, %	78.7	91.5	78.9	87.3	78.4	86.8	76.0	91.5
CRP, median, mg/L	2.4	1.8	1.9	1.6	2.2	1.2	2.6	1.2
Trough VDZ, median, µg/mL	43.6	42.4	16.2	18.6	12.6	14.2	10.4	13.3

CD, Crohn's disease; CRP, c-reactive protein; CS, corticosteroid; Q8W, every 8 weeks; UC, ulcerative colitis; VDZ, vedolizumab.

[Table. Efficacy, Safety and PK in CD (N=76) and UC (N=71) Patients Who Remained on Q8W Dosing for 56 Weeks]

Conclusion: In a clinically stable cohort, high pt persistence was observed after reducing dose frequency from VDZ Q4W to Q8W. High clinical and CS-free remission rates were maintained for 56 wk. Return to Q4W dosing was necessary in only a few pts and half of them regained clinical response afterwards. VDZ trough concentrations decreased from baseline as expected. AEs were consistent with previous reports.

Frontiers in pancreatic neoplasia
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OP218 A RANDOMISED PROSPECTIVE COMPARISON OF LIQUID-BASED CYTOLOGY WITH CONVENTIONAL SMEAR CYTOLOGY FOR ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE ASPIRATION OF SOLID PANCREATIC MASSES

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Introduction: Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) cytology is a widely used method for the diagnosis of pancreatic neoplasms. Liquid-based cytology (LBC) analysis has been developed to overcome the disadvantages of conventional smear cytology (CS) in which contaminants such as blood, mucin, necrosis and artefactual aggregation of lymphoid cells, block the background of cytology slides [1]. The aim of this study was to evaluate the efficacy of LBC in the diagnosis of pancreatic neoplasms compared to CS.

Aims & Methods: We randomly assigned patients with suspected pancreatic cancer who required histologic confirmation to receive EUS-FNA cytology by either LBC or CS for the first pass. Nineteen to 25G needles (median 22G) were used at the discretion of each echoendoscopist. The second pass was performed with the technique not used for the first pass, and the last pass was allocated to core biopsy. The cytology slides were independently reviewed by two pathologists, and the diagnostic accuracy of the CS and LBC method was assessed for the primary outcome. Secondary outcomes included the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for each method. Gold standard was defined as the final diagnosis of combined results from CS, LBC, core biopsy, and surgically obtained histology or at least 6 months follow-up for benign lesions. The sample size was calculated to determine the noninferiority of LBC compared to CS regarding diagnostic accuracy with acceptable margin of 10%. The reported accuracy of CS was approximately 90% [2]. With an alpha level of 5%, 90% power, and a dropout rate of 15%, the planned sample size was 170 cases.

Results: From April 2018 to March 2019, a total of 170 patients were enrolled in this study. Mean age was 64.8 years (range 37 - 88), and 95 patients (55.9%) were male. The median size of masses was 3.0cm (range 1.3-11.0), and the lesions were located as follows: 59 (34.7%) in the head, 24 (14.1%) in the uncinated process, 38 (22.4%) in the body, 40 (23.5%) in the tail, and 8 (4.7%) in the junction of the body and tail. Of the 170 cases, 165 lesions were malignant: pancreatic ductal adenocarcinoma (n = 163), neuroendocrine carcinoma (n = 2), and 5 lesions were benign conditions associated with chronic pancreatitis. No statistically significant differences were observed in age, sex, needle gauges, tumor size, and tumor location

between the two groups. The diagnostic accuracy, sensitivity, specificity, PPV, and NPV of LBC versus CS were 87.4% versus 83.9%, 87.1% versus 83.3%, 100% versus 100%, 100% versus100%, and 16.0% versus 16.1% (Table 1). When LBC combined with core biopsy, the diagnostic accuracy for pancreatic cancer was higher than that of LBC only (95.3% versus 87.4%, p = 0.01). There were 3 (1.76%) and 9 (5.29%) unsatisfactory samples for diagnosis in LBC and CS, respectively. Blood clots were much less observed in LBC than in CS (0.59% versus 64.1%), and the nuclear feature was similarly preserved in two groups.

Conclusion: Our study shows diagnostic utility of LBC was comparable to that of CS. Cytomorphologic features of ductal adenocarcinoma in LBC did not significantly differ from those in CS, and less frequent bloody backgrounds allow better visibility in LBC method.

Characteristic	Accuracy % (n/N)	Sensitivity % (n/N)	Specificity % (n/N)	PPV % (n/N)	NPV (%) (n/N)
LBC	87.4 (146/167)	87.1 (142/163)	100 (4/4)	100 (142/142)	16.0 (4/25)
CS	83.9 (135/161)	83.3 (130/156)	100 (5/5)	100 (130/130)	16.1 (5/31)
p value	0.37	0.34	0.99	0.99	0.99

[Table 1. Comparisons of operative characteristics]

References: 1. Hoda, R.S., C. VandenBussche, and S.A. Hoda, Liquid-Based Specimen Collection, Preparation, and Morphology, in Diagnostic Liquid-Based Cytology. 2017, Springer Berlin Heidelberg: Berlin, Heidelberg. p. 1-12. 2. Yeon, M.H., et al., Comparison of liquid-based cytology (CellPrep-Plus) and conventional smears in pancreaticobiliary disease. The Korean journal of internal medicine, 2018. 33(5): p. 883-892.

Disclosure: Nothing to disclose

OP219 ROLE OF HISTOLOGICAL SUBTYPES ON THE RISK OF HIGH GRADE DYSPLASIA CANCER IN OPERATED IPMNS: A LARGE SINGLE CENTER STUDY

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Introduction: Intraductal papillary mucinous neoplasms (IPMNs) suffer from low preoperative diagnostic accuracy. No method is available to accurately predict the grade of dysplasia of an IPMNs before surgery. Branch duct IPMNs (BD-IPMNs) and main duct-involving IPMNs (MD IPMNs) display different risks of progression to cancer and have different managements according to guidelines. IPMNs can also display different histological subtypes such as pancreatobiliary (PB) gastro foveolar (GF) oncocitic (O) and intestinal (I). The influence of such subtypes on the risks of harboring high-grade dysplasia cancer (HGD/C) in relation to different kinds of IPMNs is unknown.

Aims & Methods: To investigate the risk of HGD/C according to different histological subtypes. Single center, retrospective study on a prospectively collected cohort of patients operated for suspect malignant IPMN between 2007 and 2017 at HPB Disease Unit, Karolinska Hospital, Stockholm. Data about demographics, known risk factors for PDAC, pathological features were recorded. The inclusion criterion was the presence of histologically proved IPMNs. The exclusion criteria were the presence of a synchronous PDAC, positive margins for high grade dysplasia/cancer, or unknown histological subtype. Chi square and fisher test were used to analyze categorical variables, and statistically significant results were evaluated through sex and age adjusted univariable and multivariable logistic regression analysis. A sub-analysis was performed in BD and MD-IPMNs to assess the prevalence of different subtypes and the risk of harboring HGD/C.

Results: Among the 273 operated patients, 176 were included in the final analysis. In the BD-IPMN displaying HGD cancer the prevalence of GF subtype was significantly lower when compared to other subtypes (3.8% vs 100%, p=0.007). PB subtype was much more prevalent (66.7% vs 4%, p=0.02). The prevalence of HGD/cancer was not significantly higher for cyst dimension above 40 mm (25% vs 44%, p=0.62).

At univariable logistic regression analysis PB phenotype was associated with an increased risk of displaying HGD/C (OR 47.21; 95% CI 1.8-1184.7, p=0.01). In the MD-IPMN group displaying HGD/C the prevalence of GF subtypes was significantly lower when compared to other subtypes (45.4% vs 74.4%, p=0.001), while I subtype was much more prevalent (70.7% vs 46.2%, p=0.007).

No statistically significant differences were found for PB and O subtypes. At univariable logistic regression analysis GF was associated with a decreased risk of displaying HGD/C (OR 0.29; 95% CI 0.12-0.66, p=0.003) while I subtype was associated with higher risk (OR 2.85 95% CI 1.29-6.28, p=0.009). At multivariable logistic regression analysis adjusted even for MPD diameter GF subtype was confirmed to be associated to a decreased risk (OR 0.37 95% CI 0.15-0.95, p=0.03).

Conclusion: GF subtype associated with a decreased risk of HGD/C in BD-IPMN and in MD IPMN irrespectively from cyst dimension and MPD diameter. Intestinal subtypes might be associated to an increased of HGD/cancer risk in MD IPMNs and pancreatobiliary might be associated to an increase risk of HGD/cancer in BD IPMNs

Disclosure: Nothing to disclose

OP220 UPDATED INTERNATIONAL CANCER OF THE PANCREAS SCREENING (CAPS) CONSORTIUM GUIDELINES ON THE MANAGEMENT OF PATIENTS WITH INCREASED RISK FOR FAMILIAL PANCREATIC CANCER

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Introduction: The international Cancer of the Pancreas Screening (CAPS) Consortium has recommended specific guidelines for the management of individuals with increased risk of pancreatic cancer (high-risk individuals; HRI) arising from a familial clustering of the disease or associated with germline mutations.

Aims & Methods: Our aim was to update the 2013 CAPS consensus guidelines on the management of HRI. A modified Delphi approach was used, consisting of a systematic review of the literature, an international multidisciplinary development workgroup meeting, and two rounds of online voting. Based on pre-defined criteria, experts in the field of familial pancreatic cancer were invited to vote on statements using a 7-point Likert scale. An *a priori* threshold of 75% agreement ('Strongly agree' or 'Agree') was used to establish consensus statements.

Results: 76 experts, from 7 disciplines, 11 countries and 4 continents, completed two rounds of voting (response rate 84%). Consensus was reached on more statements than the previous guidelines (55 versus 34). The goals of surveillance (to identify T1N0M0 margin-negative pancreatic cancer and high-grade dysplastic precursor lesions) remained unchanged.

Experts now also agreed that surveillance should commence at least by the age of 50 or 10 years younger than onset in the family, or when diabetes develops. There was still no agreement on the age to stop surveillance. Added as eligible for surveillance were *CDKN2A* p16 mutation carriers without a pancreatic cancer family history, and *ATM* mutation carriers with one affected first-degree relative. Experts also agreed that baseline surveillance should still include both endoscopic ultrasound (EUS) and MRI/MRCP, and not CT, ERCP, or abdominal ultrasound.

Both modalities should also be used for follow-up, but there was no consensus on whether to alternate these modalities, or on the optimal surveillance intervals when lesions are detected. Serum carbohydrate antigen 19-9 was recommended when worrisome features are found on imaging. Fasting blood glucose testing should be performed routinely, a new diagnosis of diabetes should prompt for immediate investigations. In HRI below 50 years of age, a new diagnosis of diabetes should lead to initiation of surveillance.

The surveillance interval in case of no or low-risk findings should be 12 months. EUS-fine needle aspiration is recommended for detected cysts with worrisome features, solid lesions ≥5 mm, or main pancreatic duct strictures (with or without associated mass). Main areas of disagreement included if and how surveillance should be performed for hereditary pancreatitis, and the management of indeterminate lesions.

Conclusion: Surveillance is recommended for selected HRI to detect early pancreatic cancer and its high-grade precursors, and should be performed in expertise centers, by multidisciplinary teams, preferably within a research setting.

Disclosure: JEH received research funding from Abbott and Cook Medical; she is a consultant to Boston Scientific, Cook Medical, and Medtronics. DLC is a consultant to Tramedico. MJB received research funding from Boston Scientific, Cook Medical, Pentax Medical, 3M; he is a consultant to Boston Scientific, Cook Medical, Pentax Medical, Mylan, MediRisk, and Medicom. PF is a consultant to Olympus, Cook Medical, Ethicon Endosurgery and received research funding from Boston Scientific. REB has received research funding from Immunovia and Freenome. The other authors have nothing to disclose.

OP221 METHODOLOGY OF PANCREATIC JUICE COLLECTION FROM THE DUODENUM FOR BIOMARKER DISCOVERY AND EARLY DETECTION OF PANCREATIC CANCER

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Introduction: Pancreatic cancer (PC) is a deadly disease for which early detection of high-grade precursor lesions provides the only chance of cure. Surveillance by imaging (even EUS and MRI combined) in individuals at risk to develop PC does not enable timely detection[1]. Hence, there is an urgent need for reliable biomarkers. Pancreatic juice (PJ) is a promising biomarker source as it is in direct contact with the pancreatic ductal epithelial lining from which PC arises.

Aims & Methods: We aimed to determine the technique and duration of duodenal PJ collection after secretin stimulation that results in the highest yield of cell-free DNA, exosomes for miRNA analysis, proteins and cells (organoid growth).

PJ from patients suspected of sporadic PC and high-risk individuals, under surveillance for hereditary predisposition for PC (FPC), was collected from the duodenum during EUS after secretin stimulation. For each subject, two collection techniques (i.e. suction by a through-the-scope catheter positioned close to the ampulla or the endoscopic channel) and two time periods (i.e. the first and second four minutes) were compared. PJ

was snap frozen < 10 minutes after collection and stored at -80°C. DNA extraction was compared between the NucleoSpin and Maxwell cfDNA kit. The yield of DNA (Quant-iT dsDNA Assay), the cfDNA/gDNA-ratio (i.e. 75bp/300bp-ratio; qPCR) and %mutated KRAS (dPCR; KRAS Multiplex Kit) were compared. Exosomes were isolated and analyzed with Nanoparticle Tracking Analysis (NTA). Total protein, cytokine and (pancreas specific) PLA2G1B concentrations were quantified with Lowry assay and ELISA. Organoids were grown, based on Broutier et al.[2], from cellular content of PJ. Also, usefulness of a protease or superase inhibitor was tested. For statistical analysis, either a Friedman's or Wilcoxon signed-rank test was performed.

Results: Presence of pancreatic content was confirmed by PLA2G1B in all PJ collection methods (32 samples, 8 individuals), with exception of 6 FPC samples that were collected with a catheter. The NucleoSpin kit resulted in a higher DNA concentration and cfDNA/gDNA-ratio (p=0.025, p< 0.0001) than the Maxwell kit. Collection through the endoscopic channel during the second time period resulted in the highest yield of DNA (p=0.017, p=0.039), albeit with a lower cfDNA/gDNA ratio (p=0.039). cfDNA/gDNA ratio was highest in the first four minutes (P=0.002); independent of collection technique. Mutated KRAS was detected in all samples (%mutated KRAS: 0.09-1.01); indiscriminate of DNA extraction technique, collection technique or duration.

Exosomes (size range: 81.6-244.6 nm, 2 FPC kindreds) were present in all 8 analyzed samples. Yields were highest in samples collected with a catheter. The overall protein concentration of PJ collected through the endoscopic channel during the first four minutes was highest (64 samples, p=0.02). IL-8, IL10, IFN-γ and TGF-β concentrations did not differ between the collection methods. IL-6, IL-13 and TNF-α were not detectable. 16/65 (25%) PJ samples that were seeded for organoids grew into organoids, of which 85% had been collected in the first four minutes. The addition of inhibitors to PJ during collection did not improve any of the biomarkers tested.

Conclusion: We show feasibility of DNA, exosome and protein quantification and organoid growth from PJ. Duodenal collection during EUS in the first four minutes after secretin injection resulted in a high yield of cfDNA, exosomes, proteins and organoids. According to PLA2G1B concentrations, the use of a catheter did not result in higher yields or a more concentrated collection of PJ.

References: 1. K.A. Overbeek, I.J.M. Levink, I.C.A.W. Konings, F. Harinck, B. Koopmann, M.G.E. Ausems, A. Wagner, P. Fockens, B. Groot Koerkamp, M.G.H. Besselink, M. van der Vlugt, F.P. Vleggaar, J.W Poley, D.L. Cahen, J.E. van Hooft, M.J. Bruno. On behalf of the Dutch Familial Pancreatic Cancer Surveillance Study work group. 12 years of prospective pancreatic cancer surveillance: results of the dutch nationwide program in high-risk individuals. Abstract, UEGW. 2019. 2. Broutier L, Andersson-Rolf A, Hindley CJ, Boj SF, Clevers H, Koo BK et al. Culture and establishment of self-renewing human and mouse adult liver and pancreas 3D organoids and their genetic manipulation. Nat Protoc. 2016;11(9):1724-43.

Disclosure: Djuna Cahen is a member of the Tramedico clinical advisory board.

OP222 NEW THERAPEUTIC METHOD FOR UNRESECTABLE PANCREATIC CANCER - THE IMPACT OF HIGH-INTENSITY FOCUSED ULTRASOUND (HIFU) THERAPY

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Introduction: Even with recent advances in the diagnostic imaging technology, most cases of pancreatic cancer (PC) are diagnosed at an unresectable stage. The therapeutic effect of chemotherapy and chemoradiotherapy for unresectable PC was not satisfactory. High-intensity focused ultrasound (HIFU) is expected as new advanced therapy for unresectable PC. HIFU therapy with chemotherapy is being promoted as new method to control local advance by ablation tumor.

Aims & Methods: We have evaluated the therapeutic effect of HIFU therapy in locally advanced and metastatic PC. We treated PC patients by HIFU as optional local therapy as well as systemic chemo / chemo-radiotherapy, with whom an agreement was obtained in adequate IC, from the end of 2008 in our hospital.

This study took approval of member of ethic society of our hospital. HIFU device used is FEP-BY02 (Yuande Bio-Medical Engineering Co.LTD., China). The subjects were 176 PC patients, i.e. 88 cases in stage III, 88 cases in stage IV. Performance status (PS) was PS:0 ; 85, PS:1; 87, and PS:2; 4 cases. Gender ratio was 90 male and 86 female. Mean age was 64.0±11.8 years, The details of therapy before HIFU treatment (overlap) was radiochemotherapy in 42, chemotherapy in 97, arterial infusion chemotherapy in 5, immunotherapy in 8, operation in 22, Irreversible electroporation (IRE) in 3 ,and BSC in 13 cases.

Results: All tumors were visualized by HIFU monitor system. Tumor location was head in 49, uncus in 21, body in 73, body~tail in 7, tail in 4, and others (recurrence) in 22 cases. Treatment data was followed; mean tumor size before and after therapy was 33.3±10.9 and 33.8±11.7 mm, mean treatment sessions: 2.1±0.7 times, mean total treatment time: 89.4±66.8 min, mean total number of irradiation: 1709.6±1125.7 shots.

The effects of HIFU therapy were the following; the rate of complete tumor ablation was 90.3 %, the rate of symptom relief effect was 63.8%, the effectiveness of primary lesion was CR:0, PR:21, SD:105, PD:47 cases, primary disease control rate (DCR) more than SD was 71.0%. The therapy after HIFU treatment was operation in 8, chemotherapy in 143, immunotherapies in 4, and best supportive care (BSC) in 22 cases. MST after diagnosis in HIFU with chemotherapy and chemotherapy alone (100 patients in our hospital) was 772.3 vs 346.6 days, respectively ($p<0.05$).

The mean duration to HIFU therapy from the diagnosis (including the pre-therapy period) was 391.5 ± 390.0 days (median: 288.5 days). MST after HIFU therapy was 379.8 days. Combination therapy of HIFU with chemotherapy was better result than common chemotherapy alone.

Conclusion: This study suggested that HIFU therapy has the potential of new method of combination therapy for PC.

Disclosure: Nothing to disclose

OP223 PREDICTING CONDITIONAL SURVIVAL DURING FOLLOW-UP AFTER RESECTION FOR PANCREATIC CANCER: A POPULATION-BASED STUDY

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Introduction: Pancreatic ductal adenocarcinoma is one of the most lethal cancers. Survival estimates are traditionally calculated from the time of diagnosis or at the time of surgery. Since many patients with pancreatic ductal adenocarcinoma decease within the first year, 5-year overall or relative survival estimates change considerably when surviving the first years postoperatively. Conditional survival (CS) accounts for the time already survived after resection and may be more informative for patients. This population-based study aims to assess CS and to develop a nomogram predicting 5-year survival at a predefined period after resection of pancreatic ductal adenocarcinoma.

Aims & Methods: Patients with resected pancreatic ductal adenocarcinoma were included from the Netherlands Cancer Registry (2005-2016). Conditional survival was calculated as the probability of 5-year survival in patients who already survived 1, 2, 3 and 4 years after resection of pancreatic

ductal adenocarcinoma using the Kaplan-Meier method. The Cox proportional hazards model was used to evaluate known predictors of overall survival. A prediction model, based on tumor differentiation, resection margin, lymph node ratio and adjuvant therapy, was constructed.

Results: Overall, 3,082 patients were included with a median age of 67 years (IQR 60-73). Median overall survival was 18 months (95%CI 17-18 months) with a 5-year survival of 15%. The probability of 5-year survival after resection increased from 15% directly after resection to 23%, 42%, 61% and 82% per additional year survived (1, 2, 3 and 4 years, respectively, Table 1). The created nomogram had an optimism-adjusted C-statistic of 0.64 (95% CI 0.63-0.65). The probability to achieve 5-year survival, when measured 1 year after surgery, varied from 1 to 58% depending on the patient- and tumor characteristics included in the nomogram.

	Survival probability to reach X years								
Given years of survival	0	1	2	3	4	5	6	7	8
Number at risk	3082	2054	1001	585	367	246	176	125	88
0	100	67	37	25	18	15	13	12	10
1		100	55	38	28	23	20	17	15
2			100	68	50	42	36	31	28
3				100	74	61	53	46	41
4					100	82	71	62	55
5						100	86	75	67

Each column represents the years survived from surgery and each row represents the percentage to reach a certain total survival time from that point of survived years. For example, if a patient has survived 2 years after surgery, the probability to achieve 3-year survival after surgery is 68% and to achieve 5-year survival after surgery is 42%.

[Table 1. Conditional survival from the time of pancreatic resection in 3,082 patients, given 1 to 5 years survival after surgery]

Conclusion: This nationwide study showed the added value of conditional survival for patient who underwent resection for pancreatic ductal adenocarcinoma. A nomogram was created to provide insight to patients regarding their survival probabilities during follow-up. It could be recommended to inform pancreatic cancer patients about CS, especially those who survive the first year after resection.

Disclosure: Nothing to disclose

IBD: Basic Science I
14:00-15:30 / B5

OP224 THE BRANCHED-CHAIN AMINO ACID TRANSPORTER CD98 HEAVY CHAIN FACILITATES THE DEVELOPMENT OF COLONIC MACROPHAGES ASSOCIATED WITH DECREASED APOPTOSIS IN MACROPHAGE PROGENITORS

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Introduction: Monocytes and macrophages maintain the integrity of the gut by clearing apoptotic cell bodies and microorganisms that have crossed the epithelial barrier (1,2).A comprehensive macrophage development is critical for gut macrophages, which evolve from blood monocytes through a 'monocyte waterfall'-developmental trajectory (3,4). The underlying mechanisms of the macrophage development in the gut remains elusive.

Aims & Methods: To assess the role of branched-chain amino acids for the development of gut macrophages, we generated an inducible knock-out mouse model for the branched-chain amino acid transporter CD98hc in CX3CR1[+]intestinal macrophages.

Results: CD98hc is highly expressed on monocyte-macrophage dendritic cell progenitors, the common monocyte progenitors, and the monocytes in the bone marrow. In the gut, extravasated monocytes, intermediates of the 'monocyte waterfall'-development and macrophages express CD98hc. Stimulation of bone marrow-derived macrophages with LPS + IFN-γ (M1 conditions) or with IL-4 + IL-13 (M2 conditions) did not change CD98hc

expression. As tissue-resident macrophages develop from the yolk sac, the CD98hc expression was determined in the embryonic yolk sac (E8.5), Kupffer cells and Langerhans cells. The macrophages of the yolk sac revealed a lower CD98hc expression compared to the tissue-resident Kupffer cells and Langerhans cells. We next generated an inducible knock-out mouse system. CD98hc$^{\Delta CX3CR1}$ mice were generated by breeding Cx3cr-1^{CreER} mice with CD98hc$^{flox/flox}$ mice for the tamoxifen-inducible silencing of CD98hc. Tamoxifen-injection into CD98hc$^{\Delta CX3CR1}$ mice lead to the deletion in colonic macrophages and liver Kupffer cells but not in Langerhans cells. The deletion of CD98hc in macrophages attenuated the severity of dextran sodium sulfate (DSS) induced-colitis clinically, endoscopically, and histologically. After quality filtering, a total of 3,213 (1863 control and 1,350 CD98hc cKO) cells were obtained for scRNA-seq.

The observation of cells on a principal component analysis (PCA) or tSNE visualization, patterns of expression of cluster-specific genes, hypervariable genes and arbitrarily chosen monocytes and macrophages marker genes suggested a differentiation trajectory from monocytes to macrophages. The calculation of the relative proportion of control and CD98hc-deficient cells, across clusters and across the PCA space, indicated an enrichment of CD98hc-deficient cells in monocyte clusters, which was also apparent when the relative proportions of control and CD98hc-deficient cells projected on the nodes of FlowSOM trees.

These results indicate a block in the 'monocyte waterfall'-development to mature macrophages in the colonic lamina propria of tamoxifen-treated CD98hc$^{\Delta CX3CR1}$ mice. To further gain insights into molecular mechanisms involved in the developmental arrest in CD98hc deficient macrophages, we looked for genes differentially expressed between tamoxifen- or corn oil-treated CD98hc$^{\Delta CX3CR1}$ mice within each cluster along the developmental trajectory. The "pseudo-bulk" samples used for this analysis indicated an enrichment of apoptosis-associated genes, such as *Bcl2l11*, *Tnf*, and *Osm* in tamoxifen-treated CD98hc$^{\Delta CX3CR1}$ mice. Consequently, the numbers of macrophages but not monocytes were significantly reduced after CD98hc silencing, which is highly expressed in biopsies of patients with quiescent and active ulcerative colitis or Crohn's disease.

Conclusion: Our results demonstrate that the deletion of CD98hc results in a developmental arrest of intestinal macrophages. CD98hc plays a pivotal role in the development of intestinal macrophages.

References: 1. Smythies, LE et al. J Clin Invest 115, 66-75 (2005). 2. Kamada, N et al. J Clin Invest 118, 2269-2280 (2008) 3. Bain CC et al. Mucosal Immunol 6, 498-510 (2013) 4. Schridde A et al. Mucosal Immunol 10, 1387-1399.
Disclosure: Nothing to disclose

OP225 MITOCHONDRIAL IMPAIRMENT IN CROHN'S DISEASE DRIVES INTESTINAL STEM CELL TRANSITION TOWARDS DYSFUNCTIONAL PANETH CELLS

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Introduction: Altered intestinal epithelial cell (IEC) homeostasis is associated with chronic intestinal pathologies like inflammatory bowel diseases (IBD). Paneth cells (PC) reside in close proximity to Lgr5$^+$ intestinal stem cells (ISC) localized at the crypt base, supporting epithelial renewal/homeostasis. PC produce antimicrobial peptides and niche factors necessary for the maintenance of Lgr5$^+$ ISCs. Impaired PC function contributes to the ileal pathogenesis of Crohn's disease (CD). The aim of this study was to characterize the role of mitochondrial function on the ISC niche including PC.

Aims & Methods: To determine the impact of mitochondria on the ISC niche, we used a mouse model for CD-like ileitis (TNF$^{\Delta ARE}$ mice), and ileal tissue samples from CD patients. Impact of mitochondrial impairment on ISC and PC was evaluated in mice with a tamoxifen-inducible ISC specific knockout for the mitochondrial chaperone Hsp60 (Hsp60$^{\Delta ISC}$). Small intestinal organoids from mice and humans were generated to illustrate alterations of stem cell and PC phenotypes after treatment with dichloroacetate (DCA) and oligomycin. In addition, we performed transcriptional analyses, *in situ* hybridization, and immunostaining (IHC and IF) in tissue sections and organoid cultures to dissect molecular mechanisms.

Results: In TNF$^{\Delta ARE}$ mice, ileal inflammation correlated with reduced PC granularity and diffuse lysozyme (Lyz) staining. Impaired PC function was further indicated by diminished expression of the ISC-niche factor (*Dll4*) and antimicrobial peptides (*Ang4*, *Defa5*). Ileal tissue sections from CD patients confirmed distorted PC appearance in inflamed regions. Most importantly, the appearance of a low-granular PC and re-localization of Lgr5+ cells in non-inflamed tissues predicted disease recurrence of CD patients after surgical resection. Parallel to PC dysfunction, the intestinal epithelium developed signs of an activated mitochondrial unfolded protein response and loss of stemness indicated by reduced expression levels of *Lgr5* in the crypt base of TNF$^{\Delta ARE}$ mice as well as CD patients. ISC-specific deletion of HSP60 led to elevated numbers of dysfunctional PC and transient reduction of *Lgr5* expression, confirming the importance of mitochondrial homeostasis in regulating PC function and ISC maintenance. Increased numbers of *Lgr5$^+$*-Lyz$^+$ cells and HSP60$^-$-Lyz$^+$ cells together with absence of apoptosis or necrosis at the crypt base indicated differentiation of ISC into dysfunctional PC upon mitochondrial impairment.

Underlining the importance of mitochondrial function for ISC niche maintenance, inhibition of mitochondrial respiration using oligomycin in murine and human intestinal organoids decreased expression of *Lgr5* and antimicrobial peptides (*Lyz* and *Defa5*). In line with reduced stemness *in vivo*, TNF$^{\Delta ARE}$ mice-derived crypts were not able to give rise to organoids *ex vivo*. However, DCA-mediated inhibition of glycolysis, forcing cells to shift to mitochondrial respiration, reverted the oligomycin-mediated distortion of PC functions in organoids and rescued TNF$^{\Delta ARE}$ mice-derived crypt cultures to form sustainable organoids.

Conclusion: We provide evidence that mitochondrial impairment drives the stem cell niche towards a dysfunctional PC phenotype, and is predictive for disease recurrence of CD patients after surgical resection. Maintenance of mitochondrial respiration may represent a novel drug target to antagonize PC dysfunction in the pathogenesis of CD.
Disclosure: Nothing to disclose

OP226 ULCERATIVE COLITIS IS CHARACTERIZED BY AN INTENSE AND DYSFUNCTIONAL MUCOSAL AND SYSTEMIC B CELL RESPONSE

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Introduction: The lack of clear B-cell associated drivers of mucosal inflammation and the failure of the Rituximab trial in ulcerative colitis (UC) has largely dampened the enthusiasm for B-cell focused research in Inflammatory Bowel Diseases. However, emerging data as well clues in existing literature suggest that the humoral immune system participates in and perhaps drives the pathophysiology of UC.

Aims & Methods: In the present study, we systematically examined the B cell phenotype and function in patients with UC.

Blood and colonic biopsies were collected from UC patients as well as healthy controls at the Mount Sinai hospital. B cells were characterized using multiparameter flow cytometry and immunohistochemistry. In a subset of patients we examined the heavy chain immunoglobulin gene (IgH) repertoire at the single-cell level. We also deciphered the B cell transcriptomic profile and key B-cell clusters as well as their interactions with other cell types using single-cell RNA sequencing (10x genomic) in the colonic mucosa.

Results: We enrolled 65 active UC patients, 15 patients with quiescent disease and 30 healthy controls from whom we obtained blood samples. 58% of the patients were not under any immunomodulator. Whereas there were no changes in the frequency of CD19+ B cells and B cell subsets in blood, circulating plasmablasts (CD19+/intCD27+CD38hi) were markedly expanded in active UC patients (0.56% vs 0.12%, p< 0.0001). They up-regulated the β7-intregrin and CXCR3 while down-regulating β1-integrin. Both IgA and IgG plasmablasts were expanded in circulation. Expansion of β7+plasmablasts correlated with disease activity and systemic inflammation. Subsequent analyses of plasma cells in the colonic mucosa, from 20 inflamed mucosa, 19 non-inflamed mucosa from UC patients and 13 healthy colonic biopsies,

revealed the reshaping of the B cell landscape in the inflamed mucosa. Indeed, short-lived plasma cells (CD45+CD19+CD27+CD38hi) and Ki67+ plasmablasts were massively expanded in the inflamed mucosa along with an increased frequency of naïve and germinal center B cells. The study of the IgH gene sequencing from single-cell sorted short-lived plasma cells showed the skewing of isotype toward an increase of IgG and a decrease of IgA2 in UC. In addition, their repertoire diversity was significantly reduced. Further, clones sequenced from UC patients presented more somatic hypermutations and a longer complementary-determining region 3 (CDR3) suggesting a reduced maturation state.

Single-cell RNA sequencing of lamina propria cells demonstrated the highly proliferative state of colonic plasmablasts during active UC that were also increased in frequency while virtually absent in healthy controls. IgG plasma cells expressing the chemokine receptors CXCR4 were also found in greater frequency in the inflamed mucosa. These changes in the antibody-secreting cells compartment were accompanied by an increase in naïve and germinal center B cells as well as in a cluster of CXCL13-expressing T cells.

Conclusion: We show that an intense and acute B cell response is ongoing in active UC as evidenced by the expansion of circulating β7+plasmablasts that leads to an increase of short-lived PC and highly proliferative plasmablasts in the colonic mucosa. This B cell response likely participates in the inflammatory process as they have skewed isotype usage, they differentially express chemokine receptors and they have modified IgH gene features. This study, along with key recent works, suggests a potential interest in targeting specifically intestinal antibody-secreting cells as a therapeutic strategy in UC.

Disclosure: Nothing to disclose

OP227 MUTATIONS IN THE X-LINKED INHIBITOR OF APOPTOSIS PROTEIN PROMOTE SUSCEPTIBILITY TO MICROBIOTA-INDUCED INTESTINAL INFLAMMATION

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Introduction: Mutations in the gene encoding the X-linked inhibitor of apoptosis protein (XIAP) form the basis for one of the most common Mendelian forms of Crohn's disease. However, the mechanisms which link *XIAP* mutations to CD are poorly understood.
Aims & Methods: We investigated *Xiap⁻/⁻* mice and wildtype (WT) littermates under constitutive conditions in a specific pathogen-free (SPF) environment as well as upon exposure to dextran-sodium sulfate (DSS) or the pathobiont *Helicobacter hepaticus*.
Results: Deficiency in XIAP was associated with a selective loss of Paneth cells as a result of increased Paneth cell death. Remaining Paneth cells showed ultrastructural defects, including aberrant positioning of granules, nuclear condensation and fragmentation, and loss of mitochondrial structure.

This was associated with reduced abundance of Paneth cell-derived antimicrobial peptides and impaired bacterial control associated with dense colonization of intestinal crypts by commensal bacteria, increased abundance of mucosa-adherent bacteria and an altered intestinal microbial composition. Under SPF conditions, these alterations were not sufficient to elicit spontaneous intestinal inflammation.

However, upon exposure to the pathobiont *Helicobacter hepaticus*, *Xiap⁻/⁻* mice showed impaired clearance of *Helicobacter hepaticus* and developed granulomatous ileitis, which was not observed in WT littermates. Reconstitution of antimicrobial activity by adenoviral delivery of alpha defensin 5 restored the clearance of *Helicobacter hepaticus* in *Xiap⁻/⁻* mice and prevented ileal granuloma formation.

Moreover, in accordance with long range effects of Paneth cell-derived antimicrobial peptides in the colon, *Xiap⁻/⁻* mice showed increased susceptibility towards DSS compared to WT mice. Intriguingly, DSS also elicited ileal pathology such as villus blunting in *Xiap⁻/⁻* mice, which was not observed in WT mice.

Conclusion: Defects in XIAP are associated with loss of Paneth cells and increased susceptibility to chemical and microbiota-induced intestinal inflammation. As such, these data provide novel insight into the mechanisms that link XIAP mutations to intestinal inflammation and highlight the microbiota as a potential therapeutic target in patients with *XIAP* mutations and CD.
Disclosure: Nothing to disclose

OP228 THE TRANSCRIPTOMIC LANDSCAPE OF HUMAN COLONIC ORGANOIDS AND ITS REMODELLING BY CANONICAL CYTOKINES PROVIDES KEY FUNCTIONAL AND CLINICAL INSIGHTS INTO INFLAMMATORY BOWEL DISEASE

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Introduction: The immune- epithelial interactions are central in our current understanding of inflammatory bowel disease (IBD) pathogenesis. Cytokines have been shown to play an integral part in this cross-talk, with some considered pro-inflammatory (e.g. IFNγ, TNFα) and others protective (e.g. IL22).
Aims & Methods: Since most of the work informing our current understanding of cytokine mediated epithelial responses is based on pre-clinical models we set out to define and compare the transcriptional programmes regulated by the canonical cytokines IFNγ(TH1), IL13 (TH2), IL17A(TH17), IL22 (TH22) and TNFα, as a pro-inflammatory control, in human colonic organoids (colonoids) and associate them to disease phenotypes and therapeutic trajectories in IBD.

Whole transcriptome profiling of cytokine treated human colonoids (n=4) was performed using the Illumina platform. Pathway analysis was performed using the Ingenuity database while gene set variation analysis (GSVA) and weighted gene correlation network analysis (WGCNA) were used to associate cytokine regulated modules to phenotypes by interrogating whole biopsy transcriptomic profiles of our own UC cohort (n=16) and reposited datasets (GSE16879, n=73, GSE23597, n=206). Flow cytometry of human intestinal lamina propria mononuclear cells (LPMC) corroborated our transcriptomic analysis while the functional relevance of our findings was confirmed by using the TRUC model of colitis.
Results: A large functional overlap was found between IFNγ, IL22 and TNFα transcriptional programmes with key pathogenic pathways upregulated by all three cytokines (e.g. IL6, NF-kB, TREM1, TLR signalling, acute phase response, neutrophil chemotaxis). GSVA revealed enrichment of all cytokine regulated transcriptional modules in active inflammation while there was no difference in activated module number or type between UC and colonic CD. Intriguingly, patients with the same endoscopic activity had a gradient of activated cytokine regulated modules. Those with ≥2 modules enriched had a higher risk of non-response to anti-TNFα therapy in both IBD phenotypes [relative risk: 2.9, 95%CI(1.7, 6)]. A strong, positive correlation was seen between IL22, IFNγ and TNFα enrichment scores which was also validated by identifying a population of polyfunctional CD4+ T cells being enriched in the mucosa of IBD patients with active disease producing all three cytokines. WGCNA revealed a neutrophil chemotaxis chemokine module to be the pathway most strongly associated with anti-TNFα non-response. This module was primarily upregulated by IL22 and TNFα. In a TNFα and IL22 dependent model of colitis IL22 blockade downregulates the same chemokine module and improves colitis while the use of a neutrophil chemokine receptor (CXCR2) blocker abrogates disease.
Conclusion: Our study provides novel insights into the human gut immune-epithelial interactome and paves the way for a more granular immunophenotyping of IBD. It highlights that the simultaneous activation of modules regulated by multiple canonical cytokines is associated with non-response to anti-TNFα. Targeting of these shared pathogenic pathways may hold the key to overcoming non-response to biological therapies.
Disclosure: Nothing to disclose

OP229 IDENTIFICATION OF A CYTOTOXIC CD127^{+} INNATE LYMPHOID CELL SUBSET THAT IS EXPANDED IN PATIENTS WITH CROHN'S DISEASE

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Introduction: Crohn's disease is an inflammatory disorder within the intestines as a consequence of dysregulated immune responses. Innate Lymphoid Cells (ILCs), including helper ILCs and Natural Killer (NK) cells, regulate intestinal homeostasis and provide protective immunity, but also contribute to pathology when not properly controlled.

Previously we demonstrated that the increased frequency of non-cytotoxic IFN-γ-producing ILC1s in Crohn's disease resection specimen inversely correlated with a decreased frequency of ILC3s, while the frequency of NK cells were not altered[1,2].

Aims & Methods: Combining flow cytometry, *ex vivo* culture methods, and whole transcriptomic analysis methods of human fetal, non-inflamed and Crohn's disease resection specimen, we demonstrate here the identification of a previously unrecognized population of cytotoxic IFN-γ-producing ILC in the intestinal lamina propria, that are distinct from NK cells.

Results: These cells are characterized by the expression of the ILC-defining markers CD127 (also known as IL7Rα) and CD200R1.

In addition, these cells express CD94, a marker that was previously thought to be restricted to NK cells. This ILC population is highly increased in inflamed intestinal resection specimen when compared to non-inflamed tissue and was virtually absent in fetal intestines or peripheral blood. *Ex vivo* cloning experiments demonstrated that conventional helper ILCs, including ILC3s and ILC1s, acquired the cytotoxic, IFN-γ-producing CD94^{+} phenotype when exposed to IL-12, a cytokine that is prominently abundant in inflamed intestines of Crohn's disease patients.

We furthermore demonstrated that the identified cell population induced cell death of K562 target cells at a similar degree as NK cells whereas CD94^{-} ILC1 and ILC3 failed to kill these target cells

Conclusion: Taken together, we have identified a population of cytotoxic and IFN-γ-producing ILCs that is expanded at the expense of ILC3s in inflamed intestines of Crohn's disease patients where they may contribute to pathology.

References: 1. Bernink, J.H., Peters, C.P., Munneke, M., te Velde, A.A., Meijer, S.L., et al. (2013) Human Type 1 Innate Lymphoid Cells accumulate in inflamed mucosal tissues. Nat. Immunol. 14, 221-229 2. Bernink J.H., Krabbendam, L., Germar, K., de Jong, E., Gronke et al. (2015) Interleukin-12 and -23 Control Plasticity of CD127+ Group 1 and Group 2 Innate Lymphoid Cells in the Intestinal Lamina Propria. Immunity. 43(1), 146-160

Disclosure: Nothing to disclose

How to improve the diagnosis of GORD
14:00-15:30 / E1

OP230 INCREASED SENSITIVITY OF COUGH REFLEX IS NOT THE MECHANISM OF COUGH ATTRIBUTED TO LARYNGOPHARYNGEAL REFLUX

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Introduction: Coughing is often attributed to laryngophayngeal reflux (LPR). It is assumed that acid in the gastroesophageal reflux (GER) that reaches the laryngopharyngeal area stimulates or sensitizes respiratory nerve terminals mediating cough. This premise allows for formulation of several testable hypotheses. If the stimulation of respiratory nerves by acidic LPR is responsible for coughing then a) acidic LPR should correlate with coughing, b) proton pump inhibitor (PPI) treatment should reduce both coughing and acidic LPR. On the other hand, if sensitization of respiratory nerves by acidic LPR is responsible for coughing then a) cough sensitivity should correlate with coughing, b) PPI treatment should reduce both coughing and cough sensitivity. Here we addressed these hypotheses.

Aims & Methods: Consecutive patients referred for suspected LPR were evaluated and those with positive reflux symptom index (RSI>13) and/or reflux finding score (RFS >7) were enrolled. LPR was inferred from pharyngeal reflux. Pharyngeal reflux was evaluated by simultaneous pharyngeal and distal esophageal 24-hour pH/impedance. Pharyngeal reflux events with the maximum drop of pH at levels 6.0, 5.5, 5.0, 4.5, and 4.0 were determined to perform analysis independent of the assumption how acidic pharyngeal reflux is required to influence cough. Cough reflex sensitivity was determined as the lowest concentration of capsaicin causing at least 2 coughs (C2) by single breath capsaicin inhalation challenge using doubling capsaicin concentrations (0.49-1000μM). For statistical analysis C2 values were -log transformed. Troublesome coughing was evaluated on the scale 0-5.

Results: 27 patients diagnosed with LPR were enrolled. The number of pharyngeal reflux events (median[interquartile range]) with pH 6.0, 5.5, 5.0, 4.5 and 4.0 was 14[8-21], 4[2-7], 1[0-2], 1[0-1] and 0[0-1], respectively. There was no correlation between coughing and the number of pharyngeal reflux episodes at any pH level (Pearson coefficients R ranged from -0.17 to 0.23, P=NS). There was also no correlation between coughing and the cough reflex sensitivity C2 (R=-0.1, P=NS). 17 patients completed PPI treatment. In 11 patients RSI was normalized by PPI (PPI-responders). In PPI-responders the troublesome cough was substantially reduced by >60% (2.3±0.6 vs. 0.9±0.1, P< 0.01). However, strikingly, there was no change in cough reflex sensitivity in PPI-responders. The capsaicin C2 threshold was 13[1.6-32]μM vs. 7.8[3.1-19]μM before and after PPI (P=0.11). Furthermore, PPI treatment did not appreciably reduce acidic pharyngeal reflux.

Conclusion: The lack of correlation between the cough sensitivity and coughing and the lack of change in cough sensitivity despite substantial improvement of coughing by PPI strongly argue that an increased cough reflex sensitivity is not the mechanism of cough attributed to LPR. Dual pharyngeal and distal esophageal 24-hour pH/impedance monitoring did not identify simple relationship between acidic reflux and coughing suggesting that this relationship is more complex. Supported by VEGA 1/0304/19.

Disclosure: Nothing to disclose

OP231 RISK FACTORS OF FUTURE ONSET OF REFLUX ESOPHAGITIS: A LONGITUDINAL CASE-CONTROL STUDY USING LONG-TERM HEALTH CHECKUP RECORDS IN JAPAN

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Introduction: Reflux esophagitis (RE) is a disease in which the reflux of gastric contents into the esophagus causes superficial erosion of the mucosa of the lower esophagus, and its prevalence and burden have recently increased Risk factors of RE proposed in previous studies included obesity, being male, hiatal hernia, absence of atrophic gastritis, advanced age, diabetes drinking smoking, metabolic syndrome, *Helicobacter pylori* (*H. pylori*) negative, However, these risk factors of RE have been investigated in many cross-sectional studies, little is known about predictive factors associated with future onset of RE. We investigated time courses of clinical parameters before RE onset by a longitudinal case-control study using long-term health checkup records.

Aims & Methods: We conducted a retrospective study using to investigate factors associated with future RE onset using long-term health checkup records in Japan. We used health checkup records between April 2004 and March 2014 at nine institutions in Japan. Subjects who were newly diagnosed as RE between April 2009 and March 2014 were included in the analysis as case subjects. For each case subject, two subjects who had no RE diagnosis between April 2004 and March 2014 and were matched for age, sex, and participating institutions with the corresponding case were included as control subjects. The time courses of clinical parameters of RE subjects were compared with those of control group by the restricted maximum likelihood method for repeated measures or multivariate logistic analysis. We also implemented cross-sectional comparisons for each of the five years prior to RE onset.

Results: Initial data were obtained from 230,056 individuals, and 2,066 RE subjects and 4,132 control subjects were finally included in the analysis. The time courses of body mass index (BMI) (p < 0.001), abdominal circumference (AC) (p < 0.001), fasting blood sugar (FBS) (p = 0.039), serum triglyceride (TG) (p = 0.010), glutamate oxaloacetate transaminase (p = 0.044), glutamic pyruvic transaminase (GPT) (p = 0.005), γ-glutamyl transpeptidase (p < 0.001), and percentages with acid reflux symptoms (p = 0.004), feeling of fullness (p = 0.019), and hiatal hernia (p < 0.001) in the RE group were significantly worse than in the control group. In cross-sectional comparisons at the year of RE onset, BMI (p < 0.001), AC (p < 0.001), FBS (p = 0.006), systolic blood pressure (p = 0.011), TG (p < 0.001), uric acid (p = 0.002), GOT (p < 0.001), GPT (p < 0.001), γ-GTP (p < 0.001), amount of alcohol (p < 0.001), smoking (p = 0.008), and percentage with acid reflux symptoms (p < 0.001), feeling of fullness (p = 0.046), hiatal hernia (p < 0.001), hypertension (p = 0.003), and hyperlipidemia (p = 0.044) in the case group were higher than in the control group, and high-density lipoprotein cholesterol (p = 0.007) and percentage with atrophic gastritis (p < 0.001) in the case group were lower. Among them, BMI, AC, TG, GPT, and percentages with acid reflux symptoms and atrophic gastritis showed significant differences for five years prior to RE onset consecutively between the groups.

Conclusion: The RE group displayed a more rapid worsening of the clinical parameters associated with lifestyle diseases, including obesity, diabetes, hyperlipidemia, and fatty liver compared with the non-RE group. These results suggest that RE is a lifestyle disease and thus lifestyle guidance may help to prevent RE onset.

Disclosure: Nothing to disclose

OP232 EXACERBATION OF GASTROESOPHAGEAL REFLUX SYMPTOMS AFTER DISCONTINUATION OF PROTON PUMP INHIBITORS IS NOT ASSOCIATED WITH INCREASED ESOPHAGEAL ACID EXPOSURE

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Introduction: Almost universally, proton pump inhibitors (PPIs) are used for initial management of heartburn symptoms. After an initial PPI course, there is often an attempt to stop medication. However, it is a very common complaint that reflux symptoms exacerbate on stopping PPIs. Mechanisms have been postulated as resumption of esophageal acid exposure and rebound acid hypersecretion, however data on this are limited.

Aims & Methods: We aimed to study the impact of stopping long-term PPIs in patients with heartburn, and its association with esophageal acid exposure on objective testing.

We prospectively evaluated patients with heartburn on long-term PPIs (>8 weeks), referred to the Royal London Hospital Upper GI Physiology Unit. All completed an online questionnaire following a minimum of a 7-day PPI discontinuation. The questionnaire addressed presence and exacerbation of symptoms (heartburn, regurgitation, epigastric pain/burn, and excessive belch/bloating) since stopping PPI. Patients were asked if heartburn symptom had exacerbated since stopping PPI (yes/no). In those who had exacerbation, symptom intensity and frequency were assessed on a 10 point Likert scale (0 = no exacerbation of symptoms; 10 = extreme symptom exacerbation). Then, all patients underwent High Resolution Manometry (HRM) and 24-hour multichannel impedance pH study (MII-pH) based on our standard protocol. We measured esophageal acid exposure time (AET), the number of total reflux and proximal extent episodes, esophageal bolus exposure time%, and gastric pH < 4 time %. All data are presented as median with interquartile range. We used Fisher exact test for comparison of ratios, Mann-Whitney U test for the comparison of continuous variables, and Spearman´s Rank Correlation Coefficient for investigating correlations.

Results: 28 patients were studied. After stopping PPIs, 21 patients (75%) had exacerbation of heartburn ("exacerbation group"), 7 patients had no exacerbation of heartburn ("non-exacerbation group"). Heartburn exacerbation severity in the exacerbation group was rated as mean 6.72 out of 10 on the Likert scale. These patients also reported similar exacerbation of epigastric pain, bloating and belching. AET in the exacerbation group was not significantly higher than in the non-exacerbation group (3.5% [1.7-8.7] vs 3.4% [1.6-7.5], NS). The proportion of patients with physiological

acid exposure (< 4.2%) was not different between the exacerbation and non-exacerbation groups (11 of 21 patients vs. 4 of 7 patients respectively). Similarly, gastric pH< 4 time% was not different between groups (88.6% [77.4-92.7] vs 85.9% [78.8-90.6]). There were no significant correlations between AET/gastric pH< 4 time% and the severity of the exacerbation of each symptom on stopping PPIs. Other MII-pH parameters (the number of reflux episodes, proximal extent, and bolus exposure time%) did not show significant difference.

Conclusion: Our study shows that exacerbation of reflux symptoms after the discontinuation of PPIs occurs in the majority of patients. However, this appears to occur regardless of whether there is excessive esophageal acid exposure, and in at least half is associated with completely normal AET. Not just heartburn, but all recorded upper GI symptoms exacerbated on stopping PPI in most patients. The results suggest that acid-independent mechanisms may have a role in symptom exacerbation on stopping PPI. One potential hypothesis is that sudden withdrawal of PPI-related anti-inflammatory effects induce hypersensitivity of the GI viscera. Further studies are required.

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OP233 ABNORMAL POST REFLUX SWALLOW INDUCED PERISTALTIC WAVE (PSPW) INDEX ON PH-IMPEDANCE MONITORING ASSOCIATES WITH HYPOMOTILE ESOPHAGEAL MOTOR PATTERNS ON ESOPHAGEAL HIGH RESOLUTION MANOMETRY (HRM)

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Introduction: Post-reflux Swallow-induced Peristaltic Wave (PSPW) participates in reflux clearance through primary peristalsis, and abnormal PSPW index is a marker for higher reflux burden on pH impedance monitoring. Impaired primary esophageal body peristalsis on HRM also associates with abnormal reflux burden; peristalsis can augment following multiple rapid swallows (MRS), termed contraction reserve. The relationship between PSPW and esophageal body contraction metrics on HRM in the context of reflux disease remains unknown.

Aims & Methods: Our aim was to determine whether a relationship existed between PSPW and esophageal body contraction patterns on HRM in patients being evaluated for reflux disease. Clinical presentation, HRM, and ambulatory pH-impedance studies performed on patients with persisting reflux symptoms were reviewed from five centers (4 in Europe and 1 in US) for this preliminary report. Incomplete studies, achalasia, esophageal outflow obstruction, and prior foregut surgery were exclusions. HRM studies were analyzed according to CC 3.0, and proportions of intact (distal contractile integral, DCI>450 mmHg.cm.s), fragmented (intact with ≥5 cm breaks), ineffective (DCI< 450 mmHg.cm.s), and failed (DCI< 100 mmHg.cm.s) were recorded. The ratio of MRS esophageal body contraction vigor (using distal contractile integral, DCI) to mean contraction vigor from single swallows >1 defined presence of contraction reserve. Total, upright and supine acid exposure time (AET) were extracted from pH-impedance studies (abnormal when total AET>6%, upright AET>6% and supine AET>2%). PSPW was defined as an antegrade swallow within 30 s of completion of an impedance detected reflux episode, and PSPW index was calculated as the proportion of reflux episodes with PSPW on the 24 hour pH impedance study. Univariate comparisons, ANOVA, and linear regression were utilized to investigate potential correlations between PSPW index and contraction patterns.

Results: Of 269 patients (53.1 ± 0.9 yr, 62% F), abnormal AET proportions were found in 77 (28.6%), 111 (41.2%), and 108 (40.1%) for total, upright and supine AET, respectively. Median PSPW index was 0.50, range 0.04-0.89. PSPW index declined progressively with increasing proportions of hypomotile patterns (p< 0.001 for each comparison by ANOVA, Table); there was corresponding increase in AET (p< 0.001 for each comparison by ANOVA). MRS data was available for 140 patients, of which 76.4% had contraction reserve. There was no direct correlation between PSPW index and presence or absence of contraction reserve. However, within ineffective esophageal motility, PSPW was more robust when post MRS DCI was ≥1000 mmHg.cm.s compared to < 1000 mmHg (0.50±0.02 vs. 0.43 ±0.3, respectively, p=0.049) When controlling for physiologic acid burden, regression analysis demonstrated positive correlation between AET and PSPW index (p≤0.02 for each comparison).

	100% intact	<50% ineffective	50-70% ineffective	≥80% ineffective	Absent contractility
PSPW index*	0.60±0.02	0.54 ±0.02	0.52±0.14	0.46±0.03	0.42±0.44
Total AET* (%)	4.5±0.90	5.0±0.5	6.4±1.7	6.9±1.1	12.3±3.7
Upright AET* (%)	4.5±0.6	5.6±0.1	6.5±1.8	7.7±1.0	11.6±3.6
Supine AET* (%)	3.8±1.3	4.3±0.8	5.7±1.9	6.1±1.7	13.2±6.0

*p < 0.001 across groups by ANOVA

[Comparison of PSPW index and acid burden across esophageal body motor patterns]

Conclusion: PSPW index correlates with esophageal body motor pattern, and both associate with abnormal reflux burden. Abnormal PSPW index demonstrates a corresponding gradient of hypomotility on HRM, suggesting that both PSPW and HRM complement evaluation of neuromuscular integrity of esophageal motor function.
Disclosure: Nothing to disclose

OP234 EXTENDED BRAVO STUDIES (UP TO 96HOURS) INCREASES DIAGNOSTIC YIELD OF GASTRO-ESOPHAGEAL REFLUX DISEASE (GERD) IN PATIENTS WITH NORMAL MULTICHANNEL INTRALUMINAL IMPEDANCE-PH (MII-PH) STUDIES

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Introduction: MII-pH catheter studies measure both acid and non-acid reflux and are considered nowadays to be the gold standard in the diagnosis of GERD. Wireless pH capsule (Bravo) may increase the diagnostic yield of standard 24hr catheter-based studies with prolonged monitoring by overcoming the limitation of day-to-day reflux variability and patients are able to perform activities of daily living without the discomfort of the nasal catheter. This study aims to assess the additional diagnostic yield of extended Bravo recordings (up to 96 hours) in patients with negative 24hr MII-pH results.
Aims & Methods: A total of 44 patients with typical GERD symptoms but negative 24hr MII-pH studies off proton pump inhibitor(PPI) were referred for Bravo capsule studies. Bravo studies were performed off PPI over an extended period beyond 48hrs (up to 96hrs). Bravo cases positive for AET were analysed using the Bravo 'Worst Day Analysis' (WDA) and 'Average Day Analysis' (ADA). Reference values for MII-pH and Bravo equivalent were adopted from internationally established studies (Table 1). Subgroup analyses were subsequently made on cohorts whose MII-pH showed normal AET with (A) normal number of total reflux events (TRE), (B) normal number of non-acid reflux (NAR) events and (C) increased number of NAR events. Subgroups (B) and (C) have normal number of acid reflux events. Statistical analysis was performed using SPSS.
Results: study group (male=14, female=30) with a mean age of 48 years, successfully completed Bravo studies up to 96 hours in 77.3% and beyond 48 hours in 97.7%. Using the WDA and ADA respectively, Bravo (AET cut-off >4.2%) captured an additional 59.1% and 43.2% of patients with increased AET (p< 0.001) in cases with normal AET on MII-pH. In MII-pH subgroups (A), (B) and (C), Bravo WDA was able to reveal an additional positive AET of 61.8%(p< 0.001), 60.9%(p< 0.001) and 50.0%(p=0.016) respectively compared to MII-pH while Bravo ADA showed a similar albeit smaller additional yield of 44.1% (p< 0.001), 43.5% (p< 0.002) and 35.7% (not sig-

nificant). Results were similar using other internationally published Bravo AET limits of >4.4% and >5.3%. Inclusion of symptom reflux association in Bravo cases with increased AET also showed additional diagnostic yield over MII-pH ranging from 42.9-47.7% (p≤0.031) across all subgroups.
Conclusion: Extended Bravo studies managed to procure a diagnosis of GERD in more than half of cases with an initial normal MII-pH but persistent symptoms. Half of the patients with increased NAR events on MII-pH also showed positive acid reflux on prolonged testing using Bravo. This additional yield has the potential to alter diagnosis from functional heartburn/hypersensitive esophagus to GERD in difficult cases and affect management by intensifying acid suppression therapy.
Disclosure: Nothing to disclose

OP235 ROLE OF REFLUX IN THE PATHOGENESIS OF EOSINOPHILIC ESOPHAGITIS -COMPREHENSIVE APPRAISAL WITH OFF- AND ON-PPI IMPEDANCE-PH MONITORING

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Introduction: The relationship between eosinophilic esophagitis (EoE) and gastroesofageal reflux disease (GERD) has not been fully elucidated, as well as the mechanisms of response to proton pump inhibitor (PPI) therapy. Comprehensive assessment of reflux by impedance-pH monitoring could clarify these issues
Aims & Methods: A prospective multicenter study comparing EoE and GERD patients with healthy controls was carried out. Patients were evaluated off- and on- PPI; impedance-pH appraisal included chemical clearance, assessed with post-reflux swallow-induced peristaltic wave (PSPW) index, and mucosal integrity measured with mean nocturnal baseline impedance (MNBI) in the distal and mid esophagus
Results: Sixty consecutive EoE patients entered the study, and were compared to 60 age- and sex-matched healthy controls and to 60 typical GERD cases. Number of total and acid refluxes were higher while PSPW index and distal MNBI were significantly lower in EoE than in healthy controls. On therapy, all reflux parameters and MNBI improved in the 40 PPI-responsive EoE cases but PSPW index was the only variable independently associated with PPI responsiveness (OR 1.143, 95% CI 1.049-1.247, P=0.002). In PPI-refractory patients, number of total refluxes and PSPW index were not modified by therapy. Distal MNBI improved much more in PPI-responsive than in PPI-refractory cases. Off-PPI, MNBI values in mid and distal esophagus were comparably low in PPI-refractory but not in PPI-responsive EoE
Conclusion: Reflux plays a role in the pathogenesis of EoE, more relevant in PPI-responsive cases. PPIs mainly act by improving chemical clearance, i.e. by an anti-reflux action, thus supporting their long-term prescription in PPI-responsive EoE
Disclosure: Nothing to disclose

Big data to robotics
14:00-15:30 / F2

OP236 A THREE-DIMENSIONAL PRINTED PELVIC MODEL IS USEFUL FOR LATERAL PELVIC NODE DISSECTION IN RECTAL CANCER

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Introduction: In patients with advanced lower rectal cancer, the complex pelvic anatomy renders lateral pelvic node dissection (LPND) challenging. Though laparoscopic and robotic surgery have decreased the invasiveness of LPND, the absence of tactile sensation increases the risk of blood vessel and nerve injury. Recently, three-dimensional (3D) printing of models for preoperative simulation or intraoperative navigation has been described for liver [1], kidney [2], and pancreas surgery [3]. Subjective assessments have confirmed the utility of 3D-printed models for understanding spatial anatomy.

Aims & Methods: We evaluated the utility of printing a 3D pelvic model for LPND.

We included 22 patients who underwent LPND for rectal cancer between June 2017 and February 2019. Using CT scans, 3D pelvic images and models were constructed and printed, respectively. Thirty colorectal surgeons subjectively evaluated the utility of 3D pelvic models based on a 5-point Likert scale questionnaire (1 = strongly disagree to 5 = strongly agree).

Production of the 3D pelvic model

A colorectal surgeon constructed a 3D image from 0.5-mm thin-slice images obtained using an enhanced multi-detector CT. The organ structure was manually segmented to define the region of interest on each CT slice in the axial view and converted into a stereolithography file to generate the 3D virtual model. The 3D models were printed with white polylactic acid of 2.85-mm diameter using an 3D Printer. The models were finalized by removing the support filament and were coloured manually.

Results:

Patient characteristics: The patients included 13 males and nine females; of these, five underwent open surgery, 12 underwent laparoscopic surgery and five underwent robotic surgery. LPND was performed on the left side in eight patients, right side in seven patients and bilaterally in seven patients. Lateral pelvic lymph node metastasis was observed in 19 sides.

Questionnaire results: The average Likert score for the question 'Would a 3D model be useful for understanding pelvic anatomy?' was 4.7. Cases with enlarged pelvic lymph nodes (4.8 ± 0.44) scored higher than those without metastasized lymph nodes (4.4 ± 0.77, p = 0.02). For spatial comprehension of pelvic anatomy, 3D models scored higher (4.83) than 3D images (4.36, p < 0.001). The ease of use of 3D models and images were scored 4.20 and 4.60, respectively (p = 0.015).

Production time of 3D pelvic models: With experience, the 3D image reconstruction time decreased to 150 min. The printing time for the model was approximately 22 h, and the finalizing time was approximately 1 h. In total, it took about a day to produce one 3D pelvic model.

Conclusion: 3D pelvic models helped to understand pelvic anatomy for LPND.

References: [1] Oshiro Y, Mitani J, Okada T, et al. A novel three-dimensional print of liver vessels and tumors in hepatectomy. Surg Today 2017; 47: 521-524. [2] Chandak P, Byrne N, Coleman A, et al. Patient-specific 3D Printing: A Novel Technique for Complex Pediatric Renal Transplantation. Ann Surg 2019; 269: e18-e23. [3] Marconi S, Pugliese L, Botti M, et al. Value of 3D printing for the comprehension of surgical anatomy. Surg Endosc 2017; 31: 4102-4110.

Disclosure: Nothing to disclose

OP237 ARTIFICIAL INTELLIGENCE IDENTIFIES BARRETT'S NEOPLASIA WITH HIGH ACCURACY USING NBI-ZOOM VIDEOS: A MULTICENTER INTERNATIONAL STUDY

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Introduction: The endoscopic diagnosis of Barrett's esophagus (BE) neoplasia generally consists of primary detection in overview, followed by targeted inspection using Narrow Band Imaging (NBI). Endoscopists have difficulties evaluating NBI-zoom imagery, resulting in suboptimal diagnostic accuracy and poor inter-observer agreement. Computer-aided diagnosis (CAD), using deep learning techniques, has shown promising results in gastrointestinal endoscopy. Therefore, we envisioned that CAD might be able to assist endoscopists in the interpretation of NBI-zoom imagery. Aim To demonstrate feasibility of a deep-learning CAD system for the evaluation of unaltered NBI-zoom videos in BE.

Aims & Methods: We used a step-wise approach using 4 different endoscopic datasets to train our deep learning network (ResNet-UNet hybrid architecture). First, our CAD system was pre-trained using 494,364 labelled images of a variety of endoscopic imagery, named GastroNet. Next, 690 BE neoplasia and 557 non-dysplastic (ND)BE white light endoscopy overview images were used for refinement training. To further improve the CAD system, we used 71 NDBE and 112 neoplastic NBI-zoom *images* from 50 non-dysplastic and 50 neoplastic patients. Finally, the CAD system was trained and validated with a fourth prospectively-collected, and histologically-confirmed, dataset of 77 NDBE and 37 neoplastic (high grade dysplasia/adenocarcinoma) unaltered NBI-zoom *videos*. Performance was evaluated using fourfold cross-validation. Majority voting by the CAD system was applied in our automated video analysis, in which a video was classified as neoplastic if more than 50% of its sequential frames were suspicious for neoplasia. The primary outcome was reported as diagnostic accuracy of the CAD system for classification of neoplastic BE in NBI-zoom images and videos.

Results: The CAD system demonstrated an accuracy, sensitivity and specificity for detection of BE neoplasia using NBI-zoom *images* of 84%, 88%, and 78%, respectively. In total, 18873 individual video frames were analyzed by the CAD system. Accuracy, sensitivity and specificity for BE neoplasia detection using NBI-zoom *videos* were 93% (106/114), 86% (32/37), 97% (75/77). Mean assessment time per video was 0.64 seconds (SD ± 0.02), corresponding to 391 frames per second.

Conclusion: We are the first to report high diagnostic accuracy on prospectively-collected and histologically-confirmed unaltered NBI-zoom *videos* with fast corresponding assessment time, thereby showing feasibility of neoplasia characterization in BE using CAD systems. Future work will focus on optimizing our current CAD system and validation using separate prospectively-collected datasets.

Disclosure: J.J. Bergman: NinePoint Medical, Fuji Film, Olympus, Pentax, CDx diagnostics, Cernostics, Medtronic, Erbe, Boston Scientific, Cook.

Evidence-based improvements in surgical outcomes

14:00-15:30 / Barcelona

OP238 PRETREATMENT TUMOR-DNA SEQUENCING OF KIT AND PDGFRA IN ENDOSONOGRAPHY-GUIDED BIOPSIES OPTIMIZES THE PREOPERATIVE MANAGEMENT OF GASTROINTESTINAL STROMAL TUMORS

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Introduction: Down-sizing tyrosine kinase inhibitor (TKI) therapy increases the chance of organ-preserving, radical resection in selected patients with gastrointestinal stromal tumor (GIST). We aimed to evaluate systematic, immediate DNA-sequencing of *KIT* and *PDGFRA* in pretreatment GIST-tissue to guide downsizing TKI-therapy and optimize pre-operative tumor response.
Aims & Methods: All patients being candidates for downsizing therapy of a suspected GIST [the study cohort (SC)] were prospectively included January 2014 - March 2018. Patients were subjected to pretreatment, endosonography-guided fine-needle biopsy (EUS-FNB) or transabdominal ultrasound-guided needle biopsy (TUS-NB) followed by immediate tumor-DNA-sequencing (< 2 weeks). A historic (2006-2013) reference cohort (RC) underwent work-up without sequencing before downsizing imatinib (n=42). The rate of optimal downsizing therapy (Thera$_{OPT}$) was calculated and the induced tumor size reduction (TR$_{max}$, %) was evaluated by CT-scan.
Results: The success rate of pretreatment tumor-DNA-sequencing in the study cohort (n=81) was 77/81 (95%) [EUS-FNB: 71/74 (96%); TUS-NB: 6/7 (86%)] with mutations localized in *KIT* (n=58), in *PDGFRA* (n=18), or neither gene, WT, (n=5). In patients with a final indication for down-sizing therapy, the Thera$_{OPT}$ was higher in the SC compared with the RC, 61/63 (97 %) *vs* 33/42 (79 %), p=0.006, leading to a significantly higher TR$_{max}$ (32 %) *vs* (19 %), p=0.001, among patients treated with standard dose imatinib.
Conclusion: Pretreatment endosonography-guided biopsy sampling followed by immediate tumor-DNA sequencing of *KIT* and *PDGFRA* is highly accurate and valuable for the guidance of downsizing TKI-therapy in GIST. This approach minimizes the maltreatment with inappropriate regimens and leads to improved tumor size reduction before surgery.
Disclosure: Nothing to disclose

OP239 IMMUNONUTRITION TO IMPROVE THE QUALITY OF LIFE OF UPPER GASTROINTESTINAL CANCER PATIENTS UNDERGOING NEOADJUVANT TREATMENT PRIOR TO SURGERY (NEOIMMUNE): DOUBLE BLIND RANDOMIZED CONTROLLED MULTI-CENTER CLINICAL TRIAL

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Introduction: Malnutrition, is very frequent in oesophagogastric cancers, and is associated with negative outcomes including increased morbidity, poor tumour response, poor tolerance to treatment and decreased quality of life (QOL). Immunonutrition in gastro-intestinal cancer surgery has been shown to efficient in perioperative period in reducing the risk of infectious complications.
Aims & Methods: The aim of this randomized controlled trial was to evaluate if immunonutrition during neoadjuvant treatment prior to surgery will improve patients' QOL, reduce postoperative morbidity and reduce haematological and mucosal toxicities.
Study Design: Double blind randomized controlled multi-center clinical trial. Included patients had untreated non-metastatic Upper GI tumor, aged 18 ≥years with a life expectancy of >3months. The study was powered for 80% power to detect a difference in EORTC-QLQC30 with standard deviation of 15 between the groups, permitting 179 randomized to received

immunonutrition with IMPACT® formula and 179 randomized to receive an isocaloric control during neoadjuvant therapy. The primary end-point for the study was QOL as measured by the EORTC-QLQ-C30. Secondary end-points included diarrhoea, mucositis, haematologic toxicity, nutritional status, compliance and response to neoadjuvant therapy, postoperative morbidity and length of hospital stay.
Statistical Analysis: An intention-to-treat analysis will be employed, and univariate analysis (ANOVA) was performed to compare scores, with an analysis of co-variance using ANCOVA also performed.
n° EUDRACT: **2011-A00716-35**
Results: The study was terminated prior to completion of recruitment at the interim analysis stage, as reviewers felt the sample size was underestimated given the true effect of IMPACT formula. 300 patients were randomized; 148 to the IMPACT group and 152 to the control-formula group. Patient groups were well balanced in terms of age, sex, ethnicity, BMI, clinical tumour stage, utilisation of neoadjuvant therapy and medical co-morbidities.
No significant differences between groups in changes, at diagnosis and 30 days postoperatively, were identified in global health score (p=0.112) and time to global health deterioration (p=0.527), physical functioning (p=0.976), role functioning (p=0.777), emotional functioning (p=0.545), cognitive functioning (p=0.207), social functioning (p=0.968) and fatigue score (p=0.920). No significant differences in changes, at diagnosis, after neoadjuvant therapy and 30 days postoperatively were seen in pain, nausea and vomiting, dyspnea, insomnia, appetite loss and change in bowel habit. Analysis of EORTC-OG25 in changes 30-days postoperatively showed with IMPACT® improvements in time to pain and discomfort (p=0.007). Multivariate analysis for global health score deterioration showed no significant effect of IMPACT® administration (Hazard ratio = 1.18; 95% confidence interval 0.843 to 1.652).
Within the IMPACT® group toxicity during neoadjuvant treatment, tumor regression, postoperative complications, length of hospital stay and survival were unaffected.
Conclusion: The results of this large multi-center blind RCT fail to demonstrate any large benefit in terms of HRQOL to the utilization of immunonutrition during neoadjuvant therapy in patients with esophageal or gastric cancer. Furthermore no significant improvements were observed in secondary outcomes including 30-day postoperative complications.
Disclosure: Nothing to disclose

OP240 LAPAROSCOPIC VERSUS OPEN GASTRECTOMY FOR GASTRIC CANCER, RESULTS OF A MULTICENTER PROSPECTIVELY RANDOMIZED CONTROLLED TRIAL (LOGICA-TRIAL)

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Introduction: Open gastrectomy is the preferred surgical approach for gastric cancer worldwide. This procedure is associated with considerable morbidity. Meta-analyses have shown an advantage in short-term outcomes of laparoscopic gastrectomy compared to open procedures, with similar oncologic outcomes. However, the included series are mostly from Asia with early gastric cancer. It is unclear whether these results can be extrapolated to the Western population with mostly advanced gastric cancer. In this randomized controlled multicenter trial from the Netherlands, we assessed the outcomes of laparoscopic versus open gastrectomy.
Aims & Methods: Between 2015-2018, patients with resectable (cT1-4a, N0-3b, M0) gastric adenocarcinoma were randomly assigned to either laparoscopic (105 patients) or open (105 patients) gastrectomy, in 10 participating

centers in the Netherlands. Inclusion criteria were age ≥18 years, European Clinical Oncology Group performance status 0, 1 or 2 and informed consent. The primary outcome was postoperative hospital stay (days). Secondary outcome were postoperative morbidity and mortality, oncologic outcome, readmissions, quality of life and cost-effectiveness.

Results: This is a late breaking abstract. The last study patient was operated on in November 2018. The data are not yet mature at the moment of writing this abstract. We would like to present our primary endpoint and secondary endpoints at the UEGWEEK 2019

Conclusion: See above

Disclosure: Nothing to disclose

OP241 RANDOMIZED CONTROLLED TRIAL ASSESSING THE EFFECTIVENESS OF 5-HT$_3$ RECEPTOR ANTAGONIST (RAMOSETRON (IRRIBOW®)) FOR THE TREATMENT OF ANTERIOR RESECTION SYNDROME IN MALE PATIENTS WITH RECTAL CANCER

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Introduction: Anterior resection syndrome, including fecal urgency, frequency and incontinence can develop after sphincter-saving surgery for rectal cancer in 60-90% of the patients, but there has been no effective treatment.

Aims & Methods: We performed a randomized controlled trial to assess the effectiveness of ramosetron (Irribow®), a 5-HT$_3$ receptor antagonists, for the treatment of anterior resection syndrome.

Male patients with symptoms of anterior resection syndrome after rectal cancer surgery (after ileostomy take-down if ileostomy was performed) were enrolled and randomly assigned to take the ramosetron (Irribow®) 5mg daily (n=48) or conservative treatment (n=50) for 1 month. Low anterior resection syndrome (LARS) score[1] was calculated by questionnaire before and after 1 month after treatment. Primary endpoint was the difference in proportion of severe LARS. The study design was a superiority test with 30% of difference margin, 80% of power and 5% type I error. Analyses were based on the intension-to-treat population. Secondary endpoint was the difference of patients' quality of life by the questionnaire of EORTC QLQ-C30. This study is registered with ClinicalTrials.gov, number NCT02869984.

Results: The mean age was 61.4±9.3 and 59.9±9.9 years in the ramosetron and control group, respectively (p=0.927). Tumor distance from the anal verge was 6.9±3.8 and 7.9±4.3cm (p=0.254) and stage of the tumor was not different between the two groups (Stage III/IV, 20 (41.7%) vs 17 (34.0%), p=0.434). The mean LARS score (36.0±5.9 vs 34.4±6.8, p=0.215) and stool frequency (12.6±7.7 vs 12.6±7.2, p=0.987) before treatment were also similar.

All patients had more than 4 times/day of stool frequency before treatment. The LARS score significantly decreased to 29.6±9.3 after 1 month in ramosetron group (p< 0.001) and the LARS score after 1 month in the ramosetron group was significantly lower than control group (29.6±9.3 vs 34.6±7.6, p=0.004). The mean changes in LARS score (1 month - baseline) was -6.48 in ramosetron, compared to 0.16 in control group (p<0.001).

The proportions of severe LARS (LARS score, ≥30) after 1 month was 58.3% (n=28/48) in ramosetron group vs 82.0% (n=41/50) in the control group, with the difference of 23.7% being statistical significance (95% CI=5.58~39.98%, p=0.011). The stool frequency after 1 month was 7.1/day and 10.5/day in the ramosetron and control group (p=0.004), and the patients who had the stool frequency less than 4 times/day were 13 (27.1%) in ramosetron compared to only 1 (2.0%) in the control group (p< 0.001). The quality of life after 1 month was significantly better in ramosetron group in terms of general health status (70.7±18.6 vs 62.7±17.5, p=0.031), physical functioning (88.6±11.25 vs 82.4±17.18, p=0.038), emotional functioning (90.5±11.78 vs 81.5±20.98, p=0.011) and cognitive functioning (91.7±12.4 vs 85.0±17.6, p=0.032).

Conclusion: Although we did not reach the intended superiority margin of 30% with ramosetron (Irribow®) treatment for anterior resection syndrome, our results showed significantly better LARS score and quality of life in the ramosetron treatment group. Ramosetron (Irribow®) treatment may be applied for selective patients who had severe symptoms of anterior resection syndrome after rectal cancer surgery.

References: 1. Emmertsen KJ, Laurberg S. Low anterior resection syndrome score: development and validation of a symptom-based scoring system for bowel dysfunction after low anterior resection for rectal cancer. Ann Surg 2012;255:922-8

OP242 MULTICENTER, RANDOMIZED CONTROLLED TRIAL OF NASOGASTRIC TUBE WITH WATER-SOLUBLE CONTRAST AGENT *VERSUS* LONG TUBE FOR SMALL BOWEL OBSTRUCTION

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Introduction: Small bowel obstruction (SBO) is a frequently occurred gastrointestinal emergency and the most frequent cause is adhesion after abdominal surgery, accounting for 50-80%. Gastrointestinal decompression is applied to SBO without any findings of strangulation and ischemia. Decompression with nasogastric tube (NGT) is a standard treatment for SBO in Western countries based on the old small trial that showed no significant differences between NGT and long tube (LT). On the other hand, LT seemed to be more effective than NGT in a recent Asian trial. Moreover, some studies have reported that administration of water-soluble contrast, gastrografin, thorough NGT (NGT-G) is useful for determining indication of surgical treatment and it is more effective treatment than NGT alone. However, there have been no comparative studies between LT and NGT-G. We thus conducted a randomized controlled trial to evaluate the efficacy of NGT-G for patients with SBO.

Aims & Methods: In this multicenter, open label, randomized controlled trial, patients with SBO from 11 Japanese institutions were randomly assigned by a computer-based randomization to receive LT or NGT-G between July 2016 and November 2018. Patients who assigned to the NGT-G group could receive LT placement appropriately, when SBO is not improved over 24 h. The primary end point was non-inferiority of NGT-G to LT for non-surgery rate (treatment success rate). According to pre-planned protocol, efficacy analysis was on the basis of initially randomized group (intention-to-treat analysis). Based on the results of previous studies, we estimated 85% non-surgery rate of both groups, and 95.3% CI lower limit of -15% non-surgery rate would be accepted as a lower margin for inferiority with NGT-G to LT because the previous lowest success rate of LT was 70%. According to O'Brien Fleming type α spending rule, 1 sided α levels of 0.0015 and 0.0235 were defined for the interim and final analysis, respectively. Hence, pre-planned sample size was 220 overall 1-sided-α and β errors of 0.025 and 0.20, and allowing an approximate 10% dropout rate.

Results: In total, 224 patients with SBO were enrolled to this trial and 223 patients after exclusion of 1 consent withdrawal were finally analyzed including 111 patients in the LT group and 110 patients in the NGT-G group. Baseline characteristics including laboratory data and physical findings were well balanced between 2 groups. The treatment success rate without non-surgical management was 87.4% in the LT group and 91.1% in the NGT-G group, and difference between LT and NGT-G was 3.7% (95.3% CI; -5.55 to 12.91; non-inferiority *P*= 0.00002923). Among 112 patients in the NGT-G group, 86 patients improved by NGT-G alone (86.7%), 16 patients did by NGT-G followed by LT and 10 patients underwent surgery. Non-surgery rate of NGT-G alone was significantly lower than LT (*P*=0.039).

Expectedly, median insertion time was much shorter in the NGT-G group than in the LT group (1 min vs. 25 min; P= 0.0001). No significant differences were found for relief time of abdominal symptoms and duration of hospitalization between 2 groups. In the LT and NGT-G arms, adverse event rates ≥ grade 3 were 1.8% and 0% (P=0.247) and the mortality rates were 0.91% and 0% (P=0.498), respectively.

Conclusion: NGT-G is an effective alternative to LT as the first-line treatment for SBO. Sequential strategy, NGT-G followed by LT, would be a novel standard treatment for SBO.

(University Hospital Medical Network Clinical Trials Registry, Number: UMIN000022669)

Disclosure: Nothing to disclose

OP243 ENDOSCOPIC ULTRASOUND VS PERCUTANEOUS MANAGEMENT OF POST-OPERATIVE PANCREATIC FISTULA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Post-operative pancreatic fistula (POPF) is a difficult to manage complication with significant morbidity and mortality. Mortality rates as high as 40% have been reported. Surgical and percutaneous drainage (PCD) are the usual first line of treatment. Studies have reported endoscopic ultrasound and/or standard endoscopy (END) guided management of POPF with conflicting results. Data comparing the outcomes of END vs PCD in POPF management is limited.

Aims & Methods: We conducted a comprehensive search of multiple electronic databases and conference proceedings (earliest inception through September 2018) to identify studies that reported on the clinical outcomes of END and PCD in the management of POPF. Our goal was to estimate and compare the pooled rates of technical success, clinical success, adverse events and POPF recurrence with END and PCD. The collected data was matched between the END and PCD management groups. The baseline patient characteristics, symptomatology, indication for surgery, time-to-drain placement, and the number of drains used were comparable between the groups. Meta-analysis was conducted using the comprehensive meta-analysis software.

Results: 4 studies (99 patients) reported outcomes with EUS and/or endoscopy (END) in POPF management, and 4 studies (225 patients) reported outcomes with PCD in POPF management.1.

Technical success: The pooled rate of technical success in END-POPF was 97.6% (95% CI 88.4-99.5, I²=0) and in PCD-POPF was 95.2% (95% CI 84.1-98.7, I²=63.4%). The difference was not statistically significant, p=0.52.2.

Clinical success: The pooled rate of clinical success in END-POPF was 90.8% (95% CI 82.3-95.5, I²=0%) and in PCD-POPF was 78.0% (95% CI 70.5-84.0, I²=0%). The difference was statistically significant, p=0.02.3.

Adverse events: There were a total of 2 adverse events and 7 recurrences in END-POPF group, and a total of 8 adverse events and 17 recurrences in PCD-POPF group.The pooled rate of adverse events in END-POPF was 4.9% (95% CI 1.7-13.1, I²=0%) and PCD-POPF was 5.9% (95% CI 3.4-10.0, I²=0%). There was no statistical significance to the difference, p=0.74. Data was insufficient to calculate pooled rates of recurrence in the groups.

POPF (95% CI, I2)	EUS/END	PCD	P-value
Technical Success	97.6% (88.4-99.5, 0)	95.2% (84.1-98.7, 63.4)	0.52
Clinical Success	90.8% (82.3-95.5, 0)	78% (70.5-84, 42.5)	0.02
Adverse Events	4.9% (1.7-13.1, 0)	5.9% (3.4-10, 0)	0.74

[Summary of pooled results. POPF(pancreatic post-operative fistula), EUS(endosonography), END (endoscopy) PCD (percutaneous drainage)]

Conclusion: Our meta-analysis shows that endoscopic ultrasound and/or standard endoscopy guided management of POPF gives significantly better clinical success as compared to PCD. Use of standard endoscopy in the

management of pancreatic fistula is outdated. Well-conducted direct-comparison studies are needed evaluating endoscopic ultrasound to PCD in the treatment of POPF. Indirect comparison, variability in the type of stents used, variability in the number of repeat procedures, and heterogeneity were the limitations of our study.

Disclosure: Nothing to disclose

Duodenal flat mucosa: Coeliac and beyond
16:00-17:30 / A2

OP244 USE OF MICRO-CT IMAGING OF INTESTINAL BIOPSIES TO IMPROVE THE DIAGNOSTICS OF CELIAC DISEASE

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Introduction: Traditional histopathology is too inaccurate for early stage mucosal injury and short-term challenge studies in celiac disease, and the often misoriented biopsies are prone to wrong interpretation. X-ray microtomography (micro-CT) is an imaging technique which could provide freely orientable 3D images for accurate measurements of mucosal morphometry and surface areas. We investigated the use of micro-CT in the examination of small-bowel biopsies.

Aims & Methods: Duodenal samples from 12 endoscopies were selected for the micro-CT imaging. The specimens represented celiac disease patients with different stages of injury and nondiagnosed subjects with morphologically normal mucosa. The micro-CT procedure was tested with variable staining solutions, source voltages and filters to optimize the practicability and resolution. The data were reconstructed into digital 3D images and virtually cut for measurement of villous length crypt depth ratios. Mucosal surface areas were measured utilizing computer-assisted point cloud analysis. The results were compared with routine histopathology and quantitative histomorphometry performed with paraffin-embedded biopsies.

Results: Practical staining and imaging protocol with optimal resolution was accomplished using specific I E-solution, 100 kV acceleration voltage and 10W source power. Micro-CT imaging was feasible both for previously taken paraffin biopsies and fresh biopsies. It was also possible to do routine histopathology after the imaging. The formed 3D images allowed freely orientable digital images for exact morphometry and demonstrated duodenal injury in samples interpreted as normal in traditional histology. Furthermore, micro-CT enabled reproducible measurements of the mucosal surface areas, which makes it possible to detect previously indistinguishable differences between samples e.g. minor changes during gluten-free diet.

Conclusion: We established a unique micro-CT method for digital analysis of duodenal biopsies. The improved diagnostic accuracy and possibility to measure biologically meaningful surface areas provide a powerful tool for future clinical and pharmaceutical studies.

Disclosure: Nothing to disclose

OP245 DIAGNOSTIC ACCURACY OF THE COELIAC INTRAEPITHELIAL LYMPHOGRAM ASSESSED BY FLOW CYTOMETRY FOR COELIAC DISEASE (CD) DIAGNOSIS IN PATIENTS WITH SERONEGATIVE VILLOUS ATROPHY (SNVA)

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Introduction: Causes of SNVA can be grouped as CD- and non-CD related. Despite several sets of international guidelines on CD, there is no consensus on how to approach subjects with seronegative CD. Coeliac lymphogram has been advocated as a useful tool in doubtful CD cases.

Aims & Methods: To evaluate the accuracy of the increase in CD3^{+} T-cell receptor gamma delta^{+} (TCRγδ) intraepithelial lymphocytes (IEL), with or without the concomitant decrease of CD3^{-} IEL, in samples of duodenal mucosa for the diagnosis of CD in patients with SNVA.

Seventy-four consecutive patients with SNVA were included (45.3±2.5 years; 67% women). Serum anti-TG2 was negative in all cases. In all of them, duodenal biopsies to assess TCRγδ^{+} and CD3^{-} IEL by flow cytometry were obtained at the index endoscopy. The increase in TCRγδ^{+} *plus* decrease in CD3^{-} IEL defined the coeliac lymphogram. CD was diagnosed on the basis of a clinical and histological remission after a GFD. Sensitivity (S), specificity (Sp), positive and negative likelihood ratios (LR) were calculated. Values of +LR >10 and -LR < 0.10 were associated with a convincing diagnostic evidence.

Results: CD was diagnosed in 46 patients, and non-coeliac SNVA in 28. Non-coeliac causes of SNVA were: olmesartan (8), giardiasis (4), Crohn's disease (2), other enteropathies (6), and idiopathic (8). CD patients were younger (39±3 vs. 55±3 yrs; p=0.001), more often showed HLA-DQ2/8 (97.6% vs. 61%; p=0.002), and had a more severe histology (61% vs. 32% Marsh 3b-c; p=0.056), as compared to non-coeliac SNVA. Coeliac lymphogram was associated with a S of 87% (95% CI, 73-95), Sp of 96.4% (CI, 80-100), +LR of 24.3 (CI, 3.5-167) and -LR of 0.13 (CI, 0.06-0.28). Evaluating only TCRγδ[+] yielded a S of 91% (CI, 78-97), Sp of 86% (CI, 66-95), +LR of 6.4 (CI, 2.6-16) and -LR of 0.10 (0.04-0.26). Two olmesartan enteropathies and 1 giardiasis had an isolated increase in TCRγδ[+] and another olmesartan enteropathy presented with the coeliac lymphogram.

Conclusion: The coeliac lymphogram assessed by flow cytometry in duodenal biopsy samples was associated with a high level of diagnostic evidence either against or in favour of CD in patients with SNVA.

Disclosure: Nothing to disclose

Trends in treatment and detection of upper GI bleeding
16:00-17:30 / B2

OP246 OUTCOMES OF UPPER GASTROINTESTINAL BLEEDING ARE SIMILAR BETWEEN DIRECT ORAL ANTICOAGULANTS AND VITAMIN K ANTAGONISTS: A SUB-GROUP ANALYSIS OF A FRENCH PROSPECTIVE MULTICENTER STUDY

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Introduction: Management of oral anticoagulants remains challenging during upper gastrointestinal bleeding (UGIB). Outcomes of UGIB are not worse in patients treated with vitamin K antagonists (VKA) but a reversion of the anticoagulation can be easily done contrary to direct oral anticoagulants (DOACs) (1). DOACs belong to a new therapeutic class with conflicting results on the associated risk of UGIB that might be increased (2). Later studies showed a different bleeding risk according to the type of DOACs (3,4), but data are mostly retrospective with a low level of evidence. This study aimed to describe epidemiology, endoscopic management and outcomes of UGIB in patients treated with anticoagulants.

Aims & Methods: From November 2017 to October 2018 a prospective multicenter study in French general hospitals enrolled all consecutive patients with UGIB. Data were collected with an e-CRF. All patients treated with an anticoagulant at the time of the UGIB were retrieved from the cohort and assessed. Main outcomes were mortality at 6 weeks, rebleeding during the first 6 weeks and need for non-endoscopic treatment (surgery, radio-embolisation).

Results: Among the 2498 patients included, 475 (19%) had an oral anticoagulant: 267 (56.2%) with VKA (Warfarin 67 (25%), Fluindione 200 (75%)) and 208 (43.8%) had DOACs (Dabigatran 21 (10%), Rivaroxaban 114 (55%), Apixaban 73 (35%)). This subgroup of patients consisted of 65% men, mean age was 78.2 and mean Charlson score was 3.2. Aspirin was ongoing for 100 patients (21%), and 55 (11.6%) had other antiplatelets agent (APA). Baseline characteristics were broadly similar between VKA and DOACs except for the association of kidney failure and cirrhosis. Gastroscopy was performed in 470 patients (98.9%), described as normal in 73 (15.3%) and showed active bleeding in 117 (24.9%). The aetiology of UGIB was peptic for 289 (60.8%) patients, portal hypertension for 43 (9%), vascular and tumoral for 41 (8.6%) and 27 (5.7%), respectively, without difference between VKA and DOACs. Endoscopic treatment was performed in 128 (26.9%) patients; bleeding resolution was possible in 95 (20%). The mortality rate at 6 weeks was 12.4% (59 patients) (VKA 16.1%, DOACs 7.8%, p< 0,01). Factors associated with mortality by univariate analysis were Charlson index ≥5, anticoagulation by VKA, presence of shock at admis-

sion, peptic lesion in endoscopy, Rockall Score >2 and Blatchford ≥14; only Charlson index remained significant in the multivariate analysis (OR 4.14, p< 0.0001). Re-bleeding happened in 56 patients (11.8%) (VKA 30 (11.2%/), DOACs 26 (12.5%), p=0.71). By multivariate analysis: co-medication with APA was associated with a higher risk (OR 2.72, p=0,009) whereas beta-blockers were protective (OR=0.41, p=0,0072). Non-endoscopic treatment was performed in 18 (3.8%) patients (VKA 10 (2.1%), DOACs 8 (1.6%) p=0.95).Tumoral origin of the bleeding was the only factor associated by multivariate analysis (OR=6.66, p=0.0064).

Conclusion: DOACs do not alter outcomes of UGIB as compared to VKA. Comorbidities and associated treatment seem to be the most important factors worsening prognosis of UGIB.

References: 1. Nahon S, Hagège H, Latrive JP, Rosa I, Nalet B, Bour B, et al. Epidemiological and prognostic factors involved in upper gastrointestinal bleeding: results of a French prospective multicenter study. Endoscopy. 2012 Nov;44(11):998-1008. 2. Ruff CT, Giugliano RP, Braunwald E, Hoffman EB, Deenadayalu N, Ezekowitz MD, et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. Lancet Lond Engl. 2014 Mar 15;383(9921):955-62. 3. Abraham NS, Noseworthy PA, Yao X, Sangaralingham LR, Shah ND. Gastrointestinal Safety of Direct Oral Anticoagulants: A Large Population-Based Study. Gastroenterology. 2017;152(5):1014-1022.e1. 4. Miller CS, Dorreen A, Martel M, Huynh T, Barkun AN. Risk of Gastrointestinal Bleeding in Patients Taking Non-Vitamin K Antagonist Oral Anticoagulants: A Systematic Review and Meta-analysis. Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc. 2017 Nov;15(11):1674-1683.e3.

Disclosure: Nothing to disclose

OP247 OUTCOMES ON THE USE OF HEMOSPRAY IN UPPER GASTROINTESTINAL BLEEDS SECONDARY TO TUMOURS: OUTCOMES FROM THE MULTICENTRE INTERNATIONAL HEMOSPRAY REGISTRY

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Introduction: Upper gastrointestinal bleeding (UGIB) is a leading cause of morbidity with a 7% mortality in the United Kingdom (UK). Upper GI tumours account for 2-4% of UGI bleeds. These patients are often challenging to treat due to the diffuse nature of the neoplastic bleeding lesions, high bleeding recurrence rates and the significant transfusion requirements with a resultant poor quality of life. Hemospray (Cook Medical, North Carolina, USA) is a novel haemostatic powder for GI bleeding.

The primary aim was to look at the outcomes of all UGIBs secondary to tumoural bleeding who had Hemospray therapy in 14 centres worldwide.

Aims & Methods: Data was prospectively collected on the use of hemospray from specialist centres in the UK, France, Germany and the USA (Jan'16-March'19). Hemospray was used during emergency endoscopy for UGIBs secondary to upper GI tumours at the discretion of the endoscopist as a monotherapy, dual-therapy with standard haemostatic techniques or rescue therapy once standard methods have failed. Haemostasis was defined as the cessation of bleeding within 5 minutes of the application of hemospray. Rebleeding was defined as a sustained drop in Hb (>2g/l), haematemesis or melaena with haemodynamic instability after the index endoscopy.

Results: 84 patients with UGIB secondary to tumours of the GI tract were recruited (57 males, 27 females, 24/84 (29%) oesophageal, 56/84 (67%) gastric, 4/84 (5%) doudenal). The median Blatchford score at baseline for all patients was 10 (IQR, 7-12). The median rockall score was 8 (IQR,7-9). The median size of lesions was 25mm (IQR, 11-40mm).

Immediate haemostasis was achieved in 81/84 **(96%)** of patients, 11/70 (16%) patients had a rebleed, 2/73 (3%) patients died within 7 days, 14/73 (19%) patients died within 30 days (all-cause mortality). Based on the baseline average total rockall score, the expected rebleed rate is 25-40%, and expected mortality rate was 40-45% in our cohort.

Haemostasis was achieved in 51/51 (100%) patients in the hemospray monotherapy group, 16/19 (84%) patients in the combination therapy group and 8/8 (100%) of patients in the rescue therapy group (Table 1).

	Monotherapy (n=57)	Combination therapy (n=19)	Rescue therapy (n=8)
Haemostasis	57/57 (100%)	16/19 (84%)	8/8 (100%)
Median Rockall score	8 (IQR,7-9)	8 (IQR, 7-9)	7 (IQR, 5-8)
Median Blatchford score	10 (IQR, 7-12)	9 (IQR, 7-15)	11 (IQR, 10-13)
Rockall 7 and 8: Predicted re-bleed rate: 25-40%			
Re-bleed	7/49 (14%)	3/13 (23%)	1/8 (13%)
Rockall 7 predicted mortality rate: 20-30%, Rockall 8 predicted mortality rate: 40-45%			
7-day mortality	2/49 (4%)	0	0
30-day mortality	10/49 (20%)	4/16 (25%)	0

[Outcomes in the different hemospray subgroups]

100% (4/4) haemostasis was achieved in the duodenal tumour cohort, 98% (55/56) in the gastric cohort and 92% (22/24) haemostasis in the oesophageal tumour group. The highest rebleed rate was in duodenal tumours, 1/4 (25%), and highest all cause 30-day mortality in the oesophageal tumour group, 7/20 (35%).

Conclusion: Hemospray is an effective endoscopic tool for achieving immediate haemostasis in UGIBs secondary to upper GI tumours, which are generally considered difficult bleeds to treat, with 100% haemostasis levels and lowest re-bleed levels in the monotherapy group.

When considering average rockall score the rebleed and mortality rate is better than predicted rates. Haemostasis is achieved in the majority allowing for patient stabilization and thereby providing time for patients to have urgent surgery or radiotherapy to treat the underlying tumour.

Disclosure: Nothing to disclose

OP248 NOVEL HEMOSTATIC ADHESIVE POWDER APPLICATION IN NONVARICEAL UPPER GASTROINTESTINAL BLEEDING

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Introduction: A new hemostatic adhesive powder (UI-EWD) was developed to improve the high re-bleeding rate and technical challenge in application of current available hemostatic powders.

Aims & Methods: The aim of current study was to assess the performance of UI-EWD in nonvariceal upper gastrointestinal bleeding (NVUGIB).

A total of 56 consecutive patients receiving UI-EWD for endoscopic hemostasis in NVUGIB were retrospectively reviewed. UI-EWD was used as a monotherapy. The main outcomes were success rate of immediate hemostasis and rate of re-bleeding within 30 days. Outcomes were analyzed by reviewing patient medical records.

Results: The etiology of bleeding was post-endoscopic therapy bleeding in 46 (82.1%), peptic ulcer in 8 (14.3%), tumor in 1 (1.8%) and other in 1 (1.8%). The UI-EWD was successfully applied at bleeding site in all

cases. The success rate of immediate hemostasis was 96.4% (54/56). Re-bleeding within 30 days occurred in 2/54 (3.7%) of patients who achieved immediate hemostasis. The adverse event related to use of UI-EWD was not occurred.

Conclusion: UI-EWD had a high success rate for immediate hemostasis in NVUGIB when used as monotherapy and showed promising result in prevention of re-bleeding.

References: 1 Hearnshaw SA, Logan RF, Lowe D, et al. Acute upper gastrointestinal bleeding in the UK: patient characteristics, diagnoses and outcomes in the 2007 UK audit. Gut 2011; 60: 1327-1335 2 Barkun AN, Bardou M, Kuipers EJ, et al. International consensus recommendations on the management of patients with nonvariceal upper gastrointestinal bleeding. Ann Intern Med 2010; 152: 101-113 3 Yau AHL, Ou G, Galorport C, et al. Safety and efficacy of Hemospray® in upper gastrointestinal bleeding. Canadian Journal of Gastroenterology and Hepatology 2014; 28: 72-76 4 Smith LA, Stanley AJ, Bergman JJ, et al. Hemospray application in nonvariceal upper gastrointestinal bleeding: results of the Survey to Evaluate the Application of Hemospray in the Luminal Tract. J Clin Gastroenterol 2014; 48: e89-e92

Disclosure: Nothing to disclose

OP249 RANDOMISED CONTROLLED TRIAL OF EARLY CAPSULE ENDOSCOPY VERSUS COLONOSCOPY FOLLOWING NEGATIVE GASTROSCOPY IN ACUTE GASTRO-INTESTINAL BLEEDING

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Introduction: A proportion of patients with suspected acute upper gastrointestinal bleed (UGIB) characterised by malaena or malaena and haematemsis, have a negative initial gastroscopy. The traditional approach is to perform colonoscopy as the second investigation, however diagnostic yield is low.[1,2] Small bowel bleeding is likely in this cohort. Capsule endoscopy can safely and effectively visualise small bowel bleeding with high sensitivity in the acute setting.[3,4] The aim of this study is to investigate whether capsule endoscopy is superior to colonoscopy as a second investigation in patients with suspected UGIB but negative initial gastroscopy.

Aims & Methods: This is a single centre randomised control trial, which commenced in June 2017. Local ethics approval was obtained (ID 31035). Informed consent was obtained from all patients. All patients admitted to our hospital with acute bleeding as defined above but with negative gastroscopy were considered for the study. Patients who consented for the study were then randomised to either capsule endoscopy or colonoscopy as the second investigation. If the test was not diagnostic, the patient underwent the other investigation or other interventions as clinically required. Our primary outcome was the diagnostic yield of each modality. Secondary outcomes measured were length of stay, transfusion requirements and number of diagnostic tests required. We also recorded baseline patient characteristics.

Results: 20 patients have been randomised to date, 12 males and eight females. Mean age was 69 years and baseline patient characteristics were similar in both groups. 11 patients received capsule endoscopy and nine patients received colonoscopy as the second investigation after negative gastroscopy. Diagnostic yield was 91% in the capsule endoscopy arm and 22% in the colonoscopy arm. Six out of nine patients in the colonoscopy group underwent subsequent capsule endoscopy, which was normal in four cases and in the other two revealed mid small bowel angioectasia and a jejunal diverticulum. Table 1 highlights secondary outcome data. 12-month data was available for four patients from the colonoscopy group and four patients from the capsule group. One patient from each group was readmitted to hospital with recurrent GI bleeding, though neither required further investigation. Regrading complications in our cohort, one patient had capsule retention without obstruction due to strictures. Two had incomplete capsule studies with capsule passing within 48 hours. One diagnosed a gastrointestinal stromal tumour in the gastric antrum and the second temporarily retained in a small bowel diverticulum.

Conclusion: Data from our study suggests capsule endoscopy has a significantly higher diagnostic yield than colonoscopy in patients with suspected acute UGIB and negative gastroscopy. It is well established that an early capsule study is crucial in making a timely diagnosis of small bowel bleeding and allows early intervention. This is expected to decrease overall morbidity and mortality, particularly in the elderly and those with co-morbidities in whom capsule endoscopy is well tolerated. To our knowledge, this is the first randomised controlled trial in this context.

Outcome	Capsule endoscopy (n=11)	Colonoscopy (n=9)
Packed Red Blood Cells (n), Mean (SD)	2.0 (2.4)	2.9 (3.1)
Length of stay (days), Mean (SD)	8.7 (3.9)	8.3 (2.7)
Number of other investigations required, Mean (SD)	1.2 (0.4)	0.9 (0.6)

[Table 1. Secondary Outcomes]

References: 1. Laine L, Shah A. Randomized trial or urgent vs. elective colonoscopy in patients hospitalized with lower GI bleeding. American Journal of Gastroenterology 2010; 105: 5969-41 2. Raju G, Gerson L, Das A, Lewis B. American Gastroenterological Association (AGA) institute technical review on obscure gastrointestinal bleeding. Gastroenterology 2007; 133: 1697-717. 3. Delvaux M, Fassler I, Gay C. Clinical usefulness of the endoscopic video capsule as the initial intestinal investigation in patients with obscure digestive bleeding: validation of a diagnostic strategy based on the patient outcome after 12 months. Endoscopy 2004; 36: 1067-73. 4. Schlag C, Menzel C, Nennstiel S, Neu B, Phillip V, Schuster T, Schmid R, Delius S. Emergency video capsule endoscopy in patients with acute severe GI bleeding and negative upper endoscopy results. Clinical Endoscopy 2015; 81:889-895

Disclosure: Nothing to disclose

OP250 ARTIFICIAL INTELLIGENCE USING A CONVOLUTIONAL NEURAL NETWORK FOR AUTOMATIC DETECTION OF SMALL-BOWEL ANGIOECTASIA IN CAPSULE ENDOSCOPY IMAGES

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Introduction: Although small-bowel angioectasia is frequently diagnosed via capsule endoscopy (CE) in patients with obscure gastrointestinal bleeding, a computer-aided detection method has not been established. We aimed to construct an artificial intelligence system with deep learning that can automatically detect angioectasia in CE images.

Aims & Methods: We retrospectively examined 169 patients (training image set: 141 patients, validation image set: 28 patients) with small-bowel angioectasia diagnosed via CE and 20 patients with no abnormal findings on CE at Hiroshima University Hospital, the University of Tokyo, and Sendai Kousei Hospital. CE was performed using a Pillcam™SB2 or SB3 CE device (Covidien Japan Inc., Tokyo, Japan). We trained a deep convolutional neural network (CNN) system based on Single Shot Multibox Detector, using 2,237 CE images of angioectasia. For a validation image set, 10,488 independent images were prepared. Of these, 488 images showed angioectasia in the small-bowel, and 10,000 images showed normal mucosa in the small-bowel. We manually annotated all of angioectasia with rectangular bounding boxes in the validation set. The trained CNN also shaped the region of angioectasia with rectangular bounding boxes in the validation set and outputted the probability score of angioectasia (range, 0-1). We evaluated the ability of CNN to discriminate between whether each image included angioectasia or not using the probability score. In addition, we evaluated the ability of CNN to identify angioectasia correctly. The receiver operating characteristic (ROC) curve was plotted by varying the threshold of the probability score, and the area under the curve (AUC) was calculated for assessing the discrimination. The sensitivity, specificity, positive predictive value, and negative predictive value of CNN's ability to detect angioectasia were calculated, using cut-off values for the probability score according to the Youden index.

Results: The AUC of CNN used to detect angioectasia was 0.999. The cut-off value for the probability score was 0.36. At this cut-off value, the sensitivity, specificity, positive predictive value, and negative predictive value of

CNN were 98.8%, 99.1%, 84.3%, and 99.9%, respectively. The sensitivities of CNN for angioectasia Type 1a and Type 1b were 83.3% (15/18) and 99.4% (467/470). The detectability of small-bowel angioectasia Type 1b by CNN is significantly higher than the detectability of type 1a (*P*< 0.001). False-negative images (n=6) were classified into two categories based on the cause of the false-negative read: poorly focused (67%, 4/6) and laterality or partialness (33%, 2/6). On the other hand, false-positive images (n=90) were classified into five categories based on the reason as follows: vascular dilation of normal mucosa (40%, 36/90), foam (30%, 27/90), fold (18%, 16/90), debris (9%, 8/90), and normal mucosa (3%, 3/90). The trained CNN required 323 seconds to evaluate the images, with an average speed of 32.5 images per second. The correct discrimination rate was 83.3% (15/18) in Type 1a and 98.9% (465/470) in Type 1b. The cause of incorrect discrimination for angioectasia was bleeding from angioectasia Type 1b. The correct discrimination rate for small-bowel angioectasia Type 1b by CNN is significantly higher than the detectability of Type 1a (*P*=0.002).
Conclusion: We developed and validated a new system based on CNN to automatically detect angioectasia in CE images. This may be the crucial step for a daily-use diagnostic software for CE images to reduce the burden on the physicians and oversight.
Disclosure: Nothing to disclose

OP251 CLINICAL PERFORMANCE OF A NEW SOFTWARE TO AUTOMATICALLY DETECT ANGIOECTASIAS IN SMALL BOWEL CAPSULE ENDOSCOPY

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Introduction: Video Capsule Endoscopy (VCE) revolutionized the diagnosis and management of obscure gastrointestinal bleeding, though the rate of detection of small bowel lesions by the physician is still disappointing. Our group developed a novel algorithm (CMEMS-Uminho[1]) to automatically detect angioectasias which display greater accuracy in VCE static frames than other methods previously published.
Aims & Methods: We aimed to evaluate the algorithm overall performance and assess its diagnostic yield and usability in clinical practice. Algorithm overall performance was determined using 54 full-length VCE recordings. To assess its diagnostic yield and usability in clinical practice, 38 VCE examinations with the clinical diagnosis of angioectasias consecutively performed (2017-2018) were evaluated by three physicians with different experiences. CMEMS-Uminho algorithm was also applied. The performance of CMEMS-Uminho algorithm was defined by a positive concordance between a frame automatically selected by the software and a study independent capsule endoscopist.
Results: Overall performance in complete VCE recordings was 77,7% and diagnostic yield was 94,7%. There were significant differences between physicians in regard to global detection rate (p< 0,001), detection rate per capsule (p< 0,001), diagnostic yield (p=0,007), true positive rate (p< 0,001), time (p< 0,001) and speed viewing (p< 0,001). The application of CMEMS-Uminho algorithm significantly enhanced all readers' global detection rate (p< 0,001) and the differences between them were no longer observed.
Conclusion: CMEMS-Uminho algorithm detained a good overall performance and was able to enhance physicians' performance, suggesting a potential usability of this tool in clinical practice.
References: 1. Vieira P, Silva C, Costa D, Vaz I, Rolanda C, Lima C (2019) Automatic Segmentation and Detection of Small Bowel Angioectasias in WCE Images. Annals of Biomedical Engineering. doi: 10.1007/s10439-019-02248-7
Disclosure: Nothing to disclose

Cirrhosis and liver cancer
16:00-17:30 / B3

OP252 LONG-TERM EVOLUTION OF HEPATOCELLULAR ADENOMAS AT MR IMAGING FOLLOW-UP

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Introduction: Hepatocellular adenomas (HCAs) are rare benign liver tumors. Guidelines recommend continued surveillance for patients diagnosed with HCAs, but these recommendations are mainly based on small series or experts' opinion. The aims of this study were to analyze the long-term course of evolution of HCAs including solitary and multiple lesions, and to identify predictive features of progression.
Aims & Methods: We retrospectively included consecutive patients with pathology-proven (i.e., biopsy or surgery) and subtyped solitary and multiple HCAs between January 2004 and December 2015. Exclusion criteria were:
(a) preoperative or follow-up MR imaging was not available;
(b) patients treated with locoregional therapies or transplantation, and lack of pretreatment MR imaging follow-up;
(c) inadequate MR imaging protocol.
Reference standard was pathologic analysis. For each patient the following information were assessed:
(a) aspect of non tumoral liver;
(b) subtype of HCA according to the updated classification published by Nault J et al;
(c) hemorrhage and malignant foci within the lesion.
All MR exams performed by each patient were analyzed by two radiologists with expertise on liver imaging.
Tumor evolution was evaluated using the Response Evaluation Criteria in Solid Tumors (RECISTv1.1) thresholds.
Results: Our final study population consisted of 118 patients (mean age, 40 ± 10 years; range 18-69 years, 10 men and 108 women), including 41 patients with a solitary HCA and 77 patients with multiple HCAs.
In 44 HCAs with micro- and/or macroscopic hemorrhage detected at pathology, 26 were inflammatory, 8 were HNF-1α inactivated, 5 were sonic-hedgehog, 4 were ß-catenin mutated exon 3 and 1 was ß-catenin mutated exon 7-8. Malignancy was detected among ß-catenin mutated HCAs in five patients with ß-catenin mutation -four with ß-catenin mutation in exon 3 and one with ß-catenin mutated in exon 7-8 HCA -, and two patients with inflammatory HCAs.
Median follow-up of the entire study population was 5.0 years, and it was not significantly different between the solitary and multiple HCAs cohorts (5.1 years vs. 4.9 years, respectively, *p*= 0.624).
Overall, 37 of 41(90%) patients with solitary HCAs and 55 of 77 (71%) patients with multiple HCAs showed stable or regressive disease (i.e. >30% size decrease). After resection of solitary HCAs, new lesions appeared only in 2 of 29 (7%) patients, both with HCAs at-risk of malignancy (i.e. ß-catenin mutated HCAs or foci of malignancy within the tumor).
Patients with multiple HNF-1α inactivated HCAs showed a higher rate of progression compared to patients with multiple inflammatory HCAs (11 of 26 [42.3%] vs. 7 of 37 [18.9%], *p*= 0.043).
Patients with progressive disease had a lower weight and BMI at diagnosis. Of note, neither surgery nor presence of ß-catenin mutated subtype had an impact on progression (*p*= 1.000, *p*= 0.667), while presence of multiple HCAs was associated with higher probability of progressive disease compared to solitary HCAs (22/77 [28.6%] vs. 4/41 [10.8%], respectively; *p*= 0.020). However, the number of lesions at diagnosis in patients with multiple HCAs was not significantly associated with progressive disease (*p*= 0.541).
Conclusion: Seventy-eight percent of HCAs showed long-term stability or regression. After resection of solitary HCAs, tumor progression occurred only in HCAs at-risk of malignancy. Patients with multiple HCAs were more

likely to show progressive disease, with HNF-1α inactivated HCAs being the most common subtype showing progression.

References: 1. European Association for the Study of the Liver (EASL) EASL Clinical Practice Guidelines on the management of benign liver tumours. J Hepatol 2016; 65:386-398. 2. Bonder A, Afdhal N. Evaluation of liver lesions. Clin Liver Dis 2012;16: 271-283. 3. Karhunen PJ. Benign hepatic tumours and tumour like conditions in men. J Clin Pathol 1986; 39:183-188. 4. Nault JC, Couchy G, Balabaud C, et al. Molecular Classification of Hepatocellular Adenoma Associates With Risk Factors, Bleeding, and Malignant Transformation. Gastroenterology 2017; 152:880-894. 5. Van Aalten SM, De Man RA, Ijzermans JNM, Terkivatan T. Systematic review of haemorrhage and rupture of hepatocellular adenomas. British Journal of Surgery 2012; 99:911-916. 6. Bioulac-Sage P, Laumonier H, Couchy G, et al. Hepatocellular adenoma management and phenotypic classification: the Bordeaux experience. Hepatology 2009; 50:481-489

Disclosure: None related to this study Dominique Valla discloses the following not related to this study: Laboratoire Servier : "Liver safety committee for Agomelatine"

OP253 HEPATOCYTE-SPECIFIC DELETION OF MTOR ACCELERATES LIVER TUMOR GROWTH

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Introduction: The mTOR protein is an essential component of mTORC1 and mTORC2, two multi-protein complexes of central importance for the regulation of cell proliferation, metabolism and autophagy. Activation of the mTOR pathway is frequently found in cancer, resulting in the notion that targeting mTOR represents a useful approach for cancer therapy. Of note, mTOR inhibitors have thus far failed to demonstrate significant antiproliferative efficacy in the majority of cancer types. It is therefore of pivotal importance to better understand the functional significance of the mTOR protein for the pathogenesis of cancer.

Aims & Methods: We sought to characterize the cell type-specific role of mTOR for the pathogenesis of primary and secondary liver tumors. To this end, we established a liver epithelial cell (LEC)-specific knock-out (KO) of mTOR via the Cre/loxP-system (termed mTOR[LEC] mice). We characterized the growth of primary (non-alcoholic steatohepatitis-associated hepatocellular carcinoma (NASH-HCC)) and secondary (colorectal cancer liver metastasis (CRC-LM)) liver tumors in mTOR[LEC] mice compared to wildtype controls.

Results: mTOR[LEC] mice were viable and developed normally, arguing for a non-essential role of mTOR in LECs for hepatic development. Strikingly, tumor nodules in both the NASH-HCC as well as the CRC-LM model were significantly larger in mTOR[LEC] mice compared to controls. As both primary and secondary liver tumors were affected, we hypothesized that the KO of mTOR in LECs resulted in the formation of a pro-tumorigenic microenvironment in the liver. To further analyze this, we determined the expression of pro-inflammatory genes in WT versus KO livers. While the expression of COX-2, HIF-1a, TNF-a and IL-6 was not affected, IL-1b gene expression was found to be significantly higher in the livers of mTOR[LEC] mice. Furthermore, mTOR[LEC] mice displayed periportal leukocyte accumulation that was absent in livers from wildtype mice. The functional relevance of this finding for the accelerated liver tumor formation in mTOR[LEC] mice is currently being evaluated by us.

Conclusion: We show an unexpected acceleration of liver tumor growth upon functional deletion of mTOR specifically in liver epithelial cells. These results argue against the widely accepted perception of mTOR as an eligible target for cancer therapy. Our results add a further layer of complexity to the biology of mTOR and suggest that cell and tissue type-specific factors need to be considered in order to comprehend the complexity of mTOR.

Disclosure: The authors declare no competing interests

OP254 MIR-21 IS INCREASED IN EXPERIMENTAL AND HUMAN NASH-ASSOCIATED HCC, CONTRIBUTING TO HEPATOCARCINOGENESIS

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Introduction: The molecular mechanisms governing the progression of non-alcoholic steatohepatitis (NASH) towards hepatocellular carcinoma (HCC) remains elusive. We have recently shown that concomitant miR-NA-21 (miR-21) ablation and farnesoid X receptor (FXR) activation prevents NASH development in mice.

Aims & Methods: Here, we aimed to evaluate the role of miR-21 in NASH-associated carcinogenesis. miR-21 expression was evaluated in two independent cohorts of patients. In the San Sebastian cohort (n=160), RNA was isolated from formalin-fixed, parafin-embbeded liver biopsies obtained from obese patients. miR-21 expression was measured by qPCR and correlated with histopathological and serological findings. In the TCGA cohort, miR-21 expression was evaluated by miRNA sequencing (miRseq) using liver samples from patients with NASH-associated HCC obtained after surgical resection (n=19) and compared with surrounding liver tissue (n=50). In parallel, wild-type (WT) and miR-21 KO C57BL/6N mice were fed either a choline-sufficient, amino acid-defined control diet (CSAA; n=28) or a choline-deficient, amino acid-defined diet (CDAA; n=28) for 32 and 66 weeks. Serum was collected for biochemical analyses and liver samples processed for histological analysis and measurement of miR-21, its targets and metabolic relevant genes, as well as pro-inflammatory/pro-fibrogenic cytokines. A profiler PCR array was used to evaluate the expression of liver cancer-related genes.

Results: miR-21 levels were increased with disease severity (steatosis, lobular inflammation, ballooning, fibrosis and NAS score) while no correlation with serum data was observed in the San Sebastian cohort. Noteworthy, miR-21 levels were markedly increased in the tumor tissue of patients with NASH-HCC, when compared with surrounding liver in the TCGA cohort. WT mice fed the CDAA diet for 32 weeks developed macrovesicular steatosis, hepatocyte ballooning, NASH and fibrosis, concomitantly with accumulation of perivascular lymphoid cells and macrophage agglomerates. CDAA-fed miR-21 KO mice exhibited increased activation of PPARalpha target genes, augmented mitochondrial activity and decreased fatty acid serum levels, compared with WT mice. After 66 weeks, all WT mice on the CDAA diet developed at least one preneoplastic nodule (~5.2 nodules/animal), with one animal developing trabecular HCC. miR-21 expression was increased in CDAA-fed mice and further increased in HCC, concomitantly with decreased expression of its targets (PTEN, PDCD4, CDK2AP1 and PPARalpha). In addition, livers presented with mitochondrial dysfunction, hyperplastic foci and anisokaryosis, as well as phenotypically altered and highly proliferative (Ki-67 positive) hepatocytes. Increased levels of pro-inflammatory/fibrogenic markers were particularlly evident in pre-neoplastic liver tissues, alongside higher activation of oncogenic pathways. Strikingly, CDAA-fed miR-21 KO mice for 66 weeks displayed serum ALT levels similar to control animals and, compared with CDAA WT-fed mice, the NAS score (< 5); number of liver nodules (~2.3 nodules/animal); hepatocyte profliferation and expression of oncogenes were all significantly reduced, with the pro-inflammatory/fibrogenic milleau reversed to almost baseline controls.

Conclusion: Overall, activation of the miR-21 pathway appears to contribute to NASH-associated carcinogenesis, with its inhibiton halting HCC development. Targeting miR-21 may constitute an appealing therapeutic approach to ameilorate NASH and its progression towards HCC. (PTDC/BIM-MEC/0895/2014, PTDC/MED-PAT/31882/2017, SFRH/BD/88212/2012, SAICTPAC/0019/2015 FCT, PT).

Disclosure: Nothing to disclose

OP255 GENOME-WIDE ASSOCIATION STUDY OF LIVER CORRECTED T1 MAGNETIC RESONANCE IMAGING IDENTIFIES A MISSENSE VARIANT IN SLC39A8 AND YIELDS NEW INSIGHTS INTO MECHANISMS UNDERLYING LIVER INFLAMMATION AND FIBROSIS

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Introduction: Steatohepatitis and subsequent fibrosis affect approximately one in ten middle-aged adults, and are progressive conditions which in turn may lead to cirrhosis, hepatocellular carcinoma and death.[1] The genetic background of steatohepatitis and fibrosis is unknown since liver biopsy is an invasive procedure with significant risks.

A promising, non-invasive proxy measure of liver inflammation and fibrosis is corrected T1 (cT1) magnetic resonance imaging (MRI). cT1 MRI measures are associated with histological liver fibrosis and liver disease outcomes. cT1 MRI has already been used as a non-invasive outcome in randomised controlled trials for NASH,[2] and is an established technique for the assessment of myocardial fibrosis.

Aims & Methods: In this study, we aimed to explore the genetic susceptibility underlying hepatic cT1 MRI measures as a proxy for underlying steatohepatitis and fibrosis.

We used data from the UK Biobank study which is a prospective study of 500,000 individuals recruited at age 40-69 years old across the UK. We derived cT1 measures from abdominal MRI scans in 2,501 unrelated participants. We divided our data into a discovery set of 2,289 white British individuals and a validation set of 212 European but not white-British individuals.

We performed a genome-wide association study (GWAS) in 2,289 white British individuals from UK Biobank using 11,977,111 imputed variants. We adjusted for age, sex, BMI and principal components. We performed a sensitivity analysis where we adjust for all the covariates except BMI. We validated the GWAS significant variants (p-value < 5×10^{-8}) in our validation set of 212 European but not white-British individuals.

Results: The GWAS of liver cT1 MRI measures in 2,289 unrelated individuals of white British ancestry identified one independent variant that reached GWAS significant threshold (rs13107325 in *SLC39A8*, p = 3.44 x 10^{-32}). The missense G > T variant (rs13107325) was associated with 0.67 standard deviations (SD) higher cT1 measures (95% confidence interval [0.56, 0.78]). In our validation set, the association between rs13107325 and cT1 measures was replicated (p = 0.002).

The same missense G > T variant has been shown previously to be associated with higher alcohol intake, higher blood pressure, higher body-mass index, lower brain grey matter volume, less diverse human microbiome composition, higher risk of schizophrenia and higher risk of Crohn's disease.[3-5]

Conclusion: We identified a highly significant, novel association between a G > T missense variant in *SLC39A8* and cT1 MRI liver measures, a non-invasive marker of fibrosis and inflammation, in an unselected, prospective, population-based cohort. Validation is required in larger independent cohorts.

SLC39A8 encodes ZIP8, a divalent cation importer capable of transporting zinc, iron, manganese and selinate, and is one of the most pleiotropic genes in the human genome. Hepatic ZIP8 deficiency in mice was previously associated with liver inflammation and fibrosis, as well as neoplastic changes consistent with hepatocellular carcinoma.[6]

Future studies are needed to determine whether interventions targeting pathways regulated by *SLC39A8* might be attractive therapeutic options to prevent liver disease in at risk individuals.

References: 1) Costas, Javier. 2018. "The Highly Pleiotropic Gene SLC39A8 as an Opportunity to Gain Insight into the Molecular Pathogenesis of Schizophrenia." American Journal of Medical Genetics. 177 (2): 274-83. 2) Elliott, Lloyd T., Kevin Sharp, Fidel Alfaro-Almagro, et al. 2018. "Genome-Wide Association Studies of Brain Imaging Phenotypes in UK Biobank." Nature 562 (7726): 210-16. 3) Harrison, Stephen A., Stephen J. Rossi, Angelo H. Paredes, et al. 2019. "NGM282 Improves Liver Fibrosis and Histology in 12 Weeks in Patients with Nonalcoholic Steatohepatitis." Hepatology , February. https://doi.org/10.1002/hep.30590 4) Li, Dalin, Jean-Paul Achkar, Talin Haritunians, et al. 2016. "A Pleiotropic Missense Variant in SLC39A8 Is Associated With Crohn's Disease and Human Gut Microbiome Composition."

Gastroenterology 151 (4): 724-32. 5) Liu, Liu, Xiangrong Geng, Yihong Cai, Bryan Copple, et al. 2018. "Hepatic ZIP8 Deficiency Is Associated with Disrupted Selenium Homeostasis, Liver Pathology, and Tumor Formation." American Journal of Physiology. Gastrointestinal and Liver Physiology 315 (4): G569-79. 6) Williams, Christopher D., Joel Stengel, Michael I. Asike, et al. 2011. "Prevalence of Nonalcoholic Fatty Liver Disease and Nonalcoholic Steatohepatitis among a Largely Middle-Aged Population Utilizing Ultrasound and Liver Biopsy: A Prospective Study." Gastroenterology 140 (1): 124-31.

Disclosure: RB and HW are shareholders in Perspectum Diagnostics. RB is an employer of Perspectum Diagnostics.

OP256 VOLUMETRIC-CT ASSESSMENT OF SARCOPENIA IN LIVER TRANSPLANT RECIPIENTS

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Introduction: Today, sarcopenia is widely considered as a factor influencing the prognosis in the liver transplant. Among the various available methods, the analysis of muscle mass on a single CT slice at L3 level is currently considered the gold standard for the diagnosis while other methods are currently a matter of investigation.

Aims & Methods: Our aim was to evaluate the prognostic role of sarcopenia assessed through the analysis of muscle mass of the whole abdomen by means of a volumetric-CT analysis.

We evaluated 101 pre-transplant CT scans (venous phase) of adult patients with cirrhosis who underwent LT between 01/01/2016 and 31/10/2018 at our centre. We measured the muscle volume of the abdomen, using a 3D method, from the iliac crests to the base of the heart, excluding visceral content by segmentation. Images were analyzed with Volume Viewer software (GE Medical Systems). Abdominal muscle volume was indexed by height squared (cm3/m2). The lower quartile of indexed muscle volume in the analyzed population was set as a cut-off for significantly reduced muscle mass. A Cox proportional regression-model was used for post-LT survival analysis.

Results: 80 subjects were male (79.2%). The mean age of the study population was 54.8 ± 10.3 years. The prevalent etiology was alcoholic liver cirrhosis (31.7%) followed by HCV (21.8%), cholestatic liver disease (11.9%) and HBV (10.9%). HCC was present in 41.6% of subjects. The mean MELD score was 16.8 ± 7.4. Volumetric cut-offs for lower quartile of indexed abdominal muscle volume were 583.7 cm3/m2 for women and 629.9 cm3/m2 for men. A statistically significant difference in post-LT survival was found using these cut-offs in the study population as an indicator of significant sarcopenia (HR 7; 95% CI 2.3-21.6, *p* = 0.001).

Conclusion: Muscle mass estimate assessed by volumetric analysis appear to be a reliable predictor of post-LT mortality. 3D analysis has the advantage of analyzing a wider portion of the body compared with the standard single-CT slice methods so providing a more reliable estimate of whole-body muscle mass. This method should be further investigated in larger cohorts to confirm its diagnostic performance compared with the standard bi-dimensional analysis.

Disclosure: Nothing to disclose

OP257 LIVER DISORDER DUE TO PD-1 INHIBITORS IN THE CLINICAL SETTING

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Introduction: Recently, cases in which immune checkpoint inhibitors are administered as a new option for the treatment of cancer have been increasing. They are known to lead to immune-related adverse events (hereafter referred to as 'irAEs'), but the actual state of liver disorders as irAEs in clinical settings are not clear. We studied the liver disorders in cases where Nivolumab and Pembrolizumab were administered in our hospital.

Aims & Methods: The subjects were 103 patients (male, 74; female, 29) who were given Nivolumab and/or Pembrolizumab from July 2015 to February 2019. Seventy patients were given Nivolumab (hereafter 'group N'), 31 patients were given Pembrolizumab (hereafter 'group P'), and 2 patients were given the two drugs separately (hereafter 'group NP'). Carcinomas studied were 65 cases of lung cancer, 7 cases of renal cancer, 6 cases of stomach cancer, 5 cases of malignant melanoma, and 20 cases of other cancers. We reviewed whether or not there was presence of liver disorder after the administration of the drugs, and on how they were managed after the liver disorder manifested.

Results: Liver disorder was found in 5 patients in group N (7.1%); 2 of them had grade 1, and 3 of them had grade 3. In the 2 patients with grade 1, Nivolumab was continued but the liver disorder remitted spontaneously. In 2 patients with grade 3, Nivolumab was discontinued and the liver disorder remitted. In the 1 patient with grade 3, mPSL was given with Nivolumab continued, but the liver disorder did not improve, but when Nivolumab was discontinued, the liver disorder improved. In group P, liver disorder was found in 3 patients (9.7%); 2 of them had grade 1 and 1 had grade 3.

In 1 patient with grade 1, Pembrolizumab was continued, but the liver disorder remitted spontaneously. In the other patient with grade 1, Pembrolizumab was discontinued because of another severe irAE, and with the administration of PSL 1mg/kg, the disorder remitted. As the patient with grade 3 did not remit rapidly after administering PSL 60mg (1mg/kg), mycophenolate mofetil (hereafter MMF) was added, with which the disorder remitted. After then, MMF was discontinued, and PSL was decreased to 10mg, after which the liver disorder relapsed. MMR 1g was resumed, and the liver disorder improved. Liver disorder was not found in the NP group. None of the 8 patients who developed liver disorder had history of autoimmune disease.

Conclusion: Among patients with mild liver disorder, there were many in whom administration of PD-1 inhibitors could be continued. In patients with severe liver disorder, discontinuation of the drugs was required in all of them, but all of them remitted by the discontinuation of the drug and administration of immunosuppressive agents. There were also patients whose liver disorder relapsed by a decrease in the dosage of the immunosuppressive agents.

Disclosure: Nothing to disclose

Intestinal epithelium in health and disease
16:00-17:30 / B5

OP258 DUODENAL MUCOSAL RESURFACING (DMR) COMBINED WITH GLP-1-RA MAY ELIMINATE INSULIN THERAPY AND IMPROVE METABOLIC HEALTH IN TYPE 2 DIABETES

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Introduction: Duodenal mucosal resurfacing (DMR) is an endoscopic intervention in which the duodenal mucosa is ablated by hydrothermal energy. DMR improves glycemic control in type 2 diabetes (T2D) through altered metabolic signaling from the duodenum causing insulin sensitization. We studied the feasibility of eliminating insulin therapy in T2D by combining DMR with GLP-1r agonism (liraglutide) and lifestyle counseling.

Aims & Methods: Single arm, single center study in 16 insulin treated T2D patients (HbA1c ≤64 mmol/mol; basal insulin < 1U/kg/day, c-peptide ≥0.5 nmol/l). Day 1, DMR is administered and insulin therapy discontinued. Day 14, liraglutide is introduced (titrated to 1.8 mg/day) and life style counseling is administered throughout. Primary endpoint: percentage of patients free of insulin and HbA1c ≤59 mmol/mol at 6 months.

Results: Enrolment has been completed (n=16) and 12 patients have reached 6 months with 10/12 (83%) insulin-free and able to maintain glycemic control (HbA1c -6.2 mmol/mol, p=0.002, FPG -2.5 mmol/l, p=0.086, AUC glucose MMT -916 mmol/l*min, p<0.001, iAUC glucose MMT -332 mmol/l*min, p< 0.001, peak glucose MMT -3.9 mmol/l, p<0.001), with

improvement across multiple metabolic parameters (weight -5.0 kg, p<0.001, BMI -2.4 kg/m², p<0.001, HOMA-IR -4.7, p=0.003, ALT -7.9 U/l, p=0.008, MRI-PDFF -44.2%, SBP -4.0 mmHg, p 0.344, DBP -2.0 mmHg, p=0.475)(Table 1).

Conclusion: Single endoscopic DMR, combined with liraglutide and lifestyle counseling, may effectively eliminate the need for insulin therapy in T2D while improving glucose regulation and overall metabolic health. This treatment approach is a promising alternative that appears to shift insulin-treated T2D patients to a state of better overall metabolic health.

Disclosure: Nothing to disclose

	Baseline (n=12)	6 months (n=10)*	p-value
Age	61 ± 8		
Daily insulin dose (IU)	37 ± 28	0	
Weight (kg)	96 ± 23	91 ± 22	<0.001
HbA1c (mmol/mol)	58.5 ± 5.4	52.3 ± 6.2	0.002
Insulin (pmol/l)	120 ± 60	64 ± 49	0.011
HOMA-IR	8.1 ± 4.4	3.4 ± 3	0.003
ALT (U/l)	25.9 ± 8.7	18 ± 4.8	0.008
MRI-PDFF % (change)†	8.5 ± 4.6	5.2 ± 3.2 (-44.2)	0.064

Data are mean ± standard deviation. Data represent measurements at baseline and 6 months after initiation of the combined approach of DMR (Duodenal Mucosal Resurfacing), liraglutide and lifestyle counselling instead of basal insulin. BMI: Body Mass Index, HbA1c: Glycated hemoglobin A1c, FPG: Fasting Plasma Glucose, HOMA-IR: Homeostatic Model Assessment of Insulin Resistance, AST: Aspartate Transaminase, ALT: Alanine Transaminase, ABPM: 24-hour ambulatory blood pressure monitoring, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, MMT: Mixed Meal Test, AUC: Area under the curve, iAUC: Incremental area under the curve. P-values based on paired student's t-tests (n=10 vs. n=10). *Two subjects were excluded in whom insulin was reintroduced based on high HbA1c levels at 6 months. †Data at 6 months from 7 patients

[Table 1. Baseline characteristics and 6 months follow-up measurements]

OP259 DECREASED INTESTINAL ACETYLCHOLINESTERASE IN PATIENTS WITH DIABETES: AN *IN VIVO* STUDY WITH ¹¹C-DONEPEZIL PET/CT

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Introduction: Gastrointestinal (GI) neuropathy is a serious complication to diabetes mellitus (DM). Most intrinsic and extrinsic neurons controlling GI motility are cholinergic with nerve endings located within the myenteric plexus. Radioactive Donepezil binds with high affinity to acetylcholinesterase in the synaptic clefts and thereby serve as an *in vivo* marker of cholinergic innervation.

Aims & Methods: Nineteen patients with DM type 1 and GI symptoms were compared to nineteen age and gender-matched HC by means of ¹¹C-Donepezil PET/CT scan and validated questionnaires for assessment of GI symptoms.

In the present study we aimed to compare the density of cholinergic innervation of the gut in patients with DM and healthy controls (HC) by means of ¹¹C-Donepezil PET/CT.

Results: All Patients had severe GI symptoms when assessed by standard questionnaires. Compared to HC, the DM patients had significantly larger volumes of the small intestine (DM: median 557 cm³ interquartile range (IQR 446-697) vs. HC median: 448 cm³ (IQR 341-518) (*p*< 0.01)) while their ¹¹C-Donepezil PET signal was lower (DM: median 7.09 SUV (IQR 5.94-7.99) vs. HC: median 9.51 SUV (IQR 7.48-10.85) (*p*= 0.04)).In the colon, differences did not reach statistical significance (DM: median 1064 cm³ (IQR 882-1312) vs. HC: median 939 cm³ (IQR 785-1008) (*p*= 0.13)) (DM: median 1.20 SUV (IQR 1.05-1.36) vs. HC: median 1.33 SUV (IQR 1.19-1.57) (*p*= 0.07)). Furthermore, DM patients had reduced pancreatic volume (DM: median 53 cm³ (IQR 41-69) vs. HC: median 98 cm³ (IQR 82-110) (*p*< 0.01)) and ¹¹C-Donepezil PET signal of the pancreas (DM: median 13.14 SUV interquartile range (IQR 9.58-15.82) vs. HC: median 21.46 SUV (IQR 18.97;24.06) (*p*< 0.01)).

Conclusion: We found that patients with DM and severe bowel symptoms had distended small intestines and reduced cholinergic innervation of the gut. ^{11}C-Donepezil PET/CT holds promise as a non-invasive method for *in vivo* assessment of dysmotility and intestinal neuropathy in DM.
Disclosure: Nothing to disclose

OP260 MEMBRANE MUCIN MUC17 IS A NOVEL INTESTINAL BARRIER COMPONENT REGULATED BY BACTERIAL SIGNALS

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Introduction: Intestinal epithelium defends the host against environmental insults while permitting nutrient extraction and grafting of microbiota. Contact with bacteria and bacterial products at early stages of life is necessary for intestinal maturity and priming of intestinal epithelial cells (IECs) as well the host immune system[1]. However, there is critical knowledge gap concerning how the host senses the gut microbiota. Membrane mucin Muc17 is a dynamic glycoprotein expressed on apical membrane of IECs, where it extends up to 1 μm into the intestinal lumen[2]. We suggest that Muc17 is an ideal docking site for gut bacteria and could act as a novel epithelial immune receptor in intestine. However, the regulation of Muc17 remains unknown.
Aims & Methods: The aim of this work is to determine the role of Muc17 in intestinal barrier function. Ileum of wild type postnatal mice, human enterocyte-like Caco-2 cells and intestinal organoids were used as experimental models. Expression of Muc17 and epithelial barrier genes were investigated using immunofluorescence, quantitative RT-PCR and western blot.
Results: Establishment of an adult microbiota is a critical event in postnatal intestinal development. Consequently, we asked if the emergence of an adult-type microbiota upon weaning regulates Muc17. In adult mice with a conventional microbiota, Muc17 covers the apical membranes of IECs in the small intestine and colon.
In stark contrast to adult animals, Muc17 was restricted to intracellular vesicles in the ileum of neonatal mice, and localized to apical surfaces only after the suckling-weaning transition, at postnatal day P21. In order to gain insight in the epithelial program(s) underlying Muc17 maturation, we assessed expression of epithelial barrier genes and cytokines during postnatal development (P9-P33). We observed a specific increase in Muc17 expression with age, reaching a peak at P24.
Other upregulated genes were the cytokines Il-22 and Ifn-γ and antimicrobial proteins such as Reg3-β, Reg3-γ and Zg16. However, Toll-like receptors (TLRs) and downstream regulators were unaffected in ileum during the suckling-weaning transition.
Next, we investigated the signaling pathways downstream of Il-22 and Ifn-γ in epithelial-only intestinal organoids. Only stimulation of organoids with Il-22, Ifn-γ or the combination of Il-22 and Ifn-γ upregulated Muc17, whereas ligands for TLRs did not elevate Muc17 levels.
Conclusion: In summary, our study shows that Muc17 is associated with important genes that form the epithelial barrier in the small intestine. Expression of Muc17 and antimicrobial peptides is regulated by cytokines Il-22 and Ifn-γ produced by immune cells in the lamina propria, generating a robust epithelial barrier against the gut microbiota. We suggest that the establishment of this epithelial barrier, including membrane mucin Muc17, requires environmental signals from an adult-type consortium of microbiota.
References: 1. Knoop KA et al., Microbial antigen encounter during a pre-weaning interval is critical for tolerance to gut bacteria. Sci Immunol. 2017 Dec 15;2(18). pii: eaao1314. 2. Pelaseyed T et al., The mucus and mucins of the goblet cells and enterocytes provide the first defense line of the gastrointestinal tract and interact with the immune system. Immunol Rev. 2014 Jul;260(1):8-20.
Disclosure: Nothing to disclose

OP261 XBP1 GOVERNS ENDOPLASMIC RETICULUM STRESS DRIVEN STING SIGNALING IN THE INTESTINAL EPITHELIUM

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Introduction: Endoplasmic reticulum stress (ER-stress), defective autophagy and a dysbiotic microbiota are hallmarks of inflammatory bowel disease (IBD) pathophysiology. Recent findings indicate that Stimulator of Interferon Genes (STING) might be involved in IBD pathophysiology in a mechanism involving excessive IFN-I secretion and consecutive necroptotic cell death[i][ii][iii]. To which extent IBD risk genes involved in the ER-Stress axis such as *XBP1* are necessary to coordinate intrinsic STING activation is not known.
Aims & Methods: We hypothesized that STING signaling might be dysregulated in context of ER-stress and inflammation in the intestinal epithelium. We therefore investigated the crosstalk between ER-stress and the STING pathway, focussing on the IRE1/XBP1 branch of the unfolded protein response (UPR) as hypomorphic *XBP1* variants have been shown to cause ER-stress and thereby confer risk for IBD[i]. Intestinal organoids were derived from IBD patients and tested on their ability to induce ER-stress driven STING signaling. RNA sequencing data from biopsies were analysed for correlation of ER-stress and STING singaling signatures in context of IBD. Mice with a conditional epithelial deletion of *Xbp1* and/or *Atg16l1* (*Xbp1*[ΔIEC], *Xbp1/Atg16l1*[ΔIEC]) were used to study STING signaling in context of ER-stress and defective autophagy. STING signaling was induced either chemically, via dsDNA or using vita-PAMPs such as L. monocytogenes or cytomegaliavirus.
Results: Analysis of ileal biopsies and human organoids from IBD patients revealed a strong correlation of ER-stress marker genes and STING expression in a disease-dependent manner with highest upregulation in inflamed tissue. Surprisingly, ER-stress induction itself via TM treatment induced robust STING-dependent IFN-I induction. In contrast, chronic ER-stress in *Xbp1*-deficient intestinal epithelial cells lead to STING degradation and subsequently impaired pathogen induced IFN-I production. These finding were confirmed *in vivo*, as the STING/IFN-I pathway was strongly impaired in *Xbp1*[ΔIEC] mice. Mechanistically, we show that impaired STING-dependent IFN-I induction was due to Atg16l1-driven autophagic removal of STING, as STING-dependent IFN-I induction was partially recovered in the *Xbp1/Atg16l1*[ΔIEC] mice and organoids.
Conclusion: Our data suggests that the STING/IFN-I pathway is tightly regulated by ER-stress in intestinal epithelial cells. Mechanistically, acute ER-stress directly induces IFN-I release via STING activation. In contrast, chronic ER-stress, such as in the context of Xbp1 deficiency, induces autophagy-dependent STING degradation and renders epithelial cells vulnerable to bacterial or viral infections. Hence our data implicate a novel mechanism of the IBD risk gene *XBP1* on epithelial defense response against pathogens and provides an interesting link to explain the drastically increased vulnerability of IBD patients towards intestinal viral infections
References: Howell, Kate Joanne, et al. „DNA methylation and transcription patterns in intestinal epithelial cells from pediatric patients with inflammatory bowel diseases differentiate disease subtypes and associate with outcome.“ Gastroenterology 154.3 (2018): 585-598. Samie, Mohammad, et al. „Selective autophagy of the adaptor TRIF regulates innate inflammatory signaling.“ Nature immunology 19.3 (2018): 246. Aden, Konrad, et al. „ATG16L1 orchestrates interleukin-22 signaling in the intestinal epithelium via cGAS-STING.“ Journal of Experimental Medicine 215.11 (2018): 2868-2886. Kaser, Arthur, et al. „XBP1 links ER stress to intestinal inflammation and confers genetic risk for human inflammatory bowel disease.“ Cell 134.5 (2008): 743-756.
Disclosure: no conflict of interest

OP262 HYPERSENSITIVITY TO OXIDATIVE LYSOSOME DAMAGE CAUSES DEATH OF ENTEROCYTES IN MICROVILLUS INCLUSION DISEASE

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Introduction: Microvillus inclusion disease (MVID) is a fatal enteropathy, characterized by intractable diarrhea and malabsorption associated with unexplained villus atrophy. MVID is caused by mutations in MYO5B encoding myosin-Vb, known for its role in the recycling of cell surface proteins. Although recycling and degradation pathways of cell surface proteins are connected, the impact of the loss of myosin-Vb on the degradative route remains unclear.

Aims & Methods: The aim of this study was to investigate the impact of myosin-Vb loss-of-function on the late endo-lysosomal system. Immunolabeling on tissues of MVID patients with MYO5B mutations and Myo5B knockout mice was performed, together with functional studies in a MVID cell model to address causal relationships between phenotypes and myosin-Vb expression and underlying mechanisms.

Results: Loss of myosin-Vb had a profound impact on the late endolysosomal system, causing

1) alterations in the morphology and spatial distribution of late endo-lysosomes,

2) the accumulation of iron in lysosomes,

3) an iron-mediated hypersensitivity to oxidative stress-induced lysosome membrane rupture and

4) resultant cell death.

The availability of the small GTPase rab7 was identified as a rate-limiting factor for the development of the late endo-lysosomal phenotype. Iron chelation and antioxidant treatment restored the phenotype.

Conclusion: Myosin-Vb, concurrent with its role in plasma membrane homeostasis, is important for late endolysosomal homeostasis. Hypersensitivity of myosin-Vb-depleted cells to oxidative lysosomal membrane permeabilization and cell death should be considered part of MVID pathogenesis. This property underlies a potential clinically relevant and druggable mechanism to explain the extensive villus atrophy in MVID.

Disclosure: Nothing to disclose

OP263 NEW AND SIMPLE DIAGNOSTIC TEST FOR INCREASED INTESTINAL PERMEABILITY BASED ON PLATELET COUNT

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Introduction: The main pathological process associated to increased intestinal permeability is the translocation of toxic products, predominantly endotoxins/lipopolysaccharides (LPS) from the intestinal tract into the microcirculation (1).

In the bloodstream, LPS is distributed in varying proportions bound by LPS-binding protein, several other acute phase proteins, lipoproteins, soluble CD14, and even more relevant for our study, by cells bearing TLR4 such as platelets (2,3). LPS leads to preactivated platelets that have a lower threshold to be aggregated in presence of the physiological agonists, thrombin and collagen, but also by other molecules such as heparin (4,5).

Aims & Methods: The aim of this study was to validate a simple, fast and reliable test for screening LPS-loaded platelets as an indirect biomarker for increased intestinal permeability. This test named PANDA (acronym for PlAtelet's Number in Different Anticoagulants) consists in the measurement of the mean platelet number in blood samples collected into EDTA and heparin.

To explore this issue, we analyzed the platelet number from patients with gastrointestinal diseases and a group of healthy persons in blood samples anticoagulated with EDTA or heparin, but also in presence of hirudin or citrate in order to investigate the contribution of Ca^{2+} in platelet's aggrega-

tion. Finally, we also evaluated whether the PANDA test can be used for monitoring the gut barrier function in 30 patients under treatment with a new oxygenated simethicone emulsion (6).

Results: A notably lower number of platelets was found in heparinized blood compared to EDTA-anticoagulated blood from patients with a gut barrier dysfunction but not from healthy volunteers. These results suggested that when LPS translocates into blood, it binds to platelets leading to a preactivated state in which they have a lower threshold to be aggregated in presence of heparin. In order to confirm this hypothesis, LPS was added to heparinized and EDTA-anticoagulated blood samples collected from both groups. LPS led to a significant reduction of platelet counts only in heparinized blood samples from control subjects but not in patients where the LPS-binding sites on platelets could already be saturated. LPS did not influence platelet number in EDTA-blood samples at all.

Moreover, platelet's aggregation can not be attributed to the higher Ca^{2+} concentration in heparinized samples compared to EDTA-blood samples. If this were so, how can we explain the lack of aggregation in heparinized blood from control subjects? Furthermore, in blood samples from some patients either the platelet number in citrated blood was very similar to that of heparinized blood or platelet counts found in heparinized blood were even lower than those of hirudin-blood samples in spite of the same external Ca^{2+} concentration in these samples.

Finally, we have investigated whether PANDA test could be useful for monitoring the reconstitution of gut barrier function. We found that the platelet's number in heparinized blood was notably lower compared to EDTA-blood before beginning of treatment.

However, the difference in platelet's number in presence of these both anticoagulants decreased notably during the course of a simethicone treatment.

Conclusion: Our results demonstrated that PANDA test can be used for screening LPS-loaded platelets as an indirect diagnostic biomarker for increased intestinal permeability and also for monitoring the gut barrier function during the treatment of gastrointestinal diseases.

References: 1. Laukoetter MG, Nava P, Nusrat A. Role of the intestinal barrier in inflammatory bowel disease. World J Gastroenterol 2008;14:401-407. 2. Kopp F, Kupsch S, Schromm AB. Lipopolysaccharide-binding protein is bound and internalized by host cells and colocalizes with LPS in the cytoplasm: Implications for a role of LBP in intracellular LPS-signaling. Biochim Biophys Acta 2016;1863:660-672. 3. Ståhl AI., et al., 2006. Lipopolysaccharide from enterohemorrhagic Escherichia coli binds to platelets through TLR4 and CD62 and is detected on circulating platelets in patients with hemolytic uremic syndrome. Blood 108:167-176. 4. Zhang G, Han J, Welch E, Ye R, Voyno-Yasenetskaya T,Malik AB, Du X, Li Z. LPS stimulates platelet secretion and potentiates platelet aggregation via TLR4/MyD88 and the cGMP-dependent protein kinase pathway. J Immunol 2009;182:7997-8004. 5. Gao C, Boylan B, Fang J, Wilcox D, Newman D and Newman P. Heparin promotes platelet responsiveness by potentiating αIIbβ3-mediated outside-in signaling. Blood 2011;117:4946-4952. 6. Meier R, Steuerwald M. 2007. Review of the Therapeutic use of simethicone in gastroenterology. Schweiz. Zschr. Ganzheits Medizin 19:380-387.

Disclosure: Nothing to disclose

Improving colorectal cancer screening
16:00-17:30 / C2

OP264 ADENOMA DETECTION RATE IN ASYMPTOMATIC FECAL IMMUNOCHEMICAL TEST POSITIVE COHORTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Adenoma detection rate (ADR) is a well-accepted quality indicator of screening colonoscopy and is defined as the proportion of patients who have one or more adenoma detected while undergoing screening colonoscopy. In a recent guideline, the US multi society task force on CRC prevention proposed an ADR benchmark of >35% for females and >45% for males in fecal immunochemical test (FIT) positive asymptomatic population. This, however, is based out of low quality evidence.

Aims & Methods: We conducted this meta-analysis to estimate the pooled threshold of ADR in FIT-positive asymptomatic population undergoing colonoscopy. We conducted a comprehensive search of several databases and conference proceedings including PubMed, EMBASE, Google-Scholar, LILACS, and Web of Science databases (earliest inception to January 2019). We followed the Preferred Reporting items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, by using predefined protocol, to identify studies reporting the detection of adenoma by colonoscopy in FIT-positive population. Random-effects model was used for analysis. Heterogeneity between study-specific estimates was calculated using Cochran Q statistical test and I^2 statistics. Publication bias was ascertained, qualitatively, by visual inspection of funnel plot and quantitatively, by the Egger test.

Results: From an initial total of 480 studies, 73 records were screened and 48 full-length articles were assessed. 21 studies were included in the final analysis. All included patients were aged more than 50 years. In the included 21 studies, 129,975 cases were positive for FIT, of which 105,731 cases underwent a screening colonoscopy. 50,247 cases were identified with a colorectal adenoma, 12,343 cases were diagnosed with advanced adenoma, and 4,211 cases were diagnosed with colorectal cancer. The pooled rate of adenoma detection rate (ADR) in FIT-positive asymptomatic individuals was 45.4% (95% CI 37.3-53.8, I^2=99.8). The pooled rate of advanced adenoma detection rate (aADR) was 19.4% (95% CI 14.2-25.8, I^2=99.6) and the pooled rate of colorectal cancer detection rate (CDR) was 3.8% (95% CI 2.8-5.0, I^2=97.9). Based on visual inspection of the funnel plot as well as quantitative measurement that used the Egger regression test, there was no evidence of publication bias (Egger's p-value=0.37).

Conclusion: From a total of 21 good quality studies that evaluated 129,975 participants, we report a pooled adenoma detection rate (ADR) of 45.4%, a pooled advanced-ADR of 19.4%, and a pooled CDR of 3.8% in FIT-positive asymptomatic individuals. To the best of our knowledge, this study is the largest and most up-to-date meta-analysis reporting on the pooled results of colonoscopy findings in FIT-positive asymptomatic population.

Disclosure: Nothing to disclose

OP265 THE PREDICTIVE EFFECT OF A HIGH-QUALITY SINGLE NEGATIVE SCREENING COLONOSCOPY IN INDIVIDUALS WITH FAMILY HISTORY OF COLORECTAL CANCER EXCEEDS 10 YEARS

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Introduction: Despite limited evidence, current guidelines recommend to repeat screening colonoscopy in individuals with family history (FH) of colorectal cancer (CRC) every 5 years.

Aims & Methods: To assess the long-term risk (>5 years) of CRC and CRC death in individuals with and without a family history of colorectal cancer (at least one first-degree relative with CRC) after high- and low-quality single negative screening colonoscopy, as compared with the general population.

We conducted an analysis of the database records of all colonoscopies performed between October 1st 2000, and December 31st 2011 as part of the Polish CRC screening program.

All subjects with and without FH of CRC who underwent a single negative colonoscopy (defined as the absence of any neoplastic lesions) were identified and followed for CRC and CRC death through the National Cancer Registry over the median of 10.2 years and up to 17.4 years. High-quality colonoscopy was defined as an examination with cecal intubation, adequate bowel preparation (very good, good or sufficient per the Aronchick scale) performed by an endoscopist with an adenoma detection rate ≥20%. Standardized incidence and mortality ratios (SIRs and SMRs) were calculated by comparing the observed values against the values for the general Polish population.

Results: Out of 206,685 individuals who underwent screening colonoscopy with a negative result, we identified 40,798 individuals with FH of CRC. Overall, throughout a 17.4-year period following a high-quality single negative colonoscopy there was no significant difference in risk of CRC and CRC death between subjects with FH of CRC and those without FH of CRC (high-quality screening colonoscopy yielded SIR of 0.33 (95% CI, 0.19-0.53) and SMR of 0.04 (95% CI, 0.00-0.24) in subjects with FH of CRC and SIR of 0.24 (95% CI, 0.19-0.30) and SMR of 0.17 (95% CI, 0.11-0.25) in subjects without FH of CRC. Among individuals with FH who underwent high-quality colonoscopy, the risk of colorectal cancer and colorectal cancer death between 5 and 10 years after examination did not differ significantly from the earlier period of observation (Table 1).

	Years following negative colonoscopy					
	0-5.0	5.1-10.0	Entire follow-up period	0-5.0	5.1-10.0	Entire follow-up period
	Individuals with family history of CRC			Individuals without family history of CRC		
High-quality colonoscopy						
SIR (95% CI)	0.23 (0.08-0.50)	0.40 (0.17-0.79)	0.33 (0.19-0.53)	0.19 (0.13-0.27)	0.30 (0.22-0.42)	0.24 (0.19-0.30)
SMR (95% CI)	0.08 (0.00-0.46)	0.00 (0.00-0.41)	0.04 (0.00-0.24)	0.09 (0.04-0.18)	0.21 (0.11-0.36)	0.17 (0.11-0.25)
Low-quality colonoscopy						
SIR (95% CI)	0.57 (0.39-0.81)	1.04 (0.77-1.37)	0.79 (0.64-0.96)	0.36 (0.30-0.43)	0.63 (0.54-0.72)	0.52 (0.47-0.57)
SMR (95% CI)	0.24 (0.09-0.52)	0.82 (0.48-1.29)	0.50 (0.33-0.72)	0.17 (0.11-0.24)	0.51 (0.40-0.64)	0.38 (0.32-0.45)

[SIRs and SMRs of individuals with and without FH of colorectal cancer according to the quality and the time from single negative screening colonoscopy]

Conversely, low-quality screening colonoscopy was not associated with a significant reduction in colorectal cancer risk among the individuals with FH of colorectal cancer between 5 and 10 years after colonoscopy.

Conclusion: Our results suggest that 5-year screening interval for individuals with FH of CRC could be safely prolonged to 10 years providing that the quality of baseline colonoscopy was high.

Disclosure: JR received honoraria/consultation fees from Ipsen, Polpharma, Takeda, Alfa Sigma, Krka, Promed, and travel grant from Abbvie and Alfa Wassermann. MFK recived honoraria/consultation fees from Olympus, Fujifilm, Alfa Sigma and Norgine.

OP266 SHOULD ADENOMA DETECTION RATES BE AGE BASED?

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Introduction: Adenoma detection rate (ADR) is a measure of the quality of the colonoscopic examination, and in the UK a minimum target of 15% has been set for the whole population. Given the pathogenesis of adenomas, colonoscopists who examine a higher proportion of younger patients might be expected to encounter fewer adenomas, and as such not produce equivalent ADRs to those dealing predominantly with older patients.

Aims & Methods: We set out to establish ADRs in patients of different age groups. We interrogated the endoscopy reporting system at a District General Hospital in South London over a 3-year period. We divided the patients into three age groups, and then determined the crude rate of polyp detection for each. From each age group we selected a sample of 100 consecutive patients who had polyps on their colonoscopy, and reviewed the histological diagnoses to determine the proportion of polyps which were clinically important i.e. adenomas, sessile or serrate lesions, and carcinomas. Chi-square testing was used to compare the different age groups for: the crude polyp detection rates, the rate of clinically important lesions in our samples, and the extrapolated number of clinically important lesions for the 3-year data set.

Results: A total of 7928 colonoscopies were performed in this time period. Table 1 below summarises the lesion detection rates in the three age groups examined.

	20-39 year old	40-59 year old	60-90 year old
Total number of colonoscopies performed	639	2519	4770
Number of colonoscopies in which polyps were detected	102	605	1662
Crude rate of polyp detection	16.0% p value (20-39yo vs. 40-59yo) <0.001	24.0% p value (40-59yo vs. 60-90yo) <0.001	34.8% p value (20-39yo vs. 60-90yo) <0.001
Number of adenomas, sessile or serrated lesions, and carcinomas in a sample of 100	49	67	76
Predicted rates of clinically important polyps	7.8% p value (20-39yo vs. 40-59yo) <0.001	16.1% p value (40-59yo vs. 60-90yo) <0.001	26.5% p value (20-39yo vs. 60-90yo) <0.001

[Table 1]

Conclusion: Our data suggests there is a significant difference in ADRs in different age groups, and that clinically important polyps are more likely to be found in older people. This adds to the body of evidence that ADRs increase with age. Future key performance indicators for colonoscopies should take this into account.

References: Kaminski MF, Regula J, Kraszewska E, Polkowski M, Wojciechowska U, Didkowska J, Zwierko M, Rupinski M, Nowacki MP, Butruk E. Quality indicators for colonoscopy and the risk of interval cancer. N Engl J Med. 2010 May 13;362(19):1795-803. doi:10.1056/NEJMoa0907667. Corley, DA., et al. Adenoma Detection Rate and Risk of Colorectal Cancer and Death. N Engl J Med 2014; 370:1298-1306 DOI: 10.1056/NEJMoa1309086 Diamond SJ, Enestvedt BK, Jiang Z, et al. Adenoma detection rate increases with each decade of life after 50 years of age. Gastrointest Endosc. 2011;74(1):135-40.

Disclosure: Nothing to disclose

OP267 EFFICACY AND TOLERABILITY OF SINGLE DOSE *VS.* SPLIT DOSE POLYETHYLENE GLYCOL FOR COLONIC PREPARATION IN CHILDREN: A RANDOMIZED CONTROL STUDY

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Introduction: Polyethylene glycol (PEG) solution is the most effective colon cleansing agent but volume related adverse effects are common. Though split-dose PEG is used in adults, there is no pediatric study so-far comparing split-dose with single-dose PEG.

Aims & Methods: The aim of this study was to find the efficacy and tolerability of split-dose as compared to single-dose PEG for bowel preparation in pediatric patients.

Consecutive children (1-18 years) were randomized into either single-dose or split-dose PEG. Single-dose group received 4000mL/1.73m² PEG solution day before colonoscopy while split-dose group received half dose day before and the remaining half on the day of colonoscopy. Effectiveness of bowel preparation was assessed on Aronchik scale, by the endoscopist who was blinded to the type of preparation. Inter-observer variability was analyzed by comparing with independent scoring by the blinded trained endoscopy-nurse. The trial was registered with Clinical Trials Registry of India. (Trail number 2017/08/009303).

Results: Of the 220 randomized children, 179 completed the study (split-dose: 93, single-dose: 86) The mean age of the study population was 138.12 (57.84) months (72.6% males). Age, gender distribution, body surface area (BSA), volume of PEG solution ingested, proportion of in-patients and previous history of colonoscopy were comparable between the single-dose and split-dose PEG groups. The efficacy of bowel preparation was better with split-dose (satisfactory preparation: 76.34% *vs.* 43.02%, p< 0.001) with almost perfect inter-observer agreement (k=0.803). Nausea, vomiting and sleep disturbance were significantly less in split-dose than single-dose group (p< 0.05). Split-dose patients were able to drink PEG solution faster (p=0.002). Total sleep duration and uninterrupted sleep duration was also better in split-dose group as compared to single-dose (p=0.001).

Parameters	Single dose PEG (N=86)	Split dose PEG (N=93)	P value
Mean duration of drinking (SD) in hours	5.15 (1.18)	4.65 (0.93)	0.002
Pain abdomen, n (%)	7 (8.1)	3 (3.2)	0.199
Abdominal distension, n(%)	6 (7)	2(2.2)	0.156
Vomiting, n (%)	36(41.9)	21(22.6)	0.007
Sleep disturbance,n(%)	49(57)	13(14)	0.001
Mean duration uninterrupted sleep (SD) in hours	4.23 (1.83)	6.05 (1.34)	0.001
Last stool liquid consistency, n (%)	72(83.7)	90(96.8)	0.003
Satisfactory preparation (Excellent and Good on Aronchik score), n (%)	37(43.02)	71(76.34)	<0.001
Ileoscopy, n(%)	83(96.5)	93(100)	0.109

[Comparisons of tolerability and efficacy between single dose versus split dose Polyehylene glycol]

Conclusion: Split-dose PEG is more effective than single-dose for colonoscopic preparation in pediatric population. At the same time it causes lower volume related side effects of bowel preparation and improved sleep quality which are of paramount importance for children.

Disclosure: Nothing to disclose

OP268 WATER EXCHANGE (WE) SIGNIFICANTLY INCREASES DETECTION RATE OF SESSILE SERRATED POLYPS COMPARED WITH AIR (AI) OR CARBON DIOXIDE (CO2) INSUFFLATION - POOLED DATA ANALYSIS OF THREE RANDOMIZED CONTROLLED TRIALS

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Introduction: Important advances were made in understanding the impact of water exchange (WE) colonoscopy in the past decade. The cardinal feature and key to the success of WE is, during the insertion phase, the near-complete suction removal of infused water used to aid insertion.[1] A network meta-analysis in 2018 summarized the data and reported that WE provided the highest adenoma detection rate[2]; but the impact on the detection rate of sessile serrated polyps was not addressed. These lesions can be found anywhere in the colon and are more common in the proximal and right colon. The endoscopic features of sessile serrated polyps make their real-time identification challenging. Given their subtle appearance and their definite potential for transformation to malignancy, a method that enhances their endoscopic detection is desirable.

The finding of sessile serrated polyps was mentioned in several randomized controlled trials (RCTs) comparing WE with air (AI) or carbon dioxide (CO2) insufflation.

Aims & Methods: By pooling the data in three RCTs[3-5] to minimize the pitfall of type II error, the aim of this report is to assess the impact of WE (vs. AI or CO2) on detection rate of sessile serrated polyps. Three RCTs with data on sessile serrated polyps when the standardized WE method was compared with AI or CO2 insufflation were identified. Demographic and procedural data were tabulated. Data on sessile serrated polyps were pooled and analyzed.

Results: Table 1 summarizes the studies selected for pooled analysis based on available data. WE significantly increased detection rate of sessile serrated polyps from 3.2% to 4.9% (*P=0.0054, Fisher Exact test).

Conclusion: The pooled data show WE significantly increased detection rate of sessile serrated polyps. The improved outcome adds value to colonoscopy performed with the WE method. The enhanced value justifies incorporation of WE into colorectal cancer screening programs, to set the stage for future studies to assess the impact of WE on minimizing the development of colorectal cancers.

Pooled Data of References 3, 4, 5		
Method	Water Exchange	Air Insufflation
No. of patients	2053	2043
No. of colonoscopists	20	20
Mean age, year	57	57
Male, no. (%)	1088 (53%)	1121 (55%)
Screening, no.(%)	865 (42%)	919 (45%)
Cecal intubation no. (%)	2020 (98%)	2001 (98%)
Withdrawal time (min)	7.1 to 20	7.2 to 22
Bowel prep regimen	Split-dose	Split-dose
Sessile polyp detection rate	101/ 2053 (4.9%)*	65/2043 (3.2%)

[Table 1: Details of randomized controlled trials selected for analysis]

References: 1. Leung FW, et al. Water infusion without near-complete removal during insertion by any other name is still water immersion (WI). Gastrointestinal Endoscopy 2019;89(3):599-601. 2. Fuccio L, et al. Water exchange colonoscopy increases adenoma detection rate: a systematic review with network meta-analysis of randomized controlled studies. Gastrointest Endosc. 2018;88(4):589-597. 3. Garborg K, et al. Water exchange versus carbon dioxide insufflation in unsedated colonoscopy: a multicenter randomized controlled trial. Endoscopy. 2015 Mar;47(3):192-9. 4. Jia H, et al. Water exchange method significantly improves adenoma detection rate: a multicenter, randomized controlled trial. Am J Gastroenterol. 2017;112(4):568-576. 5. Leung JW, et al. A prospective RCT comparing combined chromoendoscopy with water exchange (CWE) vs. water exchange (WE) vs. air insufflation (AI) in adenoma detection in screening colonoscopy. United European Gastroenterology J. 2019 Feb. https://doi.org/10.1177/2050640619832196

Disclosure: Nothing to disclose

OP269 FACTORS ASSOCIATED WITH MECHANICAL AND SYSTEMIC ADVERSE EVENTS AFTER COLONOSCOPY (FRANCE, 2010-2015)

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Introduction: More than one million colonoscopies are performed every year in France. They are associated with risks of mechanical and systemic serious adverse events (SAEs).

Aims & Methods: In this study, we attempted to identify the factors associated with mechanical (colonic perforation, gastrointestinal bleeding, splenic injury) and systemic (shock, myocardial infarction, stroke, pulmonary embolism, acute renal failure, urolithiasis) SAEs after colonoscopy. We analysed data from the French national claims databases (SNDS). A total of 4,088,799 patients, 30 years or older, undergoing a first screening or diagnostic colonoscopy between 2010 and 2015 were identified. SAE rates were estimated, and risk factors associated with SAEs were identified using multilevel logistic regression models, adjusted for patient, colonoscopy, endoscopist, and facility characteristics.

Results: Perforation rates ranged from 3.5 (stringent definition) to 7.3 (broad definition) per

10,000 procedures, bleeding rates ranged from 6.5 to 23.1 per 10,000 procedures, and splenic injury rates ranged from 0.20 to 0.34 per 10,000 procedures. The 5-day SAE incidence rate was 2.8/10,000 procedures for shock, 0.87/10,000 for myocardial infarction, 1.9/10,000 for stroke, 2.9/10,000 for pulmonary embolism, 5.5/10,000 for acute renal failure, and 3.3/10,000 for urolithiasis.

Increasing age was associated with an increasing incidence of mechanical and systemic SAEs. Cancer andcardiovascular comorbidities were associated with mechanical SAEs. A higher number of pre-existing conditions was associated with shock and acute renal failure. Polypectomy, especially of polyps larger than 1 cm, was associated with an increased risk of perforation (OR=4.1; 95% CI, 3.4-5.0) and bleeding (OR=13.3; 95% CI, 11.7-15.1). Mechanical SAEs were associated with the endoscopist's experience, while systemic SAEs were more frequent in public hospitals than in private clinics.

Conclusion: SAEs related to colonoscopy are more frequent in older patients and in those with comorbidities. Systemic SAEs are more frequent in public hospitals, reflecting patient selection processes. The risk of both mechanical and systemic SAEs should be taken into account when deciding colonoscopy, particularly in elderly patients with multiple pre-existing conditions

Disclosure: Franck Carbonnel received personal fees from Medtronic for board participation

New ways to predict response in IBD

16:00-17:30 / E1

OP270 EARLY DYNAMICS OF PERIPHERAL BLOOD GENE EXPRESSION AND DNA METHYLATION PREDICT RESPONSE TO ANTI-TNFA THERAPY IN A PROSPECTIVE MULTI-OMICS ANALYSIS IN IBD PATIENTS

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Introduction: Biologics targeting tumor necrosis factor α (TNFα) are successfully used to treat chronic immune mediated diseases including inflammatory bowel disease (IBD). However, the utility of these therapies is significantly impacted by high primary and secondary non-response rates. Hence, it is crucial to find biomarkers that could predict therapeutic response before or in the initial stages of the treatment. Here, we aim to understand the dynamic molecular changes that lead to remission in IBD patients newly receiving anti-TNFα therapy.

Aims & Methods: In total 14 biologic-naïve IBD patients, who underwent first time anti-TNFα treatment with infliximab, were recruited into a molecular medicine study with a dense sampling scheme at the University Hospital Kiel for hypothesis generation and 45 patients for confirmation of findings. Clinical response was assessed using symptom based clinical disease scores (HBI/MAYO) and endoscopy. In the hypothesis generation cohort, 7 patients attained remission within a time frame of 14 weeks. Whole blood from the patients before and 4, 24, 72 hours, 2, 6 and 14 weeks after therapy was collected. RNA and DNA isolated from the 98 blood samples were used for systematic multi-OMICS profiling including RNA sequencing and DNA methylation profiling by EPIC arrays, respectively.

Results: We found that target engagement of anti-TNFα led to fast and drastic downregulation of overall gene expression in the whole blood transcriptome irrespective of therapy outcome. Pairwise comparisons and impulse-modelling identified a higher number of differentially expressed genes in patients who later attained remission. Co-expression analysis identified gene modules involved in innate immune response and inflammatory response showing different expression profiles in remission and non-remission groups. These modules were characterized by decrease in expression in the early timepoints (24h to 2 weeks) in the remission group. 763 out of 3889 remission associated genes correlated significantly with differentially methylation variable positions (MVPs), indicating a potential epigenetic control of remission-associated gene modules. The identified methylation sites were enriched for binding motifs of transcription factors related to immune and inflammatory processes such as BATF, NFKB, STAT3 and CEBPB. Selected pairs of differentially expressed transcripts and MVPs were verified in a confirmatory cohort of 45 IBD patients receiving first time treatment with infliximab or vedolizumab, demonstrating overlapping and unique signals between biologics.

Conclusion: We show that successful induction of remission through anti-TNFα therapy drastically alters the whole blood transcriptome and methylome in the first 2 weeks during therapy initiation. Our results suggest that transcriptional changes associated with remission are highly dynamic in nature and might be partially regulated by epigenetic mechanisms. The contrast of gene modules integrated across Omics-layers can be used to decipher predictive molecular signatures of remission. Further clinical studies are required to evaluate the utility of such signatures for clinical decisions between continuation of therapy and early switching to other MOA.

Disclosure: Nothing to disclose

OP271 TERMINAL ILEUM THICKNESS IS A PREDICTIVE MARKER FOR INFLIXIMAB THERAPY IN CROHN´S DISEASE

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Introduction: While achieving mucosal healing has been associated with long-term response to therapy of Crohn's disease (CD), little is known about the significance of terminal ileum (TI) transmural thickness in predicting of clinical outcomes.

Aims & Methods: In this retrospective chart review, we examined the correlation between transmural TI thickness during maintenance phase (week 14 and above) and the clinical outcome of CD in a cohort of patients treated with infliximab. Intestinal ultrasonography (IUS) was used in all patients to determine TI transmural thickness. TI transmural response was defined as TI< 4mm. Treatment failure was defined as treatment discontinuation due to inefficacy, dose escalation, or surgery. IUS parameters and clinical data were assessed during follow up.

Results: Sixty CD patients receiving infliximab therapy (60% male, mean age 32.6 years, mean duration of disease-9.6 years, 92% anti-TNF-naïve) were included in the study. All patients had ileal or ileo-colonic disease. Thirty nine patients (65%) achieved transmural response. The mean duration of follow-up was 11.2 months. After a median follow-up of 9.5 months, 22(36.6%) patients developed treatment failure. On univariate analysis, the only variables associated with treatment failure were: TI thickness of 3.1 (3.62-6.72) mm vs 1.4 (1.8-3) mm, p value <0.0001 in patients with and without treatment failure, respectively, and IFX trough level (IFX-TL) of 6.6 (0.13-6.97) mcg/ml vs 3.9 (3.9-7.8) mcg/ml level, p = 0.008. There was a significant correlation between failure to achieve transmural response and treatment failure (18/24 (75%) vs 4/36 (11.1%)) in patients with treatment failure and without treatment failure, respectively (OR-17.55 95%, CI -4.0-76, p=0.02). Other than IFX-TL and TI- thickness there were no clinical or demographic parameter that were associated with the risk of treatment failure.

On multivariate analysis, only terminal ileum thickness> 4 mm was associated with the risk of treatment failure (p= 0.002); IFX-TL did no retain statistical significance on multivariate analysis (P= 0.695)

Conclusion: Our findings suggest that failure to achieve transmural response to infliximab can predict subsequent treatment failure in CD patients, indicating transmural response as a potential novel valuable therapeutic target.

Disclosure: Nothing to disclose

OP272 TRANSMURAL HEALING ASSESSED USING MRI IS ASSOCIATED WITH BETTER OUTCOMES AND IS A POTENTIAL THERAPEUTIC TARGET IN PATIENTS WITH CROHN´S DISEASE

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Introduction: The poor acceptability of repeated colonoscopies limits the use of endoscopic mucosal healing as therapeutic target in patients with Crohn's disease (CD). MRI is better accepted than endoscopy, is able to perform a concomitant transmural assessment of ileocolonic inflammation and to detect CD complications.

Aims & Methods: We aimed to evaluate whether transmural healing assessed using MRI scores was associated with decreased risk of surgery, hospitalization and therapeutic intensification in patients with CD.

From a database including all the consecutive patients who performed anMRI to assess luminal CD between January 2012 and June 2018 in our IBD unit, we selected all the patients with CD (> 18 yearsold) who underwent two MRI with:

1) objective signs of inflammation on the 1st MRI,

2) the second MRI performed to assess therapeutic efficacy,

3) follow-up > 6 months and no surgery between the two MRI.

All the patients underwent MRI assessing the small bowel and the colon using a standardized protocol (no bowel cleansing the day before and no colonic distension). Complete transmural healing was defined as normalization of MRI. Partial transmural healing was defined as a decrease of at least 25 % of Clermont score or MaRIA in each active segment. Results were expressed as Hazard Ratio (HR) and 95% confidence interval [95% CI].

Results: Overall, 443 patients undergoing 889 MRI were screened for the study. Among them 274 patients were included (mean age 33.1 ± 15.8 years, median CD duration = 7.0 [2.013.0] years, 36.4 % smokers, 31.4 % prior intestinal resection, L1 = 51.5 %, L2 = 5.5 % and L3 = 43.1 %, 25.9 % perianal lesions, 35,4 % stricturing CD and 31.0 % fistulizing CD). At the time of the second MRI, the patients received one or several medications among: steroids (6.3 %), immunosuppressants (45.2 %), antiTNF agents (65.7 %) or ustekinumab (2.6 %). The median interval between the 2 IRM was 9.2 months [6.0 - 14.1].

Overall, 53 patients had a CD-related bowel resection, 72 patients (26.3 %) required CD-related hospitalization and 163 patients (59.5 %) needed therapeutic intensification (median follow-up = 14.9 mois [4.3 - 31.4]). In multivariate analysis (Cox model), complete or partial transmural healing was associated with reduced risk of surgery (HR = 0.13 [0.05 - 0.38] ; p < 0.001), of subsequent hospitalization (HR = 0.25 [0.11- 0.56] ; p = 0.001) and therapeutic intensification (HR = 0.08 [0.03 - 0.20] ; p < 0.001). Complete transmural healing showed a lower risk of therapeutic intensification compared to partial transmural healing (p < 0.05).

Conclusion: Transmural healing assessed using MRI scores is associated with favourable outcomes in patients with CD and should be used as therapeutic target both in daily practice and clinical trials.

Disclosure: Nothing to disclose

OP273 MOLECULAR TRAJECTORIES OF REMISSION IN BIOLOGICS THERAPY OF IBD: PRIVATE DRUG SPECIFIC-SIGNATURES VS. COMMON TRANSCRIPT MODULES

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Introduction: Inflammatory bowel disease (IBD) is characterized by inadequate destructive immune responses fueled by a complex dysregulation of the mucosal cytokine network. Targeted therapies block pivotal pathophysiological principles (e.g. cytokines, signalling, leukocyte adhesion). Currently, no biomarkers for predicting or defining molecular remission across therapies are available, although it can be assumed that disease control with mucosal healing -regardless of the drug-specific MOA- is characterized by a shared molecular signature across therapies. Currently, the dynamics of shared gene expression networks (e.g. remodelling of extracellular matrix, epithelial regeneration) associated with molecular remission is unclear. A blueprint of unifying principles of molecular remission is needed to disentangle drug-specific immunological network alterations associated with existing and novel compounds. The aim of this study thus was to identify a drug-independent core expression signature in mucosal biopsies that might be applicable for an early prediction of molecular remission.

Aims & Methods: Patients with IBD that were treated with various biologics, including anti-TNFa (Infliximab, IFX), a4b7-integrin antagonist (Vedolizumab, VDZ) were enrolled into a prospective clinical and molecular characterization program with multiple planned endoscopies (up to 10 endoscopies over 14 weeks) and RNASeq from intestinal biopsies. In addition, Additional data were included from Phase IIa molecular medicine following the same setup and clinical trial in which Olamkicept (OLA), a sgp130Fc fusion protein specifically inhibiting the IL-6 trans-signaling pathway was administered open label. In all cases, biopsies from the sig-

moid colon were collected before (0h) and at several time points (+4h, +24h, 2 weeks, 6 weeks, and 14 weeks) after drug exposure. In total 55 patients were analyzed (UC: 29, CD: 26) and were exposed to the following biologic therapies (IFX: 19, VDZ: 20, OLA: 16). 36% of patients achieved clinical remission, whereas 21% were clear failures

Results: All investigated biologic treatments downregulated genes starting at 2 weeks after treatment. Importantly, this downregulation preceded the attenuation of clinical response parameters (HBI, Mayo). The majority of early downregulated genes were highly drug-specific and showed little overlap between the different biologic treatments; with only 1% of downregulated genes being shared amongst treatments at week 2, 2% at week 6, while at week 14 21% of all downregulated genes detected were shared between one or more treatments.

We identified a core set of eight differentially expressed genes, which were downregulated in mucosal tissues at week 14 in all remission patients in a drug-independent manner. These genes comprised e.g. Toll-like receptor 2 (TLR2), chemokine receptor 2 (CXCR2) and a cytokine receptor (CSFR). Importantly, using this 8-gene score, we were able to define a threshold of the dynamic behavior of the marker set that was able to predict clinical remission status already at week 2.

Conclusion: Our data indicate that different biologic therapies produce private transcriptomal signatures. However, changes also comprise drug-independent longitudinal changes of specific transcript modules, which were already detectable at an early timepoint (i.e. week 2) and were predictive of clinical remission at week 14. A prospective multicenter clinical study is ongoing to evaluate whether this information can be used to develop a "treat and test" strategy to decide already at early timepoints of exposure, which therapy is best for a patient.

Disclosure: Nothing to disclose

OP274 INTEGRIN EXPRESSION CHANGES ON THE T CELL SUBSETS INFLUENCE THE RESPONSE TO VEDOLIZUMAB IN INFLAMMATORY BOWEL DISEASE PATIENTS

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Introduction: Vedolizumab is a gut-selective alpha4beta7 integrin inhibitor approved for the treatment of Ulcerative Colitis (UC) and Crohn's disease (CD). The exact mechanism of action remains to be unraveled and there is no consensus whether the response to vedolizumab is associated with integrin expression profiles of the innate, adaptive immunity or both. Response prediction to vedolizumab is particularly relevant since it is a rather slow-acting molecule.

Aims & Methods: We investigated whether baseline levels and/or early changes in the integrin-expressing T cell subsets during the induction phase can predict the response to vedolizumab in inflammatory bowel disease (IBD) patients.

In this prospective multi-centric study, 71 patients with CD (n=28) or UC (n=43) with moderate-to-severe disease were included at the start of vedolizumab treatment. The response to vedolizumab was determined on a clinical, biochemical and endoscopic level at the end of the induction phase (week (W)14). The clinical response was defined as a drop in the Harvey Bradshaw index (HBI) of at least 3 points for CD and a reduction in Mayo score of at least 3 points with no rectal bleeding for UC. The biochemical response was defined as a 50% reduction of CRP or when the CRP normalized (< 10 mg/l) for CD and a 50% reduction or normalization (< 250mg/g) of calprotectin for UC. The endoscopic response was evaluated positive when there was a drop of at least 1 point in the SES-CD score for CD or the endoscopic Mayo score for UC. During the induction phase, peripheral blood mononuclear cells (PBMCs) were collected at W0, W2,

W6, W10 (only CD) and W14, before vedolizumab administration. Variation between the different centers was reduced by isolating the cells 6h after blood collection. The PBMCs were analyzed by flow cytometry to evaluate the CD4+/CD8+ Alpha4Beta7+, Alpha4Beta1+, AlphaEBeta7+ and Alpha-EBeta1+ T cell populations. Based on the distribution of the data, statistics were performed by an independent sample t-test or a Mann-Whitney U test.

Results: The flow cytometry analyses revealed that only the CD4+ Alpha-4Beta7+ T cell subset at baseline was significantly increased in UC patients with a favorable clinical (P= 0.042), biochemical (P=0.025) and endoscopic response (P= 0.054). This was not the case in CD. In CD, the baseline number of CD4+ Alpha4Beta1+ T cells was lower in clinical (P= 0.094) and biochemical responders (P= 0.004). In addition, lower baseline CD4+ AlphaEBeta1+ T cells and the CD8+ AlphaEBeta1+ T cells were also associated with a biochemical response in CD (P= 0.032 and P= 0.025), respectively. No other significant baseline or delta change differences were identified between the responders and non-responders in the other investigated T cell subsets in both UC and CD.

Conclusion: This prospective cohort study showed that in UC patients, clinical, biochemical and endoscopic response to vedolizumab treatment is associated with a high number of CD4+ Alpha4Beta7+ T cells in circulation at baseline. In CD patients, the relationship is less clear and the response is rather linked to a low number of Beta1+ T cells. A second cohort is being recruited to confirm our findings. The final aim is to build a predictive model that is feasible for use in clinical practice.

Disclosure: Support provided by Takeda.

OP275 GUT MICROBIAL METABOLIC FUNCTIONS ARE ASSOCIATED WITH ANTI-TNF EFFICACY IN IBD PATIENTS

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Introduction: An impaired interplay of the mucosal immune system and gut microbiota plays a critical role in the pathogenesis of human chronic inflammatory bowel disease (IBD).The impact of targeted cytokine blockade on intestinal microbial communities is still poorly understood. Here, we investigate the effect of anti-TNFα treatment on gut microbial community structure and functional properties in a prospective, longitudinal two-step study. We correlate our findings to therapeutic outcome and investigate fecal metabolite patterns associated with microbiota shifts upon therapy initiation.

Aims & Methods: We recruited two cohorts of patients initiating anti-TNFα therapy. Cohort #1 included IBD (n=12) and rheumatic disease (RD; n=17) patients who were exposed to anti-TNFα therapy were enrolled for longitudinal stool sampling at baseline and 2, 6 and 30 weeks after therapy induction. Specificity of the findings was assessed in an independent cohort #2 of 23 IBD patients (13 UC, 10 CD) treated with anti-TNFα or anti-α4β7 integrin. Intestinal microbial community structures were studied by V3-V4 16S rRNA gene amplicon sequencing. In-silico analysis of metabolic interactions among microbial species were performed to identify key metabolites indicative of clinical remission status. Stool metabolomics was performed in a subset of samples to validate functional predictions associated with therapy outcome.

Results: anti-TNFα treatment restores microbial diversity in IBD patients, but not RD patients. Assessment of microbial diversity indices is not suitable for the differentiation between remission and non-remission status in IBD patients. In contrast, in-silico analysis of microbial metabolite ex-

change shows an extensive perturbation of microbial metabolic cooperativity, which discriminates between anti-TNFα remitter and non-remitter. Inferred microbial metabolite exchange indicates e.g. altered inter-microbial metabolism of SCFA. Stool metabolomics validated increased butyrate to be associated with remission status.

Conclusion: We show that anti-TNFα treatment increases the gut microbial diversity and coupling of cross-feeding metabolic interactions towards the state of healthy individuals. Assessment of metabolic interactions in responders and non-responders to therapy may identify predictive microbial metabolite markers as well as aid our understanding how the intestinal microbiota modulates therapy outcome in IBD.

Disclosure: Konrad Aden has received funding from Pfizer to execute parts of this study. The grant did not affect study design at any time point. All other authors have nothing to disclose

New frontiers in pancreatic neoplasias
16:00-17:30 / F2

OP276 AGE, OVERWEIGHT AND INITIAL CYST SIZE ARE ASSOCIATED WITH THE RISK OF PROGRESSION OF BD-IPMN UNDERGOING FOLLOW-UP

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Introduction: Current guidelines do not suggest personalizing the follow-up of BD-IPMN without suspicious signs of malignancies according with their initial features of with patients' characteristics. Furthermore, the need to maintain follow-up (FU) in the long-term is debated.

Aims & Methods: To investigate the occurrence of progression of the cystic lesions and of Worrisome Features (WF) constituting a relative indication for surgery and analyse factors associated with them in a prospective cohort of IPMN-BD under FU. Data on BD-IPMNs diagnosed 2003-2017, without any indication for surgery at diagnosis and under FU in two institutions, were input in a prospective database containing initial patients' and cysts' characteristics. The primary outcome was the progression of the cyst defined as either an increased cyst's size (>2 mm), development of a new cyst or appearance of any indication for surgery. Occurrence of WF was separately considered as a secondary outcome. Fisher test and Student's t-test were used to analyze categorical and continuous variables. Survival probability was calculated with the Kaplan-Meier curve and Cox analysis employed to calculate hazard ratios (HR). A p< 0.05 was considered statistically significant.

Results: Of 530 BD-IPMN with mean age of 65.2 years, 62.4% were female, 54.7% were multifocal and the initial mean size of the largest cyst was 14.3 mm. The mean length of FU was 58.9 months. 32 deaths were recorded, of which 3 pancreas-related. 265 patients had any progression (50%) and 82 (15.5%) developed WFs or HRS; 13 patients were operated (2.8%) of whom 5 had a carcinoma. The rate of progression and occurrence of WFs were 101.9/1000 p-y and 31.5/1000 p-y. The mean time to any progression was 43.7 months and the mean time to WFs was 54.2 and 14% of patients developed the first progression event and 4.5% WF or HRS after 60 months. A ROC curve identified the cut-off of 15 mm as best discriminator of progression (sensitivity 67.9%, specificity 44.5%) and of WF/HRS appearance (sensitivity 64.6%, specificity 67.2%). In a multivariate Cox regression analysis, among initial patients' and cysts' characteristics: age (HR 1.01 per year; 95%CI 0.99-1.02; 0.060), BMI>25 (HR=1.32; 95%CI 1.02-1.71; 0.030), and cyst diameter >15mm (HR 1.32; 95%CI 1.03-1.69; 0.025) were associated with any progression. Only age (HR 1.026; 95%CI 1.00-1.048; 0.022) and

initial cyst diameter>15mm (HR 3.35; 95%CI 2.12-5.30; < 0.0001) were associated with development of WFs or HRS during follow-up. Sex, smoking, family history of any cancer or of pancreatic cancer, alcohol intake and multifocal cysts were not associated with progression risk, while previous diabetes was significant only at the univariate analysis.

Conclusion: In this cohort of BD-IPMNs, the rate of progression and of occurrence of WFs were 10% and 3% per year. A quote of these events occurred after 5 years of negative FU. Age, overweight and initial cyst size>15mm are predictors of progression. These data support the role of metabolic factors in determining progression of BD-IPMNs and offer the opportunity to tailor follow-up intervals based on simple criteria available at diagnosis.

Disclosure: Nothing to disclose

OP277 OXALIPLATIN AND 5-FLUOROURACIL (FOLFOX) IN ADVANCED WELL-DIFFERENTIATED DIGESTIVE NEUROENDOCRINE TUMORS: A MULTICENTER NATIONAL RETROSPECTIVE STUDY FROM THE FRENCH GROUP OF ENDOCRINE TUMORS (GTE)

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Introduction: Oxaliplatin-based regimens have shown promising antitumor activity in digestive neuroendocrine tumors (NETs), however the available data are limited. Our aim was to assess the tumor response and survival in a large series of patients treated with oxaliplatin and 5-fluorouracil (FOLFOX) for advanced digestive NETs.
Aims & Methods: All patients with advanced well-differentiated digestive NETs treated with at least 3 cycles of FOLFOX between 2004 and 2018 in 12 centers of the French GTE, were retrospectively included. Best response according to the RECIST 1.1 criteria, progression-free survival (PFS) and overall survival (OS) were evaluated. The prognostic factors for PFS were investigated by multivariate analysis using a Cox proportional hazard model including variables with a p value ≤ 0.20 in univariate analysis.
Results: One hundred and forty-nine patients were included. Primary tumor location was pancreas (n=88), small intestine (n=37), stomach (n=7), rectum (n=4) and unknown without lung tumor at CT scan (n=13). Partial response rate was of 31% for pancreatic NETs, 13% for small intestine NETs, 14% for gastric NETs, 25% for rectal NETs and 38% for unknown primary NETs. Median PFS were, respectively, 9, 9, 14, 4 and 6 months, and median OS were 30, 28, 31, 25 and 15 months. Significant poor prognostic factors for PFS after FOLFOX in digestive NETs were: progressive disease (HR=2.5, p=0.018), hepatic involvement > 50% (HR=1.8, p=0.009), prior targeted therapy (HR=1.5, p=0.048) and rectal primary tumor (HR=4.2, p=0.01). Among pancreatic NETs, the 9 insulinomas had a 22 months PFS versus 9 months for the others (p=0.025), and serum glucose normalization was obtained in 8 out of 9 cases.
Conclusion: FOLFOX has a promising clinical activity, especially in insulinomas.
Disclosure: Nothing to disclose

Bile duct stone management
16:00-17:30 / F3

OP278 ENDOSCOPIC MANAGEMENT OF DIFFICULT BILE DUCT STONES: RESULTS OF A RANDOMIZED TRIAL

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Introduction: Although ERCP is the reference standard, the optimal approach to efficient treatment of difficult bile duct stones is not standardized. While single operator cholangioscopy-guided laser lithotripsy (SOC-LL) and large balloon sphincteroplasty (LBS) are effective rescue techniques, their precise roles in the treatment algorithm is unclear.
Aims & Methods: To evaluate the role of SOC-LL and LBS for the treatment of difficult bile duct stones.
Patients with difficult bile duct stones were randomized to undergo SOC-LL or LBS. Difficult bile duct stones were defined as stones (≥12mm) that failed retrieval attempts using balloons or baskets and required advanced interventions. The main outcome measure was procedural efficiency defined as the ability to achieve ductal clearance without the need to cross-over to alternate treatment modality or require adjunctive mechanical lithotripsy. The secondary outcome measure was treatment costs.
Results: 66 patients were randomized equally to either cohort over a 2-year period. There was no significant difference in stone size (median, 15mm [IQR 12-18] vs. 14mm [IQR 12-15], p=0.097), number of stones (median, 3 [IQR 1-4] vs 3 [IQR 1-4, p=0.92]) or stone-duct size ratio (stone size/diameter of distal common bile duct in mm; median, 1.5 [IQR 1.0-1.8] vs. 1.3 [IQR 1.0-1.3], p=0.098) between the SOC-LL and LBS cohorts, respectively. More patients randomized to LBS required mechanical lithotripsy (33.3 vs. 3.0%, p=0.001) or cross-over to SOC-LL (27.3 vs. 6.1%, p=0.021) to achieve ductal clearance. On multivariate logistic regression analysis, after adjusting for patient demographics, stone characteristics and procedure details, not using SOC-LL (OR 13.5 [95% CI, 3.11-58.4], p=0.001) and stone-duct size ratio ≥1.2 (Odds ratio (OR) 5.0 [95% CI, 1.21-20.6], p=0.026) were significantly associated with procedural inefficiency. Although the procedural cost for SOC-LL was higher, there was no significant difference in total treatment costs between cohorts by generalized linear models (SOC-LL $16,684 vs. LBS $10,626; p=0.097).
Conclusion: When standard maneuvers fail, utilizing SOC-LL for the treatment of difficult bile duct stones should be the preferred first-line approach, particularly when size of the stone exceeds that of the distal bile duct.
Disclosure: Ji Young Bang, Shyam Varadarajulu and Robert Hawes are Consultants for Boston Scientific Corp. and Olympus America Inc.

OP279 EUS-DIRECTED TRANSGASTRIC ERCP (EDGE) VS LAPAROSCOPIC ASSISTED ERCP (LA-ERCP) VS ENTEROSCOPY ASSISTED ERCP (E-ERCP): A SINGLE CENTER EXPERIENCE

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Introduction: EUS-directed Transgastric ERCP (EDGE) is a novel technique for managing pancreaticobiliary diseases in patients with a history of Roux-en-Y Gastric Bypass (RYGB). Laparoscopic-assisted ERCP (LA-ERCP) and Enteroscopy-assisted ERCP (E-ERCP) are the current standard of care and these procedures can be challenging with limited success.
Aims & Methods: The aim of this study was to compare outcomes of EDGE, LA-ERCP and E-ERCP at a single tertiary-care academic center. Patients with a history of RYGB who underwent these procedures between January 2015 and March 2019 were included. Patient demographics, procedure time, technical success and complications of each group were recorded. Technical success was defined as cannulation of the intended duct. 'Difficulty of procedure' was defined as level of difficulty documented by per-

forming endoscopist or defined as difficult if there was performance of precut sphincterotomy or >2 failed attempted cannulations of intended duct. Statistical analysis was performed using SPSS 23 (IBM, Armonk, NY).
Results: Forty-eight patients (18 EDGE, 19 LA-ERCP and 11 E-ERCP) were included in this study. Mean procedure time for EDGE patients was 72 ± 27 minutes, compared to 150 ± 58 and 108 ± 39 minutes for LA-ERCP and E-ERCP, respectively (p= < 0.01). The difficulty level was recorded as 'not difficult' for 100% (18/18) of EDGE procedures, compared to 79% (15/19) for LA-ERCP and 45% (5/11) for E-ERCP patients (p=< 0.01). Technical success for EDGE was 100% (18/18) compared to 89% (17/19) and 82% (9/11) for LA-ERCP and E-ERCP, respectively (p=0.21). While none of the EDGE patients developed post-procedure pancreatitis, this was observed in 5% (1/19) of LA-ERCP and 9% (1/11) of E-ERCP patients (p=0.47). The hospital length of stay was shorter for EDGE patients at 1.09 days, compared to 2.35 and 3.47 days for LA-ERCP and E-ERCP, respectively (p=0.04).

	EDGE (n=18)	LA-ERCP (n=19)	E-ERCP (n=11)	p-value
Age (mean)	61.78 +/- 11	61.52 +/- 13	68 +/- 16	0.39
Gender (F)	78% (14)	68% (13)	64% (7)	0.69
Indications:				0.96
Choledocholithiasis	39% (7)	68% (13)	27% (3)	
CBD Dilation	28% (5)	0% (0)	9% (1)	
PD Dilation	11% (2)	0% (0)	0% (0)	
Biliary leak/sludge/stricture	28% (5)	0% (0)	27% (3)	
Cholangitis	0% (0)	5% (1)	18% (2)	
Pancreatitis	0% (0)	11% (2)	18% (2)	
Papillary stenosis	0% (0)	5% (1)	0% (0)	

[Baseline Characteristics of patients]

Conclusion: Our study indicates that EDGE is characterized by significantly shorter procedure time and lower rates of procedural difficulty when compared to LA-ERCP and E-ERCP. We also observed non-statistically significant trend towards superior safety and efficacy profile of EDGE.
Disclosure: Nothing to disclose

Risk assessment, diagnosis and management in colon cancer
16:00-17:30 / Barcelona

OP280 EUS-GUIDED PORTAL VENOUS BLOOD ACQUISITION FOR CIRCULATING TUMOUR CELLS IN PATIENTS WITH COLORECTAL CANCER

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Introduction: Analysis of circulating tumour cells (CTCs) has potential to be a prognostic marker for metastasis in different types of cancer (1). As opposed to peripheral blood collection, the use of endoscopic ultrasound (EUS) to acquire portal venous blood (PVA) for circulating tumour cells (CTC) enumeration has only been described for pancreatic cancer. The role of EUS- PVA in enumerating CTC's for other types of cancer is uncertain.
Aims & Methods: Hence, the aim of the current study is to perform a feasibility study on EUS PVA for enumerating and characterising CTC's in patients suffering from colorectal cancers. We hypothesise that EUS-guided PVA is safe, feasible and effective in obtaining CTC.
Patients suffering from stage 2 to 4 colorectal carcinomas were recruited. Recruited patients had one 9 ml aliquots of peripheral blood collected at the same time of the EUS procedure. The patient then underwent EUS-PVA and two sets of 9 ml aliquots of portal venous blood were collected (PVB). During EUS-PVA, the liver was first assessed for presence of occult metastasis from the duodenum (right lobe) and also the stomach (left lobe).

Under EUS-guidance, the left and right PVs were identified. After verifying flow signal by Doppler, a 19-gauge EUS-FNA needle was advanced transhepatically into the portal vein and two sets of 9 ml aliquots of blood were aspirated. The puncture site was then be monitored under EUS for 3 minutes to observe for any bleeding before the needle was withdrawn. Epithelial-derived CTCs were sorted magnetically based on expression of epithelial cell adhesion molecules. Only those with a proper morphology and found to be CD45 negative and positive for cytokeratins 8 and 18 were considered to be CTCs.
Results: This prospective, single-centre study was performed in the Prince of Wales Hospital in Hong Kong between December 2016 and March 2019. 56 patients with stage 2 and 3 colorectal carcinomas were recruited. Technical success was 100% and none of the patients suffered from adverse events. The colonic tumors were located in the ascending colon (11%), transverse colon (11%), descending colon (7%), sigmoid colon (50%), rectum (21%). 85% of the patients had T2 and T3 tumours and 42.9% were node positive. CTCs were obtained in 80.5% of the PVA and 37.5% in peripheral blood. The mean (S.D.) of CTCs obtained by EUS-guided PVA was significantly higher than that in peripheral blood samples [154.6 (213.4) vs 6.78 (11.2), P< 0.0001].
Conclusion: This study has shown that EUS-guided PVA to be a safe, feasible and effective method in collecting CTCs for enumeration and characterisation in colonic cancer. More CTC's were obtained from the portal vein and the numbers were significantly higher than that of peripheral blood. Further studies are required to be performed to evaluate its potential as a prognostic marker for survival and liver metastasis in colorectal cancer patients.
References: 1. Cristofanilli M, Budd G, Ellis M et al. Circulating Tumor Cells, Disease Progression, and Survival in Metastatic Breast Cancer. New England Journal of Medicine. 2004;351(8):781-791. doi:10.1056/nejmoa040766
2. Catenacci D, Chapman C, Xu P et al. Acquisition of Portal Venous Circulating Tumor Cells From Patients With Pancreaticobiliary Cancers by Endoscopic Ultrasound. Gastroenterology. 2015;149(7):1794-1803.e4. doi:10.1053/j.gastro.2015.08.050
Disclosure: Nothing to disclose

OP281 CLINICAL IMPORTANCE OF COLONOSCOPY IN PATIENTS WITH EARLY GASTRIC CANCER TREATED BY ENDOSCOPIC SUBMUCOSAL DISSECTION (COMPARISON WITH PATIENTS WITH POSITIVE FECAL IMMUNOCHEMICAL TEST RESULTS)

Yamaguchi Y., Ebi M., Tashiro T., Yamamoto K., Ozeki T., Sugiyama T., Adachi K., Hijikata Y., Ogasawara N., Funaki Y., Sasaki M., Kasugai K.
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Introduction: Second primary cancers are a leading cause of morbidity and mortality among cancer survivors all over the world. Colorectal neoplasms are the most commonly observed tumors in patients with gastric cancer.
Aims & Methods: We examined the usefulness of colonoscopy (CS) for patients undergoing gastric endoscopic submucosal dissection (ESD). Of the 312 patients who underwent ESD for early gastric cancer in the 3 years between January 2015 and December 2017, 143 patients receiving CS were included (ESD group) in this study. And 874 asymptomatic patients who underwent CS because of positive fecal immunochemical test (FIT) during the same period were selected (FIT group). Propensity score matching was used to adjust baseline characteristics (BMI, alcohol, smoking, diabetes mellitus, hypertension, hyperlipidemia, liver disease, renal failure and other organs cancer) between two groups. In this study, we compared with the background of two groups and statistically analyzed.
Results: The total number of colorectal neoplasm were found in 90 cases (62.9%) in the ESD group, on the other hand, 81 cases (56.6%) in the FIT group (*p*=0.012). Advanced adenoma and carcinoma (AAC) were found 30 cases (20.1%) of ESD group and 16 cases (11.2%) of FIT group (*p*< 0.01).
Conclusion: In patients undergoing gastric ESD, CS appears to be necessary for detecting synchronous double neoplasms.
Disclosure: Nothing to disclose

OP282 BACTERIAL ALTERATIONS IN POST-CHOLECYSTECTOMY PATIENTS ARE ASSOCIATED WITH COLORECTAL CANCER

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Introduction: Previous studies showed that cholecystectomy increased the enterohepatic recirculation rates and the secretion rate of bile acids, which made an increased exposure of the bile acid pool to gut bacteria. However, what kind of alteration after cholecystectomy in patients was unclear. Moreover, many meta-analyses also indicated inconsistent incidences of colorectal cancer (CRC) in patients after cholecystectomy. Thus, our study was to investigate the changes and roles of bacterial microbiota after cholecystectomy and tried to clarify the clinical significance of the changes.

Aims & Methods: 104 subjects were recruited for two groups, post-cholecystectomy patients (PC, n=52) and healthy controls (HC, n=52). 9 of PC patients had precancerous lesions and CRC (preCA_CRC), which confirmed by colonoscopy mucosal pathology. The demographic data and basic clinical data of each group were recorded. Qualified stool samples were collected for 16S rRNA gene V3-4 region amplicons seqencing to profile the overall structure of the bacterial microbiota. Based on the Operational Taxonomic Units (OTUs), bacterial composition, functional annotation, and the correlation with environmental factors were analyzed respectively.

Results: The species richness of gut bacterial microbiota was increased in PC patients, and the composition was quite changed. At the genus level, the abundance of *Bacteroides, Parabacteroides* which took part in bile acid metabolism and *Prevotella* which could promote inflammation increased; the abundance of *Faecalibacterium* which participated in butyrate and short-chain fatty acids biosynthesis and *Bifidobacterium* which could inhibit inflammation decreased. *Megamonas funiformis* and *Lactobacillus mucosae* were characteristic species which could distinguish PC patients from HC. Functional analysis showed that pathways in cancer, especially in CRC, were enriched in PC group. We collected about 10 kinds of indexes as environmental factors for correlation analysis with bacterial composition. Furthermore, the duration after cholecystectomy was the critical factor, which mainly affected the composition of the bacterial microbiota. Although there was no statistical difference, preCA_CRC patients had lower species richness than the subjects of the cancer-free patients after cholecystectomy. The abundance of *Sutterella* and *Flavonifractor*, two protective genera further decreased in preCA_CRC patients, additionally, the abundance of *Megamonas funiformis* was significantly negatively correlated with the progression of CRC.

Conclusion: Our study showed a specific alteration in PC patients, and the duration after cholecystectomy was the critical factor which affected the bacterial composition. *Megamonas funiformis* was not only the characteristic species of PC patients, but also associated with the progression of CRC. These findings suggest that it is necessary to pay more attention to the long-term follow-up of PC patients, and *Megamonas funiformis* may play a pivotal role in related-disease studies.

Disclosure: Nothing to disclose

OP283 COLORECTAL CANCER DRIVES LOSS OF SIRP ALPHA AND INCREASED CD103 ON LAMINA PROPRIA DENDRITIC CELLS IN MACROSCOPICALLY HEALTHY COLONIC MUCOSA: A PATHWAY FOR IMMUNE EVASION?

Pring E.[1,2], Durant L.[3], Noble A.[3], Gould L.[4], Fletcher J.[4], Dilke S.[3], Malietzis G.[5], Athanasiou T.[2,6], Jenkins J.T.[7], Knight S.C.[8]
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Introduction: Dendritic cells (DC) are the major antigen presenting cells of the immune system and orchestrate downstream cellular immune responsesorchestrate the cellular immune response. Within the colonic mucosa, DC populations can be subdivided based on expression of SIRP-alpha (CD172a) and CD103 (alpha E integrin). SIRP-alpha inhibits Fc receptor mediated functions in cells bearing its receptor (CD47) and in doing so recognises the CD47 expressing cell as "self". SIRP-alpha expressed on myeloid cells (DCs and macrophages), via the CD47/SIRP-alpha axis, plays an essential role in "self" recognition, protecting healthy cells from phagocytosis.

CD103 is a mucosal tissue marker and CD103+DC play a vital role in maintaining intestinal immune homeostasis by promoting protective immune responses, including upregulation of gut-homing markers on T cells thus inducing a "tolerogenic" immune response. CD103 expressing DCs are responsible for upregulating CCR9 and $\alpha4\beta7$ - cell surface markers on T cell subtypes essential for homing to mucosal surfaces including the gut.

Aims & Methods: The aim of this study was to explore the effect colorectal cancer has on this important immunological axis in the gut and in doing so identify a further pathway by which cancer evades the immune system. Colonic biopsies were taken from macroscopically healthy mucosa in disease free subjects (n=12) at colonoscopy and colorectal cancer (CRC) patients (n=8) at the time of surgery. Lamina-propria leucocytes were isolated by enzymatic tissue digestion which was performed in a two stage process with DTT and EDTA followed by collagenase and liberase. Cell surface staining was performed using fluorochrome antibodies for SIRP-alpha and CD103. Expression of SIRP-alpha and CD103 on DCs was examined by flow cytometry.

Results: Proportions of CD103-veSIRPa+ve and CD103+SIRPa+ DC populations were significantly reduced in the CRC group (p< 0.0001 and p< 0.0002) whilst CD103+veSIRPa-ve and CD103-veSIRPa-ve DC populations were significantly increased in the CRC group (p< 0.0015 and p< 0.0001).

Conclusion: Many cancers themselves highly express CD47 which allows evasion of the cellular immune response. Herein we demonstrate changes to DC signalling in cancer perhaps reducing an appropriate aggressive response to CRC by loss of SIRP-alpha expression. Notably these immunological changes are taking place in what appears "healthy" bowel tissue away from the tumour site.

Disclosure: Nothing to disclose

OP284 WITHDRAWN

OP285 IS DECOMPRESSING STOMA BETTER THAN STENT AS BRIDGE TO SURGERY FOR LEFT-SIDED OBSTRUCTIVE COLON CANCER? A NATIONWIDE, PROPENSITY-SCORE MATCHED ANALYSIS

Veld J.[1], Amelung F.[2], Borstlap W.[1], van Halsema E.[1], Consten E.[2], Siersema P.[3], ter Borg F.[4], van der Zaag E.[5], de Wilt H.[3], Fockens P.[1], Bemelman W.[1], van Hooft J.E.[1], Tanis P.[1]

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Introduction: Bridge to elective surgery with self-expandable stent (SEMS) placement is still a debated alternative to emergency resection of left-sided obstructive colon cancer (LSOCC) because of oncological concerns. Another bridge to surgery strategy is decompressing stoma construction. However, studies comparing decompressing stoma and SEMS are scarce. If we could directly compare these two methods, we may improve treatment and consequently health-related outcomes such as mortality and morbidity in patients with LSOCC.

Aims & Methods: Our aim was to directly compare decompressing stoma and SEMS as bridge to surgery strategies for LSOCC. All patients with LSOCC who were treated with curative intent between 2009 and 2016 were included from the Dutch ColoRectal Audit, a prospective, (mandatory) national registry. Additional diagnosic, procedural, and long-term outcome data were retrospectively collected through individual patient files. Patients with locally advanced tumours were excluded from the analysis. Following propensity-score matching, patients treated with a decompressing stoma were compared with patients treated with SEMS placement as bridge to surgery.

Results: Seventy-five of 77 Dutch hospitals completed data of 345 decompressing stoma and 229 SEMS patients treated with curative intent. Propensity-score matching resulted in two groups of each 121 patients. Median follow-up was 36 (IQR 15-59) months and 31 (IQR 15-56) months, respectively (p=0.593). Decompressing stoma patients showed more primary anastomoses (86% versus 75%, p=0.024), more stomas after resection (67% versus 29%, p< 0.001), fewer major resection-related complications (6% versus 15%, p=0.023), and more reinterventions including stoma reversal (58% versus 28%, p< 0.001). Following decompressing stoma and SEMS, 3-year locoregional recurrence was 12% and 19% (HR 0.62, 95% CI 0.30-1.28, p=0.200), 3-year disease free survival 64% and 57% (HR 0.90, 95% CI 0.61-1.33, p=0.600), and 3-year overall survival 78% and 72% (HR 0.77, 95% CI 0.48-1.22, p=0.260), respectively.

Conclusion: This nationwide, propensity-score matched study comparing decompressing stoma and SEMS for non-locally advanced LSOCC revealed both advantages and disadvantages of either of the two bridging techniques. Based on the currently available evidence, there is no scientific basis to recommend one over the other.

Disclosure: J.V. Veld, F.J. Amelung, W.A.A. Borstlap, E.E. van Halsema, E.C.J. Consten, P.D. Siersema, F. ter Borg, E.S. van der Zaag, J.H.W. de Wilt, P. Fockens, W.A. Bemelman, J.E. van Hooft, and P.J. Tanis have no conflicts of interests or financial ties to disclose for this specific study. The study was funded by unrestricted research grants from Citrienfonds and Dutch Cancer Society (KWF). Outside of the submitted work, J.E. van Hooft received a grant from Cook Medicals and a consultancy fee from Boston Scientific and Medtronics. P.D. Siersema receives grant support from Pentax Medical, Norgine, EndoStim and Motus GI, and is on the advisory board of Pentax, Ella-CS and Boston Scientific.

HPB on fire
16:00–17:30 / Hotspot

OP286 DEVELOPMENT AND VALIDATION OF A PATIENT REPORTED OUTCOME MEASUREMENT IN ACUTE PANCREATITIS: THE PAN-PROMISE STUDY

de-Madaria E.[1], Sánchez-Marin C.[1], Carrillo I.[2], Chooklin S.[3], Mejuto R.[4], Mauriz V.[4], Márta K.[5], Hegyi P.[6], Barbu S.[7], Lauret-Braña E.[8], Gomes A.P.[9], Martins R.[9], Lourenço L.C.[9], Nunes V.[9], Matia R.[9], Ruiz-Rebollo L.[10], Garcia-Rayado G.[11], Lozada-Hernández E.E.[12], Pereira J.A.[13], Negoi I.[14], Espina S.[15], Bernal V.[15], Bajador-Andreu E.[15], Kamal A.[16], Hollenbach M.[17], Litvin A.[18], Marra-Lopez Valenciano C.[19], Bolado F.[19], Vargas R.D.[20], Czako L.[21], Gasiorowska A.[22], Fraile-González M.[23], Abando-Zurimendi A.[23], Cheon Y.K.[24], Triantafyllou K.[25], Gatos C.[25], Romero-Mosquera B.[26], Rodríguez-Oballe J.A.[27], Miguel-Salas I.[27], Pascual-Moreno I.[28], Singh V.K.[16], Mira J.J.[2]

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Introduction: The development of clinical trials in acute pancreatitis (AP) is limited by the absence of adequate outcome variables. Organ failure (OF) and mortality are infrequent, so thousands of patients are needed to detect differences among treatment arms. Despite being the patients the center of the medical act, their assessment is rarely considered.

Aims & Methods: PAN-PROMISE aims to develop and validate a Patient Reported Outcome Measurement scale (PROMS) in AP. Reliability, content validity, apparent, construct and empirical validity indexes were calculated. Firstly, a qualitative study was carried out in patients and gastroenterologists from 2 centers; 7 symptoms were retrieved and the PROMS instrument was designed (PROMISE scale).

Afterwards, an international prospective multicenter cohort (29 centers from 15 countries, 527 patients) was performed to validate the instrument. PROMISE scale was measured in the 1st 24h, 48h, 5th and 7th day, at discharge and 15d after discharge.

Results: The 7 items of PROMISE are grouped into a coherent measure giving rise to a single dimension with factor saturations of the items that exceed the minimum of 0.50: between 0.63 and 0.75, explained variance 45.1% in the mild cases and 0.57-0.73, variance explained 43.3% in the moderate-to-severe cases. The internal consistency of the relationships between the items exceeds the degree of adjustment required for a new instrument of this type: Cronbach's Alpha= 0.77 in mild cases and 0.76 in moderate-to-severe. The stability of the measurement calculated by test-retest (at discharge and 15d after discharge) confirms the reproducibility of the measurement with values in the Student's T statistic without statistical significance, p> 0.05 (the clinical improvement at discharge is sustained after an adequate temporary period). The total PROMISE score was directly related to the health status score of the EORTC QLQ-C30 quality of life scale (beta -1.34, 95% CI -2.55, -0.13). PROMISE allows detecting changes in the clinical evolution of patients during hospital admission: total value

of the scale (maximum 35) at admission 33.1 48h 19.6, 5ºd 11.1, 7ºd 7.7, at discharge 5.3 (p < 0.0001). Mild cases presented lower scores in the evolution than moderate-to-severe severe ones (p < 0.001) except at discharge.
Conclusion: The PROMISE scale satisfies standardized criteria of reliability and validity. PROMISE can be used to test new therapeutic interventions in AP to detect differences in the patients´ assessment of their symptoms.
Disclosure: Nothing to disclose

OP287 PRELIMINARY DATA OF THE PINEAPPLE-P STUDY: 30-80% OF ACUTE PEDIATRIC PANCREATITIS IS NOT DIAGNOSED DUE TO THE LOW AWARENESS

Mosztbacher D.[1,2], Parniczky A.[2,3], Juhász M.F.[2], Tél B.[1], Erős A.[1], Nagy A.[4], Tokodi I.[5], Kaán K.[1], Horváth E.[1], Ila V.[6], Tóth A.[7], Demcsák A.[7,8], Kadenczki O.[9], Ocskay K.[2], Dohos D.[2], Szentesi A.[2,10], Hegyi P.[2,10], Hungarian Pancreatic Study Group

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Introduction: Abdominal pain is one of the most common complaints in childhood and it is responsible for 10-20% of emergency visits. One of the causes of abdominal pain in children is acute pancreatitis (AP). Our retrospective data collection shows that the prevalence of acute pediatric pancreatitis (APP) depends on the diagnostic awareness, hence ranges between 0.2-1.14% in children with abdominal pain.
Aims & Methods: The aim of the PINEAPPLE-P study is to estimate the real worldwide incidence of APP in children with abdominal pain. Furthermore, we would like to develop an EBM guideline to establish a scoring system in order to evaluate the necessity of diagnostic steps for APP in children with abdominal pain. Patients were divided into two groups: 1) abdominal pain with APP (APP group) 2) abdominal pain without APP (non-APP group). PINEAPPLE (Pain In Early phase of Pediatric Pancreatitis) is a registered (ISRCTN35618458), observational, multinational clinical trial (http://www.ncbi.nlm.nih.gov/pubmed/26641250). In the PINEAPPLE-P subtrial detailed patient data are collected, serum pancreatic enzyme measurement (sPEM) and abdominal imaging are performed prospectively for children with abdominal pain turning up at ER units. Until now 769 patients have been enrolled.
Results: 1.7% (13/769) of the children with abdominal pain was diagnosed with APP. The diagnosis was based on the fulfilment of all three diagnostic criteria (abdominal pain, sPEM elevation more than three times upper limit of normal, alteration on imaging characteristic for AP) in 6 patients (46.2%). Beside the abdominal pain in 5 cases (38.5%) the sPEM elevation and in 2 cases (15.4%) the imaging were positive for APP. Epigastric (46.2%) and left upper abdominal pain (23.1%) occurred significantly more often in children with APP than in non-APP group (p=0.004, p=0.01). Patients with APP had abdominal pain for significantly longer period of time than non-APP patients (151.4±256.8 hours vs 70.2±140.9 hours; p=0.0043). Significantly more patients had positive family history for pancreatitis in APP group compared to non-APP group (53.8% vs 13.8%; p< 0.0001). Positive family history of pancreatitis and upper abdominal pain outstanding more than 3 days were characteristic for APP.
Conclusion: The real incidence rate of APP is 1.7%. Diagnostic workup for APP should be performed in children with upper abdominal pain outstanding more than 3 days and positive family history for pancreatitis.
Disclosure: Nothing to disclose

OP288 THE ROLE OF HBSAG LEVELS IN THE OUTCOMES OF NON-CIRRHOTIC PATIENTS WITH HBEAG-NEGATIVE CHRONIC HEPATITIS B WHO DISCONTINUE LONG-TERM ANTIVIRAL THERAPY

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Introduction: HBsAg serum levels at the end of treatment (EOT) have been associated with subsequent HBsAg loss in patients with HBeAg- negative chronic hepatitis B (CHBe-) who discontinue long-term nucleos(t)ide analogues (NA). However, their prognostic value for predicting post-NA relapse remains uncertain. This study assessed relapse, retreatment and HBsAg loss rates based on HBsAg levels at EOT in a large cohort of non-cirrhotic CHBe- patients from 4 liver clinics in Greece.
Aims & Methods: The study included 136 patients (M/F: 87/49, age: 55±23 years) who discontinued NA therapy after a minimum on-NA virological remission of 5.65± 2.39 years and had at least 12 months of post-NA follow-up. Patients with coinfection, cirrhosis, cancer or liver transplantation were excluded. Patient characteristics before therapy as well as ALT, HBV DNA and HBsAg levels at EOT and post-NA were recorded. Patients were divided in 3 groups based on EOT HBsAg levels: A:≤100 IU/mL, B:>100-1000 IU/mL, C:>1000 IU/mL. Study endpoints were virological relapse (HBV DNA>2000 IU/mL), clinical relapse (HBV DNA>20,000 IU/mL & ALT>ULN), retreatment and HBsAg loss.
Results: The median post-NA follow-up was 20 (IQR: 14-66) months. Cumulative rates of virological relapse did not differ significantly among patients of group A, B, C being 46%, 62%, 46% at 6 and 51%, 67%, 77% at 12 months, respectively (log-rank, P=0.25). Cumulative rates of clinical relapse were significantly different among groups A, B, C and were 16%, 30%, 36% at 6 and 16%, 30%, 44% at 12 months, respectively (log-rank, P=0.03). No new case of clinical relapse was observed after 12 months and only two cases of virological relapse were observed between 12 and 24 months of post-NA follow-up. Cumulative retreatment rates differed significantly between group A, B, C being 8%, 18%, 29% at 6 and 8%, 22%, 32% at 12 months, respectively (log-rank, P=0.01). Finally, cumulative rates of HBsAg loss also differed significantly among groups A, B, C being 40%, 9%, 7% at 12 months, respectively (log-rank, P< 0.001).
Conclusion: Post-NA outcomes differ significantly in CHBe- patients with different EOT HBsAg. Patients with EOT HBsAg ≤100 IU/mL have significantly lower risk of clinical relapse or retreatment and higher probability of HBsAg loss. Therefore, non-cirrhotic CHBe- patients with HBsAg ≤100 IU/mL can safely stop antiviral therapy and often achieve post-NA functional cure (HBsAg loss) in the first 12 months after discontinuation.
Disclosure: Nothing to disclose

OP289 SIMULTANEOUS BARIATRIC SURGERY AND LIVER TRANSPLANT ASSOCIATED WITH WORSE OUTCOMES

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Introduction: Obesity is directly linked with development of non-alcoholic steatohepatitis (NASH), which is one of the leading indications for

liver transplantation (LT). Bariatric surgery (BS) in the pre-LT setting has emerged as a successful treatment option for obesity, which improves transplant-free survival and other outcomes, or is used as a way to decrease the BMI and positively influence the patient's transplant candidacy status. BS at the time of transplant (i.e. Sleeve Gastrectomy) has been argued to decrease costs, length of stay (LOS), stress and pain in small studies. To date, larger studies examining outcomes lack.

Aims & Methods: The aim was to determine inpatient outcomes of patients undergoing simultaneous BS and LT compared to LT alone. Case-control study using the 2012-2016 NIS. All patients with ICD9-10CM procedural codes for LT were included. Patients who did not undergo BS with a BMI< 30kg/m², and patients undergoing LT after having undergone BS during the same admission were excluded. The cohort was stratified into two groups depending on whether they had undergone simultaneous BS at the time of LT or not. Primary outcome was determining the odds of inpatient mortality in patients undergoing simultaneous BS at the time of LT compared to patients who underwent LT alone. Secondary outcomes included determining inpatient morbidity, resource utilization, hospital length of stay (LOS), and inflation-adjusted total hospital costs and charges. Multivariate regression analyses were used to adjust for age, gender, Charlson Comorbidity Index, income in patient zip code, hospital region, location, size and teaching status.

Results: A total of 32,580 patients were identified as having LT in the study period, of which 255 underwent simultaneous BS. The mean patient age was 30.1 years in patients who underwent simultaneous BS compared to 55.7 years in patients who underwent LT alone (49% and 39% were female, respectively). For the primary outcome, patients undergoing simultaneous BS had adjusted mortality odds of 14.01 (p< 0.01) compared to patients undergoing LT alone.

For the secondary outcomes, patients with simultaneous BS also had increased odds of shock and total parenteral nutrition (TPN), compared to LT alone. Patients undergoing simultaneous BS had increased additional adjusted hospital costs, additional hospitalization charges and LOS (Table 1).

Variable	Adj. OR / Adj. Mean	95%CI	p-value
Inpatient Mortality	14.05	4.76-41.49	<0.01
Shock	5.73	2.36-13.91	<0.01
TPN	9.42	2.58-34.34	<0.01
AKI	0.73	0.37-1.43	0.36
Multi-organ failure	1.04	0.56-1.98	0.89
ICU	1.55	0.75-3.24	0.24
Additional Adjusted Costs	$177,698	93309,262088	<0.01
Additional Adjusted Charges	$555,072	283609,826536	<0.01
Additional Adjusted LOS (days)	29.1	16.7,41.4	<0.01

[Adjusted odds ratio and additional adjusted means in patients undergoing simultaneous BS at the time of LT compared to patients undergoing LT alone.]

Conclusion: Patients undergoing simultaneous bariatric surgery at the time of liver transplant display increased odds of inpatient mortality, morbidity, hospital costs, charges and length of hospitalization during the index admission for liver transplant. The outcomes may vary significantly with existing studies, as not only sleeve gastrectomies were included in this study, but all varieties of bariatric surgical procedures. This may reflect the burden that an additional surgical procedure may impose on patients undergoing a liver transplant. Large prospective studies are needed to better elucidate the outcomes of patients not only during the index admission for liver transplant, but also in the longer term.

Disclosure: Nothing to disclose

OP290 ITALIAN MULTICENTRIC SURVEY ON DAILY PRACTICE FOR AUTOIMMUNE PANCREATITIS: CLINICAL PRESENTATION, DIAGNOSIS, TREATMENT AND EVOLUTION TOWARD PANCREATIC INSUFFICIENCY

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Introduction: Autoimmune pancreatitis (AIP) is a peculiar form of chronic pancreatitis of presumed autoimmune etiology. Several guidelines have been published in recent years. An attempt to unify the different guidelines have hesitated in the International Consensus Diagnostic Criteria (ICDC) guidelines for AIP. However the application of these guidelines can be complex and articulated. Furthermore the natural history, the best treatment strategy and the final evolution of this relatively new disease is not well known.

Aims & Methods: The aim of this study is to analyze, in a large cohort of patients from several Italian centers, representative of all national area, the daily practice in "real lyfe" regarding AIP, in terms of diagnosis, treatments, relapses, long-term outcomes and adherence to the ICDC guidelines. This observational multicenter retrospective survey was promoted and coordinated by the Italian Association of Hospital Gastroenterologists (AIGO), and was endorsed by AISP (Italian Association for the Study of the Pancreas). Data from 173 AIP patients from 14 different institutions in Italy, distributed along the entire national territory, were retrospectively analyzed.

Results: 106 patients were classified as type 1 AIP, 48 as type 2 AIP and 19 as AIP-Not Otherwise Specified. Epidemiological, clinical, radiological, serological characteristics, relapses and outcome were similar to the previously reported ones for different types of AIP. However, in our cohort endoscopic histology was available merely in 86/173 (49.7%). Pancreatic EUS-FNA/B cyto-histology was obtained more frequently in AIP1 (57/106 patients, 53.8%) compared with AIP2 (13/48 patients, 27.1%) (p< 0.01), and was judged diagnostic for AIP in 43/57 (75.4%) AIP1, 10/13 (76.9%) AIP2 (p= 0.91). EUS-FNA/B of the pancreas was performed mostly in the focal form of AIP (85% of cases).

In the overall cohort an endoscopic histology diagnostic for AIP was obtained in only 61/173 (35.2%) of patients.

Most patients (123/173, 71.1%) were initially treated with steroids with a success rate of 92%. A maintenance steroid therapy was administered in 31/123 (25.2%).

Immunosuppressant drugs were rarely used (10.9%) and Rituximab in only 1.7%.

Steroid trial for diagnosis of AIP was performed in only 75/173 patients (43.3%) of patients and it was considered positive, in accordance to ICDC criteria, in 70/75 (93.3%).

Applying the ICDC criteria to our cohort of patients, a diagnostic mismatch in sub-classification between type 1 and type 2 AIP was founded in about one-third of cases, and 26 (15.2%) patients did not have enough diagnostic criteria for any type of AIP.

Fecal elastase-1 was evaluated in 31.2%, and it was pathologic in 59.2% of cases.

Conclusion: In our cohort of AIP patients, although diagnosis and classification for subtype was frequently possible, the low use of histology and steroid trial for diagnosis of AIP is probably responsible for a mismatch in subclassification. These findings showed that the ICDC Criteria for AIP are difficult to apply in daily-clinical practice, confirming what previously observed by other authors, and the need for modification and simplification of such criteria.

The majority of patients received steroids as initial treatment and as maintenance therapy, with a very high response rate. Immunosuppresants and Rituximab were rarely used.

Finally, the rate of exocrine pancreatic insufficiency development is not routinely investigated during the follow up of AIP, but is rather common in AIP patients. Fecal elastase test is inexpensive, non-invasive, and largely available, its use should be recommended.

Disclosure: Nothing to disclose

OP291 PRECISION ONCOLOGY IN PANCREATOBILIARY CANCERS: A LONGITUDINAL STUDY

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Introduction: Next-generation sequencing is widely used to identify therapeutic options for advanced cancer patients, but its utility in patients with pancreatobiliary cancer is not fully understood. We evaluated the rate of biologically actionable mutations and their impact on therapeutic decision-making in patients with pancreatobiliary cancers.

Aims & Methods: We conducted a retrospective cohort study of patients seen at Taussig Cancer Institute, Cleveland Clinic between 2013-16 with incurable solid tumor malignancies, in whom FoundationOne™ (Cambridge, MA) tumor genomic profiling was ordered. Genomics tumor board (GTB) recommendations and treatment decisions (on label, off label, or clinical trials) based on said recommendations were reviewed.

Results: Six hundred patients with solid tumor malignancies were included, of whom 53 had pancreatobiliary malignancies. For these, median age was 59.6 years, 62.2% (33/53) of patients were female, 86.8% (46/53) were Caucasian, and 11.3% (6/53) were African American. Eight samples (15.1%) had inadequate tissue. Twenty-seven (60%) had biologically actionable alterations. Of these, 21 were recommended treatment including clinical trials (N=19) or off-label drugs (N=2). The most common actionable targets for therapy were FGFR (5/21) and CDKN2 (3/21). Of patients with recommendations, only two (9.5%) received genomics-driven therapy compared to 31.7% (86/271) of patients with other solid tumor malignancies (p=0.03). One received an IDH1 inhibitor and a second received dabrafenib and trametinib for a BRAF alteration; both on clinical trials. At time of last follow-up, best responses were unknown and partial response, respectively.

Unavailability of local clinical trials (9.5%) and clinical trial ineligibility (9.5%) (i.e. low performance scores, other co-morbidities) were common reasons for lack of actionability.

Conclusion: Benefit from next-generation sequencing in the pancreatobiliary population is low with only 4.4% of tested patients eventually receiving genomics-based therapy. Benefit to patients will not improve until access to clinical trials is enhanced and/or patients are evaluated for these trials earlier in the course of their disease, when their functional status is likely to be higher.

Disclosure: Nothing to disclose

OP292 CANCER RISK IN PRIMARY SCLEROSING CHOLANGITIS

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Introduction: Primary sclerosing cholangitis (PSC) is a rare inflammatory bile duct disease closely associated to inflammatory bowel disease (IBD). The lifetime risk for cholangiocarcinoma is 10-20%. The risk for gallbladder cancer and colorectal cancer is also increased. The risk for extra intestinal cancer is less studied.

Aims & Methods: The aim of the present study was to evaluate risk of all cancers in a large well-defined cohort of PSC patients in Sweden. We have performed a national prospective matched cohort study of 1769 PSC patients from six university hospitals in Sweden. All patients were diagnosed according to accepted criteria. The cohort was linked to the national registers of cancer, death and the patient register. Through Statistics Sweden we were provided with up to ten controls for each PSC patient matched for sex, age and residence at time of diagnosis.

Patients were followed from one year after date of PSC diagnosis (index date) until date of first cancer diagnosis, liver transplantation, death, emigration date or the 31st of December 2016.

Kaplan Meier method was used to evaluate the cumulative risk of the different subgroups of cancer in PSC patients and their controls. In addition, we calculated sub distribution hazard ratio (SHR) using competing risks regression model.

Results: After exclusion, using index date, end of follow up or censoring events, 1430 PSC patients remained for final analyzis. Mean patient follow up time was 15.3 years (range 0.02-47.0). A concomitant IBD diagnosis was present in 88 % of the PSC patients. The hazard ratio for any cancer was 3.3 (95 % CI 2.9-3.7) in PSC patients compared to their matched controls. The risk of hepatobiliary cancer (cholangiocarcinoma, hepatocellular cancer and gallbladder cancer), pancreatic cancer, colorectal cancer, ventricular cancer, non-melanoma skin cancer and lymphoma was increased in PSC patients compared to their matched controls.

Conclusion: In this large cohort of well-defined PSC patients from Sweden we show, for the first time, an increased risk of ventricular cancer, non-melanoma skin cancer and lymphoma. The previously known high risk of hepatobiliary and colorectal cancer was confirmed.

Disclosure: Nothing to disclose

OP293 THE DIAGNOSTIC YIELD OF MAPPING BIOPSY AND ITS IMPACT ON SURGICAL CURABILITY IN EXTRAHEPATIC CHOLANGIOCARCINOMA

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Introduction: Surgery with negative tumor margin (R0 resection) offers survival benefits in patients with extrahepatic cholangiocarcinoma (ECC). Accurate preoperative diagnosis, especially for longitudinal cancer spread is required to plan an optimal surgery to achieve R0 resection. However, the diagnostic yield of transpapillary mapping biopsy (MB) for possible surgical ductal margins (PSDMs) and its impact on the operative curability remains unclear.

Aims & Methods: Between 2003 and 2018, 190 patients with ECC (85 perihilar and 105 distal) who underwent surgical resection after preoperative evaluation with ERCP were retrospectively examined. PSDMs were determined according to the planned surgery, and the diagnostic yield of MB for PSDMs was assessed based on the resected specimens as the gold standard. We also compared the operative curability in patients with and without preoperative MB for PSDMs.

Results: A total of 186 preoperative MB procedures were performed in 75 patients, and 242 samples were obtained from PSDMs under fluoroscopic

or cholangioscopic guidance. Among them, 88% (177/201) of samples obtained under fluoroscopic guidance included sufficient materials for the diagnosis (86% and 96% at the possible proximal and distal margin, respectively). On the other hand, 80% (88/110) of samples obtained under cholangioscopic guidance included sufficient materials (79% and 100% at the proximal and the distal margin, respectively). When MB for 75 proximal and 24 distal margins after radical surgical resection (33 pancreatico-duodenectomy, 24 hepatectomy, and 18 hepatopancreatoduodenectomy) was evaluated, MB under fluoroscopic guidance provided the diagnostic accuracy of 65% and 67% at proximal and distal margins, respectively. On the other hand, MB under cholangioscopic guidance provided the diagnostic accuracy of 61% and 72% at proximal and distal margins. Macroscopic residual cancer was observed in 20% (17% at the proximal margin, 6% at the distal margin) and R0 resection rate was 48%. MB for PSDMs was associated with an improved R0 resection rate (56% vs 43%, P = 0.08) and a lower incidence of macroscopic residual cancer at the surgical ductal margins (12% vs 20%, P = 0.10).

Conclusion: MB for PSDMs improved the possibility of curative resection in patients with ECC. Insufficient sampling for the proximal margin may result in the limited accuracy of the MB, especially under the cholangioscpoic guidance. The dedicated devices for MB should be developed.

Disclosure: Nothing to disclose

OP294 13 YEARS OF PROSPECTIVE PANCREATIC CANCER SURVEILLANCE: RESULTS OF THE DUTCH NATIONWIDE PROGRAM IN HIGH-RISK INDIVIDUALS

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Introduction: Surveillance of individuals at high risk for pancreatic ductal adenocarcinoma (PDAC) may reduce pancreatic cancer-related mortality.

Aims & Methods: Our aim was to determine the yield of a nationwide pancreatic cancer surveillance program in high-risk individuals in the Netherlands during a 13-year follow-up. From 2006 through 2019, asymptomatic individuals with an estimated more than 10-fold increased lifetime PDAC risk were enrolled. Surveillance commenced at the age of 50 or 10 years younger than cancer onset in the family, and ended at the age of 75. Surveillance was performed every 12 months with both MRI and EUS. For worrisome features the surveillance interval was shortened to 3 or 6 months or surgery was performed.

Results: 344 individuals from 229 families were enrolled (mean age 54 (SD 10.0) years, 44% male). 156 (45%) were germline mutation carriers and 188 (55%) were familial pancreatic cancer kindred. They were followed for a median of 44 (IQR 74) months and a total of 1616 person-years. Cystic lesions were found in 185 (54%) participants, which were ≥1 cm in 43 (13%). 14 (4.1%) participants underwent surgery for a suspect lesion (3 at baseline, 11 during follow-up). Pathological results in these patients revealed PDAC in 4 patients, low-grade precursor lesions in 7, a 5-mm neuroendocrine tumor in 1, autoimmune pancreatitis in 1, and no lesion in the resected specimen in 1. In total, 7 (2%) patients developed PDAC (median age 56 years, IQR 23). Two were diagnosed at baseline and underwent resection. Histology revealed a margin negative T2N1M0 and T1N0M0. Both patients died after 32 months. Another 5 individuals developed PDAC during follow-up, all of whom had prior abnormalities visible on both EUS and MRI (presumed side branch IPMN in 4, an indeterminate lesion in 2, a moderately dilated common bile duct in 1, and a main pancreatic duct stricture without visible mass in 1 case). Of the 5 PDACs detected at follow-up, 3 (60%) were irresectable (survival 1-4 months), two of which had presented as symptomatic interval carcinomas, of which one appeared to have arisen separately from the known side branch IPMN. One of the 5 underwent an irradical resection (T3N1M0, survival 18 months), and one was radically resected (T1N0M0, alive, 18 months after diagnosis). The overall median survival for the 6 deceased PDAC patients was 11 (IQR 30) months.

Conclusion: In this relatively young cohort of individuals at high risk for PDAC, timely identification of relevant resectable lesions proved challenging with surveillance based on imaging alone with EUS and MRI. The quantitative effect of surveillance on resectability rates and survival remain difficult to assess because of the limited number of cases and possible lead-time bias. Biomarkers may hold better promise to improve the outcome of surveillance in individuals at high risk for PDAC.

Disclosure: PF is a consultant to Olympus, Cook Medical, Ethicon Endo-surgery and received research funding from Boston Scientific. DLC is a consultant to Tramedico. JEH received research funding from Abbott and Cook Medical. She is a consultant to Boston Scientific, Cook Medical, and Medtronics. MJB received research funding from Boston Scientific, Cook Medical, Pentax Medical, 3M. He is a consultant to Boston Scientific, Cook Medical, Pentax Medical, Mylan, MediRisk, and Medicom. The other authors have nothing to disclose.

What's hot in cold snaring

OP295 REAL TIME DIAGNOSTIC ACCURACY OF BLUE LIGHT IMAGING WITH MAGNIFICATION (BLI) IN THE CHARACTERISATION OF SESSILE SERRATED POLYPS (SSPS) AND ADVANCED HISTOLOGY WITHIN COLO-RECTAL POLYPS

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Introduction: Blue light imaging (BLI) is a novel modality for image enhanced endoscopy. Using the short wavelength of the absorption spectrum of haemoglobin and specific white light spectral colours emitted by 4 LED lights enhances the visualisation of vascular and surface pattern morphology within colonic polyps. In addition, magnification endoscopy with BLI is expected to enhance characterization and detection of advanced pathology such as high grade dysplasia (HGD) or submucosal invasion. Our study aims to assess the accuracy of BLI in characterizing SSPs and its ability to accurately predict advanced pathology.
Aims & Methods: A retrospective analysis was performed of a prospectively collected database in a single tertiary hospital. Hospital ethical board approval was obtained and informed consent was attained from all patients. Data from all colonoscopy utilising BLI and magnification were collected for 12 months from October 2017.Data was collected on polyp location, size, morphology and polyp type and presence of advanced pathology. Mucous cap, indefinite margins, type 2 open pits and dilated branching vessels were used as additional criteria for predicting SSPs. Endoscopic prediction was compared to histology to determine accuracy.
Results: 155 polyps were assessed in 68 procedures during the study period. Of these, 112 (72%) were in the proximal colon, 28 in the distal colon (18%) and 15 (10%) in the rectum. 62 polyps were diminutive (40%) and 17 were 6-10 mm (11%). 76 polyps were >10mm in size (49%) of which 43 were between 20-50 mm and 12 were >50 mm in size. 65 polyps were of Paris 1s morphology (41.9%), 80 were Paris 2a (50.3%) and 10 had combined morphology. BLI with magnification detected 55 SSPs of which 54 were confirmed at pathology (sensitivity 98.1%, specificity 99%, PPV 98%, NPV 99%, accuracy 98.7%). Adenomas were predicted in 100 polyps with HGD in 11 polyps and submucosal invasion in 6 polyps. Pathology confirmed submucosal invasion in all predicted polyps but did not detect HGD in 2 lesions. Pathology identified an additional 2 proximal colon polyps with focal HGD and 1 small focus of early submucosal invasion in a >50 mm polyp where endoscopy predicted HGD. Detailed results are in table 1.

Polyp characterisation	Sensitivity	Specificity	PPV	NPV
SSP	98.1(90-99)	99 (94-99)	98 (89-99)	99 (95-100)
Advanced pathology(HGD + SM invasion)	88 (62-97)	98 (94-99)	88 (62-97)	98 (94-99)
SM invasion	85 (42-99)	100 (96-100)	100 (51-100)	99 (95-99)

[Table 1]

Conclusion: As a novel modality, BLI with magnification has enhanced ability to visualise and characterize vascular and pit pattern morphology of colo-rectal polyps. Our study utilised these features and specific criteria for SSPs for accurate prediction of polyp type and advanced pathology. The results indicate high diagnostic accuracy for BLI in differentiation of SSPs as well as prediction of HGD and submucosal invasion. Prediction of advanced pathology is crucial in determining the ideal therapeutic strategy. Our study highlights the potential use of BLI and magnification in this regard.
Disclosure: Nothing to disclose

OP296 CONTINUOUS ANTICOAGULATION AND COLD SNARE POLYPECTOMY VERSUS HEPARIN BRIDGING AND HOT SNARE POLYPECTOMY IN PATIENTS ON ANTICOAGULANTS WITH SUBCENTIMETER POLYPS: A RANDOMIZED CONTROLLED TRIAL

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Introduction: Management of anticoagulants for patients undergoing polypectomy is still controversial, and cold snare polypectomy (CSP) is reported as a less hemorrhagic procedure.
Aims & Methods: To investigate the efficiency of continuous administration of anticoagulants with CSP (CA+CSP) compared to periprocedural heparin bridging with hot snare polypectomy (HB+HSP) for subcentimeter colorectal polyps. Patients taking anticoagulants (warfarin or direct oral anticoagulants) and having at least one non-pedunculated subcentimeter colorectal polyp. Patients were randomly assigned to undergo HB+HSP or CA+CSP. Follow-up of patients was performed 28 days postoperatively. The primary endpoint was incidence of polypectomy-related major bleeding: i) poorly controlledintra-proceduralbleedingor ii) post-polypectomy bleeding requiring endoscopic hemostasis.
Results: A total of 184 patients were enrolled, with 90 allocated to the HB+HSP group, 92 to the CA+CSP group, and 2 refusals. The occurrence of polypectomy-related major bleedingin the HB+HSP and CA+CSP groups was 12.0% [95% confidence interval (CI), 5.1 to 19.1] and 4.7% [95% CI, 0.2 to 9.2], respectively. Inter-group difference for the primary endpoint was +7.3% with the lower limit of two-sided 90% CI of 0.4% [95% CI, -1.0 to 15.7], which demonstrated non-inferiority of CA+CSP. The mean procedure time for each polypand hospitalization periodwere longer in the HB+HSP group than in the CA+CSP group.
Conclusion: CA+CSP for subcentimeter colorectal polyps in patients taking anticoagulants did not increase the incidence of polypectomy-related major bleedingcompared with HB+HSP, with a shorter procedure time and hospitalization period.
Disclosure: Nothing to disclose

OP297 THE SAFETY OF COLD SNARE POLYPECTOMY FOR PATIENTS ON ANTITHROMBOTIC THERAPY

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Introduction: Cold snare polypectomy (CSP) is a more efficacious and safer polypectomy technique without electrocautery, therefore it is widely used for the removal of subcentimeter polyps. Recent studies have revealed that delayed post-polypectomy bleeding (DPPB) and perforation are few observed in CSP. The use of antithrombotic agents for prophylaxis or treatment of thromboembolic events is expected to increase with the aging of the population. The management of antithrombotic agent use in patients undergoing CSP is a very important issue in clinical practice. However the safety of CSP in patients who are currently on antithrombotic therapy haven't been fully evaluated.

Aims & Methods: The aim of this study was to elucidate the safety of CSP in patients who are currently on antithrombotic therapy. 3341 consecutive patients with colorectal polyps were removed by CSP between March 2016 and March 2019. We retrospectively assessed the characteristics of polyps, the histological results, the rates of DPPB. DPPB was defined as significant bleeding requiring endoscopic treatment within 2 weeks after CSP.

Results: 6236 polyps in 3341 patients (male/female; 2511/830) were removed by CSP. There were 1310 polyps (21.4%) in 621 patients (antiplatelets agent users 403, anticoagulants agent users 172 and both agent users 64) in the antithrombotic group, and this group was divided into two groups: the continuation group (group A; 637 polyps, 339 patients) and the interruption group (group B; 569 polyps, 282 patients). And there were 5030 polyps (79.6%) in 2720 patients in the non-antithrombotic group (group C). The baseline characteristics of the lesions (size, location, morphology, resection number, and institution) in three groups weren't significantly different in univariate or multivariate analyses. As for adverse events, the overall rate of DPPB was 0.18% (6/3341). DPPB occurred 0.59% (2/339) in group A, 0.35% (1/282) in group B, 0.11% (3/2720) in group C, showing no significant differences from three groups (p = 0.09). In the rates of DPPB of the antithrombotic group (group A and group B), there were no significant differences depending upon the antithrombotic agents used (warfarin group, DOAC group, antiplatelet group, multiple antithrombotic group). Of the 6 cases of DPPB in CSP, 3 cases were located in sigmoid colon, all polyps were more than 5mm in diameter. Patients in the antithrombotic group in whom DPPB occurred included 2 aspirin users with 2 polyps and 1 aspirin plus rivaroxaban user with 2 polyps. All DPPB occurred within 24 hours, and transfusion and surgery were not necessary. In all cases, no perforation and fetal adverse events were occurred.

Conclusion: It is noteworthy that continued use of all of the antithrombotic agents in patients undergoing CSP didn't increase the risk of DPPB, even in patients receiving multiple antithrombotic agents. Thus, CSP can be performed with a high level of safety, even in patients receiving antithrombotic agents. In addition, there were no significant differences of rates of DPPB between the continuation group and the interruption group. So our results suggest that we may not be necessary for cessation of the antithrombotic therapy in CSP, and it is possible to reduce the risk of thromboembolism. In the future, prospective, randomized studies are necessary to confirm our results.

Disclosure: Nothing to disclose

OP298 INCOMPLETE RESECTION OF 4-20MM COLORECTAL POLYPS WHEN USING COLD SNARE POLYPECTOMY

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Introduction: Cold snare polypectomy has been recently been recommended as preferred polypectomy approach for up to 10mm colorectal polyps. We were interested to evaluate expansion of cold snare polypectomy for up to 20mm colorectal polyps and associated efficacy and safety.

Aims & Methods: This prospective studyincluded adults (age 45-80) presenting for a screening, surveillance or diagnostic colonoscopy at one academic center. The primary endpoint was the Incomplete Resection Rates (IRR) for 4-20mm neoplastic colorectal polyps. Secondary outcomes included technical feasibility of cold snare polypectomy and associated complication rates. "Easy" polypectomy was defined as immediate polyp resection upon first closure of the snare while "difficult" was defined as having to open and close the snare multiple times and/or using mechanical force (e.g. guillotine technique)to complete the cold snare polyp removal. Incomplete resection was defined by the presence of remnant tissue in marginal biopsies after polypectomy.

Results: The study included 413 patients (mean age 63; female 48.2%). Polyp and adenoma detection rates were 54.5% and 36.4%, respectively. A total of 182 colorectal polyps 4-20mm were found and initial removal was attempted using cold snare. In 75.3% cold snare resection was easy, in 12.1% difficult and in 9.9% conversion was required. The IRR for adenomatous polyps was 14.8%. The IRR for neoplastic polyps was 16.8%. Among neoplastic polyps incomplete resection was more frequent for SSP (36.4%) than for adenomatous polyps (14.8%, p=0.018). The IRR for hyperplastic polyps was 20.0%. The IRR for all 4-20mm polyps (combining neoplastic and hyperplastic polyps) was 17.6%. The risk of incomplete resection varied with polyp size (15.8% for 4-5 mm, 22.2% for 6-9 mm and 15.8% for 10-20 mm) and incomplete resection occurred more frequently when immediate polyps resection was difficult (IRR 42.1%). Intraprocedural bleeding requiring endoscopic intervention (treatment with clip or injection) occurred in 4.4%.

Conclusion: In this multi-endoscopist study using systematic cold snare polypectomy for up to 20mm colorectal polyps IRR was found more often than in other recent studies reporting outcomes for cold snare polypectomy. Technical difficulty to resect the polyp was associated with higher IRRs.

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OP299 CLINICAL IMPORTANCE OF COLD POLYPECTOMY DURING INSERTION PHASE IN LEFT SIDE COLON AND RECTUM: A MULTI-CENTRE RANDOMISED CONTROLLED TRIAL (PRESECT STUDY)

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Introduction: Although small and diminutive colorectal polyps are often found unintentionally during insertion phase (IP) of colonoscopy, removal of polyps during IP is not common in the current practice. These polyps, especially in the left side colon are often challenging to re-detect during withdrawal phase (WP) and may even become undetectable. As time-consumption of the re-inspection process is not negligible, instant resection of polyps should be considered. With the global spread of cold polypectomy and carbon dioxide (CO_2) gas insufflation, polypectomy during IP became less of a burden to endoscopists.

Aims & Methods: The aim of this prospective multi-centre randomized trial was to investigate the clinical benefits of instant removal of polyps upon scope insertion. We have set the primary outcome as total procedure time to confirm that polypectomy during IP facilitates the entire colonoscopy procedure and improves time efficiency. Secondary outcomes include the number of missed or 'hiding' polyps. Hiding polyp is defined as a polyp detected during insertion, however lost in withdrawal phase which was eventually found after re-inspection.

Patients with at least one target lesion (adenomas or SSAP < 10mm, hyperplastic polyps 6mm < 10mm in left side colon) detected during IP were divided into two groups and received cold snare or forceps polypectomy under CO2 gas insufflation: study group removed polyps during both IP and WP, where control group removed polyps during WP only. Patients were randomized into the two groups as soon as a target lesion is detected during IP. 20 senior endoscopists from 7 institutions were involved in this trial.

Results: A total of 1451 patients were recruited for the trial from April 2018 to March 2019. 300 (26.2%) patients had at least one detectable target lesion during IP, and 220 patients (120 in study group, 100 in control group) were eligible for full assessment. Mean total procedure time was significantly shorter (18:51 vs 22:18, -15.4%, p=0.0004) and mean pure cecal intubation time was similar between two groups (7:25 vs 7:33 p=0.9318). Mean number of polyps resected per patient was 2.1 in both groups. In the control group, out of 107 polyps found during IP, 48 polyps (44.8%) were not found in the first withdrawal action and 7 (6.5%) polyps were completely lost. Time consumption for re-searching these hiding or missed polyps was 2:54 in average. One case (1%) of delayed post-polypectomy bleeding in control group was reported as an adverse event.

	Polypectomy upon insertion and withdrawal	Polypectomy upon withdrawal only	P-value
n	120	100	NA
Total number of polyps	254	210	0.9011
Mean number of polyps per patient	2.1	2.1	NA
Mean total procedure time (min:sec)	18:51	22:18	0.0004
Mean pure cecal intubation time (min:sec)	7:26	7:27	0.9318
Mean polypectomy time (min:sec)	2:03	1:59	0.7562
Number of ‚hiding' polyps	NA	41(38.3%)	NA
Number of missed polyps	NA	7 (6.5%)	NA

[Main outcomes of PRESECT study.]

Conclusion: Polypectomy during IP in the left side colon improves the time efficiency of colonoscopy and reduces total procedure time without experiencing any disadvantages.
Disclosure: Nothing to disclose

OP300 COLD SNARE POLYPECTOMY VS HOT SNARE POLYPECTOMY VS (APC) FOR SMALL(5-9MM) LEFT-SIDED COLORECTAL POLYPS: A PROSPECTIVE RANDOMIZED TRIAL

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Introduction: The optimal technique for the removal of small colorectal polys is debatable. We aimed to compare the recurrence rates among three endoscopic treatment modalities for 5-9mm left-sided colorectal polyps.
Aims & Methods: Consecutive adults referred for elective colonoscopy (1/2015-1/2018) who had at least one polyp of eligible size (5-9mm) located distally to the splenic flexure were randomly assigned (1:1:1) to one of three treatment modalities: 1) cold snare polypectomy (CSP), 2) hot snare polypectomy (HSP) and 3) APC ablation (50-60W, flow: 2lt/min). The polyp site was marked with endoscopic tattoo and a follow-up colonoscopy with scar biopsies was performed 6-18 months after the index procedure. Outcomes were the polyp recurrence rate and the occurrence of complications.
Results: A total of 119 patients were enrolled, of whom 112 (62.5% males, mean age 61.1±9.9 years) with 121 polyps (CSP: 39, HSP: 45, APC: 37) returned for follow-up colonoscopy. The mean polyp size was 6.7±0.91mm, 58% were located in the sigmoid, 33% in the rectum and 8% in the descending colon. The majority of polyps resected by CSP or HSP were histopathologically proven to be neoplastic (tubular adenomas: 25.9%, tubulovillous adenomas: 11.1%, sessile serrate adenomas/polyps: 17.5%). No cases of delayed bleeding or perforation occurred in the study. Scar biopsies at follow-up colonoscopy (performed after a mean interval of 13.4 ±3.8 months) revealed a total of 6 (4.96%) cases of polyp recurrence, showing no significant difference among the three treatment groups [CSP: 3/39 (7.7%), HSP: 1/45 (2.2%), APC: 2/37 (5.4%), P=0.51).
Conclusion: CSP, HSP and APC ablation are effective and safe treatment modalities for 5-9mm left-sided colorectal polyps. The present randomized study could not detect any differences in the polyp recurrence rates among the three endoscopic techniques.
Disclosure: Nothing to disclose

What causes (recurrent) acute pancreatitis?
08:30-10:00 / B2

OP301 ETIOLOGY OF CHRONIC PANCREATITIS IN CHILDREN - ANALYSIS OF 423 CASES

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Introduction: Chronic pancreatitis (CP) is of a rare occurrence in childhood. The etiology of CP in children is varied and includes anatomic anomalies, gene mutations, metabolic disorders and others.
Aims & Methods: The aim of this study was to investigate the etiological aspects of CP in children from well-defined homogenous single-centre cohort. 423 children with CP (aged: 0.6-18 years; mean 10; F-220, M-203)

hospitalized between 1988 and 2019 were enrolled into the study. The diagnosis of CP was established according to INSPIRE recommendations. Clinical and epidemiological data were recorded and analyzed. All patients were screened for mutations in the high-risk genes associated with CP (*CFTR, CTRC, PRSS1, SPINK1, CPA1, CEL-HYB*). All children had preceding imaging studies, including US, CT, MRCP and/or ERCP.

Results: Gene mutations were found in 279 children **(66%)** (*SPINK1* mutation in 118 children, *CTRC* in 108 patients, *CFTR* in 61 patients, *PRSS1* in 55 children, *CEL-HYB* in 8 and *CPA1* in 4; 75 pts (17.7%) have 2 or more mutations).

Anatomic anomalies of pancreatic duct were diagnosed in 69 patients (16.3%) (43-pancreas divisum, 9-ansa pancreatica, 7-ABPU, 2-two main pancreatic ducts, 8-other).

Toxic-metabolic risk factors were found in 63 children (14.9%) with chronic pancreatitis, with dominance of lipid disturbances. Hyperlipidemia was present in 35 patients (8.3%), including isolated in 15 patients (3.5%) and coexisting with obesity/metabolic syndrome in 20 (4.7%). CP associated with medication was present in 15 (3.5%) children (mostly with anti-epilepsy drugs). Alcohol abuse history was present in 7 (1.7%) patients. Smoking (>5 cigarettes/day) history was present in 8 (1.8%) children. Five patients (1.2%) from these groups had history of both- alcohol abuse and cigarettes smoking. Chronic renal failure was present in 4 (1%), mitochondrial cytopathies in 2 (0.5%) and hypercalcemia (hyperparathyroidism) in 2 (0.5%) patients with CP.

CP was associated with biliary tract diseases in 38 patients (8.9%). Auto-immune pancreatitis was diagnosed in 14 children (3.3%). Idiopathic CP was diagnosed in 37 children (8.7%).

Conclusion: 1. Gene mutations and anatomic anomalies of pancreatic duct are the most common etiologic factors of CP in children.

2. CP is a multifactorial disease.

3. Our data demonstrate the need for genetic testing in children with CP.

Disclosure: Nothing to disclose

OP302 METABOLIC SYNDROME FACTORS WORSEN THE OUTCOME OF ACUTE PANCREATITIS

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Introduction: Several studies have confirmed the effect of obesity (OB), hyperlipidemia (HL) and diabetes mellitus (DM) on the outcome of acute pancreatitis (AP). However, there is no data regarding the association between hypertension (HT) and the outcome of AP. Furthermore, no study has examined yet the independent effects of these four factors, neither the effect of their different combinations.

Aims & Methods: Our aim is to understand how these four factors of metabolic syndrome (MetS) and their combinations effect the outcome of AP. The Hungarian Pancreatic Study Group has prospectively collected clinical data from AP patients between 2012 and 2017. Our cohort contains 1257 cases from 28 centers of which 906 cases had information on all four examined factors of MetS. For the individual effect analysis, patient groups were formed based on the WHO classification of BMI and the presence of other MetS factors, namely HT, HL and DM. Logistic regression was performed to analyze the independent effects of these four factors. For the joint effect analysis, patient groups were defined according to the combinations of the MetS factors.

Results: OB and HT significantly increased the risk for severe AP (OR=2.153 and OR=2.3861 respectively). OB and HT patients stayed significantly longer in the hospital (10.4d vs. 12.1d, p=0.008 and 10.5d vs. 11.8d, p=0.020) and had increased risk for systemic complications (OR = 1.993 and OR=2.830

respectively). HL increased the risk for moderately severe AP, for local complications (OR = 1.552) and for renal failure (OR = 2.166). DM increased the risk of systemic complications, though, the difference was not significant. In the independent effect analysis, only HT was an independent risk factor for mortality and severity (OR=5.900, p=0.020 and OR=3.895, p=0.001 respectively). OB is an independent risk factor for renal failure (OR=2.968, p=0.007), HT for respiratory failure (OR=2.667, p=0.024) and renal failure (OR=7.565, p=0.007) and HL for fluid collections (OR=1.415, p=0.037) and diabetes as a complication (OR=2.373, p=0.013).

In the joint effect analysis, the rate of severe AP elevates with the number of MetS factors (2.6%, 4.7%, 6.1%, 8.5% and 6.0% with 0, 1, 2, 3 and 4 factors respectively).

Conclusion: MetS factors increase the risk of mortality, severe AP and complications. Hypertension proved to be an independent risk factor for mortality and severity of AP. The more MetS factors are present, the higher is the risk of worse outcome in AP.

Disclosure: Nothing to disclose

OP303 QUANTIFYING THE RISK OF DRUG INDUCED PANCREATITIS WITH ACE INHIBITORS AND STATINS USING A LARGE ELECTRONIC MEDICAL RECORD PLATFORM

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Introduction: Acute pancreatitis (AP) is one of the most common causes of gastrointestinal-associated hospitalizations in the United States, with mortality rates as high as 30% for acute severe pancreatitis. Angiotensin-converting enzyme inhibitors (ACEi) and hydroxymethylglutaryl-coenzyme A reductase inhibitors, also known as 'statins', are often prescribed to patients with hypertension and hyperlipidemia and have been implicated in causing AP. The quantitative risk for AP and incremental risk when used together is unknown.

Aims & Methods: Using IBD Explorys (1999-2019), a HIPAA-enabled web platform that includes clinical data from over 63 million unique individuals with accompanying lab data, we aimed to quantify the risk for drug-induced AP with ACEi and statins. AP cases were identified using a combination of ICD and SNOMED codes, and AP episodes secondary to alcohol, gallstones, triglycerides or common class 1 drugs associated with AP were excluded. Odds ratios (OR) with corresponding 95% confidence intervals (CI) are reported.

Results: A total of 280,740 patients with AP meeting our inclusion criteria were identified, the majority of which had been exposed to statin alone (32%), ACEi alone (31%), or both (19%). Among all patients exposed to these medications, AP was observed in 1.5% (n=90,120/5,959,500) of patients exposed to statin alone, 1.9% (n=86,870/4,705,640) of patients exposed to ACEi alone, and 1.9% (n=54,590/2,879,850) of patients exposed to both a statin and ACEi. Compared to the general population, exposure to these medications conferred a 5-6 fold increased risk for AP not related to alcohol, gallstones, triglycerides, or common class 1 drugs associated with AP. (Table 1)

Medication	Odds Ratio	Confidence interval (95%)
HMG-CoA reductase inhibitor (statin)	4.97	(4.93, 5.01)
ACE inhibitor	6.12	(6.07, 6.17)
ACEi + Statin	5.72	(5.67, 5.78)

[Table !: Odds ratio (with 95% confidence intervals) for acute pancreatitis with exposure to a statin, ACE inhibitor, or both]

Conclusion: Approximately 1.5-2% of patients exposed to a statin or ACEi develop AP, and exposure to these medications is associated with a 5-6 fold increased risk for developing AP not attributed to alcohol, gallstones, triglycerides, or other drugs commonly associated with AP.

Disclosure: Nothing to disclose

OP304 DEVELOPMENT OF A MODEL TO DETERMINE THE RISK OF RECURRENCE OF ACUTE BILIARY PANCREATITIS BEFORE CHOLECYSTECTOMY: A MULTICENTRE, RETROSPECTIVE COHORT STUDY

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Introduction: International guidelines of acute pancreatitis (AP) recommend cholecystectomy during the index admission of patients with acute biliary pancreatitis (ABP). This recommendation is not consistently followed, thus increasing the risk of recurrence of ABP.

Aims & Methods: Our aim was to develop a model to determine the risk of recurrence of ABP to prioritise patients on surgical waiting list.

Multicentre, retrospective cohort study of patients with a first episode of ABP from January 2010 to December 2015. Biliary aetiology was defined by the presence of stones, or sludge/microlithiasis in the CBD or gallbladder at abdominal ultrasound, EUS or MRCP, together with the absence of AP relapse after cholecystectomy. Laboratory liver tests (AST, ALT, AP, GGT and bilirubin) at admission were recorded. Primary outcome was the risk of ABP recurrence during the six-month period after the first episode. Survival analysis was performed using the Kaplan-Meier method. Cox regression analysis was performed to calculate hazard ratios (HR). Significant risk factors associated with the risk of ABP recurrence were scored accordingly and three risk categories (low, intermediate and high) were defined.

Results: 498 patients with a first episode of ABP were included. Median time to cholecystectomy was 136 days (range 72-206 days). Patients waiting more than 6 months for cholecystectomy were excluded. 352 patients were finally included (mean age 67.6 years, range 51.6 to 77,4, 199 female). ABP relapsed in 89 patients (25.3%). Serum alkaline phosphatase (AP), previous endoscopic sphincterotomy (EE) and the severity of the first episode of ABP were significantly associated with ABP recurrence. Scores assigned identified patients with ABP who recur with a c-statistic of 0.59 (95% CI, 0.55-0.64, p<0.001), HR 2.64 (95% CI 1.61-4.32). Patients in the high, intermediate and low risk group had a recurrence rate of 30.7%, 18.7% and 0%, respectively.

Level of Alkaline Phosphatase	Points
0 to 263 (Normal limit)	5
264 to 526 (2 ULN)	4
527 to 789 (3 ULN)	3
790 to 1052 (4 ULN)	2
> 1052	0
Severity of AP	
Mild AP	4
Moderate AP	2
Severe AP	0
ERCP	
No	4
Yes	0

Low risk: 4 to 8 points Intermediate: 9 to 11 points High risk: 12 to 13 points

[RABP Score]

Conclusion: A score system (recurrence acute biliary pancreatitis -RABP-score) based on serum levels of AP at admission, EE and severity of AP allows identifying patients with ABP at low, intermediate and high-risk groups of recurrence. This score might be used to prioritise patients in surgical waiting list for cholecystectomy.

Disclosure: Nothing to disclose

OP305 INVESTIGATING THE EARLY PHASE OF CHRONIC PANCREATITIS: THE GOULASHPLUS TRIAL PROTOCOL AND THE RESULTS OF THE FIRST 14 MONTH

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Introduction: Acute pancreatitis (AP) is an inflammatory condition, which can lead to late consequences. In 20 % of patients recurrent AP (RAP) develops and in 7-12 % chronic pancreatitis (CP) will occur. However, we do not have sufficient information to establish an evidence-based statement to define early CP, or how to prevent its development.

Aims & Methods: The aim of the GOULASH-PLUS study is to understand the influencing factors and to determine, which parameters should be measured to detect the early phase of CP.

This is an observational prospective follow-up study of the GOULASH-trial. Patients' selection: individuals enrolled in the GOULASH study will be approached and asked to join this longitudinal study. Participants will be followed up at 1-2-3-4-5 and 6 years after the episode of AP. Anamnestic data will be collected by the following questionnaires: i) FFQ ii) SF-36 iii) physical activity questionnaire iv) stress questionnaire. Genetic tests will be performed for the genes already known to be associated with CP. The exocrine pancreatic, liver and kidney functions will be determined by several laboratory tests, stool sample analyses and imaging will be performed. The endocrine function will be measured by an oral glucose tolerance test (OGTT) and HbA1C. Blood and stool samples will be stored in the biobank for later measurements. Now, the participation in the first 14 months and the changes in the endocrine function were analyzed.

Results: During the first 14 months 93 out of the 126 patients attended the first year control, thus the enrolment rate was 73.8 %. Their mean age was 54+13.3 years and 57 (61.2%) were male. Mild, moderate and severe AP was observed in 69 (74%), 19 (21%) and 5 (5%) patients during their index admission. Out of 18 (19.4%) of them was admitted with recurrent AP episode. At the first year follow-up, 9 patients were newly diagnosed with diabetes, and 21 patients had impaired glucose tolerance. The incidence of diabetes increased after the first year of AP from 12.9% to 22.7%, at 45.3% of the patient´s carbohydrate metabolism disorder could be detected. Patients who were admitted with moderate or severe AP were more likely to develop diabetes (5 from 24 patients; 20.8%) than patients with mild AP (4 from 69 patients; 5.8%).

Conclusion: The development of carbohydrate metabolism disorder is frequent in AP, it shows correlation with the severity of AP, therefore the follow-up of these patients is likely to be beneficial.

Disclosure: Nothing to disclose

OP306 ACUTE PANCREATITIS AND MUCIN PHENOTYPE OF INTRADUCTAL PAPILLARY MUCINOUS NEOPLASM OF PANCREAS

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Introduction: Acute pancreatitis (AP) occasionally occurred in patients with intraductal papillary mucinous neoplasm (IPMN). The influence of mucin phenotype of IPMN on the occurrence of AP remains controversial.
Aims & Methods: We investigated the relationship between mucin phenotype of IPMN and AP, including pancreatic hyperenzymemia. This study included 163 patients with IPMN who had surgery at our hospital between January 2000 and December 2016. The relationship between mucin phenotype of IPMN and AP (or pancreatic hyperenzymemia) was investigated. Mucin phenotype of IPMN was classified as Gastric type (G type: N=101), Intestinal type (I type: N=45), Pancreatobiliary type (PB type: N=11) and Oncocystic type (O type: N=2).
Results: 11% (18/163) of IPMN cases developed AP and 55.6% (10/18) of AP cases have recurrent episode (2-4 times). Age, gender, BMI, diabetes, alcohol consumption (more than 50g/day), drinking habits, and smoking status (current smoking) were not associated with the incidence of AP. In addition, there was no association of the incidence of AP with the diameter of main pancreatic duct, mural nodules, and the diameter of IPMN. In mucin phenotype, AP was significantly more frequently occurred in pancreatobiliary type (PB type: with AP vs. without AP, 27.8% [5/18] vs. 4.1% [6/145], P = 0.003) and intestinal type (I-type: with AP vs. without AP, 50.0% [9/18] vs 24.8% [36/145], P = 0.046). In the 5 cases of PB type with AP, 4 cases were intraductal mass in the main pancreatic duct, and 1 case had the compression of the main pancreatic duct by the intraductal mass in the branch pancreatic duct. In Intestinal IPMN cases with AP, 88.9% (8/9) had dilated main pancreatic duct by hyper mucin production. The elevation of serum pancreatic enzymes (serum amylase, serum lipase, serum elastase-I) was not significantly related to mucin phenotype of IPMN.
Conclusion: PB type and intestinal type IPMN were significantly associated with AP. PB type sometimes display intraductal mass with poor mucin production in the main or branch pancreatic duct, while intestinal type is characterized by abundant mucin production. These mucin phenotype might be closely associated the occurrence of AP in IPMN.
Disclosure: Nothing to disclose

From bench to bedside in pancreatic cancer
08:30-10:00 / B3

OP307 A MULTI-INSTITUTIONAL STUDY ASSESSING PREVALENCE OF DELETERIOUS GERMLINE MUTATIONS IN PANCREATIC CANCER

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Introduction: Pancreatic cancer is being increasingly associated with germline implications. Some large single-center studies have reported results ranging from 3.9% to 19.8% of patients found to have germline variants [Shindo, *JCO* 2017; Lowery, *JNCI* 2018].
Aims & Methods: We aim to further delineate prevalence of deleterious germline mutations in pancreatic cancer using a multi-institutional data set. We also aim to analyze predictive factors such as mutant allele frequency (MAF, in %) in germline versus somatic calls. We sequenced 23 genes in DNA prepared from clinical tissue and blood specimens submitted to Tempus Labs. Germline variants and somatic variants were processed separately. Germline variants were determined to be deleterious through the sum effect of a combination of *in silico* predictors, population

databases, and internal evaluations. Tumor-normal comparisons were used to define somatic versus germline, and MAFs were calculated for each.
Results: A total of 234 patient samples from 17 institutions were analyzed. Of these, 12 (5.1%) had predicted deleterious germline variants involving 8 different genes: *BRCA1* (n = 3), *CHEK2* (n = 3), *ATM* (n = 1), *MLH1* (n = 1), *MUTYH* (n = 1), *PALB2* (n = 1), *SMAD4* (n = 1), *TP53* (n = 1). For most somatic alterations, the MAFs were found to be greater than the germline deleterious alterations, with the latter approaching ~50% in most cases.
Conclusion: This multi-institutional study identifies 5% of patients with pancreatic cancer to have deleterious germline alterations. Somatic variant testing, particularly when paired with germline, can be used as a screening method for genetic counseling referrals, especially with MAF analyses of paired tumor-normal samples.
Disclosure: Nothing to disclose

OP308 GENE CO-EXPRESSION NETWORK ANALYSIS OF PRECURSOR LESIONS IN FAMILIAL PANCREATIC CANCER

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Introduction: An estimated fraction of up to 10% of all pancreatic cancers is attributed to familial pancreatic cancer (FPC) with an accumulated lifetime risk of up to 38.5% for pancreatic ductal adenocarcinoma (PDAC) (1). The process of progression from pre-malignant lesions to the formation of invasive PDAC is thought to take around 10 years (2). High grade Pancreatic Intraepithelial Neoplasia (PanIN) are aggressive pre-malignant lesions, associated with elevated risk for progressing to PDAC (3-5). To date, no genetic mutations with strong association to FPC related PanIN lesions are known. A thorough depiction of dysregulated gene activity in high grade PanIN lesions in patients with FPC can help to characterize the molecular events during the development and progression of familial PanIN lesions to PDAC.
Aims & Methods: We performed weighted gene co-expression network analysis (WGCNA) to identify genes associated with FPC related PanIN lesions using gene expression profiles of 33,000 genes measured by Affymetrix GeneChip HG-U133 arrays on 13 pancreatectomy specimens with PanIN lesions (stage 2-3) from FPC patients, 6 pancreatectomy specimens with PDAC from sporadic pancreatic cancer (SPC) patients, and 4 specimens of normal donor pancreatic tissue (6). Microarray data were analyzed using R package *WGCNA*.
Results: WGCNA detected co-expressed genes as modules/clusters and summarized each module by a representative gene: the module eigengene. Correlation analysis identified 2 up-regulated modules or co-expressed gene clusters (p< 1e-05) and 2 down-regulated modules (p< 1e-05) in FPC compared to SPC. The upregulated gene modules include 5 significant genes (p< 1e-06) consisting of *FMO4, FMO2, CORO1B, TPP1, CIB4*.
The down-regulated gene modules include 170 significant genes (p< 1e-06), among them 13 highly significant genes (p< 1e-10) consisting of: *COL10A1, SAMD9, PLPP4, COMP, POSTN, IGHV4-31, THBS2, MMP9, FNDC1, HOPX, TMEM200A, INHBA, SULF1*. The down-regulated modules are significantly enriched for Gene Ontology (GO) terms functionally related to: extracellular structure organization, cell-substrate junction, focal adhesion, collagen binding, extracellular vesicle, etc. In addition, we identified common modules shared by both FPC and SPC - with 2 commonly up-regulated modules (p< 4e-12) and 1 commonly down-regulated module (p< 1e-17) as compared with normal pancreatic tissue.
The common up-regulated modules include 1054 highly significant genes (p< 1e-06) with 14 top significant genes (p< 1e-16) consisting of: *ID2B/ID2, OGFOD1, COL3A1, HOPX, SULF1, ELK3, HLA-DRB1, PMP22, CYAT1, PLPP4, COL1A2, SFRP4, SPARC, THBS2*. In the common down-regulated module, 214 genes were differentially expressed in comparison with normal pancreatic tissue (p< 1e-06), among them 15 were top significant genes (p< 1e-12) consisting of: *UTP14A, PGM3, SLC1A4, PHGDH, MRM3, GMPPA, SNORD14D, NSA2, NUBP1, CCT4, IGBP1, FMOD, AADAC, ASNS, LANCL2*. The common down-regulated module is enriched for GO terms related to functions in: cotranslational protein targeting to membrane, peptide metabolic process, structural constituent of ribosome, etc.

Conclusion: The differential molecular pathology of FPC and SPC involves multiple co-expressed gene clusters significantly enriched for GO terms including functions in extracellular activities and focal adhesion. Meanwhile, both FPC and SPC share strong gene co-expression patterns functionally related to intracellular activities. These findings provide reference for genomic characterization of the molecular events during the development and progression of PanIN lesions to PDAC in FPC.

References: 1. Brune KA, Lau B, Palmisano E, Canto M, Goggins MG, Hruban RH, et al. Importance of age of onset in pancreatic cancer kindreds. Journal of the National Cancer Institute. 2010;102(2):119-26. 2. Yachida S, Jones S, Bozic I, Antal T, Leary R, Fu B, et al. Distant metastasis occurs late during the genetic evolution of pancreatic cancer. Nature. 2010;467(7319):1114-7. 3. Diaz KE, Lucas AL. Familial Pancreatic Ductal Adenocarcinoma. The American journal of pathology. 2019;189(1):36-43. 4. Hruban RH, Canto MI, Goggins M, Schulick R, Klein AP. Update on familial pancreatic cancer. Advances in surgery. 2010;44:293-311. 5. Welinsky S, Lucas AL. Familial Pancreatic Cancer and the Future of Directed Screening. Gut and liver. 2017;11(6):761-70. 6. Crnogorac-Jurcevic T, Chelala C, Barry S, Harada T, Bhakta V, Lattimore S, Jurcevic S, Bronner M, Lemoine NR, Brentnall TA. Molecular analysis of precursor lesions in familial pancreatic cancer. PLoS One. 2013;8(1):e54830. doi: 10.1371/journal.pone.0054830.
Disclosure: Nothing to disclose

OP309 GASTROKINE 1 AND 2 IN PANCREATIC CARCINOGENESIS: ONE FAMILY WITH TWO DISTINCT ROLES?

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Introduction: Late detection of pancreatic ductal adenocarcinoma (PDAC) and limited treatment options lead to poor survival of PDAC patients. A better understanding of the pathomechanism of PDAC development will help identify new therapeutic approaches. An early event during tumorigenesis is the development of pre-malignant lesions such as pancreatic intraepithelial neoplasia (PanIN). While studying a K-Ras driven mouse model (KC mice) of PDAC, which recapitulates the stepwise progression of pancreatic cancer, we serendipitously identified Gastrokine 1 (GKN1) and Gastrokine 2 (GKN2) in early PanIN lesions. Importantly, we confirmed the presence of GKN1 and GKN2 in human pancreatic premalignant lesions. GKNs are proteins derived from gastric epithelium, where they maintain gastric homeostasis and act as tumor suppressors. Therefore, we aim to investigate the function of this PanIN-specific GKN1 and GKN2 expression, to understand the early events that underlie the development of premalignant lesions leading to pancreatic carcinogenesis.
Aims & Methods: We intercrossed KC mice with GKN1-/- or GKN2-/- mice. GKN1-/- KC, GKN2-/- KC and GKN+/+ KC pups were analyzed at the age of 3- and 9 months to quantify PanIN lesions and assess tumor development via histology. Furthermore, qRT-PCR and western blots were used to analyze genes and proteins (relevant for apoptosis, EMT or tissue remodeling and stroma composition) involved in tumorigenic processes. For all compared groups we analyzed the proliferation index and measured differences in pancreatic cyst sizes. In vitro, acinar transdifferentiation experiments were performed with cells isolated from all groups. A lentiviral construct overexpressing mouse GKN1 or GKN2 was generated to transduce Panc02 mouse pancreatic cancer cells to confirm the results in-vitro.
Results: Absence of GKN1 or GKN2 dramatically accelerated the development of PanIN lesions in KC mice. 3 months old GKN1-/-KC and GKN2-/-KC mice showed more extensive ADM and PanIN lesions compared to GKN+/+ KC mice, coinciding with significant upregulation of genes involved in PanIN development, cytokine and chemokine expression as well as tissue remodeling. Interestingly, the mRNA expression analysis also revealed a significant difference in apoptosis regulation in GKN1-/- KC mice. Analysis of cleaved Caspase-3, FAS protein and activated cleaved Caspase-8 point towards a decreased apoptosis in the absence of GKN1 and suggests a possible involvement of GKN1 in the activation of the extrinsic apoptotic pathway. The histological comparison at 9-months showed that GKN1-/- KC mice developed a collagen-rich dense stroma around the pancreatic lesions compared to sparse stroma in KC animals. GKN1-/- KC mice showed an increased tumor incidence (40.7% vs 13%) and a more differentiated

tumor phenotype. On the other hand, the histological evaluation shows that 9 month old GKN2-/- KC mice display a change of pancreatic tissue architecture resulting in big cystic lesions. In context of tumor incidence, GKN2-/-KC mice reveal a comparable incidence to GKN+/+ KC mice.
Conclusion: We conclude that the absence of GKN1 or GKN2 leads to accelerated PanIN development. Based on our results, we suggest that GKN1 influences apoptosis avoidance at an early age through the extrinsic apoptosis pathway. Apoptosis avoidance and development of a dense stromal reaction in later stages leads to an increased tumor incidence. GKN2 plays an important role in maintaining pancreatic architecture during PanIN formation, especially influencing the cyst size and proliferation.
Disclosure: Nothing to disclose

OP310 HOW DOES INTESTINAL TYPE INTRADUCTAL PAPILLARY MUCINOUS NEOPLASM EMERGE?

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Introduction: Intestinal intraductal papillary mucinous neoplasms (IPMNs) are often concurrent with gastric type components, and gastric IPMNs are assumed the origin of intestinal IPMNs. However, the molecular mechanism underlying the development and evolution of intestinal IPMN is not known.
Aims & Methods: To establish the molecular progression model of intestinal IPMN, we performed triple staining for CDX2, MUC2, and alcian blue, as intestinal differentiation markers, and double immunostaining for p21 and Ki-67, as cell cycle regulatory markers, on 61 intestinal IPMNs. Mutation analyses of $KRAS$ and $GNAS$ of intestinal and gastric components, individually, were performed using droplet digital PCR (QX200, Bio-Rad) and targeted amplicon sequencing (Ion S5, Thermo Fisher) in 25 cases.
Results: Histologically, intestinal features appear gradually in gastric type neoplasms those being IPMNs (n=32, 54%) or incipient PanIN-like lesions (n=20, 30%) in size. Triple staining for CDX2, MUC2 and alcian blue revealed that CDX2 expression appeared to precede MUC2 expression and morphological changes into intestinal phenotypes in gastric type epithelia. With MUC2 expression, intestinal morphological features, such as elongated nuclei, high-columnar epithelia, and nuclear stratification, became obvious. Cytoplasmic alcian blue-positive mucin and papillary growth seemed to become prominent as MUC2 expression increased. These results suggest that CDX2 may induce the characteristic biochemical and morphological transition of gastric-type epithelia into intestinal-type epithelia.
Expression of p21 and Ki-67 seemed to be accelerated by CDX2 expression as follows: the labeling index of p21 was 17.9±24.0% in gastric IPMNs and 52.4±22.1% in intestinal IPMNs (p< 0.05). The labeling index of Ki-67 was 4.3±1.9% in gastric IPMNs and 34.0±16.8% in intestinal IPMNs (p< 0.05). Double immunostaining for p21 and Ki-67 revealed that p21 positive cells tended to distribute in apex while Ki-67 positive cells did base of papillae, which resembles those in normal intestinal mucosa. Hence, intestinal IPMNs may have an adenomatous phase, in which the balance of differentiation and proliferation of neoplasm is regulated. This regulated trend seemed to disappear with the progression of grade and development of invasion (low-grade IPMN versus high-grade IPMN, p< 0.05, and versus invasive cancer, p< 0.05).
Finally, all intestinal IPMNs concurrent with gastric IPMN (n=18) or with incipient PanIN-like lesions (n=7) shared identical $KRAS$ and $GNAS$ profiles with the gastric type epithelia. Intestinal IPMNs seemed to arise from $GNAS/KRAS$ mutant (n=14, 78%) and $GNAS$ mutant (n=4, 22%) gastric IPMNs. Also, intestinal IPMNs seemed to arise from $GNAS/KRAS$ mutant (n=4, 57%) and $GNAS$ mutant (n=3, 43%) incipient PanIN-like lesions, namely incipient IPMNs. Variant allele frequencies (VAFs) of $GNAS$ and $KRAS$ increased with the transition of gastric IPMNs into intestinal IPMNs as follows: VAFs of $GNAS$ in gastric and intestinal IPMNs were 20.8±15.3% and 40.2±18.4% (p< 0.05, n=18), respectively. VAFs of $KRAS$ in gastric and intestinal IPMNs were 23.1±12.1% and 33.8±12.4% (p< 0.05, n=14), respec-

tively. Moreover, VAFs of *GNAS* and *KRAS* increased from incipient IPMN foci (7.5±6.9% and 3.5±3.7%) to mature intestinal IPMNs (47.1±16.1% and 42.8±13.0%, n=7 and n=3, p< 0.05 and p=0.0702).

Conclusion: Intestinal IPMNs may arise in *GNAS*-mutant gastric type IPMNs, in which CDX2 is supposed to play a critical role in the process of intestinal differentiation and progression by inducing the expression of MUC2 and p21 with some unknown growth-promoting molecules.

Disclosure: Nothing to disclose

OP311 DISCOVERY OF GASTROKINES IN EARLY PANCREATIC CANCER PRECURSORS AND THEIR POTENTIAL UTILITY AS A BIOMARKER

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Introduction: Current diagnostic methods are unable to detect pancreatic ductal adenocarcinoma (PDAC) at early, possibly treatable stages. Such early event in the malignant transformation is the development of pancreatic intraepithelial neoplasia (PanIN), the most common PDAC precursor. PanINs are classified according to their grade of dysplasia into PanIN-1A, PanIN-1B, PanIN-2 and PanIN-3. Molecular events occurring in the stepwise progression from premalignant PanIN lesions to PDAC development are largely unknown. A detailed knowledge of the critical biological changes responsible for pancreatic tumorigenesis is essential for the development of early diagnostic and preventive strategies.

The aim of our project is the identification of such key processes through the characterization of PanINs, focusing on two proteins - gastrokine 1 and gastrokine 2- that has so far not been shown in the pancreas. Gastrokines (GKNs) have been almost exclusively described in the stomach with a suggested role in gastric epithelial homeostasis and as tumor suppressor.

Aims & Methods: First, a comprehensive gene expression analysis was performed in human PanIN samples. The results were validated with qRT-PCR in an independent cohort of pancreatic cancer patients. The presence of GKNs was verified by immunohistochemistry (IHC). The *KRAS* gene driven KC (*p48[+/Cre];Kras[+/G12D]*) mouse model is a well-established model for pancreatic cancer, recapitulating the morphological features of PDAC development. Pancreatic tissues of KC mice were characterized by whole genome microarray analysis, qPCR, western blotting and IHC. Using a 3D mouse primary acinar cell culture model, we induced acinar cell transdifferentiation, to test GKNs expression. GKNs in mouse pancreatic juice were detected with mass spectrometry and in serum by western blot.

Results: Molecular analysis of patient samples and KC pancreas revealed high expression of gastrokines (GKN1 & GKN2) on dysplastic cells. GKN1 and GKN2 are co-expressed specifically on low-grade PanIN lesions (PanIN1B and PanIN2) in human and mice, where their expression is restricted to the cytoplasm of dysplastic epithelium. These proteins are absent in healthy acinar and ductal cells, as well as on tumor cells. Also high grade PanIN lesions are negative for GKNs.

We further assessed if inflammation can drive GKNs expression, however infiltrating inflammatory cells in human and mouse samples do not express GKNs. Furthermore, GKNs are undetectable in mouse models of pancreatic inflammation. Analysis of KC mice revealed continuous increase in GKNs from 4-52 weeks of age corresponding to an increase in the PanIN harboring area. During in-vitro transdifferentiation, expression of GKNs increased progressively parallel to the number of newly formed lesions in the culture. We confirmed secretion of GKNs in the pancreatic juice, and detected GKNs in the serum of KC mice. We further observed the presence of GKN1 in human pancreatic cyst fluid in some IPMNs and PDAC with cystic component.

Conclusion: In this study, for the first time, we report association of gastrokines with early pancreatic cancer precursors in human and mouse pancreatic tissues. Their progressive increase in developing PanIN lesions and their secretion in serum, pancreatic juice and cyst fluid suggest that gastrokines could become promising biomarker(s) in PDAC diagnostic or

screening. Collectively, the discovery of GKNs opens up avenues to test these proteins in patient cohorts and to further study their role in PanIN and PDAC development.

Disclosure: Nothing to disclose

OP312 PANCREATIC CANCER CELLS ACCESS NERVES VIA TGFBETA1-MEDIATED TRANSDIFFERENTIATION OF PERINEURAL EPITHELIAL CELLS INTO MESENCHYMAL-LIKE CELLS

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Introduction: Mechanisms of "neural invasion" in pancreatic cancer are widely unclear. Classically, cancer cells are assumed to actively break or mechanically disrupt the perineural barrier to find access into nerves. However, for this hypothesis to be true, the cancer cells would need to exert destructive-toxic effects on the cells that compose the perineural barrier. Here, we hypothesized an alternative mechanism of cancer cell entry into nerves, i.e. the "transdifferentiation" of perineural epithelial cells of the outermost nerve sheath in the cancer micro-environment.

Aims & Methods: Human perineural epithelial cells were cultured within the supernatants of different human pancreatic cancer cell lines and analyzed for markers of epithelial-mesenchymal-transition (EMT). The integrity of the perineural epithelial cell linings was analyzed in human pancreatic cancer tissues by quantitative immunohistochemistry of circumferential perineural GLUT1 staining. Transcriptomic arrays were performed with perineural epithelial cells to decipher the transcriptomic changes in the cancer-induced transdifferentiation process. Levels of different EMT inducers were analysed by ElLISA within pancreatic cancer cell supernatants. Genetically engineered mice with precursors of pancreatic cancer (p48-Cre;LSL-KrasG12D/"KC") and pancreas-specific TGFbeta1 overexpression (KC;TGFbeta1ov+/) were analysed for the perineural integrity.

Results: Treatment of human perineural epithelial cells (HPEC) with supernatants of three different human pancreatic cancer cell lines resulted in morphological alterations in the perineural cells that were reminiscent of EMT. Accordingly, cancer-conditioned perineural epithelial cells overexpressed Vimentin and N-Cadherine, and downregulated E-cadherine. The transcriptomic analysis of the cancer-conditioned, perineural epithelial cells revealed expression changes that pointed out towards an EMT signature. Among the different potential mediators of EMT, the only factor that was specifically enriched in the supernatants of human pancreatic cancer cell lines was TGFbeta1. Accordingly, increasing concentrations of TGFbeta1 in the culture medium of human perineural epithelial cells resulted in prominent EMT-like changes in the perineural cells. In human pancreatic cancer tissues, GLUT1-expressing perineural epithelial barrier cells were widely lost as opposed to the intact barrier around nerves in normal pancreas. Moreover, analysis of the perineural integrity in KC;TGFbeta1ov+/ revealed prominent loss of perineural integrity upon TGFbeta1 overexpression when compared to KC mice.

Conclusion: Cancer cell-induced transdifferentiation of perineural epithelial cells seems to be the initial mechanistic event that enables pancreatic cancer cell access into nerves. In this context, TGFbeta1 signaling seems to be of paramount importance in mediating neural invasion in pancreatic cancer and is thus of potential therapeutic relevance.

Disclosure: Nothing to disclose

Towards early diagnosis of gastric cancer
08:30-10:00 / E1

OP313 COMPREHENSIVE BIOINFORMATIC ANALYSIS OF ABERRANTLY EXPRESSED PROFILES OF MIRNAS AND LNCRNAS WITH THE ASSOCIATED CERNA NETWORK IN GASTRIC CANCER

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Introduction: Increasing evidence has highlighted the critical roles of miRNAs as biomarkers and therapeutic targets for cancer. MiRNAs are also regarded as a major part of competing endogenous RNA (ceRNA) network due to its regulation on protein-coding gene expression by acting as sponges. However, functional roles of miRNA-mediated ceRNAs in gastric cancer (GC) remain unclear.

Aims & Methods: To clarify relevant potential mechanisms, we comprehensively compared the expression profiles of mRNAs, lncRNAs and miRNAs between 55 GC tissues and 55 non-tumor tissues, based on GEO databases. Then, we selected most relevant genes through GO and pathway analysis, together with target gene prediction. We also set up a ceRNA network through the certain algorithm.

Results: 299 lncRNAs and 1118 mRNAs were identified as aberrantly expressed in all of the four databases (GSE67354, GSE78775, GSE79973 and GSE19826). After screening by GO and pathway analysis, 364 significant mRNAs were selected (p< 0.05) and they had correlations with tumorigenesis and/or progression of GC. Further screening was performed using targeting gene prediction and 179 mRNAs were chosen. Then, a dysregulated miRNA-associated ceRNA network was successfully constructed, which inculdes 70 lncRNAs, 11 miRNAs and 112 mRNAs. Finally, 2 out of the 11 dysregulated miRNAs functioned as prognostic biomarkers for GC patients according to the overall survival analysis, which is a higher expression of hsa-miR-125-5p and hsa-miR-130-3p represented a lower prognosis rate (P=0.0259 and 0.0236, respectively). We then examined the miRNAs' expression in our 30 GC tissues and 30 controls. MiR-125 and miR-130 were both decreased in GC tissues.

Conclusion: Our study identified novel miRNAs as candidate prognostic biomarkers and potential therapeutic targets for GC, based on large-scale sample size. More importantly, the newly identified ceRNA network will be beneficial for improving the understanding of miRNA-mediated ceRNA regulatory mechanisms in the pathogenesis of GC.

Disclosure: Nothing to disclose

OP314 POTENTIAL OF URINARY MICRORNA BIOMARKER PANEL FOR THE EARLY DETECTION OF GASTRIC CANCER

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Introduction: Gastric cancer (GC) is one of the most common malignancies in the world. Although endoscopy is a gold standard for the diagnosis of this disease, comprehensive screening endoscopy would be invasive, expensive and could result in significant complications. To date, there is a significant lack of useful GC biomarkers. We thus conducted this study to discover non-invasive biomarkers for the early diagnosis of GC, consisting of urinary microRNAs (miRNAs).

Aims & Methods: A cohort of 306 patients composed of 153 patients with GC and 153 age- and sex-matched healthy controls (HCs) were randomly divided into three groups: the discovery cohort (4 pairs); the training cohort (95 pairs); the validation cohort (54 pairs). Moreover, age- and sex-matched 32 pairs with serum samples were also enrolled in the serum cohort.

Results: Baseline clinical characteristics were well balanced and no significant differences were noted except for *H. pylori* status. More than 60 % of patients with GC were stage I and around 50 % could undergo curative endoscopic resection in this study.

A miRNA microarray analysis detected 22 urinary miRNAs with significantly aberrant expressions between the two groups in the discovery cohort. Two miRNAs, miR-6807-5p and miR-6856-5p, were found to be highly expressed in the urine of GC patients compared to HCs in the training cohort. A multivariate analysis has demonstrated that urinary levels of these 2 miRNAs were independent biomarkers for diagnosis of GC, as well as *H. pylori* status

In the validation cohort, urinary miR-6807-5p and miR-6856-5p showed significantly higher expression levels in the GC group, and the combination biomarker panel of miR-6807-5p, miR-6856-5p, and *H. pylori* status also showed excellent diagnostic performance (AUC = 0.885). In addition, serum levels of miR-6807-5p and miR-6856-5p were significantly higher in the GC group.

Conclusion: A novel biomarker panel consisted of urinary miR-6807-5p, miR-6856-5p, and *H. pylori* status enabled early and non-invasive detection of GC.

Disclosure: Nothing to disclose

OP315 DETECTION OF GASTRIC CANCER USING A SERUM MICRORNA ASSAY

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Introduction: High mortality from gastric cancer is related to the late manifestation of its symptoms. A blood-based non-invasive biomarker with the ability to detect all stages of gastric cancer could significantly improve patient outcomes.

Aims & Methods: We aimed to develop a novel serum miRNA assay for diagnosis of gastric cancer.

We developed a multi-target miRNA assay from a discovery study involving 892 gastric cancer and control subjects from Singapore and Korea. Using RT-qPCR, we quantified the expressions of 578 serum miRNAs and constructed a 12-miR biomarker panel through multi-variant data analysis. The results were generated with the use of a logistic-regression algorithm, with the value of 40 or more considered to be positive. We subsequently validated this multi-miR assay in a large prospective cohort. The cohort included subjects of all ethnicities (Chinese, Malay, Indian, and others) age 40 years old and above presenting with an indication for upper GI endoscopy at the National University Hospital and Tan Tock Seng Hospital, Singapore between 2013 and 2016. All participants had undergone endoscopy. In addition to miRNA profiling, sera was routinely assayed for *H. pylori* antibodies with Western Blot Assay (MP BIOMEDICALS, USA), as well as levels of pepsinogen I and II using latex agglutination turbidimetric immunoassay kit (Eiken, Japan). The performance of the miRNA assay was compared with serological markers such as *H.pylori* antibody and Pepsinogen index. A positive serum Pepsinogen index was defined as pepsinogen I level ≤70 ng/ml and a pepsinogen I/II ratio ≤3.0. All participants had given informed consent.

Results: Out of the 4566 subjects with the mean age of 57±10, 53% were male, 76% were Chinese, 55% were *H.pylori* serology positive, and 5.3% were positive for Pepsinogen index. There were 125 gastric cancer cases detected. The 12-miR assay achieved an Area-Under-Curve (AUC) of 0.84, significantly outperforming (p-value< 0.01) that of *H.pylori* (AUC of 0.64) and Pepsinogen index (AUC of 0.57). The sensitivity of the miRNA assay in detecting early (stage 0-2) and late (stage 3-4) stage gastric cancer was 82.6% (95% CI, 68.6% to 92.2%) and 88.4% (95% CI, 78.4% to 94.9%) respectively at a specificity of 70.0% (95% CI, 67.8% to 71.9%). In com-

parison, *H.pylori* showed a sensitivity of 80.4% at a specificity of 44.3% whereas the Pepsinogen index showed sensitivity of 18.2% at a specificity of 95.0%. Using the miRNA assay as a pre-screening tool could potentially reduce number of endoscopy needed by 62% in detecting one case of gastric cancer.

Conclusion: Our serum miRNA panel is a useful, non-invasive screening test for gastric cancer. It can reduce unnecessary diagnostic endoscopy too.

Disclosure: Nothing to disclose

OP316 CELL-FREE DNA AMOUNT AND MUTATION PROFILE ANALYSIS FOR GASTRIC CANCER PATIENTS

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Introduction: Cell-free DNA (cfDNA) is released into the blood stream in various ways including at the death of cells or by active secretion. CfDNA also harbors genetic aberrations from malignant tissue (1). It was shown that cfDNA could be a powerful disease state and relapse monitoring analyte (2). New minimally invasive diagnostic procedures for circulating molecules are in demand because standard diagnostics are not able to analyze the cancer mutation profile changes over the course of treatment. However, there is a lack of comparative studies conducted in gastric cancer comparing tumor tissue DNA and cfDNA mutation profiles.

Aims & Methods: The aim of a study was to compare tumor tissue DNA and cfDNA mutation profiles and evaluate correlation of cfDNA amount and TNM stage for gastric cancer patients.

The study was approved by the Kaunas regional biomedical research ethics committee (No. Nr. BE-2-10). Gastric cancer tissue and blood were collected from 30 patients who were recruited at the Department of Gastroenterology, Lithuanian University of Health Sciences Hospital during the period 2010 - 2018. Tumour tissue was obtained from the primary lesion of the resected specimen or biopsy and stored at -80°C. Peripheral blood was drawn using a K2EDTA tubes at admission (before surgery). Sequencing libraries were prepared using TrueSeq Nano Libraries and samples of cfDNA pilot study were done in two replicates. Genomic DNA (gDNA) of tumor tissue and cfDNA were analyzed for mutations in cancer related genes using xGen Pan-Cancer Panel (IDT) consisting of 7816 xGen Lockdown Probes spanning 800 kb of the human genome, for enrichment of 127 significantly mutated genes implicated across 12 tumor tissue types for deeper sequencing coverage. Libraries were pair-end sequenced on an Illumina NextSeq 500. Individual reads were mapped to hg19 using BWA mem keeping only primary mappings. Variant calling for stand-alone plasma samples was performed using VarDict which enables scaling linearly to sequencing depth and ultra-deep sequencing application to detect tumor DNA circulating in blood. Strand filter was enabled to reduce false positive variants originating from only one strand. All variants were annotated using Variant Effect Predictor (3) and validated using the Integrative Genomics Viewer (4).

Results: Overall, 16 patients had mutations detected in gastric cancer related genes. Most frequently mutated genes in our study were *TP53*, *BRCA2*, *NOTCH1*, *CHECK2*, ERBB4 and KRAS. Yield of cfDNA is significantly increased for gastric cancer patients compared to healthy controls and generally corelated with gastric cancer TNM stage (R=0.55, p=0.012).

Conclusion: Our results demonstrate moderate correlation of total cfDNA amount and tumor stage. cfDNA reflects mutation profile in gastric cancer tissue DNA therefore may enable cfDNA analysis for monitoring disease stage of gastric cancer patients.

References: 1. Bettegowda, C. et al. Detection of circulating tumor DNA in early- and late-stage human malignancies. Science translational medicine 6, 224ra224, https://doi.org/10.1126/scitranslmed.3007094 (2014). 2. Phallen, J. et al. Direct detection of early-stage cancers using circulating tumor DNA. Science translational medicine 9, https://doi.org/10.1126/scitranslmed.aan2415 (2017). 3. McLaren, W. et al. The Ensembl Variant Effect Predictor. Genome Biology Jun 6;17(1):122, doi:10.1186/s13059-016-0974-4

(2016). 4. Robinson, J. T. et al. Integrative genomics viewer. Nature biotechnology 29, 24-26, https://doi.org/10.1038/nbt.1754 (2011).
Disclosure: Nothing to disclose

OP317 ENDOSCOPIC THREE CATEGORICAL DIAGNOSIS OF *HELICOBACTER PYLORI* INFECTION USING LINKED COLOR IMAGING AND DEEP LEARNING: A SINGLE-CENTER PROSPECTIVE STUDY

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Introduction: *Helicobacter pylori* (HP) eradication is a critical therapeutic approach to reduce gastric cancer mortality. In Japan, 1.5 million people undergo HP eradication annually. Three categories of HP infection status that coexist in the Japanese society are identified, i.e., non-infection (without a history of infection, HP_0), current infection (HP_1), and after eradication treatment (HP_2). Despite successful HP eradication, the risk of gastric cancer persists for patients who already show progression of mucosal atrophy and intestinal metaplasia[1]. Because each category shows a different risk of developing gastric cancer, diagnosis to stratify examinees into three categories is important. The authors find it beneficial to create a novel computer-aided endoscopic diagnosis (CAD) system for classifying HP infection status using linked color imaging (LCI) and deep learning (DL)[2]. LCI is a new image-enhanced endoscopic technique that enhances slight differences in mucosal color, whereas DL is a machine learning technology that imitates the neural network of the brain.

Aims & Methods: This prospective study aims to create a CAD system that can classify HP infection status into three categories using LCI and DL. The candidate subjects were examinees who underwent esophagogastroduodenoscopy (EGD) and who were tested for serum HP antibodies (HPab) or urea breath test (UBT) at our medical clinic. This study grouped the subjects under three categories: non-infection (HPab < 3 U/ml, n = 121, HP_0), current infection (HP ab ≥10 U/ml, n = 144, HP_1), and after eradication (UBT < 2.5 ‰, n = 119, HP_2). HP eradication treatment was performed at our clinic. All 384 subjects were allocated to a training group (n= 294; HP_0 = 91, HP_1 = 114, and HP_2 = 89) or a test group (n = 90; HP_0 = 30, HP_1 = 30, and HP_2 = 30) to evaluate the diagnostic accuracy of CAD. From the training group, 12,836 LCI pictures linked with HP infection status were generated. The accuracy of CAD was assessed by comparing the output data from the test group with the actual data on HP infection status. The endoscopic equipment was EG-L 580 NW or EG-6400 N (Fujifilm Co.). The DL model with 22 deep convolutional layers for CAD was adopted. R (version 3.3.2.) was used for statistical analyses.

Results: The areas under the curve of receiver operating characteristics of the CAD were 0.90 (HP_0; 95% CI, 0.833-0.959), 0.82 (HP_1; 95% CI, 0.727-0.905), and 0.73 (HP_2; 95% CI, 0.612-0.852).

Conclusion: Patients after HP eradication show negative reaction in most noninvasive HP infection tests; therefore, we cannot distinguish HP_0 from HP_2. In such a case, EGD is the only objective examination to achieve three categorical classifications because EGD recognizes mucosal atrophy and intestinal metaplasia of patients with eradicated HP. The CAD system demonstrated good accuracy in classifying HP infection status into three categories using LCI. In particular, the accuracy of HP non-infection with very low risk of gastric cancer was excellent. The authors infer that reducing EGD examination for HP_0 category can help simplify gastric cancer screening programs.

References: 1)Kobayashi M, Sato Y, Terai S. Endoscopic surveillance of gastric cancers after Helicobacter pylori eradication. World J Gastroenterol. 2015; 21(37): 10553-10562. 2)Nakashima H, Kawahira H, Kawachi H, Sakaki N. Artificial intelligence diagnosis of Helicobacter pylori infection using blue laser imaging-bright and linked color imaging: a single-center prospective study. Annals of Gastroenterology. 2018; 31: 462-468
Disclosure: Nothing to disclose

OP318 EFFICACY OF LINKED COLOR IMAGING IN SCREENING INTESTINAL METAPLASIA AND EARLY GASTRIC CANCER: A MULTICENTER RANDOMIZED CONTROL CLINICAL TRIAL

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Introduction: Minor mucosal lesions in the stomach are prone to be missed under white light (WL) endoscopy. Linked color imaging (LCI) can improve the endoscopic diagnosis, and LCI-based endoscopic criteria were proposed. We conducted this randomized clinical trial to investigate LCI's diagnostic efficacy for gastric intestinal metaplasia (GIM) and early gastric cancer (EGC)/high-grade intraepithelial neoplasms (HGINs).

Aims & Methods: Consecutive adult patients who had indications for gastroduodenoendoscopy were selected and randomly divided into two groups. In Group A (n=914), the patients received the WL endoscopy followed by LCI endoscopic examination. In Group B (n=914), the patients received LCI, followed by the WL mode for gastroscopy. The diagnostic efficacies of LCI and WL were evaluated and compared.

Results: LCI was superior to WL in diagnosing EGC/HGINs. GIM was manifested as "Purple in Mist" (PIM) under LCI. For GIM, the accuracy, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) [95% confidence interval] of WL were lower than those of LCI (0.676 [0.654-0.699] vs. 0.877 [0.861-892]; 0.650 [0.612-0.688] vs. 0.870 [0.843-0.896]; 0.693 [0.664-0.721] vs. 0.880 [0.862-0.898]; 0.564 [0.527-0.600] vs. 0.784 [0.753-0.815]; and 0.764 [0.736-0.792] vs. 0.931 [0.916-0.946], respectively). For differentiated EGC/HGINs, the accuracy, sensitivity, specificity, PPV and NPV of LCI were higher than those of WL (0.770 [0.729-0.812] vs. 0.664 [0.626-0.703]; 0.825 [0.726-0.923] vs. 0.632 [0.506-0.577]; 0.761 [0.716-0.806] vs. 0.668 [0.627-0.709]; 0.367 [0.284-0.451] vs. 0.175 [0.122-0.227]; and 0.963 [0.940-0.985] vs. 0.942 [0.918-0.966], respectively).

Conclusion: Our data supported the idea that LCI could improve the endoscopic diagnosis of GIM and EGC/HGINs, which can be used for screening and surveillance (ClinicalTrials.gov ID: NCT03092414).

Disclosure: Nothing to disclose

Biomarker-based classification of IBD
08:30-10:00 / Barcelona

OP319 POLYGENIC RISK SCORES IDENTIFY GENETIC AETIOLOGY OF INFLAMMATORY BOWEL DISEASE PHENOTYPES BEYOND KNOWN DISEASE SUSCEPTIBILITY LOCI

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Introduction: Genome-wide association studies (GWAS) have greatly improved our understanding of the genetic background of inflammatory bowel disease (IBD), with up to 240 genetic susceptibility loci identified. Clinical disease phenotypes are very heterogeneous and are, rather than the disease itself, the main determinant of patient well-being. However, only few genetic contributors to disease phenotypes have been identified through conventional GWAS. Polygenic risk scores (PRS), which aggregate the effects of thousands of trait-associated genetic variants discovered in GWASs, are powerful tools to estimate individual-specific genetic propensities and predict outcomes, even when used in relatively small deeply-phenotyped cohorts. In this present study, we use polygenic risk scores of twelve IBD-affiliated traits to uncover mechanisms which contribute to clinical phenotypes.

Aims & Methods: Detailed clinical characteristics of patients with IBD were obtained from two independent cohorts (cohort A: n=1,097 and cohort B: n=2,697). All patients were genotyped using the Global Screening Array, and over 12 million genetic variants were imputed using the Haplotype Reference Consortium panel. PRS were constructed for CD, UC and ten different traits and their associations with IBD disease phenotypes were evaluated using linear regression models. Significant (P< 0.05 after 10,000 rounds of permutation) PRS-phenotype associations identified in cohort A were put forward for replication in cohort B followed by a meta-analysis.

Results: In total, six PRS-phenotype associations remained significant after permutation and were replicated in the independent cohort. The composite genetic risk for CD susceptibility showed association with the subphenotype fibrostenotic CD (Montreal B2 [R^2 = 4.6%; P = 4.0E-7]) and ileocaecal resection (R^2 = 4.3%, P =6.3E-11), and remained significantly associated after correcting for CD disease location and age at diagnosis, even after excluding known contributing factors (*NOD2, MST1* and *MHC*). The composite UC susceptibility genetic risk (R^2 = 6.5%; P = 2.9E-4) and primary sclerosing cholangitis susceptibility (PSC) genetic risk (R^2 = 1.3%; P = 1.2E-3) were associated with colonic CD (Montreal L2). Moreover, polygenic scoring revealed shared genetic aetiology of affiliated diseases: polygenic risk for rheumatoid arthritis was associated with ulcerative proctitis (Montreal E1) (R^2 = 3.6%; P = 2.3E-4) and coeliac disease genetic risk (R^2= 2.6%; P = 1.4E-4) was associated with PSC. The polygenic risk for development of pulmonary fibrosis was nominally significantly associated with the risk of fibrostenotic CD in both cohorts (R^2 = 1.5%, [cohort A: unadjusted P= 0.018 and unadjusted P = 0.02 [cohort B]).

Conclusion: The cumulative genetic burden of CD is associated with more complicated clinical disease phenotypes, suggesting biological signals beyond known genome-wide significant disease susceptibility genetic variants. We validate the putatively shared genetic aetiology of PSC and UC with colonic CD. Moreover, our results suggest shared genetic aetiology between the development of pulmonary fibrosis and fibrostenotic CD. These results further our understanding of specific IBD phenotypes and might be used to better stratify patients or to provide new therapeutic targets.

Disclosure: Nothing to disclose

OP320 GENOME-WIDE ANALYSES IDENTIFY NOVEL GENETIC VARIANTS THAT INTERACT WITH TOBACCO SMOKE AND AFFECT RISK FOR DEVELOPMENT OF INFLAMMATORY BOWEL DISEASE

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Introduction: Inflammatory Bowel Disease (IBD) is characterized by a complex etiology with an interplay between genetic, environmental, microbial, and immunologic factors. A divergent effect of smoking behavior in the two subtypes of IBD, Crohn's Disease (CD) and Ulcerative Colitis (UC), supports the existence of gene-environment interactions (GxE). Several genetic variants have already been found to interact with tobacco smoke in modifying the risk for IBD. However, in previous studies, gene-smoking interactions in IBD were detected based on genome-wide Immunochip-data with poor coverage. Therefore, we performed a case-only study using over 12 million genetic variants with an excellent genome-wide content from Illumina Global Screening Array (GSA).

Aims & Methods: In this study, we aimed to identify novel gene-smoking interactions that could potentially affect IBD, CD or UC. Genetic data were obtained from 1,097 IBD patients (CD n= 500, UC n = 402) of European ancestry of the University Medical Center Groningen (UMCG) through GSA. After quality control (QC) and imputation 12,130,010 genetic variants were available for genome-wide association studies. Smoking status was defined as 'never smoking', 'ever smoking', 'current smoking' or 'former smoking'. Multivariable logistic regression analyses (age- and sex-adjusted) were performed to compare different groups of smokers (ever vs never

smokers, current vs never smokers, former vs never smokers, and current vs never and former smokers). All analyses were performed in the total IBD cohort, and for CD and UC separately.

Results: We observed an overall number of 2,109 statistically significant (p< 5.0x10^{-5}) single nucleotide polymorphisms (SNPs). However, some SNPs referred to unknown genes or belonged to the same gene. Five significant SNPs, rs1878558 (*SLCO3A1*), rs6680523 (*RASSF5*), rs7141581 (*SLC25A21*), rs6818043 (*ARHGAP10*), and rs240952 (*REV3L*) were detected within loci that were previously associated with nicotine dependence or differences in smoking cessation. The directions of their odds ratios (ORs) indicated that our phenotype data were reliable. We detected several significant SNPs that refer to immune regulating pathway genes (e.g. rs6680523 *RASSF4*, rs11738246 *LNPEP*, rs74660825 *PRKCB*, rs144226221 *CBLB*, and rs160357 *CREB5*). Many other significant SNPs that we detected refer to dopaminergic signaling genes, calcium-associated genes, and nucleic acid binding genes.

Several nominally significant SNPs (p < 0.01) had an opposite OR direction in CD and UC: 216 SNPs in ever vs never smokers, 97 SNPs in current vs never smokers, 202 SNPs in former vs never smokers, and 98 SNPs in current smokers vs never and former smokers. The results imply that a smoking associated SNP protects against the one subtype of IBD, whereas the same gene-smoking interaction increases the risk for development of the other subtype of IBD.

Conclusion: In this study, we identified multiple novel genetic variants that interact with smoking status and affect the risk for development of IBD, CD or UC. In our cohort of 1,097 IBD patients, we were able to reproduce smoking-associated genetic risk variants that have previously been identified in non-diseased populations. We detected genetic risk variants that yielded an opposite direction in CD and UC, thus indicating a distinct effect of gene-smoking interactions on disease development. Our results, especially the divergent effect of gene-smoking interactions in CD and UC, provide a better insight into the contribution of gene-smoking interactions to the etiology of IBD.

Disclosure: Nothing to disclose

OP321 INTEGRATION OF WHOLE-EXOME SEQUENCING, GENOME WIDE GENOTYPING AND RNA SEQUENCING OF INTESTINAL BIOPSIES IN INFLAMMATORY BOWEL DISEASE IDENTIFIES INFLAMMATION-DEPENDENT EFFECTS

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Introduction: Inflammatory bowel disease (IBD) is a chronic immune-mediated disease, characterized by intermittent inflammation in the gastrointestinal tract. Although currently >240 genetic risk loci are known to be associated with this disease, it is still poorly understood how these genetic variants contribute to disease development. The effect of genetic variation on gene expression (defined as expression quantitative trait loci— *cis*-eQTLs) has mostly been studied by combining GWAS and transcriptome data from peripheral blood. However, the importance of studying these eQTLs in the disease- tissue and in the right disease- context is increasingly being recognized. We set out to examine the effect of genetic variants on gene expression in intestinal mucosal biopsies of IBD patients, in both inflamed and non-inflamed conditions, to identify inflammation-dependent eQTLs.

Aims & Methods: We collected 299 snap-frozen intestinal biopsies from 171 IBD patients, 113 deriving from non-inflamed tissue and 186 from inflamed tissue. Mucosal transcription profiles were determined by RNA-sequencing and genotypes were obtained by Whole Exome Sequencing (WES) combined with Genome Wide Screening Array (GSA) data. In total, 28,746 genes and SNPs located in +/- 500kb genomic regions surrounding these genes were included for identifying *cis*-eQTLs. *cis*-eQTLs were identified using linear mixed models and by regressing out the effect of potential confounding variables as visualized in the first 18 Principle Coordinates. To explore the effect of genetic variants in the context of inflammation, we then assessed the *cis*-eQTLs in inflamed versus non-inflamed tissue.

Results: Overall, 419,858 *cis*-eQTLs were found to be significant in gut tissue, after adjusting for inflammation effect (FDR< 0.05). We replicated 84.22% of these in the publicly available intestinal dataset of the Genotype-Tissue Expression (GTEx) consortium, showing robustness of our method. The inflammation-interaction analysis revealed 1.140 inflammation-dependent *cis*-eQTLs in 157 unique genes (FDR< 0.1). We identified inflammation-dependent *cis*-eQTLs involving known IBD-risk genes (*IL26, HLA-DQA1, HLA-DQA2, TNFSF11*), cytokines and growth factors (*DKK1, FGF12, PENK, STC2*), and genes encoding immune cell receptor (segments) (*IL17RB, TRAV34, TRAV8, TREML4*). Enrichment analyses of the associated genes revealed that inflammation-dependent *cis*-eQTL genes are mainly involved in immune responses and ion transport.

Conclusion: In this study we identify genetic variants that influence mucosal gene expression in patients with IBD, both dependent and independent of inflammation status. We observe that the inflammation-dependent *cis*-eQTL genes are mainly involved in immune responses, which suggests that differences in the genetic background of patients drive differences in the mucosal immune response in IBD. Overall, our results show local and context specific *cis*-eQTLs, which are potential leads for understanding disease pathogenesis and drug target identification.

Disclosure: Nothing to disclose

OP322 MICROBIOME AND FECAL BIOMARKERS CAN DIAGNOSE AND CLASSIFY INFLAMMATORY BOWEL DISEASE

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Introduction: Irritable Bowel Syndrome (IBS) and Inflammatory Bowel Diseases (IBD) are chronic disorders of the gut, with prevalence exceeding 10% in the European population. Currently, these diseases are frequently diagnosed by exclusion of other gastrointestinal disorders using multiple, often invasive, clinical procedures. The only biomarker for IBD currently utilised in clinical practice is fecal calprotectin test (FCal), which has high sensitivity but suffers from moderate specificity. Improvements in metagenomic sequencing have enabled cost-efficient profiling of gut microbiota, opening an opportunity to utilise the gut microbiome for diagnosis of IBD and IBS. In addition, our previous research identified that fecal measurements of human beta defensin 2 (HBD2) and Chromogranin A (ChrA) proteins are associated with composition of gut microbiota and diagnosis of IBS.

Aims & Methods: The primary aim of this study was to use features of microbiome and fecal biomarkers FCal, HBD2 and ChrA to train models for non-invasive diagnosis of IBD and IBS. Secondary aim was to test if gut microbiome can be utilised to classify type of IBD (Crohn's disease vs ulcerative colitis) and clinical parameters of the disease (such as disease activity and location).

We used whole metagenome sequencing to analyse composition and function of microbiome of fecal samples of 181 IBS patient, 380 IBD cases and 859 healthy controls (HC), and measured HBD2, FCal and ChrA in all samples. A total of 521 microbiome features (244 bacterial taxa and 277 biochemical pathways) were used to train machine-learning classifiers (random forests, support vector machines and neural networks) for classification of samples as HC, IBD or IBS cases, and to classify type of IBD (Crohn's disease (CD) vs Ulcerative colitis (UC)), clinical parameters of the disease (based on Montreal classifications), and disease activity. The models were put forward for validation on a dataset generated using 16S sequencing to assess the reproducibility of the approach.

Results: Fecal measurement of HBD2 showed high predictive power for differentiating between IBD vs IBS (Sensitivity = 0.9, Specificity = 0.8, Area under ROC curve (AUC) = 0.89), outperforming FCal (Sensitivity = 0.85, Specificity = 0.6, AUC = 0.79). The ChrA, however, showed low predictive power (Sensitivity = 0.6, Specificity = 0.55, AUC = 0.57). Additionally, combining HBD2 and FCal increased the predictive power above individual biomarkers (Sensitivity = 0.9, Specificity = 0.85, AUC = 0.94).

Models trained using microbiome features demonstrated predictive power in line with HBD2 (AUC = 0.88) with an added advantage classification of

disease location (AUC = 0.82 for classification of colonic vs ileal disease) and type of disease (AUC = 0.88 for classification of UC vs CD). Finally, integration of biomarkers and microbiome features further increased the predictive power of the model (Sensitivity and Specificity > 0.9, AUC > 0.95 for IBD vs IBS). Models build on metagenomic-sequencing data replicated well by using 16S data (and vice-versa), with Sensitivity and Specificity within 10% of the original model.

Conclusion: We demonstrate that HBD2 is a novel biomarker for IBD with potential to improve specificity of IBD diagnosis, especially when combined with FCal. Additionally, we show that features of gut microbiome, in combination with already used fecal biomarkers, are strong predictors for differentiating IBD and IBS, with additional potential of classifying location and type of IBD. These results have a potential to improve non-invasive pre-screening for IBD in clinical practice.

Disclosure: Nothing to disclose

OP323 USEFULNESS OF ACP 353 (ANTI-CROHN´S DISEASE PEPTIDE 353) AS A NEW BIOMARKER IN THE DIAGNOSIS OF INFLAMMATORY BOWEL DISEASE: A MULTICENTER STUDY

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Introduction: We isolated an antigenic peptide (TCP 353) specific for patients with Crohn's disease (CD) from the blood using the phage display method and found that its antibody titer (ACP 353) would be a biomarker specific for CD (Clin Exp Immunol 2011 and J Gastroenterol 2014). In multicenter studies, we have clarified the specificity of TCP for novel serum biomarkers centered on ACP 353. Here, we analyzed the specificity of ACP 353 IgG for CD and the improvement in the diagnostic ability of the combination of ACP 353 IgG and a novel serum biomarker and examined its usefulness in the diagnosis of inflammatory bowel disease (IBD).

Aims & Methods: Subjects were patients with intestinal diseases who visited Kurume University Hospital, Fukuoka University Chikushi Hospital and Kyushu University Hospital between December 2016 and September 2017. ACP 353 IgG, glycoprotein 2 (GP2) IgG and antibodies against Saccharomyces cerevisiae (ASCA) IgG levels were mesured as a marker for CD and proteinase 3- antineutrophil cytoplasmic antibody (PR3-ANCA) and myeloperoxidase (MPO)-ANCA levels as a marker for ulcerative colitis (UC).

Results: There were 334 patients, including 108 with CD, 88 with UC, 23 with IBD-unclassified (IBD-U), 32 with other intestinal diseases (Irritable bowel syndrome, etc.), and 83 healthy people. The cutoff value was positive above the mean human healthy value plus 3 SD. The mean ± SE/positive rates of ACP 353 were as follows: CD, 54.7 ± 34.8 U/mL/34.3%; UC, 1.6 ± 0.15 U/mL/1.1%; IBD-U, 1.41 ± 0.12 U/mL/0%, others, 1 .19 ± 0.1 U/mL/0%; and healthy, 2.14 ± 0.06 U/mL/0%. The sensitivities/specificities of the markers were as follows: ACP 353 IgG, 34.3/97.8; GP2 IgG, 36.1/98.2; and ASCA IgG, 15.7/96.5 for CD, PR3-ANCA, 31.8/96.3; and MPO-ANCA, 0/100 for UC. Next, the specificity of the biomarker was fixed at 95%, and the sensitivity was compared. The sensitivities (%) of the biomarkers were as follows: ACP353 IgG, 34.3; GP2 IgG, 42.6; ASCA IgG, 26.9; ACP 353 IgG + GP2 IgG + ASCA IgG, 41.7; and ACP 353 IgG + GP 2 IgG + ASCA IgG + PR3-ANCA, 63.

Conclusion: The high specificities of the IBD novel biomarkers ACP 353, GP2 and PR3-ANCA were demonstrated. In the future, with the aim of multi-facility joint research on a nationwide scale, we would like to clarify the usefulness of new biomarkers centered on ACP 353 for the Japanese population.

Disclosure: Nothing to disclose

OP324 MYENTERIC PLEXITIS AND POST-OPERATIVE RECURRENCE IN CROHN'S DISEASE: THE ROLE OF ENTERIC GLIAL CELLS AND INTER-CELLULAR ADHESION MOLECULE-1

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Introduction: Half of Crohn´s disease (CD) patients require surgery within 20 years of diagnosis, and post-operative recurrence (POR) is frequent. Among the risk factors of POR, the presence of myenteric plexitis (≥ one immune cell in contact with myenteric ganglia) at the proximal resection margin has been incorporated in the European guidelines. However, this criterion is rarely used, as little is known about the involved mechanisms. Our objectives were to determine which cells of the enteric nervous system interact with T cells, and to identify the molecules responsible for these interactions.

Aims & Methods: Our objectives were to determine which cells of the enteric nervous system interact with T cells, and to identify the molecules responsible for these interactions.

In vivo: 29 patients (20 CD, 9 cancer) who underwent an ileocolonic resection were included. Full-thickness slices of the proximal resection margin were analysed by immunohistochemistry (IHC) to identify enteric glial cells (S100β), neurons (Hu) and T cells (CD3, CD4, CD8). T cells in contact with ganglia of the myenteric plexus were counted on each slide.

In vitro: To analyse neuro-immune interactions, human enteric glial cells (EGC) were co-cultured with T cells which were activated by anti-CD3/CD28 antibodies beforehand. To determine the impact of inflammatory conditions, EGC were pre-treated with lipopolysaccharide (LPS) or IL-1β/TNFα (IT). Immunocytochemistry (ICC) was used to analyse the adhesion of T cells to EGC. The expression of adhesion molecules was determined by qPCR, western blot and ICC.

Results: IHC showed the presence of T cells, CD4^{+} and CD8^{+}, in contact with EGC of myenteric ganglia in both CD and control patients. The number of T cells per ganglion was significantly higher in CD patients (5.6 ± 0.9) as compared to controls (1.2 ± 0.2) (p< 0.001), with a threshold of 1.7 T cell per ganglion, and was twice higher in CD patients suffering from POR (7.1 ± 1.4) as compared to those in whom CD did not recur (3.6 ± 0.9) (p=0.175). POR was systematic above 7.7 T cells per ganglion.

In vitro, pre-treatment of EGC with LPS and IT significantly increased the number of T cells in contact with EGC, respectively by a factor of 2.7 (± 0.7) (p< 0.01) and 2.1 (± 0.3) (p< 0.01) as compared to the control condition. These inflammatory stimuli were associated with an overexpression of ICAM-1 in EGC as measured by qPCR, while the expression of MAdCAM and NCAM was not increased. This upregulation of ICAM-1 was confirmed at the protein level.

Conclusion: Our results indicate that T cells interact with EGC *in vitro* and *in vivo*. These interactions are increased under inflammatory conditions and are associated with an upregulation of ICAM-1. This suggests a role of EGC in the formation of plexitis, possibly through the binding of LFA-1 to ICAM-1. Further experiments will be carried out to confirm this possibility.

Disclosure: Nothing to disclose

Highlights in oesophageal cancer: What's hot?

10:30-12:00 / A1

OP325 DETECTION OF BARRETT'S ESOPHAGUS BY MOLECULAR ENDOSCOPIC IMAGING USING NANOPARTICLES

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Introduction: Barrett's esophagus (BE) is recognized as a premalignant condition of esophageal cancer. Despite recent advancements in treatment strategies its prognosis is still very poor. Early detection may allow for more effective surveillance. Endoscopic surveillance for detecting premalignant lesions in BE is challenging because of their flat appearance without any noticeable morphological change. Molecular endoscopic imaging (MEI) allows for in vivo visualization and characterization of biological processes that occur on a cellular or sub-cellular level. Several MEI studies in the past using fluorescent-labeled antibodies were carried out to detect disease-specific targets. However, antibodies may confer allergic reactions, and their diffusion across epithelial borders and delivery to target structures is slow due to their high molecular weight. In contrast, nanoparticles have high surface area to volume ratio and no apparent toxicity. Therefore functionalizing the surface of nanoparticle with antibodies and stronger fluorophores allow for targeting minute amounts of structures. In addition they can also be loaded with ligands to multiple biomarkers. To date, no data is available on the use of nanoparticles for MEI

Aims & Methods: To assess the diagnostic applicability of MEI with nanoparticles for diagnosis of Barrett's esophagus. In addition, the results were compared with traditional MEI using specific labeled Muc-2 antibodies and standard histopathology.

Patients undergoing endoscopic surveillance of known Barrett's esophagus were recruited for the study. First, careful inspection of the Barrett's segment was performed with high-definition white-light imaging and chromoendoscopy. Then biopsies were collected from the Barrett's mucosa and rinsed in PBS. Afterwards, biopsy specimens were incubated with FITC labeled Muc-2 antibodies or biodegradable, pH sensitive nanoparticles coupled with FITC conjugated Muc-2 antibodies. After washing in PBS to remove unbound antibody, MEI was performed using the probe-based confocal imaging system. Squamous epithelium and gastric tissue samples were considered as controls. Fluorescence intensity from Barrett's mucosa and control specimens were compared, followed by histological confirmation.

Results: 30 specimens were successively analyzed. Squamous epithelium or gastric mucosa showed no antibody binding demonstrating the high specificity of the technique. Fluorescence signals were noted for traditional MEI using Muc-2 antibodies in intestinal type Barrett's metaplasia corresponding to goblet cells in the histopathological examination. A significantly higher fluorescence was found with nanoparticles coupled with FITC conjugated Muc-2 antibodies. MEI with nanoparticles for prediction of Barrett's metaplasia was consistent in all cases with histological analyses.

Conclusion: This is the first study showing the feasibility of using nanoparticles for molecular endoscopic imaging. Highly-specific nanoparticles can visualize Barrett's metaplasia more efficiently than conventional MEI. With the unique potential of nanoparticles allowing coupled to multiple biomarkers, future research is focused to identify different grades of dysplasia in affected patients. In addition, NPs can be loaded with cytotoxic materials to apply for targeted therapy.

Disclosure: Nothing to disclose

OP326 FACTORS PREDICTING MISSED DIAGNOSES OF OESOPHAGOGASTRIC CANCER: A CASE CONTROL STUDY OF PATIENTS HAVING GASTROSCOPY

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Introduction: There are unprecedented pressures facing endoscopy services worldwide. In the United Kingdom, there has been an over 40% increase in gastroscopy and 80% increase in colonoscopy delivery in the last 10 years. Oesophagogastric (OG) cancers diagnosed in patients who have had a gastroscopy within the preceding three years are considered to have had cancers missed and occur in 11% cases in the Western population [Menon and Trudgill, EIO 2014]. We examine patient, endoscopist and service level factors that may affect rates of missed OG cancers.

Aims & Methods: Patients diagnosed with OG cancer who had undergone gastroscopy within the preceding three years (the cases) were identified from endoscopy and OG cancer databases between January 2013 and December 2017 at Sheffield Teaching Hospitals, Sheffield, United Kingdom. Patient factors (age, gender, location of missed cancer and indication for gastroscopy), endoscopist factors (professional background, training status, procedural volume and use of sedation) and service pressures (number, types and time of procedures) at the time of the index procedure (at which a missed cancer is presumed) were examined and compared to two control groups. The first comprised the cases at the time of their subsequent diagnostic gastroscopy to control for patient factors. However, lesions in this group would be more endoscopically obvious than early cancers which are typically smaller, more focal lesions. Therefore a second control group comprised patients diagnosed as having benign focal lesions (of ≤ 10mm) matched (in terms of endoscopist, procedural date, patient age, gender and location of cancer) to each of the cases.

Results: We identified 627 patients diagnosed with oesophageal (50.9%) and gastric (48.8%) cancer of whom there were 48 (7.7%) cases considered to have missed cancers in the preceding three years. Missed gastric cancer was more common in male patients (OR 3.0, 95% CI 1.32- 6.91). There were fewer cases of missed oesophageal cancer amongst those who were examined for dysphagia (OR 0.16, 95% CI 0.05 - 0.50), but more cases amongst those examined for anaemia (OR 5.36, 95% CI 1.87 - 15.41). Univariate analysis suggested that greater total numbers of procedures (on lists including upper and lower endoscopy) or greater number of gastroscopies on a list, or gastroscopy only lists, were associated with missed cancers. However, only greater total numbers of procedures were associated with missed cancers on multivariate analysis (OR 2.16, 95% CI 1.19 - 3.91). When missed cancer cases were compared to the control group in which benign focal lesions were diagnosed, only a greater number of procedures on a list (OR 1.25, 95% CI 1.02 - 1.52) was associated with a risk of a missed lesion. There was no association between use of sedation, endoscopist experience or professional background or time of day and risk of missed cancers.

Conclusion: 7.7% of patients diagnosed with OG cancer could have been diagnosed and treated earlier. Our study suggests that there may be risk of missed pathology during gastroscopy performed on more populated endoscopy lists. The use of sedation, endoscopist background, or time of procedure did not increase the risk of missed cancer procedures.

References: Menon S, Trudgill N. How commonly is upper gastrointestinal cancer missed at endoscopy? A meta-analysis. Endosc Int Open 2014; 2(2): E46-50.

Disclosure: Nothing to disclose

OP327 LONG-TERM OVERALL SURVIVAL AFTER ENDOSCOPIC MUCOSAL RESECTION FOR ESOPHAGEAL HIGH-GRADE DYSPLASIA AND EARLY ADENOCARCINOMA: A NATIONWIDE REGISTRY LINKAGE STUDY

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Introduction: Endoscopic therapy, particularly endoscopic mucosal resection (EMR), is recommended by current guidelines for patients with esophageal high-grade dysplasia (HGD) or early adenocarcinoma (EAC). Long-term outcome data based on large cohorts is limited. In this study, we aimed to evaluate the long-term outcome of EMR in patients with esophageal HGD/EAC based on nationwide data from daily clinical practice. We also investigated factors associated with overall survival.

Aims & Methods: Registered patients in the period 2005-2015 with HGD/EAC of the esophagus or gastroesophageal junction treated with EMR were identified from the Netherlands Cancer Registry (NCR). Clinicopathological data, including age at diagnosis, year of treatment, disease stage, surgical resection and vital status were retrieved from the NCR. Through record linkage with the nationwide Dutch Pathology Registry (PALGA), additional pathological data were obtained. Patients with no available pathology reports of an EMR specimen were excluded. The primary outcome was overall survival.

Secondary outcomes were the number of en-bloc resections, R0-resections (margins free from dysplasia/EAC) and proportion having undergone surgical resection. Estimated overall survival rates were compared with log-rank analysis. Multivariable Cox regression models were used to investigate the association between clinicopathological variables and overall survival.

Results: A total of 898 primary EMR procedures for HGD/EAC were included. The mean age at diagnosis was 67 [±10.5] years, median follow-up time 4.8 [IQR 3.0-6.8] years. Local tumor stage after primary EMR was 12% HGD (pTm1), 68% intramucosal (pTm2-3) and 21% submucosal (pTsm1-3) EAC, with 10-year overall survival rates of 73%, 58% and 49%, respectively (p<0.001, see table 1). In total, 118 patients (21%) had an en-bloc EMR with 42% complete resection rate.

Following piecemeal EMR (mean specimens 3.3 [±2.6]), R0-resection of the vertical margins was 73%. R0-resections increased over time from 53% in 2005 to 75% in 2015. After radical EMR without lymphovascular invasion, 28/558 (5%) underwent surgical resection during follow-up (4% intramucosal vs 14% submucosal EAC, (p<0.001). Factors associated with overall survival were pTsm1-3 (HR 2.5, 95% CI 1.4 - 4.4), pTm2-3 (HR 1.9, 95% CI 1.1 - 3.3), presence of signet ring cells (HR 1.7, 95 CI% 1.0 - 2.7), lymphovascular invasion (HR 1.6, 95 CI% 1.0 - 2.5), R1-resection (HR 1.5, 95% CI 1.1 - 2.0), age (HR 1.1, 95 CI% 1.0 - 1.1) and surgical resection (HR 0.5, 95% CI 0.3 - 0.8).

	Overall		R0-resection		R1-resection	
pT stage	5-year OS	10-year OS	5-year OS	10-year OS	5-year OS	10-year OS
m1 (HGD)	88%	73%	89%	75%	86%	67%
m2-3	76%	58%	79%	61%	69%	51%
sm1-3	65%	49%	80%	57%	55%	44%

[Table 1. Overall survival (OS) rates according to radicality of primary EMR.]

Conclusion: EMR is a highly effective treatment for esophageal HGD/EAC with excellent long-term survival in daily clinical practice. Pathologic factors, i.e. depth of tumor invasion, presence of signet ring cells and lymphovascular invasion, were the strongest predictors of poor overall survival.

Disclosure: Nothing to disclose

OP328 CONDITIONAL SURVIVAL IN PATIENTS WITH RESECTABLE ESOPHAGEAL CANCER

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Introduction: Most provided survival rates in current literature are static, calculated from the day of surgery. But as time proceeds after surgery, the risk of death in esophageal cancer patients changes. Conditional survival accounts for the time already survived after surgery and may be informative in addition to conventional estimates during follow-up.

Aims & Methods: The aim of this study was to assess conditional survival in esophageal cancer patients and to design a nomogram predicting the conditional probability of survival for esophageal cancer patients after surgery. Consecutive patients with esophageal cancer who received neoadjuvant chemoradiation followed by an esophagectomy between January 2004 and 2019 in the Amsterdam UMC, location AMC, The Netherlands were included in this retrospective study. Patients with distant metastases, who underwent salvage surgery, or who died within 30 days after resection due to complications were excluded. Conditional survival was defined as the probability of surviving "y" years after already surviving for "x" years. The used formula was: $CS_{(x|y)} = S_{(x+y)}/S_{(x)}$ with $S_{(x)}$ representing the overall survival at "x" years. Cox proportional hazard models were used to evaluate predictors for overall survival. A nomogram was constructed to predict 5-year survival directly after surgery and given 1-, 2-, 3- and 4-years survival after surgery, based on the coefficients of the predictors in the multivariable Cox proportional hazard model, using a penalized LASSO (Least Absolute Shrinkage and Selector Operator) method. C-statistic which is presented with optimism adjusted for by bootstrapping.

Results: 660 patients were included in this study. The median overall survival was 46.4 months (95%CI 39.1 - 53.8). The probability to achieve 5-year overall survival after resection increased from 46% directly after surgery to 55%, 67%, 79% and 88% per additional year survived. The more years patients have already survived, the better their chances of additional years of survival are. This increase flattens after more years have passed. The conditional overall survival probability is shown in table 1. ypN-stage was the strongest predictor for overall survival in multivariable analysis (HR 2.53, 95%CI 1.90 - 3.36; HR 3.17, 95%CI 2.27 - 4.43 and HR 6.50, 95%CI 4.28 - 9.87, respectively for ypN1, ypN2, ypN3 with ypN0 as reference, all p< 0.001), followed by pulmonary complications (HR 1.16, 95%CI 1.88 - 0.002, p=0.002), cardiac comorbidity (HR 1.27, 95%CI 1.01 - 1.60, p=0.040) and ypT-stage (HR for ypT2-3 in relation to ypT0 1.461, 95%CI 1.02 - 2.09, p=0.039). These variables were included in the nomogram. The nomogram predicted 5-year survival using these predictors and number of years already survived with a C-statistic of 0.70.

Total years of survival	Years already survived by patients							
	0	1	2	3	4	5	6	7
1	83							
2	69	83						
3	58	69	84					
4	52	62	75	90				
5	46	55	67	79	88			
6	41	49	60	71	79	90		
7	38	46	55	66	73	83	93	
8	33	40	48	58	64	73	81	88

[Table 1. Conditional survival estimates]

Conclusion: The proposed nomogram showed an accurate prediction of survival in patients after esophageal cancer surgery, taking the years already survived after surgery into account. This nomogram can be helpful in counselling patients in the follow-up after surgery.

Disclosure: Nothing to disclose

OP329 DYNAMICS OF BODY COMPOSITION PARAMETERS IN RESECTED PATIENTS WITH ADENOCARCINOMA OF THE ESOPHAGOGASTRIC JUNCTION TYPE 1 AND 2

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Introduction: Preoperative sarcopenia is a predictor of poor prognosis of esophageal cancer after esophagectomy. and can influence surgical complications. Less is known about the influence of surgical resection on body composition. The aim of this study is to examine the dynamics of body composition parameters of resected patients with adenocarcinoma of the esophagogastric junction (AEJ) Siewert type I and II.

Aims & Methods: 172 patients with AEJ Siewert type I and II who underwent esophagectomy in the Department of Surgery, Klinikum Rechts der Isar, 2007-2009 and 2014-2015, were screened for this retrospective study. Computed tomography (CT) images prior to surgery (timepoint 1, T1) as well as 6 (T2) and 12 months (T3) after esophagectomy were assessed using Slice-O-Matic® software version 4.3. Following body compositions parameters were estimated: subcutaneous adipose tissue area index (SATI), visceral tissue area index (VATI), intramuscular tissue area index (IMATI), total adipose tissue area index (TATI), as well as skeletal muscle mass index (SMAI). 157 patients had CT at T1, and only 59 patients had CTs at T1, T2, and T3. Sarcopenia was defined by consensus thresholds before surgery with the cut-off points for SMI (skeletal muscle tissue area index) < 52.4 cm^2/m^2 for male and < 38.5 cm^2/m^2 for female patients.

Results: Preoperative sarcopenia occurred in 53% of patients. 76% of patients were sarcopenic 6 months and 72% 12 months after surgery. Sarcopenic and non-sarcopenic groups differ in absolute and relative weight loss, BMI, albumin, hemoglobin, SMAI and SATI, but not in cholinesterase, c-reactive protein, TATI, VATI and IMATI. Median survival rate was 3,9 (range: 0.2-11.3) years in the non-sarcopenic group and 2,8 (range: 0.2-11.2) years in the sarcopenic group (p = 0.006). The median values for decrease in body composition parameters 6 months after surgery were for TATI 55 cm/m2 (50%) in non-sarcopenic group and 52 cm2/m2 (51%) in sarcopenic group, for VATI 32 cm/m2 (64%) in both non-sarcopenic group and sarcopenic groups, for SATI 19 cm/m2 (33%) in non-sarcopenic group and 16 cm2/m2 (39%) in sarcopenic group, for IMATI 1 cm/m2 (33%) in non-sarcopenic group and 1 cm2/m2 (20%) in sarcopenic group, for SMAI 5 cm/m2 (9%) in non-sarcopenic group and 2 cm2/m2 (4%) in sarcopenic group.

The median values for decrease in body composition parameters 12 months after surgery were for TATI 60 cm/m2 (55%) in non-sarcopenic group and 46 cm2/m2 (46%) in sarcopenic group , for VATI 35 cm/m2 (70%) in non-sarcopenic group and 31 cm/m2 (62%) in sarcopenic group, for SATI 21 cm/m2 (36%) in non-sarcopenic group and 14 cm2/m2 (34%) in sarcopenic group, for IMATI 1 cm/m2 (33%) in non-sarcopenic group and 1 cm2/m2 (20%) in sarcopenic group, for SMAI 4 cm/m2 (7%) in non-sarcopenic group and 2 cm2/m2 (4%) in sarcopenic group. The significant differences between sarcopenic and non-sarcopenic groups were observed regarding change in SMAI (sarcopenic group lost less skeletal muscle 6 and 12 months after surgery), as well as change in IMATI (sarcopenic group lost less intramuscular adipose tissue 6 months after surgery) and SATI (sarcopenic group lost less subcutaneous adipose tissue 12 months after surgery).

Conclusion: To our knowledge, it is the first study demonstrating dramatical loss of adipose and skeletal muscle tissue 6 and 12 months after esophagectomy in AEJ Siewert type I and II patients. No significant changes in body composition parameters occur between 6 and 12 months after surgery.

Disclosure: Nothing to disclose

OP330 IRRADIATION STENTS PROLONG SURVIVAL COMPARED TO REGULAR STENTS IN END-STAGE ESOPHAGEAL CANCER: META-ANALYSIS AND SYSTEMATIC REVIEW

Tinusz B.[1], Soós A.[1], Hegyi P.[1], Sarlós P.[2], Szapáry L.[1], Erős A.[1], Feczák D.[1], Szakács Z.[1], Márta K.[1], Erőss B.[1]

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Introduction: Esophageal cancer is the eighth most common cancer worldwide and the sixth leading cause for cancer-related mortality. Such high mortality underlines the importance of palliative treatment options. Currently, there are no universally accepted international guidelines on whether additional oncological treatment is required besides stenting in the palliative care of esophageal cancer.

Aims & Methods: Our aim was to compare the effectiveness and safety of stent insertion alone to stent insertion combined with any modality of active oncological treatment in the palliative care of esophageal cancer.

A meta-analysis and systematic review were performed according to the PRISMA Statement. We searched 6 databases (PubMed, EMBASE, the Cochrane Library, Web of Science, clinicaltrials.gov, and the WHO Global Health Library) for papers on the palliative treatment of esophageal cancer. Patients receiving stent insertion only (control group) were compared to patients receiving chemotherapy, radiotherapy, chemo-radiotherapy or brachytherapy in addition to stent treatment (intervention group). Meta-analytical calculations were performed by using STATA v15.1. For mean survival time and grade of dysphagia within 3 days of stenting weighted mean differences (WMD) were calculated. For complications of stenting (such as chest pain, hemorrhage, deaths due to hemorrhage, stent migration and restenosis, tracheoesophageal fistula formation and development of pneumonia) pooled odds ratios (OR) were calculated. WMDs and ORs were interpreted with 95% confidence intervals (CI). The protocol of the study was registered prior on PROSPERO under the registration number CRD42018093921.

Results: Out of 9038 articles yielded by our search, 11 met the pre-defined inclusion and exclusion criteria. These contained a total of 838 esophageal cancer patients, out of which 374 and 464 patients belonged to the intervention and control groups, respectively. Patients in the intervention group had significantly longer mean survival time (WMD, 1.56; 95% CI, 0.66-2.46). This significance was still present when analyzing the subgroup of patients where irradiation stents were utilized as intervention (WMD, 1.93; 95% CI, 0.78-3.09), however, the significance disappeared when only looking at patients receiving other modalities of oncological treatment (WMD, 0.72; 95% CI -1.26-2.70). We found no significant difference in any complications of stenting between the two groups. Our systematic review suggested that additional treatment is more effective in the long-term relief of dysphagia than stenting alone.

Conclusion: Our results indicate that the utilization of irradiation stents prolong the survival of patients in the palliative treatment of esophageal cancers as compared to conventional stent insertion. Moreover, additional oncological treatment may be more effective in the long-term relief of dysphagia as compared to stenting alone. Further studies are warranted.

Disclosure: Nothing to disclose

An integrated view of microbiome in IBD
10:30-12:00 / A3

OP331 FECAL SCFA MEASUREMENT AND MICROBIOME METABOTYPE SHIFTS IN NUTRITIONAL THERAPY OF PEDIATRIC CROHN'S DISEASE

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Introduction: Changes in gut bacterial community structure are associated with Crohn's Disease (CD) and response to therapy. A recently completed randomized controlled trial (RCT) showed improved sustained remission with the Crohn's Disease Exclusion Diet + Partial Enteral Nutrition (CDED+PEN) as compared with Exclusive Enteral Nutrition (EEN)[1]. Whole metagenome analysis paired with metabolite assays can help elucidate how changes in abundance impact microbiome function.

Aims & Methods: To examine changes in the functional network and fecal SCFA concentration in CD patients reaching remission after 6 weeks of nutritional therapy (n=53). Stool samples were collected from patients at weeks 0, 6 and 12 and whole shotgun sequence data were obtained. Stool SCFA analysis was available for 128 samples (48 patients). Mann-Whitney U (unpaired) and Wilcoxon signed rank tests (for paired samples) were used to compare SCFA measurements at different time points.

In total 146 CD patient samples were combined with 26 healthy controls (Lewis et al.[2]), and characterized using HUMAnN2. Reactions, substrates and products for genes with an enzymatic commission were input to an unsupervised Bayesian analysis of community metabolism (BiomeNet). Statistical analysis of community metabolism and SCFA concentrations were performed using R. Non-negative matrix factorization (NMF) and Structural topic models (STM) were used to identify patient-associated microbial metabotypes.

Results: Unsupervised analyses revealed two metabotypes. All healthy controls possessed one metabotype (M1). CD patients possessed a mixture of two metabotypes (M1 & M2), with mixtures related to stage of treatment. CD patients achieving remission showed a steady increase in the M1 contribution as nutritional therapy progressed.

Fecal SCFA concentrations did not change significantly across the 3 timepoints in CDED+PEN, but there was a significant drop in butyrate in the EEN group compared with CDED+PEN at week 6 (p=0.00028).

However, SCFA concentrations were associated with M1 and M2 mixtures in patients. M1 was associated with higher concentrations in butyrate (p=0.012), valerate (p=1.2e-6) and iso-butyrate (p=0.008). Genes involved in the 4-aminobutyrate, and crotonoyl-CoA to butyrate pathways, (p=0.03 to 0.0001) were associated with M1 and a different pattern of associated genes was identified in M2. Changes in fecal SCFA concentrations, though associated with M1, were not associated with clinical remission at week 6 in CDED+PEN. In EEN, there was a significant drop between week 0 and week 6 in butyrate concentration (Mann-Whitney p=0.0018 and Wilcoxon signed rank test p=0.0046).

The butyrate-related change in community function is attributable to shifts in bacterial species abundance, notably *Bacteroides* and *Clostridium*.

Conclusion: Diet-induced remission samples were associated with a metabotype that characterized healthy controls and genes involved in the 4-aminobutyrate pathway, and crotonoyl-CoA to butyrate pathway. Although the higher concentrations of butyrate and other SCFA, associated with M1, agree with past work suggesting that butyrate levels are associated with reduced inflammation, we did not measure an increase in fecal butyrate in the CDED+PEN group.

Conversely, remission achieved with EEN is associated with a decrease in butyrate at week 6. An expansion of Firmicutes and decrease in Proteobacteria was observed in both diets by week 6. This suggests that other metabolic processes are important in the microbiome community function shift associated with achieving remission.

References: 1. Levine A, Wine E, Assa A, Sigall Boneh R, Shaoul R, Kori M, Cohen S, Peleg S, Shamaly H, On A, Millman P, Abramas L, Ziv-Baran T, Grant S, Abitbol G, Dunn KA, Bielawski JP, Van Limbergen J. Crohn's Disease Exclusion Diet Plus Partial Enteral Nutrition Induces Sustained Remission in a Randomized Controlled Trial. Gastroenterology 2019 in press. 2. Lewis JD, Chen EZ, Baldassano RN, Otley AR, Griffiths AM, Lee D, Bittinger K, Bailey A, Friedman ES, Hoffmann C, Albenberg L, Sinha R, Compher C, Gilroy E, Nessel L, Grant A, Chehoud C, Li H, Wu GD, Bushman FD. Inflammation, Antibiotics, and Diet as Environmental Stressors of the Gut Microbiome in Pediatric Crohn´s Disease. Cell Host Microbe. 2017 Aug 9;22(2):247.

Disclosure: Nothing to disclose

OP332 WHOLE EXOME SEQUENCING ANALYSES REVEAL GENE-MICROBIOTA INTERACTIONS IN THE CONTEXT OF INFLAMMATORY BOWEL DISEASE

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Introduction: A large number of host genetic factors, as well as changes in the gut microbiota, are known to determine etiology and pathogenesis of inflammatory bowel disease (IBD). The knowledge on the interaction between these two factors is, however, still limited. In order to characterize these interactions, in depth determination of the host genetics and gut microbiota is necessary. Here we aimed to identify genetic factors relevant for maintenance of the gut microbiome in the context of IBD.

Aims & Methods: We performed whole exome sequencing of the host genome, and whole genome shotgun sequencing of fecal samples of 524 IBD patients and 939 controls from population-based cohort. The interaction between exonic variants, microbial taxa and metabolic pathways was explored using a four step approach: 1) Bidirectional meta-analysis between the two cohorts to identify common variants 2) A targeted meta-analyses of IBD risk loci and protein truncating variants (PTVs) 3) A gene-based burden test to detect rare mutations that affect microbial features, and 4) an interaction analysis to identify IBD-specific microbial quantitative trait loci (mbQTLs).

Results: We tested 170,000 protein coding variants and 641 microbial features and identified 25 associations between genetic variants and gut microbial features (FDR< 0.05). Among common variants, a strong mbQTL was observed for deletion near the IBD-risk *IL17REL* gene that was correlated to *Alistipes indistinctus* abundance, which is known to be decreased in IBD patients. The gene-based burden test revealed that mutations in an IBD-related gene *CYP2D6*, a major component of phase I drug metabolism, were associated with decreased level of bacterial biosynthesis of vitamin K (PWY-5838). Moreover, *GPR151* gene, known to be protective against obesity and type II diabetes, was found to be associated with a decrease in bacterial degradation of glucose. The interaction analysis revealed another association between *TNFSF15* and *glycogen degradation* specific to IBD.

Conclusion: We performed the largest, high resolution, genome-microbiome association study to date, that utilizes whole exome sequencing and metagenomics sequencing methods. Disease specific interactions were explored in the context of IBD, including the effect of risk loci and protein truncating variants. These results highlight the importance of host genetics in the maintenance of gut microbiome homeostasis critical for prevention of IBD.

Disclosure: Nothing to disclose

OP333 INTEGRATED MICROBIOTA AND METABOLITE PROFILES IN HUMAN AND MICE IDENTIFIED FUNCTIONAL SIGNATURES IN CROHN'S DISEASE WITH A LINK TO SULFATE METABOLISM

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Introduction: Dysbiosis and metabolic alterations of the gut microbiome have been implicated in inflammatory bowel diseases (IBD). The aim of this study is to identify functional microbiome signatures associated with disease outcome or response to therapy in patients with IBD, and to mechanistically characterize their pathogenic potential using gnotobiotic humanized mice and an integrative multi-omics approach.

Aims & Methods: We studied 35 Crohn's disease (CD) patients for a period of 5-years after autologous hematopoietic stem cell transplantation (HSCT) therapy. Fecal samples were collected both at baseline and at different time points during follow-up. To characterize changes in gut microbiome and metabolome, we performed 16S rRNA gene sequencing, global 16S predicted metagenomes, shotgun metagenomic sequencing and untargeted metabolomics. To address the functional impact of microbial dysbiosis, we established a humanized IBD mouse model by colonizing germfree (GF) Il-10$^{-/-}$ mice with selected fecal samples from CD patients at different disease states.

Results: Temporal fluctuations in gut microbiota composition and metabolite profiles reflected the individual patient-related variations and the differences in disease activity. Fecal microbiome of patients with active disease was enriched in microbial taxa involved in sulfur metabolism such as *Eshericia Shigella* and *Fusobacterium* as well as a high proportion of sulfate reducing bacteria such as *Desulfovibrio* and *Campylobacter*. Fecal metabolic profiling confirmed an increased abundance of sulfated metabolites (bile acids, polyphenols and biogenic amines). Predicted metagenomes from 16S rRNA gene profiling revealed enrichment of functional genes associated with sulfate and ion transport system metabolism in IBD patients with active disease. In contrast, increased abundance of several basic biosynthetic processes correlated with remission. Transplantation of microbiota from patients with active or inactive disease was reproducibly sufficient to recreate disease phenotype in recipient Il-10$^{-/-}$ GF mice. Humanized mice reflected the dysbiotic features of their respective human donors and inflammation was driven by a variety of individual community profiles. Using a machine-learning algorithm, we identified a microbiome signature that discriminates inflamed from non-inflamed humanized mice characterized by an overabundance of B*acteroides fragillis* and *Desulfovibrio*. In accordance with the signature identified in humans, enrichment of sulfated metabolites was indicative for inflamed phenotypes, together with an abundance of genes mapping to sulfate metabolism, Type II, IV and VI secretion systems. Integration of microbiota and metabolite profiles from human and mice improved the predictive modelling of disease outcome significantly and identified a network of functionally relevant bacteria-metabolite interactions linked to disease activity in CD.

Conclusion: Our data prove that despite the heterogeneity of CD patients gut microbiome at the taxonomic level, shared functional signatures correlate with disease severity. Multi-omics data integration improved the clinical outcome prediction and identified a signature involving sulfur metabolism and detoxification to be relevant in disease outcome.

Disclosure: Nothing to disclose

OP334 IMPACT OF 41 COMMONLY USED DRUGS ON THE COMPOSITION, METABOLIC FUNCTION AND RESISTOME OF THE GUT MICROBIOME

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Introduction: The human gut microbiota composition is influenced by numerous factors including medication. Moreover, there is increasing evidence that the gut ecosystem plays an essential role in drug responses and efficacy. To further understand these drug-microbiota interactions in the context of polypharmacy, we studied the relations between commonly used drugs and gut microbial changes in the general population as well as in patients affected by gastrointestinal disorders.

Aims & Methods: We performed metagenomics sequencing of 1883 fresh frozen fecal samples from three independent cohorts:

1) a population-based cohort,

2) patients with inflammatory bowel disease and

3) patients with irritable bowel syndrome intermixed with healthy controls. Taxonomic and potential metabolic profiles were predicted for all samples. In each cohort, we investigated differences between drug users and non-users in two steps: first, by looking at the effect of single medication use, and second, considering the use of multiple drugs per participant. Finally, cohort-specific results were combined in a meta-analysis using an inverse-variance-based approach.

Results: Out of 41 drugs categories, 18 were associated with changes in gut microbiota composition and/or function, with proton-pump inhibitors (PPIs), metformin, antibiotics and laxatives having the largest impact. After correcting for polypharmacy, seven drug categories remained significant (FDR< 0.05), and associated to changes in 46 taxa and pathways. For example, the abundance of *Eubacterium ramulus* was associated with the use of SSRI antidepressants. The gut microbiota of PPI users was characterized by an increased abundance of upper gastrointestinal tract bacteria and by the increase of fatty acid biosynthesis pathways. While these changes in microbial functions were mainly driven by the expansion of *Streptococcus* species in the fecal samples of PPI users, in metformin users an enrichment of *Escherichia coli*-derived metabolic pathways was observed. The use of oral steroids was associated with an enrichment of methanogenic bacteria. Methanogenic bacteria have been associated with obesity and an increase in BMI, a known side effect of oral steroids use. Finally, we identified an increase in antibiotic resistance mechanisms related to eight different medication categories

Conclusion: We provide evidence for extensive changes in taxonomic structure, metabolic activity and resistome in relation to commonly used drugs. Changes in the gut microbiota can increase the risk of enteric infections, obesity and other disorders, therefore, these associations need to be functionally investigated given the importance of the gut microbiota in health and the widespread use of many drugs.

Disclosure: Nothing to disclose

OP335 *BACTEROIDES FRAGILIS* IS MORE PREVALENT IN CROHN'S DISEASE EXACERBATIONS WHILE STRENGTHENING THE INTESTINAL EPITHELIAL BARRIER IN A STRAIN-DEPENDENT MANNER

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Introduction: Crohn's disease (CD) is a chronic relapsing inflammatory gastro-intestinal disease with a high disease burden. Until today, the pathophysiology is not completely understood. Next to host genetics and environmental factors, impaired intestinal barrier function and microbiota seem to play a role in the onset and course of CD. Among others, *Bacteroides fragilis* has frequently been associated with CD. In addition, recombinant *B. fragilis* toxin (Bft) was found to disrupt the intestinal epithelial barrier *in vitro* by cleaving the adherens junction protein E-cadherin. Furthermore, Ubiquitin was found as a potential virulence factor, acting on host immune response.

Aims & Methods: This study aims to investigate the role of *B. fragilis* in the pathophysiology of CD, focusing on prevalence and its interaction with the intestinal epithelial barrier.

To investigate the presence of *B. fragilis*, *B. fragilis* toxin (Bft) and Ubiquitin, we selected 183 CD patients with active or remissive state from our extensive population-based IBD South Limburg cohort. Disease activity was determined by faecal calprotectin levels (< 100 µg/g = remission; ≥250 µg/g = exacerbation) and faecal DNA was investigated by qPCR. Data were analysed using Chi-square test.

To examine the impact of *B. fragilis* on the intestinal epithelial barrier, we subsequently cultured and isolated six *B. fragilis* strains with various genetic profiles of *bft* and *ubiquitin* from two healthy subjects, three CD patients and one ATCC strain (25285). Differences in coding sequences and secreted metabolites between bacterial strains were examined by whole-genome sequencing using MiSeq and Nuclear Magnetic Resonance (NMR) Spectroscopy, respectively. Next, bacteria-free culture supernatant as well as outer membrane vesicles (OMVs) were isolated and luminally applied to colonic adenocarcinoma-derived Caco-2 cell monolayers. After 24 h incubation, the difference in transepithelial electrical resistance (TEER) was determined and compared to the vehicle control.

Results: *B. fragilis* prevalence was 15 % higher (p<0.023) in active CD patients compared to remission. *Bft* and *ubiquitin* prevalence was comparable in both groups. Interestingly, TEER results demonstrate that luminally applied concentrated culture supernatant of *bft* positive *B. fragilis* strains increased the TEER (p<0.001) compared to *bft* negative strains or vehicle control, suggesting an improved epithelial integrity. This effect even overruled tight junction-dependent barrier disruption by TNF-α and IFN-γ. However, isolated OMVs of *bft* positive or *bft* negative strains did not show any alterations in TEER. Among the *B. fragilis* genomes 160 to 18875 SNPs were observed (Split Kmer Analysis). *bft* positive and *bft* negative strains cannot be discriminated by other known coding sequences than the pathogenicity island, containing *bft* and Metalloprotease II. NMR analysis did not reveal clear differences in metabolic profiles between the supernatants of the strains.

Conclusion: This study confirms in a large well-defined patient cohort that *B. fragilis*, but not *bft* or *ubiquitin* positive strains specifically, is more prevalent in active CD, suggesting that it might play a role in exacerbations. Surprisingly, *B. fragilis* components did not impair the epithelial barrier and components of *bft* positive strains even improved intestinal barrier function, which warrants further investigation. This unexpected finding stresses the relevance of extending current research on the functional role of relevant microorganisms.

Disclosure: Nothing to disclose

OP336 GUT MICROBIOTA IN PRIMARY SCLEROSING CHOLANGITIS IS CHARACTERIZED BY SPECIFIC COMPOSITION OF FUNGI

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Introduction: Primary sclerosing cholangitis (PSC) is a progressive disorder of biliary tree which can lead to end-stage liver disease, liver transplantation or even death. Colitis accompanying PSC (in up to 80% of patients) is considered to be a phenotype of IBD inflammatory bowel disease (IBD) distinct from ulcerative colitis (UC) and is often referred to as PSC-IBD. Gut microbiota presumably plays an important role in both PSC and IBD pathogenesis. Several recent studies described the features of gut bacterial microbiota composition in PSC. However, disruption of gut fungal microbiota (mycobiota) has not yet been properly investigated.

Aims & Methods: The aim of this study was to characterize gut mycobiota composition in patients with PSC, PSC-IBD and UC. Stool samples were prospectively collected and relevant clinical data obtained from 109 study participants: 50 PSC patients with (n = 38) or without (n = 12) concomitant IBD, 32 controls with UC and 27 healthy controls (HC). After standardised DNA extraction, amplification and library preparation, sequencing of the ITS1 gene was performed using Illumina MiSeq platform. Acquired data were processed in QIIME employing MaAsLin and LEfSe tools for analysis of the output results.

Results: Mycobial profiles did not reveal significant shifts between the study groups when calculated for various alpha - diversity indices (Shannon, Chao 1, Simpson, Observed OTUs). Furthermore, there was no statistically significant distinction among phenotypes when describing beta - diversity with both Bray - Curtis and Binary Jaccard index. However, PSC was characterized by high relative abundance of several genera as compared to healthy controls: *Candida* (5.2% vs 2.5%), *Lysurus* (20.7% vs 11.7%) and *Cladosporium* (1.2% vs 0.6%). Furthermore, relative abundance of genus *Rhodosporidium* clearly distinguished PSC-IBD from UC (14.4% vs 2.8%). Such differences were further tracked down to the species level, identifying major taxa responsible for respective shifts: *Candida albicans*, *Lysurus cruciatus*, C*ladosporium herbarum* and *Rhodosporidium Babjevae*. Subsequent multivariate analysis determined high abundance of *Cladosporium herbarum sp.* to be tightly associated with presence of PSC (p ≤ 0.05).

Conclusion: PSC is characterized by specific features of gut fungal microbiota composition. Intestinal mycobiota profiles differ between IBD subphenotypes (PSC-IBD and UC). High abundance of *Cladosporium herbarum sp.* (exceedingly common plant pathogen) in PSC may suggest an association with certain dietary habits.

Disclosure: Nothing to disclose

Seeing is believing: Improving polyp detection
10:30-12:00 / B2

OP337 IMPROVED ADENOMA DETECTION WITH ENDOANGEL: A RANDOMIZED CONTROLLED TRIAL

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Introduction: Colonoscopy is a pivotal procedure in the detection and diagnosis of lower gastrointestinal lesions. However, there are significant variations in colonoscopy performance among endoscopists, impairing the discovery of colorectal cancers and precursor lesions. The aim of this study was to construct a real-time quality improving system, ENDOANGEL, to monitor real-time withdrawal speed, time colonoscopy insertion and withdrawal, and remind endoscopists of blind spots caused by scope slipping, and evaluating its effectiveness in improving the adenoma yield of everyday colonoscopy.

Aims & Methods: ENDOANGEL system was developed using the methods of deep neural networks and perceptual hash algorithm. Patients referred because of health examination, symptoms, surveillance were recruited from Renmin hospital of Wuhan University. Enrolled patients were ran-

domly assigned to ENDOANGEL-assisted colonoscopy (EAC) and normal colonoscopy (NC). The primary end point was the adenoma detection rate (ADR) in colonoscopy with or without ENDOANGEL.

Results: 388 and 391 patients were analyzed in EAC and NC respectively. ADR was significantly higher in EAC compared with the NC (13.56% vs 21.91%, *P* = 0.049). Polyp detection rate (PDR) was significantly increased from 37.08% to 51.29% with the assistance of ENDOANGEL (*P* < 0.001). Mean withdrawal was 2.32 minute longer with EAC (*P* < 0.001), with no difference in caecal intubation rate or insertion time. There was no significant adverse event.

Conclusion: ENDOANGEL significantly improved adenoma yield in colonoscopy and could be used to improve the quality of everyday endoscopy.

Disclosure: Nothing to disclose

OP338 ENDOCUFF-ASSISTED COLONOSCOPY VS STANDARD COLONOSCOPY ON ADENOMA DETECTION RATE IN ROUTINE PRACTICE: A CLUSTER-RANDOMIZED CROSSOVER TRIAL ON 2058 PATIENTS

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Introduction: Endocuff Vision (ECV) is a device supposed to improve polyp detection. This device has recently changed with the marketing of a second generation (ECV) very different from the first (Endocuff Device). If interest of the first generation of this device is still debated, little data is available on the second generation. The aim of this study was to evaluate the interest of ECV on adenoma detection rate (ADR) in routine colonoscopy. The secondary aim was to determine in which endoscopists the ECV is the most useful.

Aims & Methods: This cluster-randomized crossover trial compared endocuff-assisted (ECV+) to standard colonoscopy (ECV-). Randomization determined which team (of 11 endoscopists each, matched on ADR, age and activity volume) started with ECV + and which team by ECV-. A switch of the 2 teams was made at half of the inclusions.

The main criterion was ADR. Secondary objectives were polyp detection rate (PDR), advanced neoplasia detection rate (ANDR) and serrated polyp detection rate (SPDR).

Results: 2058 patients were included (1032 ECV- vs 1026 ECV+). Both groups were comparable except for age (58.5±13y vs. 59.25±12y, P=0.001). ADR was significantly improved in ECV group in multivariate analysis (OR 1.49, CI95% 1.2-1.82, P=10⁻⁵). Benefit of ECV was significant for PDR (46.2% vs 37.7%, P< 0.001) but not for ANDR (11.1% vs 9.2%, P=0.17) nor SPDR (12.5% vs 11.9%, P=0.74).

Regarding ADR upon physicians, ECV significantly improved ADR in the medium (42 vs. 30%, P=0.005) and high detectors (46 vs. 32%, P< 0.001) groups but not in the low detectors group (31 vs. 26%, P=0.16).

Conclusion: We showed a significant increase in ADR and PDR in ECV group with a gain of approximately 10%. This benefit was significant in medium and high detectors, but not in low detectors. In contrast, we did not show significant impact of ECV on ANDR and SPDR.

Trial registered at ClinicalTrials.gov (NCT03344055)

Disclosure: Nothing to disclose

OP339 IMPACT OF DIGITAL PATIENT REINFORCEMENT ON HIGH QUALITY COLONOSCOPY PREPARATION IN CRC SCREENING: RESULTS FROM THE MULTI-CENTER COLOPRAPP-STUDY

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Introduction: Sufficient bowel preparation is crucial for successful screening and surveillance colonoscopy. However, the rates of inadequate preparation are still high. We investigated the effects of reinforced patient education using a smartphone application for colonoscopy preparation in CRC-screening.

Aims & Methods: In this prospective, endoscopist-blinded, multi-center study standard instructions pertaining to split-dose preparation were provided orally and in a written format to all patients during the initial appointment. Patients (n=500) were randomly assigned (1:1) to group that received reinforced education starting 3 days before the colonoscopy (APP group) or control group without further education. The primary outcome was quality of bowel preparation according to the Boston Bowel Preparation Scale (BBPS). The secondary outcomes included polyp and adenoma detection rate (PDR, ADR), compliance with low fibre diet and split-dose laxative intake and patients' perceived discomfort of the preparation procedure.

Results: The mean BBPS score was significantly higher in the APP group (7.6±0.1) than in the control group (6.7±0.1) (p< 0.0001). The percentage of patients with insufficient bowel preparation was significantly lower in the APP group (8%) than in the control group (17%) (p=0.002). The ADR was significantly higher in the APP group (35 vs. 28%) (p=0.0081). Significantly more flat adenomas were detected in the right colon in the APP group (p=0.004). Using the smartphone application was accompanied by a lower level of discomfort during preparation and a higher rate of compliance regarding correct laxative intake and diet restrictions.

Conclusion: Reinforced patient education using a smartphone application for optimized bowel preparation during the final 3 days before colonoscopy increased bowel cleanliness, adenoma detection and reduced discomfort in CRC screening and surveillance patients.

Disclosure: B. Walter: Consultancies for Norgine Pharma

OP340 LINKED COLOR IMAGING IMPROVES DETECTION RATE OF SESSILE SERRATED ADENOMA/POLYP IN THE COLON: A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

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Introduction: Colorectal cancer (CRC) is one of the leading causes of cancer deaths worldwide. Endoscopic surveillance for premalignant polyps in the colorectum is a crucial strategy for reducing CRC-related mortality. It has been reported that colorectal polyps in the right-side colon are often missed during conventional colonoscopy. Sessile serrated adenoma/polyp (SSA/P) predominantly occurs in the right-side colon, and is a precursor lesion of the cancer with microsatellite instability. It is more difficult to detect SSA/P with conventional colonoscopy than adenomatous lesion because SSA/P commonly presents as a flat and faded color lesion. To improve endoscopic sensitivity in detection of SSA/P is putative for reduction of mortality of CRC. Linked color imaging (LCI) is a novel image-enhanced endoscopy that emphasizes color contrast between red and white areas and has been widely used for the diagnosis of gastrointestinal diseases including neoplastic lesions.

Aims & Methods: This study aimed to evaluate the utility of LCI for SSA/P detection in a prospective randomized controlled trial (RCT) and was conducted at Tokushima University Hospital between 2015 and 2018. Patients underwent modified back-to-back colonoscopies with white light image (WLI) and LCI. Patients were randomly allocated to 1 of the 2 arms at a 1:1 ratio using a sealed envelope method: (A) WLI-LCI group: first inspection with WLI followed by a second inspection with LCI; (B) LCI-WLI group: first inspection with LCI followed by a second inspection with WLI. Polyps detected during the first inspection were removed by snare or biopsied. Polyps detected during the second inspection were classified as additional polyps, and were also removed or biopsied. The primary outcome of the study was the additional SSA/P detection rate in WLI-LCI and LCI-WLI groups. The secondary outcomes were the positive detection rate for additional SSA/P lesions in the second inspection per subject and the morphological features of additionally detected SSA/P.

Results: A total of 60 patients participated the clinical trial and 52 were eligible; 26 each in the WLI-LCI and LCI-WLI groups. There was no statistically significant difference in inspection time, bowel preparation score, patients´ characteristics between the 2 groups. In the WLI-LCI group, 32 SSA/P were detected in the first inspection and 9 were additionally detected. In the LCI-WLI group, 34 SSA/P were detected in the first inspection and 1 was additionally detected. The additional detection rate of SSA/P in the second inspection in the WLI-LCI group was significantly higher than that in the LCI-WLI group (21.9% vs 2.9%, p< 0.05). The prevalence of additional SSA/P lesions in the second inspection per subject was significantly higher in the WLI-LCI group versus the LCI-WLI group (30.8% vs 3.8%, p< 0.05). The SSA/P lesions of smaller, non-mucus, same color as the background mucosa, and located at the transverse colon were detected more frequently in the second inspection with LCI. It was indicated that hyperplastic polyp and adenoma in the right colon were also additionally detected in the second inspection in the WLI-LCI group by the sub-analysis.

Conclusion: This RCT results demonstrated the superiority of LCI to WLI in SSA/P detection by highly improved additional detection rate of SSA/P. Our data will be warranted by a multicenter, larger-scale trial recruiting a more general patient population to compare detectability of SSA/P with LCI and WLI. The study was registered at the University Hospital Medical Information Network-Clinical Trials Registry (UMIN 000017599).

References: Fujimoto D, Muguruma N, Okamoto K, Fujino Y, Kagemoto K, Okada Y, Takaoka Y, Mitsui Y, Kitamura S, Kimura T, Miyamoto H, Bando Y, Sonoda T, Takayama T. Linked color imaging enhances endoscopic detection of sessile serrated adenoma/polyps. Endosc Int Open. 2018.

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OP341 MICROVESSELS OBSERVATION IN COLORECTAL ENDOCYTOSCOPY IS USEFUL IN PREDICTING PATHOLOGICAL DIAGNOSIS

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Introduction: To date, narrow-band imaging (NBI) could make it possible to analyze the surface microvessels of colorectal lesions for differentiating neoplasms from non-neoplasms and for predicting the histropathological diagnosis. Endocytoscopy (EC) is the next generation of ultra-magnification endoscopy that allow visualization of the glandular structure and cellular atypia *in vivo*. In addition, when using EC with NBI (EC-NBI), it enables *in vivo* observation of blood vessels in more detail compared to conventional magnification power without the use of any dye solution.

Aims & Methods: The study included 502 patients who underwent complete colonoscopy and endoscopic or surgical treatment between April 2006 and June 2016. A total of 669 lesions (61 Non-neoplastic polyps, 372

adenomas, 75 intramucosal cancer, 21 slightly invasive submucosal cancer (SMs) and 140 massively invasive submucosal cancer.) were retrospectively evaluated. We used the Kudo classification for the degree of submucosal invasion and classified cancers accordingly(1). SMs cancer without vessel permeation does not metastasize. In contrast, SMm lesions show a substantial proportion (~10%) of lymph node metastasis. We named the ultra-magnified microvessel findings as endocytoscopic vascular (ECV) pattern and classified into the following 3 groups: EC-V1, the surface microvessels were very fine obscure; EC-V2, the surface microvessels were more clearly seen and showed a regular vessel network, and their caliber and arrangement were uniform; and EC-V3, the surface microvessels were thick, and their caliber and arrangement were non-homogeneous.

Results: The sensitivity, specificity and accuracy of EC-V1 for diagnosis of hyperplastic polyp were 91.8%, 98.7% and 98.1%, respectively. Similarly the sensitivity, specificity and accuracy of EC-V3 for diagnosis of SMm were 82.1%, 98.3% and 94.9%, respectively

Conclusion: Endocytoscopic vascular pattern was useful for predicting the histopathology of colorectal lesions.

Disclosure: Nothing to disclose

OP342 EFFECT OF PRECEDING BIOPSY ON THE RESULTS OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR COLORECTAL LATERALLY SPREADING TUMOR

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Introduction: Forceps biopsies are usually performed before endoscopic submucosal dissection (ESD) for colonic laterally spreading tumors (LSTs). However, preceding biopsy is commonly believed to possibly inhibit complete tumor resection by causing blurring of tumor borders and tissue fibrosis.

Aims & Methods: The aims were to investigate whether the preceding biopsy of colorectal LST affects complete endoscopic tumor resection and increases the risk of complications. We retrospectively reviewed the medical records of patients with colorectal LSTs who underwent ESD at our center during an 8-year period. Patients were divided into two groups according to whether they underwent biopsy of the tumor before ESD. In addition, the characteristics of patients and tumors, including the completeness of tumor resection, were investigated.

Results: Of 288 patients (174 men) enrolled in this study, 194 (67.4%, preceding biopsy group) underwent biopsies before ESD, whereas 94 (32.6%, no biopsy group) did not. There were no significant differences in age, sex, comorbidity, medication history, tumor location, and final pathologic result between both groups. Tumor size was larger (*p*=0.002) and LST-G tumor was more common (*p*=0.003) in the preceding biopsy group than in the no biopsy group. No significant difference was seen in ESD outcomes, including procedure time, hospitalization period, incidence of complications, en bloc resection rate, resection margin status, and incidence of surgical operation, between both groups.

Conclusion: Biopsy of LST is commonly performed before endoscopic resection. Contrary to popular belief, it does not increase the incomplete tumor resection rate and incidence of complications.

Disclosure: Nothing to disclose

Enteropathies: From bench to bedside
10:30-12:00 / B3

OP343 DIAGNOSTIC ACCURACY OF SERUM FIBROBLAST GROWTH FACTOR 19 (FGF19) AND TOTAL FECAL BILE ACIDS AS BIOMARKERS FOR BILE ACID MALABSORPTION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES, MICROSCOPIC COLITIS AND IRRITABLE BOWEL SYNDROME

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Introduction: Excessive amounts of bile acids (BAs) entering the colon due to bile acid malabsorption (BAM) cause chronic bile acid diarrhoea (BAD). The [75]Selenium homocholic acid taurine (SeHCAT) test is the "gold standard", but is not generally available. Fibroblast growth factor 19 (FGF19) is the ileal hormone providing feedback inhibition of BAs and one possible biomarker of BAM that demonstrate a correlation with SeHCAT, but little is known about the mechanisms of dysregulation in patients with inflammatory bowel disease (IBD), IBD after ileal resection (IBD-IR), irritable bowel syndrome with diarrhea (IBS-D) and microscopic colitis (MC).
Aims & Methods: The aim was to evaluate the diagnostic accuracy of serum levels of FGF19, total free faecal bile acids (TFFBA) for finding BAM in patients active IBD, IBD in remission, IBD after ilea resection, IBS-D and MC. Methods: We enrolled 109 adult patients with chronic diarrhoea and 11 healthy controls who underwent standard laboratory tests, colonoscopy, serum FGF19, fecal calprotectin (FC), TFFBA. Patients were divided into six groups: 30 patients with active IBD, 21 patients with IBD in remission, 21 patients with IBD after surgery (IBD-IL), 23 patients with IBS- D, 14 patients with MC and 11 healthy control subjects. Fasting serum FGF19, TFFBA were measured by ELISA test and FC by the quantitative immunochromatographic method
Results: Diagnosis of BAM based on levels of FGF19 below 30 pg/ml was confirmed in 65 of 109 patients (59,6%) and excluded in 44 (40,4.%) compare to healthy controls. Mean levels of FGF19 in patients with IBD active were 263.06 pg/mL, IBD remission were 367.2 pg/mL, IBD-IR were 57.1 pg/mL, IBS-D were 447,5 pg/mL, MC were 403,7 pg/mL and healthy controls were with 585,6 pg/mL (p- 0,003, Welch test). A cut-off concentration of FGF19 of 136,7 pg/mL or lower identified patients with active IBD and diarrhea attributable to BAM with 70.9% sensitivity, 72,7% specificity and an AUROC 0.79 (p-0,005). The number of IBD patients in remission with up to 4 bowel movements daily was 16 (76.2%) and concentration of FGF19 below 136,7 pg/ml were in 76,2% of the patients, which corresponds with BAD as a co-factor in the diarrhea pathogenesis in these IBD patients. A cut-off concentration of FGF19 of 32,88 pg/mL or lower identified patients with IBD-IL and MC with diarrhea attributable to BAM with 90,5% sensitivity, 81,8% specificity and an AUROC 0.93 (p< 0.01).
The overall sensitivity and specificity of FGF19 for finding BAM in patients with IBD and MC compare to healthy controls were 76.2% and 72,7%, respectively for a cut-off value of 136,7 pg/ml., which will lead to accurate prediction of BAM in 72% of the IBD and MC patients. In patients with IBS-D, serum concentration of FGF19 shows no significant difference compare to healthy controls (p-0,71). TFFBA shows no significant difference between all the groups and compare to healthy controls.
Conclusion: BAM is common and very under-diagnosed condition in patients with chronic diarrhea. FGF19 could be used for screening biomarker for BAM in patients with IBD, IBD after surgery (ileal resection) and MC, because there is effective additional treatment with bile acid binder's for this patients. We observed significantly lower serum concentrations of FGF19 in patients with IBD with IR, compared to healthy controls. A cut-off concentration of FGF19 below of 30,04 pg/mL identifies patients with diarrhea likely attributable to BAM with an AUROC value of 0.93. Further bigger studies are needed to establish the efficacy of FGF19 in patients with suspected bile acid malabsorption.

References: 1. Mottacki N, Simrén M, Bajor A. Review article: bile acid diarrhoea - pathogenesis, diagnosis and management. Aliment Pharmacol Ther . 2016 Apr;43(8):884-98. Available from: http://doi.wiley.com/10.1111/apt.13570 2. Pattni SS, Brydon WG, Dew T, Johnston IM, Nolan JD, Srinivas M, et al. Fibroblast growth factor 19 in patients with bile acid diarrhoea: a prospective comparison of FGF19 serum assay and SeHCAT retention. Aliment Pharmacol Ther. 2013 Oct;38(8):967-76. Available from: http://doi.wiley.com/10.1111/apt.12466 3. Battat R, Duijvestein M, Casteele N Vande, Singh S, Dulai PS, Valasek MA, et al. Serum Concentrations of 7α-hydroxy-4-cholesten-3-one are Associated with Bile Acid Diarrhea in Patients with Crohn's Disease. Clin Gastroenterol Hepatol . 2018 Nov; Available from: https://linkinghub.elsevier.com/retrieve/pii/S1542356518312552 4. Vijay-vargiya P, Camilleri M, Carlson P, Lueke A, O'Neill J, Burton D, et al. Performance characteristics of serum C4 and FGF19 measurements to exclude the diagnosis of bile acid diarrhoea in IBS-diarrhoea and functional diarrhoea. Aliment Pharmacol Ther. 2017 Sep;46(6):581-8. Available from: http://doi.wiley.com/10.1111/apt.14214
Disclosure: Nothing to disclose

OP344 CYTOKINE RESPONSES TO GLUTEN AND GLIADIN IN MUCOSAL IMMUNE CELL POPULATIONS FROM FUNCTIONAL DYSPEPSIA PATIENTS

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Introduction: Non-coeliac gluten or wheat sensitivity (NCWS) describes a condition by which ingestion of wheat products induce gastrointestinal symptoms, in the absence of coeliac disease or wheat allergy. Symptoms of epigastric pain and post-prandial fullness are often described by these patients, demonstrating some overlap of symptomology with functional dyspepsia (FD). In addition, an association between FD and foods containing wheat components have been reported in a number of observational studies; however, the mechanism behind this link has not been elucidated.
Aims & Methods: This study aimed to examine whether antigens present in gluten or gliadin could provoke an immune response from duodenal mononuclear cells isolated from patients with FD.
Lamina propria mononuclear cells (LPMCs) were isolated from duodenal biopsies taken from patients with FD diagnosed by Rome III criteria (n=14) and non-dyspeptic controls (n=8). The cells were cultured and exposed to gluten (1 mg/mL) or gliadin (1mg/mL) for 24 hours. The supernatant was collected and a cytometric bead array used to analyse the concentrations of Th1, Th2 and Th17 cytokines (IL-2, IL-4, IL-6, IL-10, TNF, IFN-γ, and IL-17a).
Results: When LPMCs were stimulated with gliadin, a significant increase in the concentration of IL-17a was produced from FD patient cells compared to non-FD controls (*p*=0.047). There was no significant response observed for IL-17a in response to gluten for FD or control. When the cohort was classified by self-reported NCWS, FD patients with NCWS had increased IL-17a concentrations when compared to non-FD controls with no NCWS (*p*=0.0001). Interestingly, FD patients without NCWS had significantly increased IL-17a levels when compared to the NWCS positive FD group when treated with both gluten (*p*=0.002) and gliadin (*p*=0.009).
Stimulation with gluten produced a decreased TNF level trending towards significance (*p*=0.061) in FD patients when compared to controls. FD patients with NCWS had significantly decreased levels of TNF compared to controls with NCWS (*p*=0.006) and controls without NCWS (*p*=0.030). An increase in TNF level in FD patients without NCWS compared to FD patients with NCWS was approaching significance (*p*=0.052).There was no change in TNF level following exposure to gliadin.
Conclusion: Gluten and gliadin, components of wheat, stimulate immune responses from duodenal LPMCs from FD patients, characterised by an increase in IL-17a concentration and a decrease in TNF levels in cell culture supernatants.
These results indicate that NCWS may be a subtype of FD, and that dietary antigens from wheat products may induce symptoms of FD in some. The increased IL-17 concentration in cells from FD patients following stimulation with gliadin suggests Th17 immune pathways warrant further inves-

tigation in NCWS and FD. Further characterisation of these antigens as potential triggers for a subset of FD could allow for the elucidation of the immune mechanisms driving symptom onset and subtle inflammation in patients.

Disclosure: Nothing to disclose

OP345 MAST CELL DENSITY AND MAST CELL-NERVE INTERACTIONS CORRELATE WITH SEVERITY OF ABDOMINAL PAIN AND BLOATING IN PATIENTS WITH NON-CELIAC GLUTEN / WHEAT SENSITIVITY

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Introduction: Non-celiac gluten/wheat sensitivity (NCG/WS) is characterized by gastrointestinal (GI) and extra-intestinal symptoms triggered by gluten-containing foods. Hitherto, despite many efforts, different aspects of this disorder, i.e. epidemiology, pathophysiology, diagnostic biomarkers and mechanisms underlying symptom generation remain unsolved. Furthermore, the overlap of clinical signs with functional GI disorders, including functional dyspepsia (FD) and irritable bowel syndrome, make the diagnosis of NCG/WS challenging in daily practice. Based on the hypothesis that innate, more than adaptive, immunity is involved in NCG/WS, we designed this study aimed to investigate the role of neuro-immune interactions in GI symptom generation in patients with NCG/WS, focusing on the upper gut, specifically on duodenal submucosal neurons and mast cells (MCs).

Aims & Methods: Patients with self-reported NCG/WS (n=34), celiac disease (CD; n=28), FD (n=13) and healthy controls (HC; n=24) were recruited and examined with upper GI endoscopy to obtain routine duodenal biopsies. NCG/WS and CD patients were recruited according to the diagnostic work-up, including serological and genetic tests and histopathological evaluation, while FD patients were selected based on Rome IV criteria. All subjects were invited to fill an appropriate symptom questionnaire (modified GI symptom rating scale). Submucosal whole-mount preparations were analyzed by immunohistochemistry to obtain quantitative data on neuronal and MC density and the percentage of MC in close vicinity to submucosal nerve endings. Appropriate statistical tests were applied to compare the three groups in terms of symptoms, neuronal and MCs density and MCs-nerves distance (D). These results were correlated to the clinical features.

Results: There were significant differences among the three pathological groups in terms of the number of GI symptoms (P< 0.0001) and the presence and severity of bloating and abdominal pain (P< 0.0001), with NCG/WS groups showing the highest scores. Bowel habit changes were similar among the three groups (P=0.08). Immunohistochemistry showed absence of neuronal cells abnormalities in the enteric submucosal plexus of all the three pathological groups. In NCG/WS, MCs density was not different from HC, while was slightly increased vs. CD (P=0.07), and significantly decreased vs. FD (P< 0.05). The percentage of MCs close to nerves (D< 15 mm) was similarly increased in all three pathological groups *vs.* HC (P< 0.001). Specifically, we identified that in NCG/WS, CD, and FD patients, 60% of the total MCs present in the tissues were localized in the range of 15 mm from the closest nerve fiber.

Moreover, 45% of the total MCs were localized in the range of 5 mm, as opposed to the 20% found in HC. In NCG/WS, MCs infiltration correlated to bloating (P=0.001) and abdominal pain severity (P=0.03), and the per-

centage of MCs in proximity to neurons correlated with the number of GI symptoms (D< 5 mm; P=0.05), bloating and abdominal pain severity (D< 15um; P=0.01). In FD MC density correlated to the number of GI symptoms (P=0.03) and with the presence of pain (P=0.05). In NCG/WS, CD and FD, MCs density and MC-nerve spatial relation did not correlate to bowel habit.

Conclusion: This study provided a morphological basis indicating that submucosal MCs infiltration and MCs-nerve interactions in the upper GI tract of NCG/WS patients contribute to patient reported GI symptoms generation and maintenance, i.e. abdominal pain and bloating severity.

Disclosure: Nothing to disclose

OP346 THE IMPACT OF CLINICAL PRESENTATION OF COELIAC DISEASE ON DIAGNOSTIC DELAYS IN CHILDREN IN CENTRAL EUROPE

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Introduction: Due to a broader use of serological screening tests, more coeliac disease (CD) patients with non-classical presentation have been diagnosed during the past decades. However, limited awareness of the diversity of clinical presentation of CD among health care professionals (HCP) contributes to continued frequently missed diagnoses.

Aims & Methods: The aim of our study was to assess the impact of the clinical presentation on diagnostic delays in children with CD in Central European (CE) region.

Paediatric gastroenterologists (PaedGI) in five CE countries retrospectively submitted anonymised medical records of all their symptomatic patients aged < 19 years with CD diagnosis in 2016. Based on clinical presentation, patients were classified as classical CD (presenting with signs and symptoms of malabsorption), non-classical CD (any other symptoms) and dermatitis herpetiformis Duhring (DHD). Classical CD patients were subdivided into those with and those without diarrhoea, and non-classical CD into those with gastrointestinal and those with non-gastrointestinal symptoms (appetite loss, fatigue, irritability, headache, joint pain, skin rash (not DHD)).

We analysed diagnostic delays in relation to clinical presentation at diagnosis. Diagnostic delays were calculated as the time gap between first CD related symptoms to confirmed CD diagnosis, and subdivided into the duration between first symptoms and first visit to the PaedGI, and from this visit to final diagnosis. Kruskal-Wallis H test with post hoc tests were used for the analysis (IBM SPSS Statistics 22.0 for Windows).

Results: Data from 393 symptomatic children (65% female) from Croatia, Hungary, Germany, Italy and Slovenia were included (Table 1). Median age at diagnosis was 7 years (range 7m-18.5y). Patients with classical CD tended to have a slightly shorter median diagnostic delay (6m) compared to those with non-classical CD (7m) and DHD (8m) (NS). Further analysis showed that the median duration from first symptoms to the first visit to the PaedGI was the same (5m) in children with classical CD (n=264) and non-classical CD (n=122) whereas it tended to be slightly longer (7m) in children with DHD (n=7) (NS). Median duration from the first visit to the PaedGI to the confirmation of CD was found to be significantly longer in non-classical compared to classical presentation (p< 0.05).

Within classical CD group longer diagnostic delay was found in patients without diarrhoea (8m) compared to those with diarrhoea (5m) (NS), which can be attributed to significantly longer duration from symptoms to PaedGI in patients without diarrhoea (6m) compared to those with diarrhoea (4m) (p< 0.05).

In patients with non-classical CD, diagnostic delay with GI symptoms was slightly longer (7m) compared to non-GI symptoms (6m) (NS).

	Classical CD	Non-classical CD	Skin DHD
Number of patients N=393 (%)	264 (67.2%)	122 (31.0%)	7 (1.8%)
Time from first symptom until first visit to PaedGI Median (range)	5m (0-10y)	5m (0-6y)	7m (1m-1.5y)
Time from first visit to PaedGI until diagnosis* Median (range)	1m (0-2.5y)	1m⁑ (0-5y)	1m (0-1m)
Time from symptoms to diagnosis (diagnostic delay) Median (range)	6m (0-10y)	7m (0-6y)	8m (1m-1.5y)

*PaedGI - paediatric gastroenterologist; m - month; y - year; DHD - dermatitis herpetiformis Duhring *p<0.05 ⁑significance (p<0.05) vs Classical CD*

[Diagnostic delays and clinical presentation of coeliac disease]

Conclusion: Clinical presentation at CD diagnosis has some, although relatively small effect on diagnostic delays. Delays were longer in patients presenting with non-classical symptoms or dermatitis herpetiformis Duhring compared to malabsorption. Lack of awareness about different clinical presentations of CD may contribute to prolonged delays. Further efforts to raise the awareness and knowledge among HCPs appear necessary.
*Study was co-financed by Interreg CE programme (CE 111, Focus IN CD)
Disclosure: Nothing to disclose

OP347 CELIAC FACTS - ONLINE COURSES ON CELIAC DISEASE FOR HEALTH CARE PROFESSIONALS AND PATIENTS AND WEB-APP IMPLEMENTING THE UPDATED DIAGNOSTIC GUIDELINES

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Introduction: Celiac disease (CD) requires a life-long gluten-free diet to treat symptoms and avoid long-term health consequences. A correct and early diagnosis is of utmost importance. However, many health-care professionals (HCPs) have poor knowledge of CD, leading to impaired patient care. Most patients seek more details on CD online with the risk of misinformation. To improve this situation we developed online courses on CD within the „Focus IN CD" project (Interreg Central Europe Projekt CE111).
Aims & Methods: Twelve project partners from Germany, Slovenia, Hungary, Italy & Croatia developed free, autodidactic online-courses with comprehensive, understandable, varied and evidence-based content, tailored to the target group. Project partners and external reviewers revised the drafts before the online implementation. Adult patients, parents of pediatric patients, and HCPs are currently evaluating the courses before and after their use by completing anonymous online questionnaires. A Web based App was planned to provide detailed pathways and explanations for physicians to diagnose CD during childhood and adolescence.
Results: The courses contain written explanations illustrated by graphics, interactive elements, explain movies, self-tests and a dictionary. The HCP's course comprises two units (background & diagnosis, treatment & follow-up), published in parallel to diagnostic guidelines of the European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) updated in 2019. The patient's course includes four units (background, diagnosis, treatment, living with CD) and explains the medical background in lay terms. Furthermore, the Web-App provides two separate pathways for the generalist (GP/ paediatrician) and the specialist (pediatric gastroenterologist) according to the new ESPGHAN guidelines. Therefore the physician can easily follow the diagnostic flow scheme by choosing the relevant options while getting background information and advice how to proceed

and make the correct diagnosis. The courses and Web-App are accessible via www.celiacfacts.eu (English), www.zoeliakie-verstehen.de (German), www.coeliakia.info (Hungarian), www.poznam-celiakijo.com (Slovenian), www.sveocelijakiji.hr (Croatian) and www.celiachia-info.it (Italian). Preliminary data of the evaluation show a significant knowledge improve and high user satisfaction.
Conclusion: The online courses "Celiac Facts" increase the knowledge of celiac disease among health care practitioners and patients while the Web-App facilitates a correct diagnosis. These innovative tools may improve patient care. More language versions are intended.
Disclosure: The Focus IN CD project was funded by Interreg CENTRAL EUROPE (European Regional Development Fund), project no. CE111

OP348 A DURUM WHEAT VARIETY-BASED PRODUCT IS EFFECTIVE IN REDUCING SYMPTOMS IN PATIENTS WITH NON-CELIAC GLUTEN SENSITIVITY: A DOUBLE-BLIND RANDOMIZED CROSS-OVER TRIAL

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Introduction: Patients with non-celiac gluten sensitivity (NCGS) do not have celiac disease but their symptoms improve after a gluten-free diet. However, to date, it is uncertain if the gluten or other components of the wheat are responsible for these symptoms.
Aims & Methods: The aim of this study was to compare the effects of an organic durum wheat variety and of a standard commercial wheat in patients with known NCGS.
We performed a double-blind randomized cross-over trial of 42 patients (mean age 45 years, 8 men) with NCGS diagnosed according to the Salerno criteria and adherence to GFD for at least 12 weeks from screening. Enrolled subjects were randomly assigned to one the following groups of treatment: A) a 2-week diet with Senatore Cappelli wheat variety pasta; B) a 2-week diet with standard commercial pasta. Then, after a 2-week washout period on gluten-free diet, each patient crossed over to the other treatment group. Symptoms were assessed through a modified version of the Gastrointestinal Symptom Rating Scale (GSRS), tailored on NCGS.
Results: Between April 2018 and July 2018, 42 patients with NCGS were enrolled in the study (70.6% female) 34 patients completed the study. Patients reported lower overall symptoms scores after eating Senatore Cappelli pasta than standard pasta (p=0.03), and also significantly lower scores in several specific gastrointestinal and extra-intestinal symptoms after eating Senatore Cappelli pasta than standard pasta specifically bloating (p=0.04), abdominal distention (p=0.004), eructation (p=0.01), flatus (p=0.02), feeling of incomplete evacuation (p=0.001), dermatitis (p=0.01) and limb numbness (p=0.03).
Conclusion: In our study patients with NCGS experienced lower gastro-intestinal and extra-intestinal symptom scores after eating the Senatore Cappelli wheat variety than a standard commercial wheat. Should our preliminary results be confirmed by further studies, new dietary alternatives may be available to patients with NCGS, with consequent health, economic, and social benefits
Disclosure: Nothing to disclose

Video Case Session
10:30-12:00 / F1

OP349 GEL IMMERSION ENDOSCOPY FOR COLONIC DIVERTICULAR BLEEDING

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Introduction: Diverticular bleeding(DB) is most common cause of lower gastrointestinal bleeding. Despite 75% of diverticular bleeding achieve hemostasis naturally, 25% of DB have the stigmata of recent hemorrhage(SRH)

and need treatment such as Endoclips and Endoscopic Band Ligation(EBL). SRH includes active bleeding, non bleeding visible vessels and adherent clots. Compared with left sided DB, right sided DB tends to be massive bleeding.[1] In Asia, right sided DB is more common than left sided DB.[2] In massive bleeding cases, it's difficult to identify the SRH due to inappropriate endoscopic view with a large amount of bleeding and clot. Therefore to achieve hemostasis in DB, to get clear endoscopic filed is important. Although water jet endoscopy was one of the good device, active bleeding and flesh clot make water muddy immediately and disturb good visual filed.Gel immersion endoscopy has been reported to achieve hemostasis besides difficult visual filed in gastrointestinal bleeding.[3]

Aims & Methods: Our aim is to confirm the effectiveness of gel immersion endoscopy for the massive DB case.

Results: The case was 72 year old female who admitted our hospital with massive hemotochezia. CT scan revealed the extravasation at hepatic flexure. Urgent colonoscopy was performed after bowel preparation.Because of massive bleeding and clot, it was difficult to identify SRH. So Gel(OS-1 jelly: Otsuka Pharmaceuticals Factory, Tokushima, Japan) was used to get clear view. We injected the OS-1 gel through the BioShield irrigator(US Endoscopy, Mentor, Ohio).Gel clean the visual filed instead of clot.After Gel injection, bleeding source was seen clearly. Small non bleeding visible vessel was identified. Then marking clip was done. Colonoscopy was re-inserted with Endoscopic Band Ligation(EBL) device.EBL was successfully done and hemostasis was achieved. At the top of EBL lesion, visible vessel was confirmed.

Conclusion: Gel immersion endoscopy was effective technique in massive diverticular bleeding.

References: 1)Khoury W. Massive and recurrent diverticular hemorrhage, risk factors and treatment. Int J Surg 2016; 33: 136-139 2) Imaeda H. The Burden of Diverticular Disease and Its Complications: West versus East. Inflamm Intest Dis 2018; 3: 61-68 3) Yano T. Gel immersion endoscopy: a novel method to secure the visual field during endoscopy in bleeding patients. Gastrointestinal Endoscopy 2016;83(4):

Disclosure: Nothing to disclose

OP350 ENDOSCOPIC RESECTION OF A CHOLEDOCOCELE

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Introduction: Coledococele is a very rare finding in upper GI endoscopy and it is liable to endoscopic resection only in a few times.

Aims & Methods: A 17 years old caucasian man referred to our endoscopic unit for a recent episode of pancreatits. A MRCP showed regular caliber of the common bile duct, with an isolated cystic-like dilatation of its distal part. Our preliminary duodenoscopy and EUS detected a pre-papillary choledococele of 25-30 mm containing 3 biliary stones and ascribable to the biliary dilatation type III, according to the Todani classification.

Results: The choledococele was handled like an ampulloma and removed en-bloc with the hot snare; it was too large to pass through the oesophageal lumen, so we cut it in the stomach and took it out in two parts. At the cut edge the biliary and pancreatic orifice could be clearly seen: we performed both sphinterotomies and decided to proctect the Wirsung orifice against the risk of pancreatitis using a plastic stent. At the end of the procedure, the cut edge was closed by two clips.

Conclusion: The control after 2 months showed the spontaneous expulsion of the pancreatic stent and a regular scar of the papillary area.

Disclosure: Nothing to disclose

OP351 HOW TO MODIFY THE AXIS OF A SEMS PLACED FOR GASTRIC ANTRAL NEOPLASIA: A SIMPLE TRICK

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Introduction: Self-expandable metallic stents (SEMSs) may be used to effectively palliate malignant gastric outlet obstructions (GOOs), but their utility and efficacy in patients with gastric antral neoplasia in not completely clear. One of the reason why gastric SEMS can be inefficacy is possibly due to the impact of the proximal end of the stent to the great curvature of the gastric body.

Aims & Methods: .The aim of our treatment was the modification of the proximal part of the SEMS, to restore the normal anatomy of the stomach. Three patients unfit for surgery underwent SEMS placement for gastric antral neoplasia (two F of 25 and 56 years old and one M 57 years old). In the first patients a SEMS 22 x 90 mm was placed, in the second a 22 x 60 mm and in the third patient a 22 x 90 mm was placed inside a previous 22 x 60 mm

Results: Because of the normal anatomy of the stomach, after placing a SEMS for gastric antral neoplasia, the proximal end of the stent can bit on the great curvature of the gastric body. This can results in a GOO due to the impact of the stent. With a standard clip we catch the upper part of the proximal end of the stent, closing the clip inside the mesh of the body of the SEMS. This trick allow to the upper part of the stent the completely modification of the axis, restoring the normal anatomy of the stomach. All of the patients restart oral intake the day after without any complication or vomiting.

Conclusion: In presence of gastric antral neoplasia causing GOO undergone SEMS placement, the modification of the axis of the stent with a standard clip is a simple trick to restore the normal anatomy, allowing to the patients a correct oral intake.

Disclosure: Nothing to disclose

OP352 ACETIC ACID IN COMBINATION WITH BLUE LIGHT IMAGING: A NEW METHOD TO IMPROVE THE DETECTION OF RECURRING SESSILE SERRATED LESIONS IN THE COLON

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Introduction: Sessile serrated lesions (SSLs) have a high risk of incomplete endoscopic resection, and any recurrent lesion at the site of resection is often difficult to delineate due to the development of mucosal scars in the area.[1] Our previous experience have demonstrated that acetic acid (AA) spray along with indigocarmine is of substantial benefit for the delineation of SSLs.[2] Recently, a new image enhanced endoscopy technique, blue light imaging (BLI), has been developed and the benefits in assessing colonic polyps has been reported.[3] Nevertheless, the combined use of AA and BLI has not yet been presented.

Aims & Methods: The aim is to describe the first experience of AA and BLI in two recurrent SSLs.

Colonoscopy with a magnifying function and BLI (EC-760ZP-VM, Fujifilm Co., Tokyo, Japan) was used. The acetic acid (5%) was diluted in lukewarm water to derive a solution with a concentration of 1.7%. The solution was sprayed directly through the working channel of the endoscope on to the suspicious lesions. Thereafter the polyps were assessed and characterized prior to endoscopic removal.

Results: Acetic acid improved the visibility of the recurrent SSLs in both cases. In combination with BLI, the delineation of the lesion was more easily performed, and thus facilitated precise and radical resection, which was achieved in both cases. The use of acetic acid in a concentration of less than 2% was safe and no adverse events were recorded.

Conclusion: The combination of acetic acid and BLI could be an excellent method to improve the visualization of recurrent SSLs and thereby increasing the possibility to perform complete endoscopic resections. The acetic acid spray was both easy to prepare and use.

References: 1 Pohl H, et al. Incomplete polyp resection during colonoscopy-results of the complete adenoma resection (CARE) study. Gastroenterology. 2013;144:74-80. 2 Yamamoto S, et al. Acetic acid-indigocarmine mixture for evaluating the margins of sessile serrated adenomas/polyps. Dig Endosc. 2017;29:817-8. 3 Bisschops R, et al. BASIC (BLI Adenoma Serrated International Classification) classification for colorectal polyp characterization with blue light imaging. Endoscopy. 2018;50:211-20.
Disclosure: Nothing to disclose

OP353 SALINE-IMMERSION THERAPEUTIC ENDOSCOPY (SITE) FACILITATED UNROOFING OF A LARGE, SYMPTOMATIC ILEAL LIPOMA AT DOUBLE-BALLOON ENTEROSCOPY (DBE)

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Introduction: Lipomas of the gastrointestinal (GI) tract are common, benign and usually present as innocuous findings. Larger ones (>2cm in diameter), particularly those involving the ileum, may present with clinical symptoms such as abdominal pain (caused by intussusception) and iron deficiency anaemia (IDA) or obscure GI bleeding (OGIB) (caused by overlying mucosal ulceration); these cases warrant intervention and often end up being referred for surgery. We describe a minimally invasive endoscopic alternative to surgical resection for the management of these lesions.
Aims & Methods: A 60-year-old man presented with recurrent, cramping abdominal pain and OGIB. A magnetic resonance enterography (MRE) revealed a 2.5 cm submucosal lesion in the distal ileum, in keeping with a large lipoma. In light of these findings and the clinical presentation, we perform a saline-immersion retrograde DBE under conscious sedation, for further evaluation and minimally invasive, definitive endotherapy.
At DBE the lesion was identified at around 40cm proximal to the ileocaecal valve. The endoscopic appearances revealed a 2.5 cm sessile submucosal, lumen-filling lesion with a positive 'pillow sign'. Although the overlying mucosa appeared mostly unremarkable, a small, healed ulcer (which would account for the patient's IDA and OGIB) was identified on the medial surface of the lesion.
Endotherapy was deemed feasible and this was facilitated by the buoyancy properties provided by SITE. In order to reduce the risk of perforation and bleeding, an endoscopic loop ligating device was first deployed tightly at the base of the lesion. A ball-tip, needle-type endoscopic submucosal dissection (ESD) knife was then used to incise and unroof the lesion. This allowed for exposure and spontaneous extrusion of the lipomatous tissue (already under pressure from the loop-lighting device). Saline-immersion allowed for maintenance of a clear visual field, through avoidance of clouding of the endoscopic lens and flotation of extruded micelles of fatty tissue. A submucosal tattoo and a clip were placed as endoscopic and radiological markers, respectively. The procedure was performed under antibiotic cover. No significant immediate, early or late adverse events were encountered.
Results: Histopathological examination of retrieved tissue showed mature adipocytes with fibrofatty submucosal changes, in keeping with a submucosal lipoma. No dysplasia or sarcomatous transformation was identified. The patient's symptoms have resolved completely post-endotherapy.
Conclusion: Our case demonstrates the safety and usefulness of minimally invasive endotherapy of symptomatic large ileal lipomas. The combination of DBE with SITE-facilitated unroofing, after securing the lipoma's base with a loop-ligation device, allows for safe, spontaneous extrusion of the benign lipomatous tissue and avoids the need for operative surgery in symptomatic patients.
Disclosure: Dr Despott and Dr Murino receive research/ education support from Aquilant Medical, Fujifilm, Olympus, Pentax Medical, Boston scientific and GI supply. All others authors have no conflicts of interest to disclosure.

OP354 MUCOSAL ENTRY DEHISCENCE AND ESOPHAGEAL LEAK AFTER POEM

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Introduction: Per-oral endoscopic myotomy (POEM) has been a minimally invasive technique for the treatment of achalasia. While most of the cases in the Northern are performed for idiopathic achalasia, in our country the majority of the patients treated with POEM are Chagasic patients. Many of them have per-oral endoscopic myotomy after recrudescence of dysphagia many years after surgical esophagogastric myotomy with partial fundoplication.
Aims & Methods: To present the case and the treatment of mucosal entry dehiscence and esophageal leak after a per-oral endoscopic myotomy.
Results: A 49 years old female with advanced Chagas achalasia presenting recurrence of dysphagia (Eckardt 6) 15 years after a cardiomyotomy and partial fundoplication was submitted to POEM. Control esophagogram the next day showed no leak. However, she presented a severe vomiting episode. Liquids were introduced the following day, and the patient discharged asymptomatic on the postoperative day 3. After 48 hours, she returned complaining about chest pain and vomiting. Physical examination and leukogram were normal. Computed tomography (CT) with oral contrast showed dehiscence of the mucosal entry (mucosotomy) in the esophagus and esophageal blocked leakage to the posterior mediastinum. Broad-spectrum antibiotics, proton-pump inhibitor (PPI) and placement of nasoenteric feeding tube were adopted. Follow-up CT after 10 days showed the persistence of the esophageal leakage. Upper gastrointestinal endoscopy (UGE) showed a proximal mucosotomy on the mucosal entry topography with fibrin clots and an hemoclip inside it. The hemoclip was pulled-out and then the endoscope advanced inside the tunnel. A distal orifice communicating the submucosal tunnel to the esophageal lumen was identified 3 centimeters forward, guiding the drainage of the esophageal leakage and preventing the formation of fluid collection. Section of the mucosal flap over the submucosal tunnel was the therapeutic choice as previous surgery fibrosis and inflammatory tissue around blocked the leakage and contained the infection. PPI and sucralfate were prescribed. Liquid diet was introduced 2 days after and the patient discharged with semi-liquid diet 4 days after. The patient was asymptomatic 30 days after the new procedure, and UGE revealed a small amount of fibrin over the blocked wall. PPI was maintained and pasty diet introduced. UGE after 90 days showed the blocked wall almost wholly re-epithelialized and Los Angeles B esophagitis. Due to improving but still present reflux the patient is still on PPI and will have a 6-months UGE control.
Conclusion: Mucosal flap section could be safely performed as the leakage was blocked. Avoiding severe vomiting after POEM is an important step to prevent mucosal entry dehiscence. Previous surgery for achalasia may be a factor that helps block esophageal leakage in case of mucosotomy.
Disclosure: Nothing to disclose

OP355 MULTIPLE BULBAR NEUROENDOCRINE TUMORS RESECTED BY PRE-PYLORIC TUNNELING ESD

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Introduction: A 61 years-old patient underwent an esophagogastroduodenoscopy (EGD)for epigastric pain. It revealed multiples sub-mucosal lesions of the duodenal bulb, between 5 and 16 mm, the two largest being juxta-pyloric. Biopsies revealed grade I neuroendocrine tumors (Rindi I, Ki67< 2%). Work-up included an endoscopic ultrasound that showed a T1 tumor with no regional lymphadenopathies and a positron emission tomography-computed tomography (PET/CT) scan using ^{68}Ga-DOTA-TATE (somatostatin [SST]-analog)that came back negative.

Aims & Methods: After discussion in the multidisciplinary oncological board, a decision was made to perform an endoscopic submucosal dissection (ESD) of the largest tumors, followed by an endoscopic mucosal resection (EMR) for the remaining small lesion.

Results: Knowing the close contact between the two largest bulbar NETs and the pylorus, the procedure was started with gastric submucosal tunneling 2 cm proximal from the pylorus according to the pocket-ESD method, to be able to reach the deep submucosa of the juxta-pyloric bulb in a tangential axis with the ESD knife. The dissection was conducted alongside the pylorus sphincter before digging under the Brunner glands under the NET lesions. A clip and thread traction system was set up on the flap after lateral opening, followed by distal incision. En-bloc, complete endoscopic resection was achieved with a tiny bulbar muscular tear easily closed by clips.

The patient had no symptoms after the resection. Histopathological examination of the specimen showed 3 grade I neuroendocrine tumors. Lateral margins were free from malignancy, while one of the vertical margins was in contact with the tumor cells. There was no lymphovascular invasion and the lesion was classified pT2mNx. Given the well differentiation of the tumor, endoscopic follow-up was proposed. The patient underwent control EGD at three months and resection of the small remaining lesion by cap-band-assisted EMR. At that time no recurrence was discovered.

Conclusion: Pre-pyloric tunneling ESD is feasible and safe for bulbar submucosal lesions.

Disclosure: Nothing to disclose

OP356 ENDOSCOPIC SUTURING TO REDUCE THE RISK OF COMPLICATIONS AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION OF A RECURRENT RECTAL POLYP

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Introduction: Recurrent colorectal polyps present a challenge for the endoscopist due to the presence of submucosal fibrosis. In these cases, endoscopic mucosal resection (EMR) is often unsuccessful thus submucosal dissection (ESD) is the preferred technique. The risk of muscle layer damage and subsequent perforation is increased in performing ESD for recurrent colorectal polyps. As such, wound closure after resection may reduce the risk of complications.

Aims & Methods: This video demonstrates closure of a rectal ESD defect using an overstitch device designed for use with a flexible endoscope. A 74 year-old man presented with a recurrent laterally-spreading tumor (LST) in the mid-rectum (initial size 65mm with pathology showing focal high-grade dysplasia). Previous piecemeal EMR had been performed but at follow-up endoscopy 6 months later a large recurrent adenoma was identified. We anticipated significant submucosal fibrosis particularly in the scarred center of the lesion.

Furthermore, the previous histology and location of the lesion predicted an increased risk for covert submucosal invasion thus ESD would likely be the best option for a complete en bloc resection. If indeed the center of the lesion was tethered to the muscle layer, we further anticipated some degree of muscle injury during ESD so we were prepared to close the defect via endoscopic suturing.

Results: A detailed examination of the lesion under high-definition white-light, linked-color imaging and blue-light imaging in addition to optical zoom + under water magnification revealed a mid-rectal 40x30mm granular-type LST with Paris type IIa+IIc morphology and Kudo IIIL/IV pit pattern. Standard ESD was then performed using a HybridKnife (ERBE Elektromedezin, GE) by incising the mucosa around the lesion followed by stepwise ESD. As anticipated, the center of the lesion was adherent to the muscularis propria thus very careful dissection was required with cutting of some superficial muscle fibres in this area to preserve an en bloc resection. No major bleeding or intra-procedural perforation occurred.

After ESD was completed, further examination of the resection bed revealed no definite signs of deep muscle injury or perforation. However, given there was intentional incision of the muscle layer in the center of the lesion, wound closure was optimal. The resected area was too large to attempt clip closure therefore we elected to perform endoscopic suturing using an overstitch device (Apollo Endosurgery Inc., USA). Two running sutures were completed to tightly appose the edges of the resection

bed and completely seal the mucosal defect. Total procedure time was 165 minutes. No delayed complications occurred. Final pathology revealed low-grade dysplasia only.

Conclusion: Endoscopic suturing is a viable option when full closure of a mucosal defect is desired.

Disclosure: Nothing to disclose

OP357 ENDOSCOPIC MECHANICAL LITHOTRIPSY FOR SIGMOID GALLSTONE ILEUS

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Introduction: Gallstone ileus is an uncommon condition accounting for 1-4% of all causes of mechanical intestinal obstruction. The usual site for stone impaction is the terminal ileum or ileo-caecal valve. Intestinal obstruction caused by gallstone impaction in the large bowel is a very rare entity. We present a case of colonic gallstone ileus, at the level of sigmoid colon, which was successfully treated with endoscopic mechanical lithotripsy.

Aims & Methods: A 60 year old man was admitted with a 5 day history of upper colicky abdominal pain, high grade fever and darkening of urine. Initial blood tests showed, WBC 9.8 x10^9/L, CRP 270 mg/L, Bilirubin 44mmol/L, ALT 48 iu/L, and Alkaline phosphatase 170 iu/L (NR< 130). An ultrasound scan of abdomen and MRCP showed multiple stones in the gallbladder and in the common bile duct. Hence, an ERCP was performed 2 days later and strangely, 4 litres of fluid was seen in the stomach despite a prior overnight fast. After aspirating the fluid, the pylorus was found to be widely patent and two small ulcers were noted in the duodenum just proximal to the normal looking ampulla. After a wire guided biliary cannulation, the cholangiogram confirmed common bile duct stones. A sphincterotomy was performed and the bile duct stones were extracted with a balloon catheter. However, the final occlusion cholangiogram showed a possible cholecysto-duodenal fistula. Despite a successful ERCP, the patient failed to show clinical improvement and developed vomiting and abdominal distension with a rise in the WBC to 28x10^9/L. A CT scan 2 days after the ERCP confirmed a cholecysto-duodenal fistula together with dilated small bowel loops and a large gallstone impacted in the sigmoid colon. Hence, a flexible sigmoidoscopy was performed confirming the presence of a 3cm gallstone obstructing the narrow sigmoid colon. Initially, a large polypectomy snare was used to grasp the stone but it was not possible to extract the stone through the narrow sigmoid colon. Therefore, a 3cm diameter Olympus Lithocrush Basket was used to crush the gallstone into smaller pieces, which then passed spontaneously.

Results: The patient recovered and went home two days later.

Conclusion: Gallstone ileus involving the large bowel is an uncommon condition. The stone usually fistulates from the gallbladder directly to the colon rather than to the duodenum as in this case. Colonic gallstone ileus is usually seen in old age and in patients with multiple co-morbidities where surgical intervention is associated with an increased risk of morbidity and mortality. Hence, less invasive techniques such as colonoscopy with mechanical lithotripsy of the impacted gallstone should be tried prior to considering surgical intervention.

Disclosure: Nothing to disclose

Oncology: Basic mechanisms
10:30-12:00 / Barcelona

OP358 THE CHICK EMBRYO CHORIOALLANTOIC MEMBRANE ASSAY: *IN OVO* MODEL FOR PERSONALIZED ASSESSMENT AND EVALUATION OF THE MOST EFFECTIVE THERAPEUTIC APPROACH IN CANCER THERAPY

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Introduction: "Personalized medicine," is tailoring and maximize medical treatment to a single person.
Aims & Methods: To generate a personalized, quick and reliable screening system for effective evaluation of different therapeutic options using 3D tumors in a „humanized egg".
At day 3, 2ml of albumin was pulled out from fertilized eggs to separate the CAM from the eggshell and a small window in the eggshell has been made. On day 6-7, single cells suspension or tissues, derived from cancer patients, were transplanted onto the CAM and visible tumors were developed („CAM-PDX"). Human immune cells were inoculated on day 9-10 and then drugs, mAbs and Immuno/chemo-therapy, were applied via the yolk sac. Tumor growth was measured, weighted, stained and monitored by caliper and IVIS imaging platform.
Results: Histology and IHC analysis confirmed that the established tumors retained their characteristics. Positive Ki-67 staining confirmed that cancer cells proliferate while the treated tumors showed reduced staining. Anti-CD24 mAb, FOLFOX and cetuximab, given as single agent or combinations, successfully inhibited CRC cells growth (by 70-75%). Detection of active caspase-3 confirmed these results. Biopsies from human specimens, were successfully established and expanded by serial passages allows generation of bio-bank. The stimulated human PBMCs demonstrated enhanced proliferation *in vitro* and *in ovo*, even after 5 days in the egg.
Conclusion: The CAM is an ideal, effective, economical and powerful avatar-based precision medicine approach to predict the best protocol for cancer therapy.
Disclosure: Nothing to disclose

OP359 METHYLATION ANALYSIS OF NON-AMPULLARY DUODENAL PRECANCEROUS LESIONS

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Introduction: Because duodenal epithelial tumors are rare, their biological and clinical characteristics are not yet fully understood.
Aims & Methods: To clarify the molecular and clinicopathological characteristics of non-ampullary duodenal lesions, we assessed DNA methylation of cancer-associated genes in a cohort of non-ampullary duodenal precancerous lesions. One-hundred and two non-ampullary duodenal premalignant lesions including 95 intestinal-type tumors (90 intestinal-type adenomas and 5 intestinal-type non-invasive carcinomas) and 7 gastric-type tumors (2 pyloric gland adenomas and 5 non-invasive carcinomas) as well as adjacent normal tissues (n = 15) from 102 individuals were investigated. According to the revised Vienna classification, intestinal-type tumors were classified as 32 Category 3 tumors (low grade adenomas) and 63 Category 4 tumors (high grade adenomas and non-invasive carcinomas).
Also, gastric-type tumors were classified as 2 Category 3 tumors (pyloric gland adenomas) and 5 Category 4 tumors (non-invasive carcinomas). After extracting DNA from formalin-fixed paraffin embedded (FFPE) sections, we assessed the methylation status of CpG island methylator phenotype (CIMP) markers including *CACNA1G*, *IGF2*, *NEUROG1*, *RUNX3*, and *SOCS1* as well as *MLH1* using bisulfite pyrosequencing. A cutoff value of 15% was used to define genes as methylation-positive. Tumors were defined as CIMP-positive when methylation was detected in two or more out of five methylation markers.
Results: Tumors with CIMP were seen in 20 intestinal-type tumors (21.1%) and 3 gastric-type tumors (42.9%), respectively. In intestinal-type tumors, prevalence of CIMP-positive lesions was higher in non-invasive carcinomas (40%) than in adenoma (20.2%) or normal mucosa (0%, P < 0.01). In gastric-type tumors, CIMP was detected more frequently in non-invasive carcinomas (60%) than in normal mucosa (0%, P < 0.01). As for intestinal-type tumors, prevalence of CIMP-positive lesions was significantly higher in Category 4 tumor than in normal mucosa (25.8% vs. 0%, P = 0.03). As for methylation levels of each cancer-associated gene, we found that the methylation levels of *CACNA1G*, *NEUROG1*, *RUNX3*, and *SOCS1* were significantly higher in intestinal-type non-invasive carcinomas than in intestinal-type adenomas or normal mucosa. However, there were no significant differences when intestinal-type tumors were classified according to the revised Vienna classification.
Conclusion: Genome-wide hypermethylation of cancer-associated genes estimated by CIMP were associated with development of non-invasive carcinomas other than adenoma formation during carcinogenesis of non-ampullary duodenal precancerous lesions. Especially for intestinal-type tumors, epigenetic silencing of *CACNA1G*, *NEUROG1*, *RUNX3*, and *SOCS1* was significantly associated with development of non-invasive carcinomas from adenomas.
Disclosure: Nothing to disclose

OP360 TLR4-DRIVEN SPONTANEOUS TUMORIGENESIS IS MEDIATED BY MICROBIAL-INDUCED EPITHELIAL PRODUCTION OF REACTIVE OXYGEN SPECIES

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Introduction: Duodenal adenocarcinoma (DA) is a rare malignancy with a poorly defined pathogenesis. Previous studies have identified histopathological similarities between DA and colorectal cancer (CRC) as well as an increased risk in CRC patients to develop DA. We have shown that toll-like receptor 4 (TLR4), a receptor for Gram negative bacteria, is overexpressed in intestinal epithelial cells (IECs) of CRC patient adenomas. To mimic over-activation of epithelial TLR4 in an animal model, we developed the villin-TLR4 mice, which express a constitutively active form of TLR4 under the promoter of villin.
In this model, we have demonstrated that epithelial TLR4 signaling induces gut dysbiosis, production of reactive oxygen species (ROS), and increased susceptibility to colitis-associated cancer. Furthermore, we have also reported that these mice develop spontaneous duodenal adenomas before 12 weeks of age.
Aims & Methods: Here, we took advantage of this spontaneous model of DA to test the hypothesis that epithelial TLR4 activation promotes tumor initiation by shaping the microbiome and inducing reactive oxygen species (ROS). Villin-TLR4 mice and their wild-type (WT) littermates were either rederived into germ-free conditions or treated with the ROS scavenger apocynin from birth. At 12 weeks, mice were euthanized and tumor area in vilin-TLR4 mice was measured. IECs from non-involved areas were iso-

lated by EDTA chelation and analyzed for H_2O_2 production by means of Amplex Red and expression of NADPH oxidase 1 (Nox1) and dual oxidase 2 (Duox2) transcripts by means of qPCR.

Results: Constitutive activation of epithelial TLR4 significantly increased the expression of Nox1, p22 phox, Duox2, and DuoxA2 transcripts in vil-lin-TLR4 IECs when compared to those of WT littermates. Rederivation of villin-TLR4 into germ-free conditions significantly reduced the epithelial expression of DuoxA2, which was accompanied by a significant reduction in the production of H_2O_2. In the absence of a microbiota, duodenal tumor initiation was abrogated in 5 out of the 6 mice and the tumor area was dramatically reduced in the only mouse that developed DA. Chronic administration of apocynin did not inhibit epithelial NADPH oxidase activity or expression, but significantly reduced the tumor area in 5 out of the 8 mice and prevented tumor formation in 3 out of the 8 mice, demonstrating that ROS play an important role in this model of tumorigenesis.

Conclusion: Our findings demonstrate that TLR4-driven spontaneous tumorigenesis is dependent on the presence of a microbiota that induces DuoxA2 upregulation and the release of ROS. In addition, our observations suggest that similar to CRC, DA is also dependent on the microbiota. We speculate that TLR4 activation induces dysbiosis, which in turn feeds forward ROS production by IECs, leading to tumor initiation.

Disclosure: Nothing to disclose

OP361 YAP/TAZ PLAYS A POTENTIAL ROLE IN TUMOR INITIATION IN THE INTESTINE AND CAN BE REGULATED BY THE MICROENVIRONMENT

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Introduction: The stromal microenvironment plays a key role in regulating adult stem cell niches and can play a dual role in tumor development. Depending on the tissue context, stromal cells may either promote or inhibit tumor growth, however the precise cellular and molecular mechanism remain largely unknown.

Aims & Methods: We aimed to identify tumor initiation signaling pathway(s) that is regulated by the stromal microenvironment. To study this, we employed wild type and mutated (Apc+/1638N) murine intestinal organoid cultures and crypt-myofibroblast co-cultures, microarray analysis, real-time PCR and immunohistochemistry staining of human colorectal cancer samples.

Results: Microarray analysis revealed that genes associated with YAP signaling are upregulated in both mutated intestinal organoids and wild type organoids from an indirect crypt-myofibroblast co-cultures, that was confirmed with real-time PCR. Inhibition of YAP signaling with cytochalasin D resulted in reduced number and decreased diameter of tumor-like crypts (spheroids). Immunohistochemistry staining of human colorectal cancer samples showed that strong activation YAP/TAZ in dysplastic epithelium correlated with strong infiltration of aSMA+ stromal cells.

Conclusion: We discovered that YAP/TAZ signaling in the intestinal epithelium can be regulated either intrinsically by an oncogenic mutation or extrinsically by secreted factors from the stromal microenvironment. This study highlights the important role of the microenvironment in regulating epithelial cell plasticity and suggests that aSMA+ stromal cells can contribute to tumor initiation. Therefore, aSMA+ stromal cells should be considered in the future as cellular targets for anti-cancer therapies.

Disclosure: Nothing to disclose

OP362 COMPREHENSIVE MOLECULAR ANALYSIS IDENTIFIES DRIVER MUTATIONS IN METASTASES OF SPORADIC WELL-DIFFERENTIATED NEUROENDOCRINE TUMOURS OF THE SMALL INTESTINE

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Introduction: Small intestinal neuroendocrine tumours (SI-NETs) represent a heterogeneous group of rare tumours. At present, the genetic make-up of SI-NETs is poorly elucidated. In contrast to adenocarcinomas and neuroendocrine carcinomas (NECs), well differentiated SI-NETs are relatively indolent tumours. NECs share oncogenic pathways with adenocarcinomas whilst SI-NETs are mutationally quiet. The prognosis and treatment of SI-NETs is currently based on traditional criteria, which do not predict clinical outcomes for individual patients nor provide a rationale for targeted therapy.

Aims & Methods: The aim is to perform a comprehensive genetic characterization of metastatic SI-NETs. This study, which is largely based on genomic tumour data collected as part of the Center of Personalised Cancer Treatment (CPCT) study from patients of the Netherlands Cancer Institute, entails whole genome sequencing (WGS) of 29 metastasized SI-NETs (group 1) and next generation panel sequencing (NGS) of 7 SI-NET liver metastases (group 2). Diagnosis was confirmed by histopathological examination according to the WHO classification of neuroendocrine tumours (NETs) 2018. For group 1, WGS included assessment of somatic mutations in all cancer related driver genes (>500), somatic copy number variations, gene disruptions (including gene fusions), tumour mutational burden (TMB) and microsatellite status. In group 2, NGS was performed in a diagnostic setting with a cancer hotspot mutation panel of 58 genes. Our cohort consisted of metastatic well-differentiated SI-NETs of which 19% (7/36) were grade 1, 69% (25/36) grade 2 and 11% (4/36) grade 3. Association between tumour grade and genetic features was assessed using the Man-Whitney U test.

Results: Somatic mutations were identified in 66% of SI-NETs by WGS (n=29) and 43% by NGS (n=7). Of SI-NET metastases (n=36), 36% showed driver mutations in tumour suppressor genes (e.g. TP53, RB1, ATM, CD-KN1B, CTNNB1, SMAD2) and 8% of metastases showed mutations in proto-oncogenes (KRAS, NRAS, MET). In group 1 (N=29), allelic loss of chromosome 18 was present in 63%. Other recurrent events were complete loss of CDKN2A and CDKN1B (both 7%). All tumours in group 1 were microsatellite stable (median 0.029, IQR 0.022-0.046) and showed low TMB (median 1.10, IQR 0.86-1.33). Solely 13% of all driver mutations unveiled by WGS would have been detected using panel NGS. No association between tumour grade and genetic characteristics was found.

Conclusion: Metastasized SI-NETs are mutationally quiet tumours and allelic loss of chromosome 18 is common, which is in accordance with earlier studies on primary SI-NETs. Surprisingly, 44% of metastasized well differentiated SI-NETs harbour driver mutations in proto-oncogenes and tumour suppressor genes. Thus, the presence of driver mutations is not exclusive to neuroendocrine carcinomas or adenocarcinomas and does not contribute to the distinction between well differentiated NETs and poorly differentiated NECs during pathological assessment. Targetable genetic alterations were detected in 19% of patients, including the BRCAness, the cyclin D/cyclin-dependent kinases 4 and 6 -retinoblastoma protein and the HGF/MET pathway, rendering these patients eligible for targeted therapy which provides them with new treatment options. These mutations may be missed in the routine clinical setting when hot-spot NGS panels are used. In the immediate future, we will continue to assess the additional value of WGS in SI-NETs in terms of biomarker identification, additional standard treatment options and eligibility for trial inclusion.

Disclosure: Nothing to disclose

OP363 REGULATION OF LYMPHANGIOGENESIS BY PANETH CELLS IN NORMAL PHYSIOLOGY AND EXPERIMENTAL PORTAL HYPERTENSION

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Introduction: The mesenteric lymphatic network contributes to the transport of fluid and intestinal mucosal associated immune cells along the gut-liver axis. We have previously reported a decrease in intestinal vascularization and number of Paneth cells along with diminished lymphangiogenesis in absence of intestinal microflora [1]. However, the association of Paneth cells with the regulation of lymphatic vascular development is unknown.
Aims & Methods: We hypothesized that Paneth cells, as part of the innate intestinal immune system, regulate the development of lymphatic vessels and affect portal pressure under the control of intestinal bacteria.
We induced Paneth cell depletion in Math-1 Lox/LoxVillcre[ERT2] mice by injecting three consecutive doses of tamoxifen and performed partial portal vein ligation (PPVL) to induce portal hypertension. After 14 days, intestinal and mesenteric lymphatic vessels were assessed by immunohistochemistry (IHC) using lymphatic vessel endothelial hyaluronic acid receptor 1(Lyve-1) antibody. The lymphatic vessels were quantified using Metamorph to calculate pixel ratio. Expression of genes involved in the regulation of lymphatic vessels was evaluated by RT[2] profiler PCR array in intestinal tissue. Additionally, the expression of specific genes involved in lymphangiogenesis was evaluated separately by quantitative PCR. Intestinal organoids from control and Paneth cell depleted mice were exposed to different bacterial derived products. Proteomic analysis of conditioned media was performed using MaxQuant to analyse differentially regulated proteins in lymphangiogenesis in the absence of Paneth cells and/or in portal hypertension.
Results: Portal pressure was significantly attenuated in Paneth cell depleted mice compared to control mice after PPVL (n=11/group, 9.78±1.23 cmH$_2$O vs 11.45±1.41 cmH$_2$O, respectively, p<0.002). Depletion of Paneth cells resulted in a significantly decreased density of lymphatic vessels compared to control as assessed by IHC (n=5, pixel ratio), in the intestine (0.176% ±0.12 vs 0.367%±0.15, p=0.01) and in the mesentery (0.160%±0.06 vs 0.404%±0.20 p=0.001). Quantitative PCR showed a decreased expression of genes involved in the regulation of lymphangiogenesis, including VEGF-C, VEGF-D, VEGF-A, Nrp2, Angpt-2, Tie-1, Tie-2, TGF-α, HGF and CXCL-1 in Paneth cell depleted mice. Moreover, the expression of specific markers of lymphangiogenesis such as transcription factor Prox-1 or growth factor VEGFR3 and protein FOX-C2 were significantly decreased in Paneth cell depleted mice after PPVL. In the absence of Paneth cells, proteomic analyses showed a significant downregulation of several proteins involved in lymphatic vessel development and morphogenesis, as well as in processes of lipid metabolism and transport.
Conclusion: In the absence of Paneth cells, the intestinal and mesenteric lymphatic vessel networks were significantly underdeveloped. This was associated with an attenuated portal hypertension. These findings suggest that Paneth cells not only play an antimicrobial role in the intestine, but also contribute to the regulation of lymphatic vessels and portal pressure.
References: 1. Moghadamrad S, McCoy KD, Geuking MB, et al. Attenuated portal hypertension in germ-free mice: Function of bacterial flora on the development of mesenteric lymphatic and blood vessels. Hepatology 2015;61:1685-95.
Disclosure: The authors declare no conflict of interest. These data has been presented as an e-poster in ILC-2019 in Vienna.

Hot topics in gastric cancer
10:30-12:00 / Hotspot

OP365 EVALUATING THE ACCURACY OF DISCHARGING PATIENTS FROM SURVEILLANCE FOR GASTRIC PREMALIGNANT LESIONS ACCORDING TO THE MAPS GUIDELINE IN A LOW RISK POPULATION: A PROSPECTIVE COHORT STUDY

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Introduction: Intestinal type gastric cancer follows a cascade of premalignant lesions which makes gastric cancer suitable for screening and surveillance. The Management of epithelial precancerous conditions and lesions in the stomach (MAPS) guideline (first published in 2012 and revised in 2019) advises an histological-led diagnosis by performing random biopsies, in order to stage the extent and severity of premalignant gastric lesions, and determine if surveillance is recommended. No surveillance is deemed necessary for atrophic gastritis (AG) or intestinal metaplasia (IM) limited to either antrum or corpus. However, random biopsies may not properly reflect the extent of the lesions. The aim of this study was to assess the appropriateness of discharging patients from further surveillance according to the guideline in daily practice.
Aims & Methods: Patients were included from the multicenter, prospectively followed PROREGAL cohort initiated in 2009 in which patients were identified with AG, IM and/or dysplasia of the gastric mucosa at index endoscopy (t0). In the PROREGAL protocol each patient underwent a first surveillance endoscopy with random biopsies one year after the index endoscopy (t1), and in case no high or low grade dysplasia was present, a second surveillance endoscopy was performed three years after the index endoscopy (t2). Further surveillance interval was in accordance with the MAPS guideline. For the current study, patients excluded from further surveillance according to MAPS-2012 were re-invited to undergo a follow-up endoscopy after three years (t3). Patients were included in the current study 1) if they met the MAPS-2012 or MAPS-2019 guideline recommendations to stop surveillance based on the outcome of the latest endoscopy (t1 or t2), and 2) underwent a subsequent follow-up endoscopy (t2 or t3) not included in the guideline recommendations. An inappropriate discharge from follow-up was defined if premalignant gastric lesions were present at t2 or t3 that gave reason to resume surveillance.
Results: The PROREGAL cohort comprises 334 patients. Between 2009 and 2019,113 patients were supposed to be discharged according to MAPS-2012 but underwent follow up endoscopy according to the PROREGAL protocol. In 38/113 (33.6%; 95%CI 25.2-43.2) patients (progressions of) gastric lesions for which surveillance is recommended were found at t2 or t3. If MAPS-2019 was followed, inclusion increased to 173 patients who were supposed to be discharged from surveillance. In 62/173(35.8%; 95%CI 28.8-43.5) of these patients, gastric lesions for which surveillance is recommended were present at t2 or t3. In two cases high grade dysplasia (both corpus) and in one case gastric adenocarcinoma of the angulus was diagnosed.
Conclusion: 1/3rd of patients who are discharged from gastric cancer surveillance according to MAPS recommendations appeared to be misclassified as low risk according to results found at follow-up endoscopy. Three of them had developed high grade dysplasia or gastric cancer. Therefore improvement of endoscopic and histological staging of premalignant gastric lesions is warranted.
Disclosure: Nothing to disclose

OP366 DIFFERENTIAL EXPRESSION OF LONG NON-CODING RNA HOTAIR IN GASTRIC CANCER AND PRENEOPLASTIC CONDITIONS

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Introduction: HOTAIR is long non-coding RNAs that plays an important role in gene regulation and has been shown to be upregulated in various tumors, including gastric cancer (GC). Recent studies reported that high expression of HOTAIR can promote tumor growth in vitro influencing patient prognosis including worse survival.
Aims & Methods: The aim of this study was to evaluate HOTAIR expression in preneoplastic gastric conditions and GC as well as to assess the clinicopathological and prognostic value of HOTAIR in GC patients. HOTAIR expression was analyzed in tissue samples of 81 GC patient (paired samples from tumor and corresponding adjacent gastric mucosa), 50 atrophic gastritis (AG) patients, 22 chronic gastritis (NACG) patients, and 16 controls. In addition, HOTAIR expression was evaluated in serum of 23 GC patients. Samples were obtained from 2 University hospitals in Lithuania and Germany. Total RNA was extracted using RNeasy Plus Universal Mini Kit. Quantitative HOTAIR expression analysis was performed using SYBR Green assay. HOTAIR expression was further correlated with genome-wide methylation using surrogate LINE-1 methylation by bisulfite pyrosequencing. GC patient's survival was evaluated using Kaplan-Meier analyses.
Results: HOTAIR was undetectable in histologically confirmed normal gastric mucosa samples from control group and NACG. HOTAIR expression was found in 24% of patients with AG. The HOTAIR positivity was strongly related to intestinal metaplasia (64.7%) and expression was positively associated with the grade of intestinal metaplasia (p< 0.001). Paired GC samples analysis revealed higher positivity rate of HOTAIR in tumor tissue compared to adjacent gastric mucosa (65.4% vs 8.6%, p< 0.001). HOTAIR was only sporadically detectable in serum samples of GC patients; however, with very low level of reproducibility.
Overall, tumor positivity for HOTAIR expression was associated with shorter overall survival in GC patients compared to patients without detectable HOTAIR expression; however, the difference did not reach statistical significance (p=0.074). HOTAIR positive tumors showed lower genome-wide LINE-1 methylation level compared to HOTAIR negative tumors (p=0.024).
Conclusion: Our data provide a novel evidence for a distinct expression pattern of HOTAIR in gastric mucosa. HOTAIR expression increases in stepwise manner in correlation to progression of preneoplastic condition of Correa´s cascade. These results indicate that HOTAIR might be involved in the development of GC.
Disclosure: Nothing to disclose

OP367 INVESTIGATION OF MECHANISTIC ROLE OF HOTAIR AND PCDH10 IN GASTRIC CARCINOGENESIS

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Introduction: Long non-coding RNA (LncRNA)s are rapidly emerging as new players in cancer biology and contribute to epigenetically to regulate DNA methylation. HOX transcript antisense intergenic RNA (HOTAIR) is one of the well-studied lncRNAs that regulate gene expression by mediating the modulation of chromatin structure. Protocadherin 10 (PCDH10) is well-known tumor suppressor genes and aberrant methylation of the PCDH10 is a frequent event in gastric cancers.
Aims & Methods: We aimed to investigate the epigenetic mechanism of lncRNA HOTAIR related with PCDH10 in gastric cancer.
Materials and methods: We collected 30 fresh gastric cancer tissue and paired adjacent gastric tissue samples and we used gastric cancer cell lines. We investigated mechanism of HOTAIR on apoptosis, cell proliferation, cell cycle analysis as indicators of carcinogenesis and metastasis of

gastric cancer. We analyzed expression of HOTAIR and PCDH10 in gastric cancer tissues and paired adjacent gastric tissue and perform methylation-specific PCR to identify the interaction between HOTAIR and PCDH10 in cancer cell line.
Results: The expression of HOTAIR was found to be higher in gastric cancer tissue compared with adjacent non-tumor gastric tissue. Using MKN 28 and MKN 74 cells, we demonstrated that HOTAIR repressed apoptosis, was associated with cell cycle progression, and controlled the invasion and migration of gastric cancer cells. PCDH10 expression was significantly decreased in gastric cancer tissues compared with adjacent non-tumor gastric tissue. The treatment of siHOTAIRs increased the transcriptional level of PCDH10, furthermore, PCDH10 protein was also upregulated by siHOTAIRs in gastric cell lines. We observed that HOTAIR induced PCDH10 methylation in gastric cell lines via methylation-specific PCR.
Conclusion: We identified a novel epigenetic mechanism involving the methylation of PCHD10 by lncRNA HOTAIR in gastric cancer and demonstrated that the HOTAIR modulated cell proliferation and the invasion and migration of gastric cancer cell We identified a novel epigenetic mechanism involving the methylation of PCHD10 by lncRNA HOTAIR in gastric cancer and demonstrated that the HOTAIR modulated cell proliferation and the invasion and migration of gastric cancer cell.
Disclosure: Nothing to disclose

OP368 CLINICAL AND MOLECULAR CHARACTERIZATION OF EARLY ONSET GASTRIC CANCER (≤ 50 YEARS): ANALYSIS OF A NATIONAL MULTICENTRE STUDY

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Introduction: Gastric adenocarcinoma (GC) is a common tumour with high morbidity and mortality. Although most GCs are sporadic, familial aggregation can be observed in approximately 10% of cases and hereditary GC, i.e. in the context of a germline mutation, accounts up to 5% of all cases. Only 7% of patients are diagnosed before age 50. The clinical and molecular characteristics of early onset GC had been poorly described.
Aims & Methods: To describe the clinical, histological and molecular characteristics of early onset GC (≤ 50 years old).
From 1999 through 2018, patients with early onset GC were retrospectively recruited at 4 Spanish centres. Personal and, family history, tumour-related information and tumour immunohistochemistry (IHC) of DNA mismatch repair proteins (MMR) (MLH1, MSH2, MSH6 and PMS2) status were registered. Germinal genetic analysis was performed in patients who met criteria of a hereditary syndrome associated with GC (ie. hereditary diffuse gastric cancer, Peutz-Jeghers syndrome, Lynch syndrome, familial adenomatous polyposis, hereditary breast and ovarian syndrome, juvenile polyposis and Li -Fraumeni syndrome).
Results: 308 patients were included, 118 (38%) were women. The median age at diagnosis was 43 years (range 17-50). The tumours were located mainly at body and antrum, 55% and 25% respectively. Histologically, 75% were diffuse, 17% intestinal and 18% mixed or unclassifiable. An advanced stage (III/IV) at diagnosis was present in 78% cases. With regard to environmental risk factors: and *Helicobacter pylori* infection was detected in 24/82 (29%) cases, 78/167 (46%) patients had regular smoking habit and 51/105 (20%) were moderate/severe alcohol consumers.
Family history was available in 108 cases: familial aggregation of GC was present in 15 (13.8%) cases and 5 (4.6%) met criteria for familial GC. IHC of MMR was performed in 88 (28.5%) tumours: 3/88 (3.4%) showed loss of expression in MLH1/PMS2, without an associated germline mutation. Fifteen genetic analyses were performed, detecting a germline mutation in 3 (20%) cases: *BRCA2*, *TP53* and *CDH1* (Table 1).
Conclusion: Most of early-onset GCs are histologically diffuse and diagnosed at an advanced stage. In this subgroup of patients, DNA mismatch repair system deficiency is an infrequent event and likely not very useful. Familial aggregation is present only in 13% of cases; however, in 20%

of the patients who meet criteria for genetic study, a germline mutation is found (*BRCA2, CDH1, TP53*). These results demonstrate that early-onset GC has a marked genetic heterogeneity, reinforce the importance of an adequate genetic counselling (complete family history) and enhance the emerging use of multigene panels.

Disclosure: Nothing to disclose

Age at diagnosis	Gender	Family history of GC	Family history of other tumours	IHC	Germline gene mutation
40	Female	No	Breast Ovarian	MMR+	BRCA2
38	Male	Yes	No	MMR+	CDH1
34	Male	No	Breast Colon	MMR+	TP53

[Table 1: Characteristics of patients with germline gene mutation]

OP369 CHARACTERISTICS AND RISK FACTORS OF INTERVAL GASTRIC NEOPLASMS DETECTED IN SCREENING ENDOSCOPY AMONG ASYMPTOMATIC HEALTHY ADULTS

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Introduction: In Korea, where gastric cancer is highly prevalent, regular upper endoscopy every other year is recommended for gastric cancer (GC) screening among individuals over 40 years old. However, even under such regular screening endoscopy, some are still diagnosed to have advanced gastric neoplasms.

Aims & Methods: This study was designed to identify characteristics and risk factors of interval gastric neoplasms detected in screening endoscopy. Medical records of individuals who were newly diagnosed with gastric neoplasms in screening upper gastrointestinal endoscopy between January 2004 and May 2016 were reviewed. Among them, those who had previous endoscopy within 2 years were enrolled. Their endoscopic finding, family history of GC, cigarette smoking, and *Helicobacter pylori* (*H. pylori*) infection status were analyzed. Those with positive results in anti-*H. pylori* IgG, CLO test or histologic findings of *H. pylori* were considered to have *H. pylori* infection.

Results: During the study period, 625 patients were newly diagnosed with gastric neoplasm. Among them, 300 patients underwent previous endoscopy within 2 years (median 12 months; Interquartile range: 11-15 months). Three patients with previous gastrectomy or unclear final pathology were excluded. Among the 297 neoplasms, 246 were endoscopically treatable gastric neoplasms (ET-GN) and 51 were endoscopically untreatable gastric neoplasms (EUT-GN) according to the criteria for endoscopic submucosal dissection. About 80% of EUT-GNs were undifferentiated cancers (40/51) and about 30% of them showed submucosal invasion (13/40). EUT-GN were less commonly located at the antrum compared with ET-GN (29.4% vs. 58.1%, p < 0.001) and their median size was 2.0 cm. In multivariable analysis, EUT-GN was highly related with age < 60 (OR, 2.091; 95% CI, 1.028-4.255, p = 0.042), *H. pylori* infection (OR, 2.814; 95% CI: 1.195-6.625, p 0.018), and absent or mild atrophic gastritis (OR, 2.673; 95% CI, 1.251-5.724, p = 0.011). Overall and disease-free survival were not significantly different between the two groups, however, EUT-GN showed a tendency of short disease-free survival.

Conclusion: Current screening interval of 2 years seems unsatisfactory to detect rapid-growing gastric neoplasms, such as undifferentiated cancers, early enough. Those neoplasms tended to develop in young adults with current *H. pylori* infection without severe atrophic gastritis. More intense screening is warranted for subgroup of young adults with *H. pylori* infection even if they do not have gastric atrophy.

Disclosure: Nothing to disclose

OP370 ENDOSCOPIC TREATMENT OF EARLY GASTRIC NEOPLASIA IN THE WEST : EXPERIENCE FROM THREE EUROPEAN TERTIARY CENTRES

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Introduction: Endoscopic submucosal dissection (ESD) is a technique first developed in Japan to enable en-bloc endoscopic resection of early gastric neoplasia. The high prevalence of gastric neoplasia allowed for greater opportunity to train and refine the technique in the Far East. The same is not applicable to the West where the prevalence of gastric neoplasia is low.

Aims & Methods: We aim to review the efficacy and safety of ESD for early gastric neoplasia from three large European referral centres. Data was prospectively collected on an electronic database. We analysed this database and patient's electronic record. Parameters related to ESD outcome were collected.

Results: A total of 175 gastric neoplasia were resected between 2009 and 2017 (152 ESD, 23 hybrid ESD), 51.4% were in proximal stomach. Mean size was 29mm. Only 13 (7.42%) were sub-epithelial lesions. Table (1) shows outcomes and procedure-related complications. The overall en-bloc resection, R0 (deep), and R0 (deep and lateral) rates were 92.5%, 83.4%, and 61% , respectively. Proximal location of the lesion was a predictor for R1 outcome (p value 0.011). Size of the lesion was not significantly related to the R0 rate. The overall adverse event rate was 11.3%. There was no 30-day procedure related mortality. Recurrence at 3 months occurred in 7 patients (4%).

Conclusion: This is the largest western gastric ESD series, demonstrating the feasibility and safety of this technique in an European setting. Despite the low R0 rate, our recurrence rate is low and comparable to Japanese data.Reasons behind good clinical outcome (very low recurrence) despite an average technical outcome (R0) remains uncertain.This raises a possibility that in the west, R-1 should not automatically be considered as an indication for surgery.

Disclosure: PB received research grants and honorarium from Pentax, Boston, Fuji, Olympus, and 3D Matrix.

OP371 SHORT- AND LONG-TERM OUTCOMES OF GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION FOR ABSOLUTE-INDICATION LESIONS AND EXPANDED-INDICATION LESIONS

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Introduction: Endoscopic submucosal dissection (ESD) is an effective treatment method for early gastric neoplasms, and its indication is being expanded. According to 2018 Japanese gastric cancer treatment guidelines, for differentiated-type gastric cancer (>2 cm without UL, ≤ 3cm with UL) treatment, expanded-indication of ESD became absolute-indication. Expanded-indication for undifferentiated-type gastric cancer (≤2 cm) is also expected to become an absolute-indication. These claims were based on evidence from high-volume centers, and it is important to check their applicability to actual clinical practice.

Aims & Methods: Our study aimed to evaluate and compare the clinical outcomes of ESD to early gastric cancers for absolute-indication lesions and that for expanded-indication lesions. The subjects were 490 patients who collectively presented with 574 early gastric cancers diagnosed with absolute-indication lesions or expanded-indication lesions. All patients underwent ESD at our hospital between June 2007 and August 2018. The

patients were segregated into two groups: absolute-indication lesions (group A: 294 patients with 331 collective lesions) and expanded-indication lesions (group B: 233 patients with 243 collective lesions). We evaluated the clinicopathological findings, and short- and long-term outcomes including the local and distant recurrence rates, and overall survival (OS) and disease-specific survival (DSS) rates.

Results: The patients' mean ages were 72.9 years (group A) and 71.4 years (group B), and the male-to-female ratios were 232/62 (group A) and 177/56 (group B). The mean tumor size in group B (22.9 mm) was significantly larger than that of group A (10.2 mm) (p < 0.01). Histopathological findings revealed that the rates of differentiated-type were 100 % (331/331) in group A and 88.9 % (216/243) in group B (p < 0.01). Regarding tumor depth, intramucosal carcinomas were 100 % (331/331) in group A and 81.9 % (199/243) in group B, and shallow submucosal invasive carcinomas (< 500 μm) were 0 % (0/331) in group A and 18.1 % (44/243) in group B (p < 0.01). The *en bloc* resection rates were 99.7 % (330/331) in group A and 95.9 % (233/243) in group B (p< 0.01), and the curative resection rates were 98.5 % (326/331) in group A and 93.8 % (228/243) in group B (p< 0.01). Regarding adverse events, postoperative hemorrhage rates were 2.42 % (8/331) in group A and 4.94 % (12/243) in group B, and perforation rates during the procedure were 0.30 % (1/331) in group A and 0.82 % (2/243) in group B. There were no significant differences in adverse events. Regarding long-term outcomes, the local and distant recurrence rates were 0.30 % (1/331) and 0 % (0/331) in group A and 0.41 % (1/243) and 0 % (0/243) in group B, respectively (n.s.). Regarding survival analysis, the mean follow-up periods in group A and group B were 55.1±35.6 and 47.0±35.4 months, respectively. The 3- and 5-year OS rates were 92.7 % and 90.1 % in group A, and 94.1 % and 88.7 % in group B (using the Kaplan-Meier method and long-rank test), respectively. The 5-year DSS rates were 100 % in both groups. No significantly difference was observed in the survival rates.

Conclusion: The short-term outcomes of expanded-indication lesions were inferior to those of absolute-indication lesions, despite both being acceptable. In addition, expanded-indication lesions had excellent long-term prognosis, equivalent to absolute-indication lesions. Therefore, expansion of the indication of gastric ESD to actual clinical practice is appropriate.

Disclosure: Nothing to disclose

OP372 DO THE SUPPRESSION OF PROLIFERATIVE CAPACITY OF GASTRIC CANCER CELLS DUE TO *HELICOBACTER PYLORI* ERADICATION AFFECT THE FINDINGS OF MICROSURFACE PATTERNS ON MAGNIFYING ENDOSCOPY WITH NARROW-BAND IMAGING?

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Introduction: In Japan, *Helicobacter pylori* (HP) eradication therapy is already spread, but gastric cancer is frequently detected, even after eradication (post-eradication gastric cancer). The detection of lesions or the diagnosis of the margin of the lesions is considered to be more difficult in post-eradication gastric cancer than in HP-uneradicated gastric cancer. Regarding the underlying reason, it has been reported that the Ki-67 index is low in post-eradication gastric cancer, indicating that the proliferative capacity of tumor cells is suppressed [1-3]. However, whether differences in cell proliferative capacities between post-eradication and uneradicated gastric cancer are associated with the microsurface pattern (MSP) has not been determined.

Aims & Methods: This study included 122 lesions of differentiated early gastric cancer (63 lesions of post-eradication gastric cancer and 59 lesions of uneradicated gastric cancer) treated with endoscopic submucosal dissection (ESD) at our hospital between January 2014 and December 2017. Under magnifying endoscopy with narrow-band imaging (M-NBI), all lesions were resected in an en bloc fashion by using ESD. The middle sections of the resected specimens were immunostained for Ki-67 (MIB-1). The Ki-67 index was then calculated and compared to determine whether it was different between post-eradication and uneradicated gastric cancer. In addition, according to the MSP using the vessel plus surface classification system, the lesions were divided into the following 4 groups: group A of post-eradication gastric cancer with a regular MSP, group B of post-eradication gastric cancer with an irregular MSP, group C of uneradicated gastric cancer with a regular MSP, and group D of uneradicated gastric cancer with an irregular MSP. In each group, the Ki-67 index was calculated and analyzed using the Tukey-Kramer test to determine whether the cell proliferative capacity was associated with M-NBI findings.The Ki-67 index was defined as a value calculated using the following formula: Ki-67-positive cell count / total epithelial cell count per magnification of 200 times. To match the result for the visible range of NBI, the index was calculated in an area that was located 200 μm from the superficial portion of the mucous membrane.

Results: The mean Ki-67 index score of all the lesions was 24.8% for post-eradication gastric cancer and 38.2% for uneradicated gastric cancer. The score was significantly lower for the former (P < 0.001), suggesting that eradication suppressed the proliferative capacity of tumor cells. According to the MSP findings, there were 20 lesions in group A (31.7%), 43 lesions in group B (68.3%), 5 lesions in group C (8.5%), and 54 lesions in group D (91.5%). The mean Ki-67 index scores were 19.6% in group A, 27.1% in group B, 31.6% in group C, and 38.8% in group D. The Ki-67 index scores in groups A and B were significantly lower than the score in group D (P < 0.001 and P < 0.01, respectively), whereas no significant difference in the scores was observed between groups A and B. No association was detected between decreased Ki-67 index scores due to eradication and MSP findings.

Conclusion: In post-eradication gastric cancer, the Ki-67 index was generally lower than in uneradicated gastric cancer, and the proliferative capacity of the tumor cells was suppressed. However, M-NBI did not show any association between different MSP findings and the cell proliferative capacity. The previously reported view appeared unlikely.

References: 1. Kodama M et al. Endoscopic and immunohistochemical characteristics of gastric cancer with versus without Helicobacter pylori eradication. Digestion. 2018;97:288-297. 2. Shichijo S et al. Characteristics and predictors of gastric cancer after Helicobacter pylori eradication. World J Gastroenterol. 2018;24(20):2163-2172. 3. Kitamura Y et al. Characteristic epithelium with low-grade atypia appears on the surface of gastric cancer after successful Helicobacter pylori eradication therapy. Helicobacter. 2014;19(4):289-295.

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Poster presentations
Monday, October 21, 2019
Tuesday, October 22, 2019
Wednesday, October 23, 2019

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UNITED EUROPEAN GASTROENTEROLOGY

Ⓢ**SAGE**

Poster Presentations
Monday, October 21, 2019

Liver and Biliary I
10:30-17:00 / Poster Exhibition - Hall 7

P0001 WITHDRAWN

P0002 INTERLEUKIN 10 INDUCED SENESCENCE OF HEPATIC STELLATE CELLS VIA STAT3-P53/P21 SIGNAL PATHWAY TO ATTENUATE LIVER FIBROSIS

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Introduction: Hepatic fibrosis is a wound healing process which results in deposition of excessive abnormal extracellular matrix (ECM) in response to chronic liver injury[1].Activated hepatic stellate cells (HSCs) are the major sources of ECM, therefore, phenotype reversion or retardation of proliferation or induction of senescence in activated HSCs is an appropriate therapeutic strategy for liver fibrosis[2].Cytokine plays an important role in senescence of activated HSCs. Our previous studies have shown that interleukin-10 (IL-10) attenuates the carbon tetrachloride (CCL_4) - and porcine serum-induced liver fibrosis in rats. However, little is known about the mechanism of IL-10 regulated anti-fibrosis and activated HSCs senescence.
Aims & Methods: To uncover the underlying pathway by which IL-10 mediates activated HSCs senescence to attenuates liver fibrosis.Rat liver fibrosis was induced by intraperitoneal injection of 40% CCL_4 dissolved in olive oil (2 mL/kg) twice a week. From the 4th week, rIL-10 plasmid DNA was transferred into fibrotic rats for 5 weeks by hydrodynamics-based transfection (HBT). Hematoxylin and eosin stain, Masson and Sirius Red stain were used to evaluate degree of fibrosis; α-smooth muscle actin and senescence-associated-β-galactosidase (SA-β-Gal) stain were used to detect senescence of activated HSCs in fibrotic liver. In vitro, primary rat HSCs isolated by collagenase perfusion and density gradient centrifugation were cultured for 7 d and then treated with or without IL-10 for 24h. Cell proliferation, cell cycle, SA-β-Gal activity and expression of senescent marker protein P53 and P21 were detected to analyze the senescence of activated HSCs. Pifithin-α (a specific inhibitor of P53) or Cryptotanshinone (a specific inhibitor of signal transducers and activators of transcription 3) was used to block expression of P53 or p-STAT3 signal transduction in primary HSCs or HSC-T6 cells presence/absence of IL-10, respectively. SA-β-Gal stain and Western Blot analysis was used to detect HSCs senescence and expression of signaling protein p-STAT3/ STAT3 and senescence marker protein P53 and P21.
Results: In vivo, IL-10 gene treatment by HBT attenuated inflammatory response, deposition of collagen and numbers of activated HSCs and enhanced the activity of SA-β-Gal in fibrotic liver and then promoted senescence of activated HSCs. In vitro, IL-10 treatment inhibited the cell proliferation, blocked the cell cycle, and increased the activity of SA-β-Gal and the expression of senescence marker protein P53 and P21. Blocking expression of P53 with Pifithin-α reduced the number of SA-β-Gal positive HSCs and protein expression of P53 and P21. IL-10 treatment also increased the expression of total STAT3 and p-STAT3 and promoted p-STAT3 translocation from cytoplasm to nucleus. Blocking p-STAT3 with cryptotanshinone reduced protein expression of p-STAT3, STAT3, P53 and P21 and the number of SA-β-Gal positive activated HSCs.
Conclusion: IL-10 gene treatment attenuates CCL_4-induced liver fibrosis by promoting the senescence of activated HSCs and underlying mechanism is that IL-10 could up-regulate the expression of senescence protein P53 and P21 in activated HSCs via STAT3 pathway.
References: [1] K.S. Nallagangula, S.K. Nagaraj, L. Venkataswamy, M. Chandrappa, Liver fibrosis: a compilation on the biomarkers status and their significance during disease progression, Future Science OA 4 (2018) O250. [2] D. Ezhilarasan, E. Sokal, M. Najimi, Hepatic fibrosis: It is time to go with hepatic stellate cell-specific therapeutic targets, HEPATOB PANCREAT DIS 17 (2018) 192-197.
Disclosure: Nothing to disclose

P0003 CD1D AS A DIRECT, NKT CELL-INDEPENDENT REGULATOR OF HEPATIC LIPID METABOLISM AND INFLAMMATION IN NONALCOHOLIC FATTY LIVER DISEASE

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Introduction: Natural Killer T (NKT) cells recognize lipid antigens in the context of the atypical MHC class I protein CD1d. Based on the study of mice deficient in CD1d, which lack both CD1d and NKT cells, recent work has suggested a critical role of NKT cells in the regulation of metabolic and inflammatory progression in nonalcoholic fatty liver disease (NAFLD). However, since CD1d can associate with a substantial proportion of cellular lipids and can compete with other substrates for lipid transfer proteins, we asked the question of whether CD1d may directly regulate hepatic lipid metabolism and inflammation in an NKT cell-independent manner.
Aims & Methods: To examine potential NKT cell-independent roles of CD1d in hepatic metabolism, CD1d-proficient and CD1d-deficient littermates were analyzed on a Rag1^{-/-} background, thus lacking mature T and B cells including NKT cells. Analyses were performed both on a high fat diet (HFD, 60% kcal from fat, for 16 weeks) and control diet. Hepatic, adipose tissue, and plasma lipids were analyzed by shotgun lipidomics. Hepatic cytokine levels (qPCR), lipid droplet distribution (oil red O staining), hepatocyte damage (alanine aminotransferase (ALT)), and glucose metabolism were evaluated.
Results: CD1d-deficiency on a *Rag1^{-/-}* background was associated with a selective decrease in hepatic levels of triglycerides on normal diet and triglycerides and cholesterol esters on HFD. Hepatic TNFα expression was increased in response to a HFD with significantly lower expression of TNFα in CD1d-deficient Rag1^{-/-} compared to CD1d-proficient Rag1^{-/-} mice. Accordingly, serum ALT activity was lower in CD1d-deficient compared to CD1d-proficient Rag1^{-/-} mice. Moreover, CD1d-deficient Rag1^{-/-} mice had reduced levels of fasting glucose in response to a HFD, compared with CD1d-proficient mice.
Conclusion: Our data demonstrate that CD1d can regulate hepatic lipid and carbohydrate metabolism in an NKT cell-independent manner and promote hepatic inflammation in response to a metabolic challenge. Liver export of TG and CE from hepatocytes is regulated by the microsomal triglyceride transfer protein (MTP) which loads neutral lipids onto apolipoprotein B (ApoB) to assemble very low density lipoproteins (VLDL). Since MTP is also responsible for lipid transfer onto CD1d, we hypothesize that CD1d-dependent regulation of hepatic lipid metabolism results from competition between CD1d and ApoB for lipid transfer activity of MTP. This hypothesis is currently being experimentally addressed.
Disclosure: Nothing to disclose

P0004 INFLAMMATORY BOWEL DISEASES DO NOT AFFECT ENHANCED LIVER FIBROSIS TEST RELIABILITY IN ASSESSING LIVER FIBROSIS

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Introduction: The Enhanced Liver Fibrosis (ELF) test was established in 2004 as a non-invasive serum test for liver fibrosis based on an algorithm that combins measurements of the concentration of three markers of fibrosis, hyaluronic acid (HA), tissue inhibitor of matrix metalloproteinases-1 (TIMP-1) and aminoterminal propeptide of type III procollagen (PIIINP). Since then, a series of studies has demonstrated the validity of ELF as a diagnostic and prognostic tool in a variety of chronic liver diseases (CLD), including primary sclerosing cholangitis (PSC). Nevertheless, in these studies, exacting protocols were followed that excluded patients with fibrogenic co-morbidities involving organs other than the liver to avoid any confounding of the relationship between ELF and liver fibrosis. Inflammatory bowel diseases (IBD) are known to cause fibrotic changes of the bowel wall and to be associated to liver diseases, especially PSC in patients affected by ulcerative colitis (UC).

Aims & Methods: In order to investigate whether IBD may confound ELF test results in the assessment of liver fibrosis in CLD patients, we prospectively collected data of IBD patients who did not have liver disease followed up at three IBD centres in North Italy since 2008. A cohort of healthy controls (HC) was enrolled over the same period. Demographic and clinical data were recorded and sera were storred for ELF testing. Serum samples were then processed in the same laboratory (iQur Limited), and the impact of IBD on ELF results was investigated by comparing the ELF scores of participants with different IBD phenotypes between IBD groups and healthy controls (HC). Data were analysed with the IBM SPSS software.

Results: Overall, 137 patients suffering from IBD, comprising 107 Crohn's disease (CD) and 31 by ulcerative colitis (UC), (mean age 36±15 years; M:F ratio 1.5:1) were consecutively enrolled (mean disease duration 84±89.9 months) as well as 27 healthy volunteers (mean age 32±11.3 years; M:F ratio 1:1) as a control group. The ELF results of IBD patients (mean 8.38 ng/ml, sd 1.03) were compared to those of HC (mean 8.13 ng/ml; sd 0.78) and no significant difference was found (p=0.15). Furthermore, each CD phenotype was compared to the whole recruited population, and no significant difference was found between these groups and the rest of the cohort (luminal p=0.16; stricturing p=0.09; penetrating p=0.97). No significant difference was highlighted in direct comparison between phenotypes. Likewise, UC patients' ELF results were compared to those of the rest of the recruited population and no significant difference emerged (p=0.31). No correlation was found between ELF score and either gender or age. Disease activity, measured at sampling in 70 CD (Crohn's disease activity index, CDAI) and 27 UC patients (Clinical Activity Index. CAI), showed no correlation with ELF score (r_s=0.07; p=0.52 in CD and r_s=0.005, p=0.98 in UC).

Conclusion: We found that the ELF score is not influenced by IBD, regardless of CD phenotype or IBD clinical activity, and thus, it can be used as a reliable tool to detect and follow up liver fibrosis in CLD patients.

References: 1. Rosenberg WM, Voelker M, Thiel R, Becka M, Burt A, Schuppan D, Hubscher S, Roskams T, Pinzani M, Arthur MJ; European Liver Fibrosis Group. Serum markers detect the presence of liver fibrosis: a cohort study. Gastroenterology. 2004 Dec;127(6):1704-13 2. Vesterhus M, Hov JR, Holm A, Schrumpf E, Nygård S, Godang K, et al. Enhanced Liver Fibrosis Score Predicts Transplant-Free Survival in Primary Sclerosing Cholangitis. Hepatology. 2015; 62:188-197. 3. de Vries EMG, Färkkilä M, Milkiewicz P, Hov JR, Eksteen B, Thorburn D, Chazouillères O, Pares A, Nygård S, Gilja OH, Wunsch E, Invernizzi P, Carbone M, Bernuzzi F, Boberg KM, Røsjø H, Rosenberg W, Beuers UH, Ponsioen CY, Karlsen TH, Vesterhus M. Enhanced

liver fibrosis test predicts transplant-free survival in primary sclerosing cholangitis, a multi-centre study. Liver Int. 2017 Oct;37(10):1554-1561 4. Bettenworth D, Rieder F. Pathogenesis of Intestinal Fibrosis in Inflammatory Bowel Disease and Perspectives for Therapeutic Implication. Dig Dis. 2017;35(1-2):25-31.
Disclosure: Nothing to disclose

P0005 RILPIVIRINE-INDUCED ANTI-INFLAMMATORY EFFECTS IN LIVER DISEASES INVOLVE THE ACTIVATION OF STAT6 SIGNALING PATHWAYS IN MACROPHAGES

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Introduction: Rilpivirine (RPV) is an antiretroviral drug widely used in anti-HIV therapy, which is generally considered safe for the liver and not associated with hepatotoxicity in these patients. Although there are few data on the effects of this drug on the liver in the presence of other chronic hepatic complications, our group has previously described that treatment with RPV induces a clear anti-steatotic, anti-inflammatory and anti-fibrotic effect in murine models of non-alcoholic fatty liver disease (NAFLD) and fibrosis induced by carbon tetrachloride (CCl_4).

Aims & Methods: To determine the molecular mechanisms by which RPV exerts its anti-inflammatory properties in chronic liver diseases, focusing on its actions on hepatic macrophages.
In vivo, the effects of RPV on the progression of NAFLD in a nutritional model in C57BL/6 mice (12 weeks) and in a model of CCl_4-induced fibrosis (4 weeks) were analyzed. *In vitro*, monocyte-derived macrophages (MDMs) were obtained from human peripheral blood mononuclear cells isolated from healthy donors. MDMs were treated with clinically relevant concentrations of RPV (1-8 μM) for 48 h. The molecular routes involved were studied using RT-PCR, Western Blot and determinations of enzymatic activity.

Results: The data obtained in both animal models revealed the anti-inflammatory potential of RPV, reducing the gene expression of pro-inflammatory markers (TNFα, IL1β, Caspase 1 and NLRP3), as well as the activity of the MPO enzyme and the macrophage infiltration into the liver. In addition, RPV significantly decreased the activation of the NF-κB and NLRP3 inflammasome pathways, and induced the expression of LXRα. RPV also increased the hepatic expression of *Stat6, Pparg* and *Arg1* in our mouse models. Interestingly, STAT6/PPARG/ARG1 pathway activation by RPV was confirmed in MDMs, showing a positive correlation *in vitro*.

Conclusion: Beyond its well-described role in antiretroviral therapy, RPV has a clear anti-inflammatory effect in different models of chronic liver diseases, associated with its actions on liver macrophages and the activation of STAT6-mediated pathways. Our results may be clinically relevant in the management of chronic liver diseases such as NAFLD, although more studies are needed to clarify the mechanisms involved.

Disclosure: Nothing to disclose

P0006 FIBROGENESIS OF NONALCOHOLIC STEATOHEPATITIS BEGINS AROUND CHOLESTEROL-LADEN MACROPHAGE IN THE EXPERIMENTAL MOUSE MODEL

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Introduction: The pathogenesis of fibrosis in nonalcoholic steatohepatitis (NASH) may be different from that in viral hepatitis since they show different histopathological findings of fibrosis.The major feature of NASH-related fibrosis is elongation of fine fiber around living cells rather than remarkable necrosis. The mechanisms involved in progression to fibrosis remain largely unknown, thus therapies to prevent or delay the disease progression remain limited.

Aims & Methods: We examined the pathogenesis of fibrosis using mice fed with our new diet which could induce fibrotic NASH. Nine-week-old male A/J mice were fed with the high-fat/cholesterol/cholate (HFCC) diet or standard chow for nine weeks.

Results: Histological steatohepatitis including steatosis, lobular inflammation and fibrosis (stage 1 or 2) were seen in A/J mice fed the HFCC diet. Some of the blue-stained fibers by azan stain were surrounding bright and multinuclear giant cells. These cells were positively stained by mac-2, suggesting that they were macrophages. A polarized light microscope identified cholesterol crystals characterized by a Maltese cross inside their macrophages. Platelet-derived growth factor (PDGF) is secreted by activated macrophages and activates stellate cells to become myofibroblast that produces collagen fibers. We observed PDGF-receptorβ-positive cell, that is myofibroblast, surrounded the giant cells. Histological severity including fibrosis and the number of giant cells dose-dependently worsened with increasing cholesterol intake.

Conclusion: Cholesterol-phagocytic macrophage could be a key player of development of fibrosis in NASH. Our model could capture the onset of NASH fibrosis and could be suitable for evaluation of drug efficacy targeting macrophages.

Disclosure: Nothing to disclose

P0007 LIVER FIBROSIS WITH TWO-DIMENSIONAL SHEAR WAVE ELASTOGRAPHY IN PATIENTS WITH PRIMARY BILIARY CHOLANGITIS

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Introduction: Primary biliary cholangitis (PBC) is a slowly progressive cholestatic disease. The accurate evaluation the degree of liver fibrosis is important for determining medical management and prognosis of PBC patients. Although liver biopsy remains the reference standard to assess liver fibrosis, it is limited by its invasiveness and potential complications [1]. Recently, Two-dimensional shear wave elastography (2D-SWE), a noninvasive method for measuring liver stiffness has been developed with several advantages. First, it can be used to measure liver stiffness values on the basis of anatomic information to avoid nontarget structure and elastic artifacts and to improve measurement reliability. Second, it can be used in patients with ascites. This method has good diagnostic accuracy for the staging of liver fibrosis in patients with chronic liver disease [2-4]. However, studies focused on patients with PBC are relatively rare and all of them include not only PBC, but also other autoimmune etiology related chronic liver disease [5].

Therefore, this retrospective study is to investigate the diagnostic accuracy of 2D-SWE for the noninvasive staging of liver fibrosis in patients with PBC by using histologic analysis as a reference standard.

Aims & Methods: To investigate the diagnostic accuracy of 2D-SWE for the noninvasive staging of liver fibrosis in patients with PBC by using histologic analysis as a reference standard. Patients with PBC who underwent liver biopsy and 2D-SWE were consecutively enrolled. Spearman's correlation was applied to evaluate the correlation between Liver stiffness (LS) of 2D-SWE and liver fibrosis stage by liver biopsy Receiver operating characteristic (ROC) curves were constructed to assess the overall accuracy and to identify optimal cut-off values.

Results: The characteristics of the diagnostic performance were determined for 120 patients with PBC. Spearman's correlation between LS of 2D-SWE and liver fibrosis stage was 0.686,p< 0.001. The areas under the ROC curves of significant fibrosis (≥ S2), severe fibrosis (≥ S3), and cirrhosis (S4) were 0.799, 0.902, and 0.942, respectively. and the optimal cut-off values associated with significant fibrosis, severe fibrosis, and cirrhosis were 8.45kPa, 10.9kPa and 14.05 kPa, respectively. 2D-SWE showed sensitivity of 72.4% and specificity of 73% for significant fibrosis, sensitivity of 86.8% and specificity of 84.1% for severe fibrosis, sensitivity of 86.7% and specificity of 86.7% for cirrhosis.

Conclusion: 2D-SWE shows promising diagnostic performance for assessing liver fibrosis stages in patients with PBC, especially for severe fibrosis, and cirrhosis.

References: 1. Rockey, D.C., et al., Liver biopsy. Hepatology, 2009. 49(3): p. 1017-44. 2. Gao, Y., et al., Liver Fibrosis with Two-dimensional US Shear-Wave Elastography in Participants with Chronic Hepatitis B: A Prospective Multicenter Study. Radiology, 2018. 289(2): p. 407-415. 3. Herrmann, E., et al., Assessment of biopsy-proven liver fibrosis by two-dimensional shear wave elastography: An individual patient data-based meta-analysis. Hepatology, 2018. 67(1): p. 260-272. 4. Zhuang, Y., et al., Two-dimensional Shear-Wave Elastography Performance in the Noninvasive Evaluation of Liver Fibrosis in Patients with Chronic Hepatitis B: Comparison with Serum Fibrosis Indexes. Radiology, 2017. 283(3): p. 873-882. 5. Zeng, J., et al., Non-invasive assessment of liver fibrosis using two-dimensional shear wave elastography in patients with autoimmune liver diseases. World J Gastroenterol, 2017. 23(26): p. 4839-4846.
Disclosure: Nothing to disclose

P0008 CIRCULATING BLOOD MICROBIOME SIGNATURES IN PATIENTS WITH LIVER CIRRHOSIS AND PORTAL HYPERTENSION

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Introduction: Studies from recent years have shown that intestinal microbiome is linked to the development of liver cirrhosis and disease related complications. Portal hypertension (PH) is a complication of advanced liver disease that causes blood retention in the portal vein system. PH leads to increased intestinal permeability ("leaky gut"), translocation of bacteria and their metabolites into the blood. In the last two years, studies have shown changes in circulating microbiome in patients with liver disease, however, circulating microbiome in patients with PH has not been assessed yet.

Aims & Methods:

Aim of the study: To detect changes in circulating blood microbiome in patients with portal hypertension.

Tasks of the study:

1. To determine composition of circulating blood microbiome in patients with portal hypertension.

2. To asses differences of circulating blood microbiome between patients and healthy control subjects.

3. To asses changes in circulating blood microbiome in relation to the degree of portal hypertension.

Methods: Study cohort included 58 patients with liver cirrhosis and 46 healthy control (HC) subjects. Collection of biological material (blood plasma samples from hepatic and peripheral venous blood from liver cirrhosis patients and peripheral venous blood from HC subjects) also measurements of hepatic venous pressure gradient (for liver cirrhosis patients) was performed at Department of Gastroenterology of Lithuanian University of Health Sciences, Kaunas Clinics. Bacterial DNA from blood plasma samples was obtained using QIAamp Circulating Nucleic Acid (Qiagen) isolation kit. 16S rRNA gene sequencing of V1-V2 variable regions was used to determine bacterial composition. Raw sequencing data was processed into the table of amplicon sequencing variants through DADA2 workflow. Data analysis was performed using publicly available R statistic packages.

Results: Taxonomic composition analysis at the phylum level revealed that blood microbiome was predominated by *Proteobacteria (66.3%, 58.3%, 53.91%), Bacteroidetes(10.8%, 13.2%, 12.5%), Actinobacteria(12%, 10.8%, 11.5%)* and *Firmicutes (10.9%, 17.6%, 22%)* in samples from peripheral blood of HC subjects, peripheral blood of PH patients and blood from hepatic vein of PH patients respectively. α-diversity was not significantly different between HC and PH patients, nor between different compartments in PH patients (Shannon index - 4.02, 4.22, 4.15, p >0.05). Bacterial community structure did not show significant clustering between neither HC and PH patients nor between different compartments in PH patients. Differential abundance analysis revealed differently abundant genera between HC and PH patients with an increase in abundance of *Tepidimonas, Enterobacter, Prevotella, Parabacteroides* in PH patients. Subgroup analysis of PH patients with different degree of PH revealed no significant differences in composition at phylum level, α-diversity or β-diversity, however *Parasutterella* genus was found to be differentialy abundant with increasing levels in patients with higher degree of PH.

Conclusion: Circulating blood microbiota comprises of four main phyla - *Proteobacteria, Bacteroidetes, Actinobacteria* and *Firmicutes.* Genera of *Tepidimonas, Enterobacter, Prevotella, Parabacteroides was* found to be in-

creased in patients with portal hypertension compared to healthy controls. *Parasutterella* genus was associated with higher degree of portal hypertension.
Disclosure: Nothing to disclose

P0009 PATIENT ATTITUDES TOWARDS FAECAL SAMPLING FOR GUT MICROBIOME STUDIES AND CLINICAL CARE REVEAL POSITIVE ENGAGEMENT AND ROOM FOR IMPROVEMENT

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Introduction: Faecal sample collection is crucial for gut microbiome research and its clinical applications. However, while patients and healthy volunteers are routinely asked to provide stool samples, their attitudes towards sampling remain largely unknown. Here we investigate the attitudes of 780 Dutch patients, including participants in a large Inflammatory Bowel Disease (IBD) cohort, and population controls, to identify barriers to sample collection and provide recommendations for gut microbiome researchers and clinicians.
Aims & Methods: We sent questionnaires designed in cooperation with the psychologist of our IBD centre including questions about living situation, experiences with faecal sample collection, information about the type of toilet and perceptions of storing faecal samples in their freezer to 660 IBD patients and 112 non-gastroenterology patients who had previously been approached to participate in gut microbiome studies.
The questionnaire recipients in the IBD cohort comprised both patients previously willing to collect a stool sample for research (n=577, IBD-Willing) and patients previously not willing to do so (n=83, IBD-Unwilling).
We also conducted 478 brief interviews with participants in our general population cohort who had collected stool samples. Statistical analysis of the data comprising Fisher's exact tests and Chi-square tests was performed using R.
Results: 97.4% of respondents reported that they had willingly participated in stool sample collection for gut microbiome research, and most respondents (82.9%) and interviewees (95.6%) indicated willingness to participate again, with motivations for participating being mainly altruistic (57.0%). Most patients thought the collection process was easy (84.9%). Only 26.2% of the patients who responded felt the collection of faecal samples was dirty and most of the population controls interviewed perceived faecal sample collection as 'not inconvenient at all' (49.8%) or 'not inconvenient' (28.7%).
A minority of respondents (19.1%) did not understand why the faecal sample needed to be frozen according to our protocol. This is an important observation because the clarity of the written instructions was associated with future willingness to collect stool samples (P=0.046), and knowing the purpose of freezing stool (stopping bacterial growth) was associated with future willingness to freeze the stool samples (P=0.003). Responses indicated that storing stool samples in a home freezer for a prolonged time was the main barrier to participation (52.6%), but clear explanations of the sampling procedures and their purpose increased willingness to collect and freeze samples (P=0.046, P=0.003).
Conclusion: In conclusion, patients and healthy controls experience some barriers to participate in stool sample collection project. To account for participant concerns, we wrote the following four recommendations:
(1) Gut microbiome researchers and clinicians should explain why their collection protocol was designed in a specific way.
(2) In studies where a time-series of many stool samples needs to be collected and frozen, researchers should consider providing participants with a small freezer.
(3) Researchers and clinicians should inform participating patients and healthy volunteers about the outcome of the research.
Disclosure: Nothing to disclose

P0010 INFECTIONS IN CIRRHOSIS: A CHANGING EPIDEMIOLOGIC SETTING

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Introduction: : Bacterial and fungal infections represent a leading cause of decompensation and death in hospitalized patients with cirrhosis. Even if a great proportion of infections in cirrhosis are culture-negative, the analysis of microbiological findings is of utmost importance to assess local epidemiology, prevalence of multidrug resistant (MDR) strains and therefore address early empirical therapy.
Aims & Methods: To retrospectively analyze epidemiology of culture-positive infections (CP-I) in a cohort of hospitalized patients with cirrhosis.
All patients with cirrhosis consecutively admitted at Multivisceral Transplant Unit, Padua University Hospital, over 2 years period, were enrolled. Amongst patients with infection we analyzed CP-I in relation to epidemiology of fungal and bacterial strains and clinical outcome. Bacterial or fungal colonizations were not included.
Results: One-hundred ninety-two patients during 433 hospitalizations were analyzed in the study period. 156 CP-I (fungal/bacterial 15/139) occurred in 77 (40.1%) patients (M/F 51/26, median [IQR] age 55.3 [13] years, 48% alcohol-related disease, 22% viral-related; 36.3% waitlisted for liver transplantation; Child-Pugh and MELD score 11 [3] and 24 [12], respectively. 82% CP-I were hospital-acquired, being the urinary tract (38,9%) and blood (23,4%) the most common sources.
Amongst bacterial CP-I, gram positive (G+) strains occurred more frequently than gram negative (G-) ones (56.2% vs 43.8%).
Enterococcus faecium, E. Coli and Enterococcus faecalis accounted for 26.7%, 16.5% and 13.6% of all bacterial CP-I. Prevalence of MDR CP-I was 35.5% (32,5% amongst G+ and 37,5% amongst G-).
Considering fungal infections, they were mostly from the urinary tract and caused by Candida *spp*.
17 out of 77 patients experienced an episode of sepsis-related multiorgan failure requiring ICU admission. In-hospital transplant free survival was 55.8%.
Conclusion: Identification of infective agent in about half of hospitalized patients with decompensated cirrhosis. The increasing prevalence of gram positive and MDR bacterial strains, should be taken into account for antibiotic stewardship and early empiric therapy.
Disclosure: Nothing to disclose

P0011 CHARACTERIZATION OF BIOPSY PROVEN NON-ALCOHOLIC FATTY LIVER DISEASE IN HEALTHY NON-OBESE AND LEAN INDIVIDUALS

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is frequently seen among non-obese overweight individuals and more interestingly among lean subjects (those with normal body mass index). This study aimed to investigate prevalence and risk factors of NAFLD based on liver biopsy in a cluster of healthy non-obese and lean individuals.

Aims & Methods: In a cross-sectional study, adult (>18 years) healthy individuals who were first degree relatives of patients who had undergone liver transplantation between July 2012 and October 2018 were included. Liver biopsy was performed, as a routine pre-transplant work-up, for all the study participants to evaluate liver histology before living donor. Non-obese individuals were those with body mass index (BMI) < 30 Kg/m2. Lean individuals were defined as participants with BMI < 25 Kg/m2.

Results: Totally 310 patients were included. Seventy six individuals (24.5 %) had NAFL and 30 patients (9.67 %) had non-alcoholic steatohepatitis (NASH) among non-obese population. In univariate analysis, higher BMI, serum cholesterol, LDL, ALT, alkaline phosphatase and uric acid were associated with NAFLD in non-obese individuals (P< 0.05). In regression analysis, higher BMI and LDL were independently associated with NAFLD in non-obese individuals (P< 0.05). In multivariate regression analysis, only higher BMI was marginally associated with NASH in non-obese compared to those without NASH (Odds ratio: 2.52, 95 % CI: 0.097-6.54; P=0.05).

Totally, 246 individuals were lean. 55 individuals (22.3 %) had NAFL and 20 individuals (8.2 %) had NASH in their liver biopsies. In univariate analysis, serum triglyceride, cholesterol, LDL, ALT, alkaline phosphatase and uric acid were associated with NAFL among lean individuals (P< 0.05). In regression analysis, serum uric acid was associated with NAFL (Odds ratio: 1.70, 95 % CI: 1.18- 2.45; P=0.004) and NASH in lean individuals (Odds ratio: 1.98, 95 % CI: 1.27- 3.10; P=0.003).

Conclusion: NAFLD/NASH is prevalent even in a healthy lean population when evaluated by liver biopsy. Higher BMI and serum uric acid were two major risks of NAFLD/ NASH in non-obese and lean individuals.

Univariate				Multivariate analysis		
	With NASH	Without NASH	P-value	OR	95 % CI	P-value
Age (year)	31.88 ± 6.64	32.64 ± 7.19	0.668			
Sex (m/f)	10/10	95/131	0.636			
BMI (kg/m2)	22.47 ± 2.1	21.76 ± 2.15	0.747			
FBS	90.84 ± 9.77	88.93 ± 10.56	0.450			
TG	152.15 ± 79.00	99.81 ± 57.25	<0.001	1.004	0.99-1.01	0.334
Cholesterol	181.95 ± 35.82	168.62 ± 37.20	0.127			
HDL	44.76 ± 9.42	46.67 ± 11.50	0.508			
LDL	105.58 ± 36.10	97.89 ± 30.51	0.329			
AST	23.80 ± 12.50	20.01 ± 7.18	0.037	1.020	0.96-1.08	0.518
ALT	27.55 ± 13.43	19.37 ± 11.54	0.003	1.005	0.96-1.04	0.834
ALK.Phos	205.35 ± 76.25	194.43 ± 66.08	0.486			
Uric acid	4.93 ± 1.40	3.50 ± 1.14	<0.001	1.98	1.27- 3.10	0.003

[Characteristics of lean patients with and without NASH]

References: 1. Fracanzani AL, Petta S, Lombardi R, Pisano G, Russello M, Consonni D, Di Marco V, Cammà C, Mensi L, Dongiovanni P, Valenti L, Craxì A, Fargion S. Liver and Cardiovascular Damage in Patients With Lean Nonalcoholic Fatty Liver Disease, and Association With Visceral Obesity. Clin Gastroenterol Hepatol 2017; 15(10):1604-1611.e1. 2. Golabi P, Paik J, Fukui N, Locklear CT, de Avilla L, Younossi ZM. Patients With Lean Nonalcoholic Fatty Liver Disease Are Metabolically Abnormal and Have a Higher Risk for Mortality. Clin Diabetes 2019; 37(1):65-72.

Disclosure: Nothing to disclose

P0012 DISTRIBUTION OF GLYTATHIONE-S-TRANSFERASE T1 AND GLYTATHIONE-S-TRANSFERASE M1 NULL GENOTYPES IN NONALCOHOLIC FATTY LIVER DISEASE PATIENTS AND THEIR ASSOCIATION WITH CYTOKINE AND ADIPOKINE PROFILES

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Introduction: Nonalcoholic fatty liver disease (NAFLD) is the most common hepatic disease worldwide. Possible role of genetic factors, involved in the NAFLD development and course is discussed. The aim of the study was to investigate distribution of glutathione-S-transferase T1 (GSTT1) and GSTM1 null genotypes in NAFLD patients and their association with cytokine and adipokine profiles.

Aims & Methods: The deletion polymorphism of GSTT1 and GSTM1 genes was studied in 104 NAFLD patients and 45 healthy individuals (control group). Biochemical parameters, tumor necrosis factor-α (TNF-α), interleukin 10 (Il-10), transforming growth factor-β_1, leptin, adiponectin blood levels were investigated.

Results: Among the NAFLD patients deletion of the GSTT1 gene was established in 18 individuals (17.3%), normal genotype in 86 patients (82.7%). In the group of healthy individuals, the deletion of the GSTT1 gene was observed in 6 cases (13.3%), normal genotype in 39 (86.7%), which was not significantly different from the distribution of the genotypes among NAFLD patients.

The deletion of GSTM1 gene among NAFLD patients was diagnosed in 52 cases (50.0%), normal genotype was observed in 52 patients (50.0%). In the control group, the deletion of the GSTM1 gene was detected in 23 individuals (51.1%), normal genotype - in 22 (48.9%), which also was not significantly different from the distribution of genotypes in NAFLD patients.

Higher direct bilirubin level in the blood by 18.5% (p = 0.049) was found in NAFLD patients with null genotype of the GSTT1 gene, as compared to patients with normal genotype. The analysis of probable dependence of pro- and anti-inflammatory cytokines and adypokine content on the deletion polymorphism of the GSTT1 gene in NAFLD patients showed a two-fold (p = 0.01) higher TNF-α level in the blood of patients with null genotype as compared to patients with normal genotype of the GSTT1 gene. Higher concentration of leptin in the blood at 37.1% (p = 0.04) was observed in patients with null-genotype of GSTM1 gene in comparison with patients with normal genotype.

Conclusion: Distribution of GSTT1 and GSTM1 null genotypes in NAFLD patients did not differ significantly from healthy individuals. However NAFLD patients null genotype carriers were characterized by more aggravated changes of proinflammatory TNF-α and those with deletion of GSTM1 gene by higher leptin plasma levels as compared to patients with normal genotypes of proper genes.

Disclosure: Nothing to disclose

P0013 THE MECHANISM OF NEGATIVE REGULATION OF FABP1 BY NF-KB/IL-6 ON INVASION AND METASTASIS OF HEPATOCELLULAR CARCINOMA

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Introduction: Breaking the homeostasis of lipid metabolism is a key risk factor for invasion and metastasis of hepatocellular carcinoma (HCC). The synthesis, transport and catabolism of free fatty acids (FFA) are regulated by fatty acid-binding proteins (FABPs). The biological role of FABPs in regulating free fatty acid (FFA) synthesis and metabolism in tumorigenesis and development is one of the hotspots in the basic and clinical research of tumor microenvironment.

It has been found that the expression of FABPs can be regulated by the signal pathway of NF-kappa B/IL-6. The specific mechanism of action is not clear.

Aims & Methods: Immunohistochemistry was used to detect the expression of liver fatty acid-binding proteins (L-FABP, FABP1) and P65 on HCC tissue microarray. Lentivirus with high or low expression of FABP1 was used to infect Huh7 cell line in vitro. The effects of different FABP1 expression on lipid synthesis, invasion and metastasis of cancer cells were further studied, meanwhile, apoptosis was detected by flow cytometry. Affymetrix Gene Chip microRNAs Arrays gene chip were used to analyze the expression profile of miRNAs in the Huh7 and HepG2 cells induced by IL-6, and RT-PCR was used to verify the results of microarray. Bioinformatics analysis was used to predict target genes of miRNAs, western-blot and fluorescent reporter assay were used to study the target genes. Finally, the role of miR-603 in the proliferation and invasion of HCC cells were studied by Edu Assay kit and transwell methods.

Results: The expression of FABP1 in cancer tissues was significantly lower than that in adjacent tissues in nearly 90% HCC patients, and the expression level of FABP1 in adjacent tissues was correlated with the survival time of HCC patients (P < 0.01). The FABP1 could be absorbed by Huh-7 cells and the intracellular lipid synthesis was enhanced in the Huh7 cells with FABP1 over expression, but the down regulation of FABP1 can decreased the lipid synthesis. Flow cytometry study showed that the over expression of FABP1 can improve the apoptosis of HCC cells. The microarray results showed that the expression profile of miRNAs was significantly changed in the Huh7 and HepG2 cells induced by IL-6. RT-PCR results showed that the miR-603 was up-regulated in HCC tissues when compared with adjacent tumor tissues. Bioinformatic method revealed that there were 7 binding sites in the region 1424-1431 of miRNA-603 to FABP1 3'UTR. In vitro cell studies, it was showed that high expression of miR-603 could inhibit the expression of FABP1 protein. Furthermore, it was showed that high expression of miR-603 could promote the proliferation and migration of HCC cells.

Conclusion: NF-KB/IL-6 can negatively regulate FABP1 expression through miR-603. High expression of FABP1 can promote lipid synthesis in HCC cells and enhance the lipotoxicity, then inhibit invasion and metastasis of cancer cells.

Disclosure: The authors declare that they have no competing interests.

P0014 SERPINA1 AND HSD17B13 GENE VARIANTS IN LIVER FIBROSIS AND CIRRHOSIS

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Introduction: Previous studies identified single nucleotide polymorphisms (SNPs) of the SERPINA1 gene as risk factors for developing liver cirrhosis of different aetiology and HSD17B13 gene variant association with reduced chronic liver disease risk.

Aims & Methods: In this study, we tried to evaluate SERPINA1 rs28929474 and rs17580 SNPs association with the risk of hepatic fibrosis or liver cirrhosis and HSD17B13 rs10433937 SNP protective trait against chronic liver injury. The study was conducted at the Department of Gastroenterology in Lithuanian University of Health Sciences Hospital and included 302 patients with liver cirrhosis, 127 patients with liver fibrosis, and 548 controls. SNPs were genotyped by quantitative PCR, using TaqMan allelic discrimination assays. Adjusted p value of < 0.016 was considered significant.

Results: Genotype distributions of SERPINA1 and HSD17B13 SNPs were in Hardy-Weinberg equilibrium. SERPINA1 rs28929474 was not associated with liver fibrosis or cirrhosis. HSD17B13 rs10433937 also showed no significance to liver injury, but genotype GG showed tendency to be protective against liver fibrosis (aOR 0.37, p=0.03). SERPINA1 rs17580 was associated with higher risk of developing hepatic fibrosis (aOR 3.42, p=0.001) and showed tendency towards development of liver cirrhosis (aOR 2.59, p=0.02).

Moreover, SERPINA1 rs17580 genotype AT was also associated with increased liver fibrosis risk (aOR 3.28, p=0.008) and showed tendency to increased liver cirrhosis risk (aOR 2.55, p=0.02).

Conclusion: We found that SERPINA1 rs17580 confers an increased risk of developing liver fibrosis, while SERPINA1 rs28929474 and HSD17B13 rs10433937 are not associated with liver injury.

Disclosure: Nothing to disclose

P0015 C282Y/H63D COMPOUND HETEROZYGOSITY CAUSES SIGNIFICANTLY ELEVATED IRON OVERLOAD AND ASSOCIATED DISEASES

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Introduction: Hereditary Hemochromatosis (HH) occurs due to mutations in the HFE gene. Homozygosity for the C282Y mutation is the most common genotype found in HH patients. Other genotypes are found less frequently in HH patients, indicating variable degrees of penetrance. We studied the penetrance of patients with the C282Y/H63D genotype in developing clinically significant iron overload and iron overload-related disease.

Aims & Methods: We have completed a retrospective analysis on every individual within Newfoundland & Labrador (NL) who were diagnosed as C282Y/H63D compound heterozygote between 1996 and 2009 through molecular genetics study. Data collection was completed in St. John's, NL using electronic health records on multiple clinically relevant parameters - ferritin, transferrin saturation, aspartate aminotransferase (AST) levels, alanine aminotransferase (ALT) levels and liver biopsy results. As available, data were collected for up to 10 years following the initial molecular genetics study to assess the development of iron overload and associated clinical sequelae. Iron overload categories were classified based on previously published definitions from the HealthIron Study (Allen et al., 2008). Evidence of ironoverload-related disease was the most severe category and required both documented iron overload with concurrent development of hepatocellular carcinoma, cirrhosis or fibrosis on liver biopsy, tenderness/effusion of the second and third metacarpophalangeal joints, elevated AST (>45 IU/L) or ALT (>40 IU/L) levels, or by diagnosis of symptoms associated with HH by a physician. Documented iron overload was determined by serum ferritin >1000 µg/L, or hepatic iron staining 3 or 4. Provisional iron overload was determined by elevated serum ferritin and transferrin saturation: >300 µg/L and >55% for men and postmenopausal women, >200 µg/L and >45% for premenopausal women, respectively. Patients who did not meet the criteria for either documented or provisional iron overload were considered to have no evidence of clinically significant iron overload.

Results: Between 1996 and 2009, 275 individuals in NL tested positive for C282Y/H63D compound heterozygosity. However, only 247 individuals had electronic health records available for review. At baseline, 4% of all patients exhibited iron overload-related disease on the background of documented iron overload. Including these individuals, 8.1% of all patients met the criteria for documented iron overload, while an additional 16.2% met the criteria for provisional iron overload. The remaining 75.7% of all patients at baseline did not show any evidence of iron overload. When the data from the next 10 years were analyzed, the proportion of patients with iron overload-related disease on the background of documented iron overload increased to 5.3%. Including these individuals, the total number of patients with documented iron overload increased to 10.1%, while the proportion of patients with provisional iron overload increased to 23.1%. As a result, the number of patients with no evidence of iron overload decreased to 66.8% at the end of our study period. Looking specifically at the development of iron overload-related disease, one patient with documented iron overload and two patients with provisional iron overload at baseline progressed to iron overload-related disease throughout our study.

Conclusion: C282Y/H63D compound heterozygosity is associated with increased iron overload and this results in iron overload-related disease in a significant proportion of patients.

References: Allen KJ, Gurrin LC, Constantine CC, et al. Iron overload-related disease in HFE hereditary hemochromatosis. N Engl J Med 2008; 358:221-30.

Disclosure: Nothing to disclose

P0016 PREVALENCE OF SMALL INTESTINAL BACTERIAL OVERGROWTH SYNDROME IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE/NON-ALCOHOLIC STEATOHEPATITIS: A CROSS-SECTIONAL STUDY

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is a multifactorial wide-spectrum disorder. Small intestinal bacterial overgrowth (SIBO) is characterized by the increase in the number and/or type of colonic bacteria in the upper gastrointestinal tract. SIBO through energy salvage and inflammation induction could be considered one pathophysiological factor for NAFLD development and progression.
Aims & Methods: Consecutive patients with histological, biochemical or radiological diagnosis of any stage of NAFLD (NAFLD, NASH, cirrhosis) underwent upper gastrointestinal endoscopy. Duodenal juice (2cc) was aspirated from the 3rd-4^{th}part of duodenum in sterile traps. SIBO was defined as $\geq 10^3$aerobes CFU/ml of duodenal aspirate and/or presence of colonic type bacteria. Patients without any liver disease undergoing gastroscopy due to GERD comprised the healthy control (HC) group. Concentrations (pg/ml) of tumor necrosis factor-alpha (TNFα), interleukin (IL)-1βand IL-6 were also measured in the duodenal fluid. The primary endpoint was to compare SIBO prevalence among patients with different disease stages and healthy controls.
Results: We enrolled 125 patients (51 NAFLD, 27 NASH, 17 cirrhotics and 30 HC) aged 54±11.9yrs and weight 88.3±19.6kg (NAFLD vs. HC 90.7±19.1 vs. 80.8±19.6kg, p=0.02). Overall, SIBO was diagnosed in 23/125 (18.4%) patients, with Gram (-) bacteria being the predominant species (14/23; 60.8%, Table). SIBO prevalence was higher among NAFLD/NASH or cirrhosis subjects compared to HC (14/78; 17.9% vs. 1/30; 3.3%, p=0.04 and 8/17; 47.1% vs. 1/30; 3.3%, p< 0.001, respectively). Patients with NASH had higher SIBO prevalence (6/21; 22.2%) compared to NAFLD individuals (8/51; 15.7%), but this difference did not reach statistical significance. Among patients with liver disease, cirrhotics had a higher SIBO prevalence compared to NAFLD/NASH individuals (47.1% vs. 17.9%, p=0.02). Mean concentration of TNF-a, IL-1b and IL-6 did not differ among the different groups.
Conclusion: The prevalence of SIBO is significantly higher in patients with NAFLD compared to healthy controls, and SIBO is more prevalent in cirrhotics compared to uncomplicated NAFLD or NASH individuals.
Disclosure: Nothing to disclose

P0017 NONALCOHOLIC STEATOHEPATITIS: AN INFREQUENT ENTITY IN THE WESTERN WORLD?

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Introduction: The incidence of nonalcoholic Steatohepatitis (NASH) is rising, along with the increase of associated risk factors, specially overweight, in the Western world. The diagnosis requires an exhaustive study of liver disease, whereby its frequency based on population studies is difficult to determine. The relative prevalence among all causes of liver disease may be elucidative.
Aims & Methods: The aim of this study is to evaluate the burden of NASH in a hepatology consultation and to characterize this population of patients. It was performed a retrospective observational study of consecutive patients observed in a Hepatology consultation, by three different doctors, in a central hospital of Lisbon in the year of 2017.
Patients with nonalcoholic fatty liver disease (NAFLD) and NASH were studied. NASH diagnosis was established based on the existence of hepatic steatosis and ALT elevation and after exclusion of other etiologic factors for liver disease (including an alcohol consumption <20 and 30 g/day for women and men, respectively). Cirrhosis was determined based on histologic findings, unequivocal imaging or hepatic elastography (FibroScan)>14kPa.
Results: Among the 1268 patients analyzed, 69 (5.4%) had NAFLD, of whom 56 (4.4%) had NASH [age 56.7 ± 14.4; 27 (48.2%) female].
Twenty-five (44.6%) patients had type 2 diabetes mellitus; 32 (57.1%) hypertension; 40 (71.4%) dyslipidemia. All patients were overweight (BMI 31.1 ± 5.8, min.25.1- max.39.5 kg/m²).
Sixteen (28.6%) patients were cirrhotic. The initial ALT was 65±48 (20-234) U/L.
Among patients with NASH, 54% lost weight. Normalization of ALT was found in 84% (21/25) of those who lost weight.
Patients with ALT normalization had a weight loss that did not differ significantly from those who did not normalize ALT (10.3 ± 12% and 9.2 ± 5.36%, respectively, p = 0.46).
Conclusion: NASH has a low prevalence in hepatology consultation. However, cirrhosis occurs in a significant proportion of those patients. The prescription of diet and lifestyle changes has a role in this patients.
Disclosure: Nothing to disclose

P0018 EVALUATION OF THE PRESENCE OF HEPATIC STEATOSIS MEASURED BY CAP-FIBROSCAN IN PATIENTS WITH PSORIASIS

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Introduction: Different studies have reported a high prevalence of non-alcoholic fatty liver disease (NAFLD) in patients with psoriasis, using analytical, histological or ultrasound evaluations. To date, there are no studies that analyze the usefulness of CAP-fibroscan and the assessment of body composition by bioimpedance in this group of patients.
Aims & Methods: Knowing the prevalence of hepatic steatosis (HS) in patients with Pso and HA using CAP-fibroscan and analyze the relationship with serological indices, anthropometric, analytical and body composition variables: fat mass index (FMI) and visceral fat (VF) measurements by electrical bioimpedance (BIE). Prospective study of patients with PS and HA from our hospital. Anthropometric, analytical, elastometric and body composition variables were collected.
Results: Descriptive analysis: 107 patients were recognized (45% women), mean age 48.4 ± 12.7 years. 80% with PSo and 20% HA.
Anthropometry: 4.7% were overweight and 57% were obese (100% HA and 83.9% Pso). The mean BMI was 27.1 ± 7.6. 56% had a high waist circumference (WC) (69% women and 45% men).
Comorbidity: 17% HBP, 7% diabetes, 25% dyslipidemia and 29% metabolic syndrome (MtS).
CAP-Fibroscan: 56% had moderate-severe HS (CAP> 248 dB / m) and 31.4% severe (CAP> 280 dB / m).
Liver Stiffnes: 74% were F0-1, 20% F2, 3% F3 and 3% F4. BIE: 69% had high FMI levels (63.3% women vs 86.7% men) and 43% VF (66.7% women vs 23.3% men).
Inferential analysis: There was a good correlation between HS measured by CAP and anthropometric parameters (WC and BMI), serological indexes FLI and HSI, and FMI and VF (p < 0.05).
Patients with HA were younger, more obese, with > liver stiffness (LS),> CAP,> FLI,> FMI and> VF than patients with Pso (p < 0.05). Women with HS had > LS 7.8 vs 5.4 KPa (p < 0.05). Patients with comorbidity had higher HS, higher score in FLI and HSI,> LV and >% FMI and high VF and a higher average age.
The hypertensive males had a VF high in 100% vs non-hypertense (p < 0.05). The high VF in males was significantly higher in terms of age (54 vs 39.7 years), BMI (37.3 vs 30.7), CAP (260 vs 226.8), FLI and HSI index, and the same occurred with the high FMI and age (54 vs 31.1), BMI (36.6 vs 30.38) and the FLI and HSI index.

Moderate-severe HS (CAP> 248 dB / m) was significantly associated with BMI, FLI, HSI, VF and the presence of MtS (p < 0.05). Patients with MtS had a CAP> 248dB / m in 76.2% vs 46.9% (p < 0.05).

Conclusion: The prevalence of moderate-severe HS by CAP in patients with Pso and HA in our series is 56% and this is associated with the presence of obesity, MtS, cardiovascular comorbidity and high fat mass. Up to 25% have advanced fibrosis data. This group of patients would have to be evaluated in the Hepatology units for NAFLD screening and to rule out significant liver disease.

Disclosure: Nothing to disclose

P0019 ROLE OF ADIPONECTIN, LEPTIN AND IGF-1 AS CIRCULATING BIOMARKERS IN NON-ALCOHOLIC FATTY LIVER DISEASE

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Introduction: Non-alcoholic fatty liver disease (NAFLD) encompasses a spectrum of conditions from the benign hepatic steatosis to non-alcoholic steatohepatitis (NASH), which may progress to liver cirrhosis and/or hepatocellular carcinoma. The gold standard method to distinguish steatosis from NASH is liver biopsy.

However, this is an invasive procedure with risk of complications, which provides a two-dimensional estimation of a particular biopsy, and is subjected to individual evaluation by a pathologist. All these limitations prompt the need to discover and validate new accurate diagnostic biomarkers.

Aims & Methods: Here, we aimed to assess the performance of circulating levels of adiponectin, leptin and insulin-like growth factor-I (IGF-1) as potential non-invasive biomarkers in NAFLD. Serum levels of adiponectin, leptin and IGF-1 were evaluated in discovery (n = 59) and validation (n = 145) cohorts of morbidly obese patients, with clinical and biopsy-proven diagnosis of NAFLD, using specific enzyme-linked immunosorbent assays. Hormone levels were correlated with histology findings, clinical parameters, presence of comorbidities and *PNPLA3* genotype. Sera of disease-free individuals, lean and obese, were also analyzed in both cohorts (n = 20 and n = 32, validation and discovery cohorts, respectively).

Results: The results showed that in the discovery cohort, adiponectin was significantly lower in patients with NASH compared to steatosis (*p* < 0.05) or healthy individuals (*p* < 0.01), and the area under the receiver-operating characteristic (AUROC) was 0.79 (95% CI = 0.62 - 0.96; *p* < 0.01). The same trend was observed in the validation cohort. Further adiponectin decreased with histologic severity of steatosis (*p* < 0.005), inflammation and fibrosis (*p* < 0.05), and showed an inverse correlation with serum alanine aminotransferase (ALT) and triglycerides (*p* = 0.0023 and *p* = 0.0055, respectively), supporting a role for this hormone in NAFLD pathophysiology.

In both cohorts, leptin levels were significantly increased in patients with steatosis or NASH when compared to healthy lean controls (*p* < 0.005 and *p* <0.0001), showing an AUROC of ~ 0.9 (*p* < 0.05 and *p* < 0.0001 for discovery and validation cohorts, respectively). Circulating leptin levels were similar between lean and obese controls, suggesting that obesity is not a confounding factor. Finally, although IGF-I concentrations were significantly diminished in patients with steatosis or NASH, compared with controls (*p* < 0.05) in the discovery cohort, IGF-1 levels were similar between control individuals and patients with NAFLD in the validation cohort. Strikingly, IGF-1 levels were significantly lower in more severe fibrosis (*p* < 0.005) in the validation cohort, with an AUROC value of 0.71 (95% CI = 0.6 - 0.82; *p* < 0.01).

Conclusion: In conclusion, these hormones are potentially valuable tools for non-invasive stratification of patients with NAFLD. In particular, leptin might discriminate the presence of NAFLD, while IGF-1 could be a biomarker of advanced fibrosis. Further studies should analyze these hormones in a lean NAFLD control group and the performance of multivariate analysis to assess the impact of confounding factors and the potential of combined biomarker parameters.

Disclosure: Nothing to disclose

P0020 CHEMERIN AS A NON-INVASIVE SERUM MARKER FOR DIAGNOSING AND GRADING OF NON-ALCOHOLIC FATTY LIVER DISEASE

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Introduction: Patients with nonalcoholic fatty liver disease (NAFLD) and advanced liver fibrosis are at the highest risk for progressing to end-stage liver disease. Thus, identifying the severity of liver fibrosis is of major importance in guiding the subsequent management of patients. Efforts have been made to identify noninvasive indicators of liver fibrosis in patients with NAFLD. Chemerin is a recently described adipokine involved in adipogenesis and insulin resistance.

Aims & Methods: We aimed to assess the diagnostic value of serum chemerin in comparison to NAFLD fibrosis score as a non-invasive method for diagnosing and grading of NAFLD. Sixty patients with NAFLD were included. They were categorized into 3 equal subgroups according to the grade of fatty liver by ultrasonography. Thirty healthy subjects were included as controls. Serum chemerin level was measured by enzyme-linked immunoassay.

Results: Serum chemerin level was significantly higher in patients with NAFLD than controls (227.38 ± 44.72 vs. 87.58 ± 28.47 ng/ml, respectively, p≤ 0.001); moreover, it correlated positively with the grade of fatty liver (p≤ 0.001). Serum chemerin correlated positively with NAFLD fibrosis score (r = 0.988; p ≤ 0.001), age (r = 0.571; p≤ 0.001), BMI (r = 0.972; p ≤ 0.001), serum cholesterol (r = 0.942; p≤ 0.001), serum triglycerides (r = 0.915; p≤ 0.001), random blood sugar (r = 0.486; p≤ 0.001), AST (r = 0.963; p≤ 0.001), ALT (r = 0.960; p≤ 0.001), and total bilirubin (r = 0.740; p≤ 0.001), and correlated negatively with platelets (r = -0.827; p≤ 0.001) and total proteins (r = -0.290; p≤ 0.006).

For NAFLD diagnosis, serum chemerin at a cutoff > 147.8 ng/ml had area under the receiver operating characteristics curve (AUROC) = 1.000, confidence interval (CI) 95% = 1.00 - 1.00, and p≤0.001, and NAFLD fibrosis score at a cutoff > - 2.8 had AUROC = 1.000, CI 95% = 1.00 - 1.00, and p ≤0.001. Additionally, serum chemerin level above 245 ng/ml cutoff value can detect extensive fibrosis (F3-F4), with AUROC = 1.00, CI 95% = 1.00 - 1.00, sensitivity and specificity 100%. Cases within NAFLD fibrosis score gray zone had a significantly higher serum chemerin compared with cases below the gray zone, with mean level 213.83 (± 13.74) vs. 114.48 (± 35.41) ng/ml, respectively, p≤ 0.001.

Conclusion: In NAFLD patients, serum chemerin level is correlated with fatty liver grade. This study suggests that chemerin is comparable to NAFLD fibrosis score as regards detection and grading of NAFLD and of a useful utility especially in patients within NAFLD fibrosis score gray zone.

Disclosure: Nothing to disclose

P0021 SYSTEMIC EXPRESSION AND SIGNIFICANCE OF NEUTROPHIL EXTRACELLULAR TRAP (NET) COMPONENTS IN ALCOHOLIC LIVER DISEASE

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Introduction: Neutrophils release neutrophil extracellular traps (NETs) as a defense strategy in response to broad-spectrum infections, but also to sterile triggers. NETs consist of a DNA scaffold decorated with antimicrobial peptides (AMPs) including cathelicidin (LL37) and α-defensins (HNP1-3), and enzymatically active proteases including peptidyl arginine deiminase type 4 (PAD-4). NET components possess pleiotropic immunomodulating potential. Damage-associated molecular patterns (DAMPs), such as high mobility group box 1 (HMGB1), stimulate NET formation. Susceptibility to infections and inflammatory dysregulation are hallmarks of alcoholic liver disease (ALD).

Aims & Methods: We aimed to investigate the systemic concentrations of NET components such as LL37, HNP1-3, and PAD-4, and the NET promoter HMGB1 in patients with ALD and assess their implications in the disease course.

62 patients with ALD /51 males, 11 females, aged 48,94 ± 10,29/ were prospectively recruited and assigned to subgroups based on their 1/ gender, 2/ severity of liver dysfunction according to Child-Pugh and Model of End-Stage Liver Disease (MELD) scores, and modified Maddrey's Discriminant Function (mDF) 3/ presence of ALD complications, and followed for 30 days. 24 age- and sex-matched healthy volunteers served as the control group. Selected plasma components of NETs and HMGB1were quantified using immunoenzymatic ELISAs. Correlation coefficients between their blood concentrations and (i) markers of systemic inflammation [the neutrophil-to-lymphocyte ratio (NLR), C-reactive protein (CRP), white blood cell (WBC) and neutrophil (NEUT) counts], (ii) liver dysfunction severity scores (Child-Pugh, MELD, mDF), and (iii) ALD complications were calculated. The receiver operating curves (ROC) and their areas under the curve (AUCs) were checked in order to assess the accuracy of the NET component expression in predicting the degree of liver failure and the development of ALD complications.

Results: Systemic concentrations of HNP1-3, PAD-4, and HMGB1 were significantly increased in patients with ALD in comparison with controls. However, LL37 was significantly elevated only in the subgroup of ALD patients with WBC count above 15 cells/µL compared with controls and ALD patients with WBC count equal or below 15 cells/µL. No gender-related differences in NET components and HMGB1 concentrations were found. HNP1-3 levels correlated with MELD and mDF scores. ALD subgroups with MELD>20 and mDF>32 presented with significantly higher HNP1-3 concentrations. HNP1-3 levels revealed a good predictive AUC for the hepatic encephalopathy and ascites development (0.81 and 0.74, respectively), and for the survival (0.87) in patients of above 40 years of age. PAD-4 levels correlated with standard markers of inflammation (CRP, WBC, NEUT) and revealed a good predictive AUC (0.76) for the survival in the whole ALD group. No correlations of HMGB1 concentrations with markers of systemic inflammation, liver parameters, and ALD complications were found.

Conclusion: Our results reveal that systemic blood levels of NET components and the NET promoter are elevated in ALD patients and support the value of HNP1-3 and PAD-4 as biomarkers in the ALD assessment. PAD-4 seems to be an inflammatory mediator, while HNP1-3 the disease severity indicator. HNP1-3 and PAD-4 may be potentially applied as predictors of the patients' survival in ALD. The significance of LL37 and HMGB1 concentrations in patients with ALD requires further investigation.

Disclosure: Nothing to disclose

P0022 WITHDRAWN

P0023 WITHDRAWN

P0024 ROLE OF POLYMORPHISMS RS37972 RS37973 OF THE GLCCI1 GENE IN MORTALITY OF MEXICAN PATIENTS WITH ALCOHOLIC HEPATITIS

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Introduction: Alcoholic hepatitis (AH) has a mortality of 25-50%, but in some Mexican studies it reaches around 60%. Only steroid treatment impacts in AH mortality. Genetic polymorphisms (SNPs) rs37972 and r37973 of GLCCI1 gene have shown influence in steroids treatment response in various inflammatory pathologies.

Aims & Methods: To determine if SNPs rs37972 and r37973 of GLCCI1 gene confers lack of response to steroid treatment and higher mortality in patients with severe AH.A case-control study was conducted in 71 Mexican mestizo patients with severe AH. The SNPs rs37972 and r37973 of GLCCI1 gene were determined from genomic DNA by endpoint PCR. The demographic and clinical features of AH patients were collected and the response to steroid treatment was evaluated using the Lille model and its mortality. The data was analyzed with the statistical package SPSS V25.

Results: Of patients included: 62 were men (87.3%) treated with steroids. 46.5% of the patients presented response to treatment with steroids. Mortality at 24 weeks was 49.3%. The C allele of SNP rs370972 (p = 0.01 [OR 0.41 (IC95% 0.21-0.81), TT genotype of SNP rs370972 (p = 0.001 [OR 0.02 (95% CI 0.00-0.40) and AA of SNP rs37973 (p = 0.035 [OR 0.48 (95% CI 0.24-0.95), were shown as protective factors for early mortality (28 days). In evaluating mortality at 24 weeks we observed that the AG genotype of SNP rs370973 (p = ≤0.001 [OR = 13.22 (IC95% 4.72-36.78)]) and CT of SNP rs370972 (p = ≤0.001 [OR 12.0 (IC95% 4.46-32.28)) conferred higher mortality in AH patients. No association was found between the response to steroids treatment and SNPs rs370973 and rs370972 of GLCCI1 gene (p = 1.00 [IC95% 0.52 - 1.95]) in patients with AH.

Conclusion: Genetic polymorphisms of GLCCI1 gene impact in mortality of Mestizo-Mexican patients with AH. For our knowledge, this is the first study worldwide that associates the of the GLCCI1 genetic polymorphisms in patients with AH.

References: Me. Alcoholic Hepatitis a comprehesive of pathogenesis anda treatment. World J Gastroenterol. 2014 May ; 20)(20) (6279: 6286). EASL Clinical Guidelines Management of alcohol liver disease. J Hepatol. 2012 57; 399(0).

Disclosure: Nothing to disclose

P0025 DAY-4 LILLE SCORE IN EARLY PREDICTION OF CORTICOSTEROID RESPONSE FOR PATIENTS WITH SEVERE ACUTE ALCOHOLIC HEPATITIS

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Introduction: In addition to general supportive care, corticosteroids are indicated for patients with severe acute alcoholic hepatitis (SAH), defined by a Maddrey`s discriminat function (MDF) score >32 [1].
However, patients on corticosteroid therapy have a high risk of developing infections and other complications, especially during hospitalization. The introduction of Lille score helps in finding the steroid responders (< 0.45) and non-responders (>0.45) after 7 days of treatment [2].
The aim of this study is to evaluate whether using Lille score at day 4 (LM4) is as useful as Lille at day 7 (LM7), in order to determine response to therapy earlier.

Aims & Methods: A retrospective study was performed including all patients with SAH during October 2015-March 2019 in a tertiary Department of Gastroenterology and Hepatology. All consecutive patients with SAH and MDF >32, without contraindications to corticosteroids were enrolled. All patients received 40 mg of Prednisone per day and response was assessed with LM4 and LM7, according to the validated cut-off (< 0.45 responder and >0.45 non responder).

Results: A total of 40 patients out of 79 (50.6%) with acute alcoholic hepatitis had MDF>32 and received corticosteroid therapy (5 female and 35 male, mean age 51±9.2 years). All included patients had liver cirrhosis, 28/40 (70%) had Child Pugh C score. The median value MDF was 59.35±30. The mean value for Lille score at 4 days was 0.65±0.31, vs 0.5±0.35 for Lille score at 7 days, *p=0.041*. There was no difference between the proportion of patients with a responder Lille score value at 4 days versus 7 days (35% vs 45%, *p=0.36*).

Conclusion: LM4 could be used instead of LM7 in predicting the response to corticosteroids therapy in SAH to avoid a prolonged use of this therapy.

References: 1.Aspasia S. Soultati et al. Predicting utility of a model for end stage liver disease in alcoholic liver disease.World J Gastroenterol. 2006 Jul 7; 12(25): 4020-4025. 2. Louvet A. et al. The Lille model: a new tool for therapeutic strategy in patients with severe alcoholic hepatitis treated with steroids. Hepatology. 2007 Jun;45(6):1348-54.

Disclosure: Nothing to disclose

P0026 COMBINATION OF GLYCYRRHIZIN AND N-ACETYLCYSTEINE: BENEFIT OUTCOME IN A MURINE MODEL OF ACETAMINOPHEN-INDUCED LIVER FAILURE

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Introduction: Acetaminophen overdose is the most frequent cause of drug-induced liver failure in the developed countries. Despite substantial progress in the understanding of the mechanism of hepatocellular injury, N-acetylcysteine remains the only effective treatment if administered within 8 to 10 hours of ingestion of the overdose. Thus, other hepatoprotective drugs are needed for the delayed treatment of acetaminophen-induced hepatotoxicity. Glycyrrhizin, an aqueous extract of licorice root, is also known to have hepatoprotective effects.

Aims & Methods: This study aimed to investigate the efficacy of the combination of glycyrrhizin and N-acetylcysteine compared to N-acetylcysteine alone in the prevention of liver toxicity in a murine model of acetaminophen-induced liver injury. Mice fasted for 15h were treated with acetaminophen (500mg/kg) by intraperitoneal injection and separated into following groups: glycyrrhizin (200mg/kg), N-acetylcysteine (150mg/kg) and glycyrrhizin/N-acetylcysteine. In all groups, mice were sacrificed 12h following acetaminophen administration. Hematological analyses, histopathological parameters and survival rates were compared between various groups.

Results: Consistent with earlier data, intraperitoneal administration of acetaminophen in mice induced a severe liver injury characterized by release of alanine aminotransferase and centrilobular hepatocyte necrosis. Treatment with glycyrrhizin, N-acetylcysteine or N-acetylcysteine/glycyrrhizin combination, at the same time of acetaminophen, decreased significantly alanine aminotransferase levels and necrosis score. At this stage, the N-acetylcysteine/glycyrrhizin combination was as effective as N-acetylcysteine alone. Delayed administration, two hours or six hours after acetaminophen challenge, induced significant decrease of hepatocytes necrosis in group of mice treated with N-acetylcysteine/glycyrrhizin combination (p< 0,01) compared to other groups. Furthermore, the administration of N-acetylcysteine/glycyrrhizin combination was found to be associated with better survival rates. The results showed that treatment with N-acetylcysteine/glycyrrhizin combination prevented significantly (p< 0,001) mice mortality compared to N-acetylcysteine alone. Potential interference between N-acetylcysteine/glycyrrhizin treatment and acetaminophen metabolism, was evaluated and we have not demonstrated significantly differences between groups of mice.

Conclusion: Compared with N-acetylcysteine given alone, concomitant administration of glycyrrhizin decreased the liver necrosis score and improved the survival during acetaminophen-induced liver injury in mice. These results suggest for the first time that the combination of an antioxidant like N-acetylcysteine and an anti-inflammatory drug like glycyrrhizin prevented the liver damage induced by acetaminophen intoxication.

Disclosure: Nothing to disclose

P0027 THE FREQUENCY AND IMPACT ON MORTALITY OF INFECTIONS IN ACUTE ALCOHOLIC HEPATITIS

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Introduction: Acute alcoholic hepatitis is a cause of immune system dysfunction which increases the risk of infection, especially bacterial infections [1]. Infection screening in patients with acute alcoholic hepatitis is beginning to be a strategy in order to identify every minimal infection and to start treatment as soon as possible. The aim of this study was to identify the frequency and impact of infections in a cohort of acute alcoholic patients.

Aims & Methods: A retrospective cohort study was performed on a group of 79 patients with acute alcoholic hepatitis hospitalized from January 2015 to March 2019 in a tertiary Department of Gastroenterology and Hepatology. For this study we analyzed the frequency of infections occurring in these patients and their predominant location by performing hemocultures, sputocultures, urocultures, chest R-ray and ascitic fluid examination. The severe form of acute alcoholic hepatitis was defined by a Maddrey`s discriminat function (MDF) score >32 [2] and response to corticosteroid therapy was assesd by Lille score after 7 days of treatment (LM7 < 0.45 responders and >0.45 non-responders) [3].

Results: Out of all the 79 patients with acute alcoholic hepatitis (10 female and 69 male, with a mean age 53±9.5 years), 40/79 (50.6%) had severe acute alcoholic hepatitis with a MDF score >32 and 32/79 (40.5%) had a bacterial infection. All patients had liver cirrhosis (LC), 25/32 (78%) Child Pugh C score. The most common infectious agent incriminated was Klebsiella spp. 11/40 (27.5%) with pulmonary location.

In the MDF>32 group, 17/40 (42.5%) patients had infections, while in the MDF< 32 group 15/39 (38.5%) patients had infections (*p=0.719*), with no significant difference between the two groups.

17/32 (53%) patients had MDF>32 and received corticosteroid therapy. 7/17 (41.1%) were responders (LM7 < 0.45) and 10/17 (58.9%) non-responders (LM7 >0.45), with a total mortality rate of 41.1%, 2/17 (11.7%) from the responder group and 5/17 (29.4%) from the non-responder group (*p=0.2083*), with no significant difference in mortality between the two groups.

The overall mortality was 25.3%, significantly higher in the group with infections, 19% as compared to the group without infections, 6.3% (*p=0.016*).

Conclusion: Patients with acute alcoholic hepatitis have higher risk of infections and the association of infections with LC generates higher mortality, regardless the response to corticosteroid therapy.

References: 1. Grand Rounds: Alcoholic Hepatitis J Hepatol. 2018 Aug;69(2):534-543. doi: 10.1016/j.jhep.2018.05.001. Epub 2018 Jun 13. 2. Aspasia S. Soultati et al. Predicting utility of a model for end stage liver disease in alcoholic liver disease.World J Gastroenterol. 2006 Jul 7; 12(25): 4020-4025. 3. Louvet A. et al. The Lille model: a new tool for therapeutic strategy in patients with severe alcoholic hepatitis treated with steroids. Hepatology. 2007 Jun;45(6):1348-54

Disclosure: Nothing to disclose

P0028 ASSESSMENT AND OUTCOMES OF IMMUNE-CHECKPOINT INHIBITOR INDUCED HEPATOTOXICITY IN PATIENTS WITH METASTATIC MELANOMA

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Introduction: Immune checkpoint inhibitors (ICIs) are a new class of systemic anti-cancer treatment which function by targeting the inhibitory mechanisms on the hosts' immune system, inducing an immune-mediated anti-tumour effect. ICIs have improved outcomes for a subset of patients with advanced cancer such as metastatic melanoma. However, immune activation is not specific to cancer cells and often results in off-target immune-related adverse events. Hepatitis occurs in 5-10% of patients on single agents ipilimumab, nivolumab, and pembrolizumab therapy, and 25-30% of patients treated with ipilimumab/nivolumab combination therapy. We wanted to review baseline characteristics of patients with ICI induced transaminitis, and other causes associated other than treatment.

Aims & Methods: We carried out a prospective review of patients with metastatic melanoma on immune checkpoint inhibitors who developed transaminitis at our tertiary oncology centre between March 2018 and February 2019. Data are analysed based on demographics, diagnosis, immunotherapy regime, factors that would cause transaminitis such as alcohol history, pre-existing liver disease, and known liver metastasis. Transaminase elevation is graded based on CTCAE (Common Terminology Criteria for Adverse Events): Grade 1 is ALT or AST rise up to 3 times the upper limit of normal (ULN), grade 2 is 3-5 times the ULN, grade 3 is 5-20 times the ULN, grade 4 is more than 20 times the ULN. Patient's outcome is assessed by response to immunosuppressive treatment, length of immunotherapy treatment break, and immunotherapy discontinuation or change to next line of treatment.

Results: Out of 89 patients treated with ICIs (22 on combination ipilimumab/nivolumab therapy and 67 on single agent therapy of ipilimumab or pembrolizumab), 16.9% (n=15) had a rise in ALT. Of these, 8/15 had ocular melanoma, 6/15 had cutaneous melanoma, 1/15 had mucosal melanoma. 66% (n=10) patients received combination treatment and the rest had single agent treatment. 9/15 patients had liver metastasis at baseline. 3/15 had grade 1 transaminitis at presentation, 5/15 had grade 2, 7/15 had grade 3, and none presented with grade 4. The median time from first dose of ICI to ALT rise is 43 days (range 23-635). The majority of patients (8/15) developed transaminitis after 2 cycles of ICI. More patients on combination treatment had an ALT rise compared to single agent (10/22 vs. 5/62), which was statistically significant (p=0.0002).

1/15 had newly diagnosed active hepatitis B on investigations (positive HepBsAg, anti-HBc and anti-HBe) after ALT rise. 9 patients underwent imaging of liver and 3 had contributing reasons for ALT rise, including hepatic steatosis (n=1), progressive liver disease (n=1) and portal vein thrombosis (n=1).

7/15 were able to continue ICI therapy, with a median break of treatment of 91 days. Patients with contributory reasons for ALT rise other than just ICI induced had a longer break off of treatment (115 days vs 78 days).

Conclusion: We conclude that the % of patients within our Trust with hepatotoxicity from immune therapy is in line with published data. From this study we believe it is essential to review for other causes of ALT rise in patients treated with ICI, including hepatitis A, B, & C serology (essential prior to commencement of ICI), as well as liver imaging for the presence of liver metastasis, steatosis and portal vein thrombosis. Consistent with published literature, we find that patients on combination treatment were significantly more likely to develop ALT rise compared to single agent therapy (p=0.0002).

References: Haanen J., et al. Management of toxicities from immunotherapy: ESMO Clinical Practice Guidelines for diagnosis treatment and follow-up. Annals of Oncology, 2017;28((suppl_4)):p. iv119-iv142. National Cancer Institute, National Institutes of Health, U.S. Department of Health and Human Services. Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0. [last accessed March 16, 2015];NIH publication # 09-7473. Published May 29, 2009; Revised Version 4.03 June 14, 2010

Disclosure: Nothing to disclose

P0029 ETIOLOGIES OF ERECTILE DYSFUNCTION IN NON-ALCOHOLIC FATTY LIVER DISEASE

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Introduction: The relationship between non-alcholic fatty liver disease (NAFLD) and erectile dysfunciton (ED) still is not clear. Pathogenesis of ED is multifactorial with a leading cause of endothelial dysfunction. Hypertension, obesity, diabetes, abnormal lipid profile are risk factors for sexual dysfunction and also they are components of metabolic syndrome. In this cross-sectional study we aimed to investigate the relationship between NAFLD and ED.

Aims & Methods: We enrolled the male patients who were following up with NAFLD in our out-patient clinic. NAFLD diagnosis was established with imaging modalities such as ultrasound, computer tomography and magnetic resonance imaging and exclusion of other causes of hepatos-

teatosis. Sociodemographic, anthropometric and biochemical data were recorded for each patient. Index of Erectile Dysfunciton (IIEF) questionnaire fulfilled by each patients and score equal or under 21 accepted as increased risk for ED and referred to the urology specialist. Each patient was examined by same urologist for further evaluation of the etiology of ED.

Results: A total of 136 patients enrolled to the study. Mean age was 45.64 ± 11.55 years. One hundred and twenty patients (88.2%) were married, 13 patients (9.6%) were single and 3 patients (2.2%) were divorced. Grade 1 hepatosteatosis found in 41patients (30,1%), grade 2 hepatosteatosis was found in 65 patients (47,8%), grade 3 hepatosteatosis was found in 23 patients (16.9%) and grade 4 hepatosteatosis was found in 2 (1,5%) patients with USG. NAFLD diagnosis was established with MRI in 3 patients and with CT in 2 patients. Metabolic syndrome was seen in 48 patients (35.3%). Mean body mass index was 30.04 ± 5.27 kg/m², mean height was 172.48 ± 6.88 cm, mean weight was 89.95 ± 17.25 kg, mean waist circumference was 106.02 ± 13.40 cm and mean hip circumference was 106.27 ± 9.37 cm. IIEF point was below the cut-off score in 68 patients (50.0%) and these patients were referred to urologist for confirmation of ED and further investigation of etiologies and treatment. Forty-eight patients were evaluated by the urologist and ED was not confirmed in only 5 patients. Psychogenic ED was found in 19 patients (39.6%), vasculogenic ED was found in 35 patients (72.9%), drug-related ED was found in 3 patients (6.3%) and neurogenic ED was found in 6 patients(12.5%). Seventeen patients had more than one etiology for ED at the same time, 29 (21.3 %) patients described premature ejaculation and 4 (2.9%) patients described loss of sexual desire. Medical treatment was prescribed to 36 patients (75 %) for ED.

Conclusion: Erectile dysfunction may have a relation with NAFLD. IIEF questionnaire is a very practical and reliable screening tool for detection of ED. Presence of erectile dysfunction disrupts patient's quality of life and may cause psychiatric disorders. Awareness of ED in NAFLD patients is important for the early diagnosis and treatment of patients.

Disclosure: Nothing to disclose

P0030 NOVEL ORAL ANTICOAGULANTS MAY BE USED IN THE TREATMENT OF PORTAL VEIN THROMBOSIS IN PATIENTS WITH CIRRHOSIS: A SYSTEMATIC REVIEW AND COMPARATIVE META-ANALYSIS

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Introduction: Well-defined guidelines for the treatment of portal vein thrombosis (PVT) in patients with cirrhosis do not exist due to lack in robust data. Treatment options include low molecular weight heparin (LMWH), vitamin K antagonists (VKAs), and the newer oral anticoagulants (NOACs). Anticoagulation safety has been an issue in patients with cirrhosis, and the best choice of anticoagulation is unknown.

Aims & Methods: We conducted a comprehensive search of multiple databases and conference proceedings (through November 2018) to identify studies that reported on the use of LMWH, VKAs, and NOACs in the treatment of PVT in patients with cirrhosis. Goals were to evaluate the pooled rate of treatment success and bleeding with LMWH, VKAs, and NOACs, and compare the outcomes.

Results: From a total of 744 patients (17 studies), 648 were treated with some form of anticoagulation and 96 were control. 155, 315, and 70 patients were treated with LMWH, VKAs, and NOACs respectively. Baseline characteristics were comparable among the groups. Age ranged from 41 to 71 years with a predominantly male population. 144 patients were Childs A, 182 Childs B, and 121 Childs C.Pooled rate of treatment responders with anticoagulation was 66.7% (95% CI 58.3-74.1, I2=72.7) and with control was 26% (95% CI 14.2-42.7, I2=36.7). The difference was statistically significant, p=0.001. Pooled rate of bleeding was similar between these two groups (7.8%, 95% CI 4.5-13.3 and 15.4%, 95% CI 4.3-42.7, p=0.33).Pooled rates of treatment success and bleeding events were comparable between LMWH,

VKAs, and NOACs (Table-1). On meta-regression analysis, Child-Pugh classification did not seem to affect the treatment success and/ or the bleeding outcomes. The calculated 2-sided p-value of intercept was 0.39, Childs A was 0.15, Childs B was 0.11, and Childs C was 0.15.

(95% CI, I2)	Treatment responders	Bleeding
All anticoagulants	66.7% (58.3-74.1, 72.7)	7.8% (4.5-13.3, 66.2)
LMWH	60.7% (40.2-77.9, 57)	7.2% (4.5-16.6, 0)
VKA	66.0% (52.9-76.9, 80.7)	9.3% (3.8-20.6, 78.2)
NOAC	76.7% (44.6-93.4, 88.5)	7.9% (3.7-24.0, 30.3)
Control	26% (14.2-42.7, 36.7)	15.4% (4.3-42.7, 0)
p-value of statistical significance		
All anticoagulants vs control	0.001	0.33
LMWH vs VKA	0.63	0.74
NOAC vs LMWH	0.35	0.86
NOAC vs VKA	0.5	0.9

LMWH: low molecular weight heparin, VKA: vitamin K antagonists, NOAC: novel oral anticoagulants

[Summary of pooled results]

Conclusion: Our study demonstrates that anticoagulation is effective and safe in the treatment of PVT in patients with cirrhosis. Bleeding is not increased in treatment group compared to control group. Due to their similar and comparable outcomes, NOACs may be offered as a first line treatment based on patient preferences. Limitations of our study were the comparatively small sample size of patients on NOACs, heterogeneity, and indirect comparison. Well-conducted studies are warranted to ascertian the role of NOACs in the treatment of PVT in patients with cirrhosis.
Disclosure: Nothing to disclose

P0031 MULTIVARIATE ANALYSIS OF RISK FACTORS FOR MORTALITY IN ACUTE VARICEAL BLEEDING

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Introduction: Acute variceal bleeding in liver cirrhosis is an immediate life-threatening condition and a major complication of portal hypertension.
Aims & Methods: The aim of this study is to evaluate bleeding risk scores and other risk factors for predicting six-week mortality in patients with acute variceal bleeding.
We prospectively evaluated 703 consecutive patients admitted with endoscopically proven acute variceal hemorrhage (71.4% males, mean age 58 ± 10.3 years), 43% admitted with first attack of hematemesis, 14.1% Child-Turcotte-Pugh (CTP) A, 47.2% CTP B, 38.7% CTP C, 38.3% had HCC.
All patients received antibiotics and vasoactive drugs. Endoscopic treatment was individualized. The outcome was the 6-week mortality. Bleeding was controlled in 422 patients (59.9%) and 210 patients died (29.8%), (122 (17.4%) during hospitalization, 69 patients from causes not related to the acute hemorrhage (9.8%)). Rebleeding occurred in 281 patients (39.9%) after the first week. Disease severity scores (platelet-albumin-bilirubin (P-ALBI), ALBI, MELD, IMELD, MELD-Na, and UMELD) and bleeding risk scores (GB score, admission Rockall, AIMS 65 and APASL score) were calculated on admission and the full Rockall score following endoscopy. Demographic, clinical and laboratory data and the calculated scores were compared between survivors and non-survivors.
Results: Different bleeding risk scores were calculated and the significant were (the platelet-albumin-bilirubin (P-ALBI), ALBI, MELD, IMELD, MELD-Na, UMELD with the best score I MELD with AUC 0.863);The AUC of different scores is shown in table (1).
Then Demographic, clinical and laboratory data were compared between survivors and non-survivors, Multivariate models showed that Age (age> 60 years) (OR 2.6, CI (1.2 - 5.6), presence of HCC (OR 8.9) CI(3.1 - 26.1),Renal

failure (OR 4.7) CI (2 - 10.7), Early re- bleeding (OR 7120)CI(555 - 92583), Not taking NSBBS (OR .024)CI (0.004 - 0.220) , INR (OR 2.5)CI (1.1 - 6.4), and CRP (OR 1.05 CI (1 - 1.012) as P- value for all< 0.05.
Conclusion: Liver disease severity scores performed better than bleeding risk scores.
I MELD score with cut off value ≥ 40.5 is most specific predictor for 6 weeks mortality after acute variceal bleeding.
On Age, HCC, Renal failure, CRP and early re-bleeding are risk factors to predict six weeks mortality in variceal bleeding while taking NSBBs decrease mortality.
References: * Roayaie S et al. PALBI-An objective score based on platelets, albumin and bilirubin stratifies HCC patients undergoing resection and ablation better than Child's classification, Hepatology 2015; 62: 624A. • Rockall TA et al. Risk assessment after acute upper gastrointestinal hemorrhage. Gut 1996; 38: 316-21. • Saltzman JR, et al. A simple risk score accurately predicts in-hospital mortality, length stay, and cost in acute upper GI bleeding. Gastrointest Endosc. 2011;74:1215-1224 • Blatchford O et al. A risk score to predict need for treatment for upper gastrointestinal hemorrhage. Lancet 2000, 356: 1318-1321.
Disclosure: Nothing to disclose

P0032 HIGHER-DOSE OF LEVOCARNITINE MAY CONTRIBUTE TO AN EARLY REMISSION OF HYPERAMMONEMIA IN PATIENTS WITH LIVER CIRRHOSIS

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Introduction: Patients with liver cirrhosis often develop carnitine deficiency due to decreased intake from the diet and decreased biosynthesis in the body; and further, their carnitine pools in skeletal muscle are often reduced due to sarcopenia. Carnitine deficiency contributes to hyperammonemia and hepatic encephalopathy. Administration of levocarnitine activates the urea cycle, promotes ammonia metabolism, and relieve hepatic encephalopathy; however, the optimum dose of levocarnitine in patients with liver cirrhosis has not been well established. We hypothesized that administration of higher-dose of levocarnitine might promptly fill up the carnitine pool in the body and lead to an early remission of hyperammonemia and other symptoms in comparison to administration of lower-dose levocarnitine.
Aims & Methods: We aimed to compare the effect on hyperammonemia by the dose of levocarnitine in Japanese patients with liver cirrhosis. Out of the 83 patients who received levocarnitine, we included 46 cases (29 men and 17 women; median age, 68 years old) those who had hyperammonemia (at or above 70 μg/dl) at baseline and had follow-up study of serum ammonia levels. We stratified the initial levocarnitine dose into < 1500 mg/day (lower-dose group, n = 36) and 1500 mg/day or more (higher-dose group, n = 10). We performed a 2:1 matching according to the propensity score calculated from age, sex and ALBI score [1]. We compared them for the improvement of serum ammonia levels to below 70 μg/dl in 6 weeks, using Fisher's exact test and the Cox proportional hazard model.
Results: No adverse event related to levocarnitine administration was observed. In 6 weeks from the start of levocarnitine administration, 17 cases (47%) in the lower-dose group and 6 cases (60%) in the higher-dose group improved serum ammonia levels to below 70 μg/dl. After matching, the median (interquartile range) of serum ammonia levels at baseline, ALBI score, and the initial levocarnitine dose were 134 (52) μg/dl, -1.3492 (0.3528), and 750 (62) mg/day in the lower-dose group (n = 20) and 149 (124) μg/dl, -1.3402 (0.4941), and 1750 (500) mg/day in the higher-dose group (n = 10), respectively. Remission of hyperammonemia in 6 weeks was observed more often in the higher-dose group than in the lower-dose group, although the difference was not statistically significant (60% vs. 30%, P = 0.1391). The longitudinal analysis adjusted for the concomitant medication (branched-chain amino acid, rifaximin, and zinc acetate) showed that the higher-dose group had a significantly earlier ammonia normalization than the lower-dose group (adjusted hazard ratio, 4.087; 95% confidence interval, 1.169-12.289; P = 0.0275).
Conclusion: Administration of levocarnitine 1500 mg/day or more significantly remitted hyperammonemia compared with the lower dose. It may contribute to a rapid recovery from symptoms caused by carnitine deficiency.

References: [1] Johnson PJ, et al. Assessment of liver function in patients with hepatocellular carcinoma: a new evidence-based approach-the ALBI grade. J Clin Oncol. 2015;33:550-8.
Disclosure: Nothing to disclose

P0033 SARCOPENIA HELPS PREDICT THE RISK OF HEPATIC ENCEPHALOPATHY AND TRANSPLANTATION-FREE SURVIVAL AFTER TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT IN CIRRHOSIS

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Introduction: Hepatic encephalopathy (HE) remains one of the most common challenges after transjugular intrahepatic portosystemic shunt (TIPS). Sarcopenia was associated with clinical outcomes of patients with cirrhosis. This study was aimed to evaluate the association between preoperative sarcopenia and the incidence of HE and liver transplantation (LT)-free survival after TIPS with covered stents.
Aims & Methods: Preoperative CT images taken at the 3rd lumbar vertebra from 189 patients were quantified for definition of sarcopenia. Incidence of sarcopenia and post-TIPS HE, LT-free survival and the association between them were analyzed.
Results: Sarcopenia was present in 74 (39.2%) patients. HE occurred in 64 patients (33.9%) after a median time of 17.7 (IQR 4.5-28.8) months follow-up. Patients with sarcopenia had a significantly higher incidence of HE (p=0.009) and tended toward lower LT-free survival (p=0.082) than nonsarcopenic patients. The SSA score including sarcopenia (OR=1.776, p=0.024), sodium (OR=1.112, p=0.003) and age (OR=1.032, p=0.006) yielded a concordance statistic (C-statistic) of 0.714 for predicting overall HE.
The BSA score including bilirubin (OR=1.025, p=0.014), sarcopenia (OR=2.495, p=0.025) and albumin (OR=1.186, p< 0.001) generated a higher C-statistic (0.770, 95% CI 0.689-0.850) than MELD (0.639, 95% CI 0.539-0.739), MELDNa (0.685, 95% CI 0.583-0.787), MELD-sarcopenia (0.681, 95% CI 0.565-0.797) and MELD-L3SMI (0.644, 95% CI 0.538-0.750) for overall LT-free survival. The BSA score showed better discriminative performance in earlier months after TIPS. Both scores gave excellent C-statistics at 3-, 6- and 12-month for corresponding outcomes.
Conclusion: Preoperative sarcopenia independently increased incidence of HE and decreased LT-free survival after TIPS. Clinical scores including sarcopenia provided excellent discriminative performances for predicting the risk of post-TIPS HE and LT-free survival.
Disclosure: Nothing to disclose

P0034 HOW TO IDENTIFY CIRRHOTIC PATIENTS IN NEED OF PALLIATIVE CARE?

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Introduction: In end-stage liver disease, in order to select patients requiring Palliative care (PC) the Poor Prognosis Screening Criteria for Inpatients with Cirrhosis (PPSCIC) were developed. The presence of 3 criteria (out of the following 5: Child-Pugh score C, more than two admissions within the last 6 months, ongoing alcohol use in the context of known alcohol-related liver disease, unsuitability for liver transplantation, World Health Organization Performance status 3 or 4) should prompt referral to PC.
Aims & Methods: The aim of this study is the external validation of PPSCIC and its comparison to other prognostic scores, such as the Child-Pugh, UKELD and MELD-Na scores. Patients admitted to the Gastroenterology Department with liver cirrhosis, from July 2013 to December 2017 were reviewed. Those without previous diagnosis and with missing information were excluded. The PPSCIC, Child-Pugh, UKELD and MELD-Na at admission were assessed.

The defined outcomes were mortality at 6 months and mortality at 12 months. The area under the curve (AUC) of the different receiver operating characteristic (ROC) curves was calculated.
Results: A total of 260 admissions were selected from 214 different patients. The majority of the admissions were of male patients (n=194; 74.6%) and the mean age was 60.9±10.7 years. The median value for the Child-Pugh score was 10 (range 5-15), 19 (range 7-47) for MELD-Na and 55 (range 43-77) for the UKELD score. Regarding PPSCIC, 75 (28.8%) patients had 1 criterion, 70 (26.9%) had 2 criteria, 50 (19.2%) presented with 3 criteria and only 11 (4.2%) had 4 criteria. A total of 54 (20.8%) patients had no PPSCIC. The AUC for mortality at 6 months was 0.68 (95% CI: 0.61-0.74, p< 0.001) for PPSCIC, 0.67 (95% CI: 0.60-0.74, p< 0.001) for Child-Pugh, 0.74 (95% CI: 0.68-0.80, p< 0.001) for MELD-Na and 0.75 (95% CI: 0.69-0.81, p< 0.001) for UKELD. The best cut-off point for PPSCIC was >1, presenting a sensitivity of 65.7% and specificity of 59.5%. The AUC for mortality at 12 months was 0.66 (95% CI: 0.59-0.72, p< 0.001) for PPSCIC, 0.67 (95% CI: 0.60-0.73, p< 0.001) for Child-Pugh, 0.73 (95% CI: 0.67-0.79, p< 0.001) for MELD-Na and 0.74 (95% CI: 0.69-0.80, p< 0.001) for UKELD. The best cut-off point for PPSCIC was also >1, with a sensitivity of 61.7% and specificity of 59.3%.
Conclusion: The performance of PPSCIC in predicting mortality at 6 months and mortality at 12 months as a surrogate for benefit in PC was modest. Moreover, the optimal cut-off identified (>1) was different from the previously reported (>2). In fact, other prognostic scores such as the UKELD or MELD-Na revealed a greater ability to predict mortality. Therefore, the PPSCIC does not seem to be a useful tool to select patients in need of PC in our population.
Disclosure: Nothing to disclose

P0035 EFFICACY OF ATORVASTATIN PLUS ASA IN COMPARISON WITH ATORVASTATIN ALONE ON LIVER FUNCTION AND DEGREE OF FIBROSIS AMONG PATIENTS WITH CRYPTOGENIC CIRRHOSIS: A RANDOMIZED DOUBLE BLIND CLINICAL TRIAL

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Introduction: To evaluate efficacy of combination of Aspirin and atorvastatin in comparison with atorvastatin alone for improvement of liver fibrosis and function among cases of cryptogenic cirrhosis.
Aims & Methods: In this randomized double blind clinical trail, 40 patients with cryptogenic liver cirrhosis randomly allocated to receive either atorvastatin plus ASA or atorvastatin alone for a six months period and compared for viewpoint of liver function and stiffness thereafter.
Results: Overall 33 cases with cryptogenic cirrhosis included. After randomization, 16 participants in group A and 17 in group B evaluated for final analysis. Average age of patients in group A & B were 50.3± 11.2 and 47.9± 10.6 and average BMI of participants in 2 groups were 30.7± 4.2 and 30.8± 3.1 respectively. 12 patients in group A (75%) and 14 cases in group B (82%) were male. The baseline demographic characters of 2 groups were similar.
After 6 months of intervention, the decrease in average ALT level was not significant in group A (atorvastatin + ASA) while this item in group B (atorvastatin + placebo) was meaningful (P=0.009). Average Child score of participants in both groups improved significantly (P= 0.0001 & 0.002 respectively) and also the liver stiffness measurement by Fibroscan proved a significant decrease (group A; P< 0.001 & group B; P=0.007) . Despite significant decrease in degree of liver stiffness and Child score, there was not any significant difference between 2 groups (P= 0.982 & 0.611 respectively).
Conclusion: While atorvastatin is efficacious in improvement of liver fibrosis and function among cryptogenic cirrhotics, adding aspirin is unable to potentiate its positive effects although this issue worth to further be clarified in future studies.
Disclosure: Nothing to disclose

P0036 RESPONSE OF LIVER AND SPLEEN STIFFNESS TO PORTAL PRESSURE LOWERING DRUGS IN A RAT MODEL OF CIRRHOSIS

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Introduction: Liver stiffness (LS) is increasingly used to screen for liver fibrosis, in addition, spleen stiffness (SS) is an established parameter to assess portal hypertension which is tightly related to the hemodynamics of blood flow and vascular resistance. Little is known about the response of LS and SS to vasoactive substances.
Aims & Methods: We here studied LS and SS in an TAA-induced cirrhosis rat models after exposure to various vasoactive drugs using a miniaturized Fibroscan platform (µFibroscan).
We induced cirrhosis in 47 wildtype 8 weeks old adult male Wistar rats with 200 mg/Kg dosage of Thioacetamide (TAA) through intraperitoneal injection of 50 mg/ml solution 2 times per week for 6 weeks. The six groups consisted of control (sodium chloride), metoprolol, udenafil, enalapril, terlipressin and carvidelol. LS and SS were measured by µFibroscan (Echosens, Paris). The rats underwent general anesthesia with isoflurane inhalation. After anesthesia, abdominal aorta, inferior vena cava and portal vein were cannulated with 24-gauge cannula and connected to Power lab device (AD instruments) to continuously measure the mean arterial pressure (MAP), heart rate (HR) and portal vein pressure (PVP). Drugs were injected systemically and data were collected at time points 0, 15 and 30 mins.
Results: LS and SS was significantly higher in TAA treated rats than in the control group (23.8 vs 3.8 kPa and 19.6 vs 47.8 kPa, P< 0.0001). In addition, they had significantly bigger and heavier spleens (6 vs 4 cm and 2.7 vs 1 gm, P< 0.0001, respectively). In all drugs, LS and SS followed tightly the change of the portal vein pressure (r=0.681and 0.622, P< 0.01, respectively). Also, SS was significantly correlated with spleen size and weight (r=0.723 and 0.663, respectively< 0.01). Noteworthy, a significant decrease of PVP ranging from 22% to 34% (P< 0.05) was seen after 15 to 30 minutes with metoprolol, udenafil, enalapril and carvedilol which was accompanied with a significant decrease in LS and SS ranging from 18.2 to 44% (P< 0.05). (see the Table) Interestingly, with terlipressin, LS and SS only slightly decreased which could be explained by counteracting PVP and MAP. Thus, while PVP decreased by 20% (P< 0.001), MAP increased by 35% (P< 0.001). Overall, carvedilol showed the best response regarding the decrease of PVP, LS and SS. Of note, the heart rate increased after metoprolol and udenafil injection (ca. 10%, P< 0.05), while it decreased in response to terlipressin and carvedilol by ca 30% (P< 0.01).
Conclusion: LS and SS strongly correlates to PVP and responded differently to various vasoactive drugs. Combined non-invasive LS and SS measurement could be useful to monitor the patient's response and compliance to portal pressure lowering drugs.
Disclosure: Nothing to disclose

P0037 BETATROPHIN SERUM LEVEL IS POSITIVELY CORRELATED WITH INSULIN RESISTANCE AND DISEASE SEVERITY IN CIRRHOTIC PATIENTS

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Introduction: Insulin resistance (IR) is frequently associated with chronic liver disease. There has been an increase interest about betatrophin and its involvement in the compensatory response to insulin resistance.
Aims & Methods: To investigate the correlation of betatrophin level with insulin resistance and disease severity in cirrhotic patients. Sixty candidates were included and categorizes into two groups, cirrhosis group: thirty liver cirrhosis patients and control group: thirty healthy controls with matched age and sex. We excluded patients with any medical condition or receiving treatment affecting glucose metabolism. The severity of cirrhosis was classified according to Child Pugh classification and MELD score. Insulin resistance was assessed by the Homeostasis Model Assessment (HOMA-IR). Serum insulin was determined by Enzyme Linked Immuno-

sorbent Assay (ELISA), the sensitivity of the assay was 6.25 IU/ml. Human active betatrophin was analyzed by ELISA technique, the sensitivity of the assay was 0.4 ng/ml.
Results: Insulin resistance was observed in 70% of cirrhotic patients (HOMA-IR= 4 (IQR= 0.50 - 10); p= 0.005). Determinants of insulin resistance were age (p= 0.572, OR= 1.02), cirrhosis (p= 0.019, OR= 4.58) and higher betatrophin level (p= 0.165, OR= 1.04). Subjects with IR had higher betatrophin level than subjects without IR with median level (IQR) of 17.75 (10 - 23.75) vs. 8 (3.75 - 15) ng/ml, respectively, (p= 0.006).
In the overall cohort, betatrophin level correlated with fasting blood sugar (r= 0.521; p <0.001), fasting insulin (r= 0.495; p <0.001) and HOMA-IR (r= 0.405; p= 0.001). Betatrophin level was significantly higher in cirrhotic patients than controls [17.8 (8 - 30) vs. 8 (4 - 12) ng/ml, respectively, (p <0.001)]. Besides, Child-Pugh C patients had higher betatrophin level than Child-Pugh B patients [22.5 (13.25 - 40.25) vs. 15 (6.25 - 19.13) ng/ml, respectively, (p= 0.035)].
Moreover, the highest level of betatrophin was detected in patients with severe ascites followed by moderate and mild ascites [35 (13.13 - 55.25) vs. 18.75 (15 - 25) vs. 13 (2.63 - 17.25) ng/ml, respectively, (p= 0.052)]. In the cirrhosis group, betatrophin level correlated positively with Child-Pugh classification (r= 0.381; p= 0.038), MELD score (r= 0.496; p= 0.005), INR (r= 0.385, p= 0.035), and total bilirubin (r= 0.388, p= 0.034), and correlated negatively with platelets (r= -0.418, p= 0.022).
Conclusion: Plasma betatrophin is increased in cirrhotic patients; in addition, this increase is correlated with disease severity, as well as the emergence of insulin resistance.
Disclosure: Nothing to disclose

P0038 WITHDRAWN

P0039 WITHDRAWN

P0040 PREVALENCE AND PREDICTORS OF ACUTE ON CHRONIC LIVER FAILURE IN CIRRHOTIC PATIENTS HOSPITALIZED FOR VARICEAL BLEEDING

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Introduction: Acute on chronic liver failure (ACLF) is a clinical syndrome characterized by acute liver decompensation in patients with cirrhosis associated with at least one extrahepatic organ failure. This situation is frequently encountered during hospitalizations for complicated cirrhosis by variceal bleeding.
Aims & Methods: The aim of the study was to determine the prevalence and predictors factors of ACLF development in patients with variceal bleeding. A retrospective study was conducted collecting all cirrhotic patients admitted to the hepatology unit for variceal bleeding over 2-years period. We excluded patients with hepatocellular carcinoma. The diagnosis of ACLF was defined according to the criteria of CANONIC study; Grade 1: Isolated kidney failure or isolated organ failure associated with renal dysfunction (creatinine ≥15mg and < 20mg) and/or hepatic encephalopathy grade 1 or 2, or cerebral failure associated with renal dysfunction (creatinine ≥15mg and < 20mg); Grade 2: two organ failures; Grade 3: Three organ failures or more. In subgroup analysis, patients classified into 2 groups: with or without ACLF, were compared.
Results: Overall sixty-nine cirrhotic patients hospitalized for variceal bleeding were included with a sex ratio H/F=1.2. The mean age was 59 years old. The average stay at hospital was 15 days (extremes: 5-36 days). Causes of cirrhosis were: hepatitis C (43%), hepatitis B (23%), nonalcoholic steatohepatitis (15%) and primary biliary cholangitis (13%).
Average evolution of the cirrhosis was 4 years (extremes: 6 months-10 years). 44% of patients admitted for variceal bleeding developed ACLF. There was no difference of the demographics data between the two groups. In patients with ACLF, grade 1 was the most common (52.8%) followed by Grade 2 (40.6%) and Grade 3 (2%).
Bacterial infection was found in 65% of ACLF-reported patients: urinary tract infection (33%), Spontaneous bacterial peritonitis (26%), and pulmonary infection (23%). Intra-hospital mortality was of 50.5% in patients

with ACLF grade 2 and 3. Independent predictors of ACLF were high MELD at admission (p = 0.04), bacterial infection (p < 0.001) and recurrent bleeding (p = 0.06).

Conclusion: In our study, ACLF affects almost half of hospitalized patients for variceal bleeding and is associated with a short-term mortality. High MELD at admission, bacterial infection and bleeding recurrence are predictive factors for the occurrence of ACLF.

Disclosure: Nothing to disclose

P0041 PROLONGED DRAINAGE INCREASES COMPLICATIONS OF LARGE VOLUME PARACENTESIS IN REFRACTORY ASCITES

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Introduction: Large volume paracentesis (LVP) is a common procedure for symptom relief among patients who have advanced cirrhosis with refractory ascites. Prolonged ascitic drainage beyond 24 hours is frequently practised due to the concern of acute kidney injury (AKI) and circulatory dysfunction following LVP.

While prolonged drain duration could lead to secondary bacterial peritonitis (SeBP), only limited data correlates the duration of ascitic drainage with the prevalence of SeBP.

Aims & Methods: We aim to study the correlation between the duration of LVP and the prevalence of SeBP among cirrhotic patients with refractory ascites. All cirrhotic patients who underwent LVP in our institution from 2014 to 2017 were studied. Patients diagnosed with primary spontaneous bacterial peritonitis were excluded. SeBP was diagnosed based on ascitic fluid analysis with neutrophil count >250 cells/mm^3 or positive ascitic fluid culture following recent paracentesis within 7 days.

Standard dose of albumin infusion was given during LVP as per EASL guidelines. Baseline data on patient demographic, duration and complications of LVP were collected. Cases were censored at death, liver transplant or last follow-up. Analyses were performed using chi-squared test and Cox-regression models using SPSS 23.0.

Results: A total of 131 patients underwent LVP were followed-up for 1806 patients-month. The median age was 68.0 years and 86 (65.6%) were male. The median Model for End-Stage Liver Disease (MELD) score was 15; 54.2% and 45.8% were Child-Pugh class B and C respectively. The median duration of ascitic drainage was 2 days.

Overall prevalence of SeBP among these patients was 5.3%. Among patients with SeBP, 71.4% grew resistant organisms from ascitic fluid culture. Ascitic drainage beyond 24 hours significantly increased the prevalence of SeBP (0% vs 8.9%, p=0.026). Patients who developed SeBP had higher Child-Pugh scores (10.3±0.8 vs 9.5±1.2, p=0.027), higher MELD scores (17.1±1.8 vs 15.1±5.4, p=0.028), and lower serum albumin levels (22.1±3.89 vs 25.9±5.46 g/L, p=0.044).

When subgroup analysis was performed among patients with Child-Pugh scores of more than 9, drainage beyond 24 hours remained a significant predictor for SeBP (0% vs 17.9%, p=0.040). SeBP was also associated with higher risk of AKI following LVP (57.1% vs 16.1%, p=0.006) and longer inpatient stay (39.0 vs 12.5 days, p=0.024).

The 30-days readmission rate (p=0.508) and 6-month survival (p=0.327) were similar in patients with and without SeBP. The volume of ascitic fluid drained and the amount of intravenous albumin infusion given were not associated with AKI during LVP.

Conclusion: Ascitic drainage beyond 24 hours increases the risk of SeBP. As SeBP is associated with resistant organisms, higher risk of renal impairment and longer inpatient stay, ascitic drain removal within 24 hours should be considered especially among patients who have advanced cirrhosis with Child-Pugh scores of more than 9.

Disclosure: Nothing to disclose

P0042 CAROTID ARTERY STIFFENESS IN LIVER CIRRHOSIS PATIENTS

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Introduction: Liver stiffness assessment is considered a valid biomarker of cirrhosis.Carotid artery stiffness (CAS) assessment is the new gold-standard in cardiovascular and cerebral-vascular events risk-definition. In fact, it has replaced intima-media thickness measurement, not devoid of technical bias.

In LC, Hepatic encephalopathy (HE) is a frequent complication of decompensated liver cirrhosis (LC) of any cause and can overlap very often with Wernicke -Korsakoffsyndrome (WK), due to alcohol addiction.

Aims & Methods: Thus, we aimed to verify whether CAS decompensation could correlate with LC staging and/or HE/WK.

We consecutively enrolled LC patientsadmitted to the hepatology outpatient clinicof the Internal Medicine Unit of San Benedetto del Tronto General Hospital.They underwent a full LC and anophthalmic artery (OA) and CAS study at the outpatient Neurosonologic Unit of our hospital.Presence of HE and/or WK was assessed by MOCA, Digit and Stroop tests by a dedicated psychologist.

Results: We consecutively enrolled 24 LC patients (20 with alcoholic abuse, 2 with HCV- and 2 with HBV-infection, 6 of metabolic origin; mean age 64.7±10.3 years,6 F, BMI 28.1±1.1 Kg/m^2). Cirrhotic patients had significantly higher CAS index values vs. healthy subjects (beta 9.91±3.0, EP 128.45±39.30 kPa, AC 0.87±0.19mm^2/kPa, AI 16.46±5.2%, PvW 6.62±1.16 m/sec,all p<0.05).

More in detail, beta positively correlated with BMI (r=0.63); AC positively correlated with Child (r=0.67) and with OA PI (r=0.58); pvW inversely correlated with Child (r=-0.61). CAS parameters did not significantly correlate with HE and/or WK presence/grading.

Conclusion: This prospective single-center study showed for the first time the significant correlation between CAS derangement and LC staging, comorbiditiesand cerebral flow characteristics.These preliminary results suggest the possible use of CAS as biomarker for LC patients follow-up and management.

Disclosure: Nothing to disclose

P0043 CIRRHOTIC PATIENTS: IS THERE ANY ROLE TO MALNUTRITION IN PREDICTING MORTALITY?

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Introduction: Protein-caloric malnutrition and sarcopenia are common conditions in liver cirrhosis and are associated with poor prognosis and decreased survival.

However, it remains to be enlightened whether deficient nutritional status predicts mortality in liver cirrhosis.

Aims & Methods: Aim: To compare if the incorporation of sarcopenia into the Meld score (Meld-Psoas) may improve the prediction of mortality in liver cirrhosis when compared to Meld and Meld-Na scores.

Methods: retrospective study, included cirrhotic patients with computed abdominal tomography study between 2007 and 2017. Analytical parameters (creatinine, total bilirubin, INR and sodium) were analyzed and the transverse diameter of the right psoas muscle (TPMT) was determined at the cross-sectional level of L3-L4. The analytical parameters were collected within ± 7 days of the abdominal tomography.

The Meld-Psoas score: ([0.2xMELD] - [0.08xTPMT / height] +2), MELD and MELD-Na were calculated. A descriptive analysis and a ROC curve was performed to compare the predictive capability of each score to predict mortality at 6 weeks, 3, 6 and 12 months.

Results: 78 patients were included, 76.2% male gender with mean age of 56.5±11.6 years. 89.7% of the patients presented alcoholic cirrhosis. 46 patients (59%) presented ascites and 10 (12.8%) hepatic encephalopathy. Patients presented a median creatinine of 0.89 (0.4-3.89)mg/dl, a bilirubin of 1.6 (0.25-18.61) mg/dl, INR of 1.4 (0.9-3.3) and sodium of 138.0 (123-145) meq/l. Regarding the scores, they presented a median Meld of 13.0 (6-43), a Meld-Na+ of 14.0 (6-42) and Meld-Psoas of 3.1 (1.32-9.4).

Meld-Psoas presented an AUROC of 0.90 (0.81-0.95, CI95%), 0.87 (0.77-0.93) and 0.86 (0.77-0.93) and 0.87 (0.78-0.94) predicting mortality at 6 weeks, 3, 6 and 12 months respectively.

Meld presented an AUROC of 0.88 (0.79-0.94), 0.83 (0.73-0.91), 0.83 (0.73-0.91) and 0.84 (0.74-0.91) predicting mortality at 6 weeks, 3, 6 and 12 months respectively.

Meld Na+ presented an AUROC of 0.87 (0.78-0.94), 0.82 (0.72-0.90), 0.82 (0.72-0.90), 0.84 (0.74-0.91) predicting mortality at 6 weeks, 3, 6 and 12 months respectively.

Meld-Psoas of 0.71 predicts 6 week mortality with a sensitivity of 100% and a specificity of 71%.

Conclusion: The incorporation of sarcopenia in Meld score (Meld-Psoas) presented an excellent accuracy in predicting mortality of cirrhotic patients, in particular 6 week mortality, superior than the observed in previous scores (Meld, Meld-Na+).

Disclosure: Nothing to disclose

P0044 MONITORING INFLAMMATORY ACTIVITY IN CROHN'S DISEASE: SIMPLE ULTRASONOGRAPHIC SCORE VERSUS CEUS WHICH ONE TO USE?

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Introduction: Gastrointestinal Ultrasound (GIUS) is increasingly being used in Crohn's Disease (CD) as an essential tool in monitoring inflammatory activity, given its low cost and the absence of ionizing radiation exposure. In 2017 emerged a simple ultrasonographic score (SUS) that allows the accurate noninvasive assessment of inflammatory activity based on 2 parameters: bowel wall thickness (bwt) and color Doppler.

Aims & Methods: The aim of this study was therefore to compare the accuracy of bowel GIUS with SUS versus Contrast Enhanced Ultrasound (CEUS) in predicting inflammatory activity in ileocolonoscopy.

All CD patients underwent a conventional GIUS directed to terminal ileum followed by a CEUS using a microbubble contrast agent (SonoVue®). GIUS examinations were performed using a Hitachi HI VISION Avius®, employing a linear abdominal transducer. Qualitative and quantitative parameters from the sonographic analysis included maximum bowel wall thickness (bwt), semi-quantitative analysis of vascularity pattern by Doppler GIUS and quantitative measurement of contrast bowel wall enhancement using CEUS (peak intensity). SUS was calculated according to the authors = (0.0563xbwt1) + (2.0047xbtw2) + (3.0881xbwt3) + (1.0204xdoppler1) + (1.5460xdoppler2).

Disease activity was assessed by ileocolonoscopy (reference) and patients were graded as inactive (normal or mild disease) or active (moderate or severe inflammation).

Results: Thirty known CD patients were included, 60% female with median age 33.5 (17-63) years. Regarding endoscopic disease severity, 14 (46.7%) patients presented inactive disease and 16 (53.3%) patients were classified as active disease.

Median bwt was 6.1 (3-13) mm and Doppler intensity was absent in 1 patient (3.3%), mild in 7 patients (23.3%) and moderate to severe in 22 patients (73.3%). Patients presented a median SUS of 5.1 (0.1-12.4) and was not different between patients with active or inactive disease (p=0.50) with a poor capability to predict endoscopic activity in ileoscopy (AUROC 0.6, 95% CI 0.38-0.75).

Regarding CEUS, the median peak intensity was 10.9 (2.5-44) and was related with disease severity (p=0.005) with a good capability to predict endoscopic activity in ileoscopy (AUROC 0.8, 95% CI 0.61-0.92). We found that peak intensity of 7.8 is the optimal cut off point predicting active disease with a sensitivity of 87.5% and a specificity of 71.4%.

Conclusion: Although SUS is a validated score including bowel wall thickness and color Doppler parameters, in our population was not capable to predict with good accuracy endoscopic activity. CEUS is an emerging technique that must be considered routinely part of the entire sonographic evaluation in CD with good diagnostic accuracy for bowel inflammation.

Disclosure: Nothing to disclose

P0045 TARGETED VISUALIZATION OF CELL ADHESION MOLECULES IN PATIENTS WITH LIVER CIRRHOSIS BY MOLECULAR ENDOSCOPIC IMAGING

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Introduction: The degeneration of intestinal barrier integrity plays a pivotal pathophysiological role in patients with liver cirrhosis leading to bacterial translocation and the development of complications including spontaneous bacterial peritonitis, hepatic encephalopathy, hepatorenal syndrome, progression of liver injury and hepatocellular carcinoma. Previous studies have shown the potential of molecular endoscopic imaging (MEI) for identification of disease specific molecular alterations in patients with chronic inflammatory bowel disease and colorectal polyps. To date, no data is available on the applicability of MEI for cirrhotic patients.

Aims & Methods: To assess the diagnostic applicability of MEI for diagnosis of intestinal barrier function in patients with liver cirrhosis. Afterwards the results of compensated and decompensated patients and controls were compared.

Patients with confirmed liver cirrhosis and control patients undergoing surveillance gastroscopy were recruited for the study. A total of 20 samples were obtained from duodenum of the enrolled patients. Specimen were first washed with PBS and then incubated with FITC labeled Claudin-1 and Connexin-43 antibodies. After washing in PBS to remove unbound antibody, MEI was performed using the probe-based confocal imaging system with a scan rate of 12 frames per second and a scanning field of 30,000 pixels. Similar examinations were performed with specifically developed biodegradable and pH sensitive inorganic nanoparticles conjugated with FITC labeled antibodies. After MEI, specimens were fixed in 10% formalin and processed for immunohistochemical analysis.

Results: Specific fluorescence signals were observed in all samples studied, including cirrhotic patients and controls. Claudin-1 and Conexin-43 signals were highest in controls. Reduced expression was found in cirrhotic patients. Alterations were more apparent in decompensated patients compared to the compensated liver cirrhotic patients. Of note, MEI was achieved with both, traditional antibody staining and by means of nanoparticles.

Conclusion: Molecular endoscopic imaging of cell adhesion molecules in patients with liver cirrhosis is feasible and showed reduced expression in decompensated patients. The data indicated that an impaired gut barrier function in patients with liver cirrhosis might be related to disease specific complications.

Next studies should focus to assess the impact of pharmaceutical therapies, like that of non-selective beta-blockers, on the intestinal barrier function. Moreover, MEI might help in developing new specific risk scores for cirrhotic patients.

Disclosure: Nothing to disclose

P0046 HEPATITIS B SCREENING PRIOR TO CHEMOTHERAPY IN THE MIDDLE EAST: A RETROSPECTIVE COHORT STUDY

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Introduction: The global burden of hepatitis B virus (HBV) infection has been increasingly recognized, placing it among the 20 most common causes of mortality worldwide. Lebanon is considered to be of moderate endemicity. Acute infection in immunocompetent adults resolves spontaneously in the vast majority of cases. HBV DNA persists in all affected individuals, rendering them susceptible to reactivation in certain immunosuppressive conditions.

Reactivation can be asymptomatic or manifest as fatal fulminant hepatitis. Most international guidelines recommend HBV screening for patients anticipated to receive immunosuppressive therapy.

Aims & Methods: To determine screening rates and modalities of HBV screening in patients receiving chemotherapy at the American University of Beirut Medical Center (AUBMC), a leading tertiary care center in Lebanon and the Middle East, and compare it to the international recommendations. To establish local national guidelines for HBV screening in patients planned to receive chemotherapy. A retrospective cohort review of electronic medical records of all adult patients who received chemotherapeutic agents on the hematology-oncology service at AUBMC between June 2015 and June 2016 was performed. The information retrieved from the records included patient demographics, type of malignancy (solid organ or hematological), and if the patients underwent hematopoietic stem cell transplantation (HSCT) in case of hematological malignancies. The laboratory tests performed for HBV screening were reviewed and documented. Adequate screening was defined as performing all of the following tests: HBsAg, anti-HBs Abs, and anti-HBc Abs (total). Statistical analysis included simple descriptive statistics (using % for categorical variables and mean for continuous variables).

Results: A total of 1547 patients were initially screened. 277 were excluded from the study (221 were younger than 18, and 56 did not receive chemotherapy). Most of the patients were males (579 ,45.6%), and 691 (54.4%) were females with a mean age of 56 (range 18 to 96). The majority of the included patients had solid organ malignancies (888, 70%), and the rest (382, 30%) had hematologic malignancies, of whom 111 underwent HSCT. Of those included, 303 (24%) patients were screened by at least one test for HBV. 42 (3.3%) were adequately screened (7 in solid organ malignancies, and 35 in hematological malignancies, including 19 of HSCT patients); 45 (3.5%) were tested only for HBsAg and anti-HBs Abs; 8 (0.6 %) for anti-HBs Abs alone; 50 (3.9%) for HBsAg and anti-HBc Abs; and 158 (12.4%) for HBsAg alone. Of those tested, 25 patients were positive for at least one serological test. HBV DNA was performed on 20 of them.

Screening test performed	None performed	At least 1 test performed	HBsAg only	Anti-HBs Abs only	HBsAg and anti-HBs Abs	HBsAg and Anti-HBc Abs	HBsAg, anti-HBsAbs, anti-HBc Abs (combination)
Hematologic malignancy	141 (36.9%)	241 (63.1%)	123 (32.2%)	3 (0.8%)	38 (9.9%)	42 (11.0%)	35 (9.2%)
Solid malignancy	826 (93.0%)	62 (7.0%)	35 (3.9%)	5 (0.6%)	7 (0.8%)	8 (0.9%)	7 (0.8%)

[Hepatitis B screening patterns among solid and hematologic malignancies; HBsAg: HBV surface antigen]

Conclusion: Rates of screening for HBV prior to chemotherapy in a tertiary care center in the middle east are still low. When performed, screening was not always complete and adequate. Also, patients with hematologic malignancies were more likely to be screened. There is an urgent need to implement a better screening policy at AUBMC. Increased awareness among physicians is required and establishing a standardized protocol for pre-chemotherapy screening and management is needed at the institutional and national levels.

Disclosure: Nothing to disclose

P0047 TREATMENT OUTCOMES OF HEPATITIS C VIRUS RECOMBINANT FORM 2K/1B WITH SOFOSBUVIR BASED REGIMENS IN GEORGIA

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Introduction: The estimated prevalence of hepatitis C virus (HCV) infection in the Republic of Georgia is one of the highest in the world. Interestingly, latest data suggest, that up to 20% of all genotypes (GT) in Georgia belong to the HCV intergenotypic recombinant form 2k/1b (RF_2k/1b), which appears to show the highest prevalence of this recombinant virus so far reported worldwide.

Aims & Methods: The aim of our study was to define optimal treatment regimen for RF_2k/1b within hepatitis C virus elimination project in Georgia.

We retrospectively analyzed the data of GT2 patients identified by INNO-LiPA VERSANT HCV Genotype 2.0 in Medical Center Mrcheveli from May 2015 to May 2016. Partial genome sequencing of core and NS5B regions was performed for identification of RF_2k/1b variants before treatment. All interferon eligible recombinants were treated with Sofosbuvir (SOF) plus Pegilated Interferon (PegINF) plus Ribavirin (RBV) for 12 weeks and interferon ineligible patients with SOF/RBV 24 weeks. We compare SVR12 rates of RF_2k/1b to pure GT2 treated with SOF/RBV-12 or SOF/RBV-20 (depending on presence of cirrhosis). Also we performed regenotyping and partial sequencing of core and NS5B region in randomly selected 20 samples from 95 GT2 (by INNO-LiPA VERSANT) treatment failures from other medical centers treated with SOF/RBV 12 or SOF/RBV 20 weeks.

From May 2016, after SOF/LDV became available, all RF1_2k/1b patients were treated with SOL/LDV+RBV for 12 weeks, irrespective of liver damage, like GT2 patients. Only RBV ineligible patients receiving RBV free regimen - SOF/LDV for 12 weeks, like GT1 patients.

Results: A total number of 67 HCV GT2 samples by INNO-LiPA were analyzed, in which 43 (64%) RF_2k/1b were identified. Antiviral therapy in 23 out of 24 GT2 patients with SOF/RBV for 12 or 20 weeks (depending on presence of cirrhosis) was initiated and SVR12 rates was achieved in 22/23 (96%) patients. 36 out of 43 RF_2k/1b patients were treated with either SOF/PegINF/RBV for 12 weeks (n=24) or with SOF/RBV for 24 weeks (n=12) depending on interferon eligibility criteria. 23/24 (96%) patients achieved SVR 12 rates in interferon-containing group and 9/12 (75%) patients in group without interferon.

From unspecified genotype 2a/2c patients (n=446) who were treated with SOF/RBV for 12 or 20 weeks depending on presence of cirrhosis, 95/446 (21%) relapsed. Partial genome sequencing of core and NS5B regions of 20 randomly selected samples from 95 treatment failed patients was performed. All samples were consistent to RF_2k/1b.

From May 2016 to May 2018, after introduction of SOF/LDV regimen, a total number of 336 RF1_2k/1b patients were treated. 30 (9%) of patients lost from follow-up.

From total 306 patients, SVR12 were achieved in 303 patients (99%)

From 306 patients, in 294 patients, who were treated with SOF/LDV+RBV for 12 weeks, SVR rate were achieved in 292 (99%) patients.

From 306 patients, in 12 RBV ineligible patients, who were treated with SOF/LDV- 12 week, SVR rate were achieved in 11 (92%) patients.

Conclusion: Our findings suggest that treatment of RF_2k/1b patients with SOF/PegINF/RBV for 12 weeks was more effective than with SOF/RBV for 24 weeks (p = 0.061).

Also we can conclude, that SVR12 rate was significantly higher in GT2 patients, confirmed by sequencing, treated with SOF/RBV 12 or 20 weeks than in unspecified GT2, who were treated with the same regimen (p < 0.05).

Treatment of HCV RF_2k/1b with SOF/LDV regimen with or without RBV is as effective as GT1 patients.

References: Zakalashvili M, Zarkua J, Weizenegger M, et al. Identification of hepatitis C virus 2k/1b intergenotypic recombinants in Georgia. Liver Int. 2018;38:451-457 Messina JP, Humphreys I, Flaxman A et al. Global distribution and prevalence of hepatitis C virus genotypes. Hepatology 2015; 61:77-87. Mitruka K, Ward JW, Averhoff F et al. Launch of a Nationwide Hepatitis C Elimination Program--Georgia, 2015 Jul 24;64(28):753-7. Kalinina

O, Norder H, Mukomolov S et al. A natural intergenotypic recombinant of hepatitis C virus identified in St. Petersburg. J Virol 2002; 76(8):4034-4043. Hedskog C, Doehle B, Chodavarapu K et al. Characterization of hepatitis C virus intergenotypic recombinant strains and associated virological response to sofosbuvir/ribavirin. Hepatology 2015; 61(2):471-480. Susser S, Dietz J, Schlevogt B, et al. Origin, prevalence and response to therapy of hepatitis C virus genotype 2k/1b chimeras. J Hepatol. 2017; ttps://doi. org/10.1016/j.jhep.2017.05.027 Zarkua J, Zakalashvili M, Metreveli D, Identification of recombinant strains in HCV genotype 1 and 3: Is it needed? Liver Int. 2018; DOI: 10.1111/liv.13729
Disclosure: The authors report no conflicts of interest.

P0048 SAFETY AND EFFICACY OF A LOW MONITORING TREATMENT STRATEGY, WITH SECOND GENERATION DIRECT-ACTING ANTIVIRALS, IN HCV MONO INFECTED PATIENTS WITHOUT CIRRHOSIS: A PORTUGUESE REAL LIFE COHORT

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Introduction: The 2[nd]generation direct acting antivirals (DAAs) brought hope regarding elimination of chronic hepatitis C (CHC), as a global Public Health issue. Further simplification of on treatment surveillance will save costs and help physicians in scaling up treatment, representing an improvement in the "cascade of care" framework. Real life data, about efficacy and safety of low monitoring strategies, is sparse and necessary.
Aims & Methods: Prospective study with CHC patients, treated for the first time with DAAs, without ribavirine, between January 2017 and March 2018, without on treatment scheduled visits and laboratory monitoring. Exclusion criteria were: fibrosis stage F4, hepatocellular carcinoma, HIV or HBV coinfection and ongoing additive substance abuse. The outpatient clinic had 1 consultant hepatologist, 3 gastroenterology assistants and 2 hepatology nurses.
All patients had a complete baseline medical and nurse evaluation. A direct telephonic number for on demand nurse consultation was available. A medical visit, with laboratory and viral load evaluation, was scheduled 12 weeks after the end of treatment.
Results: 82 enrolled patients (63% male; 41-78 years); Genotype distribution: G1 - 38 (47% 1b), G3 - 23, G4 - 10 and G5 - 1. Treatment regimens were chosen according to EASL guidelines at the time: 65 were sofosbuvir based and 17 protease inhibitor based (29% pan genotypic).
Only one patient discontinued treatment (lost to follow up) and 4 forgotten blood collection for RVS12, despite attending the medical visit. Minor adverse events were 0,02%, without any serious adverse events.
None of the patients required on treatment medical visits. Sustained virological response (SVR12) was 94% (77/82) in intention to treat and 100% (77/77) in *per protocol* analysis.
Conclusion: In this real life cohort cohort of "easy to treat patients", a low monitoring treatment stategy, was safe and achieved high adherence and efficacy, without virologic failures. These results support the adoption of simplified treatment surveillance protocols, whenever possible, as a cost-effective tool in the achievement of CHC elimination goals.
References: 1- Shahid I, AlMalki WH, Hassan S et al Real-world challenges for hepatitis C virus medications: a critical overview. Crit Rev Microbiol. 2018 Mar;44(2):143-160 2- VanOpdorp JR, Ferrentino N, Strader DB, et al Utility of laboratory monitoring during hepatitis C treatment with ribavirin-free direct acting antiviral regimens. J Viral Hepat. 2019 doi: 10.1111/jvh.13083. 3- Marco VD, Alberti A, Angarano G et al Optimising management of patients with hepatitis C virus in the age of direct-acting antivirals: results of a Delphi consensus Eur Rev Med Pharmacol Sci 2018; 22 (20): 7024-7033. 4- Kapadia SN, Marks KM Hepatitis C Management Simplification From Test to Cure: A Framework for Primary Care Providers. Clin Ther. 2018 Aug;40(8):1234-1245. 5- EASL Recommendations on Treatment of Hepatitis C 2018 Journal of Hepatology 2018 vol. 69 j 461-511
Disclosure: Nothing to disclose

P0049 BASELINE LIVER STEATOSIS EXCEEDS ADVANCED FIBROSIS AS A PREDICTOR OF POOR OUTCOME IN CHRONIC HEPATITIS C PATIENTS WITH SUSTAINED VIROLOGIC RESPONSE

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Introduction: Sustained virological response (SVR) results in reduced incidence of hepatocellular carcinoma (HCC) and mortality among chronic hepatitis C (CHC) patients with advanced fibrosis. Both advanced fibrosis and liver steatosis (LS) may coexist in CHC patients.
Aims & Methods: The present study was design in order to evaluated the individual effects of LS and advanced fibrosis on a composite outcome of all-cause mortality and HCC in CHC patients with SVR following direct-acting antivirals (DAA) treatment. In the study we retrospectively evaluated 515 consecutive CHC patients who achieved SVR following treatment with DAA, with a mean follow up of 24 months. Baseline liver fibrosis was assessed by transient elastography and LS was validated by at least 3 independent ultrasonographic examinations.
Results: 211 of 515 patients (41%) had baseline LS. The incidence rate of of HCC were 2.61 cases (95% C.I 2.47 - 2.85) of HCC per 100 person-years in all the cohort, and 5.23 cases (95% C.I 4.85 - 5.71) per 100 person-years in patients who had LS. In addition, patients with LS had a higher cumulative rates of all-cause mortality and HCC at 2 years of follow up compared to patients without LS (15.75% and 2.79%, respectively p < 0.001), although they did not have increased incidence of advanced fibrosis or cirrhosis. Consistently, multivariate analysis showed that LS was associated with a significant 7.5-fold increased risk of all-cause mortality and HCC (HR 7.51, 95% C.I 3.61 - 13.36, p < 0.001) even upon adjustment to the components of the metabolic syndrome, whereas advanced fibrosis showed only a trend toward statistical significance (HR 2.32, 95% C.I 0.97 - 6.59, p = 0.06). Finally, when divided into four groups according to fibrosis and steatosis status at baseline, patients who had both LS and advanced fibrosis had the highest risk to develop the composite outcome (HR 17.56, 95% C.I 2.37 - 75.11, p = 0.005) while the presence of LS without advanced fibrosis at baseline was also significantly associated with the composite outcome (HR 9.21, 95% C.I 1.11 - 62.53, p = 0.030). Interestingly, the presence of advanced fibrosis without LS was not significantly associated with the composite outcome of all cause mortality and HCC (HR 1.96, p = 0.538).
Conclusion: LS is a major predictor of all-cause mortality and HCC in patients who achieved SVR following DAA treatment regardless of fibrosis stage. These patients should be rigorously screened for HCC.
Disclosure: Nothing to disclose

P0050 COMPARATIVE STUDY FOR RETREATING PATIENTS WHO FAILED TO PRIOR SOFOSBUVIR/ DACLATASVIR REGIMEN: AN OPEN LABELED RANDOMIZED TRIAL

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Introduction: Treating HCV patients with NS5A-containg protocols such as sofosbuvir/ daclatasvir (SOF/DCV) regimens is still very effective. However, a minute number of patients may experience treatment failure. Retreating those patients is still challenging due to the possibility of NS5A resistance-associated substitutions (RASs).
Aims & Methods: To compare the results of re-treating those patients with 2 different protocols.
Methods: From a total of 4585 patients treated with sofosbuvir/ daclatasvir± ribavirin regimen for 12 weeks, only 92 patients (2%) failed to achieve sustained virologic response at week 24 (SVR-24). Eighty patients were randomly re-treated either by Sofosbuvir(400mg)/Daclatasvir(60mg)/

Simeprevir(150mg)/Ribavirin (SIM-group, n=40) versus Sofosbuvir(400mg) /Ombitasvir(25mg)/ Paritaprevir(150mg) /Ritonavir(100mg) /Ribavirin (OPr-group, n=40) for 12 weeks. All recruited patients were compensated cirrhotic. Patients with decompansated liver, HBV co-infection and hepatocellular carcinoma (HCC) were excluded. The mean duration for re-start new treatment was 12±3 weeks.

Results: In SIM-group, SVR-24 was 92.5% (n=37) and 3 patients failed to achieve SVR. In OPr-group, SVR24 was 90% (n=36) and 4 patients failed. All failed-to-treat patients were males, F3/F4 fibrosis score, and diabetic. No major adverse events were reported.

Conclusion: Re-treating patients with previous NS5A failure is possible and safe with satisfactory results.

References: ClinicalTrials.gov ID: NCT03549832

Disclosure: Nothing to disclose

P0051 PREDICTORS OF DETECTION OF HBV IN PBMCS AMONG NAIVE PATIENTS WITH SERUM HBV-DNA NEGATIVITY

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Introduction: Studies tackled the extra-hepatic reservoir of hepatitis B virus (HBV), especially in those with negative peripheral viremia, are still scarce.

Aims & Methods: Therefore, we aimed to investigate the presence of HBV DNA in peripheral blood mononuclear cells (PBMCs) and evaluate different factors affecting this.

Patients and methods: Between January 2018 and December 2018, a cross-sectional study was designed to include all consecutive patients with proven CHB. From these cases, naive patients (without previous treatment) with persistently negative HBV viremia were selected. HBV DNA was tested in PBMCs All cases were tested also for anti-HBc-Ab, HBe-Ag, HBe-Ab and HCV-Ab, and quantitative HBs-Ag (qHBs-Ag). Assessment of hepatic stiffness score measurements was done by Fibroscan.

Results: A total of 1650 naive CHB patients were recruited. Out of them, 320 (19.4%) patients (75% were male [n=240], mean age was (38.4 ±12.8 years) have a persistently negative serum real-time PCR for HBV-DNA without previous treatment experience. More than half of them (n=170, 53.1%) exhibited positive HBV-DNA in PBMCs. The mean Log10 of quantitative HBV-DNA by PCR in PBMCs was 5.1±0.3 IU/ML. HCV co-infection was found in 30 patients (17.6%). Most of them had insignificant fibrosis scores (less than F2). The multivariate Logistic regression analysis for prediction of presence of detectable HBV-positive viremia in PBMCs yielded the following risk factors (OR): The presence of HBV anti-core (OR =37.2), presence of HCV-RNA (OR =1.7) and RNA (OR =1.7) and a log_{10} of qHBs-Ag more than 3 (OR =1.1).

Conclusion: A considerable number of patients with negative plasma HBV DNA are still harboring subtle form of virus within remote extra-hepatic compartments. So, dual testing for both plasma and PBMCs is mandatory especially in epidemiologic studies.

Disclosure: Nothing to disclose

P0052 OFF TRAIL TREATMENT OF HÉPATITIS C WITH HEMODIALYIS PATIENTS, RESULTS OF AN ALGERIAN COHORT

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Introduction: There is a constant growth in the number of hemodialysis patients in our country with a prevalence of 23,8% of infection with hepatitis C[1], unfortunatly there is no adapted treatment for this population in Algeria; With the risk of contamination that increases with time[2] and the complication that goes with it, we had to treat our patients with the antiviral therapy in our disposal.

Aims & Methods: Highlight the difficulties associated with the management of hemodialysis patients with viral hepatitis C (VHC), particularly with the unavailability of adapted drugs in some countries like Algeria.

Prove the effectiveness of current therapies outside consensual indications. A prospective descriptive study, including all patients treated for (VHC) on dialysis over a period of one year (January 2017-January 2018).

29 patients were treated, all included in our study.

The treatment was: Sofosbuvir 400mg / Ledipasvir 90mg +/- Ribaverine for 12 or 24 weeks.

The treatment was taken after each dialysis.

All patients received a complete clinical examination, a biological assessment with genotype identification and an assessment of liver fibrosis (fibroscan / fibrotest).

Regular monitoring every 4 weeks with assessment of tolerance, compliance, transaminases and blood count was performed.

A viral load was requested in pre-therapeutic, end of treatment and 12 weeks after the end of treatment.

Results: Total number of patients was 29, of whom 28 were naive to any treatment.

The mean age was 46 ± 20 years, with a sex ratio of close to 1

Average viral load of 500 * 10³ / ml (4.7Log)

We had to treat 7 cirrhotic patients, 5 patients had a treatment duration of 24 weeks (hemoglobin < 10g / dl); the remaining two were treated in combination with Ribaverine for 12 weeks.

Genotype 1b was found in 100% of patients.

We had 96% sustained viral response (SVR)

Only one patient had a positive viral load at week 12 (naïve non-cirrhotic patient).

28% of patients complained of headache, asthenia and only one case of severe anxiety was reported.

100% of the group treated with Ribaverine benefited from an optimization of Erythropietine injections.

No patient had to stop the treatment.

Conclusion: The renal clearance of Sofosbuvir makes it difficult to handle in patients with IRCT, however our study shows that with close and strict monitoring we get a sustained viral response in more than 95% of patients with no significant side effects, however more exhaustive studies, with dosage of active metabolites should be conducted to support our results.

References: (1) : National Algerian survey MSRH-IPA2008 on 7502 samples (2) : High Prevalence of Infection in Dialysis and Multi-Transfused Patients Involving Diverse and Novel Virus VariantsAug 2012

Disclosure: Nothing to disclose

P0053 ASSOCIATION OF GENETIC POLYMORPHISM OF TOLL LIKE RECEPTORS2(TLR2) AND (TLR4) WITH SUSCEPTIBILITY TO HCV INFECTION, RESPONSE TO TREATMENT AND PROGRESSION TO HEPATOCELLULAR CARCINOMA IN CIRRHOTIC PATIENTS

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Introduction: Chronic hepatitis C virus (HCV) infection is a major cause of chronic liver disease, leading to progressive hepatic fibrosis with long-term progression to cirrhosis and hepatocellular carcinoma (HCC).

HCV has different effects on TLR pathway stimulation which enhances proinflammatory cytokine production leading to liver damage and viral persistence by evasion of the immune response . Lipopeptide complexes of the HCV core protein were found to stimulate the innate immune response via TLR2 and TLR4. Many studies have shown that genetic variation in TLRs may affect susceptibility to infections.

Aims & Methods: In the current study 9 of single-nucleotide polymorphisms (SNPs) and haplotypes of SNPs in TLR 2 and TLR4 were investigated to clarify their association with clinical outcome of hepatitis C, response to treatment, progression to cirrhosis and development of HCC. In this study a total of 3295 individuals from 725 families were recruited and

categorized as Chronic HCV (CHC) , Spontaneous virus clearance (SVC) and control groups . The treated patients were classified into responders (RST) and non responders (NRST) .In addition to patients with liver cirrhotic(LC) and Hepatocellular carcinoma(HCC) were also included. All subjects were genotyped for 5 snips of TLR 2 and 4 snips of TLR4 and their haplotypes using allelic discrimination real-time PCR.

Results: The carriage of minor alleles in different TLR 2 SNPs is associated with HCV chronicity compared to sponatenous clearance (SVC)group.The peak of association was observed with the A allele of rs13105517 s.

The peak of risk of HCC was observed with allele C of rs3804099 (<0.0001). A strong association was also detected for the carriage of T allel of rs1816702 and the allele A of both rs13105517 and rs1898830 (*P*<0.008, 0.00001, and 0.0002 respectively).

Finally, a strong association was found with allele T of rs1816702 and allele C of rs3804099 in non-responder compared to that of responder group (P<0.0001 and 0.0029 respectively).

As regard TLR4 the peak of risk of chronicity was observed with the C allele of rs10116253 in addition to a strong association of allele A of rs5030728 and allele G of rs4986790 in CHC compared to that of SVC group(p<0.0001, <0.0001 and 0.0022) respectively. However no association with T allel of rs4986791 . The carriage of minor alleles of three SNPs of TLR4 was associated with HCC compared to that of cirrhotic group. The peak of risk with C allele of rs10116253 while a strong association was observed for allele A of rs5030728 and allele T of rs4986791 in HCC group compared to that of LC group(p< 0.001) . The carriage of rare allele of different SNPs of TLR4 was significantly higher in non-responder group compared to that of responder group (p<0.0001) with peak at allele A of rs5030728.

A signification association of haplotype CAGT of TLR4 and ATAC of TLR2 with CH and HCC groups in comparison to others.

Conclusion: There is an association of minor alleles of TLR2 and TLR4 with outcome of HCV infection, response to therapy and development of HCC in cirrhotic patients ,especially the allele A of rs13105517 and allele C of TLR4 rs10116253 are strongly associated with HCV chronicity and development of HCC.

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P0054 EFFECT OF DIRECT ACTING ANTIVIRAL THERAPY FOR HEPATITIS C- INFECTED PATIENTS ON CHANGES IN THE PARAMETERS OF LIVER FIBROSIS PROGRESSION

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Introduction: Liver fibrosis is the most important prognostic factor in chronic hepatitis C virus (HCV) patients, and Egypt shows the highest worldwide HCV prevalence. Recently, direct acting antivirals (DAAs),medicines with direct activity against HCV, were introduced for treatment of HCV with very favorable results regarding viral cure, but liver fibrosis is still an unresolved problem. Our study was done to assess to what degree viral cure results in regression of liver fibrosis

Aims & Methods: The aim of this study was to investigate the degree of liver stiffness measurement (LSM) improvement after successful HCV eradication.This study included 100 chronic HCV Egyptian patients, and was conducted at The Egyptian Liver Foundation-Beni Suef, from August 1, 2017 till February 1, 2018. LSM was obtained by FibroScan® before starting direct acting antiviral (DAA) treatment, after the end of 12 weeks of treatment, and after achieving sustained virological response-12 (SVR-12). Based on baseline LSM, patients were stratified into F2, F3 and F4 groups (METAVIR), as F0-F1 patients were excluded. LSM and laboratory data after the end of treatment and after achieving SVR-12 was compared with that before starting therapy in each fibrosis group, p-value =0.050 was statistically significant.

Results: Following DAA treatment, 100 patients achieved SVR-12. Mean baseline LSM dropped from 13.5 to 10.1 kPa post-SVR12; the maximum change occurred in F2 patients 84.3% versus 84.2%, 43.3% in F3, and F4 patients respectively (p< 0.001). At baseline, 30 patients were in the F4 group; only 11 (43.3%) regressed to non-cirrhotic range (< 12.5 kPa), while 19 (56.7%) were still cirrhotic despite achieving SVR-12 (p< 0.001). Patients showed significant improvement in Platelets count and decreased ALT levels after achieving SVR (p< 0.001).

Conclusion: Successful eradication of HCV results in significant LSM improvement; the best improvement occurs in F2 patients. But as the majority of cirrhotics are still at risk for liver decompensation and hepatocellular carcinoma development despite achieving SVR-12, early detection and treatment are highly recommended.
Disclosure: Nothing to disclose

P0055 SIMPLE SCORE FOR PREDICTORS OF HEPATOCELLULAR CARCINOMA OCCURRENCE AFTER HEPATITIS C VIRUS ERADICATION BY DIRECT-ACTING ANTIVIRAL TREATMENT

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Introduction: Hepatitis C virus (HCV) infection is a high risk factor related to liver cirrhosis (LC) and the occurrence of hepatocellular carcinoma (HCC). Interferon (IFN) / Ribavirin (RBV) combination treatment for hepatitis C was performed as a standard treatment, but the cure rate remains poor. n recent years, Direct Acting Antivirals (DAA) has been developed against HCV infection, and currently the IFN-free DAA treatment dramatically improves the cure rate to more than 90% and is also safe to use for patients with HCV. Patients with HCV treated with DAA still exhibited the occurrence of HCC. Therefore, the aim of this study is to identify predictors of hepatocellular carcinoma occurrence after DAA treatment.

Aims & Methods: The remaining task is to predict the risk of HCC in infected patients with HCV after obtaining SVR with IFN-free DAA treatment. The patient grouping with high risk of HCC need closed surveillance program. Therefore, to establish a simple scoring system using general clinical data to predict the risk of HCC after 12 week SVR (SVR 12) following DAA treatment, we evaluated the clinical features of patients who acquired SVR12 by DAA administration retrospectively.Of 1454 HCV-infected patients from September 2014 to November 2018, we enrolled 1088 who achieved sustained virologic response (SVR) and had no history of HCC treatment. We analyzed the incidence of HCC and predictors contributing to HCC occurrence after DAA treatment using patient background and blood tests before and after DAA treatment.

Results: During this study, HCC developed in 26 cases. The incidence of HCC was 0.61 %, 1.88 %, 2.82 %, and 3.71 % at 0.5,1, 1.5 and 2 years at the end of DAA treatment respectively. Multivariate analysis identified Male gender (HR=1.1902; 95% CI 1.0155- 1.3946; P=0.0316) and AFP at the start (HR=1.0023; 95% CI 1.0002 - 1. 0049; P=0.0330) as independent factors that contributed to HCC occurrence after DAA treatment. The cut-off value of AFP at the start of DAA treatment was set as 6.0 ng/mL, based on the ROC value for developing HCC based on the serum AFP level at the start of DAA treatment noted in the original set (sensitivity 0.8400 and specificity 0.6315, area under the curve 0.743). Using these factor, our novel scoring system (0 to 2 points) was developed. The incidence of HCC at 2 year was 0.52% in 0 points group, 2.37% in 1 points group and 11.77% in 2 points group.

Conclusion: Male gender and AFP ≥6 at the start of DAA treatment were the independent predictors for developing HCC after DAA treatment. For patients with these risk factors, we consider that our novel score of this study is very simple to perform before DAA treatment.
Disclosure: Nothing to disclose

P0056 SAFETY AND EFFICACY OF THE USE OF GENERIC SOFOSBUVIR AND DACLATASVIR IN THE TREATMENT OF NAÏVE CHRONIC HEPATITIS C IN HIV/HCV GENOTYPE 4 CO-INFECTED PATIENTS: AN EGYPTIAN REAL- LIFE EXPERIENCE

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Introduction: HIV and HCV co-infection is associated with an increased risk of poor health outcomes, mostly due to the negative effects of HIV infection on the natural history of HCV. HIV infection is associated with higher rates of HCV replication and therefore higher risk of development of liver fibrosis, decompensated cirrhosis and hepatocellular carcinoma. In Egypt, according to several clinical trials and real-life data, the use of utterly generic sofosbuvir and daclatasvir combination with or without generic ribavirin was well tolerated and associated with high response rate in genotype 4 (GT4) HCV mono-infected patients with different stages of liver disease. However, data are lacking regarding efficacy and safety in HIV/HCV-GT4-co-infected patients.

Aims & Methods: This prospective cohort study was conducted in the period between May 2017 and January 2019. From a wide spectrum of patients seeking Direct Acting Antivirals (DAAs) in Kasr Al-Aini Viral Hepatitis Center (KAVHC), Cairo University Hospitals, Cairo, Egypt, 50 HIV/HCV-GT4 co- infected patients were offered generic sofosbuvir and an adjusted dose of daclatasvir according to the antiretroviral therapy (ART) without ribavirin for 12 weeks.

All patients were HCV treatment naïve, with CD4 count ≥100 cells/mm3 and eligible for HCV treatment according to the national guidelines. The 13 patients who were naive to both ART and DAAs with CD4 count > 500 cells/mm3, were advised to receive DAAs firstly. Patients' demographics, laboratory data (complete blood cell counts, serum alanine and aspartate aminotransferase, total bilirubin and serum creatinine), and adverse events (AEs) were analyzed at baseline, week 4, 8, 12 on treatment and at follow-up week 4 and 12. Sustained viral response (SVR12) was defined as an undetectable HCV RNA 12 weeks after the end of treatment (EOT). Changes in HIV PCR, CD4 count and liver stiffness measurement (LSM) by transient elastography at week 12 post- treatment were assessed in comparison to baseline.

Results: The mean patients age was 34.6±10 years, 41 were males (82%), 46% reported intravenous drug use and 26% had significant liver fibrosis (≥F2). SVR12 was achieved in 48 of 50 patients (96%). SVR12 rates were comparable either the patients were receiving ART or not and either had significant liver fibrosis (≥F2) or not (All p >0.1). AEs occurred in 44 (88%) patients. Most frequent AEs: fatigue (32%), headache (20%), and nausea (12%) were mild with spontaneous recovery after EOT. No serious AEs, treatment discontinuation due to AEs or deaths were reported. HIV viral load suppression was not compromised in the patients stable on ART. All patients experienced a CD4 count increase during HCV treatment (p=0.01). LSM showed a significant decline at week 12 post-treatment when compared to baseline (7.5±5.2 vs. 6.33±3.1 kPa, p< 0.01).

Conclusion: Administration of generic daclatasvir and sofosbuvir without ribavirin for 12 weeks irrespective of liver fibrosis stage was safe and highly effective for HCV treatment naïve HIV/HCV-GT4-co-infected patients. So, patients with HIV-HCV co-infection are no longer considered as a special 'hard to treat' population in the real-life settings.

Disclosure: Nothing to disclose

P0057 NATURAL HISTORY AND PREDICTORS OF POOR OUTCOME AMONG PATIENTS WITH NON-ACETAMINOPHEN INDUCED ACUTE LIVER INJURY

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Introduction: Acute liver injury (ALI) is determined as liver insult resulting in liver damage characterized by ALI or AST ≥x10 ULN, INR ≥1.5, without hepatic encephalopathy in absence of pre existing liver disease. There is paucity of literature available over cohort of ALI patient, who is vulnerable to develop poor outcome i.e. acute liver failure (ALF) and death. In this study we have determined the characteristic of cohort of ALI patients plus the risk factors predicting the poor outcome.

Aims & Methods: Patients meeting criteria of ALI prospectively enrolled, while patients with comorbid condition affecting short term mortality e.g. with hepatocellular carcinoma were excluded. These patients were followed until complete recovery, acute liver failure (ALF), death, or liver transplantation (LT). Two subgroup analyses -one with patients with INR ≥1.5-≤1.9 vs. with INR ≥2 and second subgroup analysis with respect to patients with and without death was performed to see the difference among independent variables. Finally using linear regression model the factors responsible for death were determined.

Results: A total of 110 patients were enrolled from January 2013 to December 2017 for final analysis. Mean age was 35.1± 18.0, and 50 (45.5%) were males. The common etiology of ALI was HEV 39 (35%), followed by HAV 23 (20%), DILI among 12 (10.8%), ischemic hepatitis among 10 (9%), indeterminate etiology among 3 (2.7%), and paracetomol only among 2 (1.8%) of patients. The common symptom at presentation was fever 49 (44.5%), Nausea/Vomiting (N/V) among 49 (44.5%) followed by jaundice among 47 (42.7%). A total of 27 (24.5%) patients developed at least one of poor outcome i.e. ALF, death or LT, while rest recovered liver insult. Of 27 patients 19 (17.27%) patients developed ALF. Out of 19 ALF patients, 8 patients died, one underwent LT, and 10 recovered spontaneously. A total of 14 patient died-8 have ALF initially and 6 patients without intermediate phase of ALF. Out of 14 who died, 4 had HEV, 3 had ischemic hepatitis, 3 with indeterminate cause, two patients with HAV-HEV and dengue infection respectively. On subgroup analysis among groups-one with INR ≥1.5-≤1.9 (n=40), and second with ≥ 2 (n=70), showed difference in terms of jaundice (9 (22.5%) vs. 38 (54.2%) p 0.002), WBC (6.9 vs. 11 p < 0.001), GGT (150 vs. 61.5 p < 0.001), and development of poor outcome (3 (7.5%) vs. 24 (34.2%) p 0.002).

On regression analysis, there were no factors which were found to be responsible for having INR ≥2. On subgroup analysis with respect to death-a group with death (n=14) vs. a group without death (n=96) showed difference in INR of ≥2 (13 vs. 1 p 0.01), frequent ALOC (10 (71.4%) vs. 4 (4.1%) p 0.04), less frequent N/V (1 (1%) vs. 10 (71) p 0.002), raised PT (33 vs. 22 p 0.003), raised WBC (16.2x10^{3} vs. 10.4x10^{3} p 0.003), raised AST (5166 vs. 1834 IU/L p 0.004), raised Creatinine (2.6 vs. 1.1 mg/dl p 0.002), and longer length of hospital stay (8.36 vs. 5.04 days p 0.019) were statistically different among groups.

However, on linear regression AST (OR 1.0 (1.0-1.0) p 0.03), creatinine (OR 1.42(1.04-1.95) p 0.02), and length of hospital duration (OR 1.12(1.004-1.25) p 0.04) were found to be the predictors of death.

Conclusion: ALI is a severe disease culminating in to poor outcome in among one fourth of patients. More than half of patient with ALF can recover spontaneously; however, death is inevitable among rest of patients unless an immediate LT is performed. Patients with severely raised AST, acute renal deterioration and longer hospital stay are vulnerable to develop poor outcome.

Disclosure: Nothing to disclose

P0058 DIRECTLY ACTING ANTIVIRALS ARE SAFE AND EFFECTIVE IN HCV ELDERLY PATIENTS

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Introduction: Treatment of chronic Hepatitis C (HCV) with directly acting antivirals (DAAs) can lead to sustained virological response (SVR) in nearly 95% of patients. Treatment efficacy and safety in elderly patients has not been extensively studied.
Aims & Methods: We retrospectively analyzed treatment efficacy and safety in HCV patients ≥ 80 years of age who consecutively received DAAs at the Humanitas Research Hospital between 2015 and 2018. DAAs were given following the EASL recommendations.
Results: During the study period 976 patients received DAA treatment in our center, 40 patients (4.1%) were ≥80 years old and were included in the study. Their mean age was 81.8 years (80-88), 25 patients were female (62%), HCV genotype 1b (29 patients 72.5%) and 2 (10 patients 25%) were the most prevalent HCV genotypes. Advanced fibrosis (F3-F4) defined by transient elastography was present in 21 (52.5%), six patients had CPT score >A5 and 8 (20%) had previously failed IFN based treatment. Sofosbuvir based therapies (SOF/LDV, SOF/VEL and SOF + RBV) were given to 21 patients (52.5%), Paritaprevir/Ombitasvir/Dasabuvir was used in 3, G/P in 7 (17.5%) and Grazoprevir/Elbasvir in 9 (22.5%). Concomitant medications were common in our cohort with 39 patients (97.5%) taking at least 1 drug and 23 (57.5%) taking 4 or more concomitant drugs. In 3 cases concomitant therapy had to be modified to start DAA treatment for potential significant Drug interactions. Five patients reported side effects during treatment, side effects were always mild and no serious adverse events were reported, no patient discontinued treatment prematurely. Seven patients are still completing the follow-up and could not be assessed for SVR. In the remaining 33 patients a SVR was achieved in 32 (97%). The only treatment failure was a patient lost to follow-up after the End of treatment visit.
Conclusion: Our study shows that DAA treatment in HCV Patients older than 80 years of age is safe and effective. Due to high rate of comorbidities DDI need to be carefully assessed before starting treatment.
Disclosure: Nothing to disclose

P0059 MAC-2 BINDING PROTEIN GLYCAN ISOMER IS A RELIABLE MARKER FOR THE ASSESSMENT OF LIVER FIBROSIS GRADE IN CHRONIC HEPATITIS C PATIENTS TREATED WITH DIRECT ACTING ANTIVIRALS

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Introduction: Assessing liver fibrosis is important for predicting the efficacy of direct acting antivirals (DAAs) and patient prognosis. Non-invasive techniques to assess liver fibrosis are becoming important. Recently, serum Mac-2 binding protein glycan isomer (M2BPGi) was developed as a non-invasive marker for liver fibrosis.
Aims & Methods: The aims of this study were (1) to evaluate the diagnostic accuracy of serum M2BPGi to predict the grade of liver fibrosis in patients with chronic hepatitis C (CHC) at baseline and after achievement of a sustained virological response at 12 weeks after completion of treatment (SVR12) by DAAs and (2) to compare the results with fibrosis score (FIB4) and PAPAS index. This study included 85 patients with CHC. For 12 weeks duration, 65 patients were treated with sofosbuvir and daclatasvir, and 15 patients were treated with sofosbuvir, daclatasvir and ribavirin. We measured M2BPGi, PAPAS index, FIB4 and liver stiffness measurements (LSM) at baseline and SVR12. Serum M2BPGi was measured by M2BPGi ELISA kits, with detection range 0.625 - 20 ng/ml, sensitivity 0.1 ng/ml, intra-assay, and inter-assay coefficient of variation less than 15%. PAPAS index (platelets/age/phosphatase/AFP/AST) formula= Log (index+1) = $0.0255 + 0.0031 \times$ age (years) + $0.1483 \times$ log {ALP (U/L)} + $0.004 \times$ log {AST (U/L)} + $0.0908 \times$ log {AFP (ng/L) + 1} - $0.028 \times$ log {platelet count (10^9/L)}. LSM was performed using Fibroscan (Echosens, 502 Touch, Paris, France).

Fib4= [Age (yr.) × AST (IU/L)/platelet count (10^9/L) × ALT (IU/L)]. We classified cases according to LSM into, F0-1: < 7.1 KPa, ≥F2: ≥7.1 - < 9.5 KPa, ≥F3: ≥9.5 - < 12.5 KPa, and F4: ≥12.5 KPa.
Results: All patients achieved SVR12 (100%). M2BPGi, LSM, FIB-4 and PAPAS index decreased significantly at SVR12 [9 vs. 6.7 ng/mL (p< 0.001), 11.4 vs. 9.5 kPa (p=0.002), 1.8 vs. 1.3 (p< 0.001) and 2.2 vs. 2.1 (p=0.010), respectively]. M2BPGi correlated positively with LSM at baseline and SVR12 (r= 0.326; p= 0.003 and r= 0.612; p< 0.001, respectively), while no correlation was observed with FIB4 or PAPAS index. At baseline, M2BPGi was the best marker to distinguish patients with F4, F0-2 from F3-4 and F0-1 from F2-4 with AUROC of 0.801, 0.730 and 0.763, respectively, (P< 0.001). At SVR12, when compared with FIB4 and PAPAS index, M2BPGi had the greatest AUROC for differentiating patients with F4, F3, F0-2 from F3-4 and F0-1 from F2-4 with AUROC of 0.844, 0.893, 0.891 and 0.750, respectively, (P< 0.001).
Conclusion: Serum M2BPGi is an accurate and reliable marker for the assessment and grading of liver fibrosis before and after DAAs therapy for CHC patients. This diagnostic capability is superior to FIB4 and PAPAS index. This approach could be clinically feasible for therapeutic and investigational utility if this measurement application is commercially realized.
Disclosure: Nothing to disclose

P0060 CARDIAC ADVERSE EFFECTS OF DIRECT-ACTING ANTIVIRALS ARE POSSIBLE IRRESPECTIVE OF COADMINISTRATION WITH AMIODARONE

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Introduction: Several concerns have arisen regarding cardiac toxicity after the Food and Drug Administration published the warning about the serious slowing of the heart rate of amiodarone when taken in combination with direct acting antivirals (DAAs). Currently, little is known about the possible drug-related cardiotoxicity of DAAs.
Aims & Methods: To investigate the occurrence of cardiac adverse effects of DAAs if not coadministered with amiodarone in chronic hepatitis C (CHC) patients. We included 60 CHC patients who were eligible for DAAs therapy. They were equally categorized into 2 groups according to the presence of risk factors for cardiac disease such as diabetes, hypertension and obesity. Group I included patients without risk factors for cardiac disease, while group II included patients with risk factors for cardiac disease. We excluded patients with diagnosed cardiovascular disease, under treatment with amiodarone or other heart-rate lowering drugs and those with abnormal echocardiographic or ECG findings. All patients were treated with sofosbuvir and daclatasvir for 12 weeks. We compared echocardiographic findings, ECG and lipid profile of all patients at baseline and after achievement of sustained virological response at 12 weeks after completion of treatment (SVR12).
Results: All patients achieved SVR12 (100%). Heart rate slowed significantly at SVR12 than baseline with median (IQR) of 55 (40 - 70) vs. 70 (60 - 80) beats/min, respectively, (p=0.001). In group I, bradycardia and 1st degree heart block occurred in 8 (26.6%) and 4 (13.3%) patients, respectively, (p< 0.05). Ten (33.3%) and 7 (23.3%) patients in group II developed bradycardia and 1st degree heart block, respectively, (p=0.001). Concerning the lipid profile at SVR12, we detected a significant difference between both groups as regards serum levels of cholesterol, low density lipoprotein (LDL) and triglycerides (p< 0.001). Serum triglycerides level increased significantly in both groups at SVR12 compared with baseline; as mean level in group I was 140 ± 8.56 vs. 126.13 ± 20.80 mg/dl, respectively, (p= 0.01), and mean level in group II was 185.67 ± 12.94 vs. 125.13 ± 20.33 mg/dl, respectively, (p< 0.001). Serum cholesterol level in group II increased significantly at SVR12 compared with baseline with mean level of 280.20 ± 34.68 vs. 185.73 ± 34.93 mg/dl, respectively, (p< 0.001).
Additionally in group II, LDL serum level increased significantly at SVR12 compared with baseline with mean level of 185.80 ± 2.31 vs. 151.00 ± 13.06 mg/dl, respectively, (p< 0.001).
Conclusion: Cardiac adverse effects of DAAs are possible irrespective of the presence of cardiac disease or coadministration with amiodarone. Physicians' awareness of this risk is mandatory for optimizing patients' care.
Disclosure: Nothing to disclose

P0061 HEPATOCELLULAR CARCINOMA RECURRENCE AFTER DIRECTLY ACTING ANTIVIRALS AMONG EGYPTIAN PATIENTS INFECTED WITH GENOTYPE 4 HEPATITIS C VIRUS: A 2-YEAR FOLLOW UP STUDY

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Introduction: Hepatocellular carcinoma (HCC) is the fifth most common cancer in the world and the most common cancer in Egypt.(1)
Incidence of HCC recurrence after curative therapies without HCV treatment ranges widely among different studies. Cabibbo et al.(2) conducted a meta-analysis of 11 studies evaluating the HCC recurrence in HCV untreated patients after curative HCC treatment using surgical resection or radiofrequency ablation for tumors ≤3cm. The meta-analysis found probabilities of HCC recurrence to be 20% at 1 year and 47% at 2 years. Data regarding HCC recurrence after directly acting antivirals (DAAs) treatment are debatable.
Aims & Methods: Our aim was to study the 2-year recurrence rate of HCC in HCV patients who were treated using radiofrequency ablation (RFA) or microwave ablation (MWA) at our unit during 2016 and then received DAAs. This retrospective study included all Child-Pugh A and B patients with HCV related < 5 cm single or multiple HCCs up to 3 lesions without any vascular invasion or lymph node or distant metastasis who were treated using RFA or MWA at the Hepatobiliary Unit, University of Alexandria in the period from 1/1/2016 to 31/12/2016 and then received DAAs for HCV after ensuring no residual or recurrent HCC on triphasic CT scan. Triphasic CT scans were performed for all paients 4 weeks after the ablation procedure and every 12 weeks from the date of the ablation procedure thereafter according to our unit protocol. Those with any other cause of chronic liver disease, those who received previous HCC treatments and those with previous DAAs exposure were excluded. After these exclusions, data from 52 patients were analyzed. Significance of the obtained results was judged at the 5% level.
Results: Out of the 52 patients, 2 patients were died and 4 patients were lost for follow up before any HCC recurrence. The tumor recurrence rate at 1 year after tumor ablation among the remaining 46 patients was 30% (14 patients) and became 47.8% (22 patients) by the end of the second year. Tumor recurrence at 6 months after tumor ablation among those who had started DAAs before that time was 22.2% (8 out of 36 patients) while no one out of the 16 patients who started DAAs later experienced tumor recurrence during that period but this difference was not statistically significant (P=0.06). All of the 8 patients had started DAAs just 4 weeks after tumor ablation and the recurrence was multicentric in 50% of them.
On comparing HCC recurrence between those who started DAAs earlier than 12 weeks from the HCC ablation procedure and those who started DAAs 12 weeks or more after it, the 1-year HCC recurrence was 31.3% in the first group (10 out of 32) and 20 % in the second group (4 out of 20) (p=0.591) while the 2-year HCC recurrence was 43.8% in the first group (14 out of 32) and 40% in the second group (8 out of 20) (p=0.722)
Conclusion: Although our study included both modified Child-Pugh A and B classes and included lesions up to 5 cm, HCC recurrence rates were nearly similar to that previously reported in the era before DAAs and so we can conclude that DAAs usage after ensuring complete HCC ablation using a reliable imaging technique doesn't seem to increase HCC recurrence rates. HCC recurrence rates didn't differ significantly between those who started DAAs early after tumor ablation and those who started them later but we recommend a randomized controlled trial to confirm this point.
References: 1- Ibrahim AS, Khaled HM, Mikhail NN, et al. Cancer incidence in Egypt: Results of the National Population-Based Cancer Registry Program. J Cancer Epidemiol. 2014;2014:437971. 2- Cabibbo G, Petta S, Barbàra M, et al. A metaanalysis of single HCVuntreated arm of studies evaluating outcomes after curative treatments of HCVrelated hepatocellular carcinoma. Liver International. 2017;37:1157-66.
Disclosure: Nothing to disclose

P0062 THYROID DYSFUNCTION IS COMMUNE AMONG AUTOIMMUNE HEPATITIS PATIENTS

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Introduction: Autoimmune hepatitis is an autoimmune disorder involving the liver with several systemic manifestations. The link between autoimmune hepatitis and autoimmune thyroid disorders has been investigated with controversial results. The aim of the study was to assess whether an association exists between autoimmune hepatitis and thyroid dysfunction
Aims & Methods: Using the medical database of EMMS the Nazareth Hospital, we compared the proportion of hypo and hyperthyroidism between patients with autoimmune hepatitis and age-matched and gender-matched controls in a cross-sectional study. Univariate analysis was performed using Chi-square and student t-test and a multivariate analysis was performed using a logistic regression model.
Results: One hundred and sixty three autoimmune hepatitis patients and 1,104 age-matched and gender-matched controls were included in the study. The average age was 44.12 ± 10.5 (18-74). Fifty-seven patients (64.6%) were females. The proportion of hypothyroidism among autoimmune hepatitis patients was increased in comparison with controls (17.7vs. 4.98%, respectively, p-value < 0.001), as was hyperthyroidism (3.24 and 1.23% respectively, p-value < 0.001). Autoimmune hepatitis revealed an independent association with hypothyroidism on multivariate analysis (Odd Ratios 1.324, 95% Confidence Intervals 1.21-1.38),but not with hyperthyroidism.
Conclusion: Autoimmune hepatitis patients have a higher proportion of hypothyroidism in comparison with matched controls. Physicians treating autoimmune hepatitis subjects should consider screening for thyroid dysfunction on a regular basis.
Disclosure: Nothing to disclose

P0063 AUTOIMMUNE MARKERS ARE MORE COMMON AMONG PATIENTS WITH FATTY LIVER DISEASE: A CASE CONTROL STUDY

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Introduction: Autoimmune marker can be present in serum healthy subjects as well as among patients whit autoimmune and non-autoimmune disorder. The prevalence of autoimmune markers in tatty liver patients varies considerably.
Aims & Methods: Patients with fatty liver disease were compared with age and sex-matched controls regarding the proportion of autoimmune markers deduction in a case-control study. Chi-square and t-tests were used for univariate analysis and a logistic regression model was used for multivariate analysis. The study was performed utilizing the medical database of Clalit Health Services.
Results: The study included 519 patients with fatty liver and 2,187 age and sex-matched controls. The proportion of autoimmune markers detection in patients with fatty liver was increased compared with the prevalence in controls (19.52% and 4.68%, respectively, P< 0.001). In a multivariate analysis, fatty liver disease was associated with autoimmune markers detection (odds ratio 2.542, 95% confidence interval 2.254-2.879).
Conclusion: Patients with fatty liver disease have a greater proportion of autoimmune markers detection than matched controls.
Disclosure: Nothing to disclose

P0064 GLUCOCORTICOIDS DECREASE APOPTOSIS AND AUTOPHAGY OF HEPATOCYTES VIA PI3K/AKT/MTOR SIGNALING PATHWAY IN AUTOIMMUNE HEPATITIS

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Introduction: Autoimmune hepatitis (AIH) is distinctly characterized by massive immune cell-mediated hepatocyte destruction. Here, we investigated the effect of glucocorticoids on concanavalin A (Con A)-induced experimental autoimmune hepatitis (EAH) mice and *in vitro* to demonstrate the important role of hepatocytes.
Aims & Methods: C57BL/6 mice were injected intravenously with ConA (20 mg/kg) to generate a model of EAH. Glucocorticoids was injected intragastric administration 0.5 h after the ConA administration. The apoptosis cells percentage, levels of serum serum liver enzymes, inflammatory cytokines, pathology and other marker proteins were determined 12 h after ConA injection. *In vitro*, primary hepatocyte and the LO2 cell lines were used to examine the susceptibility of hepatocytes to ConA challenge and explore the underlying mechanisms. We then treated the hepatocytes with ConA, 3-methyladenine (3-MA), and glucocorticoids. The apoptosis rates, mitochondrial membrane potential (ΔΨm), reactive oxygen species (ROS) level, the expression of autophagy-related proteins, the formation of autophagosomes and expression of Akt/p-Akt and mTOR/p-mTOR protein were detected.
Results: Treatment with glucocorticoids reduced apoptosis cells percentage, levels of serum liver enzymes, inflammatory cytokines, and attenuated histopathological damage in EAH mice. Autophagy may play an important role in EAH. *In vitro*, the increased apoptosis rates, decreased ΔΨm level, ROS imbalance and elevated autophagy level were observed under treatment with ConA. The expression of p-Akt and p-mTOR was inhibited during this process. Glucocorticoids protected against Con A-induced hepatocyte apoptosis, decreased the autophagy related protein expression, decreased autophagosome formation and up-regulated the level of p-Akt and p-mTOR.
Conclusion: We provided evidence that underlying mechanisms of hepatocytes involved in the progression of AIH. Glucocorticoids could ameliorate Con A-induced liver injury by regulating autophagy and apoptosis on hepatocytes via PI3K/AKT/mTOR signaling pathway.
Disclosure: Nothing to disclose

P0065 WITHDRAWN

P0066 EFFICACY OF FENOFIBRATE ADD-ON THERAPY FOR PATIENTS WITH PRIMARY BILIARY CHOLANGITIS AND A SUBOPTIMAL RESPONSE TO URSODEOXYCHOLIC ACID

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Introduction: Oral ursodeoxycholic acid (UDCA) at 13-15mg/kg/day is the first line pharmacotherapy for all patients with primary biliary cholangitis (PBC). However up to 40% of PBC patients have a suboptimal response to UDCA monotherapy as defined by validated criteria, and have been shown to be at higher risk of disease progression to cirrhosis, need for liver transplant, and death (1). Due to their peroxisome proliferator-activated receptor (PPAR)-mediated anti cholestatic effects, evidence of the biochemical efficacy of add-on therapy with bezafibrate has been demonstrated in patients with ALP >1.67x upper limit normal(ULN) and/or bilirubin elevated < 2x ULN (2). However data evaluating the efficacy of fenofibrate, a more commonly used fibrate, is limited.
Aims & Methods: To evaluate the efficacy of fenofibrate in patients with PBC and a suboptimal response to UDCA monotherapy.
This was a retrospective analysis of 5 patients with PBC and serum alkaline phosphatase (ALP) 1.5x ULN despite at least 12 months of UDCA monotherapy (median treatment duration 90.2 months). They received fenofi-brate 160mg/day in addition to UDCA for 16 weeks. Biochemistry data and UK-PBC risk scores at 5-, 10- and 15- years were compared at baseline and after 16 weeks of treatment. In addition, the baseline fibroscan score and serologies were noted.
Results: .Median serum ALP levels decreased significantly at 16 weeks. However there was no significant improvement in the 5-, 10- and 15-year UK-PBC risk scores. 1 patient was cirrhotic and 1 patient had Autoimmune hepatitis(AIH)/PBC overlap syndrome. No significant adverse events were reported.
Conclusion: This study found the use of fenofibrate in combination with UDCA to be effective in improving serum ALP in PBC patients with a suboptimal response to UDCA monotherapy within 16 weeks. However, this did not appear to translate to significant reductions in the estimated probability of liver-related death or need for liver transplantation. Further studies are needed to evaluate if fenofibrate can be a viable alternative to bezafibrate as second line therapy for patients with PBC and suboptimal response to ursodeoxycholic acid.
References: 1. Corpechot C, et al. Early primary biliary cirrhosis: biochemical response to treatment and prediction of long-term outcome. J Hepatol. 2011;55:1361-1367 2. Corpechot et al. A Placebo-Controlled Trial of Bezafibrate in Primary Biliary Cholangitis. N Engl J Med. 2018 Jun 7;378(23):2171-2181
Disclosure: Nothing to disclose

P0067 WITHDRAWN

P0068 ASPARTATE-β-HYDROXYLASE PROMOTES CANCER METABOLIC SWITCH VIA P53-DEPENDENT SUPPRESSION OF MITOPHAGY IN HEPATOCELLUAR CARCINOMA

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Introduction: Metabolic reprogramming is widely observed during hepatocellular carcinoma (HCC) development. Mitophagy constitutes an important target for interventions seeking tomanipulate cell fate during metabolic reprogramming. Aspartate-β-hydroxylase (ASPH) was one of the most differentially expressed genes in HCC. However, the relationship between ASPH and cancer metabolic reprogramming remains uncharacterized.
Aims & Methods: In the this study, we aimed to explore the relationship of ASPH in the P53-dependent mitophagy, characterized the impact of ASPH on tumor metabolic reprogramming.
We constructed HCC animal model and HCC anoxic autophagy model, using lentivirus to deliver ASPH to HepG2 cell line and the CRISPR/Cas9 system to knockout ASPH, so that we can assess the effect of ASPH on mitophagy, characterized cancer metabolic reprogramming in HCC. Besides, we uncovered the biological mechanism of ASPH-induced mitophagy and cancer metabolic reprogramming using western blotting, RT-PCR, electron microscopy, immunofluorescence and transient transfection of a GFP-LC3-expressing construct.
Results: In this study, ASPH down-regulated the expression of P62, and improved the expression of P53, Atg5, Atg7 and LC3-II/LC3-I. Meanwhile, ASPH also significantly inhibited the expression of TOMM20, which reflects the oxidative phosphorylation level of tumor cells. In addition, ASPH regulated tumor metabolism reprogramming in HCC hypoxic autophagy model, including increased levels of glycolysis and pentose phosphate pathways, with the up-regulation of GLUT1, PKM2 and G6PD. However, ASPH did not affect the level of lipid metabolism and lactic acid metabolism based on the the expressions of MCT1, ACC and ACLY. Futhermore, ASPH also significantly decreased the expressions of BNIP3 and NIX proteins in HCC.
Conclusion: Our finding suggests that ASPH regulates metabolic reprogramming via P53-dependent signaling pathway in HCC. This study will provide a reliable theoretical basis for the application of ASPH as an effective target for HCC treatment.
Disclosure: Nothing to disclose

P0069 PROTECTIVE EFFECT OF BIOFABRICATED *TRIANTHEMA PORTULACASTRUM* SILVER NANOPARTICLES AGAINST HEPATOCELLULAR CARCINOMA

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Introduction: Over the recent years, nanoparticle approach for targeted drug delivery is considered as a promising therapeutic method to improve the potential of antitumor agents. *Trianthema portulacastrum* (TP) leaves have been utilized as a strong hepatoprotective in Indian traditional medicinal system.

Aims & Methods: Current study was designed to biofabricate, characterize and evaluate protective effect of TP extract mediated silver nanoparticles (AgTPNPs) against diethylnitrosamine (DEN) induced hepatocarcinoma in rat model. AgTPNPs were synthesized by co-precipitation method and different characterization techniques confirmed the formation of spherical crystalline nanoparticles with size range of 50-80 nm. FTIR results showed the existence of possible bioactive functional groups of phytoconstituents in the synthesized AgTPNPs. Liver damage in rats was induced with a single dose of DEN (200 mg/kg) as well as double dose of phenobarbital. Simultaneously, animals were administered with AgTPNPs at two dose levels (10 and 20 mg/kg p.o.) for 16 weeks. At the end of study, serum biomarkers, hematological status, antioxidants enzymes, proinflammatory cytokines, i.e., tumor necrosis factor-α, interlukin-6, interlukin-1β, and nuclear factor kappa beta (NF-kB), were examined to assess the protective effect of AgTPNPs. Histological studies were also undertaken to assess the outcomes of current study.

Results: Results demonstrated that DEN significantly induced the hepatocellular carcinoma in each group, which was significantly reversed ($p < 0.001$) by AgTPNPs in a concentration dependent manner. A significant reduction in level of serum hepatic and non-hepatic marker enzymes, oxidative stress and different inflammatory markers via direct and indirect inhibition of NF-kB expression were observed in rats administered with AgTPNPs. Histopathological study further supported the significant hepatic cellular structure recovering effect.

Conclusion: Collectively, results demonstrated that AgTPNPs potentially ameliorated the damaging effects of DEN induced hepatocellular carcinoma and it can be utilized as an effective nano technology based anti-cancer approach.

Disclosure: Nothing to disclose

P0070 ESTROGEN-INDUCED EPIGENETIC SILENCING OF IRON METABOLISM-RELATED GENES REDUCES THE GROWTH POTENTIAL OF HEPATOCELLULAR CARCINOMA CELLS

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Introduction: Hepatocellular carcinoma (HCC) is the second most common type of cancer in men and seventh in women. Several lines of evidence suggest that estrogen (E2) plays a protective role against HCC. In that, male-to-female incidence ratio is between 2:1 to 4:1, women of premenopausal age are less prone to HCC and respond more positively to chemotherapy as compared with postmenopausal women and E2 treatment in hepatocellular carcinoma (Hep-G2) cell cultures induces significant levels of apoptosis. That said, the exact mechanism underlying this protective effect of E2 against HCC is not well understood. Recent work has shown that E2 modulates the expression of multiple iron metabolism-related (IRM) genes and disrupts intracellular iron homeostasis in cancer cells. However, how E2 disrupts the expression of IRM genes and whether this has any bearing on the protective role of E2 against HCC is yet to be addressed.

Aims & Methods: Given that epigenetic modifications are involved in regulating gene expression, we hypothesized that E2 could disrupt intracellular iron metabolism by inducing epigenetic modifications in select IRM genes. To test this hypothesis, the UCSC genome browser was used to analyze the CpG islands (CGI) on the promoter regions of core IRM genes. Furthermore, Hep-G2, gastric cancer (AGS) and breast adenocarcinoma (MCF7)

cell lines were used to investigate the effect of E2 on IRM gene expression. DNA methylation was assessed by PCR, methylation-specific (MSP)-PCR, western blotting and flow cytometry. Histone modification was assessed by chromatin immunoprecipitation (ChIP) and western blotting. Cell proliferation and cell cycle analysis were performed to assess the functional significance of E2- disrupted intracellular iron metabolism.

Results: Both ferritin heavy chain-1 (*FTH1*) and transferrin receptor-1 (*TFR1*) genes were identified as having CGIs in their promoter region. E2 (20nM) treatment induced DNA methylation and inhibited the expression of *FTH1* and *TFR1* in HepG2 cells. De-methylation treatment with 5-Aza-dC rescued the downregulation of *FTH1* and *TFR1* in HepG2 cells but not in AGS or MCF7 cells. DNMT3B, PRMT5 and methylated-Histone 4 (H4R3me2s) upregulated in E2-treated HepG2 cells. The siRNA knockdown of PRMT5 inhibited E2-induced methylation of histone H4R3. Furthermore, E2 treatment recruited PRMT5 and H4R3me2s on *FTH1* but not on *TFR1*, as suggested by ChIP assay data. The siRNA knockdown of PRMT5 and DNMT3B were required to block the inhibitory effect of E2 on *FTH1*, however, knock-down of the only DNMT3B inhibited E2 induced-downregulation of *TFR1*. Suggesting *FTH1* silencing requires coordination of both, histone methylation and DNA methylation, whereas, *TFR1* is silenced only by DNA methylation. Lastly, siRNA knockdown of *FTH1* and *TFR1* in Hep-G2 cells resulted in the decreased intracellular labile iron pool, which was associated with cell cycle arrest and reduced cell growth and proliferation.

Conclusion: These findings clearly suggested that E2 disrupts intracellular iron metabolism by inducing histone and/or DNA methylation events that silences the *FTH1* and *TFR1* genes and that such changes were associated with cell cycle arrest and reduced cell growth.

Disclosure: Nothing to disclose

P0071 SAT-2 HYPOMETHYLATION AS AN EARLY DIAGNOSTIC MARKER FOR HCV-RELATED HEPATOCELLULAR CARCINOMA

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Introduction: Hepatocellular Carcinoma (HCC) is the most frequent subtype of primary liver cancer, accounting for approximately 85% of total clinical cases. In the past 20 years, the HCC incidence, in the United States, was increased by three times with a 5-year survival rate lower than 12%. The prevalence of HCC in Africa is higher than the rest of the world due to the high incidence of chronic hepatitis C virus (HCV) infection which is usually undiagnosed until late stages.< br>The precise molecular pathogenesis of HCC is very complicated and heterogeneous, leading to a delay in its diagnosis and treatment. Owing to the low sensitivity and specificity of the currently existing tumor biomarker tests (e.g., AFP) for the early detection of HCC, most patients are diagnosed and treated at advanced stages of the disease, which greatly affects the response to the available therapy and leads to poor prognosis. Thus, improving early disease detection may help to achieve a better clinical outcome for liver cancer patients.

Epigenetic analyses determine how the environmental factors interact with the genome, and thus, inducing gene expression modifications without affecting the gene sequence. Epigenetic transformations, such as alteration of DNA methylation, have been noticed in multiple cancers including HCC. Therefore, they could serve as excellent biomarkers for carcinogenesis risk estimation, diagnosis, and prognosis.

Aims & Methods: The current study was designed to investigate the potentiality of SAT-2 methylation alteration for the early detection of HCV-induced HCC and to provide key insights into the epigenetic molecular mechanisms regulating HCC development and progression.

Twenty healthy controls, 40 chronic HCV patients, 40 HCV-associated cirrhotic patients, and 50 HCV-HCC patients were enrolled in this study. Patients were subjected to full history taking, complete clinical examination, routine laboratory investigations, serological detection of HCV, AFP measurement, radiological examination (e.g abdominal ultrasonography with Doppler examination, spiral CT, and Child's Pugh scoring and grading), and SAT-2 methylation analysis by Methy-Light PCR assay following bisulfite conversion of the extracted DNA from patients' blood samples.

Results: The percent of methylated reference (PMR) of SAT-2 methylation was calculated for all samples. A significant reduction was noticed in the cirrhotic and hepatocellular carcinoma groups in comparison to the control and chronic HCV groups. The mean ± standard deviation of the PMR values were 38.58 ± 0.11 % in the control group, 41.18 ± 0.068 % in the chronic HCV group, 26.23 ± 0.086 % in the cirrhotic group, 27.28 ± 0.16 % in the HCC group.

Conclusion: Decreased DNA methylation of SAT-2, in blood samples, can be used as a reliable diagnostic tool for liver cirrhosis and hepatocarcinogenesis development in HCV-chronically infected patients.

References:
1) Fan G, Tu Y, Chen C, Sun H, Wan C, Cai X. DNA methylation biomarkers for hepatocellular carcinoma. Cancer Cell Int. 2018; 1 8:140.
2) Weisenberger DJ, Campan M, Long TI, Kim M, Woods C, Fiala E, Ehrlich M, Laird PW. Analysis of repetitive element DNA methylation by Methy-Light. Nucleic Acids Res. 2005; 33(21):6823-36.

Disclosure:

P0072 EXPRESSION OF P-STAT3 AND CMYC CORRELATES WITH P2-HNF4α EXPRESSION IN NONALCOHOLIC FATTY LIVER DISEASE (NAFLD)

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Introduction: Nonalcoholic fatty liver disease (NAFLD) is associated with the metabolic syndrome and is rapidly becoming one of the major causes of hepatic cirrhosis and hepatocellular carcinoma (HCC). There are no reliable biomarkers to predict the risk of HCC in patients with NAFLD. The protein hepatocyte nuclear factor 4 alpha (HNF4α) has been recently identified as a central gene in the pathogenesis of nonalcoholic steatohepatitis (NASH), a subset of NAFLD characterized by inflammation with increased risk for cirrhosis and HCC over NAFLD. There are two different isoforms of HNF4α, P1-HNF4α and P2-HNF4α. P2-HNF4α is expressed in fetal liver but is not usually expressed in livers of normal adult.

However, it has been reported to be expressed in HNF4α-positive HCC. Phosphorylation of STAT3 (p-STAT3) and induction of cMyc has been proposed to be major contributor to HCC progression.

Aims & Methods: The aim of this study was to determine the relationships between p-STAT3, cMyc and P2-HNF4α xpression in biopsies from livers with NAFLD as potential biomarkers of HCC risk.

Formalin-fixed paraffin-embedded liver biopsies from 50 patients with NAFLD were included in this study. Sections were stained for P1-HNF4α, P2-HNF4α, p-STAT3 and cMyc using standard immunohistochemistry staining protocols. The staining results were correlated with each other and with clinicopathologic features. Statistical analysis was performed using two-tailed Fisher's exact test; $p < 0.05$ is considered significant.

Results: All 50 biopsies, except one, were positive for nuclear expression of P1-HNF4α. Twenty-nine (58%) cases were positive for nuclear expression of P2-HNF4α, 6 (12%) were positive for nuclear p-STAT3 and 5 (10%) were positive for nuclear cMyc.

There was no significant correlation between P2-HNF4α, p-STAT3 or cMyc expression and inflammation grade or fibrosis stage. All 6 (100%) p-STAT3-positive cases were also positive for P2-HNF4α. P-SAT3-positive cases were more likely to be positive for P2-HNF4α than p-STAT3-negative cases (100% vs 42%, p = 0.03). Four of the 5 cMyc-positive cases were also positive for P2-HNF4α.

Although cMyc-positive cases were more likely to be positive for P2-HNF4α than cMyc-negative cases the difference was not statistically significant (80% vs 56%, p = 0.38). p-STAT3-positive cases were more likely to be also cMyc-positive (67% vs 2%, p = 0.0003).

Conclusion: Our results strongly suggest that STAT3 phosphorylation occurs in livers with NAFLD only in the subset with P2-HNF4α expression, and cMyc expression is strongly correlated with STAT3 phosphorylation. We hypothesize that P2-HNF4α expression is an early event in the development of HCC in NAFLD that is followed at a later step by STAT3 phosphorylation and cMyc expression. This hypothesis is currently under investigation in a larger study.

Disclosure: Nothing to disclose

P0073 RELEVANCE OF IGFBP2 SIGNALING IN HEPATOCELLULAR CARCINOMA

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Introduction: 14 million patients worldwide are affected by hepatocellular carcinoma (HCC), the most common primary malignant neoplasia of the liver (85 - 90%) with the third highest tumor mortality. Thus, novel diagnostic and therapeutic options are indispensable. The insulin like growth factor (IGF) system promotes growth and cell survival via IGF binding to the IGF receptor. Insulin like growth factor binding proteins (IGFBPs) control IGF availability by competitive binding of IGF, therefore limiting proliferative IGF effects. Thus, the impact of IGFBP2 on HCC cell viability, proliferation and migration was evaluated and effects of IGFBP2 signaling on the efficacy of HCC-relevant therapeutics were analyzed.

Aims & Methods: IGF secretion and surface levels of IGF receptors were analyzed in the human HCC cell line Hep3B. Cells were cultured with recombinant IGFBP2 (100 -1000 ng/ml). Then, cell viability was measured by MTS assay, proliferation was determined by flow cytometry and cell migration was analyzed using a wound healing model. Activation of the IGF pathway was also determined by milliplex assay. Moreover, efficacy of the HCC-relevant therapeutics bleomycin, sorafenib, regorafenib and lenvatinib in combination with different IGFBP2 concentrations was analyzed by measuring cell death using flow cytometry. Varying IGFBP2 levels were obtained by overexpression and knockdown of *IGFBP2*. Overexpression of *IGFBP2* was verified by Western Blot, while knockdown of *IGFBP2* was controlled using qPCR and ELISA.

Results: Hep3B cells displayed an intact IGF system, indicated by constant IGF secretion over 96 hours and surface expression of IGF receptors. Largely, cell viability increased in a time-dependent fashion. Most pronounced effects of up to 115% were observed after 96 h using 100 - 500 ng/ml IGFBP2 . Highest proliferation rates were induced by IGFBP2 concentrations between 100 - 250 ng/ml with a significant increase of up to 18% after 48 h compared to the control. Concordantly, IGFBP2 concentrations between 100 and 500 ng/ml resulted in enhanced cell migration after only 16 hours. Interestingly, analysis of the IGF pathway after treatment with recombinant IGFBP2 resulted in no significant changes in activation compared to the untreated control. IGFBP2 protein levels were fivefold increased after overexpression of *IGFBP2*. Knockdown of *IGFBP2* resulted in a more than 90% decrease on RNA level and a reduced secretion of more than 60% after 72 h. Remarkably, with all HCC-relevant therapeutics, cell death behaved contrariwise to IGFBP2 concentration. Reduced IGFBP2 concentrations, generated by knockdown, resulted in enhanced cell death. In contrast, a decrease of cell death rates was observed in *IGFBP2*-overexpressing cells. *IGFBP2* knockdown in cells hereby significantly increased cell death when treated with bleomycin and regorafenib (7,4% and 23,5% after 48 h). Correspondingly, *IGFBP2* overexpressing cells displayed a decrease in cell death of 11% after incubation with sorafenib.

Conclusion: Although being regarded as growth-limiting factor within the IGF-system, recombinant IGFBP2 exerted proliferative effects on HCC cells. Since an induction of IGF signaling was not observed, the exact mechanisms of action need further elucidation. Nonetheless, IGFBP2 also affected the efficacy of HCC relevant therapeutics. We therefore hypothesize that IGFBP2 has further functions independent of its role within the IGF system and elucidation of those is essential for our understanding and treatment of HCC.

Disclosure: Nothing to disclose

P0074 WITHDRAWN

P0075 CLINICAL IMPLICATIONS OF AFP LEVELS IN PATIENTS OF HEPATOCELLULAR CARCINOMA IN A REFERRAL CANCER CENTRE IN INDIA

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Introduction: α-fetoprotein (AFP) is the most studied and used marker in Hepatocellular carcinoma (HCC). It is used to predict prognosis, assess response to therapy and more controversially as a screening tool along with abdominal ultrasound in patients with hepatitis or cirrhosis who are at risk for HCC. However, not all HCC secrete elevated amounts of AFP into the serum.

Aims & Methods: Aim-To explore the relationship between AFP and various clinical variables including Barcelona Clinic Liver Cancer (BCLC) stage at presentation in patients with HCC.
Methods-Clinical data of 547 prospectively accrued patients with untreated HCC in an ongoing study at our liver clinic between June 2017 and Feb 2019 was analysed. Demographic and clinical features, investigation results including routine labs and imaging reports regarding HCC size, extent of tumour (Single lobe /Bilobar), extra hepatic spread, macro vascular invasion and BCLC stage at presentation were recorded. Patients were divided into three groups according to different cutoff values for serum AFP: Group A (< 10 ng/mL, N=103); Group B (10-400 ng/mL, N=151) and Group C (>400 ng/mL, N=293). As per aetiology patients were divided into Hepatitis B /Hepatitis C related (HBHC) or Non Hepatitis B or Hepatitis C related (NBNC) HCC.

Results: 19% (n=103) patients had normal or low serum AFP values (< 10 ng/mL). Mean age at presentation in years (±SD) was 57 (±13.3), 59 (±11.9), 54 (±12.6) in group A, B and C respectively. As per aetiology, 53 % of patients in Group A were HBHC HCC as compared to 63 % in group C (p =0.146). Mean AFP was higher in HBHC HCC as compared to NBNC but this was not statistically significant (p= .367).
Patients in group A had significantly higher mean albumin (p=0.008), lower mean Bilirubin (p=< 0.001), lower mean INR (p=0.003) and smaller mean tumour size (p=0.002) as compared to group B and C. 25 % (n=26) of patients in Group A had evidence macro vascular invasion (MVI) as compared to 40% (60) in group B and 59% (n=172) in group C (p=< 0.001).
Patients with MVI (n=260) had significantly highly mean AFP in ng/mL (98088.49) as compared to patients without it (n=287, 40555.41 p=0.003). Patients in Group A had significantly lower incidence of extra hepatic metastases (EHM) (12.6 %) as compared to Group B (19.2 %) and C (28.6%, p=0.04). Serum AFP levels differed significantly (*P* < 0.001) in the BCLC stage D vs. stage A and B.

Parameter	Group A	Group B	Group C	p value
HBHC/NBNC n (%)	55 (53.4) /48 (46.6)	85 (56.3)/66 (43.4)	185 (63.1)/108 (36.9)	.146
Albumin (g/dL) Mean (± SD)	3.61 ± 0.62	3.38 ± 0.58	3.41 ± 0.58	0.008
INR	1.12 ± 0.21	1.17 ± 0.22	1.22 ± 0.30	0.003
Bilirubin(mg/dL) Mean (± SD)	1.59 ± 2.11	1.74 ± 1.42	2.5 ± 3.95	<0.001
Size of largest lesion(cm) Mean (± SD)	7.83 ± 3.66	8.38 ± 3.53	9.19 ± 3.45	0.002
Extent of tumour n (%) Single lobe/Bilobar	67 (65)/36 (35)	87(57.6)/64 (42.4)	142 (48.5)/151 (51.5)	0.01
BCLC (n) O/A/B/C/D	1/16/47/29/10	2/10/61/61/17	1/6/66/162/58	<0.001
Cirrhosis n(%) Yes/No	74 (71.8)/29 (28.2)	124 (82.1)/27 (17.9)	229 (78.1)/64 (21.9)	0.15
Macro vascular invasion n(%) Yes/No	26 (25.2)/77 (74.8)	60 (39.7)/91 (60.3)	172 (58.7) /121 (41.3)	<0.001
Extra hepatic Metastasis n(%) Yes/No	13 (12.6)/90 (87.4)	29 (19.2)/122 (80.8)	84 (28.6)/209 (71.4)	0.04

[Comparisons among AFP (ng/mL) groups in HCC patients (n=547)]

Conclusion: Comparisons between patients with AFP levels < 10, 10-400, >400 ng/ml showed that increasing AFP levels were associated with an increased percentage of MVI and EHM and ineligibility for any curative treatment. AFP is still a reasonably reliable prognostic serum marker es-

pecially in resource limited settings. However even advanced HCC can have normal to low serum AFP. In these patients, non-AFP prognostic markers are needed, especially for small HCCs.
Disclosure: Nothing to disclose

P0076 OUTCOMES OF HEPATIC RESECTION (HR) VERSUS TRANS ARTERIAL CHEMOEMBOLIZATION (TACE) FOR SOLITARY LARGE HEPATOCELLULAR CARCINOMA: A SYSTEMIC REVIEW AND META-ANALYSIS

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Introduction: Hepatocellular Carcinoma (HCC) is the sixth most common cancer and second most common cause of cancer-related death in the world. Common treatment modalities for large HCC (>/=5 cm) are Hepatic Resection (HR) and Trans arterial Chemoembolization (TACE). However, the most optimal treatment option for treating solitary large HCC (>/= 5 cm) remains controversial.

Aims & Methods: In our study we aimed to compare long-term survival outcomes of HR versus TACE for solitary HCC.The meta-analysis was performed using the Preferred Reporting Items for Systematic Reviews for Meta-Analysis (PRISMA) guidelines. We searched PubMed, Embase, Cochrane library, Medline, Google Scholar and Science Citation Index for studies comparing HR with TACE for solitary HCC >/=5cm between 2008-2018. Keywords used were "Hepatocellular carcinoma", "liver cell carcinoma", "hepatic resection" or "liver resection" and "Trans arterial Chemoembolization" or "TACE". Quality of studies was assessed by Methodological Index for Non-Randomized Studies (MINORS). Statistical analysis was performed using Review Manager version 5.3 (RevMan) software. The primary outcome was overall survival (OS) rates at 1,3 and 5 years.

Results: Using the pre-defined search strategy, 6 retrospective cohort studies were included in the meta-analysis. The analysis was performed on a total of 1488 patients, 784 (53%) underwent Hepatic resection (HR), 704 (47%) were treated with TACE. OS rates in HR 1,3 and 5 were 87,69 and 57 % respectively. OS rates in the TACE group at 1,3, and 5 years were 71, 49, and 33% respectively. The pool hazard ratio for 3 year OS rate was 0.63 (95% CI 0.51-0.69, P< 0.0001). The pooled hazard ratio for 5 year OS rate was 0.57 (95% CI 0.45-0.79, P=0.003).

Conclusion: Based on the analysis, we conclude that the patients who underwent HR have a significantly higher 3 and 5 year overall survival rate than TACE alone. Hence, HR can be safe and effective in patients with solitary large HCC. TACE can be considered in patients with contraindications to HR. However, larger prospective trials are needed to prove this.
Disclosure: Nothing to disclose

P0077 SERUM VASCULAR ENDOTHELIAL GROWTH FACTOR AS A TUMOUR MARKER FOR HEPATOCELLULAR CARCINOMA IN PATIENTS WITH HCV-RELATED LIVER CIRRHOSIS

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Introduction: Hepatocellular carcinoma (HCC) is the sixth commonest cancer and the fourth leading cause of cancer death, accounting for 8.2% of cancer-related deaths worldwide. Being a vascular tumor, vascular endothelial growth factor (VEGF) plays a vital role in HCC pathogenesis, growth, and spread.

Aims & Methods: The aim of this study was to determine the accuracy of serum VEGF and VEGF/PLT as tumour markers for early detection of HCC in patients with hepatitis C virus (HCV)-related liver cirrhosis. We conducted a prospective cohort study on HCV patients attending the outpatient and inpatient divisions of Gastroenterology & Hepatology Department. Patients were classified into three groups: HCC group, cirrhosis group, and HCV without cirrhosis (control group).

All patients were clinically evaluated, and were subjected to the following investigations: CBC, Liver functions test, renal functions test, HCV viral markers including HCV-RNA PCR, quantitative measurement of AFP, VEGF and VEGF/PLT, in addition to abdominal U/S and dynamic imaging study for HCC patients.

Data of the three study groups were compared by the ANOVA or Kruskal Wallis test. Sensitivity, specificity, optimal cut off values and diagnostic accuracy were calculated, and ROC curves were constructed for AFP, VEGF, and VEGF/PLT.

Results: Our study included one hundred patients (HCC group: n=40, cirrhosis group: n=30, and control group: n=30). HCC patients had significantly higher serum VEGF and VEGF/PLT levels than the non-HCC groups (P=0.001). Serum VEGF and VEGF/PLT showed significant positive correlations with HCC tumor size, stage, vascular invasion and Child Pugh's classification. Moreover, a VEGF cut off value of 250 pg/ml provided 80% sensitivity and 81.7% specificity for discriminating HCC patient from non-HCC patients in comparison to AFP (65%, 83.33%, respectively). Similarly, the ratio of VEGF/PLT provided sensitivity and specificity of 77.5% and 80%, respectively which is higher than the accuracy provided by AFP. The combination of AFP, VEGF, and VEGF/PLT increased the accuracy for diagnosing HCC to >95%.

Conclusion: In HCV patients, serum VEGF and VEGF/PLT either separately or in combination with AFP are reliable biomarkers for early and accurate detection of HCC.

References: Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global Cancer Statistics 2018: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA: a cancer journal for clinicians. 2018 Sep 12; doi: 10.3322/caac.21492.

Disclosure: Nothing to disclose

P0078 ALBUMIN-BILIRUBIN GRADE (ALBI) SUGGESTS BETTER PROGNOSTIC MODEL THAN CHILD TURCOTTE PUGH (CTP) SCORE IN PREDICTING SURVIVAL FROM HEPATOCELLULAR CARCINOMA (HCC)

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Introduction: HCC is the second most frequent cause of cancer related death globally. CTP score is composed of bilirubin level, albumin level, prothrombin time, severity of ascites, and degree of hepatic encephalopathy. Among these five parameters, severity of ascites and hepatic encephalopathy are assessed by clinician and are subjective in certain degree.

The albumin-bilirubin (ALBI) grade system consists of only albumin and bilirubin levels. ALBI has been suggested by Johnson et al[1] as a simpler and more objective way to estimate liver function for patients with HCC. ALBI = (log10 bilirubin × 0.66) + (albumin × -0.085), where bilirubin is in μmol/L and albumin in g/L. ALBI ≤-2.60 or Grade 1 (showed median survival 18.5-85.6 months), ALBI >-2.60 to ≤-1.39 or Grade 2 (showed median survival 5.3-46.5 months) and ALBI >-1.39 or grade 3 (showed median survival 2.3-15.5 months).

Aims & Methods: To identify predictors of overall survival in HCC patients and validate ALBI grading system in our patients. Using the hospital informatics system, we retrospectively analysed all HCC cases between December 2013 and December 2018. We calculated CTP scores and ALBI grades at the time of diagnosis and compared them to HCC survival after diagnosis. The analysis was done using the IBM SPSS Statistics software version 25. Survival analysis was performed using the Kaplan-Meier (KM) method. We also performed receiver operating characteristic (ROC) analysis between the ALBI grades, CTP scores and death from HCC

Results: Total of 121 HCC patients were identified. 82 patients (67.8%) had liver cirrhosis at time of diagnosis. Majority of the patients had relatively good liver function (Child A 64.5%, Child B 24% and child C 11.5%). There was a significant negative relationship between both CTP score and ALBI grade and survival (p < 0.05). Mean and median survival for ALBI grade 1 were 37.7 and 26 months, ALBI grade 2 were 13.4 and 6 months and for ALBI grade 3 were 4.5 and 3 months. Mean and median survival for CTP score A were 26.3 and 15 months ,CTP score B were 9.6 and 5 months and for CTP score C were 3.2 and 2 months. Visually the KM curves showed better discriminative performance for ALBI grade than CTP score. In addition, comparison of ROC curves of CTP and ALBI for outcome of death in the

study showed that ALBI was better than CTP in detecting death from HCC.

Conclusion: We found that both CTP and ALBI have significant inverse relationship with HCC survival. However, ALBI grading system discriminates HCC survival better than CTP. ALBI does not require clinical assessment as in CTP score and hence is not subjective to assessment variability between clinicians. ALBI is easier to apply as a prognostic test for HCC survival.

References: 1. Johnson PJ, Berhane S, Kagebayashi C, et al. Assessment of liver function in patients with hepatocellular carcinoma: a new evidence-based approach-the ALBI grade. J Clin Oncol. 2015;33(6):550-8. 2. Hiraoka A, Michitaka K, Kumada T, et al. Validation and Potential of Albumin-Bilirubin Grade and Prognostication in a Nationwide Survey of 46,681 Hepatocellular Carcinoma Patients in Japan: The Need for a More Detailed Evaluation of Hepatic Function. Liver Cancer. 2017;6(4):325-336. 3. Chen B, Lin S. Albumin-bilirubin (ALBI) score at admission predicts possible outcomes in patients with acute-on-chronic liver failure. Medicine (Baltimore). 2017;96(24):e7142. 4. Lee PC, Chen YT, Chao Y, et al. Validation of the albumin-bilirubin grade-based integrated model as a predictor for sorafenib-failed hepatocellular carcinoma. Liver Int. 2018;38(2):321-330. 5. Hiraoka A, Kumada T, Kudo M, et al. Albumin-Bilirubin (ALBI) Grade as Part of the Evidence-Based Clinical Practice Guideline for HCC of the Japan Society of Hepatology: A Comparison with the Liver Damage and Child-Pugh Classifications. Liver Cancer. 2017;6(3):204-215.

Disclosure: Nothing to disclose

P0079 WITHDRAWN

P0080 DEVELOPMENT AND EXTERNAL VALIDATION OF PROGNOSTIC NOMOGRAMS IN HEPATOCELLULAR CARCINOMA PATIENTS: A POPULATION BASED STUDY

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Introduction: Hepatocellular carcinoma (HCC) is the sixth most common cancer and the second most deadly cause of cancer mortality worldwide. Improvements in treatment strategies have markedly improved the overall survival (OS) and cancer-specific survival (CSS) of HCC patients, although the long-term survival rate remains low. We attempted to construct and validate novel nomograms to predict OS and CSS in HCC patients.

Aims & Methods: A total of 15394 HCC patients were included in the study and randomly divided into a discovery set (n=10262) and an internal testing set (n=5132) obtained from the Surveillance, Epidemiology, and End Results (SEER) database. We used a univariate Cox regression analysis to screen for clinicopathological risk factors for OS and CSS in the SEER discovery set. We further performed multivariate Cox regression analysis to screen for important risk factors. All variables were screened using the forward stepwise selection method in a Cox multivariate analysis regression model. Based on univariate and multivariate Cox regression analyses, we identified independent risk factors for OS and CSS. Concordance indexes (c-indexes) were used to evaluate model discrimination. Calibration plots were constructed to validate the accuracy and reliability of the nomograms. The predictive accuracy and clinical values of the nomograms were measured by decision curve analysis (DCA).

Results: The 1-, 3- and 5-year OS rates were 63.99%, 40.91%, 30.78% and 80.10%, 58.36%, 45.19% in the SEER and the SYMH cohorts, respectively. The median CSS durations in the above four sets were 1230, 1200, 1200 and 1701 days, respectively; while the 1-, 3- and 5-year CSS rates were 73.12%, 54.25%, 45.42% and 88.68%, 69.70%, 50.23% in the SEER and the SYMH cohorts. The c-index for the OS prediction nomogram was 0.753 (95% CI, 0.745-0.761) based on age, sex, race, marital status, histological grade, TNM stage, tumor size, and surgery performed in the discovery set, while the c-indexes for TNM stage, histologic grade and tumor size for OS prediction were 0.555 (95% CI, 0.547-0.563), 0.654 (95% CI, 0.646-0.662), and 0.618 (95% CI, 0.612-0.624), respectively. Similarly, Our CSS nomogram with a c-index of 0.748 (95% CI, 0.740-0.756) was higher than the c-indexes for TNM stage, grade and tumor size. The calibration curves fit well. DCA showed that the two nomograms provided substantial clinical value. Based on risk stratification by the nomograms, in the low-, intermediate- and high-risk subgroups, the 1-year OS rates were 85.59%, 52.78%, and 20.57%, the 3-year OS rates were 63.72%, 22.64%,

and 4.38%, the 1-year CSS rates were 90.69%, 59.95%, and 23.39%, and the 3-year CSS rates were 75.23%, 31.18%, and 6.88%, respectively. Internal validation produced c-indexes of 0.758 and 0.752 for OS and CSS, respectively, while external validation in the Sun Yat-sen Memorial Hospital (SYMH) cohort produced a c-indexes of 0.702 and 0.686 for OS and CSS, respectively.

Conclusion: Based on the clinical risk factors identified in a large population-based cohort, we established practical prognostic nomograms that can objectively and accurately predict long-term OS and CSS in HCC around the world. Moreover, the internal and external cohort validation results demonstrate that these nomograms perform very well and have high accuracy and reliability. Our nomograms may enable more accurate individualized predictions of OS and CSS to help doctors better formulate individual treatment and follow-up management strategies.

Disclosure: Nothing to disclose

P0081 SORAFENIB FOR PATIENTS WITH RECURRENT HEPATOCELLULAR CARCINOMA AFTER LIVER TRANSPLANTATION: INTRINSIC RESISTANCE OR NOT?

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Introduction: The use of sorafenib in patients with hepatocellular carcinoma (HCC) recurring after orthotopic liver transplantation (OLT) may be challenging. Increased toxicity from interaction with immunosuppressants are a common issue. Also, poor outcomes have been reported. However, it has not been investigated whether these outcomes derive from a dire clinical presentation or from a resistance to sorafenib.

Aims & Methods: We aimed to compare the overall survival (OS) of sorafenib-treated post-OLT HCC with that other sorafenib-treated HCCs.
We analyzed a large retrospective-prospective database gathering the clinical data of 487 patients from 6 Italian centres, who were prescribed with sorafenib between 2008 and 2017. Eighteen patients with HCC recurring after OLT were identified. A propensity score analysis comparing their clinical and tumor characteristics with those of 90 matched controls (sorafenib in patients without OLT) was performed. Propensity score included performance status, alfa-fetoprotein >400 ng/ml, macrovascular invasion, extrahepatic spread.

Results: Characteristics of the OLT patients and matched controls are reported in Table 1.

	OLT patients (n=18)	Sorafenib controls (n=90)	P
Males	16 (88.9%)	80 (88.9%)	1.000
Age	59 (56-67)	65 (62-74)	0.101
Performance status			
- ECOG-PS 0	14 (77.8%)	71 (78.9%)	1.000
- ECOG-PS 1	4 (22.2%)	19 (21.1%)	
BCLC stage			
- Intermediate	4 (22.2%)	21 (22.2%)	1.000
- Advanced	14 (77.8%)	69 (73.8%)	
Macrovascular invasion	2 (11.1%)	16 (17.8%)	1.000
Extrahepatic spread	13 (72.2%)	65 (72.2%)	1.000
Alfa-fetoprotein>400 ng/ml	4 (22.2%)	19 (21.1%)	1.000

[Table 1]

Immunosuppressant in OLT patients included: everolimus (n=10), tacrolimus (n=4), sirolimus (n=2), cyclosporine (n=2). Toxicities were similar in the two groups.The median treatment duration [4.5 months (95%CI 3.0-6.1) vs 5.9 months (95% CI 4.0-7.9), p=0.344] was comparable as well as the rate of radiologic disease control (44.4 vs 52.5%, p=0.323). Finally, the OS was also similar [11.5 months (95%CI 9.2-13.8) vs 13.5 months (95%CI 9.7-17.3), p=0.725] in OLT and non-OLT groups, respectively.

Conclusion: Extrahepatic spread was common in patients with HCC recurring after OLT, possibly reflecting the negative effects of immunomodulation.. However, once sorafenib was started, treatment duration, radiological response and OS were comparable with those of controls. The prognosis of these patients seems to be more influenced by their clinical presentation rather than by a reduced efficacy of sorafenib.

References: 1) Zavaglia C, Airoldi A, Mancuso A, Vangeli M, Viganò R, Cordone G, Gentiluomo M, Belli LS. Adverse events affect sorafenib efficacy in patients with recurrent hepatocellular carcinoma after liver transplantation: experience at a single center and review of the literature. Eur J Gastroenterol Hepatol. 2013 Feb;25(2):180-6. 2) Vitale A, Boccagni P, Kertusha X, Zanus G, D'Amico F, Lodo E, Pastorelli D, Ramirez Morales R, Lombardi G, Senzolo M, Burra P, Cillo U. Sorafenib for the treatment of recurrent hepatocellular carcinoma after liver transplantation? Transplant Proc. 2012 Sep;44(7):1989-91 3) Mancuso, A., Mazzola, A., Cabibbo, G., Perricone, G., Enea, M., Galvano, A., Zavaglia, C., Belli, L. and Cammà, C. Survival of patients treated with sorafenib for hepatocellular carcinoma recurrence after liver transplantation: A systematic review and meta-analysis, Digestive and Liver Disease 2015, 47(4), pp. 324-330.

Disclosure: Nothing to disclose

P0082 "CHEMO-VACATION PERIOD" GAINED BY ADJUVANT HEPATECTOMY FOR SYNCHRONOUS BILATERAL MULTIPLE COLORECTAL LIVER METASTASIS

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Introduction: Recently, number of patients with synchronous bilateral multiple colorectal liver metastasis (SBM-CRLM) who underwent adjuvant hepatectomy (AH) is increasing. In such cases, surgery is often performed as one choice of multidisciplinary therapy even for patients with low possibility of complete cure. It is because most surgeons or medical oncologists consider that "chemo-vacation period" gained by AH have some possibility to give a positive impact for the patients' quality of life (QOL) and second line treatment. However, there has been no reports investigating actual period of "chemo-vacation".

Aims & Methods: The aim of this study is to investigate the surgical outcome of resected cases for SBM-CRLM and to clarify the "chemo-vacation period".
35 patients who underwent AH (2013-2018) for SBM-CRLM were examined. R0 or R1 resection was achieved in all patients. Chemo-vacation period was defined as the duration between the latest date of pre or post-operative chemotherapy and the date of re-inducing chemotherapy for the post-operative recurrence.

Results: The median number of liver metastasis was 7 (range; 2-30). Anatomical hepatectomy was performed for 25 patients (71.4%). The median hospitalization after AH was 12 days and there was no mortality. Recurrence was developed in 16 patients (45.7%). The median recurrence fee survival time, 3-year recurrence free survival rate and 3-year overall survival rate were 428 days, 48.2% and 87.1%, respectively. Re-induction of chemotherapy for the recurrence was done in 9 patients. In these cases, the median "chemo-vacation period" was 155 days.

Conclusion: Although post-operative recurrence was occurred in high rate, overall survival rate was relatively good. AH gained about 5 months of "chemo-vacation period" even in cases with recurrence.

Disclosure: Nothing to disclose

P0083 RISK FACTORS FOR SYMPTOMATIC GALLSTONE DISEASE AFTER ROUX-EN-Y GASTRIC BYPASS

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Introduction: Patients with morbid obesity are at risk for symptomatic gallstone disease after bariatric surgery. Up to 15% of patients will develop biliary symptoms within two years after surgery. Although bariatric surgery is performed widely nowadays, specific risk factors for gallstones have not been well defined. Therefore, we aimed to identify risk factors for symptomatic gallstone disease after laparoscopic Roux-en-Y gastric bypass (LRYGB).

Aims & Methods: We conducted a case-control study of patients who underwent a LRYGB between 2013 and 2015 in the MC Slotervaart (Amsterdam, The Netherlands). Primary endpoint was symptomatic gallstone disease defined as the need for cholecystectomy because of postoperative biliary symptoms within two years after surgery. We selected for each case two controls without symptomatic gallstone disease after surgery. Logistic regression analyses were used to identify risk factors for symptomatic gallstone disease.

Results: Between 2013 and 2015, 1780 primary LRYGBs were performed. We identified 233 (13.1%) cases who developed symptomatic gallstones after a median [IQR] of 9 [5-14] months, and 466 controls. Younger age [OR (95% CI) 0.98 (0.96-0.99)], female gender [OR 1.83 (1.06-3.17)], Caucasian ethnicity [OR 1.82 (1.10-3.02)], higher percent total weight loss (%TWL) at 12 months [OR 1.06 (1.04-1.09)] and preoperative pain syndrome [OR 2.72 (1.43-5.18)] were associated with an increased risk for symptomatic gallstones. In a subgroup of patients who developed symptomatic gallstones within 9 months, preoperative statin use was associated with a reduced risk [OR 0.27 (0.09-0.78)].

Conclusion: In our study, higher %TWL and preoperative pain syndrome were associated with an increased risk of symptomatic gallstones besides the traditional risk factors female gender and Caucasian ethnicity. Most factors can be used to identify high-risk patients, who might benefit from preventive measures. Whether statins can protect bariatric patients from developing gallstones should be investigated prospectively.

Disclosure: Nothing to disclose

P0084 SALVAGE TECHNIQUE FOR DOUBLE-BALLOON ENTEROSCOPY-ASSISTED ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY USING A MICRO GUIDEWIRE

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Introduction: Double-balloon enteroscopy-assisted endoscopic retrograde cholangiopancreatography (DBE-ERCP) in patients with altered gastrointestinal anatomy is a technically difficult procedure. Particularly, biliary cannulation in DBE-ERCP may be challenging for even endoscopic retrograde cholangiopancreatography (ERCP) experts because the endoscopic maneuver of double-balloon enteroscopy (DBE) is different from that of conventional duodenal endoscopy. On the contrary, micro guidewire (GT wire; 0.016-inch, 300 cm, TERUMO, Japan; GTW) designed for super-selective angiography is reported to assist in difficult biliary cannulation in ERCP (UEGW 2017 and 2018). Hence, we developed a novel biliary cannulation technique using GTW for DBE-ERCP.

Aims & Methods: We aimed to assess the usefulness of GTW in the salvage technique for biliary cannulation using DBE-ERCP. We studied 20 consecutive ERCP-naive patients with altered gastrointestinal anatomy between

August 2014 and October 2018. We attempted to perform biliary cannulation for DBE-ERCP using conventional techniques, including wire-guided cannulation or pancreatic guidewire placement with conventional guidewire (0.025 or 0.035 inch) in the first 10 min. When the endoscopists found the procedure challenging, they were permitted to switch to GTW after 10 min to achieve cannulation and change the guidewire to GTW after 60 min from initiation of the procedure. DBE-ERCP-difficult-patients were defined as those who underwent biliary cannulation with GTW. Selective biliary cannulation was performed under fluoroscopic control.

Results: The 20 consecutive ERCP-naive patients with altered gastrointestinal anatomy included 14 males and 6 females. The age (median [range]) was 77 [59-88] years. Twelve patients had common bile duct stones, 7 had malignant biliary strictures, and 1 had primary sclerosing cholangitis. All endoscopists, except one expert, were inexperienced in DBE-ERCP, despite more than 5 to 10 years of experience in ERCP (3 experts with more than 10 years and 5 trainees with 5-10 years). The conventional technique was successful in 55% (11/20) patients (con group), while it was unsuccessful in 1 case owing to worse clinical conditions during this procedure (unused GTW). Although 40% (8/20) patients who failed the biliary cannulation were considered DBE-ERCP-difficult-patients, the GTW technique was successful for biliary cannulation in 100% (8/8) cases (GTW group). Consequently, the overall success rate improved from 55% to 95% (19/20 patients). The reaching time to the blind end was not significantly different between the con group and GTW group (25 [12-69] min and 22 [15-38] min, respectively). The cannulation time (the time from advancement of the cannula out of the endoscope channel to the successful deep cannulation) in the con group was 8.8 [3-47] min. Although the switched time (the time from advancement of the cannula out of the endoscope channel to that when switched to GTW) in the GTW group was 38 [15-61] min, the cannulation time after switch to GTW was 3.8 [1.2-15] min and significantly shorter than that before switch to GTW (P=0.01, Wilcoxon signed-rank test).

Conclusion: Although the biliary cannulation in DBE-ERCP with altered gastrointestinal anatomy was difficult for inexperienced endoscopists in DBE-ERCP, the salvage technique using a micro guidewire can facilitate this procedure.

Disclosure: Nothing to disclose

P0085 A PROSPECTIVE STUDY OF TEMPORARY PLACEMENT OF A FULLY-COVERED METAL STENT FOR REFRACTORY BENIGN BILIARY STRICTURE

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Introduction: Endoscopic treatment utilizing balloon dilation and plastic stent placement has been established as a standard of care for benign biliary strictures (BBS). However, patients with recurrent or refractory strictures necessitate long duration of endoscopic, percutaneous or even surgical treatment.

Aims & Methods: The aim of this prospective exploratory trial was to evaluate the effectiveness and safety of temporary placement of a fully-covered self-expandable metal stent (FCSEMS) for patients with refractory BBS, especially with biliary anastomotic stricture after living-donor liver transplantation (LDLT) and hepaticojejunostomy anastomotic strictures (HJAS). We included patients with refractory BBS defined as strictures resistant to balloon dilation and plastic stent placement longer than six months. FCSEMS (Niti-S Kaffes stent, Taewoong medical, Gyeonggi-do, South Korea) was placed endoscopically and removed after 3 months. In cases with HJAS, FCSEMS was placed under double-balloon endoscope-assisted endoscopic retrograde cholangiopancreatography. The primary outcome was a rate of stricture resolution at FCSEMS removal. The secondary outcomes included rates of stricture recurrence and adverse events. The trial was registered to UMIN-CTR (UMIN000022164).

Results: A total of 30 patients were eligible for this study between September 2016 and February 2018. The major causes of BBS were 13 LDLT, and 12 HJAS, and the other etiology of BBS included 1 post-cholecystectomy, 2 chronic pancreatitis and 1 post-hepatectomy. The location of BBS was dis-

tal in 2, proximal or IHBD in 16, and at the site of bilio-enteric anastomosis in 12. A median time from initial biliary drainage to FCSEMS placement was 25.5 months (interquartile range [IQR] 11.0-45.1). FCSEMS was placed in 29 patients except one developing cholangitis prior to FCSEMS placement. One patient needed premature FCSEMS removal due to cholangitis on day 65. Finally, a total of 28 patients completed a planned indwelling period of 90 days and all FCSEMS were successfully removed without difficulty. The rate of stricture resolution at FCSEMS removal was 96.6%. Stricture recurrence occurred in 10.7% during a median follow-up period of 15.6 months (IQR 12.0-22.1). Adverse events were observed in 10.3%: 5 cholangitis (3 moderate and 2 mild), 1 pancreatitis (moderate) and 1 intra-abdominal air (moderate).

Conclusion: Temporary placement of FCSEMS was a feasible and effective treatment option for refractory BBS such as anastomotic strictures after LDLT and HJAS.

Disclosure: Nothing to disclose

P0086 ENDOSCOPIC SPHINTEROTOMY DOES NOT DECREASE THE RECURRENCE OF CHOLECYSTITIS

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Introduction: Although, cholecystectomy is the treatment of choice for cholecystitis, many patients with comorbidities cannot undergo this surgical treatment. Percutaneous transhepatic gallbladder drainage (PTGBD) is the other treatment option for these patients. However, afterward, removing of PTGBD is not easy due to relative high risk of recurrent cholecystitis.

Aims & Methods: The aim of our study is to evaluate the role of endoscopic sphincterotomy on reducing the recurrence of cholecysitis. The patient who underwent PTGBD due to cholecystitis between January 2011 and April 2018 in Kyungpook National University Hospital, Republic of Korea were retrospectively analyzed. After improvement of acute cholecystitis by PTGBD, scheduled removal of PTGBD was conducted. We compared recurrence rate between endoscopic sphincterotomy group with observation group after removal of PTGBD.

Results: Among total of 1,148 PTGBD cases, patients scheduled for cholecystectomy, follow up duration of less than 1 year, loss of follow up, no removal of PTGBD, direct trauma or cancer related cholecystitis, prior sphincterotomy before PTGBD, percutaneous transhepatic biliary drainage with balloon dilatation at bile duct sphincter, and secondary cholecystitis were excluded. 126 patients were enrolled in this study. Among them, 40 patients underwent endoscopic sphinterotomy after PTGBD. The other 86 patients were treated without a specific procedure. The PTGBD was removed after improvement of PTGBD. The median interval between PTGBD and sphincterotomy was 108 days (range, 0-1,988). The total recurrence rate of cholecystitis was 15.1% (19/126) in the median follow-up period of 1,159 days (range, 369-2,774 days). There was no difference of recurrence rate between endoscopic sphincterotomy and observation group by using Kaplan-Meier curves with the log-rank test (P=0.807). There was a tendency of shorter duration of recurrence in observation group than endoscopic sphincterotomy group (mean±SD days; 830±603.1 vs. 1,033±669.9, p=0.093). However, this difference is not significant statistically. The only factor that increase recurrent cholecystitis was the presence of gallstone (P=0.048, by Kaplan-Meier analysis).

Conclusion: Endoscopic sphincterotomy do not reduce recurrent cholecystitis that treated by PTGBD. Other strategies for reducing recurrent cholecytitis should be investigated for patients who cannot undergo cholecystectomy and need PTGBD.

Disclosure: Nothing to disclose

P0087 PNEUMOBILIA AND AN ABSENCE OF INTRAHEPATIC BILE DUCT DILATATION ARE PREDICTORS OF ANASTOMOTIC PATENCY AFTER CHOLEDOCHOJEJUNOSTOMY

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Introduction: Cholangitis due to anastomotic strictures after choledochojejunostomy are treated with double-balloon endoscopic retrograde cholangiography (DBERC) and dilatation. However, some patients with cholangitis did not show anastomotic strictures on endoscopic findings.

Aims & Methods:

Aim: To evaluate predictors of anastomotic strictures in patients after choledochojejunostomy.

Methods: We reviewed 367 patients with surgically altered biliary anatomy evaluated by DBERC from January 2007 to March 2017. We anticipated strictures at the choledochojejunostomy in 76 patients due to cholangitis or obstructive jaundice (21 after biliary resection, 21 after pancreaticoduodenectomy, and 34 after living donor liver transplantation). Anastomotic patency was evaluated in association with the following factors: fever, persistent cholangitis, elevation of liver enzymes, bilirubin, or CRP, pneumobilia of the intrahepatic bile ducts (IHBD), retained fluid in the afferent limb, dilatation of IHBD (>5mm) on computed tomography (CT) scan, and stones in the IHBD.

Results: Of 76 patients who underwent DBERC for suspicion of anastomotic stricture, 64 had a stricture at the anastomosis, and 12 did not. In univariate analysis, normal serum liver enzyme levels (p=0.028), absence of IHBD dilatation (p=0.037) and pneumobilia (p< 0.01) were significantly associated with anastomotic patency. In multivariate analysis, pneumobilia (p=0.01, Odds Ratio [OR]7.01) and absence of IHBD dilatation (p=0.026 OR0.06) were independent predictors of anastomotic patency. The combination of these two factors were significantly associated with anastomotic patency (p< 0.01, OR 0.03).

Conclusion: Pneumobilia and the absence of IHBD dilatation on CT scan are predictors of anastomotic patency. Patients with both factors are highly likely to have a patent anastomosis and can usually be treated without endoscopic or surgical procedure.

Disclosure: Nothing to disclose

P0088 PREDICTORS OF CONFIRMED COMMON BILE DUCT STONES AFTER A POSITIVE INTRA-OPERATIVE CHOLANGIOGRAM DURING CHOLECYSTECTOMY: LABORATORY, RADIOLOGIC, AND DEMOGRAPHIC FACTORS

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Introduction: Among patients with symptomatic gallstones, initial evaluation of suspected choledocholithiasis includes serum liver biochemical tests and transabdominal ultrasound. Patients with intermediate probability of choledocholithiasis undergo further evaluation with either pre-operative EUS or an IOC. However, the incidence of false positive results is increasing, thus subjecting patients for unnecessary interventions.

Aims & Methods: Our aim in is to evaluate the correlation between pre-operative and intra-operative findings with the presence of a CBD stone on ERCP.

This is a retrospective review of chart study, where all patients who underwent IOC during their same stay laparoscopic cholecystectomy at the American University of Beirut Medical Center, Lebanon between 2010 and 2018. All patients who were admitted for gallstone related LC were scanned. Patients with a positive IOC (filling defect, non-passage of contrast to duodenum, or dilated CBD that didn't resolve upon surgical manipulation) who were further followed with ERCP or EUS for suspected CBD stone were included. The subjects were divided into 2 groups, those with a confirmed CBD stone and those with a false positive IOC. Data col-

lected included: patient's age, gender, pre-operative laboratory results, pre-operative abdominal imaging (EUS, right abdominal ultrasound, or CT abdomen), IOC findings and post LC ERCP results were included. We used McNemar's test, paired t test, and conditional logistic regression analysis to compare the two groups.

Results: During the specified period, the files of 685 patients who had IOC during LC were scanned. Among those, 35 patients were found to have a positive IOC and were followed up endoscopically. The average age of our population was 52 ± 20 years, with a female predominance of 62.9% (22 patients).

The most common indication for LC was cholecystitis (17, 49%) followed by cholelithiasis (15, 43%). The most common IOC finding was "non-passage of contrast to the duodenum" with 29 patients, followed by filling defect in 19 patients. CBD stone was confirmed in 25 patients (71.40%).

Comparing the 2 groups, patients who had CBD stone were older, and were more likely to have a normal serum liver biochemical test (table). On pre-op imaging, none of the patients who had a false positive result had CBD dilation. Regarding IOC findings, dilated CBD on IOC was significantly associated with the presence of CBD stone on further investigations (p=0.028). On multivariate analysis, dilated CBD on IOC, was found to be an independent predictor of a CBD stone with OR= 9 [1.0-82.5, p=0.052].

Demographics and Operative variables	No evidence of CBD stones (n=10)	CBD stone (n=25)	p-value
Age, mean (SD)	46 (16)	54 (21)	0.253
Gender (female), n (%)	7 (70%)	15 (60%)	0.709
Pre-operative AST (IU/L), mean (SD)	69 (89)	131 (160)	0.154
Pre-operative ALT (IU/L), mean (SD)	131 (210)	170 (243)	0.646
Pre-operative Alkaline phosphatase (IU/L), mean (SD)	194 (197)	168 (164)	0.722
Pre-operative gGT (IU/L), mean (SD)	152 (180)	192 (232)	0.591
Pre-operative lipase (IU/L), mean (SD)	45 (42)	157 (530)	0.329
Pre-operative total bilirubin (mg/dL), mean (SD)	1 (2)	1 (1)	0.749
Pre-operative imaging			
CBD dilation on any imaging, n (%)	0 (0%)	7 (33%)	0.142
IOC abnormality			
Dilated CBD, n (%)	1 (10%)	13 (52%)	0.028
Filling defect, n (%)	7 (70%)	12 (48%)	0.285
Non-passage of contrast to duodenum, n (%)	6 (60%)	15 (60%)	1.000

[Clinical characteristics of IOC positive patients who were followed up endoscopically.]

Conclusion: IOC findings are important in guiding the post-operative management of patients with suspected CBD stones. A dilated CBD on IOC is the strongest predictor of CBD stones and should prompt further investigations.

Disclosure: Nothing to disclose

P0089 ASSESMENT OF CONSENSUS CRITERIA FOR CHOLEDOCHOLITHIASIS: ARE THEY USEFUL IN THE CLINICAL PRACTICE?

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Introduction: Biliary lithiasis is a condition that affects about 15% of the population in Europe and North America. In 10-15% of cases it is complicated by the presence of choledocholithiasis, which is suspected in the scenarios of symptomatic cholelithiasis and acute biliary pancreatitis, as well as other presentations such as de novo lithiasis in cholecystectomized patients. In Argentina, the prevalence of choledocholithiasis in patients undergoing cholecystectomy with or without suspicion is 15.1%. Choledo-

cholithiasis is associated with severe complications such as cholangitis and acute pancreatitis. The endoscopic retrograde cholangiopancreatography (ERCP) is the treatment of choice for choledocholithiasis, but is associated with 5-10% risk of complications. Therefore, an accurate selection of patients with high probability of having choledocholithiasis is essential in the management of this population.

The guide of the American Society of Gastrointestinal Endoscopy (ASGE) have proposed criteria to stratify patients into low, intermediate and high risk of choledocholithiasis using variables readily available in clinical practice. The objective of the present study was to establish the diagnostic accuracy of these criteria, as well as to evaluate the presence of additional variables that are associated with the presence of choledocholithiasis.

Aims & Methods: A cross-sectional cohort study was conducted at San Martin de La Plata Hospital during the period between 2017 and 2019. All patients older than 15 years referred for ERCP with suspected choledocholithiasis that met ASGE criteria of high and intermediate risk of choledocholithiasis were considered for inclution. Presence of stone at ERCP served as criteria standard.

Results: During the study period, 653 patients met inclusion criteria. Of the 645 patients in high risk for choledocholithiasis group, 451 were found to have stones during ERCP (69.9%). Of the 8 patients at intermediate risk for choledocholithiasis, 5 were found to have stones during ERCP (62.5%); *P*-value for the difference between groups = 0.703. The diagnostic accuracy for choledocholithiasis in the high-risk group was 70%, and for the intermediate risk group it was 30%.

The presence of choledocholithiasis on pre-ERCP imaging presented 1.5 times more probability of having stones at ERCP compared with those who did not have it (OR: 2.49, 95% CI 1.49-4.16), being the strongest predictor of choledocholithiasis. In a multivariate logistic regression analysis, an increase of alkaline phosphatase (ALP) above normal value was found as an additional variable (OR: 2.09, 95% CI 1.32-3.34). The time between the pre-ERCP imaging with evidence of choledocholithiasis and the evidence of choledocholithiasis at ERCP was 9 days (5-19), and 12 days (7-21) in patients without evidence of choledocholithiasis at ERCP (p = 0.0423).

	Predictor	OR	CI 95%
	Elevated transaminases	0.67	(0.41-1.06)
	Elevated ALP	2.09	(1.32-3.34)
ERCP indication	Suspected choledocholithiasis	Reference	
	Suspected ascending cholangitis	2.32	(0.92-7.12)
	Suspected gallstone pancreatitis	0.37	(0.11-1.21)
	Choledocholithiasis	2.7	(1.59-4.60)

[multivariate logistic regression analysis]

Conclusion: The use of ASGE criteria to predict the likelihood of choledocholithiasis are useful in high-risk patients and can be used in daily practice. The evidence of choledocholithiasis in imaging is the strongest predictor associated with the presence of stones at ERCP. The increase of serum ALP is an additional variable related to the presence of choledocholithiasis at ERCP.

Disclosure: Nothing to disclose

P0090 IDENTIFICATION OF MALIGNANT BILIARY STRICTURES VIA PROFILING OF EXHALED VOLATILE ORGANIC COMPOUNDS USING AN ELECTRONIC NOSE: A PILOT STUDY

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Introduction: Determination the dignity of biliary strictures in patients with obstructive jaundice can be challenging. Present procedures still have difficulties to differentiate between malignant and benign strictures and other methods are needed to avoid wrong diagnoses. One novel diagnostic tool could be the profiling of volatile organic compounds (VOCs) in exhaled breath via training an artificial neural network (ANN) that showed promising results in previous studies detecting other malignant tumours.

Aims & Methods: Aim of this pilot study is to investigate the diagnostic performance of a handheld electronic nose by analysing VOC patterns in exhaled breath of patients with malignant and benign biliary obstruction. In this prospective study we included 107 patients with obstructive jaundice.

Before an invasive procedure (endoscopy or surgery) was performed, exhaled breath of all patients was sampled and processed using an electronic nose device (Aeonose™, The eNose Company, Zutphen, The Netherlands). Only patients with histologically confirmed diagnosis or with bile duct stones were considered in the analysis and divided into two groups: malignant and benign biliary obstruction.

The electronic nose measurement data obtained were used for training an ANN and cross-validated using the 'Leave-10%-Out' technique. Patient characteristics, including laboratory values, were documented and analysed statistically.

Results: 60 patients with malignant (cholangiocarcinoma, pancreatic cancer, liver metastases, hepatocellular carcinoma) and 47 patients with benign (bile duct stones, chronic pancreatitis, primary sclerosing cholangitis, postoperative) biliary stenosis were compared. The trained ANN was able to distinguish between the two groups with an accuracy of 0,79 and an area under the curve of 0,82. The sensitivity and specificity were 80 (95% confidence interval [CI] 0,67-0,89) and 0,77 (95% CI 0,62-0,87), respectively. The positive predictive value to diagnose correctly a malignant biliary stricture was found to be 0,81.

Conclusion: The use of an electronic nose in combination with a competent ANN can be a new non-invasive diagnostic tool in the discrimination of obscure bile duct strictures. However further training is needed to improve the accuracy of the ANN.

Disclosure: Nothing to disclose

P0091 SINGLE-OPERATOR PERORAL CHOLANGIOSCOPY-GUIDED LITHOTRIPSY FOR DIFFICULT BILIARY STONES: A PROSPECTIVE MULTICENTER STUDY

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Introduction: ERCP is the first choice for the removal of biliary stones. In difficult stones, advanced therapeutic techniques, such as electrohydraulic lithotripsy (EHL) and laser lithotripsy (LL) have been proposed. Recently, the availability of single-operator cholangioscopy (SOC) turned these techniques more accessible and easier to perform.

Aims & Methods: We sought to evaluate the clinical efficacy and safety of SOC guided-lithotripsy using EHL or LL in patients with complex biliary stones.

A prospective study was carried out in 4 hospitals, comprising 45 consecutive patients with complicated biliary stones treated with SpyGlass DS (Boston Scientific, Marlborough, United States) guided-lithotripsy using EHL or Holmium LL. We analyzed the complete cleaning of the ducts, the incidence of adverse events, the impact of the number of stones and its location on clinical success, and the performance of the 2 lithotripsy modalities.

Results: 37 patients (82.22%) had common bile duct/common hepatic duct stones, 5 patients (11.11%) had a single cystic stump stone and 3 patients (6.66%) had intrahepatic stones. 37 patients (82.22%) were successfully treated in one procedure and the remaining 8 patients (17.77%) required additional sessions to obtain cleaning of the ducts. 28 patients were treated with LL: 24 (85.71%) achieved clinical success in a single session with a single laser fiber. 17 patients were treated with LEH: 7 patients (41.17%) were clinically successful in a single 1-fiber session; 6 patients required 2 fibers to obtain ductal cleansing in a single session.

Complications were mild in 7/45 (15.55%) patients and included fever (n = 5), cholangitis (n = 1), and mild pancreatitis (n = 1).

Conclusion: SOC guided-lithotripsy using EHL or LL in patients with difficult biliary stones is very effective and is associated with transient and mild complications. Although further studies are needed there is an apparent advantage in the use of laser technology.

Disclosure: Nothing to disclose

P0092 GALL STONE PANCREATITIS OUTCOMES IN THE ELDERLY

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Introduction: Gallstone pancreatitis is the most common cause of pancreatitis in the United States. Little is known about outcomes of gallstone pancreatitis in the elderly population. We aimed to examine the association of age with outcomes and management of acute gallstone pancreatitis

Aims & Methods: A retrospective study utilizing the 2014 National Inpatient Sample (NIS) database was performed. All Adult patient hospitalizations with a diagnosis of acute pancreatitis and gallstones were included in this study. We excluded hospitalizations with a diagnosis of acute pancreatitis from any other identifiable etiology. The outcome data including presence of organ failure, inpatient surgical procedures, length of hospital stay and mortality were obtained. Patient and outcome characteristics were compared using the Mann U Whitney test for non-normally distributed data and logistic regression was used to examine associations of elderly age with outcomes. We controlled for hospitalizations, patient and hospital-level characteristics.

Results: We identified 55,285 hospitalizations that met our inclusion criteria. 66% were ≤ 65 years compared to 33% > 65 years. Whites accounted for more admissions in both age groups (72% for age > 65 and 52% for age ≤ 65 years). Females had more episodes of acute gallstone-related pancreatitis (69% for ≤ 65 years and 61% for > 65 years). 58% of hospitalizations were in patients > 65 years with ≥ three comorbidities.

Endoscopic retrograde cholangiography (ERCP) was performed in 33% of hospitalizations > 65 years versus 20% of hospitalizations ≤ 65 years. 62% of hospitalizations ≤ 65 years had a cholecystectomy compared to only 44.7% in patients > 65 years. Finally, median length of stay was shorter in hospitalizations ≤ 65 years (4 days vs. five days; p-value < 0.001) compared to 65 and older.

On multivariable analysis, hospitalizations > 65 years were twice as likely (AOR 2.2, 95% CI 1.8- 2.8) to have acute kidney injury compared to hospitalizations ≤ 65 years.

There was no significant difference between having an acute respiratory failure (AOR 1.18, 95% CI 0.92 - 1.50) or need for mechanical ventilation (AOR 1.14, 95% CI 0.77-1.67) in patients > 65 compared to their counterparts ≤ 65 years. Patients > 65 years were 22% more likely (AOR 1.22, 95% CI 1.06 -1.41) to receive an ERCP but 31% less likely (AOR 0.69, 95% CI 0.61 - 0.79) to have a cholecystectomy (laparoscopic or open). Patients > 65 years were two times higher mortality (AOR 2.95, 95% CI 1.59 - 5.56) during hospitalization for acute pancreatitis compared to patients ≤ 65 years.

Conclusion: Results from our study show significant disparities in hospitalization outcomes in elderly patients. Hospitalizations with age > 65 had fewer cholecystectomies done during index admission compared to age ≤ 65 years. Similarly, significantly more comorbidities, end organ damage (AKI), and increased mortality was associated with elderly patients with acute gall stone pancreatitis.

Disclosure: Nothing to disclose

P0093 IMPROVING THE DIAGNOSTIC YIELD OF BILIARY BRUSH CYTOLOGY IN PANCREATOBILIARY CANCERS: A SINGLE CENTRE EXPERIENCE

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Introduction: The diagnostic sensitivity of brush cytology for malignant biliary stricture has typically reported to be low (6-64%). The perceived futility coupled with the emergence of endoscopic ultrasound (EUS) and

fine needle aspiration (FNA) with a higher reported sensitivity (74%), has curbed the enthusiasm to obtain brush cytology in suspected pancreatico-biliary malignances.

Aims & Methods: This retrospective study aims to investigate the diagnostic yield of biliary brush cytology following introduction of changes to practice in 2015 at a single centre tertiary hospital. The changes implemented in the laboratory were: (i) increased care in preparing specimens with the appointment of a chief cytology biomedical scientist, (ii) careful levelling through cell block in an attempt to reveal more entrapped tissue, and (iii) downsizing in cytopathology team to three dedicated pathologists to increase experience by maximising exposure to more cases. Endoscopic retrograde cholangiopancreatography (ERCP) operators were simultaneously encouraged to perform targeted vigorous brushing of strictures to increase cellular yield. All adult patients who had an index brush cytology for biliary stricture at ERCP from 1st January 2014 to 30th September 2018 were identified. Repeat brushing and ampullary sampling were excluded. Electronic patient record was searched for histocytopathology data, radiology report, multidisciplinary team (MDT) meeting outcome and clinic letters. Patients were considered to have a malignant outcome if (i) subsequent biopsy, FNA or resection confirmed primary or metastatic disease, or (ii) there was unequivocal radiological or clinical progression of malignant disease. Patients were considered to have a benign outcome if (i) subsequent resection was benign, or (ii) clinical follow-up for a minimum of 6 months was uneventful. Cytology positive was defined as confirmed or suspicious malignant. Cytology negative was defined as atypical, negative or non-diagnostic. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated. Differences in yield between cancers were compared using chi-squared test.

Results: 201 patients met the inclusion criteria. Mean age at presentation was 69.5 years (60% male). Cytological diagnosis were as follows: malignant 48.2%, suspicious 11.1%, atypical 14.1%, negative 25.6% and non-diagnostic 1.0%. 78.6% of biliary strictures were cancers with 54.4% pancreatic, 36.1% cholangiocarcinoma, 3.8% gallbladder, 1.9% ampullary and 3.8% metastatic or other. Diagnostic test characteristics for detecting cancer before (2014-15) and after (2016-18) changes in practice are presented in Table 1. Marked improvement in sensitivity was noted (68.7% vs 83.0%). A slight drop in specificity and PPV was due to a false positive result in a patient with primary sclerosing cholangitis. There were no statistically significant difference in brush cytology yield between pancreatic cancer and cholangiocarcinoma (P=0.84).

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
2014-15	66.7	100.0	100.0	44.4	75.0
2016-18	83.0	96.3	98.7	61.9	86.0

[Table 1: Diagnostic performance for detecting cancer in index biliary brushing of 201 patients before(2014-15) and after(2016-18) changes to practice.]

Conclusion: The sensitivity of biliary brush cytology for the detection of malignant biliary strictures in our centre is higher than reported in the literature with excellent PPV. Multifaceted changes in practice and workforce restructuring can produce comparable yield to EUS FNA. Biliary brush cytology remains a valuable tool in diagnosing pancreatobiliary cancers with no difference in yield between pancreatic cancer and cholangiocarcinoma.

References: Burnett AS, Calvert TJ, Chokshi RJ. Sensitivity of endoscopic retrograde cholangiopancreatography standard cytology: 10-y review of the literature. J Surg Res 2013;184:304-11. Burnett AS, Bailey J, Oliver JB, et al. Sensitivity of alternative testing for pancreaticobiliary cancer: a 10-y review of the literature. J Surg Res 2014;190:535-47.

Disclosure: Nothing to disclose

Pancreas I
10:30-17:00 / Poster Exhibition - Hall 7

P0094 A NOVEL APPROACH FOR STUDY OF PANCREATIC DUCTS IN MICE

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Introduction: Tissue slice technique offers several benefits compared to isolated cells that helps us to understand (patho)physiology of several organs *in situ*. The most prominent feature are intact homotypic in heterotypic interactions within the tissue. In the pancreas, this technique has been successfully applied to study acinar and endocrine islet cells; however, has never been used to investigate ductal function. Since pancreatic ductal epithelial cells (PDECs) play essential role in the physiology of the pancreas, our aim was to apply this technique to pancreatic ductal cells and thus study these cells in a more *in* vivo physiological conditions.
Aims & Methods: 8-16 weeks old C57BL/6 mice were used for the preparation of pancreatic tissue slices. Low-melting point agarose was retrogradely injected into the common bile duct that served as a scaffold for further manipulation. For morphological studies, agarose-embedded tissue was further subjected to 15 μm thick cryosectioning. In order to visualize pancreatic ducts cystic,Giemsa dye was added to the agarose that was injected into the ductal tree and visualized using light microscopy or fibrosis transmembrane conductance regulator (CFTR) immunostaining was performed. For functional calcium imaging, agarose-embedded tissue was immediately cut to 140 μm thick tissue slices; these were loaded with OGB-1 AM.
Results: Giemsa staining has shown, that the injected agarose reaches the head and body of
the pancreas, but not the tail. Strong CFTR expression was detected at the apical membrane of the ductal cells and acini, whereas islet cells were completely negative for CFTR. In order to induce changes in intracellular calcium concentration ([Ca 2+] i) chenodeoxycholic acid (CDCA,1mM) was used. Administration of CDCA, for 5 minutes, caused a robust, revesible increase in ([Ca 2+] i in most of the investigated ducts.
Conclusion: Our results confirm that the pancreas tissue slice technique is suitable for the functional investigation of PDECs. The morphology of the PDECs was not disturbed by the tissue preparation and PDECs express functional membrane proteins; moreover, PDECs routinely responded to physiological stimuli. The main advantage of this approach is that allows us to examine many PDECs simultaneously, and in an intact milieu of neighbouring cells *in situ*, a more natural condition compared to other *in vitro* approaches; additionally it allows to study heterotypic interactions with other cell types, such as the acini or the endocrine pancreas allowing for broad spectra of pathophysiological testing.
Disclosure: Nothing to disclose

P0095 CORRELATION BETWEEN PANCREATIC T1 VALUES USING MODIFIED LOOK-LOCKER INVERSION RECOVERY (MOLLI) SEQUENCE AND PANCREATIC EXOCRINE AND ENDOCRINE FUNCTION

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Introduction: Quantifying myocardial T1 values has been useful for detecting and characterizing fibrotic appearance in myocardial infarction, focal scars, and non-ischemic cardiomyopathies. Since pancreatic exocrine function decreases with chronic pancreatic fibrosis advancement, this study examined the correlation between pancreatic T1 values and pancreatic exocrine and endocrine insufficiency.
Aims & Methods: Thirty-two patients underwent abdominal contrast MRI in our department between October 2017 and February 2019. We evaluated T1 values with the MOLLI sequence, pancreatic exocrine insufficiency (PEI) by fecal elastase 1 (FE1) values, and pancreatic endocrine insufficiency using fasting insulin levels.

Results: Median cohort (9 male, 23 female) age was 71 (range: 49-84) years. Eighteen patients had pancreatic cysts, 3 had alcohol-induced chronic pancreatitis, 3 had pancreatic cancer, and 8 possessed other pancreatic features (autoimmune pancreatitis: 2, acute pancreatitis: 2, bile duct tumor: 2, idiopathic chronic pancreatitis: 1, healthy control: 1).

A significant negative correlation was found between T1 and FE1 values (r=0.69, p< 0.01), with none between T1 and fasting insulin levels in the non-insulin administration group (r=0.044, p=0.85). T1 values were significantly higher in the insulin administration group than in the non-insulin group (1655.5 vs. 898.9 msec, p< 0.01).

Conclusion: Pancreatic T1 values correlated with pancreatic exocrine function and might be useful in PEI diagnosis.

Disclosure: Nothing to disclose

P0096 DIFFERENTIAL PHOSPHORYLATION OF MITOGEN-ACTIVATED PROTEIN KINASES ASSOCIATED TO THE OBESTATIN/G-PROTEIN COUPLED RECEPTOR 39 (GPR39) SIGNALING PATHWAY IN HUMAN PANCREATIC STELLATE CELLS

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Introduction: Obestatin, a peptide derived from preproghrelin, and its receptor GPR39 have been described in the endocrine pancreas. Recent works show that obestatin exogenous administration accelerates the recovery in the course of ischemia/reperfusion-induced or cerulein-induced acute pancreatitis in rats. These data revealed the possible role on the recovery of the injured pancreas via the regulation of the activated pancreatic stellate cells, accordingly to the regenerative and/or protector role previously described for obestatin in the pancreas. The obestatin/GPR39 system regulates the proliferation, migration and invasion of the activated pancreatic stellate cells (aRLT-PSCs), as well as the expression of epithelial-mesenchymal transtition and angiogenesis markers. Our goal is to determine signaling mechanisms triggered by obestatin in these pancreatic stellate cells.

Aims & Methods: The aim of the present wotk is to determine the signaling mechanisms triggered by obestatin in the activated pancreatic stellate cells RLT-PSC.

To investigate the intracellular signalling pathways activated downstream of GPR39 in aRLT-PSC cells in response to obestatin (100 nM, 5 min), the degree of the differential activation of mitogen-activated protein kinases (MAPK) was analysed by a analysed by using a human phospho-MAPK array kit.

This protein array comprised 26 MAPKs and other serine/threonine kinases. The results were validated by immunoblot.

Results: Out of the 26 kinases analysed in the human phospho-MAPK array kit, 9 were differentially phosphorylated/dephosphorylated (P < 0.05, P <0.01, P <0.001) in the obestatin-treated (100 nM, 5 min) compared to the untreated RLT-PSCs. To examine by western blot the activation/inhibition observed on the previous MAPK array, the aRLT-PSCs cells were stimulated with obestatin (100 nM) for the indicated times (5-120 min). CREB (~39.5%), ERK2 (~33.60%), glycogen synthase kinase-3 (GSK-3) α/β (~34.3%) and GSK-3β (~26.8%) exhibited increased phosphorylation following obestatin treatment. Additionally, the proteins HSP27 (~56.55%), p38α (~61.95%), p38β (~58.92%), p38δ (~56.86%) and RSK1 (~37.77%) were partially inhibited in response to obestatin.

Conclusion: The obestatin/GPR39 system regulated the activation/inhibition of a kinase panel in the aRLT-PSCs cells, in which ERK1/2 and Akt were the key signalling nodes. These facts agree with the previously described signalling pathway for the obestatin/GPR39 system. Indeed, the obestatin-GPR39 activation triggers two routes in parallel:
1) the metabolic ERK1/2 pathway, by sequential activation of Gi, PI3K, and novel PKCε and characterized mainly by its proliferative role; and

2) the Akt pathway, mediated by β-arrestin 1 and cross-activation of EGFR, of which S6K1 is the final protein triggering effects of cell growth, proliferation and differentiation.

Disclosure: Nothing to disclose

P0097 MUTANT HNF6 PERTURBS THE PANCREATIC PROGENITOR AND BETA-CELL PROGRAM LEADING TO VARIOUS TYPES OF DIABETES IN HUMANS

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Introduction: Diabetes represents a major burden with continuously rising incidence and socioeconomic impact worldwide. Insufficient glucose homeostasis initiates a plethora of complications at multiple sites of the human body. Interestingly, several genes responsible for monogenic diabetes (rare variants) are additionally associated with multifactorial diabetes (frequent variants) pointing towards a shared disease mechanism.

Aims & Methods: Genetic screening of human diabetic cohorts and healthy controls was performed. HNF6 was deleted in human pluripotent stem cells using CrisprCas9 techniques followed by subsequent pancreatic differentiation and thorough step-wise OMICS analysis.

Results: Here, we identify the transcription factor HNF6 as a novel diabetes-causing gene. In one index patient an HNF6 mutation leading to a truncated protein caused neonatal diabetes, pancreatic hypoplasia, and early death. High-throughput targeted sequencing of different diabetic patient cohorts linked HNF6 mutations to early onset type 2 diabetes (T2D). To dissect the underlying mechanism, various human HNF6 null pluripotent stem cells (hPSC) were differentiated toward the pancreatic lineage complemented with stage-specific ATAC-, ChIP- and RNA-sequencing to investigate chromatin and gene binding as well as expression dynamics. Specifically, HNF6 shapes the differentiation of the pancreatic endoderm toward the pancreatic progenitor stage by binding a large set of pancreatic enhancers and opening stage-specific chromatin clusters for endocrine priming. HNF6 null hPSCs failed to activate NKX6.1 leading to a dramatically reduced number of pancreatic progenitors with intrinsic defects to activate the endocrine program. Mechanistically, we found protein-protein interaction of HNF6 with other core factors of the islet program and a high correlation of target gene binding. Specifically, T2D causing HNF6 variants show a perturbed activation of an NKX6.1 enhancer which is crucial for isletogenesis. In addition, HNF6 interacts with NKX2.2 to foster NKX2.2 transcription, one of the earliest and most broadly expressed islet transcription factors.

Conclusion: Our study reveals distinct HNF6 mutations being detrimental for a spectrum of diabetes types in humans and expands our knowledge how HNF6 shapes the isletogenesis program.

Disclosure: Nothing to disclose

P0098 PANCREATIC STIFFNESS VALUES USING A POINT SHEAR WAVE ELASTOGRAPHY TECHNIQUE IN PATIENTS WITH HEALTHY PANCREAS

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Introduction: In the current literature, there is only a small number of studies that have evaluated the utility of point share wave elastography for pancreatic assessment.

Aims & Methods: To assess the feasibility of Virtual Touch Quantification (VTQ) elastography for pancreas assessment, as well as the mean pancreatic stiffness values in healthy subjects.

We included 70 subjects (52.8% women, 47.2% men, average BMI=25.9±4.9 kg/m2, average age 46.8±18.4 years) with a normal pancreatic ultrasound aspect and with no history of pancreatic disease or diabetes, in whom elastography measurements were performed with a Siemens Acuson

S2000 Virtual Touch ultrasound system (Siemens AG, Erlangen, Germany) using a 4CI transducer. For each patient, 10 valid VTQ measurements of the pancreatic parenchyma were performed under fasting conditions. Reliable measurements were defined as a median value of ten pancreas stiffness measurements with a success rate ≥60% and an interquartile range interval < 30%.

Results: Out of 70 subjects, reliable measurements were acquired in 61 subjects (87.1%) by means of VTQ elastography. The mean pancreas stiffness values in healthy subjects was 1.26 m/s ± 0.1 m/s, CI 95% (1.24-1.28). There were no significant differences between the mean pancreas stiffness in men vs. women 1.25 m/s ± 0.09 m/s, CI 95% (1.21-1.28) vs. 1.28 m/s ± 0.1 m/s CI 95% (1.25-1.31) (p=0.103).

Conclusion: VTQ can be a useful tool for pancreas quantification characterized by a good feasibility (87.1%) in healthy subjects. The mean pancreas stiffness values in healthy individuals was 1.26 m/s ± 0.1m/s.

Disclosure: Nothing to disclose

P0099 MUSCLE PARAMETERS CORRELATE WITH SEVERITY DURING ACUTE PANCREATITIS UNLIKE PARAMETERS OF UN-INVOLVED FAT DEPOTS

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Introduction: Acute pancreatitis (AP) is a frequent disorder with a considerable risk of morbidity and mortality. Obesity has been reported to influence severity of AP. Recent studies indicate that the volume and distribution of visceral adipose tissue correlates with worse outcome.

Aims & Methods: The aim of this study was to investigate the association of adipose and muscle parameters with the severity grade of AP. In total 454 patients were recruited from an established European cohort and two German centres. The first contrast-enhanced computed tomography of each patient was reviewed for radiological uninvolved adipose and muscle tissue parameters at L3 level. Associations between these parameters and disease severity were analysed through univariate and multivariate logistic regression analysis. The predictive capacity of the parameters was investigated using Receiver Operating Characteristic (ROC) curves.

Results: No distinct variation was found between the AP severity groups in neither adipose tissue parameters (p-values 0.97 and 0.1 for visceral and subcutaneous fat) nor visceral muscle ratio (p-value 0.14). However, muscle mass and mean muscle attenuation differed significantly with p-values of 0.037 and 0.003 respectively. In multivariate analysis low muscle attenuation was associated with severe AP with an odds ratio of 4.09 (CI: 1.61-10.36; p-value 0.003). No body parameter presented sufficient predictive capability in ROC curve analysis.

Conclusion: Our results demonstrate that a low muscle attenuation level measured during acute pancreatitis is associated with an increased risk of severe AP, unlike parameters of uninvolved adipose tissue. Further prospective studies will help identifying underlying mechanisms and characterize the influence of body composition parameters on AP.

Disclosure: Nothing to disclose

P0100 PREDICTING RELAPSE IN IDIOPATHIC ACUTE PANCREATITIS. IS THERE A PLACE FOR EUS?

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Introduction: Natural history of idiopathic acute pancreatitis (IAP) is complex although diagnosing the etiology is a mainstay to prevent furthers episodes. The efficacy of endoscopic ultrasound (EUS) as a diagnostic tool to establish etiology has been proven in many studies but its role as a predictor of recurrence has not been deeply assessed.

Aims & Methods: Our aim is to assess the predictive ability of EUS and several clinical factors on recurrent episodes of acute pancreatitis. Patients referred to our unit for EUS after a first episode of IAP or recurrent IAP were recruited. We retrospectively analyzed data such as sex, age, liver enzymes (ALT and ALP) on hospital admission in the index episode, previous cholecystectomy, smoker condition and recurrence rates. Patients were considered to have IAP after an initial normal study including abdominal ultrasound, no evidence of significant alcohol consumption, normal triglyceride levels out of an acute episode, and blood tests. Either ERCP or cholecystectomy were performed when stones were found in EUS in common bile duct or gallbladder respectively. When EUS findings suggested chronic pancreatitis or other etiology, patients underwent conservative management and clinical follow up. Patients were followed until death and those lost to follow up were excluded.

Results: We recruited 106 patients from 2010 until 2016 and they were followed until 2018 (mean follow up of 53.59±27.79 months). Clinical and endosonographic factors assessed are shown in table 1.

	Total N = 106	Recurrence N = 29 (27.4%)	No recurrence N = 77 (72.6%)	p
Current or previous smoker, n (%)	37	10 (34.4)	27 (35)	n.s
Normal ALT and ALP, n (%)	56	20 (68.9)	36 (46.7)	0.04
Male, n (%)	52	16 (55.1)	36 (46.7)	n.s
No lithiasis on EUS	54	21 (72.4)	33 (42.8)	<0.01
Age < 65, n (%)	65	22 /75.8)	43 (55.8)	0.06
Previous cholecistectomy, (%)	28	13 (44.8)	15 (19.4)	<0.01

[Clinical and endosonographic factors. ALT: Alanine transaminase. ALP: Alkaline phosphatase. EUS: endoscopic ultrasound]

In the univariate analysis, we found that normal ALT or ALP by the time of admission and a previous cholecystectomy raised the probability of relapse (p=0.04, p < 0.01 respectively). Patients aged below 65 years old showed higher recurrence rate than older ones with a p value almost significant (p=0.06). Furthermore, findings different than lithiasis in the biliary tract on EUS also had a higher probability of a relapse (p< 0.01). When logistic regression was performed, we found that age under 65 years old (OR 3.56; CI 95% 1.21-10.44; p=0.02), previous cholecystectomy (OR 3.19; CI 95% 1.11- 9.17; p=0.03) and normal EUS or findings different than lithiasis in gallbladder or common bile duct (OR 2.87; CI 95% 1.04 - 7.87; p=0.04) were all independent risk factor for recurrence

Conclusion: Far beyond sheer endosonographic findings, physicians performing EUS for IAP assessment might be concerned about etiological diagnosis and also about prognosis and future management. Beyonds its role in diagnosis of biliary conditions that lead to an ERCP or cholecystectomy or its ability in diagnosis of chronic pancreatitis, in combination with other factors such as age or the presence of a gallbladder in situ, EUS can provide predictive information about recurrence. Our study shows that patients aged under 65 years old, with a previous cholecystectomy and no stones on EUS entail a high risk of relapse. All this information should be taken into account by pancreatologists in order to decide whether a closer clinical monitoring is needed or if some patients could be spared from follow-up, although further multicenter studies should be done in this setting.

Disclosure: Nothing to disclose

P0101 COMBINATION OF INTRAVENOUS HYDRATION AND INDOMETHACIN SUPPOSITORY IS THE MOST EFFECTIVE THERAPY FOR THE PREVENTION OF POST-ERCP PANCREATITIS - A NETWORK META-ANALYSIS

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Introduction: Acute pancreatitis as a complication of endoscopic retrograde cholangiopancreatography (PEP) has substantial morbidity and mortality. The ESGE 2014 and the HPSG 2015 guidelines suggest (i) administration of diclofenac or indomethacin and (ii) placement of a prophylactic pancreas stent to prevent PEP. The beneficial effect of hydration in the prevention of PEP has been shown, however, its effectiveness compared to other treatments has never been analyzed.

Aims & Methods: Our aim was to compare the efficacy of different fluid therapies and indomethacin suppository used in PEP prevention.

A network meta-analysis was performed on randomized trials identified from Pubmed, Embase and Cochrane Library. Studies reporting a comparison of at least two treatment options (hydration/indomethacin) and no treatment were included with at least 10 patients. The incidence rate of PEP and its severity were used as outcome parameters. Bayesian network meta-analysis with WinBUGS and NetMetaXL (Markov chain Monte Carlo method) was performed. Treatment ranking was performed based on the calculation of the surface under the cumulative ranking (SUCRA). Odd ratios (95%CI) for the dichotomous data and random effect model were used. PROSPERO reg.no.: CRD42018112698.

Results: 16/954 studies with a total number of 6070 ERCP were analyzed. The event rate of PEP was 616 (10.15%). Six treatment combinations (LR-lactated ringer alone, NS-normal saline alone, IND-indomethacin alone, NT-no treatment, LR+IND, NS+IND) were found and analyzed. The most effective treatment modality was LR+IND (SUCRA: 0.9069), the second was NS+IND (SUCRA: 0.8135), the third was LR (SUCRA: 0.6572), the fourth was NS (SUCRA: 0.2911), the fifth was IND (SUCRA: 0.2696) and the last one was NT (SUCRA:0.06173). The analysis showed that LR+IND is significantly more effective in PEP prevention than NS (OR=0.06; 95%CI: 0.00-0.69), IND (OR=0.05; 95%CI:0.00-0.64) and NT (OR=0.03;95%CI: 0.00-0.41) alone; NS+IND is also significantly more effective than NS (OR=0.12; 95%CI:0.02-0.60), IND (OR=0.09; 95%CI 0.01-0.73), and NT (OR=0.05;95%CI:0.01-0.45). However, LR or NS are not significantly better than IND alone.

Conclusion: Hydration in combination with indomethacin is more effective than hydration or indomethacin alone for PEP prevention.

Disclosure: Nothing to disclose

P0102 MANAGEMENT OF SEVERE ACUTE PANCREATITIS PATIENTS BY ENOXAPARIN

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Introduction: The problem of acute pancreatitis treatment in the present time remains unsolved, and the main difficulty is to assist patients with severe disease. Despite the success of diagnostics, intensive care, improved methods of surgical treatment, mortality in this category is 30-50%. Processes of inflammation and coagulation are enhanced each other and played the important role in the pathogenesis of severe forms of pancreatitis. Therefore, in the complex treatment of this group of patients it is important to use drugs with anticoagulant and anti-inflammatory properties.

Aims & Methods: We used enoxaparin in the treatment of 31 patients with severe acute pancreatitis (SAP) (control group included 26 patients). The drug was administered at a dose of 1 mg/kg subcutaneously once daily for 12-14 days. We are not observed the complications.

Results: The use of enoxaparin in patients with SAP contributes to the improvement of hemostasis and had an anti-inflammatory effect. Enoxaparin is improved the condition of SAP patients, considering APACHE II assessment (from 11.94 ± 1.39 to 6.96 ± 1.63; control group from 12.42 ± 1.42 to 10.18 ± 1.44, p < 0.05) and severity of organ dysfunction (SOFA) (from 5.74 ± 1.39 to 1.04 ± 1.60; control group from 5.38 ± 1.36 to 3.05 ± 1.21; p< 0.05). Three (9.68%) patients with SAP in enoxaparin group are died, and 8 (30.77%) patients in control group ($\chi 2$ =4.04; p=0.0445). We operated the 14 (45.16%) patients in main group, and 9 (34.62%) patients in control group ($\chi 2$ =0.65; p=0.4149). Two patients (14.29%) died in enoxaparin group, and 4 (44.44%) in control group ($\chi 2$ =2.58, p=0.1079).

Conclusion: Enoxaparin improves outcomes in patients with severe acute pancreatitis. Enoxaparin application reduced inflammation processes and procoagulantive status, improved the condition of patients, reduced the mortality level.

Disclosure: Nothing to disclose

P0103 CLINICAL OUTCOME OF ENDOSCOPIC TREATMENT OF SYMPTOMATIC STERILE WALLED-OFF NECROSIS

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Introduction: The majority of patients with symptomatic sterile walled-off necrosis (WON) can be treated conservatively. Endoscopic drainage might be considered in case of persisting symptoms, but frequently results in complications such as iatrogenic infection. To date, no study that solely focusses on the management of symptomatic sterile WON has been published.

Aims & Methods: We aimed to evaluate clinical outcome of patients who underwent endoscopic drainage of symptomatic sterile WON. We performed a retrospective analysis of patients with symptomatic sterile WON who were drained endoscopically between November 2001 and August 2018 in two Dutch tertiary referral hospitals. Primary endpoint was iatrogenic infection, defined as need for endoscopic transluminal necrosectomy. Secondary endpoints were total number of re-interventions, post-procedural complications, clinical success and hospital stay. Factors associated with iatrogenic infection were identified by multivariable logistic regression analysis (stepwise selection method).

Results: The study cohort consistent of 62 patients (56% male, mean age 53 years). Indications for intervention were abdominal pain (66%), gastric outlet obstruction (47%), jaundice (21%) and failure to thrive (29%). Iatrogenic infection occurred in 45 patients (73%). A median of 2 endoscopic, surgical or radiological re-interventions (IQR 0.25 - 4) per patient were performed as a result of iatrogenic infection. Post-procedural complications included bleeding (5%) and stent migration (2%). Thirty patients (48%) were re-admitted and one patient died within 30 days after the index procedure as a consequence of iatrogenic infection. Follow-up data regarding clinical outcome was available for 51 patients (median follow-up 14 months, IQR 6 - 38). Forty-four patients (86%) had complete resolution of symptoms at 1-year follow-up, but 6 patients (12%) reported ongoing symptoms of abdominal pain (n=4), nausea (n=1) and failure to thrive (n=1). Higher percentage necrosis in WON significantly increased the probability of developing iatrogenic infection (odds ratio = 35.36, 95%CI 4.06 - 1048.34).

Conclusion: This is the first study to evaluate clinical outcome of patients that were treated endoscopically for symptomatic sterile WON. Clinical success was achieved in almost all patients, but at the costs of multiple invasive procedures. Treatment of symptomatic sterile WON should therefore only be performed in patients in whom conservative management is no longer expected to result in symptom relief.

Disclosure: Nothing to disclose

P0104 RATE OF EARLY READMISSION IN ACUTE PANCREATITIS AS A QUALITY MARKER - EXPERIENCES OF A TERTIARY CARE UNIT

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Introduction: Acute pancreatitis (AP) is one of the most common hospitalisation-indicating gastrointestinal diseases. Usually, the clinical manifestation of AP is mild, but unfortunately, the mortality of severe AP reaches 30%. The early (< 30 days) readmission rate is a quality indicator of the treatment of AP, which correlates with the long-term outcome of the disease: it is the strongest prognostical factor of 1-year mortality.

Aims & Methods: To investigate the rate and cause of the early readmission among patients treated with AP at our clinic.

Our retrospective study was conducted among patients (>18 years old) treated with AP between January 2010 and December 2018 at the First Department of Medicine, University of Szeged. Personal data were collected from the Hungarian Pancreas Register and medical history data from the patient recording system (eMedsol). AP cases by whom unplanned readmission happened in 30 days were investigated. Beside epidemiological data, the cause of the AP, the mean time elapsed till readmission, its cause, duration and outcome were studied. Data of biliary - and non-biliary AP were compared concerning the above mentioned parameters, separately.

Results: 647 patients were admitted because of AP (57% men, mean age: 57,7±13 years). Of them, 28 (4,33%) patients had early readmission (mean elapsed time: 13,5±8 days). The etiology of AP in these 28 cases was: idiopathic in 46,4%, biliary in 28,5% and dietary in 10,7%. 50% of these cases were mild based on the Atlanta classification. By differentiating the cases according to biliary - non-biliary etiology the number of moderately severe AP cases was significantly higher in the non-biliary group (2 vs. 12, respectively; p=0,048). The most common causes of early readmission were pancreatic (walled off necrosis, pseudocyst) in 32,1%, biliary (cholecystitis, cholangitis) in 28,6% and recurrence in 17,8% of the cases. By investigating the biliary - non-biliary AP cases separately, the indication of readmission showed a significant difference: the cause of readmission was biliary in 65,5% and in 15% in the two groups, respectively (p=0,042). In case of non-biliary AP, readmission happened because of pancreatic cause in 35% and recurrence in 25% of the cases. None of the readmitted patients needed intensive-care treatment. 50% of cases with pancreatic complications needed surgical treatment. There was no mortality bounded to hospital treatment, 75% of the patients were safely emitted to their home after readmission.

Conclusion: The rate of early readmission in our clinic is very low compared to the international data. In case of biliary AP, we need to perform index cholecystectomy in line with the international guidelines to avoid readmission, hospitalisation and increasing hospital costs.

References: S. Munigala et al. Predictors for early readmission in acute pancreatitis (AP) in the United States (US) e A nationwide population based study. Pancreatology 17 (2017) 534-542

Disclosure: Nothing to disclose

P0105 IDIOPATHIC ACUTE PANCREATITIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A MULTICENTRIC COHORT STUDY

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Introduction: Idiopathic acute pancreatitis (IAP) in patients with inflammatory bowel disease (IBD) is not well characterized.

Aims & Methods: Retrospective study conducted at 9 Spanish centres and approved by the Ethics Committee of the steering centre. All patients with IBD and a first episode of acute pancreatitis (AP) from 1998 to 2018 were included. The primary aim was to describe the incidence, characteristics and natural history of AP labelled as idiopathic (unexplained after anamnesis, initial laboratory study and abdominal ultrasound) in patients with IBD. Secondary aims included: proportion of IAP in which a cause was found after additional diagnostic work-up, risk of AP recurrence, chronic pancreatitis, and fulfillment of autoimmune pancreatitis criteria during follow-up. Data were collected and managed using AEG-REDCap™ electronic data capture tool.

Results: We identified 185 patients with IBD (53% male; 68.7% Crohn's disease) and a first episode of AP. The cause of AP was: drug-induced in 109 (59%) patients, idiopathic in 38 (20.6%), gallstones in 34 (18.4%), alcohol in 2 (1%) and post ERCP in 2 (1%). AP severity in IAP group was moderate in 15.8% and there were no severe cases; in non-IAP patients AP was mild in 93.8%, moderate in 4.8% and severe in 1.4% (p=0.04). Ulcerative colitis was significantly more frequent in the IAP group compared to other causes (56.2% vs. 23.1%, p< 0.001).

Occurrence of AP before the diagnosis of IBD was more frequent in IAP patients compared to non-IAP (21% vs. 3.4%, p=0.001), and median time from IAP to IBD diagnosis was 7.5 months (1.7-18). Further diagnostic work-up was performed in 16/38 (42%) patients without an identifiable cause at presentation (magnetic resonance cholangiopancreatography in 13, endoscopic ultrasound in 7, and both in 4 patients), and an etiological diagnosis was reached in 6/16 (37.5%): 2 biliary, 3 autoimmune and 1 groove pancreatitis.

Five-year risk of AP recurrence was significantly higher in IAP group than in non-IAP group (28% vs. 5.1%, p< 0.001), with a median time to first recurrence of 4.4 months (2.9-12.2). Six of the eleven (54.5%) IAP patients in which AP reoccurred presented more than one recurrence.

Diagnosis of chronic pancreatitis was more frequent in IAP patients than in non-IAP group (5.2% vs. 0.6%, p=0.04) after a median time of follow-up of 6.2 years (3-10). At the last available visit a probable diagnosis of autoimmune pancreatitis type 2 was established in 5/38 patients of the IAP group (13.1%) and in one patient of the non-IAP group (0.6%), p=0.002.

Conclusion: IAP represents one out of five cases of AP in patients with IBD, it is significantly more frequent in patients with ulcerative colitis and presents a high risk of recurrence. Additional imaging studies after a first episode of IAP in IBD patients identify a cause in more than one third.

Disclosure: Nothing to disclose

P0106 EARLY ORAL REFEEDING IN ACUTE PANCREATITIS

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Introduction: In recent guidelines of acute pancreatitis treatment there is a strong agreement that enteral nutrition should be started in severe cases within 48 hours (1, 2, 3). In contrast, most guidelines do not contain any information on the optimal timing of oral refeeding after enteral nutrition. Some recently published data shows that early oral refeeding could be beneficial as it shortens the lengths of hospital stay and does not result in higher number of clinical complications and mortality (4, 5).

Aims & Methods: Early enteral nutrition in severe cases of acute pancreatitis improved mortality rate at our department in 2015. From 2018 we started to adopt an early oral refeeding approach to patients with acute pancreatitis. Early oral refeeding after enteral nutrition meant initiation of oral administration as soon as the patients experienced significant improvement of their abdominal pain and passed their CRP peak. Our aim was to compare the mortality rate before and after the change of therapeutical strategy regarding the timing of oral refeeding.

Particular emphasis was placed on patients who reached a modified Ranson score of minimum 2 as most of them were fed enterally. The modified Ranson score meant adding an extra point to the conventional Ranson score when the patient had severe abdominal pain.

We examined 220 cases of acute pancreatitis retrospectively who were treated in our department in 2018 and compared the data to the mortality rate of 2015 by two-sample T-test. The occurrence of early and late complications, the amount of fluid infusion in the first 24 hours of the treatment and the consumption of enteral formulas in 2015 and 2018 were compared as well.

Results: In 107 cases the patients reached a modified Ranson score of minimum 2 in 2018. This group had a mortality of 7.8% which was not significantly higher than the 3.9% mortality of 2015 (p=0.17).

In 49 cases the patients reached a modified Ranson score of minimum 3 in 2018. This group had a mortality of 10.2% which was not significantly higher than the 5.56% mortality of 2015 (p=0.28).

The overall mortality rate of acute pancreatitis was 3.63% in 2018 which is concordant with the international data (6).

We experienced a significant decrease in the average fluid infusion given in the first 24 hours in both the modified Ranson 2 (3462,96ml vs. 3021,05ml; p=0,000001) and modified Ranson 3 (3472,22ml vs. 3083,33ml; p=0,0006) groups.

Consumption of enteral formulas has decreased by 38.84% from 2017 to 2018, and thus saving EUR 1814.

Conclusion: The early initiation of oral refeeding did not result in a significantly higher rate of mortality.

However, the mortality rate of 2018 was higher than the mortality rate of 2015 which we attribute to the significantly lower amount of fluid infusion in the first 24 hours of the treatment.

Earlier oral refeeding is more tolerable for patients and it is more cost-effective as it results in shorter hospital stay and lower consumption of enteral formulas.

References: 1. Tenner, S., et al., American College of Gastroenterology guideline: management of acute pancreatitis. Am J Gastroenterol, 2013. 108(9): p. 1400-15; 1416; 2. IAP/APA evidence-based guidelines for the management of acute pancreatitis. Pancreatology, 2013. 13(4 Suppl 2): p. e1-15.; 3. Yokoe, M., et al., Japanese guidelines for the management of acute pancreatitis: Japanese Guidelines 2015. J Hepatobiliary Pancreat Sci, 2015. 22(6): p. 405-32.; 4. Zhao XL, Zhu SF, Xue GJ, et al. Early oral refeeding based on hunger in moderate and severe acute pancreatitis: A prospective controlled, randomized clinical trial. Nutrition 2015; 31: p.171-175.; 5. Masayasu, H., et al., Timing of oral refeeding in acute pancreatitis: A systematic review and meta-analysis, United European Gastroenterology Journal, 2016, Vol. 4(6) 725-732; 6. Carnovale, A., et al., Mortality in Acute Pancreatitis: Is It an Early or a Late Event?, JOP. J Pancreas (Online) 2005; 6(5):438-444.

Disclosure: Nothing to disclose

P0107 RECURRENT ACUTE PANCREATITIS CAN BE CONSIDERED AS EARLY CHRONIC PANCREATITIS: A METAANALYSIS OF 21,186 PATIENTS

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Introduction: Chronic pancreatitis (CP) is an irreversible end-stage disease of the pancreas. The diagnosis is usually delayed when testing potential pharmacological interventions is not possible, therefore it is not surprising, that very small amount of clinical trials are performed. It is an unmet need to diagnose the disease much earlier before the morphological and functional deterioration develop.

Aims & Methods: Our aim was to systematically review the literature and investigate whether recurrent acute pancreatitis (RAP) can be considered as early CP. A meta-analysis was performed using the preferred reporting items for systematic review and meta-analysis protocol (PRISMAP). MEDLINE, Scopus, EMBASE and the Cochrane Library databases were searched for articles in which RAP and either of AP or CP were compared. Data on etiology, gender ratio and smoking were extracted from the eligible articles. Pooled estimates were calculated with random effects model by using DerSimonian-Laird method. All meta-analytical calculations were performed using Stata 15.1 data analysis and statistical software (Stata Corp LLC, College Station, TX, USA).

Results: 21186 patients' data from 23 articles were collected. Biliary etiology was significantly higher in group AP than in RAP or CP (OR: 2.40, 95% CI:1.29-4.46; OR:5.53, 95% CI:2.76-11.07 respectively). However, the significant difference in terms of biliary etiology disappeared between RAP and CP (OR: 0.81, 95% CI: 0.40-1.63) suggesting that RAP is more similar to CP than to AP.

More male were suffering from CP than AP (OR:1.93, 95% CI: 1.32-2.82); RAP than AP (OR: 1.31, 95% CI: 1.04-1.64) and CP than RAP (OR: 1.42, 95% CI: 1.15-1.76) suggesting that RAP is a transition between AP and CP. The same transition pattern was observed in the amount of smoking (OR: 3.28, 95% CI: 1.96-5.49; OR: 1.37, 95% CI: 1.11-1.70; OR: 2.23, 95% CI: 1.81-2.75, respectively) and alcohol etiology (OR: 3.85, 95% CI: 2.61-5.67; OR: 2.02, 95% CI: 1.30-3.15; OR: 1.93, 95% CI: 1.26-2.97, respectively).

Conclusion: The above patterns of etiology, gender ratio and smoking suggest that recurrent acute pancreatitis is a transit disease between AP and CP. Therefore, RAP can be considered as early chronic pancreatitis. Detailed large cohort analysis is necessary to determine the number of recurrences, which should define and be incorporated into the nomenclature of early chronic pancreatitis.

Disclosure: Nothing to disclose

P0108 THE COMBINATION OF THE ABDOMINAL VISCERAL FAT AREA AND AGE IS A USEFUL PREDICTOR OF MORTALITY IN SEVERE ACUTE PANCREATITIS PATIENTS

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Introduction: The mortality rate for severe acute pancreatitis (SAP) is extremely high. Several scoring systems have been developed for predicting adverse outcomes in AP, such as the APACHE-II and Japan severity score by summing nine factors including age. However, each score has certain shortcomings or complex using a lot of parameters. Obesity is a well-known risk factor for acute pancreatitis and reported to be related to mortality by meta-analysis. In the present study, we aimed to evaluate the impact of abdominal visceral fat area (VFA) on mortality due to SAP and performed the prognostic stratification using VFA.

Aims & Methods: This study was a retrospective single-center cohort study that examined a total of 108 consecutive patients with SAP from April 2009 till March 2018. They were diagnosed with SAP according to the Japanese diagnostic criteria and graded by the Japan severity score (JSS). VFA *at the umbilical level* were manually assessed by computed tomography scan using the image analysis system, SYNAPSE VINCENT (Fujifilm, Tokyo, Japan). We studied the mortality of patients with SAP according to clinical characteristics including VFA. Receiver operating characteristic (ROC) curve analysis was used to determine the cut-off values for predicting mortality due to SAP.

Results: The median age was 62 years (IQR 50, 75), 67% male. The median JSS and CTseverity socre was 1 (QR 0.25, 3), 2 (QR 2, 2) based on the Japanese severity scoring system for acute pancreatitis. The cause of AP was gallstone-related in 32 (30%) patients, alcohol abuse in 42 (40%) patients, idiopathic in 10 (9.5%) patients, and the others. The median hospital stay was 29 days (IQR 20, 43). During hospital stay, 14 patients developed walled-off necrosis. Nine patients (9/108, 8.3%) died in hospital. Our analysis for mortality demonstrated that the age, JSS, and VFA cut-off values were 72 years (AUC: 0.773), 4 (AUC: 0.865) and 167cm^2 (AUC: 0.684), respectively. The mortality rates of patients with older age ($\geq$72), higher JSS ($\geq$4), and larger VFA($\geq$167) were significantly higher than those with younger (22.9% vs 1.4%, P=0.0005), lower JSS (40.3% vs 3.3%, P=0.0002), and smaller VFA (21.1% vs 5.6%, P=0.0492). We generated 4 groups using the combination of age and VFA cut-off varlues and evaluated mortality rates in each group (Age^{Old} VFT^{High} group; 50% (4/8), Age^{Old} VFT^{Small}; 15%(4/27), Age^{yong} VFT^{Large} 0%(0/10), Age^{Yong} VFT^{Small}; 1.6%(1/61), respectively).

Conclusion: Larger VFA was significantly associated with poor prognosis in elderly patients with SAP. Therefore, the combination of age and VFA at diagnosis of SAP may easily provide prognostic *stratification*.

Disclosure: Nothing to disclose

P0109 FAMILIAL MEDITERRANEAN FEVER ASSOCIATED WITH ELEVATED ODDS OF ACUTE PANCREATITIS

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Introduction: Familial Mediterranean Fever (FMF) characterized by fever and serosal inflammation. Up to 95% of patients have episodic abdominal pain secondary to peritoneal inflammation. Gastrointestinal manifestations of patients with FMF may be under reported due to a frequent history of abdominal pain in this group of patients leading to a delay in diagnosis. In particular, acute pancreatitis (AP) in patients with FMF has only been described in rare case reports.

Aims & Methods: The aim of this study is to determine if there is an association between FMF and Acute Pancreatitis by examining inpatient prevalence.

Case-control study using the NIS 2007-2015, the largest public inpatient database in the US. All patients with ICD9CM codes for FMF were included. None were excluded. The primary outcome was determining the association between FMF and AP. Secondary outcomes included determining inpatient mortality, morbidity (AKI, shock, ICU stay, TPN), resource utilization (ERCP and abdominal imaging), hospital length of stay (LOS), and inflation-adjusted total hospital costs and charges. Multivariate regression analyses were used to adjust for age, gender, Charlson Comorbidity Index, income in patient zip code, hospital region, location, size and teaching status.

Results: A total of 3,956,807 patients with AP were identified and propensity matched for selected covariates, of which 96 had FMF. The mean age was 53 years, and 49.5% were female. For the primary outcome, patients with FMF had increased adjusted odds (aOR: 1.73, p=0.02) of having AP. For secondary outcomes, patients with FMF had higher adjusted odds of AKI (aOR:3.11, p=0.05), and multi-organ failure (aOR:3.38,p=0.03) compared to the general population. There was no significant difference in mortality, or hospital costs, charges, or length of stay (LOS). All adjusted odds, and means are shown in Table 1.

Conclusion: Patients with familial Mediterranean fever had higher adjusted odds of having acute pancreatitis, along with higher odds of AKI, and multi-organ failure. It is difficult to determine what contributes to the association between acute pancreatitis and familial Mediterranean fever, but

one could speculate the inflammatory nature of familial Mediterranean fever may confer increased proclivity in triggering the acute pancreatitis inflammatory process. Familial Mediterranean fever is a relatively rare genetic disease and as such large population based studies have never been conducted, thus future studies will be needed to better understand the association between acute pancreatitis and familial Mediterranean fever.

A) Variable	aOR	95%CI	p-value
Acute Pancreatitis	1.73	1.10-2.71	0.02
Mortality	5.27	0.70-39.51	0.11
AKI	3.11	0.98-9.92	0.05
Shock	2.69	0.35-20.47	0.34
ICU	3.14	0.67-14.60	0.15
Multi-organ failure	3.38	1.13-10.13	0.03
ERCP	0.90	0.20-4.01	0.89
B) Variable	aMean	95%CI	p-value
Additional Adjusted Costs	-$1,421	-6355,3512	0.57
Additional Adjusted Charges	-$12,383	-27143,2377	0.10
Additional Adjusted Length of Stay (days)	-1.4	-3.2,0.4	0.14

[A) Adjusted Odds Ratio of Acute Pancreatitis and outcomes in patients with FMF. B) Resource Utilization in patients with acute pancreatitis and FMF.]

Disclosure: Nothing to disclose

P0110 CT-SEVERITY INDEX CAN PREDICT THE SEVERITY OF ACUTE PANCREATITIS SIMILAR THAN OTHER SCORING SYSTEMS

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Introduction: Based on the revised Atlanta classification, the severity of acute pancreatitis (AP) may be mild, moderate or severe. The management of the moderate and severe forms of the disease with necrosis and multiorgan failure remains a challenge. To predict the severity and mortality of AP different scoring systems are used. The aim of the study is to investigate, if the computed tomography severity index (CTSI) of AP can predict severity and mortality similar to other scoring systems.

Aims & Methods: A systematic search was performed in 3 databases, Pubmed, Embase and the Cochrane Library. Articles were selected if they (1) provided data from patients with AP, included different severities of the disease; (2) if they used CTSI or mCTSI and/or another prognostic score (Ranson, BISAP, APACHE II, CRP) for the evaluation of severity or mortality of the disease (3) if they contained the absolute numbers of true positive, false negative, false positive and true negative test results, or area under the curve (AUC) for severity or mortality of AP. Diagnostic odds ratios with 95% confidence intervals were calculated. The statistical analysis was performed with Stata 14 software using the METANDI module.

Results: From the 319 found articles, 36 articles were included in our metaanalysis, these contain data of 6280 patients. From the 36 articles, 11 contained AUC data about mortality. The pooled AUC for the prediction of mortality was 0.79 (95% CI 0.730.86) for CTSI; 0.87 (95% CI 0.830.90 for BISAP; 0.80 (95% CI 0.720.89) for mCTSI; 0.73 (95% CI 0.660.81) for CRP level; 0.87 (95% CI 0.810.92) for Ranson score; and 0.91 (95% CI 0.880.93) for APACHE II score. The AUC for the prediction of severity of AP were 0.80 (95% CI 0.760.85) for CTSI; 0.79, (95% CI 0.72 0.86) for BISAP; 0.83 (95% CI 0.750.91) for mCTSI; 0.73 (95% CI 0.640.83) for CRP level; 0.81 (95% CI 0.750.87) for Ranson score and 0.80 (95% CI 0.770.83) for APACHE II score.

Conclusion: The APACHE II scoring system had significantly higher predictive value for mortality than CTSI or CRP level (p=0.001; p< 0.001 respectively), while the AUC for CTSI was not statistically different from the AUC for BISAP, mCTSI, CRP or Ranson criteria. There was no statistical difference between the different scoring systems in the prediction of the severity of AP. CTSI is an easily calculated feasible scoring system for AP, which can predict the severity of AP, similar to the other scoring systems.
Disclosure: Nothing to disclose

P0111 EUS-THROUGH-THE-NEEDLE TECHNOLOGIES IN THE DIAGNOSIS AND MALIGNANCY DETECTION OF PANCREATIC CYSTS: A COMPARATIVE STUDY BETWEEN DIFFERENT TECHNOLOGIES

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Introduction: Endoscopic ultrasound (EUS) have limitations to differentiate neoplastic from non-neoplastic pancreatic cysts.
Aims & Methods: Aim: to define the role of through-the-needle technologies such as: fiberoptic probe, needle-based confocal laser-endomicroscopy (nCLE) and EUS-through-the-needle microforceps biopsy (mFB) in the diagnosis of pancreatic cyst malignancy.
Methods: a retrospective analysis of a prospectively collected database (Jan-2013 to Mar-2018). Patients ≥18 years submitted for diagnostic work-up of pancreatic cyst lesions at our institution were included. Pancreatic solid lesions were excluded. Malignancy was defined in accordance to endoscopic criterion, histopathology (Fukuoka criteria) and 6-months follow-up. Patients were allocated into two cohorts: patients evaluated via EUS alone, and those with EUS plus an additional method. The sample size of 20 patients per-cohort was estimated through the accuracy described for EUS-through-the-needle micro forceps biopsy, with a 5% margin error and a 95% confidence interval. Baseline characteristics per cohort was confirmed through the corresponding hypothesis test. Agreement between EUS malignancy detection and follow-up was stablished for each method via univariate and multivariate binary logistic regression (Odds Ratio, OR). The overall diagnostic accuracy for malignancy detection was determined for each diagnostic method. An off-line inter-observed analysis (IOA) of EUS criteria was performed by two endoscopists (JO and RV) using a randomized EUS-image-set, calculated through Cohen Kappa (k). A p-value < 0.05 was considered statistically significant. Data analysis was performed on R v.3.4.3.
Results: 129 cases were included. In 82/129 patients, EUS was performed with an additional diagnostic method: EUS-FNA (21/82), nCLE (44/82), direct intracystic mFB (36/82), cystoscopy (27/82). The median age was 67 years, 90 (69%) female, 46 (36%) lesions were on pancreatic head. There were no statistical association between baseline characteristics and study cohorts. Agreement between EUS malignancy detection and follow-up was 58.6% higher when associated with nCLE, direct intracystic mFB or cystoscopy [62/82 (75.6%) vs. 8/47 (17%); OR=15.11, 95% CI 6.06-37.65; p< 0.001]. Multivariate analysis confirmed a highest malignancy detection is reached when nCLE (OR=8.441, 95% CI 2.698-33.081; p< 0.001) and direct intracystic mFB are performed (OR=3.425, 95% CI 1.104-11.682; p=0.038), with a sensitivity, specificity, PPV, NPV and observed agreement of 78%, 100%, 100%, 89% and 92% (k=82%; p< 0.001) (table 1).

	EUS (n = 47)	EUS + nCLE (n = 44)	EUS + mFB (n = 36)	EUS + nCLE + mFB (n = 26)
Sensitivity	7/7 (100%; 59-100)	8/9 (89%; 52-100)	7/8 (88%; 47-100)	7/9 (78%; 40-97)
Specificity	1/40 (3%; 0-13)	30/35 (86%; 70-95)	23/28 (82%; 63-94)	17/17 (100%; 80-100)
Positive Preditive Value	7/46 (15%; 6-29)	8/13 (62%; 32-86)	7/12 (58%; 28-85)	7/7 (100%; 59-100)
Negative Predictive Value	1/1 (100%; 3-100)	30/31 (97%; 83-100)	23/24 (96%; 79-100)	17/19 (89%; 67-99)
Observed Agreement	8/47 (17%)	38/44 (86%)	30/36 (83%)	24/26 (92%)
Cohen Kappa (k)	0% (p=0.672)	64% (p<0.001)	59% (p<0.001)	82% (p<0.001)

[Table 1. Overall diagnostic accuracy for determining malignancy [n/T (%; 95% CI)]]

IOA (k) of EUS level of confidence, borders, lobularity, walls, diagnosis and microcyst component were 29%, 30%, 17%, 4%, 53% 54%, respectively.
Conclusion: EUS-through-the-needle direct intracystic mFB and nCLE improves malignancy detection in pancreatic cysts.
Disclosure: Nothing to disclose

P0112 INTEROBSERVER AGREEMENT AMONG EXPERT PATHOLOGISTS ON THROUGH-THE-NEEDLE MICROFORCEPS BIOPSY SAMPLES FOR EVALUATION OF PANCREATIC CYSTIC LESIONS

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Introduction: Endoscopic ultrasound (EUS) is a pivotal exam in the evaluation of pancreatic cystic lesions (PCLs). During EUS it is also possible to perform fine needle aspiration (FNA) and analysis of the cystic fluid, which is helpful in the diagnostic process while it is still controversial if it has an impact on the management of these patients. Histological samples acquired by through-the-needle microforceps biopsy (TTNB) have been demonstrated to improve the diagnostic yield of EUS sampling of PCLs. However, available data is limited to the interobserver agreement among pathologists in evaluating such samples is still unknown.
Aims & Methods: Consecutive patients with PCLs were retrieved were retrieved from the databases of participating centers between May 2016 and July 2017. TTNB slides with worrisome features were retrieved and independently evaluated for specimen adequacy, presence of lining epithelium, grade of epithelial dysplasia, presence of ovarian type stroma, and specific diagnosis by six expert pathologists from six different tertiary care centers. Cohen's kappa and Gwet's AC1 coefficients were used to assess interobserver agreement, with 95% confidence intervals.
Results: 40 TTNB slides were retrieved and evaluated in the study period. An almost perfect agreement were observed for specimen's adequacy [87%, kappa 0.16 (95% CI:0.05;0.27) and AC1 0.82 (95% CI:0.79;0.98)], presence of lesional epithelium [92%, kappa 0.61 (95% CI:0.51;0.86) and AC1 0.90 (95% CI:0.86-0.92)], epithelial dysplasia [97%, 0.43 (95% CI:0.18-0.67) and AC1, 0.97 (95% CI:0.95-0.99)] and ovarian-like stroma [93%, kappa 0.76 (95% CI:0.68-0.83) and AC1 0.90 (95% CI:0.86-0.93)]. When considering all diagnoses separately, a moderate to substantial agreement (68%) was observed [AC1 0.62 (95% CI:0.57-0.67)], similarly to what was found for mucinous cysts versus serous cyst adenoma versus other diagnoses (overall agreement, 76%; kappa, 0.62, 95% CI:0.57-0.88, AC1, 0.65 95% CI:0.59-0.70) and for mucinous cysts vs. all other diagnoses (overall agreement, 87%, kappa 0.73, 95% CI: 0.68-0.80), AC1 0.74, 95% CI:0.68-0.84). The agreement for diagnosis of mucinous cystic neoplasm vs. intraductal mucinous papillary neoplasm was almost perfect (overall agreement 94.0%, kappa 0.88, 95% CI:0.81-0.95, AC1 0.88, 95% CI:0.81-0.95).
Conclusion: Interobserver agreement between expert pathologists in the evaluation of TTNB samples from PCLs with worrisome feature was close to perfection for all the evaluated parameters, except the definitive diagnosis. When mucinous cystic lesions were compared versus all other diagnoses the agreement became substantial, thus indicating that TTNB specimen can provide important information for PCLs management decisions.
Disclosure: Nothing to disclose

P0113 CARCINOEMBRYONIC ANTIGEN LEVEL IN THE PANCREATIC JUICE IS EFFECTIVE IN MALIGNANCY DIAGNOSIS AND PREDICTION OF FUTURE MALIGNANT TRANSFORMATION OF INTRADUCTAL PAPILLARY MUCINOUS NEOPLASM OF THE PANCREAS

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Introduction: The present study aimed to determine the ability of diagnosing malignancy and predicting malignant transformation in patients with IPMN using carcinoembryonic antigen (CEA) level in the pancreatic juice.
Aims & Methods: We enrolled patients with IPMN who underwent endoscopic retrograde pancreatography (ERP) between 2002 and 2018. We examined the ability of diagnosing malignancy in 63 patients who underwent surgery (surgical group).
Furthermore, we examined the value of predicting malignant transformation in 52 patients who underwent follow-up for over 1 year after ERP (follow-up group).
Results: In the surgical group, the overall sensitivity and specificity of CEA level (≥97 ng/ml) in the pancreatic juice for diagnosing malignancy were 45% and 100%, respectively. The specificity was excellent for all IPMN types; however, the sensitivity was highest in main duct type, followed by mixed type and branch duct type.
In the follow-up group, malignant transformation was observed in four patients (7.7%) during the follow-up, and the median time until malignant transformation was 58 months. High CEA level in the pancreatic juice demonstrated a statistically significant difference in multivariate analysis and was found to be an independent predictor of malignant transformation (hazard ratio, 17; P = 0.02). The cumulative malignant transformation rate was significantly higher in the high CEA group than that in the low CEA group (5-year cumulative malignant transformation rates, 69% vs. 0%, P < 0.001).
Conclusion: CEA level in the pancreatic juice is useful not only in diagnosing malignancy but also in predicting future malignant transformations in IPMN patients receiving follow-up.
Disclosure: Nothing to disclose

P0114 FEASIBILITY OF NEXT GENERATION SEQUENCING OF ENDOSCOPIC ULTRASOUND GUIDED MICROBIOPSIES FROM PANCREATIC CYSTIC NEOPLASMS

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Introduction: Risk stratification of pancreatic cysts presents a diagnostic challenge for the multidisciplinary team, and the incidence of these lesions is on the rise due to an increased use of cross sectional imaging (1). Mucinous cysts such as Intraductal Papillary Mucinous Neoplasms (IPMNs) and Mucinous Cystic Neoplasms harbor malignant potential and may develop into pancreatic ductal adenocarcinoma. Conversely, Serous Cystic Neoplasms (SCNs) are considered benign (2).
Endoscopic Ultrasound Examination (EUS) with fine needle aspiration (FNA) of cyst fluid has been the preferred method for imaging as well as tissue procurement of pancreatic cysts (3).
Interpretation of cytology samples from pancreatic cysts is challenging. A novel microbiopsy forceps used in conjunction with EUS-FNA procedure offers new opportunities for histological examination of tissue from pancreatic cysts as well as Next Generation Sequencing (NGS), whereby identification of mutated genes controlling cell cycle and arrest may provide biomarker information in the risk assessment of pancreatic cysts.

Aims & Methods: The aim of this study was to present our initial experience with microbiopsies from pancreatic cysts by quantifying the size and cellular content of the biopsies and subject the biopsies to NGS. Microbiopsies from 27 patients were reviewed with regards to clinical data and histopathology. The biopsies were processed and areas of H&E stained tissue and numbers of neoplastic epithelial cells on the glass slides were measured digitally using a slide scanner. Of the 27 biopsies, 23 were subjected to NGS using a 50 gene cancer hotspot panel detecting point mutations in frequently altered genes such as *KRAS*, *GNAS* and *BRAF*.
Results: Of the 27 patients, 19 were IPMNs, 3 SCNs, 2 pseudocysts, 2 were non-diagnostic with regards to histopathology, and 1 was excluded due to scarce material. Mean age was 70.9 years. The cysts were mostly located in the head of the pancreas and were predominantly side-branch IPMNs of gastric subtype with low grade dysplasia. A median of 3 biopsies were obtained with a mean cross size of 1,046 µm and a mean area of 997,102 µm².
A total of 23 out of 27 biopsies were subjected to NGS, excluding pseudocysts and the biopsy with insufficient material. Furthermore, one biopsy was excluded due to insufficient amount of DNA after DNA-extraction. The biopsies subjected to NGS had a mean cell count of 308 cells. The NGS analysis yielded DNA with a mean mapped reads of 742,807 base pairs, mean of sequencing depth of 3,429 and a mean uniformity of 98.4%. Sixteen IPMNs harbored mutations in genes regulating cell cycle and repair, and three were without mutations.
Most frequent mutations were found in *KRAS* and *GNAS*, and these were often concomitant. Three SCNs were without mutations, while a non-diagnostic microbiopsy, with regards to histology, harbored a *KRAS* and *TP53* mutation and was deemed malignant after clinical follow up. Three patients underwent surgery, and the mutated genes detected in the microbiopsies were confirmed in the resected specimens. We additionally identified a *GNAS* mutation in one of the resected specimens which was not identified in the corresponding initial microbiopsy.
Conclusion: Microbiopsies offer sufficient tissue for histopathological examination as well as NGS. The latter identified mutations in genes frequently seen in IPMNs and thus, NGS of microbiopsies is a promising method that has the potential to improve diagnostic decision making. Further studies in this field are needed to validate the results.
References: 1. Kromrey ML, Bulow R, Hubner J, et al. Prospective study on the incidence, prevalence and 5-year pancreatic-related mortality of pancreatic cysts in a population-based study. Gut. 2018;67(1):138-45. 2. Brugge WR, Lauwers GY, Sahani D, et al. Cystic neoplasms of the pancreas. The New England journal of medicine. 2004;351(12):1218-26. 3. European evidence-based guidelines on pancreatic cystic neoplasms. Gut. 2018;67(5):789-804.
Disclosure: Nothing to disclose

P0115 NEW APPROACHES IN DIFFERENTIAL DIAGNOSIS WITH COMBINATION OF NEUTROPHIL TO LYMPHOCYTE INDEX, CA 19-9 AND COMPUTED TOMOGRAPHY IN MALIGNANT PANCREATIC CYSTIC LESIONS

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Introduction: Pancreatic cystic lesions (PCL) is a frequent finding on cross-sectional imaging. Mucinous cystic neoplasms (MCNs) and intraductal papillary mucinous neoplasms (IPMNs) have malignant potential. The differential diagnosis of malignant pancreatic cystic lesions is frequently difficult.
Aims & Methods: The aim of our study was to evaluate the accuracy of preoperative clinical markers in differential diagnosis of malignant PCL Ninety seven patients who underwent pancreas resection for PCL were between 2008 and 2018 reviewed retrospectively (mean age 56.5 years, range 21-79; 52 females). 14 were IPMNs (9 - benign lesions, 5 malignant), 34 were serous cystoadenomas (SCA) and 34 MCNs (19 - benign lesions, 15 malignant), 27 pseudocysts. The following factors on association with malignant PCL were assessed with logistic regression analysis: age, sex, localization of cyst, cyst size, neutrophil to lymphocyte index (NLI), serum carbohydrate antigen 19-9 (CA19-9) and the presence of enhanced

intracystic mass on computed tomography. The receiver operating characteristic (ROC) curve and area under the ROC curve (AUC) were applied to determine the best cutoff values for baseline NLI.

Results: The NLI in patients with benign PCL (1,85 ± 0,94) was significantly lower than that in patients with malignant PCLs (2,93 ± 2, 45, P=0,008). The optimal cut-off value of NLI for predicting malignant PCLs was 1,876 (AUC=0,684). In multivariable analysis NLI>1,876 (OR: 5,857; 95 % CI: 1,872- 18,326; P = 0,002), CA 19-9 > 37 U/ml (OR: 17,333; 95 % CI: 4,984 – 60,273; P = 0,0001) and the presence of enhanced intracystic mass on computed tomography (OR: 7,333; 95 % CI: 2,319 - 23,186; P = 0,0007) were independent factors of malignant PCL. Sensitivity, specificity and accuracy of the combination of NLI>1,876, CA 19-9 > 37 U/ml. and the presence of enhanced intracystic mass in predicting malignant PCL is 71,4%, 95,6% and 86,5% respectively

Conclusion: Combination of NLI>1,876 CA 19-9 > 37 U/ml. and the presence of enhanced intracystic mass on computed tomography is an effective predictor of malignant PCL

Disclosure: Nothing to disclose

P0116 EUS-GUIDED MICRO-BIOPSIES IMPROVE DIAGNOSIS OF MUCINOUS AND NON-MUCINOUS PANCREATIC CYSTS

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Introduction: Current diagnostic tools are insufficient to distinguish mucinous from non-mucinous cystic lesions in the pancreas. Since these lesions have different malignancy potential, it is crucial to establish a diagnosis to provide relevant follow-up and timely intervention. In this feasibility study, we used a through-the-needle biopsy forceps to obtain histology specimens from the cyst wall in addition to cyst fluid analyses of cystic pancreatic lesions.
Aims & Methods: Adult patients with pancreatic cysts ≥15 mm were included prospectively after a multi-disciplinary-team evaluation of CT and/or MRI images from November 2016-March 2019. The entire pancreas was examined with EUS and the size, position and morphology of the cystic lesion was recorded. A 19G EUS needle was used to puncture the cysts and a Moray Micro biopsy-forceps (US Endoscopy, OH, USA) was introduced through the needle, and 2-4 biopsies were obtained from the cyst wall under EUS guidance. The patients received prophylactic antibiotics, and from 2018 additional NSAIDs and 1 l Ringer acetate i.v. prior to procedure. The specimens were examined by a dedicated pathologist. Finally, cyst-fluid was aspirated for cytology, CEA, amylase and biobank. All patients were observed for one day post procedure.
Results: 34 patients were considered for micro-biopsies: 5 patients were not included due to age (1) solid lesions (1), inability to visualise needle (1), small cyst size and ongoing double antiplatelet therapy (1). 29 patients were included and one patient needed repeated procedure. 30 procedures were performed. 17 of patients were male, 12 female, median age was 68 years (33-77). Average cyst size: 33 x 25 mm. Twenty two of 29 patients were asymptomatic and only 4 had cyst related symptoms. Diagnostic biopsy specimen was obtained in 23/29 (79,3%) of the cases, whereas cytology was diagnostic in only 5/29 (17,2%). In five of the procedures (5/30), post-procedure pancreatitis occurred and had to be treated conservatively over 4-11 days of hospitalisation. All patients recovered without sequelae. 1/29 patients underwent surgery and postoperative histology confirmed the histology obtained by EUS microbiopsy (MCN, low grade dysplasia). Two patients developed inoperable carcinoma, both were found unfit for surgery due to tumor progression. Both these patients had cyst-fluid CEA >2000 at the time of the procedure. The other patients are currently under observation.
Conclusion: EUS-guided micro-biopsies of cystic pancreatic lesions is feasible and increases diagnostic performance significantly compared to cytology. The procedure carries a risk for post-procedure pancreatitis that must be considered, and patients should be selected carefully for this procedure.
Disclosure: Speaker honoraria: GE healthcare, Conference participation: Pharmacosmos, US equipment: Samsung Medison.

P0117 WITHDRAWN

P0118 EPIGENETIC REGULATION OF APOPTOTIC PROTEASE ACTIVATING FACTOR-1IS ASSOCIATED WITH WORSE SURVIVAL AND PROGNOSIS IN PANCREATIC CANCER

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Introduction: Apoptotic protease activating factor-1 (Apaf-1) is a critical regulator of the intrinsic pathway of apoptosis. Recent studies suggest that inactivation of the Apaf-1 by DNA methylation processis common event in numerous cancer types including pancreatic ductal adenocarcinoma (PDAC). In addition, restoring physiological levels of Apaf-1 by5-aza-2'-deoxycytidine (Decitabine) - a specific inhibitor of DNA methylation, markedly enhances chemosensitivity and rescues the apoptotic defects associated with Apaf-1 loss. While the ability of DNA hypermethylation to silence tumor suppressor genes in cancer is well established, how genes are targeted for this aberrant DNA methylation in PDAC is still unclear.
Aims & Methods: The aim of our study is to determine the association of APAF-1 expression with clinicopathological parameters and prognosis in PDAC and to assess the possible epigenetic *APAF-1* regulation mechanism by DNA methylation process.
Data of 56 patients after pancreatoduodenectomy for PDAC between 2011-2016 were analyzed. Patient's mRNA expression levels of APAF-1 was compared with normal pancreatic tissue and the correlations with clinicopathological parameters were analyzed. The Kaplan-Meier method and log-rank tests were used for survival analysis. Additionally, two linear pancreatic adenocarcinoma cell lines Capan2 and MiaPaca2 were treated with Decitabine (1mM, 5mM, 10mM concentrations) and *APAF-1* mRNA expression,apoptotic activity and viability were evaluated after 0, 24, 48 and 72 hours.
Results: The RT-PCR analysis revealed that APAF-1 mRNA expression was significantly lower in PDAC when compared to normal pancreatic tissue (p=0.002). The expression of APAF-1 mRNA was correlated with tumor stage, lymph-node metastases, lymphatic and vascular invasion (p< 0.05). Furthermore,survival analysis revealed that patients with higher APAF-1 expression were doing better in tested cohort group (p=0.033). Univariate analysis revealed that higher T stage, lymph-node metastases, perineural and lymphatic invasion were assessed as significant factors for shorter survival in PDAC patients (p< 0.05). After 24 h treatment with Decitabine (1mMand 5mM conc.) the increased expression of Apaf-1 was detected in the most of thePDAC cells and it decreased gradually with increased incubation period when compared with control group.
Decitabine inhibited the cells' proliferations and viability of Capan2 and MiaPaCa2 cells gradually with increased drug's concentration and incubation time. The strongest apoptosis rates were obtained after incubation for 48 h in the Capan2 cells despite concentrations rates of Decitabine, while MiaPaCa2 cells showed the highest apoptotic activity starting from 24 hours that intensify progressively throughout all concentrations. Presumably, Decitabine reduces APAF-1 methylation and restores its expression, thus reactivating its functions.
Conclusion: Present study shows that downregulation of pro-apoptotic Apaf-1 gene is associated with worse prognosis in PDAC.Our results suggest that the tumor-suppressive effect of Decitabine may result from the reactivation of silenced *Apaf-1* through demethylation.
Disclosure: Nothing to disclose

P0119 MIR-23B-3P PROMOTES PANCREATIC CANCER CELL TUMORIGENESIS AND METASTASIS THROUGH THE PTEN/PI3K/AKT SIGNALING PATHWAY

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Introduction: The microRNA (miRNA) miR-23b-3p plays an important role in tumor growth, proliferation, invasion, and migration. However, the role and mechanism of miR-23b-3p in pancreatic cancer (PC) development remain largely unknown.

Aims & Methods: RT-PCR was applied to verified the serum miR-23b-3p expression, Immunohistochemical (IHC) and western-blot were used to detect the proteins expression, MicroRNAs (miRNAs) mimic and inhibitor were used to change the expression levels of miR-23b-3p and the PANC-1 cell lines was used for in vitro studies, the targeted gene was verified by luciferase reporter assay as well as western-blot. Finally, the subcutaneous tumor xenograft model and the living image system were used for the in vivo studies.

Results: In this study, we found that the serum miR-23b-3p level was elevated in PC patients along with upregulation of phosphoinositide 3-kinase (PI3K) and phospho-protein kinase B (p-Akt), suggesting the possible involvement of miR-23b-3p and PI3K/Akt signaling in PC development.

In addition, miR-23b-3p was induced in response to interleukin-6 (IL-6), which is involved in PC progression. Overexpression of miR-23b-3p by an miR-23b-3p mimic, on the other hand, activated PI3K/Akt signaling in PC cells, as evidenced by miR-23b-3p-induced upregulation of phosphatidylinositol (3,4,5)-trisphosphate (PIP3) and p-Akt as well as downregulation of phosphatase and tensin homolog (PTEN). MiR-23b-3p downregulated PTEN through directly targeting the 3'-untranslated region (3'UTR) of PTEN mRNA. Importantly, overexpression of miR-23b-3p by a miR-23b-3p agomir promoted PC cell-derived tumor growth and liver metastasis in a xenograft mouse model, along with activated PI3K/Akt signaling. In contrast, knockdown of miR-23b-3p by an miR-23b-3p antagomir suppressed tumor growth and metastasis as well as PI3K/Akt signaling activity.

Furthermore, the mice in vivo imaging experiment showed over expression of miR-23b-3p can enhance the total fluorescence signals from regions of interest (ROI), and it was demonstrated that the fluorescence signals were stronger in the lung and heart when compared with control.

Conclusion: These results suggest that miR-23b-3p enhances PC cell tumorigenesis and metastasis at least partially through the PTEN/PI3K/Akt signaling pathway. Therefore, targeting miR-23b-3p or PTEN/PI3K/Akt signaling may be a potential therapeutic strategy against PC.

Disclosure: The authors declare that they have no competing interests.

P0120 NF-KAPPAB CONTROLLED CHEMOKINE SIGNALLING REGULATES ONCO-IMMUNO CROSSTALK AND APOPTOSIS RESISTANCE IN PANCREATIC CANCER

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Introduction: Pancreatic ductal adenocarcinoma (PDAC) exhibit one of the worst survival rates of all cancers. For the majority of patients, a "curative" intended resection is not feasible and the response rates to palliative therapeutic approaches remain highly unsatisfactory. One hallmark of PDAC is a profound desmoplastic stroma reaction consisting of fibroblasts, endothelial and immune cells essentially contributing to therapy resistance of PDAC. It is known that inflammation and tumorigenesis are functionally connected and controlled by the NF-kB signaling pathway, mediating apoptosis resistance.

Aims & Methods: Analyzing the role of NF-kB controlled chemokine signaling in apoptosis resistance of PDAC using unbiased expression profiling followed by translational functional analysis.

Results: By using a genome wide unbiased approach we were able to establish the chemokines CCL20 and CX3CL1 as central NF-kB target genes mediating therapy resistance. Both chemokines are acting in a paracrine fashion, leading to an increased recruitment of inflammatory cells which in turn mediate apoptosis resistance of PDAC cells. By the use of an orthotopic syngeneic transplantation PDAC model, we further dissected the relevance of the observed cancer-immune cell interaction and strengthen the value of such onco-immuno-crosstalk to tailor novel precise therapeutic interventions.

Conclusion: In conclusion, our data show a functional role of NF-kB-controlled chemokine pathways in PDAC TRAIL resistance.

The demonstrated therapy induced cross-talk of cancer cells with immune cells impairs the intended treatment response, pointing out the need of novel bi-specific treatments, which target tumor cells as well as immune cell.

Disclosure: Nothing to disclose

P0121 TXNRD2 DEFICIENCY LEADS TO LOW RAS-ACTIVITY AND DECREASED TUMOR DEVELOPMENT IN A KRAS[G12D] - DRIVEN PANCREATIC CARCINOGENESIS MOUSE MODEL

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Introduction: Reactive Oxygen Species (ROS) and oxidative defense systems are believed to play a pivotal role in pancreatic cancer development. Recent results show the driving force of ROS in the development of pancreatic ductal adenocarcinoma (PDAC), yet the role of key regulators of ROS remains elusive. We set out to investigate the impact of mitochondrial Thioredoxin reductase (Txnrd2) deletion on mitochondrial ROS (mtROS) and Kras[G12D] - driven pancreatic carcinogenesis in a mouse model.

Aims & Methods: Genetically engineered mice (GEM) were kept in appropriate housing facilities according to German animal welfare law until tumor development or designated time points, respectively. Sections from pancreas and primary metastatic sites as well as macroscopically pathological organs were fixed and processed by H&E staining and immunohistochemistry. Also, tumor cells were isolated and further experiments were performed in cell culture. Methods such as qRT-PCR, Western Blot analysis, cellular oxygen consumption analysis, protein activity pulldowns, proliferation and colony formation assays, in vivo stainings, Flow cytometry and others were performed to investigate the objective.

Results: At 12 weeks and, to a lesser degree, also in 24 weeks, we observed an increase in ADM (acinar-to-ductal metaplasia) and PanIN (pancreatic intraepithelial neoplasia) lesions in Kras[G12D]; Txnrd2[ΔPanc] mice compared to Kras[G12D] control mice. Despite this initial increase in precursor lesions, , tumor incidence was significantly lower compared to Kras[G12D] control mice. In order to gain insight into the mechanism behind this apparent discrepancy, we investigated cancer cell lines isolated from these GEM. We observed impaired proliferation and colony formation. This reduced proliferation could be linked to impairments in cell cycle, concerning mainly the S-Phase. ROS and some antioxidant enzymes were increased, however, the oxidative state of the cells remained balanced. Although we also detected a higher mitochondrial copy number in Txnrd2-deficient cells, measurement of mitochondrial bioenergetics showed no impairment of mitochondrial function and comparable O_2-consumption and extracellular acidification rates, respectively.

Interestingly, we found lightly decreased levels of mRNA-levels of RAS-isoforms, which led us to investigate RAS abundance and activity, where we could observe significant alterations in cell lines deficient of Thioredoxin Reductase 2.

Conclusion: Although there are further experiments to be pursued, we believe to have gained insight into the mechanisms behind the observed phenotype of reduced tumor incidence in Kras[G12D]; Txnrd2[ΔPanc] mice.

Disclosure: Nothing to disclose

P0122 THE EFFICACY OF REIC/DKK-3 GENE THERAPY FOR PANCREATICOBILIARY CARCINOMA

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Introduction: The reduced expression in immortalized cells (REIC)/Dkk-3 gene is down-regulated in various malignant tumors. Previous study revealed that the REIC/Dkk-3-expressing adenoviral vector (Ad-REIC) was found to induce cancer-selective apoptosis, and anti-tumor immunity.

Aims & Methods: We applied Ad-REIC to treatments of pancreaticobiliary carcinoma.The cell proliferation and the apoptotic effect of Ad-REIC were evaluated by MTT assayin the pancreatic cancer cell lines (ASPC1 and MIA-PaCa2) and cholangiocarcinoma cell lines (TFK-1 and G-415). Ad-LacZ was used as a control. The apoptosis signal was assessed by western blotting. Additionally, the effect of combined therapy with Ad-REIC and chemotherapy agents (gemcitabine, and cisplatin) was assessedin vitro. We also established the drug-resistant cancer cells (gemcitabine-resistant ASPC1, cisplatin-resistant TFK-1),and assessed the therapeutic effects of Ad-REIC therapy for drug-resistant cancer cells. The effects of Ad-REIC in vivo were assessed using the mouse xenograft model.

Results: Ad-REIC inhibited cell growth in pancreaticobiliary cancer cell lines (ASPC1:31.9±8.8%, MIAPaCa2:39.7±11.6%, TFK-1:64.5±1.7%, G-415:48.4±4.1%). Anti-tumor effect of Ad-REIC was further enhanced in combination with chemotherapy agents (ASPC1:29.1±6.8%, MIAPa-Ca2:19.7±3.1%, TFK-1:50.0±5.3%, G-415:22.0±2.0%). Ad-REIC also induced apoptosis inthe gemcitabine-resistant ASPC1 (62.7±1.3%), and the cisplatin-resistant TFK-1 (58.0±1.3%). The anti-tumor effect may be causedby the stimulation of c-Jun-N-terminal kinase pathway. Ad-REIC also achieved tumor growth inhibition in the mouse xenograft model (ASPC1: 60.7±9.9%, G-415: 43.8±22.6%).

Conclusion: Ad-REIC induced apoptosis and inhibited tumor growth in the pancreaticobiliary cancer including drug-resistant cancer cells. REIC/Dkk-3 gene therapy could be an attractive therapeutic tool for the pancreaticobiliary cancer.

Disclosure: Nothing to disclose

P0123 SMART DRUG-DELIVERY SYSTEMS FOR PANCREATIC CANCER TREATMENT

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Introduction: Pancreatic cancer is a lethal disease partly due to poor drug delivery and acquired resistance to therapy. Nanotechnology have shown promise in a wide range of biomedical applications. In particular, nanoparticles have been used to achieve controlled drug delivery and to improve treatment efficacy. The protein kinase B, also known as Akt, is overexpressed in many types of cancers, including pancreatic cancer. This protein plays a key role in multiple cellular processes such as cell proliferation and cell death. Targeting Akt is a highly attractive anti-cancer strategy and different Akt inhibitors are now in clinical development for cancer therapy.

Aims & Methods: In this project, we have developed novel polymeric nanoparticles formed by elastin-like recombinamers (ELRs) carrying a small peptide inhibitor of the protein kinase Akt. We have evaluated the kinetic uptake and subcellular localisation of these carriers by flow cytometry and confocal microscopy, respectively. Moreover, we have determined the effectiveness of the loaded nanoparticles to inactivate both established pancreatic cancer cell lines and clinically relevant patient-derived cells by MTT assays and LIVE/DEAD staining. The specific inhibition of phospho-Akt and the activation of cell death pathways after incubation with the loaded nanoparticles were evaluated by western blot analysis and protein array-based approaches.

Results: We corroborated that the ELR polymer was able to self-assemble into smart nanoparticles with a mean diameter of 72 nm when the temperature was increased above 16°C. Accumulation of nanoparticles into the cells was validated by flow cytometry. Confocal microscopy showed a lysosomal localisation of these nanoparticles. Cell viability and metabolic activity were significantly reduced after incubation with loaded nanoparticles in a time- and concentration-dependent fashion. Moreover, nanoparticles inhibited phosphorylation of Akt protein, blocked NFκB signalling pathway and triggered caspase 3-mediated apoptosis.

Conclusion: Hence, the use of these novel polymeric nanoparticles could lead to the development of more effective pancreatic cancer treatment options focused on the inhibition of Akt. The combination of these inhibitors with other treatment strategies could improve treatment outcomes.

Disclosure: Nothing to disclose

P0124 EVALUATION OF A NEW ANTI-GALECTIN 9 IMMUNOTHERAPY STRATEGY IN PANCREATIC CANCERS

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Introduction: We have previously described in an humanized mouse model of nasopharyngeal carcinoma that an anti-Galectin-9 (Gal-9) monoclonal antibody (mAb) is able to significantly limits tumor growth by specifically inhibiting the suppressive activity of human natural Tregs (Patent WO: WO2015185875). Herein, we propose to use this new specific active immunotherapy in a pancreatic cancer mouse model (KRAS^{G12D}), insofar as a high Treg prevalence has been described and correlated to the tumor progression of pancreatic cancer.

Aims & Methods: Gal-9 expression was analysed by immunohistochemistry on pancreas isolated from the KRAS^{G12D} mouse model. Treg infiltration was analyzed by flow cytometry after digestion (GentleMACS) of pancreas isolated from the KRAS^{G12D}

For in vitro study we used four PDAC cancer cell lines Capan-1, Capan-2, MIAPaCa-2, Panc-1 and perfomed RT-qPCR, Immunofluorescence, Western-blot, flow cytometry and ELISA to validate Gal-9 expression and secretion.

Results: Gal-9 expression was confirmed by immunohistochemistry on pancreas isolated from the KRAS^{G12D} mouse model. This Gal-9 expression level has been correlated to the progression of pre-cancerous lesions. Furthermore, an increase of Tregs prevalence has been observed in this transgenic model at a systemic and intratumoral level. Very interestingly, we also showed that

(i) murine Tregs expressed Gal-9 (flow cytometry, immunofluorescence and western-blot),

(ii) anti-Gal9 mAb neutralized the immunosuppression induced by recombinant murine Gal-9 (proliferation assays) and

(iii) anti-Gal9 mAb neutralized the suppressive activity of murine Tregs (MLR assay).

Further investigations performed on four human pancreatic cancer cell lines (Capan-1, Capan-2, MIAPaCa-2, Panc-1) have also confirmed the Gal-9 expression at a genomic (RT-qPCR), proteomic (Immunofluorescence, Western-blot and flow cytometry) and secreting (ELISA) level. Moreover public data from 'Gene Expression Omnibus' showed a high level of Gal-9 transcript in the pancreas of PDAC patients which is associated with decreased overall survival.

Conclusion: Our preliminary results suggest that the use of an anti-Gal-9 mAb could be considered as a new anti-tumoral immunotherapy targeting Tregs in the pancreatic cancer.

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P0125 DNA SEQUENCING OF CYTOPATHOLOGICALLY INCONCLUSIVE EUS-GUIDED FINE NEEDLE ASPIRATES FROM SOLID PANCREATIC LESIONS SUSPICIOUS FOR MALIGNANCY CONFIRMS EUS DIAGNOSIS

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Introduction: Endoscopic ultrasound (EUS) with fine-needle aspiration (FNA) is inconclusive in up to 10-15% of patients with solid pancreatic lesions (SPLs). We aimed to investigate whether supplementary genetic analyses with whole exome sequencing add diagnostic value in patients with SPLs suspicious of malignancy but inconclusive EUS-FNA.
Aims & Methods: Thirty-nine patients, who underwent EUS-FNA of a SPL were retrospectively included. Three groups were defined: 16 (41.0%) had suspected malignancy on EUS confirmed by cytology (malignant), 13 (33.3%) had suspected malignancy on EUS but benign cytology (inconclusive), and 10 (25.6%) had benign EUS imaging and cytology (benign). Areas with highest epithelial cell concentrations were macro-dissected from the FNA smears from each patient, and extracted DNA was used for whole exome sequencing by Next Generation Sequencing of a selected gene panel including 19 genes commonly mutated in cancer. Final diagnosis was verified by surgery or clinical follow-up.
Results: Pathogenic mutations in *KRAS*, *TP53*, and *PIK3CA* differed significantly between the three groups (p< 0.001, p=0.018 and p=0.026, respectively). Pathogenic mutations in *KRAS* and *TP53* were predominant in the inconclusive (54% and 31%, respectively) and malignant groups (81.3% and 50%, respectively) compared to the benign group (0%). Malignant and inconclusive diagnoses correlated strongly with poor overall survival (p< 0.001).
Conclusion: Whole exome sequencing of genes commonly mutated in pancreatic cancer may be an important adjunct in patients with SPLs suspicious for malignancy on EUS but with uncertain cytological diagnosis.
Disclosure: Nothing to disclose

P0126 WITHDRAWN

P0127 WITHDRAWN

P0128 ONCOLOGICAL OUTCOME OF CURRENT NEOADJUVANT THERAPY REGIMES IN ELDERLY PATIENTS SUFFERING FROM PANCREATIC CANCER – RESULTS OF THE RESPECT-STUDY

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Introduction: The worldwide number of people aged older than 60 years will more than triple by the year 2050. As a consequence, the absolute and relative number of elderly patients requiring oncological therapy for malignant diseases will rise leading to the question whether currently practiced treatment regimes can be applied in patients of higher age or should be adopted to age. Here, data on the impact of neoadjuvant therapy(NTx) in elderly patients with pancreatic cancer is lacking.

Aims & Methods: For this purpose, the RESPECT-study - a multinational, retrospective database - was screened for patients receiving either FOFIRINOX (FFx) or Gemcitabine/nab-paclitaxel (GNP). Subsequently, patient outcomes were compared between young and elderly patients using a cut-off age of 63 years(Comparison1) and 70 years (Comparison 2).
Results: 48.5% and 23.7% of all patients receiving NTx were older than 63 and 70 years. In both groups younger patients preferably undergo FFx (Comparison 1: 83.1% vs. 69.7%; p=0.063;
Comparison 2: 81.8% vs. 57.6%; p=0.005) with more NTx cycles (Comparison1: 6.58 vs. 5.66; p=0.057). Although dose reduction of NTx was more common in elderly patients in Comparison 1 (n=10/11.2% vs. n=23/23.9%; p=0.003), resectability (Comparison 1: n=71/79.8% vs. n=57/75.0%; p=0.575;
Comparison 2: n=102/77.3% vs. n=26/78.8%; p=1.000) did not differ between both groups. Importantly, median survival (Comparison 1: 29.867 vs. 23.1; p=0.406, Comparison 2: 28.0 vs. 21.0; p=0.499), overall survival of resected patients (Comparison 1: 36.0 vs. 28.0; p=0.453,
Comparison 2: 35.0 vs. 26.0; p=0.378) and progression-free-survival time (Comparison 1: 22.0 vs. 19.0; p=0.730, Comparison 2: 23.0 vs. 15.0; p=0.095) did not relevantly differ.
Conclusion: Results suggest that NTx is also feasible in elderly patients suffering from pancreatic cancer with an adequate resection rates, oncological response and overall survival.
Disclosure: Nothing to disclose

P0129 CAN DIGITAL SKELETAL MUSCLE INDEX PREDICT PALLIATIVE CHEMOTHERAPY UPTAKE BEFORE PATIENTS UNDERGO ENDOSCOPIC PANCREATIC BIOPSY?

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Introduction: An endoscopic ultrasound guided biopsy (EUS-B) is required prior to treatment with palliative chemotherapy for patients with suspected pancreatic ductal adenocarcinoma (PDAC). Given the urgency of treatment, EUS-B is often done prior to oncological assessment after which a significant proportion of patients do not take up chemotherapy. Low skeletal muscle index (SMI), termed sarcopenia, is common in PDAC and has been associated with poor outcomes.
Aims & Methods: We aimed to assess if novel digital software can calculate SMI using a computerised tomography (CT) image to predict palliative chemotherapy uptake in patients with suspected PDAC, and streamline EUS-B. Patients who underwent an EUS-B showing PDAC between Jan 2016 and Dec 2017 with a CT scan performed within a month prior to biopsy were included in the study. SMI was calculated by a single slice CT image taken at the level of the third lumbar vertebra.
Software was used to identify skeletal muscle (sliceOmatic, Tomovision). Sarcopenia was defined as SMI< 41(female) and < 53 cm²/m²(male). Body mass index (BMI), performance status, demographic data were also compared between patients that went on to receive chemotherapy and those who did not.
Results: EUS-Bconfirmed PDAC in 85 eligible patients during the study (median age 70;41-84 years). A total of 61/85(71%) of patients received at least one dose of chemotherapy. Sarcopenia was present in 57/85 (57.6%). Despite a raised BMI of >25 in 41/85 (48.1%) of the patients, sarcopenia was present in 25 (61.0%) of them.
Patients who did not take up chemotherapy had a lower SMI (40.5 vs 45.2 cm²/m²,p=0.04) and a poorer mean performance status (1.25 vs 0.7: t-test p=0.002). There was no difference in BMI (26.8 vs 24.6 p=0.10) in patients that did and did not take up chemotherapy. No patients with a performance status of 3 (n=3) or age >80 (n=5) proceeded to chemotherapy. In those having chemotherapy, survival was higher in non-sarcopenic patients compared to sarcopenic patients (11.8 vs 7.7 months, *p*=0.04). Survival was similar in sarcopenic patients having chemotherapy and non-sarcopenic patients who did not have chemotherapy (7.7 vs 7.4 months *p*=0.5). Patients with performance status ≥2 and sarcopenia were much less likely to receive chemotherapy compared to those with performance status 0-1 without sarcopenia (83.9% vs 37.5%, *p*=0.02).

Conclusion: Patients with PDAC and a performance status of ≥2 and low SMI were significant less likely to take up chemotherapy and had poorer survival. SMI measurement could act as part of a decision tool to assess suitability of patients to triage patients for rapid EUS-B, or clinical assessment prior to considering chemotherapy.
Disclosure: Nothing to disclose

P0130 ROLE OF ADIPONECTIN LEVELS IN TUMOR STAGING AND SURVIVAL PREDICTION IN PANCREATIC CANCER PATIENTS

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Introduction: There is increasing evidence that adipose tissue-derived hormones may significantly influence the growth and proliferation of tumor cells. We recently demonstrated the potential diagnostic role of changed adipokines levels in patients with pancreatic cancer (PC). However, the role of adiponectin in tumor proliferation in PC patients has not been well studied before.
Aims & Methods: The aims of the study were to analyze plasma concentrations of adiponectin in PC patients and to compare these concentrations to clinicopathological parameters. Baseline levels of serum adiponectin were determined in 50 consecutive patients with PC and followed up for the median period of 18 months. 50 Control subjects were matched to case patients by age, sex and BMI. The association between variables were evaluated using nonparametric Spearman's correlation test. Logistic regression analysis was used to evaluate the association of independent variables with one dependet variable.Receiver operating characteristics (ROC) analysis was employed to calculate the area under the curve (AUC). Survival analysis used the Kaplan-Meier curve.
Results: Overall median adiponectin concentrations were lower in PC patients versus control subjects (3.33 vs 6.62 mg/L, $p < 0.001$). Strong inverse correlation between adiponectin concentrations and tumor size (r= -0.934, $p < 0.01$) and Ca 19-9 levels (r= -0.495, $p < 0.01$) in PC patients were observed. Logistic regression analysis demonstrated that low adiponectin levels were independent predictors of tumor size (beta= -0,018,$p < 0.001$) and metastatic disease (OR=0.573,$p < 0.005$). At ROC analysis the diagnostic profiles of adiponectin for detecting matastatic disease (AUC 0.924; sensitivity 82%;specificity 93%) among PC patients was high. Kaplan-Meier global survival analysis revealed that low adiponectin levels were associated with poorer survival compared to patients with high adiponectin levels (log-rank (c^2): 5.02, $p < 0.001$).
Conclusion: This study identified, for the first time, an inverse correlation between adiponectin levels, tumor size and Ca 19-9 levels suggesting a potential role of adiponectin as an indicator of disease progression. Furthermore these results suggest, that serum adiponectin levels might provide prognostic information in predicting survival in PC patients. The potential role of adiponectin levels as an adjunctive indicator of advanced PC disease requires further evaluation.
Disclosure: Nothing to disclose

P0131 ACCURACY AND DIAGNOSTIC YIELD OF PERCUTANEOUS ULTRASOUND FINE NEEDLE BIOPSY IN SOLID PANCREATIC LESIONS

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Introduction: Recent advances in treatment of pancreatic adenocarcinoma are leading to an increasing use of neoadjuvant therapy before surgery, even in borderline resectable disease. This could increase the number of patients who need pancreatic biopsy, until now reserved to unresectable pancreatic cancer or metastatic dIsease.
Current guidelines suggest that an histological diagnosis of adenocarcinoma of the pancreas can be made using fine-needle aspiration (FNA) biopsy with either endoscopic ultrasonography (EUS) guidance (preferred) or computed tomography (CT). EUS-FNA is highly sensitive and specific for solid lesions and provides the benefit of additional staging information at time of biopsy: lymph node staging, vascular invasion, and prediction of resectability. Altough effective, EUS-FNA requires narcosis and is an expensive procedure. Percutaneous ultrasound-guided fine needle Biopsy (US-FNB) is a widely accepted procedure to study retroperitoneal and various abdominal lesions butit is not recommended for diagnosis of pancreatic cancer.
We aimed to assess the sensitivity, specificity, accuracy, safety and effectiveness of US-FNB in patients with suspected pancreatic lesions
Aims & Methods: In our prospective study we enrolled consecutive patients with a solid pancreatic lesion suspected for malignancy. All patients underwent, if possible, US-FNB and diagnosis of malingnancy was confirmed at follow-up, either at surgery or by the evolution of disease (eg: systematic therapy, death, development of metastatic lesions). Sensitivity, specificity and side effects were estimated.
Results: Out of 90 patient, US FNB was technically feasible in 81 patients. 60 patients were diagnosed with malignancy lesions (in detail 55 were pancreatic adenocarcinomas, 2 metastasis, 3 neuroendocrine tumor). 6 patients had mass growing pancreatitis. The sensitivity of US-FNB was 80%, specificity was 100% and accuracy 82%. Only 2 adverse effects were registered: a case of mild abdominal pain and a case of self-limiting abdominal bleeding.
Conclusion: In our study the sensitivity, specificity and accuracy in pancreatic lesions of US-FNB are equal to EUS-FNA. US-FNB is safe and effective. We do not registered any important side effect and procedure was usually well tolerated by patient. Not requiring narcosis and using simple disposable equipment US-FNB is also a cheaper technique than EUS-FNA. We suggest to evaluate its use as a valid alternative to endoscopic biopsy.
Disclosure: Nothing to disclose

P0132 PATIENT-REPORTED BURDEN OF INTENSIFIED SURVEILLANCE AND SURGERY IN HIGH-RISK INDIVIDUALS UNDER PANCREATIC CANCER SURVEILLANCE

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Introduction: Worrisome features detected in high-risk individuals participating in a pancreatic cancer surveillance program, warrant for intensified surveillance or, occasionally, surgery.
Aims & Methods: Our aim was to determine the patient-reported burden of such intensified surveillance and/or surgery, and to assess post-operative quality of life. In the course of our pancreatic cancer surveillance program, participants completed questionnaires including the Hospital Anxiety and Depression Scale (HADS, subscales range 0-21) and the Cancer Worry Scale (CWS, ranges 8-32). For individuals who underwent intensified surveillance (without leading to surgery), questionnaires before intensified surveillance, during, and ≥3 weeks after the decision to return to regular follow-up were analyzed. In addition, those who underwent intensified surveillance in the last 3 years, or surgery at any time, were invited for a semi-structured telephone interview.

Results: 34 individuals underwent intensified surveillance, of which 20 returned multiple questionnaires (response rate 59%) and 12 were invited for an interview, to which eight consented (response rate 67%). Of those who underwent surgery, 10 were interviewed (response rate 91%). The total cohort consisted of 31 individuals (12 (39%) male, median age 52 (IQR 13) years), 16 (52%) familial pancreatic cancer kindreds and 15 (48%) gene mutation carriers.

During the intensified surveillance period, cancer worries increased significantly (median CWS 14, IQR 7), as compared to before (median 12; IQR 9, P=0.007) or after (median 11, IQR 7, P=0.014), but eventually returned back to baseline (P=0.823). General anxiety and depression scores were low (both median 5, IQR 5) and not significantly influenced by the intensified surveillance period (P>0.100).

Of the 8 interviewed participants, 5 (63%) had perceived the extra visits as more burdensome or stressful than the regular visits, and 5 still experienced increased worries. They regarded intensified surveillance as something positive (2), neutral (2), negative but necessary (3) or negative (1).

Of the 10 operated patients (median 43 months since surgery, IQR 63), 5 underwent a pancreatoduodenectomy and 5 a distal pancreatectomy. Pathology revealed one T1 pancreatic ductal adenocarcinoma, 7 premalignant lesions (PanIN 1-2 or IPMN with low-moderate grade dysplasia), and 2 cases of benign disease (neuroendocrine tumor and autoimmune pancreatitis).

Afterwards, 20% developed diabetes and 70% steatorrhea. Patients judged their recovery as good (fast, no complications, 20%), fair (minor complications and/or longer recovery time than anticipated, 50%), or poor (major complications, 30%). Median quality of life scores (SF-12 PCS 56 and MCS 52) were not different from age-matched reference data from the general population.

After surgery, patients' attitude towards surveillance was unchanged (60%) or became more positive (40%), but never more negative. Knowing the pathological outcome, when asked if surgery had been justified, only 20% disagreed and all would again have chosen to undergo surgery.

Conclusion: In individuals at high risk for pancreatic cancer, intensified surveillance transiently increased cancer worries, without affecting general anxiety or depression.

Although pancreatic surgery led to substantial co-morbidity, quality of life was similar to the general population, and surgery did not negatively affect the attitude towards surveillance.

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P0133 LARGER-DIAMETER PLASTIC STENT PLACEMENT FOR PREOPERATIVE BILIARY DRAINAGE IS SIGNIFICANTLY ASSOCIATED WITH LONGER PATENCY IN PATIENTS RECEIVING NEOADJUVANT CHEMORADIATION FOR PANCREATIC CANCER

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Introduction: Neoadjuvant therapy has been investigated in the patients with resectable and borderline resectable pancreatic cancer (PC). In neoadjuvant chemotherapy, self-expandable metallic stents (SEMS) was reported to be superior to plastic stents for endoscopic biliary decompression. However, preoperative biliary drainage in PC patients receiving neoadjuvant chemoradiotherapy (NACRT) has not been fully examined. We mainly used plastic stents for biliary drainage in PC patients receiving NACRT because metallic stent placement during external irradiation could cause infiltration of inflammatory cells and fibrosis due to scattering of X-ray. In this study, we examined recurrent biliary obstruction (RBO) of preoperative biliary drainage and evaluated how the diameter of plastic stents impacts on time to RBO.

Aims & Methods: We retrospectively reviewed the data regarding 131 PC patients who received NACRT using gemcitabine or TS-1 at our institution between August 2012 and July 2017. We excluded the patients who did not receive preoperative biliary drainage and those who did not receive surgery. The definition of time to RBO was the period from the stent placement to the recurrence of biliary obstruction according to TOKYO criteria 2014. Analysis of time to RBO was performed using the Kaplan-Meier method and differences were evaluated with the log-rank test.

Results: 58 patients (pts) were included. Median age was 66; 62.1% were male; median tumor size was 22mm. All biliary obstruction was caused by pathologically-proven pancreatic head cancer. Operative procedures were pancreaticoduodenectomy (n=51), total pancreatectomy (n=2) and bypass surgery (n=5). Median time from the initial biliary drainage to surgery was 133 days. The study patients received preoperative biliary drainage in 2.9 times on average (once 10 pts; twice 12 pts; three times 20 pts; four times 8 pts; five-seven times 10 pts). Biliary drainage were plastic stents in 128 cases (75.7%), endoscopic nasal biliary drainage (ENBD) in 37 cases (21.9%), SEMS in 2 cases (1.2%) and percutaneous biliary drainage in 2 cases (1.2%). SEMS was placed after radiotherapy was completed. The ERCP-related complication rate was 1.8% (mild pancreatitis 2; bile duct injury 1). These complications were relieved with conservative treatment. Two mild pancreatitis was observed in the cases of 7-Fr plastic stent placement.

RBO occurred in 80 times (occlusion 70; distal migration 10). Cholangitis was observed at the time of RBO in 66.3% (53/80). 33.9% (20/58 pts) experienced the delay of chemotherapy due to RBO. 11.9% (7/58 pts) suffered from the delay of radiation due to RBO. Surgery was not delayed because of RBO. Median time to RBO of plastic stents was significantly longer in 10 Fr (107 days) than 49 days in 7 Fr (p=0.005) and 62 days in 8.5 Fr (p=0.030).

Conclusion: In this study primarily using plastic stents, PC patients receiving NACRT experienced preoperative biliary drainage in 2.9 times on average. 10Fr plastic stents were significantly associated with longer patency compared with smaller-diameter plastic stents. Larger-diameter plastic stents could decrease RBO and the delay of chemotherapy and radiation without increasing adverse events.

Disclosure: Nothing to disclose

P0134 TEXTURE ANALYSIS ON CONTRAST-ENHANCED COMPUTED TOMOGRAPHY IN LIVER METASTASES FROM PANCREATIC AND NON PANCREATIC NEUROENDOCRINE NEOPLASIA

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Introduction: The neuroendocrine neoplasia (NEN) were considered an heterogeneity disease in term of somatostatin receptor expression, uptake contrast enhancement in CT scan evaluation, FDG uptake, and heterogeneity of proliferative index especially for patients with multiple metastases. Tumor heterogeneity can be difficult to capture and quantify with traditional imaging tools. The recent tendency of radiology is to research reproducible parameters, extracted from the images and standardized. The technical term to explain this strand is "Radiomics". It is possible to obtain an objective evaluation in addiction to traditional subjective evaluation, using TexRAD, software of CT-Texture Analysis, that refers to mathematical methods used to analyze the attenuation value of each voxel and their distribution within the region of interest (ROI) to obtain a measure of the intralesional heterogeneity.

Aims & Methods: Compare CT-texture analysis and CT features of liver metastases (mets) in pancreatic and non-pancreatic NENs according to tumor grading. CE-CT images of liver mets in NEN patients were analysed by 3D CT texture analysis. These parameters were evaluated during arterial and portal phase: mean attenuation, standard deviation, skewness, kurtosis, entropy, mean of positive pixels and Tx_sigma. Lesions delta enhancement was also calculated. The CT exams were performed before the beginning of any medical treatment.All patients had G1 or G2 a tumor according with WHO classification.

Results: Twenty-five patients non pancreatic NENs (NP-NENs) and 23 patients pancreatic (PNENs) were included in the study.

Comparing liver mets from pNENs and non-pNENs,CT texture analysis showed that the parameter "skewness" was significantly higher in non-pNENs (p-value< 0.05).This data was also confirmed when subgroup analysis according with grading system (G1 vs G2) was performed.The parameter "mean" was significantly higher in pNENs compared with non-pNENs (p=0,0066). Furthermore, the "delta enhancement" was significantly higher (p-value< 0.05) in liver mets from pNENs."Entropy" and "Kurtosis" assessed during arterial phase were associated with higher risk of death by Cox analysis (p< 0.05).

Conclusion: This study shows that liver metastases from pNENs and non-pNENs have different CT features in terms of texture parameters. The use of radiomics in NENs could be used by the physician to plan the therapy strategy.

Disclosure: Nothing to disclose

P0135 CLINICAL UTILITY OF DIRECTIONAL EFLOW COMPARED WITH CONTRAST-ENHANCED HARMONIC EUS FOR THE DIFFERENTIAL DIAGNOSIS OF PANCREATIC AND PERIPANCREATIC SOLID MASSES

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Introduction: Contrast-enhanced harmonic endoscopic ultrasonography (CEH-EUS) can be used for differential diagnosis of pancreatic lesions by evaluating microvascular circulation and patterns of contrast enhancement[1-3]. However, routine use of CEH-EUS is limited by its high cost, the lack of contrast agent availability and expertise with this technique. Directional eFLOW (D-eFLOW) (Aloka Co., Ltd., Tokyo, Japan) was introduced as a new high-definition modality for blood flow that detects blood flow in microvessels[4]. Since it uses built-in functions, it needs no additional cost and takes less time for examination.

Aims & Methods: The purpose of this study was to investigate the usefulness of D-eFlow compared with CEH-EUS for differential diagnosis of pancreatic solid lesions, especially neuroendocrine tumors. From January 2016 to February 2019, a total of 34 patients who received EUS and D-eFLOW examination to evaluate pancreatic and peripancreatic masses were analyzed, retrospectively.

Results: Of 34 patients, D-eFLOW was performed in 34 patients and CEH-EUS was performed in 32 patients. Histological diagnosis was confirmed in 19 patients by EUS-FNA and/or surgery. Concerning the detection of the neuroendocrine tumors, D-eFLOW had higher sensitivity to CEH-EUS (100% *vs.* 91.7%), lower specificity (33.3% *vs.* 50.0%), lower positive predictive value (76.5% *vs.* 78.6%), higher negative predictive value (100% *vs.* 75%) and higher accuracy (78.9% *vs.* 77.8%). There was a good correlation between the D-eFLOW and CEH-EUS to evaluating the vascularity of tumors (correlation coefficient 0.683, *p* < 0.05).

Conclusion: In conclusion, D-eFLOW can be considered as an alternative method to CEH-EUS for the evaluation of pancreatic and peripancreatic solid tumors.

References: 1. Kitano M, Sakamoto H, Matsui U, et al. A novel perfusion imag¬ing technique of the pancreas: contrast-enhanced harmonic EUS (with video). Gastrointest Endosc 2008;67:141-150. 2. Kitano M, Sakamoto H, Matsui U, et al. Contrast-enhanced endoscopic ultrasound. Digestive Endoscopy 2014;26(Suppl. 1): 79-85 3. Fusaroli P, Spada A, Mancino MG, Caletti G. Contrast harmonic echo-endoscopic ultrasound improves accuracy in diagno¬sis of solid pancreatic masses. Clin Gastroenterol Hepatol 2010;8:629-634.e1-2. 4. Das K, Kudo M, Kitano M, et al. Diagnostic value of endoscopic ultrasound-guided directional eFLOW in solid pancreatic lesions. J Med Ultrasonics 2013;40:211-218.

Disclosure: Nothing to disclose

P0136 ENDOSCOPIC ULTRASOUND-GUIDED SINGLE-PASS FINE NEEDLE BIOPSY USING 25-GAUGE NEEDLES WITH A CORE TRAP FOR DIAGNOSING SMALL PANCREATIC NEUROENDOCRINE TUMORS: MULTICENTER PROSPECTIVE TRIAL

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Introduction: We previously reported in a prospective multicenter trial that endoscopic ultrasound-guided fine needle biopsy (EUS-FNB) using 25-gauge needles with a core trap provides histological samples of adequate quality for diagnosing and grading pancreatic neuroendocrine tumors (PNET) (UMIN000010021).

Aims & Methods: Since the number of surgical cases increased thereafter, we conducted further detailed examination in this study. Consecutive patients with hypervascular solid pancreatic masses, suspected as PNET on imaging modalities, who presented to ten Japanese referral centers from June 2016 to November 2017 were prospectively recruited. All patients underwent EUS-FNB using 25-gauge needles with a core trap (EchoTip ProCore, Cook Medical, Bloomington, Indiana, USA). After the mass was punctured, the slow-pull technique was used for biopsy. The specimen obtained by first pass was used for this study. The entire specimen was inserted into a formalin bottle and processed for histological analysis. All tissue samples were brought to a single facility where experienced pathologists reviewed them.

Results: A total of 52 patients (male/female: 24/28, median age: 63 years) were enrolled in this study. The technical success rate of EUS-FNB was 100% and tissue acquisition rate for histological analysis was 86.5%. There were no complications related to EUS-FNB. Thirty-six patients subsequently underwent pancreatic resection, and 31 patients were diagnosed as PNET (G1=28, G2=3, tumor size: 3 to 26 mm, median tumor size: 11 mm) by evaluation of the surgical specimen. The sensitivity, specificity and accuracy of EUS-FNB for the histological diagnosis of PNET were 82.1%, 100% and 84.8%, respectively. Sensitivity of EUS-FNB was 80% for tumors smaller than 10 mm, 91.7% for tumors 10 to 20 mm in size, and 80% for those larger than 20 mm. Sensitivity of EUS-FNB via transgastric access (median tumor size: 11 mm) was 84.6%, that via transduodenal bulb access (median tumor size: 15.5 mm) was 50%, and that via transduodenal 2nd portion access (median tumor size: 11 mm) was 90%. Although the sensitivity of EUS-FNB via transduodenal bulb access was low, the tumors were not smaller than those for the other route. The concordance rate of PNET grading by EUS-FNB with grade of the resected tumor was 82.6%.

Conclusion: EUS-FNB using a 25-gauge needle with a core trap via a single pass offers high accuracy for diagnosing and grading small PNET.

Disclosure: Nothing to disclose

P0137 UNAWERENESS OF HYPOGLYCAEMIA IN PATIENTS WITH INSULINOMA

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Introduction: Insulinoma is rare, but definitely most common functional neuroendocrine tumor of pancreas. In almost all cases there are benign

and sporadic. Clinical manifestation include various symptoms of hypoglycaemia, which is the result of insulin overproduction. Paradoxically, there is some patients without any clinical sign of hypoglycaemia. This patients suffer from unawereness of hypoglycaemia. In our work, we focus on presence of this syndrom in patients with insulinoma. Our aim was identify these patients, because unawereness hypoglycaemia is serious condition, which has a great influence life, and can be even life threatening.

Aims & Methods: Analysis of retrospective clinical and biochemical data was used to create file of patients. We evaluated every patient with confirmed insulinoma (biochemically, with localization technique) from 1996 to 2019 hospitalized in our department. During admission we asked patient about clinical presentations, duration of hardships and presence of spontaneous loss of conciousness. After admission, every patient underwent 72-hour fasting test on intensive unit care with monitoring vital signs, levels of blood glucose level, C-peptis and IRI. From this file of patients we selected and focus on patients with documentated episode of clinically silent hypoglycaemia. After reaching the blood glucose level under 2,2 mmol/l, we took blood for examination of C-peptid and IRI levels, gave patient gucose parenterally and stopped fasting test. These patient was monitoring closely during whole diagnostic procedure, and were reffered to surgical treatment as soon as it was possible

Results: From 1996 to 2019 there were overall 23 patients with confirmed diagnosis of insulinoma. The number of patients with unawereness hypoglycaemia events was 7 (30,43%), 4 men and 3 women. The mean age of our patiens was 50 years (from 30 to 69 years). All of these patients suffer from severe episodes of hypoglycaemia without any accompanying symptoms during hospitalization in our department. We detected hypoglycaemia either accidentally during measurement profile of glucose or when patient loss of consciousness. Mean levels of blood glucose during fasting test was 1,79 mmol/l (from 2,4 to 1). Paradoxically, none of these patients had increased levels of C-peptid and IRI during fasting test.

Conclusion: Until now, unawereness of hypoglycaemia was described only in patients with diabetes mellitus. In our work, we found presence of this syndrom in patients with insulinoma. These patients suffered from severe episodes of hypoglyceamia without any accompanying symptomts and they are also at risk of sudden death.

Disclosure: Nothing to disclose

P0138 PROGNOSTIC AND SURVIVAL FACTORS OF INTESTINAL AND PANCREATIC NEUROENDOCRINE TUMORS (IP-NETS): THE EXPERIENCE OF A TERTIARY REFERRAL CENTER

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Introduction: Intestinal and pancreatic neuroendocrine tumors (IP-NETs) represent a rare group of neoplasias, with an incidence of approximately 0.5 in 100,000 inhabitants, constituting a small percentage of intestinal and pancreatic neoplasias. The clinical presentation and biological behavior is extremely variable, reflecting large differences in survival, depending on the location, type of primary tumor, metastization and other multiple factors.

Aims & Methods: In this study, we evaluated the location, type of primary tumor as well as other relevant clinical and pathological aspects with impact on the global and disease-free survival. We retrospectively evaluated 89 patients with intestinal and pancreatic neuroendocrine tumors with a confirmed pathological diagnosis between 2008 and 2019. Patients with MEN1 (Type1 Multiple Endocrine Neoplasia) or Von Hippel-Lindau syndrome were excluded.

Results: The most frequent primary site was pancreatic (47% -57%) and intestinal (42 patients-47%). The majority of patients were female (60%). The mean age at diagnosis was 53.8 years (range 22-87 years). The median survival was 138 months. Regarding the existence of metastases at the time of diagnosis (synchronous or metachronous), they were present in 37 patients (42%). Regarding the therapeutic approach, patients underwent surgery (54%), surgery + chemotherapy (40%) or chemotherapy alone (6%), Survival was higher in patients submitted to surgery (P < 0.001). It

should be noted, that the patient's age >65 years at diagnosis (P < 0.001), primary tumor size greater than 25 mm (P = 0.02), the presence of syn­chronous metastases (P = 0.03) and the presence of a Ki67> 5% (P = 0.04) were evidenced as independent factors of adverse prognosis.

Conclusion: The clinical presentation and biological behavior of IP-NETs is considerably variable. Consistent with previously published series of cases, age less than 65 years, primary tumor size and absence of locoregional disease, angioinvasion and metastases are associated with a better prognosis.

Disclosure: Nothing to disclose

Endoscopy and Imaging I
10:30-17:00 / Poster Exhibition - Hall 7

P0139 LONG-TERM OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION VERSUS LAPAROSCOPIC RESECTION FOR GASTRIC STROMAL TUMORS LESS THAN 2 CM

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Introduction: Gastrointestinal stromal tumors (GISTs) is the most common mesenchymal gastrointestinal tumor, which accounts for about 2% of all the gastrointestinal tumors.The age-adjusted yearly incidence rate of GISTs was about 6.8 per million, with 54% men and 46% women.

Aims & Methods: Laparoscopic resection (LAP) and endoscopic submucosal dissection (ESD) is commonly used to remove small gastrointestinal stromal tumors (GISTs). However, whether LAP or ESD has more efficient outcome for small GISTs is controversial. Therefore, our Aim was to evaluate the efficacy of ESD and LAP for small GISTs and provided long-term outcomes of the two methods.

Methods: All data from 398 patients who underwent ESD or LAP for small GISTs (between 2008 and 2019) were collected from Nanfang hospital, Guangzhou, China. We made telephone calls to collect information about their recurrence rate. Clinicopathological characteristics, recurrence rate and surgical outcome were collected and blindly measured for each procedure.

Results: Among the 398 patients, 234 (58.79%) received ESD treatment, and 164 (41.21%) received LAP treatment. The clinicopathological characteristics of the patients were well balanced. There was no significant difference between LAP and ESD groups according to gender, age, tumor size and location. There was also no significant difference in follow-up time (6.65±1.84 years in ESD vs. 6.19±1.53 years in LAP group, P=0.24). However, there was a significant difference between the two groups in operating time (61.42 ± 32.85min vs. 78.68 ± 39.76 min, P=0.03), estimated blood loss (6.58 ± 12.16 ml vs. 16.35 ± 17.06 ml, P=0.02) and hospital stay (5.07 ± 2.15 days vs. 9.84 ± 3.80 days, P< 0.001). The complication rate (defined as perforation or massive hemorrhage) showed no significant difference among ESD and LAP group (2.14% vs. 1.22%; P=0.85). The recurrence rate of ESD and LAP group was 2.56% and 1.22%; P=0.56. Meanwhile, Kaplan-Meier curves for disease-free survival test showed no significant difference between two groups (P=0.86).

Conclusion: Long-term follow-up showed that ESD can be a more preferable technique for resection of small gastric stromal tumors compared with LAP. However, long-term randomized controlled trials are further needed.

Disclosure: Nothing to disclose

1st validation set	AI	Group A Endoscopists				Group B Endoscopists			
		Endoscopist I	Endoscopist II	Endoscopist III	Group A Endoscopists	Endoscopist IV	Endoscopist V	Endoscopist VI	Group B Endoscopists
Accuracy (95%CI)	91.2% (85.9%-95.0%)	69.9% (65.6%-73.6%)	65.6% (61.2%-69.8%)	69.6% (65.6%-73.7%)	69.4% (67.0%-71.7%)	69.4% (65.3%-73.4%)	74.4% (70.6%-78.2%)	61.0% (57.5%-66.2%)	68.2% (65.9%-70.6%)
AUROC (95%CI)	0.93 (0.89-0.97)	0.72 (0.68-0.77)	0.68 (0.63 -0.73)	0.68 (0.63 -0.73)	0.69 (0.67-0.72)	0.68 (0.63 -0.73)	0.76 (0.71 -0.80)	0.63 (0.58 -0.69)	0.69 (0.66-0.72)
2nd validation set									
Accuracy (95%CI)	90.4% (85.9%-95.0%)	73.6% (69.7%-77.4%)	78.0% (74.4%-81.6%)	74.0% (70.1%-77.8%)	74.7% (72.5%-77.0%)	70.0% (65.9%-74.0%)	67.2% (63.1%-71.3%)	66.0% (61.9%-70.2%)	67.7% (65.3%-70.1%)
AUROC (95%CI)	0.90 (0.87-0.93)	0.75 (0.71 -0.80)	0.78 (0.73 -0.82)	0.73 (0.69 -0.78)	0.75 (0.72-0.77)	0.68 (0.63-0.73)	0.68 (0.64-0.73)	0.67 (0.62-0.71)	0.67 (0.65-0.70)

[P0141 Table. Performances of the AI image classifier vs junior endoscopists]

P0140 ENDOSCOPIC MUCOSAL RESECTION IN THE UPPER GASTROINTESTINAL TRACT: 22-YEAR EXPERIENCE IN A SINGLE CENTER

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Introduction: Endoscopic mucosal resection (EMR) has proven to be a safe and effective technique to locally remove lesions confined to the mucosa, with the advantage of providing a complete specimen for histological analysis.

Aims & Methods: We aim to report our 22-year outcome data to measure resection success and complication rates in EMR procedures performed in a single center.

We retrospectively reviewed 176 EMR procedures (157 patients) performed in our endoscopic department from March 1, 1997 to December 10, 2018. Procedures were performed using Olympus and Fujinon singlechannel or dual-channel endoscopes with a cap or band-ligation. Endoscopic ultra-sound was performed with linear scopes, radial scopes, or miniprobes in most patients. Recurrent cancer was re-treated (with additional EMR) when necessary.

Results: Of 157 patients, 93 (59.2%) were men. Mean patient age was 66.7 (SD, 11.0) years. Fourteen patients underwent more than 1 EMR procedure, for a total of 176 EMRs analyzed. Mean follow-up was 52.3 months. Gastric adenocarcinoma was diagnosed in 31.8% of patients (50/157), followed by esophageal squamous cell carcinoma in 17.8% (28/157), esophageal adenocarcinoma (Barrett esophagus) in 14.0% (22/157), and duodenal adenocarcinoma in 8.9% (14/157). Figure 1 shows a case of esophageal adenocarcinoma (Barrett esophagus) treated with EMR using band-ligation. The remaining 43 patients were diagnosed with benign lesions, including neuroendocrine tumors, hamartomas, granular cell tumors, and gastric heterotopia in the esophagus. En bloc resection was possible in 88.5% (139/157) of patients; the remaining 18 patients underwent piecemeal EMR. Eleven (7.0%) patients had recurrent lesions during follow-up: 3 esophageal adenocarcinomas (Barrett esophagus) and 8 gastric adenocarcinomas. Bleeding occurred in 21 (13.3%) patients, successfully controlled with hemoclips. Perforations occurred in 3 (1.9%) patients; 2 of them required surgery. No procedure-related death was observed during the follow-up period.

Conclusion: Our long-term outcome data demonstrate that EMR is a safe and effective therapy for high-grade dysplasia and early upper gastrointestinal neoplasia. However, careful follow-up is particularly necessary in cases of local recurrence, when additional EMR is required.

Disclosure: Nothing to disclose

P0141 TRAINING EFFECT OF ARTIFICIAL INTELLIGENCE IMAGE CLASSIFIER ON THE PERFORMANCES OF JUNIOR ENDOSCOPISTS IN PREDICTING HISTOLOGY OF GASTRIC LESIONS

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Introduction: Accurate endoscopic prediction of the histology of a sessile gastric lesion requires training and expertise, which may not be widely available. The use of artificial intelligence (AI) assisted image classifier has been shown to have high accuracy on endoscopic diagnosis. We evaluated the potential training effects of our recently developed AI assisted image classifier on histological prediction of gastric lesions by junior endoscopists.

Aims & Methods: An AI image classifier was built on a convolutional neural network with 5 convolutional layers and 3 fully connected layers Resnet backbone. It was first trained by 2,000 endoscopic images of both non-neoplastic and neoplastic gastric lesions, as verified by final histology of either multiple biopsies or total endoscopic resection. The endoscopic images were all obtained by high-definition endoscopy series (Olympus GIF-HQ290 and CV-290 video system). Gastric pathology was based on the WHO classification with neoplastic lesions defined as the presence of gastric dysplasia, adenoma or carcinoma in the most severe histology of the lesion. For each gastric lesion, around 10 regions of interest (ROI) were randomly selected in a pixel of at least 300 x 300 dpi. The independent validation set consisted of 1000 endoscopic NBI images from 100 gastric lesions. The validation set was also reviewed by six junior endoscopists who had performed more than 1,000 upper endoscopies and with training on NBI. The first part of validation set was first commented by all endoscopists and then the prediction of AI was disclosed to three of them (Group A endoscopists) while the remaining three (Group B endoscopists) were not provided this information. All the endoscopists then reviewed the 2nd part of the validation set.

Results: The overall accuracy of AI was 90.4% (95%CI: 88.6%-92.2%) with sensitivity 97.3% (95%CI: 95.8-98.7%), specificity 84.1% (95%CI: 80.9-87.2%), PPV 84.9% (95%CI: 81.8-87.8%), NPV 97.1% (95%CI: 95.6-98.7%) and area under the ROC (AUROC) 0.91 (95%CI: 0.89-0.93). AI was more confident in the prediction of non- neoplastic lesions than neoplastic lesions (84.5% vs 81.6%, p< 0.01). AI was superior to all junior endoscopists in term of accuacy and AUROC in both validation sets. (Table 1) The performance of the 3 endoscopists who had been revealed the AI finding of 1st validation set (Group A endoscopists), significantly improved on the 2nd validation set (69.3% to 74.7%; p =0.003). However, there was no significant improvement on performance for those who were not disclosed the AI findings (Group B endoscopists).

Conclusion:]The trained AI image classifier based on non-magnified NBI images can accurately predict the presence of neoplastic component of sessile gastric lesions. The use of AI image classifier can also hasten the learning curve of junior endoscopists on histologic prediction of gastric lesions.

Disclosure: Nothing to disclose

P0142 THE SEARCH, COAGULATION AND CLIPPING (SCC) METHOD TO PREVENT DELAYED BLEEDING AFTER GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION

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Introduction: Delayed bleeding is an important complication after gastric endoscopic submucosal dissection (ESD). Post-ESD coagulation (PEC) involving prophylactic cauterization of visible blood vessels at the ulcer floor is widely performed to prevent delayed bleeding after endoscopic therapy. The bleeding rate with this approach has been reported to be 3-5.5%.The search, coagulation, and clipping (SCC) method, which involves observing the ulcer floor, identifying blood vessels, and cauterizing and clipping respective blood vessels, appears to be a good approach to prevent bleeding after ESD. However, its safety and efficacy are unclear. We compared the SCC method with post-ESD coagulation (PEC) to clarify the safety and efficacy of the SCC method for preventing delayed bleeding after gastric ESD.
Aims & Methods: This retrospective study included 601consective patients (669 lesions) who underwent gastric ESD.97 patients treated with antithrombotic therapy (97/601 16.1%). Delayed bleeding was defined as clinical post-ESD bleeding with hematemesis, melena, or anemia progression that required endoscopic examination aside from the one scheduled during second-look endoscopy.Multivariate analysis was performed to identify the significant independent factors associated with delayed bleeding and we performed propensity score matching (PSM) to reduce the effect of procedure-selection bias of SCC method. Explanatory variables consisted of location, specimen size, antithrombotic agents, procedure time, and heparin placement.
Results: Of the 601 patients, 217 underwent PEC and 384 underwent SCC. According to the clinical pathway, the second-look endoscopy was performed for all cases. One patient presented bleeding in the stomach during second-look endoscopy.Delayed bleeding was significantly less common in the SCC group than in the PEC group (10/384 2.6% vs. 16/217 7.4%; P = 0.011) Among 97 patients treated with antithrombotic therapy, the delayed bleeding rate was lower in the SCC group than in the PEC group; however, the difference was not significant (4/61 6.6% vs. 5/36 13.9%;P = 0.285). Multivariate logistic regression analysis indicated that SCC methods and heparin placement were independent and significant factors affecting the delayed bleeding (SCC methods: P = 0.011;heparin placement ;P = 0.004). PSM was performed in 154 patients in the PEC group and SCC group. There was a significant difference in the incidence of bleeding in the PEC and SCC groups (2/154 1.3% vs. 12/154 7.8%;P = 0.011). No patient had perforation/bleeding associated with the SCC method.
Conclusion: Our findings suggest that the SCC method is a simple, safe, and effective approach for preventing delayed bleeding after gastric ESD.
References: Takizawa K, Oda I, Gotoda T, Yokoi C, Matsuda T, Saito Y, et al.Routine coagulation of visible vessels may prevent delayed bleeding after endoscopic submucosal dissection−an analysis of risk factors. Endoscopy. 2008;40:179-83. Azumi M, Takeuchi M, Koseki Y, Kumagai M, Kobayashi Y, Takatsuna M , et al.The search, coagulation, and clipping (SCC) method prevents delayed bleeding after gastric endoscopic submucosal dissection. Gastric Cancer. 2018 Sep 28.
Disclosure: Nothing to disclose

P0143 COMPARISON OF RISK SCORING SYSTEMS IN PATIENTS WITH ACUTE VARICEAL UPPER GASTROINTESTINAL BLEEDING

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Introduction: The aim of this study was to compare the performance of different scoring systems (Rockall scoring system, Glasgow-Blatchford score and AIMS65) in predicting outcomes in patients with acute variceal bleeding.
Aims & Methods: Data were collected prospectively over a 6-month period in the emergency department of a university hospital. Adult patients with upper GI bleeding from variceal sources were included. Clinical outcomes were re-bleeding, duration of hospitalization, need for blood transfusion and death. Patients who required blood transfusions or suffered composite clinical outcomes were considered high-risk patients. Rockall scoring system, Glasgow-Blatchford score (GBS) and AIMS65 scores were calculated for each patient. The sensitivity and specificity of the scoring systems were calculated. The areas under the receiver operating characteristic curve (AUC) of the scores were compared.
Results: There were 100 patients in the study; of whom 76 were men and 24 were women. The mean age was 59.39±7.7 years. Endoscopy was done for all of them and the three scores were calculated. Rebleeding was observed in 35 patients. A total of 83 patients received blood transfusions and 19 patients unfortunately died within 1-month follow up period. The three scores were compared to each other as regards our outcomes by using the ROC curves as shown in figures.
Conclusion: AIMS65 was superior for predicting the re-bleeding, GBS score was superior for predicting the need for blood transfusion and no significant difference was detected as regard duration of hospitalization and mortality among the three scores.
Disclosure: Nothing to disclose

P0144 FORWARD VIEWING LINEAR (FVL) VERSUS CURVED LINEAR-ARRAY (CLA) ECHOENDOSCOPES FOR SAMPLING AND DRAINAGE OF PANCREATIC AND UPPER GI SUB-EPITHELIAL LESIONS

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Introduction: Curved linear-array [CLA] echoendoscopes and forward-viewing linear [FVL] echoendoscopes are used in sampling and draining of upper GI subepithelial lesions and pancreatic lesions. FVL echoendoscopes were designed to overcome the limitations of the CLA echoendoscopes. Only a few prospective studies have compared the 2 types of endoscopes in terms of safety, efficacy, procedure duration and ease of the procedure.
Aims & Methods: We aimed to review the currently available data that compare the CLA echoendoscope with FVL echoendoscope in terms of technical success rates, diagnostic yield, diagnostic accuracy and procedure time.
Results: A total of 3 prospective studies met the inclusion criteria for this meta-analysis. A total of 260 procedures were analyzed, which included 130 FVL and 130 CLA. There were no significant differences in the technical success rates and diagnostic yield (OR, 0.77; 95% CI, 0.14-4.40, P= 0.77 and OR, 1.21, 95% CI, 0.6- 2.44, p= 0.6), Similarly, there was no significant difference in diagnostic accuracy (OR, 0.81; 95% CI, 0.38-1.71, p=0.57). However, procedure time was significantly less for the FVL group compared to CLA (MD, -2.88, 95% CI -4.53 - -1.22, p= 0.0006).
Conclusion: Both forward-viewing and curved linear-array echoendoscopes have similar technical success rate, diagnostic yield and accuracy in sampling and draining upper GI sub-epithelial and pancreatic lesions. FVL echoendoscopes provide the benefit of shorter procedural time.
Disclosure: Nothing to disclose

P0145 HYBRID ENDOSCOPIC SUBMUCOSAL DISSECTION VS CONVENTIONAL ENDOSCOPIC SUBMUCOSAL DISSECTION IN THE TREATMENT OF EARLY GASTRIC NEOPLASMS: A MULTI-CENTER RETROSPECTIVE ANALYSIS

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Introduction: Endoscopic submucosal dissection (ESD) is a technically difficult and time-consuming procedure. Hybrid ESD (H-ESD) combines circumferential incision with partial submucosal dissection and subsequently

snaring using a single device. H-ESD is potentially a simpler and shorter procedure. Here, we report the short-term outcomes of H-ESD for early gastric neoplasms.

Aims & Methods: The aim of this study is to compare short-term outcomes of H-ESD for early gastric neoplasms with those of conventional ESD (C-ESD). In this multi-center retrospective study, we reviewed the charts of patients with early gastric neoplasms within 20 mm in diameter treated with H-ESD or C-ESD between January 2017 and October 2018 at three hospitals. Propensity score matching was performed to reduce biases. Short-term outcomes including the procedure time, the en-bloc resection rate, the complete resection rate, and the rate of adverse events (perforation/delayed bleeding) were evaluated.

Results: Among 215 patients, 29 were in the H-ESD group and 186 were in the C-ESD group. Twenty-nine pairs were created by propensity score matching. In the H-ESD group, 82.8% of lesions met the original absolute indication (limited to 20 mm in diameter dominated by differentiated adenocarcinoma without ulcer) for endoscopic resection. As a result, H-ESD required a significantly shorter median procedure time (H-ESD: 20 [interquartile range, 12-27] min vs C-ESD: 40 [30-50] min; $P < 0.001$). Other outcomes were similar among two groups and no significant differences were observed (En-bloc resection rate; 100% in both groups, Complete resection rate; 100% vs 93.1%, P = 0.49, Adverse event rate; 0% vs 3.4%, P = 1).

Conclusion: H-ESD achieved significantly shorter procedure time with high curability without increase in adverse events. Therefore, H-ESD should be selected for gastric neoplasms within original absolute indication.

Disclosure: Nothing to disclose

P0146 USEFULNESS OF 3-DIMENSIONAL FLEXIBLE ENDOSCOPY IN THE DIAGNOSIS OF GASTRIC EPITHELIAL NEOPLASIA

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Introduction: 3-dimensional (3D) visualization offers better depth recognition than 2-dimensional (2D) visualization. There are some reports that 3D rigid endoscopy in surgical fields can shorten the procedure time and reduce the complications. In contrast, the prototype of 3D flexible endoscopy has already been developed, and we have reported that it has reduced technical complications during endoscopic submucosal dissection (ESD), especially in trainees. 3D visualization might be effective in the diagnosis of cancer extent because it facilitates more clearly the recognition of ruggedness and shape of lesions than 2D.

Aims & Methods: To explore the feasibility of 3D visualization in the endoscopic diagnosis, we conducted a study to compare 2D and 3D endoscopy in the diagnosis of early gastric cancers (EGCs) and gastric adenomas. Study participants (3 experts and 6 trainees) who do not know clinical information of target lesions performed pre-ESD endoscopic assessment of EGCs and adenomas under 2D and 3D observation. In the 3D endoscopy system, 2D and 3D visualization under white light imaging or narrow band imaging are quickly changed by a food pedal. In the next, they made electrocautery markings on a half of demarcation line of EGCs and adenomas under 2D images at first, and on other half under 3D.

The markings under 2D and 3D were performed in half of the anterior and posterior wall side respectively, which side they would be on was randomly assigned. Thereafter, target lesions were resected by ESD. After procedure, participants answered visual analog scaled (VAS; 0-10, worst to best) questionnaire on ease of recognition of lesion morphology / lesion extent / total endoscopic cognition and technical ease of electrocautery marking under 2D and 3D visualization.

The main endpoint was accuracy of ESD marking, which derived from the pathological distance between the demarcation line and the markings in the excised specimens. This study was conducted after an approval of the institutional review board of our hospital.

Results: Enrolled 24 EGCs and 2 adenomas (median tumor size, 13 mm, range 3 - 32 mm) were 4 of type 0- IIa, 3 of type 0-IIb and 19 of type 0-IIc, and the types of histology of EGCs were 20 well differentiated adenocarcinomas, 3 signet-ring cell carcinomas and a poor differentiated adenocarcinoma. The distance between the demarcation line and electrocautery marking under 3D visualization was significantly shorter than under 2D (1.04 ± 0.79 mm vs 1.93 ± 1.92 mm, respectively, P = 0.040). In VAS, the

recognition of lesion morphology under 3D was easier than 2D (8.54 ± 1.10 vs 4.96 ± 1.56, respectively, P < 0.001), and that of lesion extent under 3D was easier than 2D (8.00 ± 1.20 vs 5.12 ± 1.66, respectively, P < 0.001). And ease of total endoscopic cognition under 3D (8.15 ± 1.26) was significantly higher than 2D (5.35 ± 1.72) (P < 0.001). Additionally, technical ease of electrocautery marking under 3D was higher than 2D (7.35 ± 1.32 vs 5.27 ± 1.40, respectively, P < 0.001).

Conclusion: 3D endoscopy was more accurate than 2D in the endoscopic diagnosis of extent of EGCs and adenomas. Furthermore, 3D visualization enhanced the quality of recognition of ruggedness and extent of lesions, and facilitated technically electrocautery marking before ESD. In flexible endoscopy, not only the efficiency and accuracy of procedure but also the quality of diagnosis is very important. Combined with previous results on 3D-enhanced improvement of ESD performance, 3D endoscopy is the key technological innovation in diagnosis and treatment of GI.

Disclosure: Nothing to disclose

P0147 COMPLICATIONS OF THE SHARP-POINTED FOREIGN BODY INGESTION: A PREDICTIVE MODEL

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Introduction: Foreign body ingestion is a common emergency with little complication, but with the penetrating nature, sharp-pointed objects have a high risk in making esophageal perforation and subsequent death. Emergency endoscopy is the recommended treatment and sharp-pointed foreign body retrieval is a challenge for even highly experienced gastroenterologist. To date, there is no clear risk algorithm available for sharp-pointed foreign body ingestion. It is important to identify the risk factors in order to mitigate potential morbidity and improve prognosis.

Aims & Methods: In this single-center, retrospective study, 190 consecutive patients complained of sharp-pointed foreign body ingestion, and referred to gastroenterology department of West China Hospital between August 2018 and February 2019 were included. Patients data, include age, gender, foreign body type, ingestion duration (from ingestion to taking endoscopy), computed tomography (CT) features and gastroscopy findings were recorded and analyzed with univariable analysis. Logistic regression and conditional inference tree were applied to develop a predictive model. Complications of sharp-pointed foreign body ingestion were classed into four ordered categories, including none or edema, erosion, ulcer and perforation. We aimed to recognize risk factors for the complications of sharp-pointed foreign body ingestion, and help clinicians to decide the role and timing of endoscopic intervention.

Results: Of the 190 patients, 182 had taken gastroscopy (96%). The width of sharp-pointed foreign body was identified as an independent risk factor for complications (OR=3.10, 95%CI: 2.33-5.55, P< 0.001). Conditional inference tree analysis was used to construct a risk stratification algorithm for complications. The sharp-pointed foreign body width of 1.9cm was the key discriminator (P< 0.001), and the subsequent split was ingestion duration of 24 hours (P=0.003). Therefore, patients could be stratified into four risk groups: low risk (width≦1.9cm), moderate risk I (2.5cm≧width>1.9cm and duration≦24hours), moderate risk II (width>2.5cm, duration≦24hours), and high risk (width>1.9cm, duration>24hours). To test the accuracy of conditional inference tree in predicting complications, receiver operating characteristic curve was drawn, and the area under the curve was 0.703 (95%CI: 0.543-0.862, P=0.009). In high risk group, the specificity in predicting perforation was 83.2% and sensitivity was 60%. We also examined the accuracy of CT in recognizing perforation, the specificity was 95.2%, and the sensitivity was 20%.

Conclusion: The width of sharp-pointed foreign body is the main risk factor for complications. Our predictive model including width and ingestion duration could help to differentiate the patient with a high risk in perforation.

Disclosure: Nothing to disclose

P0148 CLINICAL SIGNIFICANCE OF URGENT ENDOSCOPY FOR GASTRODUODENAL PERFORATION

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Introduction: Gastroduodenal perforation, a condition representative of acute abdomen, is potentially life-threatening if left unattended, and thus early diagnosis and treatment are necessary. The standard treatment for gastroduodenal perforation is surgery. In some cases, however, operative findings reveal spontaneous closure where the perforation site is already sealed, indicating that surgery was not necessary. An accurate diagnosis by urgent endoscopy is therefore required before choosing between surgical and conservative management.

There is presently no consensus regarding the role of urgent endoscopic examination for gastroduodenal perforation in Japan.

Aims & Methods: The aim of the study was to evaluate the clinical significance of urgent endoscopy for gastroduodenal perforation. We retrospectively investigated 156 cases of gastroduodenal perforation in 154 patients (111 men, 45 women; mean age 59±19 years) at Hiroshima City Asa Citizens Hospital between December 2005 and December 2018.

We performed urgent endoscopy for the sole purpose of identifying the location of perforation and confirming the size of the perforation in order to shorten the examination time. All procedures were performed using CO_2 insufflation with a surgeon standing by in case of complications.

Results: The primary location of gastroduodenal perforation was the stomach in 42 cases and the duodenum in 114 cases. For 40 of the 42 cases of gastric perforation (95.2%) and 100 of the 114 cases of duodenal perforation (87.7%), urgent endoscopy was performed on admission to diagnose the primary disease and confirm the exact perforation site. For gastric perforation, the endoscopic diagnosis was gastric ulcer in 32 cases, gastric carcinoma in 5, malignant lymphoma (ML) in 1, and perforation due to fish bone ingestion in 1.

Regarding the clinical course of the 42 gastric perforation cases, 31 (73.8%) underwent surgery (25 gastric ulcers, 5 gastric cancer, and 1 ML) and 11 (26.2%) were managed conservatively (8 gastric ulcers, 1 terminal case of gastric cancer, 1 ML, and 1 perforation due to fish bone ingestion).

Of these 11 cases managed conservatively, 9 cases were successful while 2 cases required delayed emergency surgery because of progression of peritonitis. It is necessary to rule out the presence of malignant tumor for cases of gastric perforation. For duodenal perforation, the endoscopic diagnosis was duodenal ulcer in all 114 cases. For the clinical course of these 114 cases, 62 cases (54.4%) underwent surgery while 52 cases (45.6%) were managed conservatively.

Of the 52 cases managed conservatively, 48 cases (92.3%) were successful while 3 cases (7.7%) required delayed emergency surgery because of progression of peritonitis. There was 1 fatal case where the patient had presented in shock on admission.

We compared clinical factors between the cases of successful conservative management and those that required surgery plus the fatal case. Multivariate analysis revealed that localized abdominal pain (with no peritoneal signs) (odds ratio [OR] 0.25; 95% confidence interval [CI] 0.08-0.75; p<0.01) and perforation diameter ≤ 5 mm (OR 0.13; 95% CI 0.04-0.36; p<0.01) were significant independent clinical factors associated with successful conservative management of duodenal ulcer perforation. No complications of urgent endoscopy were observed.

Conclusion: Urgent endoscopy in gastroduodenal perforation enabled diagnosis of the primary disease and determination of the perforation site, and was considered useful in deciding the management strategy.

References: 1. Tanaka R, Kosugi S, Sakamoto K, et al. Treatment for perforated gastric ulcer: a multi-institutional retrospective review. J Gastrointest Surg. 2013;17:2074-81 2. Satoh K, Yoshino J, Akamatsu T, et al. Evidence-based clinical practice guidelines for peptic ulcer disease 2015. J Gastroenterol. 2016;51:177-94.
Disclosure: Nothing to disclose

P0149 LONG-TERM OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR UNDIFFERENTIATED EARLY GASTRIC CANCER, BEYOND EXPANDED CRITERIA

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Introduction: Expanded indication of endoscopic submucosal dissection (ESD) for intramucosal undifferentiated early gastric cancer (EGC) up to 2 cm without lymphovascular invasion have been accepted. However, preoperative measurement of the tumor was completely not as same as postoperative one and if the postoperative tumor size would be a little more than 2 cm with R0 resection, additional surgery recommaded absolutely. Without Intramucosal undifferentiated early gastric cancer (EGC) up to 2cm in size without ulceration has been treated by endoscopic submucosal dissection (ESD) because the incidence of lymph node metastasisis negligible.

Aims: The aim of this retrospective study was to analyze the long-term outcomes of ESD carried out to treat undifferentiated EGC in two groups (group A: up to 2 cm, group B: 2-3 cm)

Patients and methods: Between January 2001 and March 2015, 104 patients with undifferentiated early gastric cancer (EGC) including poorly differentiated adenocarcinoma (PD, n=66) or signet ring cell carcinoma (SG, n=38) on preoperative biopsy underwent ESD (group A: 71cases, group B: 33cases), Total ESD speciemens were evaluated en bloc resection, R0 resection, and curative resection (CR) and to evaluate long term outcome, annual endoscopic surveillance with biopsy and CT scan were done.

Long-term outcomes analyzed in the 79 patients with undifferentiated EGC who had undergone ESD between 1999 and 2008.

Short-term outcomes were evaluated in the remaining 97 patients with undifferentiated EGC.

Results: M/F was 40/31 and 17/16. Mean follow up period in group A and B were 61.10 ± 38.12, 60.79 ±47.75. Mean age in group A and B were 52.90 ±13.62, 57.00 ±12.25.

En bloc in group A and B were achieved in 92.9%, 90.9 % of patients, respectively (NS).

R0 resection in were achieved in 87.3 %, 51.5 % of patients, respectively (p< 0.05).

Curative resection was 83.0 % in group A and group B was not include this definition.

Postoperative bleeding, perforation during the procedure, and delayed perforation were no significantly different in both groups, respectively.

Recurrence in group A and B were 5.6 %(n=4), 18.1 % (n=6), retrospectively (p< 0.01). All cases with lateral margin positive required additional ESD (n=2), desctructive therapy (n=3), or surgery (n=4) and no recurrence happened. No patient died of gastric cancer.

Conclusion: In group B, R0 resection rate was lower than group A but R0 resection in both group were not different recurrence rate with long term follow up. Carefully, undiffrented EGC with 2 to 3 cm in a size recommended ESD.

Disclosure: Nothing to disclose

P0150 COMPARATIVE STUDY OF ESD AND SURGICAL RESECTION FOR GASTRIC SETS ORIGINATED FROM MUSCULARISPROPRIA

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Introduction: Endoscopic resection for gastric subepithelialtumors(SETs) originated from the muscularispropria (GSET-PM) has offered less invasive alternatives to surgical resection.

Aims & Methods: The aims of this study were to compare endoscopic subtumoraldissection(ESD) with surgical resection for the removal of GSET-PM. This study involved 17 patients with GSET-PM removed by ESD

and 76 patients who underwent curative surgical resection. ESD was attempted in GSET-PM with well marginated tumors which was below 5cm and showed an endoluminal growth pattern according to endoscopic ultrasound(EUS) finding.

Results: ESD group were more likely to have upper portion(10/17, 58.8%) and surgery group were more likely to have mid portion(41/76, 53.8%) (p=0.039). ESD group were smaller median tumor size (25.6 mm vs 35.9 mm, p=0.037) and higher endoluminal ratio (58.5±9.1 % vs 45.8±15.4 %, p=0.002). ESD group were mostly to have Yamada type III (10/17, 58.8%) and surgery group were mostly Yamada type I (52/76, 68.4%)(p< 0.001). Complete resection by ESD was lower than by surgical resection (82.4% vs 100%, p< 0.001). In ESD group, 3 performed surgical resection after ESD (1 incompletely resection and 2 uncontrolled bleeding) and 1 showed perforation was completely resected with endoscopic closure. In surgery group, complications occurred in 6 patients (1 leakage, 1 stricture, 1 hernia and bowel obstruction, 1 wound infection and 2 worsened general condition after surgery). Although surgery group were lower in complication rate than ESD group (p=0.006), severity of complications were higher in the surgery group and there were no mortalities in the ESD group compared with 2 in the surgery group. There was no statistical difference of recurrence and the follow-up period between two group.

Conclusion: ESD can be one of good options for the resection of endoluminal GSET-PM and could be replace treatment by surgical resection in Yamada type III with a high endoluminal ratio.

Disclosure: Nothing to disclose

P0151 EFFICACY OF POLYGLYCOLIC ACID SHEETING WITH FIBRIN GLUE FOR GASTROINTESTINAL FISTULAS: A MULTICENTER RETROSPECTIVE STUDY OF THE POLYGLYCOLIC ACID (PGA) STUDY GROUP

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Introduction: Anastomotic leakage, which is one of the complications of surgical operations, sometimes causes a refractory fistula despite conservative therapy, including local drainage and decompression of the digestive tract. If a refractory fistula cannot be healed, a highly invasive reoperation may be performed in the end. Fistulas can occur after not only anastomotic leakage but also other situations, including cancer chemoradiation therapies (CRT). Polyglycolic acid (PGA) sheets (Neoveil; Gunze, Kyoto, Japan) with fibrin glue (Beriplast P Combi-Set; CSL Behring Pharma, Tokyo, Japan) have been reported to be useful for preventing perforations and delayed bleeding after endoscopic treatment [1,2]. Although it can be useful for closure of fistulas related to gastrointestinal cancer operation or chemoradiation therapies [3], large-scale multicenter treatment outcomes have not been reported.

Aims & Methods: Patients with GI fistulas endoscopically closed using PGA sheeting with fibrin glue between April 2013 and March 2018 in 18 institutions in the PGA study group, which is the affiliated study group of the Japanese Gastroenterological Endoscopy Society, were identifiedand retro-

spectively analyzed. Fistula is defined as the communication between the digestive tract and other areas (thoracic cavity, mediastinum, bronchus, abdominal cavity, etc.). Fistulas were filled with one or several pieces of PGA sheets followed by spraying fibrin glue using an endoscopic catheter. The procedure was repeated several times at 1- or 4-week intervals before fistula closure, and accompanied by nasal or percutaneous drainages, and endoscopic clipping as appropriate for each case.

Results: Fistula: Forty-five cases (hypopharyngeal/esophageal cancer 21, gastric cancer 3, pancreatic cancer 1, colon cancer 3, prostate cancer 1, and communicating organs: chest cavity 5, mediastinum 4, bronchus 10, abdominal cavity 6, and others 20) were extracted. The median fistula diameter was 5 mm (range 1-20 mm). Thirty-six cases were related with operations; and 9, with other conditions, including CRT. PGA sheets were filled at a median of 2 times (range 1-10). CRT was performed before surgery in 13 cases (29%). Infections caused by fistulas were suspected in 12 cases (22%) because pus was observed in the fistulas. Percutaneous drainage was performed in 26 cases (58%); nasal drainage, in 14 (31%); and endoscopic clipping, in 16 (36%). Complete closure was attained in 25 cases (56%). The median period until resuming diet after starting sheeting was 16 days (range 1-222 days) in the closed cases. No statistically significant differences in total protein level, fistula size, performance status, accompanying drainage, and the period between fistula occurrence and start of sheeting and fistula closure. Eleven deaths occurred, which were not related to PGA sheeting.

Conclusion: Endoscopic PGA sheeting can be expected to achieve conservative closure and inhibit highly invasive reoperation for more than half of fistula cases.

References: 1] Takimoto K, Toyonaga T, Matsuyama K. Endoscopic tissue shielding to prevent delayed perforation associated with endoscopic submucosal dissection for duodenal neoplasms. Endoscopy 2012; 44 (Suppl. 02): E414 – E415 2] Tsuji Y, Fujishiro M, Kodashima S, et al. Polyglycolic acid sheets and fibrin glue decrease the risk of bleeding after endoscopic submucosal dissection of gastric neoplasms (with video). Gastrointest Endosc. 2015;81:906-12 3] Matsuura N, Hanaoka N, Ishihara R, et al. Polyglycolic acid sheets for closure of refractory esophago-pulmonary fistula after esophagectomy Endoscopy 2016; 48: E78-E79

Disclosure: Nothing to disclose

P0152 ENDOSCOPIC SUBMUCOSAL DISSECTION USING AN DETACHABLE ROBOTIC ASSITIVE DEVICE IN A LIVE PORCINE MODEL

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Introduction: Endoscopic submucosal dissection(ESD) is a standard treatment treatment of intramucosal gastric neoplasms. However, still only highly skilled operators can perform ESD safe. One of those reason is that there is no proper counter-traction during procedure. Recently, our research team devised revolute joint-based auxiliary transluminal endoscopic robot (REXTER). In this study, we evaluated the clinical feasibility of our REXTER in a live porcine model and identify the safety and efficacy of unskilled operator performing ESD.

Aims & Methods: We perform ESD was performed to imaginary gastric lesions in nonsurvival porcine models using our novel robotic asstivie device. EAR can be mounted on GIF-Q260 endoscope and can be passed through overtube to porcine stomach, making it possible for clinical use. We devided two groups, conducted by experts and novice. We measured the time required to complete the ESD and complications involving perforation and significant bleeding in each group.

Results: Total 16 cases of ESD were done. 6 cases were conducted by experienced endoscopist and 10 cases by unskilled endoscopist. Procedure time between operator groups was similar. There was no significant time difference between operator group. There was no incidence of perforation and significant bleeding.

Conclusion: Our endosopic assitive robot showed feasibility and its safety. Our robotic device could be helpful, especially in unskilled endoscopicst.

Disclosure: Nothing to disclose

P0153 CLINICAL OUTCOMES OF ENDOSCOPIC INCISIONAL THERAPY FOR TREATING BENIGN ESOPHAGEAL STRICTURE: COMPARISON WITH BALLOON DILATION AND STENT PLACEMENT

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Introduction: Benign esophageal stricture has been treated with endoscopic methods including balloon dilation, stent placement. Despite these treatment modalities, recurrent refractory esophageal stricture impairs patient's quality of life. Recently endoscopic incisional therapy was reported as an another treatment option for benign esophageal stricture.
Aims & Methods: We investigated the efficacy and safety of endoscopic incisional therapy (EIT) compared to balloon dilation (BD) and stent placement in treating benign esophageal stricture. Subjects who underwent balloon dilation, stent placement and EIT as a first-line treatment for benign esophageal stricture between January 2009 and December 2017 were eligible. Patients treated with different treatment modality from initial event for recurrent stricture were excluded. In addition, combination treatment more than two modalities concurrently were also excluded. All the patients were administered the same treatment modality as first when the stricture recurred. The medical records were retrospectively reviewed and clinical characteristics were investigated. Stricture was defined as an inability to pass a conventional endoscope.
Results: Of total 49 patients, 31 were in BD group, 7 were in stent group and 11 were in EIT group. There was no significant difference among three groups in median age and procedure time. Most common indications for BD group and EIT group was esophagojejunostomy anastomotic stricture, 10 patients (32.3%) and 4 patients (36.4%), respectively. In stent group, radiation therapy induced stricture of 4 patients (57.1%) was most common indication of procedure. Among three groups, there were no significant difference in re-stricture rate (p=0.697, 41.9% in BD group, 28.6% in stent group and 27.3% in EIT group) and interval to the second stricture (p=0.239, median 46 days in BD group, 215 days in stent group and 46 days in EIT group). Median follow up period was 699 days in BD group, 540 days in stent group and 395 days in EIT group. Subgroup analysis of esophagojejunostomy anastomotic stricture group showed lower recurrence rate in EIT group compared to BD group (0% vs. 30%, p=0.505). There was no procedure related complication reported including bleeding, perforation and pneumothorax in three groups.

	Balloon dilatation group (n=31)	Stent group (n=7)	EIT group (n=11)	P value
Age (medina, IQR)	62 (51-69)	61 (55-66)	67 (56-73)	0.680
Sex (male/female)	23/8	6/1	6/5	0.316
Procedure time, minutes	8 (7-12)	9 (8-15)	6 (2-14)	0.243
Restricture rate	13 (41.9%)	2 (28.6%)	3 (27.3%)	0.697
Interval to the 2nd stricture, days	46 (13-90)	215 (133-297)	46 (14-93)	0.239
Recurrence number (median, IQR)	0 (0-2)	0 (0-1)	0 (0-1)	0.589
Follow up period, days	699 (219-1752)	540 (305-774)	395 (86-552)	0.123
RT-induced stricture	2 (6.5%)	4 (57.1%)	2 (18.2%)	
Short segment stricture	25 (80.6%)	2 (28.6%)	8 (72.7%)	0.024

[Table 1. Baseline patient characteristics and treatment outcome]

Conclusion: EIT is a feasible, safe and effective treatment modality with acceptable long term patency for benign esophageal strictures especially in short segment stricture such as anastomotic stricture and expected to be an alternative treatment to balloon dilation or stent placement.
Disclosure: Nothing to disclose

P0154 WHITE LIGHT IMAGING MORPHOLOGICAL FEATURES AND MAGNIFYING ENDOSCOPY WITH NARROW BAND IMAGING FOR THE OPTICAL DIAGNOSIS OF SUPERFICIAL NONAMPULLARY DUODENAL EPITHELIAL TUMORS

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Introduction: Optical diagnosis of superficial nonampullary duodenal epithelial tumors (SNADETs) is important in guiding the treatment strategy.
Aims & Methods: The aim of this study was to compare the treatment outcomes based on optical diagnosis using white light imaging (WLI) morphological features and magnifying endoscopy with narrow band imaging (MNBI).We retrospectively analyzed endoscopic and pathological data on SNADETs treated at a tertiary cancer center between Feb. 2010 to Jan. 2019. We made a decision tree model for WLI and MNBI diagnosis. Optical diagnosis of high-grade dysplasia (HGD) or carcinoma with WLI were defined based on WLI scoring system (WLS) [1] as total score of 3 points or higher; 1 point for lesion diameter >10mm, heterogeneous/no lobulation, mixed type morphology/presence of depression, isochromatic, respectively, and 2 points for red color. Diagnosis of HGD/carcinoma using MNBI was based on MNBI pattern diagnosis [2]: >2 patterns of MNBI within a lesion or presence of the pattern of obscure surface structure with abnormal vessels. Ideal treatments were cold snare polypectomy (CSP) for low-grade dysplasia (LGD) < 10mm, endoscopic mucosal resection (EMR), endoscopic submucosal dissection (ESD) or surgery for lesions >10mm or HGD/carcinoma. We compared the ideal treatment based on optical diagnosis to actual treatment results.
Results: A total of 197 patients with 218 lesions who were pre-operatively diagnosed as SNADETs were included for analysis. Final histology included non-tumor 12(5%), LGD 53 (24%), HGD 20(9%), intramucosal carcinoma 124 (57%) and submucosal invasive carcinoma 9 (4%). Proportions of ideal treatment for LGD < 10mm based on WLS, MNBI and WLS with MNBI were 89%, 79% and 97%. For HGD/carcinoma, they were 89%, 90% and 96%. Diagnostic accuracy of WLS and MNBI was 84% and 80%, respectively. When the diagnosis was similar between WLS and MNBI, the accuracy was 94%.
Conclusion: Both WLI and MNBI were useful to select appropriate treatment for SNADETs. A high diagnostic accuracy was achieved when both WLI and MNBI showed similar results.
References: [1] Kakushima N, et al. A simple endoscopic score system to differentiate between duodenal adenoma and carcinoma. Endosc Int Open. 2017;5:E763-E768. [2] Kakushima N, et al. Magnified endoscopy with narrow-band imaging for the differential diagnosis of superficial non-ampullary duodenal epithelial tumors. Scand J Gastroenterol 2019;54:128-134.
Disclosure: Nothing to disclose

P0155 CIRCULARITY IN ENDOSCOPIC ULTRASONOGRAPHY IMAGING AS A USEFUL DIAGNOSTIC INDICATOR OF GASTROINTESTINAL STROMAL TUMOURS: A RETROSPECTIVE ANALYSIS IN 51 GASTRIC CASES

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Introduction: Gastrointestinal stromal tumour (GIST) should be accurately diagnosed to determine the treatment strategy for submucosal tumours (SMTs). Although endoscopic ultrasonography (EUS)-guided fine-needle aspiration is a standard option to diagnose SMTs, it is more or less invasive and less satisfactory due to technical difficulties or possible insufficient volume of specimen. Therefore, a non-interventional diagnostic method using imaging modality is still expected.
Aims & Methods: We hypothesise that GISTs can be distinguished from other SMTs based on the shape of the tumours in EUS images because GISTs generally appear round, whereas leiomyoma, a counterpart of differential diagnosis in gastric SMTs, appear craggy. Therefore, this study aims to investigate the potential diagnostic ability of EUS findings by using

tumour circularity. A total of 51 gastric cases with SMTs 20-50 mm in diameter, diagnosed as possible GISTs by EUS and surgically removed thereafter, were retrospectively collected at two institutions. In each lesion, one EUS still image showing the maximal area was selected, and the circularity of each lesion, a surrogate indicator of roundness calculated as four pi times the area divided by the perimeter squared (0-1, 1 = a true circle), was assessed using ImageJ (ver. 1.50e; National Institutes of Health, USA) by tracing the rim of the lesion. The mean circularity between GISTs and other SMTs were compared, and its diagnostic utility, by investigating a receiver operating characteristics (ROC) curve, as well as diagnostic accuracy were evaluated. In addition, circularity between GISTs and leiomyoma was compared as a sub-analysis.

Results: In 51 SMT cases, 31 GISTs were included. The mean circularity in GISTs and others were 0.85 ± 0.07 and 0.69 ± 0.11, respectively, with statistical significance (p < 0.01). In the ROC curve, a cut-off value of 0.83 with 0.91 in the area under the curve showed maximum diagnostic accuracy (84.3%), with sensitivity and specificity of 80.6% and 90.0%, respectively. The mean circularity in eight cases of leiomyomas was significantly lower than the mean circularity in GISTs (0.63, p < 0.01).

Conclusion: These retrospective data suggest that circularity calculated using EUS imaging can be used as a non-invasive diagnostic discriminator in gastric GISTs with high accuracy rate, particularly from leiomyomas. However, further prospective analysis is expected.

Disclosure: Nothing to disclose

P0156 ROLE OF ENDOSCOPY IN SUSPICION OF ATROPHIC GASTRITIS WITH AND WITHOUT INTESTINAL METAPLASIA IN COMPARISON TO HISTOPATHOLOGY

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Introduction: Atrophic gastritis(AG) and intestinal metaplasia(IM) are established premalignant gastric lesions. Many studies using conventional white-light endoscopy(CWLE) documented a poor correlation between esophagogastroduodenoscopy(EGD) and histopathological(HP) findings for detection of precancerous gastric lesions. However, in daily practice, CWLE is still used.

Aims & Methods: Bridging the gap between endoscopy and HP in detection of chronic gastritis, AG and IM. This was a prospective single-center study involved 150 patients with endoscopic criteria of chronic gastritis, AG or IM selected from 300 patients with upper gastrointestinal symptoms who were referred for Upper GI endoscopy and met the criteria of chronic gastritis, AG or IM. They were classified into 3 groups according to HP results of gastric biopsies from targeted lesions (GI chronic non-atrophic gastritis n=86, GII AG n=42 and GIII IM n=26). Routine HP using updated Sydney system and *H.pylori* detection in gastric biopsies using Giemsa stain were done. We correlated the endoscopic criteria of chronic gastritis, AG and IM with the HP results.

Results: The sample included (73males & 75 females) with ages ranged17-75 years and mean± SD was41.96 ± 15.95. GI, GII &GIII were [42 patients (28%),82 patients (54.7%) and 26 patients (17.3%)], respectively. Smoking, DM, chronic NSIDs use, current *H.pylori* infection, and family history of *H. pylori* were highly statistically significant among the 3 groups with higher incidence of AG and IM in patients who had positive family history of *H.pylori* infection (p value < 0.001). However, age and previous *H.pylori* therapy were not significant among the groups. We correlated the standardized endoscopic findings in each group, diffuse mottling was more common in GI (74.3%, P< 0.001), visible submucosal vessels, atrophic mucosa and atrophic gastric folds predominated in GII (75.6,82.3&73.1%(P 0.005,0.4 &< 0.01)), respectively. Whitish raised lesions were more specific in GIII (85.7%)with highly statistically significant difference between the groups(P< 0.001). *H.pylori* was the most etiologic agent in all groups 132/150 patients (90%) (p-0.001). EGD could truly diagnose 36 out of 42 patients diagnosed by HP in GI,71/82 in GII and 14/26 in GIII, the sensitivity

and specificity of endoscopic suspicion of chronic gastritis was (86&88% in GI), (87&85% in GII) and (54% &100% in GII) with statistically significant difference between the 3 groups(p-0.001). The logistic regression model for risk factors was statistically significant, χ2= 25.74 and 49.32 respectively, p < 0.001. The model explained 61.0 and 70% (Nagelkerke R2) of the variance in AG or IM and correctly classified 86.3, 85.3% of cases respectively. Smokers were 36.72 and 23.73 times more likely to exhibit AG or IM. Current *H. Pylori* infection was associated with an increased likelihood of exhibiting AG.

Conclusion: CWLE has a high sensitivity and specificity for suspicion of chronic gastritis and AG, but low sensitivity and very high specificity for IM and can be used as a bridge or an alternative to HP especially with high-definition endoscopy. Targeted biopsies with image enhanced endoscopic techniques may be more practical than updated Sydney protocol.

Disclosure: Nothing to disclose

P0157 THE APPLICATION OF ARTIFICIAL INTELLIGENCE USING A CONVOLUTIONAL NEURAL NETWORK FOR DETECTING HEAD AND NECK CANCER IN ENDOSCOPIC IMAGES

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Introduction: Head and neck squamous cell carcinoma is typically diagnosed at an advanced stage, and the prognosis for patients is poor. Recently, image-enhanced endoscopy (IEE) has become popular as a new diagnostic modality for the early detection of superficial head and neck cancer. However, it is difficult for inexperienced endoscopists to detect superficial head and neck cancer because the observation of the laryngopharyngeal sites is not a standard procedure with esophagogastroduodenoscopy. Image recognition using artificial intelligence (AI) with deep learning through convolutional neural networks (CNNs) has dramatically improved and been applied increasingly frequently to medical fields for diagnostic imaging.

Aims & Methods: The aim of this study is to investigate the utility of AI for diagnosing head and neck cancers. A CNN-based diagnostic system was constructed based on the Single Shot MultiBox Detector architecture and trained using 5163 endoscopic images of laryngopharyngeal cancer. To evaluate the diagnostic accuracy, an independent test set of 1775 laryngopharyngeal images collected from 68 consecutive patients with 75 laryngopharyngeal cancer lesions was applied to the constructed CNN.

Results: The CNN correctly diagnosed 72 of 75 laryngopharyngeal cancer lesions with an overall accuracy of 91.4%, and 4 of 6 non-cancerous lesions were diagnosed as benign. The two missed benign lesions were papilloma and lymphoid follicles. The three missed malignant lesions were superficial hypopharyngeal cancer (n=2) and laryngeal cancer (n=1). The sensitivity, specificity, positive predictive value, and negative predictive value in terms of the lesions were 96.0%, 66.7%, 97.3%, and 57.1%, respectively, and the accuracy, sensitivity, and specificity in terms of the endoscopic images were 83.0%, 83.3% and 79.2%, respectively. The CNN required 47 seconds to analyze 1775 test images.

Conclusion: This CNN system for detecting laryngopharyngeal cancer was able to process numerous stored endoscopic images in a very short time with clinically relevant diagnostic ability. It may be applicable to daily clinical practice, where it can help reduce the burden on endoscopists.

Disclosure: Nothing to disclose

P0158 ENDOSCOPIC GRADING OF GASTRIC INTESTINAL METAPLASIA (EGGIM) USING NARROW BAND IMAGING ENDOSCOPY WITH NON-MAGNIFIED AND MAGNIFIED OBSERVATION

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Introduction: Gastric intestinal metaplasia (GIM) is known to associated with a risk of gastric cancer. Recent studies suggest the endoscopic findings with narrow band imaging (NBI) (light-blue crest (LBC), white opaque substance (WOS)) correlate to histological GIM, and are useful markers for a cancer risk according to the classification of endoscopic grading of GIM (EGGIM). However LBC, WOS are originally reported under magnified endoscopic observation, it is unknown the differece in classifying EGGIM between non-magnified NBI (non-M-NBI) and magnified NBI (M-NBI) observation.

Aims & Methods: To investigate the difference in classifying EGGIM between non-M-NBI and M-NBI observation, 100 consecutive patients who underwent NBI endoscopy were enrolled. Helicobacter pylori (HP) infection and the endoscopic grading of gastric atrophy were investigated. Using a high resolution endoscopy (Model GIF-H260Z or H290Z, OLYMPUS Co.), four areas in each stomach (greater and lesser curvature in each corpus and antrum) were evaluated under non-M-NBI and M-NBI (with moderate-high magnification) observation. The presence of LBC and WOS were defined into three groups (score 0 (none), 1 (focal, ≤30%), or 2 (extensive, >30%)). Furthermore, using the combination of presence of LBC, WOS, or tubulo-villous pattern, endoscopic GIM score was classified according to above three groups. Resulting from the sum of endoscopic GIM score in each of the four areas, EGGIM was defined into stage 0/I/II/III/IV according to total score 0/1-2/3-4/5-6/7-8. The concordance rate and the weighted kappa value of LBC, WOS and EGGIM were analyzed between non-M-NBI and M-NBI observation.

Results: Fifty-nine patients were defined as present positive for HP infection, 20 were past infected, 21 were uninfected subjects. Endoscopic grading of atrophy were none-mild in 46 patients, moderate in 38 and severe in 16. Of total evaluated 400 areas, LBC score 0, 1 and 2 were found in 202 (50.5%), 148 (37.0%) and 50 (12.5%) areas with non-M-NBI, while 223 (55.7%), 131 (32.8%) and 46 (11.5%) areas with M-NBI observation, respectively. WOS score 0, 1 and 2 were found in 315 (78.7%), 53 (13.3%) and 32 (8.0%) areas with non-M-NBI, while 322 (80.4%), 47 (11.8%) and 31 (7.8%) areas with M-NBI observation, respectively. Several cases with whitish mucus or marginal of tubulo-villous surface structure (marginal turbid band (MTB)) were misdiagnosed as presence of LBC with non-M-NBI. The concordance rate between non-M-NBI and M-NBI were 75.8% in LBC score and 94.5% in WOS score. The strength of agreement showed good reproducibility between non-M-NBI and M-NBI observation (weighted kappa value of 0.77 in LBC score and 0.90 in WOS score). The EGGIM were classified as follows: stage 0, I, II, III and IV were 18, 26, 26, 21 and 9 patients with non-M-NBI, while 27, 21, 32, 15 and 5 patients with M-NBI, respectively. Several cases with a discordance in the EGGIM were found because of difference in a capability of evaluated field between non-M-NBI and M-NBI observation. The concordance rate of EGGIM were 76%, and the weighted kappa value showed substantial agreement with 0.72 between non-M-NBI and M-NBI observation.

Conclusion: Using high resolution NBI endoscopy, non-M-NBI and M-NBI observation showed good agreement on evaluation of the endoscopic findings associated with GIM (LBC, WOS, EGGIM). Non-M-NBI observation for EGGIM, with capability of a wide range view, may have a similar potential for assessment of an individual risk of gastric cancer as M-NBI observation.

References: Esposito G, Pimentel-Nunes P, Angeletti S et al. Endoscopic grading of gastric intestinal metaplasia (EGGIM): a multicenter validation study. Endoscopy 2018; 21[Epub ahead of print] doi: 10.1055/a-0808-3186

Disclosure: Nothing to disclose

P0159 PREVENTIVE EFFECT OF PPIS ALONE, PPIS PLUS CYTOPROTECTIVE AGENT, AND H2RA PLUS CYTOPROTECTIVE AGENT ON BLEEDING AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION: A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

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Introduction: ESD is the most effective treatment for early gastric cancer or gastric adenoma. However, the major complication of ESD is postoperative bleeding from ulcers after the procedure.

Aims & Methods: This study aimed to evaluate the preventive effect of using a proton pump inhibitor (PPI) alone, a PPI+rebamipide combination therapy, and an H2 receptor antagonist (H2RA)+rebamipide combination therapy on bleeding after endoscopic submucosal dissection (ESD). In total, 210 patients who underwent ESD from April 2015 to July 2016 in Dong-A University Hospital were randomly assigned to the PPI-alone therapy group, the PPI+rebamipide combination therapy group, or the H2RA+rebamipide combination therapy group. We excluded patients who were lost to follow-up or who had diagnoses other than early gastric cancer or gastric adenoma. Twenty-eight days after ESD, we evaluated the ulcer bleeding ratio, gastric pH, ulcer residual ratio, and ulcer stage.

Results: This study included 149 patients (PPI-alone group: 43 patients, PPI+rebamipide group: 61 patients, H2RA+rebamipide group: 45 patients). The post-ESD bleeding ratio was not significantly different among the three groups (p=0.264). The ulcer residual ratios were 34.5±21.4%, 24.8±18.8%, and 27.6±20.2% in the PPI alone, PPI+rebamipide, and H2RA+rebamipide groups, respectively (p=0.05).

Conclusion: There was no difference in delayed bleeding after ESD among the PPI-alone, PPI+rebamipide, and H2RA+rebamipide groups at 28 days; however, PPI+rebamipide was significantly more effective in reducing the ulcer residual ratio.

Disclosure: Nothing to disclose

P0160 OPPORTUNISTIC DETECTION OF OESOPHAGOGASTRIC NEOPLASTIC AND PRE-NEOPLASTIC LESIONS DURING SCREENING COLONOSCOPY PROGRAM - A WORTHWHILE STRATEGY?

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Introduction: Endoscopic screening for colon cancer is generally accepted for screening for colorectal cancer, whereas endoscopic screening for oesophagogastric (EG) cancer alone is not cost-effective in countries with low to intermediate incidence of gastric cancer. The utility of offering an opportunistic upper endoscopy during a screening colonoscopy was evaluated as a potential strategy for detection of early EG neoplastic and pre-neoplastic lesions.

Aims & Methods: A retrospective review of a prospective database in a tertiary hospital was performed. Patients with age>40 who underwent opportunistic screening upper endoscopy and colonoscopy in the same session from January 2015 to December 2017 were included. Patients who underwent upper endoscopy for indications such as dyspepsia, weight loss and anaemia were excluded. EG neoplastic lesions were defined as EG carcinomas, and pre-neoplastic lesions were defined as Barret's oesophagus, intestinal metaplasia (IM), or atrophic gastritis.

Results: Out of 9,566 patients who underwent simultaneous upper endoscopy and colonoscopy, we identified 1,414 patients who underwent screening upper endoscopy. On colonoscopy, 491 (34.7%) patients had adenomatous polyps detected, and colorectal malignancy was detected in 20 patients (1.4%).

From our cohort, 179 (12.7%) patients undergoing opportunistic screening upper endoscopy had EG neoplastic and pre-neoplastic lesions. Of these, IM was found in 146 (10.3%) patients with 112 (7.9%) focal IM while 21 (1.4%) had extensive IM. Atrophic gastritis was detected in 23 (1.6%) patients. Also, 19 (1.3%) patients were found to have Barrett's oesophagus

with one high-grade dysplasia which was resected endoscopically. Early stage gastric cancers were diagnosed in three patients (0.2%) who underwent surgery. Two were T1bN0 and one was T2N0. Another patient was diagnosed with early MALT lymphoma.

On multivariate regression, independent risk factors for upper GI neoplastic and pre-neoplastic lesions in this population include age > 50 (Risk Ratio (RR) 2.18, 95%CI 1.15 - 4.14), p = 0.018) and having a family history of first-degree relative with gastric cancer (RR 1.60, 95% CI 1.03 - 2.48, p = 0.035).

Hence, using this strategy, the number needed to detect an incidental neoplastic or pre-neoplastic EG lesion is 7.90. At a cost of USD$500/upper endoscopy, it would cost $3950 per lesion detected.

Patient Group	Number Needed to Scope	Cost per diagnosis ($USD)
All opportunistic OGDs	7.90	3,950
Age above 50	7.42	3,710
Family History of Gastric Cancer (1st Degree)	5.65	2,825
Any one risk factor	7.74	3,870

[Table 1]

Conclusion: This observational cohort suggests the potential utility of incorporating upper endoscopy into an established screening colonoscopy program, for the purpose of detecting EG neoplastic and pre-neoplastic lesions in countries with intermediate risk. All pathologies detected are early lesions. In addition, this strategy may be more acceptable to patients as they are already planned for colonoscopy. Further studies are worthwhile to verify these observations.

Disclosure: Nothing to disclose

P0161 PERORAL ENDOSCOPIC MYOTOMY AS RESCUE-THERAPY AFTER INEFFECTIVE HELLER MYOTOMY: A SINGLE CENTRE RETROSPECTIVE EXPERIENCE

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Introduction: Heller Myotomy has been the treatment of choice for patients with achalasia for the past decades. Since 2008, Peroral Endoscopic Myotomy *(POEM)* has demonstrated excellent outcome and became the primary form of minimally invasive treatment in many centers. Although Heller myotomy is still being performed worldwide with excellent results, there are patients who are refractory to the surgical procedure.

Aims & Methods: The aim of this study is to assess the safety and efficacy of POEM as a rescue therapy in those cases in which Heller myotomy was not effective. This is a retrospective study from a prospective database in a tertiary referral single center from April 2015 to April 2019. All patients included in the study had undergone POEM after ineffective Heller myotomy. All underwent gastroscopy, barium esophagogram, and high resolution manometry, as well as CT Scan to rule out obstructive lesions at the junction prior to POEM. The approach during POEM was either anterior or posterior depending on patient's anatomy and scar of surgical myotomy. To rate the effectiveness of the procedure, we used Eckardt score and Satisfaction scale *(a numeric scale from 1 to 10, 10 to express maximum satisfaction)* upon second month follow up. Symptomatic patients were defined as those with Eckardt score≥3 or those who complained of high intensity symptoms even with Eckardt score <3. Outcome measures were as follows:
1. Clinical Success: post-POEM Eckardt score <3 or Satisfaction scale >7;
2. Technical Success: complete execution of myotomy;
3. Major Adverse Events: vital-sign instability, intensive care unit (ICU) stay, hospital readmission, conversion to open surgery, invasive postoperative procedure, blood transfusion, or prolonged (>5 days) hospitalization for functional impairment.
Exclusion Criteria: patients who did not present for routine second month follow-up post POEM.

Results: Thirty-six patients underwent POEM after ineffective Heller myotomy. Three patients were excluded because of exclusion criteria and a total of 33 patients were analyzed. Twenty-two patients had laparoscopic approach and 11 patients with open approach in previous Heller myotomy.

Thirty patients presented with Eckardt score>3 and 4 patients had high intensity symptoms. Based on Modified Chicago Classification, the type of achalasia seen were as follows: Type I/II/III= 21/2/2, and 8 unclear cases. We distinguished Straight Type from Sigmoid Type *(1 vs 32)* based on barium esophagogram.

All cases achieved Technical Success. Clinical Success was observed in 81.8% of patients. Eckardt score and Satisfaction scale were as follows: Eckardt score < 3 in 23 patients (69.6%), =3 in 2 patients (6.0%), and >3 in 7 patients (21.2%), Unknown in 1 patient (3.0%). Satisfaction scale ≥7 in 19 patients (57.5%), < 7 in 2 patients (6.0%), Unknown in 12 patients (36.3%). No patients experienced Major Adverse Events. There were few cases with discrepancy in Eckardt score and Satisfactory scale: 2 patients with Eckardt score = 3 and Satisfaction scale = 9, 1 patient with Eckardt score = 4 and Satisfaction scale = 7, 1 patient with Eckardt score = 2 with Satisfaction scale = 6.

Conclusion: According to our study, POEM can be considered a safe and effective rescue therapy in symptomatic patients with prior history of surgical myotomy. In addition, there seems to be no differences in risks in performing POEM after either laparoscopic or open Heller myotomy and clinical success was achieved in majority of patients.

Disclosure: Inoue H is an advisor of Olympus Corporation and Top Corporation. He has also received educational grants from Olympus Corp., and Takeda Pharmaceutical Co. All other authors have no conflict of interests to declare.

P0162 ESOPHAGEAL CLEANSING BEFORE POEM - A SIMPLE AND EFFECTIVE TECHNIQUE

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Introduction: Pre - procedural preparation varies from center to center. No standard method prescribed.

Conventionally, patients are put on clear liquids for 48 to 72 hours pre POEM. Then an endoscopic lavage is given the previous day. This is very cumbersome and we need a better less cumbersome preparation method

Aims & Methods: To devise a simple yet effective method for pre-procedural preparation for poem.

Methods: 100 cases between 2017 and 2019 with Achalasia Cardia were included. A Pre POEM Score for the condition of oesophageal mucosa was devised.

Pre POEM Score:

Grade 1: Clean esophagus

Grade 2: Presence of fluid and froth + crumpled / puckered but normal mucosa

Grade 3: Presence of fluid and froth, no food residue + intermittent esophageal candidiasis

Grade 4: Presence of fluid and froth with minimal food residue +/- esophageal candidiasis

Grade 5: Extensive food residue with candidial infection

Patients dived in two groups: A and B

Group A: 50 patients: Prepared with 48 hours clear liquids, 24 hours nil orally and endoscopic lavage the day before.

Group B: Our new preparation. Warm water and a carbonated drink alteranately every 15 to 20 minutes for 12 hours prior to 6 hours before the procedure. No pre procedure lavage.

To assess anesthesia aspiration risk, while intubation in POEM, we devised an 'Anesthesia Risk Score'

1. Normal risk with no fluid regurgitation
2. Minimal fluid regurgitation requiring suction once
3. Significant fluid regurgitation requiring continuous suction
4. Food and fluid regurgitation needing emergency measures

Using this we compared Group A and B in terms of requirement of lavage
- procedure time
- anaesthesia aspiration risk
- Length of hospital stay
- adverse events and
- cost effectiveness

Results: In the patients who had Grade 2 and Grade 3 pre-POEM score, the lumen clearance at the time of POEM procedure was found to be optimum in both the groups

• In patients with Grade 4 score
- Group A : two patients required additional wash prior to POEM
- Group B : all patients had good luminal clearance
• In patients with Grade 5 score
- Group A: all four patients required an additional wash prior to POEM
- Group B: one of the patients required wash prior to POEM.
• All patients had successful esophageal clearance with both approaches.
• Group B patients had
- Avoidance of an additional endoscopic procedure for esophageal lavage
- Decreased risk of aspiration.
- Decreased exposure to anesthesia/ sedation.
- Decrease in the total POEM procedure time
- Total cost to the patient was significantly decreased
- Duration of the hospital stay was reduced
Conclusion: The new simple protocol of giving warm water and a carbonated drink just 12 hours before keeping the patient nil orally for anaesthesia
- reduces the starvation time for the patient to 6 hours and hence, improves compliance.
- reduces one more procedure for esophageal lavage
- reduces the anaesthesia risk of aspiration during induction
- reduces the exposure to anaesthesia
- and reduces the hospital stay and is cost effective
We can have a randomised trial to prove the effectiveness of this simple protocol in a larger study.

Characteristics	Group A	Group B
Duration Of Symptoms, Median, months	4(1-60)	6(1-60)
Mean IRP mm Hg (Median)	17.6 (10.4-52.2)	24.2 (12.4- 65.6)
Type I Achalasia; n (%)	22 (44)	35 (70)
Type II Achalasia; n (%)	18 (36)	10 (20)
Type III Achalasia; n (%)	10 (20)	5 (10)
Grade I Mucosa; n (%)	14 (28)	12 (24)
Grade II Mucosa; n (%)	13 (26)	21 (24)
Grade III Mucosa; n (%)	13 (26)	21 (42)
Grade IV Mucosa; n (%) Gr V; n (%)	6 (12) 4 (8)	7(12) 4 (8)

[Findings]

References: •J Neurogastroenterol Motil, Vol. 18 No. 4 October, 2012 •Journal of Clinical Gastroenterology: June 1998 - vol 26 - Issue 4 p 239 •Clin Radiol 1986 Nov;37(6):589-92.
Disclosure: Nothing to disclose

P0163 NARROW-BAND-IMAGING: A RELIABLE INDICATOR OF GASTRIC DYSPLASIA

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Introduction: Gastric cancer is a major health concern worldwide, with significant morbidity and mortality rates. In western society, screening remains controversial regarding cost-efficiency issues. NBI (narrow-band-imaging) is a virtual chromoendoscopy tool that has been associated with higher detection of gastric premalignant conditions in comparison with white-light endoscopy (WLE). Endoscopic grading of gastric intestinal metaplasia (EGGIM) is a NBI grading score for metaplasia.
Aims & Methods: Assess the correlation between NBI and histological diagnosis of gastric dysplasia.
Retrospective, single center study, including consecutive patients that underwent upper endoscopy complemented with NBI for gastritis surveillance, from October 2016 to Jan 2019. Our cohort was analyzed by descriptive, parametric and non-parametric SPSS tools.
Results: We included 71 upper endoscopies complemented with NBI evaluation, 40 men (56.3%) with a mean age of 62 years old. Gastric dysplasia was detected, histologically, in 23 cases (32.4%).

The correlation between NBI targeted biopsies and histological findings was statistically significant (p< 0.001) with a Kappa coefficient of 0.81. EGGIM was associated with an increase of NBI diagnosis of dysplasia (odd 1.384; p=0.025). However, as EGGIM increases the odd of correlation between NBI and histological dysplasia decreases in 42% (odd 0.58; p = 0.041).
We report 15 gastric non polypoid lesions (Paris classification 0-IIa, 0-IIb and 0-IIc). Applying NBI, we established a concordance with histological dysplasia diagnosis of 100%.
Conclusion: NBI targeted biopsies presented a statistically significant correlation with histological findings, acknowledging an almost perfect agreement with a Kappa coefficient of 0.81. Applying NBI on non-polypoid lesions identified in WLE increases the rate of histological concordance, we report a 100% concordance. NBI is an accurate tool that, in the hands of experienced endoscopists, can lead to an easy identification of gastric dysplasia, with high concordance with histological findings.
Disclosure: Nothing to disclose

P0164 ENDOSCOPIC SUBMUCOSAL DISSECTION OF THE OESOPHAGUS AND OESOPHAGOGASTRIC JUNCTION FOR EARLY NEOPLASIA: WILL IT BE THE FUTURE?

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Introduction: Endoscopic submucosal dissection (ESD) is an endoscopic technique widely employed in Asia for resection of oesophagus and oesophagogastric junction (EGJ) neoplasms. In the West, ESD of these locations is limited to a very few centres.
Aims & Methods: This study aims to report the feasibility, safety and effectiveness of ESD for the treatment of oesophagus and EGJ early neoplasms in a Western centre.
We conducted a prospective data analysis of all consecutive oesophageal and EGJ lesions treated by ESD from October 2014 to November 2018. Location, en bloc, pathological complete resection (R0) and curative rates, procedure time, complications and local recurrence were evaluated.
Results: Thirty lesions were included from 28 patients (65-year-old [39-84]; M/F=23/5): 9 squamous cell neoplasms, 6 neoplasms in Barrett's oesophagus, 12 gastric cardia neoplasms, 2 granular cell tumours and 1 oesophageal papilloma (proximal oesophagus n=3, medial oesophagus n=8, distal oesophagus n=6, EGJ n=13). The median size of the resected specimen was 42mm (12-88). En bloc resection was achieved in all resected lesions (29/29; 1 resection was considered non-feasible due to invasion detected during the procedure). Circumferential dissection was performed in 6/29 lesions (21%). R0 was accomplished in 24/29 (83%) and resection was considered curative in 19/29 (66%). Reasons to non-curative resection were: poorly differentiated cardiac gastric adenocarcinoma (n=1), R1 (n=1), deep submucosal invasion (n=6) and Rx (n=2). There were no immediate complications such as bleeding or perforation; in the curative resected group, stenosis was diagnosed in 1 patient submitted to a circumferential resection and was managed endoscopically. No recurrence was observed within a mean follow-up of 18 months (3-53).
Conclusion: This study represents one of the largest series of oesophageal and EGJ ESD in the West. Although representing the initial experience, ESD for oesophageal and EGJ lesions was efficient and extremely safe.
Disclosure: Nothing to disclose

P0165 A STUDY OF IMPROVING IMAGE PROCESSING TO REDUCE COLOR NOISES IN OXYGEN SATURATION IMAGING ENDOSCOPY

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Introduction: Oxygen saturation (OS) imaging (FUJIFILM Corporation, Tokyo, Japan) is a novel endoscopic technology which can directly measure the tissue oxygen saturation (Sto2) of the surface of gastrointestinal tract

without any additional drugs or devices.Its principle is recognizing the difference in optical absorption spectra between oxy- and deoxy-hemoglobin by emitting two kinds of lasers from endoscopy. This imaging technology is expected to contribute to research into cancer biology which leads to clinical benefit such as prediction to efficacy of chemotherapy or radiotherapy. OS imaging supply the StO2 mapping in real time, however, the measurement of StO2 is difficult in some cases of advanced gastrointestinal cancer due to covered blood or necrotic tissue.

Therefore, the algorism for discrimination between tumors and noises due to blood or necrotic tissue on tumors is necessary to measure the precise StO2 in OS imaging.

Aims & Methods: To construct the algorithms for discriminating between tumors and its adhered substances using white light imaging (WLI) of gastrointestinal cancer, and validate the utility of it in OS imaging.

We classify color of tumors and its adhered substances in WLI into following 2 classes of 4 types (red points: red tumors (83 points) and blood (68 points); white area: white tumors (79 points) and white coat (89 points)), and plotting is made at each place in 50 endoscopic tumor images in upper digestive tract. As a result, we create scatter diagram using color data (RGB value) in WLI, which its X axis is ln(R/G) value and Y axis is ln(B/G) value. The minimum and maximum value of the X and Y axes of each classes, and linear function as discriminating algorithm for each types of areas is constructed by calculating scatter diagram to adjust color noises. Discriminating algorithms are verified by using validation datasets prepared separately from 15 images out of 50 images in this study, and classified each datasets into tumor and color noises. In addition, the comparison of StO2 value of the tumors and that of its adhered substances is conducted in the images of gastrointestinal tumors captured using OS imaging.

Results: We randomly selected 50 cases consisting of advanced gastric cancer (n=30) and advanced esophageal cancer (n=20) who are simultaneously evaluated with WLI and SO imaging, and images are analyzed.

The calculated algorithms for each areas were as follows: algorism for red area; 0.388≤x≤2.610, −0.842≤y≤0.157, Y< 0.77X-1.440; algorithms for white area; 0.119≤x≤1.079, −0.577≤y≤0.172, and Y< −0.32X+0.10. In validation datasets of 15 images, each algorithms showed the discriminating accuracy between noise due to ad and tumor in red and white area of 87.8% and 86.0%, respectively.

The analysis resulted that StO2 values (median, [range]) of the area recognized as tumor and adhered substances by algorithms are follows: all captured red area; 75.9%, [44.6.-100.0], red adhered substances; 77.6%, [44.6-100.0], red tumor; 74.9%, [62.0-86.9], all captured white area; 66.1%, [42.1-100.0], white adhered substances; 71.4%, [42.1-100.0], white tumor: 64.8%, [54.2-71.4]. Analysis of StO2 revealed that the values of tumors except for adhered substances were distributed more specific comparing with that of whole tumor.

Conclusion: The algorithm for discriminating between tumors and its adhered substances based on the annotated information using WLI can be useful for precising StO2 measurement of
gastrointestinal cancer in OS imaging.

References: nothing
Disclosure: Nothing to disclose

P0166 COMPARISON BETWEEN ENDOSCOPIC BAND LIGATION AND ARGON PLASMA COAGULATION FOR THE TREATMENT OF GASTRIC ANTRAL VASCULAR ECTASIA: A SYSTEMATIC REVIEW WITH META-ANALYSIS

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Introduction: Gastric antral vascular ectasia (GAVE) is a condition characterized by diffuse mucosal vascular ectasia causing chronic gastrointestinal blood loss and anemia. It is more common in patients with cirrhosis as well as chronic kidney disease, hematologic malignancies, scleroderma, systemic lupus erythematosus and other autoimmune diseases. Since GAVE is a cause of anemia in the above mentioned chronic illnesses, it is important to ensure a treatment that may reduce the morbidity related to GAVE in such patients. Argon plasma coagulation (APC) is one of the

most widespread endoscopic technique for GAVE, however endoscopic band ligation (EBL) has gained increasing interest. Therefore we aimed to perform a meta-analysis of studies comparing EBL versus APC.

Aims & Methods: A literature search was performed in February 2019 using the following string: (GAVE OR gastric antral vascular ectasia OR watermelon stomach AND band ligation AND APC. We selected only studies in which a direct comparison of EBL and APC was performed. For dichotomic variables, odd ratios (OR) and 95% confidence intervals (95% CI) were calculated according to the Mantel-Haenszel method. For continuous variables we calculated mean differences (MD). Heterogeneity was estimated by chi-square test and, if present, a random effect model was chosen, otherwise a fixed effect model was used. Statistical significance was set at p < 0.05 and the RevMan 5.3 software was used. All procedures followed PRISMA guidelines.

Results: Five studies were selected, enrolling overall 207 patients (93 EBL and 114 APC). Pooled effectiveness of EBL was 91.4%, statistically greater than 57.9% of APC (OR=8.4; 95% CI 3.45-20.43; p< 0.001, no heterogeneity, fixed effect). Complication rate was 27.2% and 13.0% for EBL and APC respectively, not statistically different (OR=3.09, p=0.28). EBL allowed a fewer number of endoscopy sessions than APC with a p value close to significance (MD=-1.28 95% CI -2.62-0.05; p=0.06). With EBL, the mean number of transfused blood units was lower than for APC (MD=-1.55; 95% CI -3 to -0.09; p=0.04; random effect for high heterogeneity). Post-treatment hemoglobin levels were higher in the EBL group than in APC group (MD=0.43; 95% CI 0.11-0.75; p=0.009 fixed effect, no heterogeneity) and, in comparison to baseline hemoglobin, EBL showed a significantly higher increase in levels than APC (p=0.02).

Conclusion: EBL was more effective than APC in treating GAVE since a better control of anemia, a fewer number of red cell transfusions, and a higher rise in hemoglobin levels were achieved. A non significant trend showed that less endoscopic sessions were required with EBL which could be proposed as a potential cost-effective modality compared to APC. However, the low number of patients enrolled in this analysis prompts the development of further randomized trials aiming to evaluate EBL and APC for GAVE treatment.

Disclosure: Nothing to disclose

P0167 ROBOT CONTROLLED MAGNET-ASSISTED CAPSULE GASTROSCOPY IS BETTER TOLERATED AND ACCEPTED BY PATIENTS THAN FLEXIBLE GASTROSCOPY

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Introduction: Gastroscopy is performed commonly but often poorly tolerated. Capsule endoscopy is well tolerated. Robot controlled magnet assisted capsule endoscopy (MACE) allows control of a capsule endoscope resulting in a non-invasive endoscopic examination of the upper GI tract. No controlled comparisons of patient tolerance and acceptability between MACE and gastroscopy have been performed. Post procedure Endoscopy Concerns Scale (ECS) scores correlate with patient acceptance after gastroscopy [Condon 2008, Can J Gastro]. We assess tolerance and acceptability of MACE compared to OGD using the ECS.

Aims & Methods: Patients referred for the endoscopic investigation of dyspepsia were recruited. Upper GI MACE examinations were performed followed by oral or transnasal gastroscopies. Questionnaires examined patients' tolerance to and acceptability of the endoscopies. Paired differences between median distress and ECS scores are reported (p< 0.0001***, p< 0.01**)

Results: Thirty eight (oral n=33, transnasal n=5) patients were recruited (median age 50, female 74%, sedated in 36.4% of oral gastroscopy). All patients tolerated MACE adequately with minimal discomfort in 16%. Gastroscopy was adequately tolerated in 63% with the remaining reporting moderate or severe discomfort. There was less distress (1 - 10: not at all - extremely) caused by: discomfort during (1 vs 5***), discomfort after (1 vs 2***) and pain during (1 vs 2***) the procedures, gagging (1 vs 6***), choking (1 vs 4.5***), bloating (1 vs 2**) and swallowing the capsule vs. insertion of the scope (1 vs 4***) with MACE compared to gastroscopy. The overall pre-procedure ECS score (28 vs 50 points***) and post-procedure ECS score (13 vs 32 points***) was lower after MACE compared to gastros-

copy suggesting patients are more accepting of MACE before and after the procedure compared to gastroscopy. There was a reduction in pre-procedure ECS after both MACE (median difference -15 ***) and gastroscopy (-18 ***) suggesting procedures are not as distressing as initially anticipated, however 32% of patients report a higher ECS after gastroscopy whereas all patients reported a lower ECS after MACE.

All patients would undergo, or advise a friend to undergo MACE again given the same medical circumstances compared to 71% and 79% of patients when undergoing gastroscopy. All patients would have MACE as a screening test for cancer compared to 79% of patients when undergoing gastroscopy. If biopsies were required after MACE, patients would require a further gastroscopy. When asked, in retrospect after having both procedures, if the chance of requiring biopsies was 1:20, 1:10, 1:5, 1:4 and 1:2, 91%, 91%, 82%, 73% and 73% of patients respectively would prefer to have initial MACE.

Conclusion: Patients better tolerate, are more accepting of and prefer MACE over gastroscopy. Where biopsies are required, patients would still prefer capsule endoscopy initially. Cost effectiveness of this approach should be examined.

References: Condon A, Graff L, Elliot L, Ilnyckyj A. Acceptance of colonoscopy requires more than test tolerance. Can J Gastroenterol 2008; 22(1): 41-7.
Disclosure: Nothing to disclose

P0168 ENDOSCOPIC ULTRASOUND-GUIDED GASTRO-ENTERIC ANASTOMOSIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Endoscopic ultrasound (EUS)-guided gastro-enteric anastomosis using lumen-apposing metal stents (LAMS)is emerging as an alternative, minimally invasive therapy for treating gastric outlet obstruction (GOO), as well as restoring bowel continuity in patients with surgically altered anatomy. Literature on this subject is heterogeneous, with variable reporting of techniques and outcomes.
Aims & Methods: Our aim was to perform a meta-analysis of published data on EUS-guided enteric anastomosis, providing a pooled estimate of technical and clinical outcomes.
The protocol was registered in PROSPERO (Reg. no. CRD42018111110). PubMed, Embase, Scopus, and Web of Science databases were searched until February 2019 for studies describing at least 5 patients undergoing EUS guided enteric anastomosis. Screening of titles/abstracts, full-text review, and data extraction was performed independently by two of the authors. Data regarding indication, technique, technical and clinical success, adverse events, and follow-up were collected. PRISMA methodology was used. Pooled technical and clinical success rates as well as pooled adverse events rates were calculated. Study quality, publication bias, and heterogeneity were explored.
Results: Twelve studies including 290 patients were included, published between 2016 and 2019. All studies but one were retrospective. The main procedure indication was GOO (62.4%), followed by need for ERCP (27.9%) in patients with gastric bypass surgery. Direct puncture technique was the most frequently adopted (68.2%). The pooled technical success rate (12 studies, 290 patients) was 93.5% [95% confidence interval (CI) 89.7-6.0%; I²:0%], while the clinical success rate (11 studies, 260 patients) was 90.1% [95% CI 85.5-93.4%; I²:0%]. The pooled total adverse events rate was (11 cohorts, 261 patients) was 11.7% [95% CI 8.2-16.6; I²:0%]. When stratified for adverse event severity, the mild/moderate pooled adverse event rate was 10.6% [95% CI 7 -15.6; I²:3.4%], while the severe/fatal adverse event rate was 2.9% [95% CI 1.4-6; I²:0%]. Mean procedure time was 63.5±35.7 minutes, and mean length of hospital stay was 4.9±2.7 days.
No publication bias or significant heterogeneity was found, although some included studies were graded as low quality.
Conclusion: EUS-guided enteric anastomosis, when performed by expert endoscopists in tertiary referral centres, has a high rate of technical and

clinical success. The procedure appears to be relatively safe, and a minimally invasive alternative to surgery in expert hands. Further prospective studies and technique standardisation are warranted to generalise these results.
Disclosure: Nothing to disclose

P0169 ENDOSCOPIC AND CLINICOPATHOLOGICAL FEATURES OF NON-AMPULLARY DUODENAL TUMOR BASED ON THE MUCIN PHENOTYPES

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Introduction: Superficial non-ampullary duodenal epithelial tumors (SNADET) are relatively rare. In a few studies, the association between clinicopathological features and mucin phenotypes was analyzed, and they reported that the gastric phenotype of SNADET showed more aggressive biological behavior than those of the intestinal phenotype [1-3]. However, the association between mucin phenotypes and endoscopic features in SNADET has not been well elucidated.
Aims & Methods: We aimed to clarify the clinicopathological and endoscopic features including conventional white-light imaging (WLI) and magnifying endoscopy with narrow-band imaging (M-NBI) findings based on the mucin phenotypes. We collected 65 lesions of SNADET which were resected by endoscopic procedures at our hospital between February 2013 and November 2017. Eleven lesions were excluded as follows; 3 lesions with insufficient histopathological evaluation due to specimen damage, 1 lesion diagnosed cancer arising from juvenile polyp, and 7 lesions with unclassifiable mucin phenotype. The remaining 54 lesions were classified into two groups immunohistochemically: the gastric predominant phenotype (GPP) and the intestinal predominant phenotype (IPP). Endoscopic and clinicopathological findings were compared between the two groups.
Results: There were 11 lesions of the GPP and 43 lesions of the IPP. All lesions of the GPP were located in the first portion (100%, 11/11), while lesions of IPP were located more often in the second portion (72.1%, 31/43) (p< 0.01). The mean tumor size of the GPP was larger than that of the IPP (14.4 mm [range: 7-25] vs. 10.2 mm [2-30], p< 0.05). Type 0-I (72.7%, 8/11 vs. 5/43, 11.6%, p< 0.01), reddish color (72.7%, 8/11 vs. 16/43, 37.2%, p< 0.05), lobular/granular pattern (81.8%, 9/11 vs. 4.7%, 2/43, p< 0.01), category 4/5 (mucosal high-grade neoplasia/submucosal invasion by carcinoma) in Vienna classification (81.8%, 9/11 vs. 30.2%, 13/43, p< 0.01) were observed more frequently in the GPP than in the IPP. No significant differences were observed in terms of the mean age (GPP vs. IPP=67.3 years vs. 65.2 years, p=0.72), gender (male/female=9/2 in GPP, 26/17 in IPP, p=0.29), operative method (EMR/ESD=8/3 in GPP, 30/13 in IPP, p=1.00). M-NBI findings were assessed in 48 lesions. All lesions showed demarcation line (DL) clearly (100%, 48/48). White opaque substance (WOS) (22.2%, 2/9 vs. 89.7%, 35/39, p< 0.01) and light blue crest (LBC) (0%, 0/9 vs. 43.6%, 17/39, p< 0.05) were less frequently observed in the GPP than in the IPP. Vessels within epithelial circle pattern (VEC) (66.7%, 6/9 vs. 17.9%, 7/39, p< 0.01), dense pattern (55.6%, 5/9 vs. 2.6%, 1/39, p< 0.01), and dilatation of intervening part (DIP) (100%, 9/9 vs. 12.8%, 5/39, p< 0.01) were more frequently observed in the GPP than in the IPP.
Conclusion: Endoscopic and clinicopathological features of the GPP were as follows: located in the first portion, reddish color, type 0-I, lobular/granular pattern, VEC, dense pattern, DIP, and high frequency of the category 4/5 in Vienna classification. On the other hand, those of the IPP were as follows: located in second or third portion, whitish color, type 0-IIa or IIc, WOS, LBC, and high frequency of the category 3. These features are useful to distinguish the mucin phenotypes of SNADET.
References: 1. Toba T, Inoshita N, Kaise M, Nomura K, Kuribayashi Y, Tanaka M, Yamashita S, Furuhata T, Kikuchi D, Matsui A, Mitani T, Iizuka T, Hoteya S (2018) Clinicopathological features of superficial non-ampurally duodenal epithelial tumor; gastric phenotype of histology correlates to higher malignant potency. J. Gastroenterol. 53:64-70. 2. Ushiku T, Arnason T, Fukayama M, Lauwers GY (2014) Extra-ampullary duodenal adenocarcinoma. Am. J. Surg. Pathol. 38:1484-1493. 3. Hida R, Yamamoto H, Hirahashi M, Kumagai R, Nishiyama K, Gi T, Esaki M, Kitazono T, Oda Y (2017) Duodenal

Neoplasms of Gastric Phenotype: An Immunohistochemical and Genetic Study With a Practical Approach to the Classification. Am. J. Surg. Pathol. 41:343-353.
Disclosure: Nothing to disclose

P0170 COMPARISON OF MEDICAL COST BETWEEN DUODENAL AND GASTRIC ESD

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Introduction: Duodenal ESD (D-ESD) is reported to be technically difficult and at high risk of adverse events such as bleeding and perforation. Thus, it is expected D-ESD would require more medical cost than gastric ESD (G-ESD), however, actual costs of D-ESD are still unknown, since there are only few studies.

Aims & Methods: The aim of this study was to analyze the actual cost of D-ESD and compare with G-ESD, including analysis according to the elements of procedure .This is a single-center, retrospective cross-sectional survey,Medical costs were calculated among patients who underwent D-ESD or G-ESDfrom July 2016 to June 2017. Medical costs were calculated in summation of the costs of anesthesia, costs of devices for procedure, costs of materials to prevent adverse events, costs of intervention for adverse events, and hospitalization costs. Hospitalization costs were extracted in reference to the "diagnosis procedure combination" reimbursement system in Japan. The costs of devices and materials were calculated from the number of items actually used from medical records. We analyzed by using Wilcoxon rank sum test and a *p* value < 0.05 was considered statistically significant.

Results: A total of 49 cases of D-ESD and 107 cases of G-ESD were included in the study. Total medical costs in D-ESD group was significantly higher than in G-ESD group. As for the breakdown, the costs of the anesthesia, costs of materials to prevent adverse events, and hospitalization costs were significantly higher in D-ESD group than in G-ESD group, whereas there was no difference between two groups for costs of devices used for treatment and the additional treatment for the adverse events (Table1).

Costs (€)	G-ESD (N=107)	D-ESD (N=49)	P value
Median costs of anesthesia, Eur [range]	55 [8-1,079]	142 [27-3,230]	<0.001
Median costs of devices for procedure, Eur [range]	328 [208-584]	328 [208-584]	0.338
Median costs of prevention for adverse events, Eur [range]	0 [0-697]	86 [0-839]	<0.001
Median costs of intervention for adverse event, Eur [range]	0 [0-756]	0 [0-3416]	0.904
Median hospitalization costs of, Eur [range]	1,800 [1,297-14,546]	2,086 [1.420-15,119]	<0.001
Median total medial costs, Eur [range]	2,498 [1,795-12,971]	3,232 [2,243-22,219]	<0.001

[Table1: Actual medical costs during hospitalization for ESD]

Conclusion: The medical costs of D-ESD are more expensive than G-ESD, especially for the anesthesia and prevention for adverse events.
Disclosure: Nothing to disclose

P0171 DRUG ADMINISTRATION WITH PERCUTANEOUS ENDOSCOPIC GASTROJEJUNOSTOMY: A NOVEL TREATMENT OPTION FOR PARKINSON'S DISEASE

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Introduction: The incidence of Parkinson's disease (PD) sharply increases with age and, due to the progressive aging of the world's population, the number of affected individuals is likely to exponentially increase in the near future. However, it is difficult to maintain therapeutic plasma concentrations of levodopa after oral levodopa administration in patients with advanced PD due to the narrow therapeutic range and delayed gastric emptying. Levodopa-carbidopa intestinal gel (LCIG) therapy, a new drug delivery system for patients with advanced PD, has been covered by insurance in Japan since September 2016. LCIG is administered by using a percutaneous endoscopic gastrojejunostomy (PEG-J) system and helps maintain therapeutic plasma concentrations of levodopa. However, the LCIG administration cannot be achieved without PEG-J, which is the main hindrance to its introduction. Additionally, close collaboration between neurologists and gastroenterologists is very important.

LCIG therapy was introduced in our hospital in January 2017. This study investigated the usefulness and safety of the LCIG treatment system.

Aims & Methods: In LCIG therapy, a nasojejunal (NJ) feeding tube is indwelled and a test administration of LCIG is performed. After confirming reactivity and tolerability, gastrostomy is performed by the "pull" method and a PEG-J tube is inserted. We examined 11 patients who underwent LCIG therapy at our hospital from January 2017 to September 2018. The initial six cases used PEG-J tube insertion with the standard procedure, while the more recent five cases used it with the modified procedure. The modified procedure for placement of the PEG-J tube is as follows: after guiding the PEG-J tube to the jejunum with the grasping forceps using an endoscope, pull back only the endoscope to the stomach leaving the PEG-J tube with grasping forceps at the jejunum. Then, release the PEG-J tube and pull back the grasping forceps to the stomach. This method will prevent interference between the PEG-J tube and the endoscope.

Results: Out of the 11 patients, three were male and eight were female, and the mean age was 69.5±6.4 years old. Placement of the NJ tube was performed in eight patients, and, in three patients, the NJ tube placement was skipped, and gastrostomy and PEG-J were performed. The operation time for the placement of the NJ tube was 13.1±4.8 minutes (9 to 20 minutes), and for gastrostomy and the placement of the PEG-J, it was 45.6±28.4 minutes (20 to 120 minutes). PEG-J could be safely performed in all patients. The operation time for gastrostomy and the placement of the PEG-J of the modified procedure (27±6.7 min) was significantly shorter than that of the standard procedure (61.0±30.7 min) (p< 0.05). All patients responded well to LCIG regarding neurological outcomes.

Conclusion: Although there are differences among the currently used PEG-J systems, the LCIG treatment system could be used without major problems. Moreover, the modified procedure could shorten the operation time for gastrostomy and the placement of the PEG-J. For its introduction, the close collaboration between the neurologist and the co-medical staff proved to be important. The LCIG treatment system is a new and useful treatment option for PD and requires understanding and cooperation on the part of endoscopists.
Disclosure: Nothing to disclose

P0172 POSTOPERATIVE BLEEDING RISK AFTER GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION DURING ANTITHROMBOTIC THERAPY

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Introduction: Little is known about the safety of gastric endoscopic submucosal dissection (ESD) during antithrombotic therapy. In 2017, after several guideline updates, the Japan Gastroenterological Endoscopy Society recommended ESD under the continuation of aspirin/warfarin for patients with high thrombotic risk.
Aims & Methods: We aimed to evaluate the post-ESD bleeding rate and risk factors in patients receiving antithrombotic therapy. The medical records of 622 patients with gastric neoplasms treated by ESD at Mitoyo General Hospital between April 2009 and December 2018 were retrospectively analysed. The following patient/tumour clinical parameters were analysed: age, sex, comorbidities, antithrombotic drug type, antithrombotic drug management (complete cessation, continued, or heparin replacement), macroscopic findings, location, invasion depth, resected specimen diameter, and operative time. Post-ESD bleeding was defined as an episode of hematemesis/melena or a decrease in haemoglobin (>2 g/dL).
Results: Of 622 patients, 140 underwent ESD during antithrombotic therapy. The post-ESD bleeding rate was significantly higher in patients receiving therapy than in those not receiving therapy (22.4% vs 5.4%, P=0.009; log-rank test). In a multivariate analysis, the combined use of antiplatelet and anticoagulant drugs (odds ratio [OR] 13.1, 95% confidence interval [95%CI] 1.3-132) and tumours in the lesser curve (OR 0.28, 95%CI 0.08-0.99) were significant risk factors for post-ESD bleeding, while antithrombotic therapy continuation/cessation was not.
Conclusion: Gastric ESD under the continuation of aspirin/warfarin is acceptable. However, the combined use of antiplatelet and anticoagulant drugs is associated with a higher risk of post-ESD bleeding.
References: Kato M, Uedo N, Hokimoto S, Ieko M, Higuchi K, Murakami K, et al. Guidelines for Gastroenterological Endoscopy in Patients Undergoing Antithrombotic Treatment: 2017 Appendix on Anticoagulants Including Direct Oral Anticoagulants. Digestive endoscopy : official journal of the Japan Gastroenterological Endoscopy Society. 2018;30(4):433-40.
Disclosure: Nothing to disclose

P0173 SAFETY AND DURABILITY OF PEG-J: A SINGLE-CENTRE EXPERIENCE

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Introduction: Percutaneous endoscopic gastrostomy with jejunal extension (PEG-J) is currently the gold standard for delivering levodopa-carbidopa duodenal infusion therapy in patients suffering from Parkinson's disease (PD). Data regarding the safety and durability of PEG-J are still lacking. Aim of this study was to review short- and long-term safety of PEG-J first positioning and any tube replacement in a cohort of patients with PD referred to our Endoscopy Unit.
Aims & Methods: We retrospectively collected data from 58 patients (53 with PD and 5 with other neurological conditions) with a PEG-J referred to our Endoscopy Unit between March 2010 and August 2018 (53 underwent PEG-J placement in our Unit, 5 patients elsewhere). We used descriptive statistics to define prevalence of short- and long-term adverse events (AEs) related to PEG-J placement or after any tube replacement. As many substitutions were performed electively, as suggested by the PEG-J manufacturers, Chi-square with Yates' correction was used to compare the number of AEs following tube replacement on either a programmed or on an urgent basis.

Results: Fifty-eight patients (mean age 71.5 years, F/M ratio 1.5:1) have been evaluated over the study period. Of 53 patients undergoing PEG-J placement at our Unit, no immediate AEs were reported. Short-term (within 30 days) AEs (1 kinking, 3 dislocations, and 1 obstruction of the jejunal extension) occured in 5 patients (9.43%); while delayed (after 30 days) AEs (2 obstructions, 3 tube malfunctions, and 1 pyloric ulcer) were registered in 6 patients (11.32%). The median duration of the original PEG-J was 10.66 months (range 1-24 months).
Of the 113 tube replacement performed, no immediate AEs were registered and only in 2 cases (1,76%) a second procedure was necessary within the first 30 days due to dislocation of jejunal extension. A delayed AE occurred in 21 cases (18,58%; 6 obstructions, 2 buried bumper syndromes, 6 dislocations, 7 malfunctions). The median duration was 10.96 months (range 1-34 months).
The risk of developing an AE was not reduced if tube replacement was performed electively (p=0.96). No serious complications were reported.
Conclusion: Differently from what is stated in previous literature (Devos, French Duodopa Study Group, 2009), PEG-J placement is a safe procedure, particularly in patients with PD. An elective tube replacement after one year is not strictly recommended, since the durability is variable among patients and an elective replacement does not significantly reduce the number of following AEs.
Disclosure: Nothing to disclose

P0174 LANREOTIDE AND ENDOSCOPIC GASTROSTOMY IN INTESTINAL OCCLUSION FROM GYNAECOLOGICAL CANCERS: AVIANO NATIONAL CANCER INSTITUT EXPERIENCE

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Introduction: Bowel obstruction represents a common condition of gynaecological cancer. The aim of this study was to evaluate the efficacy of a combined treatment with the somatostatin analogue Lanreotide and percutaneous endoscopic gastrostomy (PEG) in the clinical management of advanced ovarian cancer with intestinal occlusion.
Aims & Methods: 93 consecutive patients with advanced abdominopelvic carcinomatosis were enrolled in the study between November 1998 and December 2012. In particular, we investigated safety and efficacy of somatostatin analogue lanreotide, 30 mg every 10-14 days, alone or in combination with PEG.
Results: Seventy-seven patients were treated with Lanreotide, and 27 of them underwent also PEG. The median age was 52,3 years, and the median follow-up was 13 months. After 2 lanreotide administrations, we observed reduction of nausea in 56.3% of patients, of vomiting in 52.7%, of abdominal distension in 60%, and of colic pain in 67.2%. In no cases, drug-related side effects were observed. In patients who received lanreotide and PEG, there was a significant reduction in gastrointestinal secretions, with a real benefit for the patient also during the home care.
Conclusion: The integrated and combined treatment with Lanreotide 30 mg and PEG is effective in patients with advanced abdominopelvic cancers. A constant overall benefit for the quality of life was observed and the control of symptoms, which is very important especially during the home care follow-up of terminal patients.
Disclosure: Nothing to disclose

P0175 RISK FACTORS FOR BACTEREMIA AFTER LOW RISK ENDOSCOPIC PROCEDURES WITH A FOCUS ON NEUTROPENIA

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Introduction: risk for bacteremia following endoscopic procedures varies among studies. A low neutrophil count is considered by some to be a risk factor. We assessed risk factors for bacteremia in low risk endoscopic procedures and risk for post procedural complications in neutropenic patients.
Aims & Methods: A retrospective analysis of all inpatients undergoing low risk endoscopic procedure (esophago-gastro-duodenoscopy (EGD), short colonoscopy and colonoscopy) between 2005-2018 with a neutrophil level taken within 72 hours prior to procedure at our hospital. Data was retrieved using MDClone's query engine and was manually validated. Neutropenia was defined as neutrophil level < 1000 cell/μl. Primary outcome was new onset bacteremia within 48 hours after the procedure. Secondary composite endpoints in patients with neutropenia included mortality within 7 days of the procedure, new onset of fever, bacteremia or hemodynamic instability within 48 hours following the procedure. As a comparator invasive procedure, rate of new onset bacteremia was estimated following bronchoscopic procedures. Mean comparison for numerical variables was done using t-test. Categorical variables were compared using either a Chi-squared test or Fisher's exact test. The multivariate logistic regression models were built by using stepwise forward selection and backward elimination.
Results: 13168 patients were included, out of which 167 procedures were performed in the setting of neutropenia. The mean age was 61 years and EGD was the most common procedure (56%). Post-procedural bacteremia was recorded in 103 (0.8%) and 7 (4.2%) of the general cohort and patients with neutropenia, respectively. Neutropenia (OR 3.2), low albumin level (OR 0.33), male gender (OR 1.71), older age (OR 1.02), fever before procedure (OR 2.09) and ICU/hematologic department settings were associated with increased risk for bacteremia in the general study population, in both univariate and multivariate analysis. A multivariate model including these factors was predictive of bacteremia (AUC 0.82, 95% CI 0.78-0.88). Bacteremia was associated with increased risk of mortality. Among patients with neutropenia, secondary composite endpoints were more frequent in patients admitted to the hematology department and with low albumin level. Antibiotics or granulocyte stimulating factor before procedure were not associated with a decreased risk for adverse outcomes. In comparison with GI endoscopic procedure, the risk for bacteremia was significantly higher among patients that underwent bronchoscopy (1.85% vs. 0.78%, respectively), but not significant among neutropenic patients undergoing these procedures (1.8% vs. 4.2%, respectively).
Conclusion: we report a low incidence of post-endoscopic bacteremia in our center. Low neutrophil level was found to be a risk factor for bacteremia. A model highly predictive of bacteremia was developed. Further studies to assess these factors are needed.
Disclosure: Nothing to disclose

P0176 INTRAGASTRIC ADJUSTABLE BALLOON: USING THE DEVICE IN ORDER TO PROMOTE THE MOST EFFECTIVE WEIGHT LOSS-A BRAZILIAN STUDY

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Introduction: Adjustable Balloon Therapy (ABT) is an effective minimal invasive technique for weight loss, proven widely. However, there is no published study comparing results using:1- Non-modified volume during the 12-month treatment;2-Submitted to upward adjustment with a fixed volume; 3-Associated with Liraglutide and 4- A combination of items 2 and 3.

Aims & Methods: From December 2016 to December 2017 were analyzed 159 patients (mean age 37.96±22.15, female 77.85%) who underwent and completed the 12-month therapy. 40 patients maintained initial volume until retrieval (IGB group). 35 received Liraglutide daily, initiated one month after implant, mean dose 2,18±0,53 mg for 9 consecutive months (LG group). 53 underwent the upward adjustment with 200 ml of sterile saline (mean 166days ±17,11 after placement) (UP group). 34 were submitted to both Liraglutide and upward adjustment (LGUP group). 3 in the UP and 1 in the LGUP group excluded. Percentage Total Body Weight Loss(%TBWL), Percentage Excess Weight Loss(%EWL), Body Mass Index (BMI) difference analyzed after balloon retrieval by the Kruskal-Wallis and the Wilcoxon test. The p set to ≤.005
Results:

	IGB GROUP	LG GROUP	LGUP GROUP	UP GROUP
(F)BMI-(I)BMI	6.14±1.99	7.72±2.42	7.69±1.84	5.97±2.21 #
%TBWL	18.18±3.66	22.53±3.64****	22.1±3.31****	17.14±4.68
%EWL	71.66±18.45	86.62±25.09*	80.56±15.96	61.82±16.34**

[Results]

#p=0.0205;****p<0.0001;*p=0.0252;**p=0.0392
Conclusion: The LG and the LGUP group presented the highest %TBWL, %EWL and BMI difference and had no statistical difference between, emphasizing Liraglutide efficiency. However, complications regarding upward adjustment should be considered. Liraglutide costs should be summed up.
Disclosure: Nothing to disclose

P0177 FULL-FIELD OPTICAL COHERENCE TOMOGRAPHY OF THE NORMAL DIGESTIVE MUCOSA: A PROMISING TOOL FOR THE STUDY OF THE DIGESTIVE BARRIER

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Introduction: Full-field optical coherence tomography (FF-OCT) is a non-invasive imaging technique, based on interferometry, allowing dynamic acquisition of images of ex vivo specimens on a microscopic scale.
Aims & Methods:
The aim of this study was to demonstrate the feasibility of imaging normal digestive biopsies using FF-OCT.
We enrolled adult subjects scheduled for an endoscopy with biopsies, who had no history of digestive disease. We *a posteriori* excluded patients, whose biopsies showed abnormal aspects at pathological examination. Four biopsies were sampled, 2 for pathological examination, 2 for immediate FF-OCT analysis, from 5 different locations: esophagus, gastric antrum, gastric fundus, duodenum or colon. Fresh biopsies were scanned using the LL-Tech benchtop scanner in order to perform an optical slicing beneath the tissue surface at selected depths (static mode) and a measurement of intracellular activity data (dynamic mode). Biopsies were then fixed in formaldehyde, sliced in a longitudinal plane parallel to the surface and stained using hematoxylin-eosin. FF-OCT images and pathological slides were then reviewed with the assistance of a senior pathologist.
Results: We enrolled 25 patients with normal biopsies of the esophagus (n=5), gastric fundus (n=10), gastric antrum (n=10), duodenum (n=7) and colon (n=6). Specific histological structures of each organ were clearly identified in 100% of FF-OCT images. For instance, the cellular structure of esophageal squamous epithelium with papillae, gastric crypts and glands, duodenal villi and colonic crypts was clearly seen at a 1μm resolution.
Conclusion: FF-OCT allows a morphological and functional analysis of digestive tissues on fresh routine endoscopic biopsies, at a subcellular scale. It is a promising tool for the study of the digestive barrier.
Disclosure: Nothing to disclose

P0178 WITHDRAWN

P0179 LOW RESIDUE DIET DURING 3 DAYS VERSUS 1 DAY IN PREPARATION FOR COLONOSCOPY FOR POPULATION SCREENING OF COLORECTAL CANCER: NONINFERIORITY RANDOMIZED CLINICAL TRIAL

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Introduction: To improve participation in the population screening program for colorectal cancer, to guarantee the quality of the exploration and to reduce its impact on the patient, it is necessary to provide the safest and most tolerable preparation. Although numerous studies have been conducted to determine which is the best purgative preparation and its administration regimen, no randomized study has been published regarding the number of days of low residue diet. Both the European and American guidelines give little concrete and low quality recommendation regarding the number of days stating "no more than 24 hours" and "several days" respectively.
Aims & Methods: To assess the efficacy and tolerance to a low-residue diet during a day in a comparison with three days in participants referred to screening colonoscopy. An equivalence margin of 5% was defined and a low diet was assigned during a day (Group A) or three days (Group B, control) without other differences in preparation. Participants with chronic constipation were given bisacodyl 10mg the night before the colonoscopy. Boston scale was used to determine the bowel cleansing. Inadequate preparation was defined as a puntuation lesser than 2 in any segment. A Likert scale was used for assesing the tolerance to the diet. We present the results of a intermediate analysis of the study.
Results: We included 210 participants in group A and 211 in group B. An adequate randomization was achieved without observing differences in age, sex, BMI, treatment with antidepressants, cirrhosis, reduced mobility or constipation. Neither in the time elapsed from the end of the preparation until the start of the colonoscopy. In group A 2 participants had an inadecuate preparation versus 10 (4.7%) in group B. This is a difference of -3, 78% (-6, 88, -1.12% CI 90% unilateral) (p < 0.05). In trems of tolerance to diet, group A obtained a maximum tolerance score (Likert 1) in 48.5% against 29.9% in B (p < 0.05), while there were no significant differences in tolerance to the evacuating preparation, Likert 1 36.9% Vs. 29.4% (p> 0.05). There were also no differences in the adenoma detection rate, 66.7% vs. 67.8%, nor in the withdrawal time with a median of 13 minutes vs. 14 (p> 0.05). In group B, cecal intubation was not achieved due to poor cleansing in 5 participants, whereas that did not occur in group A.
Conclusion: The results of this intermediate analysis show that for the preparation of the screening colonoscopy a low residue diet for 1 day is noninferior to 3 days and offers a better tolerance.
Disclosure: Nothing to disclose

P0180 THE UTILITY OF SELF-EXPANDABLE METALLIC STENT AS A BRIDGE TO SURGERY AGAINST MALIGNANT COLORECTAL OBSTRUCTION

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Introduction: Self-expandable metallic stent (SEMS) placement for malignant colorectal obstruction has been available from 2012 in Japan. On the other hand, SEMS placement as a bridge to surgery (BTS) is not recommended as a standard treatment of symptomatic left-sided malignant colonic obstruction in the European Society of Gastrointestinal Endoscopy Clinical Guideline. This is because there have been some concerns that SEMS placement has association with worse disease-free and overall survival. Therefore, we retrospectively investigated the treatment results.

Aims & Methods: Data collection was performed on the clinical outcomes from the patients who underwent colorectal resection against malignant colorectal obstruction between January 2012 and June 2018. A total of 22 patients were included in this analysis. Eleven patients received SEMS placement as BTS (Group A), and 11 patients received nasal ileus tube or emergency surgery (Group B). We retrospectively investigated the technical and clinical success rates of SEMS placement, the short-term outcomes (postoperative complication rate and 30-day mortality rate) and the long-term outcomes (progression free survival and overall survival).
Results: The mean age of the patients was 71 years (group A) and 77 years (group B), respectively. The male-to-female ratios were 3:8 (groupA) and 9:2 (group B). Tumor sites (cecum/ ascending/ transverse/ descending/ sigmoid/ rectum) were 0/1/1/2/5/2 (group A) and 5/0/3/1/1/1 (group B). The pStages (I/II/III/IV) were 0/4/4/3 (group A) and 0/1/5/5(group B), which were no significant differences between the two groups (p=0.308). In group A, the technical and clinical success rates for SEMS was 100% (11/11) and 91% (10/11). There was one case of stent perforation, but it was coincidentally detected during the elective operation. Regarding of the short-term outcomes, the postoperative complication rate was 9% (p=0.269), and the postoperative 30-day mortality rate was 0%. As for long-term outcomes, there were no significant statistical differences between the two groups in progression free survival (p=1.000) and overall survival (p=0.768), using the Kaplan-Meier method and long-rank test.
Conclusion: In our institute relatively high technical and clinical success rates were observed after SEMS placement. There were no significant differences of short-term and long-term outcomes between the two groups. These findings may suggest that the SEMS as BTS might be one of the options as long as the placement is successfully performed.
Disclosure: Nothing to disclose

P0181 ADENOMA DETECTION WITH CHROMO-ENDOSCOPY USING ORAL INDIGO CARMINE

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Introduction: Colonoscopy is currently the reference method to detect colorectal neoplasia, yet some adenomas remain undetected. Indigo carmine staining with various methods has shown interesting results for reducing this miss rate.
Aims & Methods: The aim of this study was to determine if the standard colonoscopy prep followed by oral indigo carmine intake shows the increase in the adenoma detection rate (adenoma and adenocarcinoma; ADR) and the mean number of adenomas per patient (MAP).
We introduced the oral indigo carmine technique to every subject and prospectively collected the data, and also performed retrospective review of endoscopic reports and medical charts of consecutive patients who underwent colonoscopy before introducing this technique to compare the results.
Results: 211 subjects were included in the study (105 in indigo group). The ADR was not significantly different between the groups; 44.8% in the indigo group versus 41.5% in the standard colonoscopy group (odds ratio, 1.15; 95% confidence interval, 0.9 - 1.52, p = 0.33). MAP was significantly greater in the indigo group (1.1) than in the standard colonoscopy group (0.81; p = 0.008). For advanced adenomas, the results were 10 (9.5%) and 7 (6.6%), respectively (p = 0.13).
Conclusion: The routine use of oral indigo carmine does not lead to higher ADR regardless of higher MAP.
Disclosure: Nothing to disclose

P0182 A 10-YEAR EXPERIENCE WITH BOWEL PREPARATION: PREDICTORS AND COLONOSCOPY OUTCOMES OF INADEQUATE BOWEL CLEANSING. A LARGE COHORT STUDY

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Introduction: The last decade brought in an outstanding advancement in endoscopic equipment and awareness of colonoscopy quality indicators. However, inadequate bowel preparation is still the main obstacle for a complete, thorough and quality procedure in a sizable mass of patients, constituting one of the most leading indications for repeated procedures. In the current study we aimed to identify risk factors associated with inadequate bowel preparation and better characterize these patients in our practice.
Aims & Methods: a retrospective, large cohort, single centre study. Electronic reports of colonoscopy procedures over a 10-year period were revised. Patients were divided based on the quality of bowel preparation into adequate and non- adequate bowel preparation groups. Multivariate analysis was performed to identify variables associated with inadequate bowel preparation including age, sex, setting (inpatient/outpatient), preparation regimen and procedures' indications. We also examined the effect of inadequate preparation on colonoscopy outcome and quality indicators.
Results: 28725 patients were included in the study. Of these, 6702 (23.3%) had inadequate bowel preparation. In multivariate analysis, increased age (OR= 1.015, 95% CI= 1.013-1.017; P< 0.01), male gender (OR =1.353, 95% CI=1.286-1.423; P< 0.01) and minority population (OR =1.635, 95%CI=1.531-1.746; P< 0.01) were significantly associated with inadequate bowel preparation. Inpatient setting was among the most prominent factors associated with poor bowel preparation (OR= 2.018, 95%CI 1.884-2.163; P value< 0.01). In regard to procedures' indications, significant associations with inadequate preparation were recorded for constipation (OR =1.373, 95%CI=1.24-1.519; P< 0.01), rectal bleeding (OR = 1.473, 95%CI= 1.355-1.602) and surveillance procedures after colonic resection (OR = 1.266, 95%CI= 1.089-1.472). Evaluation of procedure's outcome and quality indicators revealed that adequate bowel preparation was associated with enhanced polyp detection rate (26.8% vs 23.6%; OR= 1.22, 95% CI= 1.109-1.347; P< 0.01), increased colorectal cancer detection rate (2.8% vs. 2.4% OR= 1.402, 95% CI=1.146-1.716; P< 0.01), as well as increased cecal (96.4% vs. 73.5%; OR= 2.243, 95% CI= 2.095-2.403) and terminal ileum detection rates (8.1% vs. 5.4%; OR= 1.243, 95% CI= 1.088-1.434), when compared to inadequate preparation.
Conclusion: In this large cohort study we outlined various factors associated with inadequate bowel preparation. Further study is underway to examine tailored preparation regimens in this population.
Disclosure: Nothing to disclose

P0183 FEASIBILITY AND SAFETY OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR RECURRENT RECTAL LESIONS THAT AFTER TRANSANAL ENDOSCOPIC MICROSURGERY

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Introduction: Transanal endoscopic microsurgery (TEM) is a well-established local resection method. Although TEM is a useful and less invasive treatment, it has been reported to be associated with local recurrence rates of 3% to 19%. Occasionally surgical treatment such as low anterior resection or abdominal perineal resection may be required for such recurrent rectal lesions, however, they can have severe effects on patients' postoperative quality of life. Recently, several studies have demonstrated the usefulness of endoscopic submucosal dissection (ESD) for residual or locally recurrent colorectal lesions after endoscopic treatment. However, the utility of ESD for recurrent rectal lesions after TEM has not been fully investigated.
Aims & Methods: Aim of this study was to evaluate the feasibility and safety of ESD for recurrent rectal lesions after TEM. This study was performed at Kobe University Hospital and Kishiwada Tokushukai Hospital, which are tertiary referral centers in Japan. It examined the outcomes of 10 consecutive lesions in 9 patients, who underwent ESD between January 2006 and March 2018 for recurrent rectal lesions after TEM. The target lesions were preoperatively assessed via conventional and magnified chromoendoscopic examinations. As ESD technique, after TEM procedures involving full-thickness resection, the resultant fibrosis can be so severe that the border between the submucosa and muscle layer, and sometimes even that between the inner circular and outer longitudinal muscles, is invisible. In such cases, dissecting at the assumed level of the submucosal layer would carry a risk of cutting into the lesion, so we employed the previously reported peranal endoscopic myectomy (PAEM) technique.
Results: All lesions were successfully resected en bloc, and the R0 resection rate was 90%. The median sizes of the resected specimens and tumors (range) were 44 mm (21-70) and 27.5 mm (5-60), respectively. In present study, the PAEM technique was used to treat 4 lesions, and all of them had negative vertical margins. The pathological diagnoses included 4 adenomas and 6 cancerous lesions. The cancerous lesions included 5 cases of mucosal cancer and 1 case of SM1 cancer. No adverse events occurred. There was no recurrence during the follow-up period (median duration: 25 months).
Conclusion: ESD for recurrent rectal lesions after TEM achieved en bloc resection for all lesions without any complications. ESD appears to be a safe and feasible treatment for recurrent rectal lesions after TEM.
References: Toyonaga T, Ohara Y, Baba S et al. Peranal endoscopic myectomy (PAEM) for rectal lesions with severe fibrosis and exhibiting the muscle-retracting sign. Endoscopy 2018 Ito S, Hotta K, Imai K et al. Treatment strategy for local recurrences after endoscopic resection of a colorectal neoplasm. Surg Endosc 2018
Disclosure: Nothing to disclose

P0184 FACTORS INVOLVED IN ENDOSCOPISTS' CHOICE FOR PROPHYLACTIC CLIPPING AFTER EMR TO PREVENT DELAYED BLEEDING: A DISCRETE CHOICE EXPERIMENT

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Introduction: Flat and sessile colorectal adenomas are often resected endoscopically using endoscopic mucosal resection (EMR). Delayed bleeding after EMR occurs in up to 10% of patients. Recently, a multicenter study reported a significant decreased delayed bleeding (DB) rate after prophylactic clipping (PC) in right sided colonic lesions >2cm. As PC is associated with significant costs, its use is considered not cost-effective for small (< 2cm) polyps and left sided polyps. The practice of PC is not yet widely adopted in guidelines and clinical practice.
Aims & Methods: Our aim was to determine which predefined variables contribute to using PC in an international group of endoscopists. We performed an international survey study among endoscopists, structured as an online discrete choice experiment (DCE) with a choice based conjoint analysis. The survey was conducted in 428 gastroenterologists of the Dutch Association of Gastroenterology and Hepatology. Additionally, 69 international EMR experts were contacted and invited to forward the survey to other colleagues with EMR experience. Relevant variables hypothesized to influence decision-making for PC were selected by a panel of four EMR experts and included previous DB, periprocedural anticoagulant use, polyp size, morphology, location, intra-procedural bleeding and visible vessel(s) in the wound surface. Respondents answered ten sets of three hypothetical case scenarios with various option combinations of all of these variables, each time choosing only one scenario for PC. Alternatively, it was possible to choose a 'none'-option if they wouldn't use PC in any of the scenarios. Part-worth utility scores and importance weights were calculated for each level of the variables with a Hierarchical Bayes regression analysis and compared between subgroups using a T-test. Subsequently, considerations that were posed by participants in the comment section of the survey were analyzed quantitatively.

Results: The survey was completed by 190 endoscopists with experience in EMR from 17 different countries. In total, 6.8% of respondents would not use PC in any of the simulated situations, whereas 30.9% never chose the none-option in the survey. Except for polyp type (flat, sessile, mixed type), all tested variables were significant in the decision-making for PC with P< 0.01.

The most important factor was anticoagulant use, accounting for 22.5% in decision-making, followed by intra-procedural bleeding (16.3%), polyp size (16.2%), polyp location (15.9%), visible vessel(s) (13.5%) and previous DB (10%). Small polyps < 2 cm were considered eligible for PC by 14% of the responders in the presence of high-weighing factors such as anticoagulant use. In a subgroup analysis, no significant differences in importance weights were found when comparing high with low to moderately experienced EMR endoscopists.

Qualitative analysis showed that other variables, not included in the survey, were also considered in clinical decision making, such as technical possibility of clipping, prophylactic coagulation of visible vessels and distance of patient's residence to the hospital.

Conclusion: PC after EMR is commonly considered useful by endoscopists, usually based on known risk factors for DB.

Anticoagulant use was the most important factor in decision-making to perform PC, independent of the experience of the endoscopist. Nonetheless, although not considered cost-effective, 1 in 7 EMR endoscopists also apply PC for adenomas < 2 cm.

Disclosure: Nothing to disclose

P0185 EFFICACY OF COUNTER TRACTION USING A CLIP WITH A LOOPED THREAD FOR COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION

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Introduction: Colorectal endoscopic submucosal dissection (ESD) remains a difficult endoscopic procedure. Several traction methods have been reported that enable an appropriate view of the submucosal layer; however, almost all these methods have limitations regarding preparation, delivery, ease or cost. We have reported a treatment strategy for colorectal ESD using a clip with a looped thread, which has been developed to resemble a ring-shaped thread counter traction.

Our original counter traction does not require any special tools or devices and can be carried out without the removal and reinsertion of a scope. Additionally, this method is very easy and only requires thirty seconds to make one looped thread.

Aims & Methods: This study was performed to evaluate the efficacy of our traction method.

A 3-0 nylon suture and a clip (HX-610-135; Olympus, Tokyo, Japan) were used as the material. Between January 2017 and November 2018, colorectal ESD was carried out on 90 lesions. These lesions were allocated either to the group before introduction of the looped thread counter traction (non-looped thread; NLT) (n=66) or to the group after introduction (looped thread; LT) (n=24). We retrospectively investigated the background factors, treatment outcomes and complications.

Results: We achieved en bloc resections of all lesions. No significant differences were detected in the background factors or in the procedure time (P=0.298). The median time of the LT group (65 min) was shorter than that of the NLT group (80 min). There were 3 cases of perforation during ESD in the NLT group compared to 0 cases in the LT group (P=0.287). There were 4 cases of post-ESD bleeding (1-7 days after ESD) in the NLT group compared to 2 cases in the LT group (P=0.749).

Conclusion: No significant differences were detected in the treatment outcomes and complications in this study. But we think this traction method is useful, and we suggest that this counter traction method may be a superior method for colorectal ESD because the length of the thread can be adjusted and more clips or looped thread can be added as needed to maintain an appropriate view of the submucosal layer. Good visualization of the submucosal layer can prevent perforation and bleeding during ESD. The greatest advantages of this traction method include the low cost and ease. This method is readily available not only in high-volume centres but also in general hospitals. In this report, we demonstrate how to make the looped thread, how to tie the thread to a clip and how to carry out this traction method.

References: Mori H, Kobara H, Nishiyama N. et al. Novel effective and repeatedly available ring-thread counter traction for safer colorectal endoscopic submucosal dissection. Surg Endosc 2017; 31(7): 3040-3047
Disclosure: Nothing to disclose

P0186 AN INTERNATIONAL SURVEY OF UPTAKE AND BARRIERS FOR IMPLEMENTATION OF THE *RESECT AND DISCARD STRATEGY*

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Introduction: Optical real-time diagnosis (=*resect-and-discard* strategy) is an alternative to histopathology for diminutive colorectal polyps. However, clinical adoption of this approach seems sparse and we were interested in evaluating potential clinical uptake and barriers for implementation of this approach.

Aims & Methods: We conducted an international survey using the "Google forms" platform. Nine endoscopy societies distributed the survey. Survey questions measured current clinical uptake and barriers for implementing the *resect-and-discard* strategy, perceived cancer risk associated with diminutive polyps and potential concerns with using CT-colonography as follow-up, as well as non-resection of diminutive polyps.

Results: 808 endoscopists participated in the survey. 84.2% (95% CI 81.6%-86.7%) of endoscopists are presently not using the *resect-and-discard* strategy and 59.9% (95% CI 56.5%-63.2%) do not believe that the *resect-and-discard* strategy is feasible for implementation in its current form. European (38.5%) and Asian (45%) endoscopists had the highest rates of *resect-and-discard* practice, while Canadian (13.8%) and American (5.1%) endoscopists had some of the lowest implementation rates. 80.3% (95% CI 77.5%-83.0%) of endoscopists believe that using the *resect-and-discard* strategy for diminutive polyps will not increase cancer risk. 48.4% (95% CI 45.0%-51.9%) of endoscopists believe that leaving diminutive polyps in place is associated with increased cancer risk. This proportion was slightly higher (54.7%; 95% CI 53.6%-60.4%) when asked if current CT-colonography screening practice might increase cancer risks.

Conclusion: Clinical uptake of *resect-and-discard* is very low. Most endoscopists believe that *resect-and-discard* is not feasible for clinical implementation in its current form. The most important barriers for implementation are fear of making an incorrect diagnosis, assigning incorrect surveillance intervals and medicolegal consequences.

Disclosure: Phillipe Willems, Roupen Djinbachian, Saskia Ditisheim, Sinan Orkut, Heiko Pohl, Alan Barkun, Mickael Bouin and Bernard Faulques have no conflicts of interest relevant to this paper to declare. Daniel von Renteln is supported by a "Fonds de Recherche du Québec Santé" career development award and has received research funding from ERBE, Ventage, Pendopharm and Pentax and is a consultant for Boston Scientific and Pendopharm. The findings, statements, and views expressed are those of the authors and do not represent the views of the Department of Veterans Affairs or the United States Government.

P0187 THE CLINICAL OUTCOMES OF ENDOSCOPIC RESECTION FOR LOCAL RECURRENCE CASES RESECTED BY CFP IN PATIENTS WITH DIMINUTIVE POLYPS

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Introduction: Cold forceps polypectomy (CFP) is often used to remove diminutive colorectal polyps. It has few adverse events and can be implemented using routine biopsy techniques. In addition, jumbo biopsy forceps are considered superior to standard ones in removing colorectal polyps. Examining the margin of resected regions using narrow band imaging (NBI)-enhanced endoscopy can also improve complete resection rate. However, even in such cases using Jumbo forceps in NBI-enhanced endoscopy, local recurrence occurs in few cases. In such cases, lesions have to be treated again and clinical outcomes are still unknown.

Aims & Methods: We investigated clinical outcomes of treatment for patients with local recurrence of diminutive polyps resected by jumbo forceps biopsy in NBI endoscopy. This multicenter, prospective, single-arm observational study was conducted at 11 institutes of the National Hospital Organization in Japan between January 2015 and September 2018 (UMIN000015969). In total, 503 patients, aged 20-75 years, with diminutive polyps (≤5 mm) were prospectively assessed, and 1015 polyps were resected by jumbo forceps biopsy in NBI endoscopy. Among these, 955 lesions from 471 patients were followed-up 1 year post-CFP to examine local recurrence in the polypectomy sites (follow-up rate; 94.1%). Finally, local recurrence occurred in 18 patients (20 lesions, 2.1%), who were enrolled in this study. We analyzed clinicopathological characteristics of primary and local recurrent lesions, as well as short- and long-term clinical outcomes of treatment for local recurrent lesions including resection rates, adverse events, and re-recurrence rate.

Results: The patients consisted of 12 men (67%) and 6 women (33%) with a median age of 68.5 years (49-74). The mean primary polyp size was 3.9±0.9 mm. The number of resected primary polyps in the right and left colon were 12 (60%) and 8 (40%), respectively. The histological diagnoses of the primary resected polyps were low-grade adenomas in all cases, and the rate of one-bite polypectomy was 55% (11/20). Immediate bleeding occurred in 1 case; delayed bleeding or perforations were not observed. The mean size of local recurrent polyps was 1.5±0.6 mm; all were less than 3 mm. Re-CFP successfully managed local recurrent polyps in all cases, and the rate of one-bite polypectomy was 90% (18/20). The histological diagnoses of local recurrent polyps were low-grade adenomas in all cases; no adverse events occurred in any cases. Additionally, 16 of 18 patients (18/20 lesions) were subjected to a 1-year follow-up examination with colonoscopy (follow-up rate; 88.9%), and no re-recurrence occurred in any cases (0/18).

Conclusion: The local recurrence rate of diminutive polyps in CFP by jumbo forceps biopsy in NBI endoscopy was acceptable. When local recurrence occurred, the size was small, and it could be treated using re-CFP.

Disclosure: Nothing to disclose

P0188 SCREENING COLONOSCOPY FINDINGS AND COMPLICATIONS IN A MULTI-CENTER STUDY IN THE UNITED STATES

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Introduction: The Colonoscopy vs. Fecal Immunochemical Testing (FIT) in Reducing Mortality from Colorectal Cancer (CONFIRM) Study, a randomized study comparing annual FIT vs. colonoscopy in average risk adults aged 50-75, recently completed enrollment and is now following participants for cancer outcomes.

Aims & Methods: To determine 1) findings on baseline colonoscopy, 2) factors associated with baseline neoplasia and 3) 30 day complication rate. Advanced adenoma (AA) was defined as any adenoma ≥1cm, with high grade dysplasia or with villous histology. Univariable logistic regression was used to determine the association between baseline variables and findings of adenomas, advanced adenomas, and sessile serrated lesions (SSLs). See table for full variable list. Variables found to be significant at p≤0.1 were included in a multivariable logistic regression model, stratified by site. Participants found to have colorectal cancer were excluded from this analysis as this study is ongoing. Coordinators reviewed medical records and telephoned participants to determine complications. All serious adverse events (SAEs) were recorded, as were non-serious adverse events (AEs) deemed to be at least possibly related to colonoscopy.

Results: 15,806/17,340 colonoscopies were complete with cecal intubation (97.3%) and adequate preparation (92.4%). Polyps were found in 66.0%. Among those without polyps, mean withdrawal time was 11.1 minutes. Non-gastroenterologists were less likely to detect polyps (0.65; 95% CI 0.58-0.77) and adenomas (Table). Trainee involvement was associated with higher polyp detection (1.24; 95% CI 1.14, 1.35). Factors associated with adenoma and AA are shown in the table. Factors associated with AA included age, male sex, smoking and alcohol use. Black race, college degree, NSAIDs and prior colonoscopy were inversely associated with AA. Independent predictors of SSL's included BMI and smoking; while Blacks had 62% reduced odds of SSL's. Former aspirin use was associated with adenomas, but this finding was modified by age.

There were 235 SAEs reported (1.3%), with 52 related (0.36%) and 38 possibly related (0.25%) to colonoscopy, including 31 serious bleeding events (.18%), 31 cardiovascular events (.18%) and 5 perforations (.03%). 585 AEs were reported (2.9%), most (84%) were mild, 15% were moderate and 0.1% were severe,

Conclusion: Our study confirms the importance of several demographic and environmental risk factors for adenomas, AA and SSL. AEs and SAEs related to colonoscopy occur in approximately 3% and 0.5% of colonoscopies, respectively.

The first two authors are co-first authors.

Disclosure: Nothing to disclose

	Adenoma N=7,222 (45.7%)	Advanced Adenoma N=1,481 (9.4%)	Sessile Serrated Lesion N=589 (3.7%)
Baseline Variable	Multivariable	Multivariable	Multivariable
Age, per year (mean 59.2)	1.05 (1.04-1.05)	1.04 (1.03-1.05)	1.01 (1.00-1.03)
Female (ref=Male, 93.4%)	0.48 (0.41-0.56)	0.66 (0.49-0.89)	NS on univariale
Race: White (72.9%)	Ref	Ref 0.81 (0.70-0.93)	Ref
Black (22.7%)	0.80 (0.73-0.88)		0.38 (0.28-0.50)
AI/AN (0.7%)	0.80 (0.55-1.18)	1.12 (0.61-2.05)	1.20 (0.52-2.75)
Asian (1.7%)	0.77 (0.59-1.01)	0.64 (0.38-1.08)	0.77 (0.38-1.58)
Other (2.0%)	1.09 (0.84-1.42)	1.12 (0.75-1.65)	0.74 (0.38-1.45)
Ethnicity: Non-Hispanic (87.7%)	Ref	NS on univariale	NS on univariale
Hispanic (12.1%)	0.81 (0.71-0.93)		
Education: ≤ High School (27.0%)	Ref	Ref	NS on univariale
Some College (34.9%)	0.93 (0.86-1.02)	0.95 (0.83-1.09)	
College Degree (37.8%)	0.90 (0.83-0.99)	0.85 (0.73-0.97)	
BMI, per unit (mean 30.3)	1.02 (1.01-1.02)	NS on univariale	1.02 (1.01-1.04)
2° Relative with CRC: none (96.0%)	Ref	Ref	Ref
At least one (4.0%)	0.97 (0.82-1.15)	0.91 (0.67-1.24)	0.61 (0.36-1.05)
Aspirin Use: Never (51.1%)	Ref		
Former Use (7.8%)	4.57 (1.54-13.56)	NS on univariale	NS on univariale
Current Use (41.0%)	1.60 (0.87-2.97)		
NSAID Use: Never (57.4%)	Ref	Ref	NS on univariale
Former use (9.8%)	1.04 (0.92-1.16)	0.88 (0.72-1.07)	
Current use (32.8%)	0.84 (0.78-0.90)	0.87 (0.77-0.98)	
Statin Use: Never (53.9%)	Ref	NS on univariale	NS on univariale
Former use (6.4%)	1.11 (0.96-1.27)		
Current use (39.6%)	1.14 (1.06-1.23)		
Smoking: Never (38.7%)	Ref	Ref	Ref
Former Smoker (38.9%)	1.16 (1.07-1.25)	1.29 (1.12-1.47)	1.38 (1.13-1.69)
Current Smoker (22.4%)	1.65 (1.51-1.81)	1.78 (1.54-2.07)	1.68 (1.34-2.12)
ETOH/day, per drink (mean 0.78)	1.03 (1.01-1.05)	1.04 (1.01-1.07)	NS on univariale
METs/day, per unit (mean 14.5)	1.00 (0.99-1.00)	NS on univariale	NS on univariale
Age*Aspirin Usage/Never	Ref		
Age*Formerly takes Aspirin	0.98 (0.96-0.99)	NS on univariale	NS on univariale
Age*Currently takes Aspirin	0.99 (0.98-1.00)		
Specialty: Gastroenterologist (89.2%)	Ref	NS on univariale	NS on univariale
Non-Gastro (8.5%)	0.73 (0.64-0.85)		
Trainee Involved: No (64.7%)	Ref	Ref	Ref
Yes (35.2%)	1.19 (1.09-1.29)	1.11 (0.99-1.25)	1.19 (1.00-1.42)
Colonoscopy at VA: Yes (99.0%)	NS on univariale	NS on univariale	Ref
No (1.0%)			1.53 (0.61-3.80)
Prior Colonoscopy: No (72.6%)	NS on univariale	Ref	NS on univariale
Yes (27.2%)		0.65 (0.57-0.75)	

[P0188 Table. Predictors of Colonoscopy Findings (OR; 95% Confidence Interval)]

P0189 USEFULNESS AND SAFETY OF COLORECTAL HYBRID ESD AND PRECUTTING EMR USING A NOVEL MULTIFUNCTIONAL SNARE FOR SSPS

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Introduction: Precutting endoscopic mucosal resection (EMR) and hybrid endoscopic submucosal dissection (ESD) have the advantages of decreased procedure time and perforation risk. Recently, a novel multifunctional snare (SOUTEN; Kaneka Medics, Tokyo, Japan) to enable easy and time-efficient hybrid ESD, involving circumferential incision and partial submucosal dissection, followed by snare resection, was introduced. The SOUTEN snare combines an 18.5-mm snare loop with a 1.5-mm needle-knife and a knob-shaped tip attached to the top of the snare loop. Sessile serrated polyps (SSPs) are increasingly recognized as a significant contributor to the epidemiologic burden of colorectal cancer; therefore, it is desirable that SSPs are resected en bloc for reliable histologic assessment of the resected specimen. We sometimes experience difficult SSP cases for en bloc EMR, in which the polyps are more than 20 mm in size or in which the border of the lesion is difficult to identify. Until now, there have been few reports regarding the outcomes of precutting EMR and hybrid ESD using SOUTEN for SSPs.

Aims & Methods: The aim of this study was to evaluate the usefulness and safety of colorectal hybrid ESD and precutting EMR for SSPs using SOUTEN. We analyzed 14 SSPs in 12 patients (2 male and 10 female, mean age: 69.1 years) who underwent hybrid ESD or precutting ESD using SOUTEN at our hospital between May 2018 and March 2019. The clinicopathological characteristics, en bloc resection rate, histological complete resection rate, curative resection rate, tumor size, specimen size, procedure time, and adverse event rate were evaluated.

Results: Of the 14 lesions, 1 (7%) was located in the cecum, 6 (43%) in the ascending colon, 6 (43%) in the transverse colon, and 1 (7%) in the descending colon. All lesions had a 0-IIa macroscopic polyp morphology, and all lesions were histopathologically identified as SSPs (low grade). Among the treatment methods, the hybrid ESD-to-precutting EMR ratio was 8/6. The mean tumor and specimen sizes were 18.2 mm, and 24.5 mm, respectively. The en bloc, histological complete, and curative resection rates were 100% (14/14), 100% (14/14), and 100% (14/14), respectively. The median procedure time was 16.5 minutes. There was no bleeding, perforation, or stricture postoperatively.

Conclusion: Hybrid ESD/precutting EMR using SOUTEN for SSPs is a safe and effective treatment option because of sufficient submucosal swelling after injection of the submucosal layer. A prospective study with a large number of cases should be conducted in the future to validate our results.

Disclosure: Nothing to disclose

P0190 COLON CLEANSING EFFICACY AND SAFETY OF 1L NER1006 IN PATIENTS WITH MILD TO MODERATE RENAL IMPAIRMENT: POST HOC ANALYSIS OF RANDOMISED PHASE 3 CLINICAL TRIALS

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Introduction: Only polyethylene glycol (PEG) bowel preparations are recommended for patients with renal failure. This post hoc analysis of randomised phase 3 clinical trials assessed the colon cleansing efficacy of the first 1L PEG, NER1006, in renally impaired versus non-renally impaired patients [1-3].

Aims & Methods: Patients received split dosing regimens of NER1006, either day-before (PM/PM), overnight (PM/AM), or morning-only (AM/AM). Cleansing efficacy was assessed by treatment blinded central readers using the Harefield Cleansing Scale (HCS). The efficacy analysis included patients with a documented renal status and colonoscopy data. Patients were stratified into creatinine clearance rate (CrCl) groups: normal renal function (≥90 mL/min), mild renal insufficiency (≥60 to < 90 mL/min), or

moderate renal insufficiency (≥30 to < 60 mL/min). Patients with severe renal insufficiency were excluded.

Results: Among 1134 randomised patients, 1016 were assessed for efficacy (renal status; 692 mild/moderate, 324 normal). No significant difference was observed in the overall cleansing success rates in mild and moderate versus normal (Table). Safety was assessed in 1028 patients. The types of TEAEs were generally consistent between mild and moderate and normal. The most common TEAEs in all patient groups were gastrointestinal i.e. nausea, vomiting and dehydration. There were numerically more TEAEs in patients with moderate renal insufficiency versus normal. However, this may reflect the patients' disease state.

Conclusion: The current efficacy and safety findings support the use of NER1006 as a bowel preparation in patients with mild to moderate renal impairment.

Successful overall colon cleansing using the HCS	Mild to moderate renal impairment: CrCl 30-<90 mL/min	Normal renal function: CrCl 90+ mL/min	P value
MORA PM/AM N=262	96% (183/190)	97% (69/71)	0.63
MORA AM/AM N=270	91% (182/200)	91% (62/68)	0.52
DAYB PM/PM N=236	64% (91/142)	67% (61/91)	0.68
NOCT PM/AM N=255	92% (147/160)	94% (88/94)	0.69

[Percentage of NER1006 patients with successful overall colon cleansing using the HCS in patients with renal-impairment vs normal renal function.]

References: 1. Bisschops R et al. Endoscopy 2019; 51(1):60-72 2. DeMicco MP et al. Gastrointestinal Endoscopy 2018; 87(3):677-687 3. Schreiber S et al. Endoscopy 2019; 51(1):73-84

Disclosure: Marco Antonio Alvarez-Gonzalez: An investigator in the MORA study and has received honoraria from Norgine for Advisory Board attendance and from Casen-Recordati for speaking and teaching Soniya Mokashi: Employee of Norgine. Cesare Hassan: An investigator in the DAYB study and received honoraria from Norgine Ltd. for advisory board attendance; no other conflicts of interest.

P0191 FEASIBILITY OF ILEAL INTUBATION IN COLONOSCOPY WITH ENDOCUFF: A PROSPECTIVE OPEN LABEL COMPARISON

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Introduction: Endocuff (EC) is a mucosal exposure device attached to the distal tip of the colonoscope. Adenoma detection rate (ADR) can be improved with EC and the examination time (without reducing the ADR) can be reduced (1,2). The use of EC influencing the ileum intubation rate (IIR) has been investigated in only two studies as secondary endpoint with contradictory results (3,4).

Aims & Methods: We prospectively analysed the use of an EC and ileum intubation at the Kantonsspital St. Gallen in Switzerland between January to December 2018 performed by 3 experienced endoscopists and 1 trainee. Scientific data security were approved by the local ethics commission (EKSG14/099). EC was only applicated for screening or follow-up colonoscopy. The withdrawal time had to be at least 6 minutes. Significance was calculated with the Fishers Exact Test. Adenoma detection rate (ADR) was determined.

Results: We included 570 patients, median age 60 years (range 21-94), 51% were male. Of the 570 colonoscopies, 63% were performed with EC (n=359). Colonoscopy with EC and intubation of the terminal ileum was achieved in 85.8% (308 of 359 patients). Without EC, the ileum was intubated in 82% (173 of 211 patients). There was no significant difference (p=0.234). ADR with EC was 45% and without EC 43%, p< 0.00001. IIR for the trainee (n=87) was 71% with EC and 76% without EC (p=0.81).

Conclusion: Colonoscopy with the use of Endocuff achieved the same ileum intubation rate as without Endocuff. The need of ileum intubation therefore is not an argument against the use of Endocuff. In contrast, the ADR significantly improves with the use of an EC.

References: 1. Rex DK, Slaven JE, Garcia J, et al. Endocuff Vision Reduces Inspection Time Without Decreasing Lesion Detection in a Randomized Colonoscopy Trial. Clin Gastroenterol Hepatol 2019. Available at: https://linkinghub.elsevier.com/retrieve/pii/S1542356519300357 [Accessed February 18, 2019]. 2. Williet N, Tournier Q, Vernet C, et al. Effect of Endocuff-assisted

colonoscopy on adenoma detection rate: meta-analysis of randomized controlled trials. Endoscopy 2018;50:846-860. 3. Floer M, Biecker E, Fitzlaff R, et al. Higher Adenoma Detection Rates with Endocuff-Assisted Colonoscopy - A Randomized Controlled Multicenter Trial. PLoS ONE 2014;9. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4255000/ [Accessed February 18, 2019]. 4. González-Fernández C, García-Rangel D, Aguilar-Olivos NE, et al. Higher adenoma detection rate with the endocuff: a randomized trial. Endoscopy 2017;49:1061-1068.

Disclosure: Nothing to disclose

P0192 1L NER1006 IMPROVES HIGH-QUALITY COLON CLEANSING VERSUS STANDARD BOWEL PREPARATIONS: POST HOC ANALYSIS OF PHASE 3 CLINICAL TRIALS USING REAL-WORLD CLEANSING ASSESSMENT BY SITE ENDOSCOPISTS

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Introduction: Colonoscopy requires bowel cleansing; high-quality cleansing facilitates lesion detection. NER1006 is a 1L polyethylene glycol (PEG) bowel preparation. This post hoc analysis of three randomised trials investigated cleansing efficacy assessed, as in clinical practice, by site endoscopists [1-3].

Aims & Methods: Patients received either a 2-day evening/morning regimen of NER1006 (N2D), 2L PEG+ascorbate (2LPEG), or oral sulfate solution (OSS); or day-before NER1006 (NDB) or sodium picosulfate plus magnesium citrate (SPMC). Morning-only NER1006 (N1D) dosing was also evaluated. Cleansing was assessed by treatment-blinded site endoscopists using the Harefield Cleansing Scale (HCS). This analysis included only patients with self-reported 100% treatment adherence. Overall cleansing success (HCS grade A or B), overall high-quality cleansing success (HCS grade A), and the proportion of high-quality segments (HCS 3-4) per treatment population were analysed.

Results: Among 1985 randomised patients, 1367 were included (Table). Overall cleansing success was higher with N2D than 2LPEG (97.5% vs 93.0%) and more patients had overall high-quality cleansing with N2D and N1D than 2LPEG (72.1% and 68.4% vs 56.0%). N2D delivered more overall high-quality cleansing than OSS (77.3% vs 69.8%). Overall cleansing success was higher with NDB than SPMC (74.5% vs 62.9%) and more patients achieved HCS Grade A with NDB than SPMC (29.0% vs 12.0%). More high-quality segments were demonstrated with N2D and N1D versus 2LPEG (87.1% and 84.4% vs 76.3%), with N2D versus OSS (89.5 % vs 84.4%) and with NDB than SPMC (60.3% vs 47.0%).

Conclusion: When assessed by site-endoscopists NER1006 delivers greater high-quality, HCS grade A, cleansing than 2LPEG, OSS, or SPMC.

Phase 3 trial	MORA			NOCT		DAYB	
Cleansing success	N2D	N1D	2LPEG	N2D	OSS	NDB	SPMC
Split dosing regimen	Overnight	Morning only	Overnight	Overnight	Overnight	Day before	Day before
Sample size: N	204	193	200	225	225	145	175
Overall cleansing success HCS Grades A+B, n/N (%)	199/204 (97.5)	180/193 (93.3)	186/200 (93.0)	211/225 (93.8)	210/225 (93.3)	108/145 (74.5)	110/175 (62.9)
Overall cleansing success, P-value	P=0.016	P=0.459		P=0.424		P=0.012	
Overall high-quality cleansing success HCS Grade A, n/N (%	147/204 (72.1)	132/193 (68.4)	112/200 (56.0)	174/225 (77.3)	157/225 (69.8)	42/145 (29.0)	21/175 (12.0)
Overall high-quality cleansing success; P-value	P<0.001	P=0.006		P=0.035		P<0.001	
High-quality segments HCS 3-4, n/N (%); P-value	888/1020 (87.1)	814/965 (84.4)	763/1000 (76.3)	1007/1125 (89.5)	950/1125 (84.4)	437/725 (60.3)	411/875 (47.0)
High-quality segments; P-value	P<0.001	P<0.001		P<0.001		P<0.001	

[High-quality colon cleansing as assessed by site endoscopists in patients with self-reported 100% treatment adherence]

References: 1. Bisschops R et al. Endoscopy 2019; 51(1):60-72 2. DeMicco MP et al. Gastrointestinal Endoscopy 2018; 87(3):677-687 3. Schreiber S et al. Endoscopy 2019; 51(1):73-84

P0193 UNDERWATER ENDOSCOPIC MUCOSAL RESECTION IMPROVES R0 RESECTION RATE OF 10-20-MM COLORECTAL POLYPS: RESULTS OF A MULTICENTER RANDOMIZED CONTROLLED TRIAL

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Introduction: Endoscopic mucosal resection (EMR) with submucosal injection is widely performed to remove colorectal polyps, and underwater EMR (UEMR) without submucosal injection has been reported to be useful for large colorectal polyps. We recently reported the results of a multicenter randomized controlled trial that compared R0 resection rates of 10-20-mm colorectal polyps between UEMR and conventional EMR (CEMR)[1].
Aims & Methods: This study aimed to reveal independent predictors for R0 resection by post hoc analysis of the multicenter randomized controlled trial conducted at five Japanese institutions (UMIN000018989). Patients aged ≥20 years with 10-20-mm colorectal mucosal lesions (adenoma, intramucosal adenocarcinoma, or sessile serrated adenoma/polyp) were randomly assigned to the UEMR or CEMR group. Only the most proximal lesion was registered. Exclusion criteria were as follows: pedunculated lesions, residual lesions after endoscopic resection, inflammatory bowel disease, familial polyposis, electrolyte abnormality, coagulopathy, or severe organ failure. In the CEMR group, mucosal resection was performed with submucosal injection in an environment of air or carbon dioxide. In the UEMR group, the colonic lumen was filled with water and EMR was performed without submucosal injection. The intergroup difference in R0 resection rates was the primary endpoint. Multivariate logistic regression analysis was used for comparison of the R0 and non-R0 groups.
Results: A total of 214 patients were enrolled between February 2016 and December 2017. Finally, 108 in the UEMR group and 102 patients in the CEMR were analyzed in an intention-to-treat analysis. The R0 resection rate of the UEMR group (69% [74/108; 95% confidence interval (CI), 59-77%]) was significantly higher than that of the CEMR group (50% [51/102; 95% CI, 40-60%]) (p = 0.011). There was no significant intergroup difference in median procedure time (165 vs. 175 s) or adverse events rate (2.8% vs. 2.0%). Multivariate analysis revealed that procedure (UEMR vs CEMR: odds ratio, 2.24 [95% CI, 1.24-4.03]) and tumor diameter (≥15 mm vs < 15 mm: odds ratio, 0.56 [95% CI, 0.31-0.99]) were independent factors of R0 resection rate (Table).

		Odds ratio [95% CI]	P value
Procedure	UMER/EMR	2.24 [1.24, 4.03]	0.007
Endoscopist	Non-expert/expert	0.83 [0.46, 1.49]	0.530
Sex	Male/female	1.21 [0.65, 2.24]	0.550
Tumor diameter	≥15 mm/<15 mm	0.56 [0.31, 0.99]	0.048
Morphology	Superficial/sessile	0.95 [0.50, 1.81]	0.890
Age	≥70 y/<70 y	0.80 [0.44, 1.45]	0.460
Location	Rectum	1.00	0.244
	Right-sided colon	0.93 [0.30, 2.87]	
	Left-sided colon	1.70 [0.52, 5.52]	

[Results of multivariate analysis for R0 resection]

Conclusion: UEMR featured an improved R0 resection rate of 10-20-mm colorectal polyps without increasing procedure time or the adverse event rate. UEMR procedure and polyp size < 15 mm were independently related to R0 resection.
References: 1) Yamashina T, Uedo N, et al. Comparison of Underwater versus Conventional Endoscopic Mucosal Resection of Intermediate-Size Colorectal Polyps. Gastroenterology 2019, in press
Disclosure: Nothing to disclose

P0194 PREDICTION OF COLON ADENOMA PATHOLOGY BY APPLICATION OF ARTIFICIAL INTELLIGENCE

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Introduction: Detection and diagnosis of colon adenoma have long been emphasized in reducing colon cancer incidence. Since confirmation of the colon cancer diagnosis is by pathology, there has been lots of efforts to find and diagnose the colonic lesion more precisely before histological analysis. To spot the polyp and predict its pathology more accurately, there has been not only promising imaging technique development but also several studies using artificial intelligence for polyp recognition and its classification. The aim of this study is to develop computer-aided diagnostic system for colon adenoma.
Aims & Methods: We labeled the colonoscopic data into 4 classes according to the final pathology; Normal, Low-grade dysplasia, High-grade dysplasia, and Adenocarcinoma. The total number of colonoscopic pictures was 2507; Normal, 903; Low-grade dysplasia, 738; High-grade dysplasia, 459; and Adenocarcinoma ,407, and we separated them into the train set and the test set. We removed unnecessary black pads from the original images, and we resized our data into 224 by 224 for modeling.
Results: We used a ResNet50 model pre-trained with Imagenet data to classify the adenoma. The model we used classified the class with 86% accurary. We used a few data augmentation methods to improve the data and utilized heatmap technique to explain the results. We also compared our data with the classification pilot test results from 6 endoscopists.
Conclusion: The trained model successfully distinguished the colon adenoma pathology. There should be follow up studies to detect and diagnose the colon adenoma in real-time practice.
Disclosure: Nothing to disclose

P0195 USEFULNESS OF MAGNIFYING NARROW-BAND IMAGING ENDOSCOPY AND MAGNIFYING CHROMOENDOSCOPY FOR DIAGNOSIS OF SESSILE SERRATED ADENOMA/POLYP WITH DYSPLASIA/ CARCINOMA

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Introduction: Sessile serrated adenoma/polyp (SSA/P), an early precursor lesion in the serrated neoplasia pathway [1], is now considered a major contributor to the failure of colonoscopy in the prevention of colorectal cancers, known as "interval cancer" [2]. Therefore, accurate diagnosis of SSA/P and its dysplastic components is endoscopically important. However, the usefulness of magnifying endoscopy for serrated lesions with dysplastic changes has not yet been fully elucidated.
Aims & Methods: The aim of this study was to verify the usefulness of magnifying narrow-band imaging (NBI) endoscopy and magnifying chromoendoscopy for the diagnosis of SSA/P with dysplasia/carcinoma. Among the endoscopically or surgically resected lesions pathologically diagnosed as SSA/P with dysplasia or invasive carcinoma at Juntendo University Hospital (Tokyo, Japan) between 2011 and 2018, 73 (from 73 patients), including 44 low-grade dysplasia (LGD), 17 high-grade dysplasia (HGD), and 12

submucosal invasive carcinoma (SIC), were assessed. We retrospectively evaluated magnifying NBI endoscopic and magnifying chromoendoscopic findings using the Japan NBI Expert Team (JNET) system [3] and Kudo's pit pattern classification [4], respectively.

Results: The clinicopathological and endoscopic characteristics of the studied lesions are summarized in Table 1. All the groups were more frequently located in the proximal colon. The SSA/P-SICs tended to be larger than the SSA/P-LGDs and SSA/P-HGDs. As for the JNET classification with magnifying NBI endoscopy, 63 SSA/P lesions (86%) exhibited type 1 and type 2A, 2B, or 3, corresponding to SSA/P and dysplasia/carcinoma, respectively. The pit pattern analysis revealed that 61 SSA/P lesions (84%) had a combination of types II (including type II-open) and III$_L$, IV, V$_I$, or V$_N$ pit patterns, corresponding to SSA/P and dysplasia/carcinoma, respectively. Furthermore, both magnifying NBI endoscopy and magnifying chromoendoscopy had high sensitivity (90%) for diagnosing SSA/P with dysplasia/carcinoma.

Conclusion: Our findings suggest that the use of magnifying NBI endoscopy and magnifying chromoendoscopy might be useful for the diagnosis of SSA/P with dysplasia/carcinoma. This increased awareness may also improve recognition and complete resection of SSA/Ps with dysplasia or invasive carcinoma, and reduce the rates of interval cancer.

Variable	SSA/P-LGD (n = 44)	SSA/P-HGD (n=17)	SSA/P-SIC (n = 12)
Age (years) *	62 ± 11 (35 - 82)	68 ± 9 (51 - 81)	72 ± 6 (60 - 79)
Sex: Male / Female	23 / 21	8 / 9	3 / 9
Location: Proximal / Distal colon	35 / 9	14 / 3	11 / 1
Size of tumour (mm)	14 ± 7 (6 - 35)	14 ± 7 (6 - 33)	20 ± 16 (6 - 65)
Macroscopic type:			
0-Ip / 0-Isp / 0-Is / 0-IIa / 0-IIa+Is / 0-IIa+IIc	1 / 4 / 2 / 16 / 19 / 2	- / 3 / 2 / 10 / 2 / -	- / 2 / 1 / 5 / 1 / 3
JNET classification **:			
Type 1 only	6 (13%)	4 (24%)	-
Type 1 + Type 2A	36 (82%)	8 (47%)	2 (17%)
Type 1 + Type 2B	2 (5%)	5 (29%)	8 (67%)
Type 1 + Type 3	-	-	2 (17%)
Pit pattern classification ***:			
Type II only	10 (23%)	2 (12%)	-
Type II + Type IIIL or IV	34 (77%)	9 (53%)	3 (25%)
Type II + Type VI or VN	-	6 (35%)	9 (75%)
Age and size of tumor are represented as mean ± SD (range).			
* SSA/P-LGD vs SSA/P-HGD, P < 0.05; SSA/P-LGD vs SSA/P-SIC, P = 0.002			
** SSA/P-LGD vs SSA/P-SIC, P < 0.001; SSA/P-HGD vs SSA/P-SIC, P = 0.024			
*** SSA/P-LGD vs SSA/P-HGD, P < 0.001; SSA/P-LGD vs SSA/P-SIC, P < 0.001			

[Table 1. Clinicopathological and endoscopic characteristics of colorectal lesions studied.]

References: 1. O'Brien MJ, Yang S, Mack C, et al. Comparison of microsatellite instability, CpG island methylation phenotype, BRAF and KRAS status in serrated polyps and traditional adenomas indicates separate pathways to distinct colorectal carcinoma end points. Am J Surg Pathol. 2006; 30: 1491-1501. 2. Sawhney MS, Farrar WD, Gudiseva S, et al. Microsatellite instability in interval colon cancers. Gastroenterology. 2006; 131: 1700-1705. 3. Sano Y, Tanaka S, Kudo SE, et al: Narrow-band imaging (NBI) magnifying endoscopic classification of colorectal tumors proposed by the Japan NBI Expert Team. Dig Endosc. 2016; 28: 526-533. 4. Kudo S, Tamura S, Nakajima T, et al. Diagnosis of colorectal tumorous lesions by magnifying endoscopy. Gastrointest Endosc. 1996; 44: 8-14.

Disclosure: Nothing to disclose

P0196 EFFECTIVENESS AND TOLERABILITY OF VERY-LOW-VOLUME PREPARATION FOR COLONOSCOPY: A PROSPECTIVE, MULTICENTER OBSERVATIONAL STUDY

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Introduction: The effectiveness of bowel cleansing is essential for a quality colonoscopy since it affects diagnostic accuracy and adenoma detection rate. Recently, a very-low-volume 1L PEG-ASC solution (Plenvu®; Norgine, Harefield, UK) has been introduced on the evidence arising from three parallel phase 3 randomized controlled trials showing non-inferiority respect to comparators [1-3].

Aims & Methods: This study aimed to assess the effectiveness and tolerability of novel 1L PEG preparation compared to 4L and 2L PEG solutions in a real-life setting and to evaluate independent factors associated with a bowel cleansing success.

All in- and out-patients aged 18 years and over scheduled for a screening, surveillance or diagnostic colonoscopy, after an afternoon only or afternoon/morning 1, 2 or 4L PEG-based preparation were consecutively enrolled from September 2018 to February 2019 in 5 Italian centres. Bowel cleansing was assessed through the Boston Bowel Preparation Scale (BBPS), a bowel cleansing success was defined as a total BBPS≥6 with a partial BBPS≥2 in each colon segment and a high-quality cleansing of the right colon as a partial BBPS=3. Tolerability was evaluated through a semi-quantitative scale with a score ranging from 0 to 10. Safety was monitored through adverse event (AE) reporting.

Results: 1289 patients meeting inclusion criteria were enrolled in the study. The mean age was 60.5±14.1 years with an equal gender balance, and the main indications of colonoscopy in 58% of cases were screening and surveillance for CRC.Overall, 490 patients performed a 4L PEG preparation (Selgesse®), 566 a 2L PEG cleansing (Moviprep® or Clensia®) and 233 a 1L PEG preparation (Plenvu®).

Overall, bowel cleansing by BBPS was 6.3±1.5, 6.2±1.5 and 7.3±1.5 (p< 0.001) while right colon cleansing was 1.7±0.6, 1.6±0.6 and 2.1±0.6 (p< 0.001) for 4L, 2L and 1L PEG preparation respectively. A bowel cleansing success was achieved in 72.4%, 74.5% and 90.1% (p< 0.001), while an high-quality cleansing of the right colon in 15.5%, 11.7% and 39.5% (p< 0.001) for 4L, 2L and 1L PEG preparation groups, respectively.

The 1L preparation was the most tolerated compared to the 2 and 4L PEG solutions, with an average score of 7.8±1.7 vs 7.1±2.0 and 7.3±2.0 (p< 0.001) respectively, in the absence of serious adverse events within any of the three groups.

At multivariate analysis, age (OR = 0.98, 95% CI = 0.97-0.99; P = 0.02), absence of diabetes (OR = 1.51, 95% CI = 1.01-2.25; P = 0.04), adequate cleansing at previous colonoscopy (OR = 2.37, 95% CI = 1.37-4.09; P = 0.002), afternoon-morning split regimen (OR = 2.52, 95% CI = 1.65-3.83; P < 0.001), low-fiber diet for at least 3 days preceding colonoscopy (OR = 2.31, 95% CI = 1.61-3.31; P< 0.001), colonoscopy within 5 hours after the end of the preparation(OR= 2.16, 95% CI = 1.30-3.60; P= 0.003) and tolerability score (OR = 1.22, 95% CI = 1.14-1.31; P< 0.001) were independently associated with a bowel cleansing success.

Conclusion: The novel 1L PEG-ASC solution (Plenvu®) presents greater effectiveness compared to higher-volume PEG preparation in terms of overall bowel cleansing and high-quality cleansing of the right colon with the advantage of a higher adherence and a significantly better tolerability profile respect to comparators. In the next future, this new very-low-volume solution will be useful to improve the tolerability of bowel preparation, increasing at the same time the adherence to CRC screening and surveillance programs.

References: 1) DeMicco MP, Clayton LB, Pilot J, et al. Novel 1 L polyethylene glycol-based bowel preparation NER1006 for overall and right-sided colon cleansing: a randomized controlled phase 3 trial versus trisulfate. GastrointestEndosc. 2018;87:677-687. 2) Bisschops R, Manning J, Clayton LB, et al. Colon cleansing efficacy and safety with 1 L NER1006 versus 2 L polyethylene glycol + ascorbate: a randomized phase 3 trial. 3) Schreiber

S, Baumgart DC, Drenth JPH, et al. Colon cleansing efficacy and safety with 1 L NER1006 versus sodium picosulfate with magnesium citrate: a randomized phase 3 trial.
Disclosure: Nothing to disclose

P0197 COMPARISON OF THE EFFECTS OF DILTIAZEM GEL WITH LIDOCAINE GEL ON REDUCING PAIN AND DISCOMFORT IN PATIENTS UNDERGOING RECTOSIGMOIDOSCOPY: A RANDOMIZED DOUBLE-BLINDED CLINICAL TRIAL

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Introduction: The current study aimed at comparing the effects of diltiazem gel, an antispasmoic drug with local pain-reducing effects, with lidocaine gel in patients undergoing flexible rectosigmoidoscopy.
Aims & Methods: This double-blinded, randomized, clinical trial was performed on 80 patients who were potential candidates for rectosigmoidoscopy. After obtaining the informed consent, the patients randomly assigned to one of the lidocaine gel (2 mL) or diltiazem gel (2 mL) group, 10 minutes prior to rectosigmoidoscopy. The level of pain in the patients during the procedure was measured using the visual analogue scale (VAS) and the results were recorded. The data were analyzed using paired samples t-test and independent t-test as well as analysis of covariance (ANOVA) with SPSS version 18. P-value < 0.05 was considered the level of significance.
Results: Of 80 patients, 35 (43.75%) were male and 45 (56.25%) female with a mean age of 51.45 ± 15.21 years. The most frequent indications for rectosigmoidoscopy were abdominal pain (46.3%) and rectorrhagia (31.3%). The mean VAS score for pain reported by the patients in the lidocaine and diltiazem groups were 3.97 ± 2.89 and 2.60 ± 2.36, respectively. The VAS score for pain in the diltiazem group was significantly lower than of the lidocaine group (P = 0.023).
Conclusion: The application of local diltiazem gel around the anus, in spite of no side effects, can effectively reduce the pain and discomfort in patients during rectosigmoidoscopy.
Disclosure: Nothing to disclose

P0198 A MULTIFUNCTIONAL SNARE: A NEW APPROACH FOR HYBRID ENDOSCOPIC SUBMUCOSAL DISSECTION IN PORCINE MODEL

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Introduction: Endoscopic submucosal dissection (ESD) has a higher rate of en bloc resection rate, more accurate histological evaluation and lower rate of local recurrence compared with endoscopic mucosal resection (EMR). However, the technical difficulty limits its use in western country. To overcome the drawback, various modified techniques have been applied. Among them, ESD with snaring (by the name of hybrid ESD) is the most commonly used technique.
Aims & Methods: We designed a new multifunctional snare to simplify hybrid ESD procedure. The new rotatable device has the following functions: submucosal injection, needle knife, snare and argon plasma coagulation (APC). Animal study on porcine model was used to test its feasibility and safety in gastric and colorectal hybrid ESD. Artificial colorectal lesions of proximately 10mm and artificial gastric lesions of about 15mm were created by APC function of the new device. Hybrid ESD was done as following : initial mucosal pre-cut, submucosal injection, circumferential cutting , snare and APC the wound. The wound was checked one week after hybrid ESD. Then, pigs were sacrificed and necropsy performed.
The primary outcome is the en bloc resection rate. The secondary outcomes are the intra- and postoperative adverse event rate (bleeding and perforation). The wound healing one week after resection was also assessed by pathology.

Results: Fifteen colorectal hybrid ESD procedures were conducted successfully in three pigs (five hybrid ESD each). The en bloc resection rate of colorectal hybrid ESD was 100% (15/15). The average size of the colorectal hybrid ESD is 10.00±1.86 mm. No adverse event was found during the procedure or one week after resection. The endoscopic examination one week after the resection showed all wound being healing. In the pathology evaluation, superficial muscularis propria damage was found in one case (1/15, 6.67%), which was covered with exudate.
Other fourteen postoperative wounds showed healing of the ulcer. Eleven gastric hybrid ESD procedures were performed. The en bloc resection rate of gastric hybrid ESD was 100% (11/11). The average size of the gastric hybrid ESD was 17.18±9.00mm. No procedure related adverse event was found.
Conclusion: The new all in one snare is feasible and safe in gastric and colonic hybrid ESD in porcine model. It can save the numbers of endoscopic accessories using during hybrid ESD procedure and simplify the ESD procedure. Further study in human is awaited
Disclosure: Nothing to disclose

P0199 FACTORS ASSOCIATED WITH ADEQUATE BOWEL PREPARATION: OBSERVATIONS FROM THE EUROPEAN COLONOSCOPY QUALITY INVESTIGATION QUESTIONNAIRE

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Introduction: The development of the procedure questionnaire, by the European Colonoscopy Quality Investigation (ECQI) Group, has been previously described in posters presented at United European Gastroenterology Week, 2015 and 2016.
Aims & Methods: To investigate the factors associated with adequate bowel preparation using questionnaire responses from across Europe. Data collection is an ongoing process. We analysed data collected between 2/6/16 and 30/4/18.
A stepwise multivariable logistic regression analysis was performed to investigate which factors are associated with achievement of adequate bowel preparation, defined as a Boston Bowel Preparation Scale (BBPS) score ≥6. Analysis was performed on the following variables: age over or under 50; gender; body mass index (BMI) categories; inpatient/outpatient status; reason for procedure; use of bowel preparation; whether the patient followed instructions; proportion of bowel preparation consumed; total volume of fluid consumed; time period since last dose of bowel preparation; dosing regimen; time of day colonoscopy was performed.
Results: Data were collected on 6455 procedures, of which whether bowel preparation was adequate (BBPS≥6) or not could be determined in 6236. Of these, there were 2884 procedures where the results of all selected variables were known: adequate bowel preparation was achieved in 86.96% of these procedures.
The first five variables most associated with adequate bowel clearance were, in order:
1. Patient following instructions (89.1% vs. 54.3%, p< 0.0001).
2. Split-dosing or same-day regimen (89.5% split-dosing and 90.8% same-day vs. 77.9% evening, p=0.004).
3. Outpatient status (88.4% vs. 77.3% inpatient, p< 0.0001).
4. Age < 50 years (93.3% vs. 85.3% > 50 years, p< 0.0001).

5. Lower time period between procedure and last intake of bowel preparation (mean 6.1 hours vs. 8.0 hours in those with inadequate bowel preparation, p=0.0030).

Conclusion: Patients following instructions is the most important factor associated with achieving adequate bowel clearance followed by using a split-dosing or same-day regimen.

Disclosure: Amaro A, Agrawal A, Hünger M, Petruzziello L, Ono A, Jover R, Toth E: Consultant & advisory board participant to Norgine. Spada C: Consultant fee from Norgine. Brink L: Consultancy & Advisory Board participant to Norgine, AMBU. Fischbach W: Consultancy & Advisory Board participant to Norgine; Speaking - Abbott, Bio Merieux, Falk; Advisory speaking - Aptalis, Fresenius Biotech, Pfizer; Advisory - Boehringer Ingelheim, med update. Kinnunen U: Consultant & advisory board participant to Norgine and Olympus (European NBI Expert Training Group). Riemann JF: In terms of ECQI, consultant to Norgine, otherwise no conflict of interest. Amlani B: Employee of Norgine. Koulaouzidis A: No relevant conflict of interest. Patai A: No conflict of interest. Pecere S: No conflict of interest.

P0200 ENDOSCOPIC MANAGEMENT OF NON-DIMINUTIVE POLYPS: OBSERVATIONS FROM THE EUROPEAN COLONOSCOPY QUALITY INVESTIGATION QUESTIONNAIRE

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Introduction: The development of the procedure questionnaire, by the European Colonoscopy Quality Investigation (ECQI) Group, has been previously presented at United European Gastroenterology Week, 2015 and 2016.[1,2] Management of pathology is a domain of colonoscopy quality according to European Society of Gastrointestinal Endoscopy (ESGE) performance measures.[3]

Aims & Methods: To assess the endoscopic interventions performed in procedures where a non-diminutive polyp was recorded. Data collection is an ongoing process: we analysed data collected between 2/6/16 and 30/4/18.

Results: Of 6445 procedures, 2621 reported a polyp (40.7%). Polyp size was missing in 35 procedures, leaving 2586 procedures with at least one polyp of known size.

Polyps >5 mm: 1294 procedures reported at least one polyp >5mm: 1156 reported an endoscopic intervention (89.3%), 136 reported that there was no endoscopic intervention (10.5%) while 2 did not answer (DNA, 0.15%). Of the 138 procedures with a polyp >5mm that did not report an endoscopic intervention, there was one procedure in which an immediate complication (vascular syncope) was reported (132 stated there were no immediate complications, 5 DNA), and 37 who reported a requirement for a non-routine (immediate) repeat procedure (no 93, DNA 8). The reasons for a repeat procedure were: 20 further treatment or intervention required, 8 insufficient bowel preparation, 3 pathology encountered, 2 adjustment of blood-thinning medication required prior to intervention, and one case each of refused consent for polypectomy, referral to specialised hospital, pain and unsafe procedure.

Polyps ≥20 mm (polyp size ≥20 mm is a subset of >5 mm): There were 280 procedures with a polyp ≥20 mm recorded. Of these procedures 227 (81.1%) reported an endoscopic intervention while 53 (18.9%) reported that they did not perform an endoscopic intervention. Tattooing was only reported in 28 procedures (10%).

Of the 53 reporting no endoscopic intervention, one reported an immediate complication (vascular syncope), while 50 reported no immediate complication and 2 DNA. A requirement for an immediate (non-routine) repeat procedure was reported in 19 procedures (no 33, DNA 1): 9 further treatment or intervention required, 5 insufficient bowel preparation, 3 pathology encountered, one referral to specialised hospital for endoscopic mucosal resection and one unsafe procedure.

Conclusion: In procedures reporting non-diminutive polyps, no immediate endoscopic intervention was reported in over 1 in 10 procedures, rising to nearly one in five for procedures reporting a polyp ≥20 mm. The ESGE specifies that "In patients undergoing removal of colorectal nonpedunculated lesions 20mm in size or larger, or with suspicious macroscopic features regardless of size, the resection site should be tattooed to improve future re-location of the resection site". This should be done in 100% of cases.[3] Our findings indicate that tattooing rates are very low, being reported in only 10% of procedures recording a polyp ≥20 mm.

Type of endoscopic intervention	Polyp size >5 mm, Number, N=1156	Polyp size ≥20 mm, Number, N=227
Endoscopic mucosal resection	154	58
Endoscopic submucosal dissection	14	6
Polypectomy (complete)	1012	159
Polypectomy (incomplete)	18	10
Argon plasma coagulation	4	1
Biopsy	41	21
Tattooing	40	28

Note: Biopsies performed were not necessarily related with polyp resection.

[Endoscopic interventions in procedures with non-diminutive polyps (multiple options possible). Note: polyp size ≥20 mm is a subset of >5 mm.]

References: 1. Riemann JF et al. Poster PO160: UEGW 2015, Oct 24-28: Barcelona. 2. Jover R et al. Poster PO165: UEGW 2016, Oct 15-19: Vienna. 3. Kaminski et al. Endoscopy 2017; 49: 378-397.

Disclosure: Amaro A, Agrawal A, Ono A, Hünger M, Petruzziello L, Toth E: Consultant & advisory board participant to Norgine. Spada C: Consultant fee from Norgine. Brink L: Consultancy & Advisory Board participant to Norgine, AMBU. Fischbach W: Consultancy and Advisory Board participant to Norgine; Speaking - Abbott, Bio Merieux, Falk; Advisory speaking - Aptalis, Fresenius Biotech, Pfizer; Advisory - Boehringer Ingelheim, med update. Kinnunen U: Norgine and Olympus (European NBI Expert Training Group. Riemann JF: In terms of ECQI, consultant to Norgine, otherwise no conflict of interest. Amlani B: Employee of Norgine. Fuccio L: No conflict of interest. Koulaouzidis A: No relevant conflict of interest.

P0201 SESSILE SERRATED LESIONS DETECTION WITH ENDOCUFF-ASSISTED COLONOSCOPY - A RANDOMIZED CONTROLLED TRIAL

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Introduction: Sessile serrated lesions (SSL) have been associated with interval colorectal cancer (CRC) since they present a faster carcinogenesis and are more difficult to detect than adenomas. Several techniques have been developed to increase the sensitivity of colonoscopy, namely the Endocuff. Studies demonstrated that Endocuff-assisted colonoscopy improves adenoma detection rate. Still, the available data of its' effectiveness in detecting SSL is very limited. The aim of this study was to compare the effectiveness in SSL detection of Endocuff-assisted colonoscopy versus conventional colonoscopy.

Aims & Methods: We performed a randomized controlled trial that included patients undergoing elective colonoscopy between June 2018 and March 2019. Patients were randomly assigned in two groups before the procedure: 1) Endocuff-assisted colonoscopy; 2) Conventional colonoscopy. The procedures were performed with high definition endoscopes. The primary endpoint was the mean number of SSL with ≥ 10 mm per colonoscopy.

Results: 170 patients were included, 57% male, with mean age of 62.4±9.9 years. In *per protocol analysis*, 81 (48%) patients performed Endocuff-assisted colonoscopy and 89 (52%) conventional colonoscopy. There were no differences in cecal intubation rate (99% vs 94%, P=0.214), in mean cecal intubation time (7.3 ± 4.1 vs 8.0 ± 4.3 minutes, P=0.260) nor in withdrawal time (12.3 ± 5.3 vs 13.1 ± 6.7 minutes, P=0.373) between procedures with and without Endocuff. SSL detection rate was higher in Endocuff-assisted colonoscopy group (9% vs 2%, P=0.027), as well as the mean number of SSL detected per colonoscopy (0,2 ± 0,5 vs 0,02 ± 0,1, P=0,021). There were no differences in the mean number of SSL ≥ 10 mm between groups (0.04 ± 0.2 vs 0.02 ± 0.1, P=0.577). There were also no differences in adenoma detection rate (72% vs 67%, P=0.554) nor in the mean number of adenomas detected per colonoscopy (1.8 ± 2.4 vs 1.7 ± 2.2, P=0.785). The rate of adverse events was similar between groups (1% vs 1%, P=0.999).
Conclusion: Endocuff-assisted colonoscopy increases SSL detection rate and the mean number of SSL per colonoscopy, but not the mean number of SSL ≥ 10 mm.
Disclosure: Nothing to disclose

P0202 ASSOCIATION OF PATIENT FACTORS WITH FLAT AND PROTRUDED LESION REPORTING: OBSERVATIONS FROM THE EUROPEAN COLONOSCOPY QUALITY INVESTIGATION QUESTIONNAIRE

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Introduction: The development of the procedure questionnaire, by the European Colonoscopy Quality Investigation (ECQI) Group, has been previously described.[1,2]
Aims & Methods: To assess the patient factors associated with flat and protruded lesion reporting, as defined by Paris classification. Data collection is an ongoing process: we analysed data collected between 2/6/16 and 30/4/18. Adequate bowel clearance was defined as a Boston Bowel Preparation Score (BBPS) ≥6.
Results: Of 6445 procedures, 2621 reported a polyp in at least one segment (40.7%). Protruded lesions were reported in 2160 procedures and flat lesions were reported in 692 procedures. In procedures with polyps reported, the proportion with flat lesions was significantly lower in the left colon segment than either transverse or right colon segments (p< 0.0001).

	Right	Transverse	Left	Any segment
Any polyp	1328	723	1645	2621
Flat lesion	346	181	329	692
Protruded lesion	1012	544	1346	2160

[Table. Procedures in which a polyp was reported by type and colon segment]

Reporting of both flat and protruded lesions varied by age (generally increasing with increasing age, p< 0.0001 overall and in all individual segments). Reporting also increased for both flat and protruded lesions in those who had received a previous total colonoscopy within the last 5 years (p< 0.0001, significant in all segments): flat lesions 13.8% vs 9.8%; protruded lesions 38.7% vs 29.2%. Flat lesion reporting was not associated with body mass index (BMI, kg/m²) (p=0.667 overall, not significant in

any individual segment), while protruded lesion reporting was generally higher in higher BMI groups (p< 0.0001 overall and in all individual segments): BMI < 18.5 17.9%, 18.5-< 25 30.5%, 25-< 30 40.0%, 30-< 35 45.6%, ≥35 42.8%.
Flat lesions were more commonly reported in inpatients (inpatients 16.2% vs 10.7% outpatients, p< 0.0001), this was significant in the left (p=0.004) and right (p< 0.0001) segments but not the transverse segment (p=0.256). Protruded lesions were more common in outpatients (inpatients 29% vs 33.4% outpatients, p=0.023), however, this was not significant in any individual segments.
The reporting of flat lesions was significantly higher in procedures reporting adequate bowel clearance (11.4% vs 8.0%, p=0.004), this was significant in the left (p=0.016) and right (p=0.01) segments but not the transverse segment (p=0.354). Conversely, reporting of protruded lesions was not changed according to bowel cleansing adequacy (p=0.317).
Conclusion: Flat lesions are less commonly reported than protruded lesions. They are significantly less likely to be reported than protruded lesions in the left colon segment compared with the transverse and right segments. Reporting of flat lesions was not associated with BMI, while higher BMI was associated with increased reporting of protruded lesions. Flat lesions were more likely to be reported in inpatients while protruded lesions were more likely in outpatients. Reporting of protruded lesions was not affected by adequacy of bowel clearance while flat lesion reporting was higher in procedures reporting adequate bowel clearance.
References: 1. Riemann JF et al. Poster P0160: UEGW 2015, Oct 24-28: Barcelona. 2. Jover R et al. Poster P0165: UEGW 2016, Oct 15-19: Vienna.
Disclosure: Toth E, Amaro A, Agrawal A, Hünger M, Ono A, Petruzziello L: Consultant & advisory board participant to Norgine. Spada C: Consultant fee from Norgine. Brink L: Consultancy & Advisory Board participant to Norgine, AMBU. Fischbach W: Consultancy and Advisory Board participant to Norgine; Speaking - Abbott, Bio Merieux, Falk; Advisory speaking - Aptalis, Fresenius Biotech, Pfizer; Advisory - Boehringer Ingelheim, med update. Kinnunen U: Norgine and Olympus (European NBI Expert Training Group). Riemann JF: In terms of ECQI, consultant to Norgine, otherwise no conflict of interest. Amlani B: Employee of Norgine. Fuccio L: No conflict of interest. Koulaouzidis A: No relevant conflict of interest.

P0203 IS ADENOMA DETECTION RATE INCREASING IN PATIENTS YOUNGER THAN AGE 50?

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Introduction: Some data in the literature suggest that adenoma detection rate (ADR) in patients younger than age 50 has increased with the passage of years, with figures ranging between 4.7% and 24.1%. These observation gives cause for the start of colorectal cancer (CRC) screening at earlier ages.
Aims & Methods: Aim: To compare the ADR in two populations belonging to two periods separated by eight years.
Methods: We retrospectively studied patients younger than 50 years old who underwent a colonoscopy in an endoscopy center from Buenos Aires, Argentina; 204 from May to October 2009 (group 1) and 709 from January 2016 to May 2017 (Group 2). We recorded the following data: age, sex, indication of colonoscopy [low risk screening, high risk screening (family antecedents of CRC) and due to symptoms or surveillance], ADR and adenocarcinoma detection rate (ACDR). Detection rates were compared using a x2 or a Fisher test as appropriate.
Results: Ninety six (47.1 %) patients from group 1 and 337 (47.5%) from group 2 were men (NS). Mean age was 40.4 +/- 7.5 years in group 1 and 39.1 +/- 7.5 years in group 2 (P = 0,03). In group 1, the indication of colonoscopy was low risk screening in 45 patients, high risk screening in 41, and symptoms or surveillance in 118. In group 2, the indication of colonoscopy was low risk screening in 116 patients, high risk screening in 97, and symptoms or surveillance in 496. In the total population, 20 adenomas were detected in group 1 (ADR 9.8%) and 66 in group 2 (ADR 9.3%) (P = 0.93). No adenocarcinoma was detected in group 1 (ACDR 0%) and 5 were detected in group 2 (ACDR 0.7%) (P = 0.59). In low risk screening patients, 7 adenomas were detected in group 1 (ADR 15.6%) and 22 in group 2 (ADR 19.0%) (P = 0.81). In high risk screening patients, 5 adenomas were detected in group 1 (ADR 12.2%) and 12 in group 2 (ADR 12.3%) (P = 1.00).

In patients who underwent endoscopy due to symptoms or surveillance, 8 adenomas were detected in group 1 (ADR 6.8%) and 32 in group 2 (ADR 6.4%) (P = 0.83).

Conclusion: We did not find significant differences in the ADR of both groups, independently of the indication of colonoscopy, suggesting that ADR has not increased with the passage of years. ACDR neither differs but we cannot reach any conclusion due to the very low prevalence of CRC.

Disclosure: Nothing to disclose

P0204 SALINE-IMMERSION THERAPEUTIC ENDOSCOPY (SITE) COMBINED WITH THE POCKET-CREATION METHOD (PCM) FOR ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) OF GASTRIC AND COLORECTAL LESIONS: EXPERIENCE FROM A TERTIARY REFERRAL CENTRE IN LONDON

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Introduction: Endoscopic submucosal dissection (ESD) is now widely accepted as a potentialy curative, minimally invasive alternative to major surgery for the endoscopic management of superficial gastric and colorectal neoplasms. Due to its several advantages, in our institution, we use the pocket-creation method (PCM) for ESD as described by Yamamoto H. et al. (1). Since 2017, we have combined this with saline-immersion therapeutic endoscopy (SITE), since in our experience, this further facilitates PCM ESD by improving view quality (through refractive magnification, and minimal lense fogging) and lesion lifting, through buoyancy.

Aims & Methods: The aim of our study is to review our centre's experience of SITE-PCM-ESD cases. Demographic, endoscopic, histopathological data of patients treated by SITE-PCM-ESD were prospectively collected from July 2017 to April 2019.

Results: ESDs were performed in 35 patients (15 women), mean age: 64.8 years. Three lesions (8.6%) were removed from the stomach, 1 from the caecum (2.86%), 6 from the ascending colon (17.14%), 14 from the sigmoid colon (40%) and 11 from the rectum (31.40%). En-bloc pure SITE-PCM-ESD resection was achieved in 23 patients (65.7%); in 3 patients (8.6%) the procedure was not completed due to the suspicion of invasive malignancy and these patients were referred for surgery. Finally, in 9 cases (25.7%) the technique was converted in an endoscopic mucosal resection (EMR) due to time constraints. One of the 3 patients who were referred for surgery did not undergo any further intervention due to risks associated with underlying comorbidities. In 1 of the other 2 cases the histopathology after surgery confirmed our suspicion of malignancy.

Details of the cases managed by pure SITE-PCM-ESD are described as follows. Median specimen size was of 45,1 mm (12-100mm). Histopathological examination showed: 1) 1 villous adenoma with low grade dysplasia, 2) 8 tubular adenoma with low grade dysplasia, 3) 3 tubular adenoma with high grade dysplasia, 4) 1 tubulovillous adenoma with high grade dysplasia, 5) 10 tubulovillous adenoma with low grade dysplasia, 6) 1 adenocarcinoma, 7) 4 neuroendocrine tumors (2 G1 rectal NET, 1 G1 gastric NET and 1 G2 gastric NET), 8) 1 serrated adenoma with low grade dysplasia 9) 1 hyperplastic gastric polyp and 10) 1 sessile serrated lesion without dysplasia. R0 resection rate was 90.32 %. Lymphovascular infiltration was suspected in the one case of malignancy (3.12%). Two patients suffered from early post-procedural rectal bleeding, warranting further endotherapy (clip placement and haemospray application); no further complications were identified. To date, 16 patients (51.6%) have completed 3 months' and 12 patients (38.7%) have completed 6 months' endoscopic follow-up respectively; none of these patients have had any evidence of disease recurrence.

Conclusion: Our series of SITE-PCM ESD showed favorable results in term of efficacy and safety. Further comparative randomised control studies are required to further evaluate potential advantages of this technique.

References: 1. Hayashi Y, Sunada K, Takahashi H, Shinhata H, Lefor AT, Tanaka A, Yamamoto H. Pocket-creation method of endoscopic submucosal dissection to achieve en bloc resection of giant colorectal subpedunculated neoplastic lesions. Endoscopy. 2014;46 E421-2.

Disclosure: Dr Despott and Dr Murino receive research/education support from Aquilant Medical, Fujifilm, Olympus and Pentax Medical. All other authors have no conflicts of interest to disclosure.

P0205 EFFICACY, SAFETY AND RESECTION OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR THE TREATMENT OF SUPERFICIAL COLORECTAL NEOPLASIA IN AN ENDOSCOPY REFERRAL CENTER

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Introduction: Endoscopic submucosal dissection (ESD) is the preferred resection technique in eastern countries for superficial colorectal neoplasia larger than 2 centimeters in size and/or suspicious of submucosal superficial invasion. Only few data on ESD for colorectal neoplasia have been published in western countries.

Aims & Methods: We aimed to assess the safety, efficacy and resection outcomes of ESD for the treatment of large colorectal lesions in our center. We retrospectively collected medical data of consecutive patients who underwent colorectal ESD between 2015 and 2018 from a prospectively recorded database. Patients with inflammatory bowel diseases and familiar polyposis were excluded.

Results: Ninety five lesions in 94 patients were included in the study (42 males, median age 69 years). Median lesion size was 30 mm. 82 (86.3%) were naïve lesions, whereas 13 (13.7%) were recurrent or remnant lesions. 24 (25.3%) lesions were located in the right colon, 21 (22.1%) in the left colon, 50 (52.6%) in the rectum. Naïve lesions were defined as laterally spreading tumors (LSTs) granular homogeneous, 2 (2.4%), LSTs granular mixed, 26 (31.7%), LSTs non granular, 37 (45.1%), sessile polyps, 17 (20.7%). Histology revealed 77 (81%) benign adenomatous lesions (with high grade dysplasia in 87%), while submucosal invasive cancer (SMIC) was present in the remaining 18 (19%) lesions. All SMICs were deeply invasive (>1000 µm).

En-bloc resection was possible in 71 (74.7%) lesions: 65/82 (79.3%) naïve and 6/13 (46.1%) non naïve. In 21(22.1%) lesions piecemeal ESD had to be performed. In the remaining 3 lesions (2 naïve), resection was stopped because of non-lifting.

Complications occurred in 13/95 (13.7%) lesions: 6 (6.3%) post-procedural bleedings (no one needed blood transfusion) and 7 (7.4%) intra-procedural perforations. Only one patient (1.05%) underwent surgical management for complication (i.e. perforation).

R0 resection was obtained in 58/71 lesions: 54/60 (90%) adenomas and 4/11 (36.4%) SMICs. R1 was due to positive vertical margins in 2/60 (3.33%) adenomas and in 7/11 (63.6%) SMICs, positive lateral margins in 3/60 (5.0%) adenomas, both vertical and lateral positive margins in 1/60 (1.7%) adenomas.

14/18 (77.8%) patients with SMIC underwent surgery; in 10/14 (71.4%) of them surgical specimen was negative for neoplasia. The remaining 4 patients were not operated for comorbidities or refusal.

57 patients had 1-4 surveillance colonoscopies (SCs): 43 of the en-bloc resection group (EBG) and 14 in the piecemeal resection group (PMG). Recurrence was observed in 2/43 (4.6%) EBG patients and in 3/14 (21.4%) PMG patients. Recurrence occurred in 2/47 (4.2%) naïve lesions and in 3/10 (30%) non naïve lesions. All recurrences were successfully treated endoscopically.

Conclusion: In our experience ESD is a safe technique for the treatment of large superficial colorectal neoplasia, with an acceptable risk of complications and a low recurrence rate considering benign lesions. Despite our adherence to the current guidelines for ESD in the treatment of superficial colorectal neoplasia, none of the SMICs of our series had a curative treatment because all of them were deep invasive cancers.

Disclosure: Nothing to disclose

P0206 RECTAL RETROFLEXION: IS IT REALLY NECESSARY?

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Introduction: Rectal retroflexion (RR) is a commonly performed maneuver during lower gastrointestinal (GI) endoscopy even if poor evidence supports its diagnostic and clinical value and international guidelines do not agree to consider it as a key performance measure.

Aims & Methods: The aim of this study was to assess the diagnostic yield of RR for neoplastic and non-neoplastic ano-rectal lesions, compared with straight view examination. The RR complications rate and the variables associated with complications were also evaluated. We prospectively enrolled all consecutive patients undergoing lower diagnostic GI endoscopy between June 2018 and February 2019 in our Institute. In all patients the endoscopist performed first straight view examination of rectum and anal canal and then RR. Mayor complications included perforation and bleeding needing endoscopic treatment. Mucosal injury without bleeding or with self-limited bleeding and pain during and after the maneuver were considered minor complications.

Results: A total of 1600 patients (woman, 59%), undergoing 1419 colonoscopies and 181 proctosigmoidoscopies were included. RR was successful in 1572 patients (98%). In 28 patients (2%) RR was unsuccessful or not performed because of narrow rectum or because the maneuver was not tolerated by the patients.

One hundred and seventeen lesions were detected in 117 patients (7.4%): 91 lesions were identified on both retroflexion and straight view (77.7%), 23 lesions only on retroflex view (19.6%) and 3 lesions only on straight view (2.5%). The 117 identified lesions were: 13 malignant anal or rectal lesions (3 squamous anal cancers, 2 distal rectal adenocarcinoma, 1 melanoma, 1 distal rectal gastrointestinal stromal tumor, 5 ano-rectal infiltrations by gynecologic cancer and 1 rectal infiltration by urologic cancer) (0.8%), 4 high-risk adenoma (0.3%), 7 low-risk adenoma (0.4%), 25 high-grade anal intraepithelial neoplasia (AIN) (1,6%), 20 low-grade AIN (1.3%), 27 hyperplastic polyps (1.7%), 21 non-neoplastic lesions -ulcerations, angiodysplasia, mucosal findings of ulcerative proctitis- (1.3%).

Lesions identified only by RR were 2 out of 13 (15%) malignant anal and rectal lesions (1 squamous anal cancer and 1 rectal infiltration by gynecologic cancer), 1 out of 4 (25%) high-risk adenoma, 2 out of 7 (16%) low-risk adenoma, 4 out of 25 (16%) high-grade AIN, 6 out of 20 (30%) low-grade AIN, 6 out of 27 (22%) hyperplastic polyps and 2 out of 21 (9%) non-neoplastic lesions.No major complications occurred. There were 161 (10%) minor complications which consisted of mild or moderate pain during RR (78%) and self-limited bleeding associated with mild or moderate pain (22%). Multivariate analysis identified age < 61 years and endoscope diameter as factors correlated to the presence of minor complications (p-value respectively 0.007 and 0.037) while sex and previous pelvic surgery and/or radiotherapy did not correlate to the occurrence of complications.

Conclusion: In our experience RR identified a low but significant number of neoplastic lesions undetected by straight view. Thus, considering that RR has a low rate of not significant complications and it is fast, repeatable and low cost, its use should be recommended in the clinical practice during lower GI endoscopy.

Disclosure: Nothing to disclose

P0207 ASSOCIATION OF ASPECTS OF PROCEDURE WITH REPORTING OF FLAT AND PROTRUDED LESIONS: OBSERVATIONS FROM THE EUROPEAN COLONOSCOPY QUALITY INVESTIGATION QUESTIONNAIRE

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Introduction: European Society of Gastrointestinal Endoscopy (ESGE) guidelines recommend the routine use of high-definition (HD) white light colonoscopy for detection of colorectal neoplasia in the average population.[1] The development of the procedure questionnaire, by the European Colonoscopy Quality Investigation (ECQI) Group, has been previously described.[2,3]

Aims & Methods: To assess how aspects of a procedure associate with reporting of flat and protruded lesions, according to Paris classification. Data collection is an ongoing process: we analysed data collected between 2/6/16 and 30/4/18.

Results: Of 6445 procedures, 2621 reported a polyp in at least one segment (40.7%). Protruded lesions were reported in 2160 procedures and flat lesions in 692 procedures. In procedures with polyps reported, the proportion with flat lesions was significantly lower in the left colon segment than either transverse or right colon segments (p< 0.0001).

Use of HD equipment significantly increases reporting of both flat lesions (13.2% vs 5.5%, p< 0.0001) and protruded lesions (35.8% vs 23.6%, p< 0.0001). HD equipment significantly increases the proportion of flat lesions in procedures where polyps are reported (p< 0.0001): significant in right (p=0.004) and left (p=0.0054) segments, but not the transverse segment (p=0.0933).

Chromoendoscopy was increasingly used when both flat lesions (23.4% vs 7.9%, p< 0.0001) and protruded lesions (61.4% vs 27.2%, p< 0.0001) were reported. Where polyps are detected, the proportion of flat lesions increases with the use of chromoendoscopy (p=0.0005): significant in transverse (p=0.0172) and left (p=0.0337) segments, but not the right segment (p=0.1176).

The use of assistive technology significantly increases flat lesion reporting (21.3% vs 10.3%, p< 0.0001), significant in all segments. Higher rates were seen with the use of Endocuff (38.5%) and cap-assisted (23.9%) versus when other assistive technologies were used (19.8%). Assistive technology does not influence reporting of protruded lesions (p=0.712).

The reporting of flat (p=0.019) and protruded (p=0.015) lesions varies according to the time of day the procedure was performed. Flat lesion reporting was highest in the morning (07:00-11:59): 13.9% vs 11.3% afternoon (12:00-17:59) vs 8.4% evening (18:00-19:59). However, this was not significant in individual segments: right (p=0.321), transverse (p=0.063) and left (p=0.069). Conversely, protruded lesion reporting was higher in the evening and afternoon than morning: morning 30.1% vs afternoon 33.8% vs evening 39.2%. This was significant in the transverse segment (p=0.008), but not the right (p=0.62) and left (p=0.065) segments.

Conclusion: Use of HD equipment improves the reporting of both flat and protruded lesions. Furthermore, its use relatively increases the reporting of flat lesions, particularly in the left colon segment, where flat lesions are less reported. Chromoendoscopy was increasingly used when both types of lesion were reported, and also relatively increased the proportion of flat lesions. Use of assistive technology improves detection of flat but not protruded lesions. Reporting of flat lesions is higher in the morning, while protruded lesions are more commonly reported in the afternoon and evening.

References: 1. Kaminski et al. Endoscopy 2014;46:435-49. 2. Riemann JF et al. Poster PO160: UEGW 2015, Oct 24-28: Barcelona. 3. Jover R et al. Poster PO165: UEGW 2016, Oct 15-19: Vienna.

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P0208 WITHDRAWN

P0209 TIME PLANNING AND LEARNING CURVE OF ENDOSCOPIC SUBMUCOSAL DISSECTION IN THE COLORECTUM: RESULTS FROM AN EXPERT WESTERN CENTER

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Introduction: Endoscopic submucosal dissection (ESD) in the large bowel has gained considerable popularity in Asian countries. However, ESD has been slow to be taken up by Western endoscopists due to the technical complexity and time-consuming nature of the procedure. We have evaluated the learning curve and time planning outcomes of ESDs in an expert Western center.

Aims & Methods: Medical records of all patients undergoing ESD at Leiden University Medical Center till 1 January 2019 were retrospectively reviewed. We used multiple linear regression to identify independent risk factors for longer ESD duration.

Results: In total, 97 ESDs were performed by two expert endoscopists. The median size of the resected lesions was 45 mm (range 8-130). Median dissection speed was 8.5 cm^2 per hour (range 0.3-31.8) and did not significantly differ between the two endoscopists. Dissection speed significantly increased per 10 ESDs by 0.8 cm^2 per hour on average (p = 0.003).

The amount of time scheduled for the procedure was ≤ 120 minutes in 31 patients, 121-239 minutes in 32 patients and ≥ 240 minutes in 34 patients. Median ESD duration was 160 minutes (range 30-720); scheduled time was exceeded > 1 hour in 12 cases (3, 4 and 5 in the ≤ 120, 121-239 and ≥ 240 minutes planning group respectively).

Time exceeding of > 1 hour was associated with a higher rate of conversion to piecemeal resection (5/12 vs. 7/85; p = 0.006). Size of the lesion was the only independent risk factor for longer ESD duration (β = 23.0; p < 0.001).

Conclusion: Although the dissection speed gradually increases with the amount of ESDs performed, ESD planning should mainly be based on the size of the lesion to be resected. Accurate time scheduling of ESDs may eventually lead to higher en bloc resection rates and easier implementation of ESD in Western endoscopy centers.

Disclosure: J.J. Boonstra is a consultant of Boston Scientific. All other authors declare no potential conflicts of interest

P0210 OUT OF HOUR COLONOSCOPY; IS THE QUALITY AS GOOD AS IN HOUR COLONOSCOPY?

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Introduction: Colonoscopy is the 'gold standard' investigation for assessment of the large bowel which detects and prevents colorectal cancer[1], as well as non-neoplastic conditions. The Joint Advisory Group (JAG) on GI Endoscopy suggests monitoring key performance indicators such as ce-

cal intubation rate (CIR) and the adenoma detection rate (ADR)[2,3]. There has been a drive to increase utilization of endoscopy units nationwide by offering out of hours (OOH) endoscopy to deal with increasing service demands. Our aim was to investigate the quality of colonoscopies carried out during evening and Saturday lists in our unit and compare against BSG standards of quality for colonoscopies.

Aims & Methods: We retrospectively collected and analyzed demographical and procedure related data for non- screening colonoscopies performed between January 2016 and April 2018. Procedures were grouped according to the day of the week and timing of session (weekday, evening and Saturday). We also compared those performed by advanced colonoscopist and non-advanced colonoscopist. Advanced colonoscopist was defined as a BCSP colonoscopist or an advanced EMR colonscopist.

Results: There were a total of 17653 colonoscopies that were carried out, 56.8% (n=10025) were less than 70 years. Table 1 summarizes the differences between weekdays, evening and Saturdays' colonoscopies regarding the CIR and ADR. We noted that the KPIs (ADR, CIR) met the JAG standards. Advanced colonoscopists had better KPIs when compared to the non-advanced colonoscopists. (Table1)

		Weekdays		Evenings		Saturdays		
		No.	Rate%	No.	Rate%	No.	Rate%	P Value
Total	ADR	14200	28.9	1391	24.4	2062	24.2	<0.001a
	CIR		90.5		90.7		91.3	0.508
Advanced colonoscopist	ADR	1728	44.2	135	32.6	334	34.7	<0.001a
	CIR		94.5		97		95.2	0.411
Non-advanced colonoscopist	ADR	12472	26.7	1256	23.5	1728	22.1	<0.001a
	CIR		89.9		90.0		90.5	0.741
Advanced vs. Non-advanced colonoscopist	p value ADR	<0.0001		0.019		0.001		
	P value CIR	<0.0001		0.007		0.005		

[Table 1]

Conclusion: JAG standards were maintained during colonoscopies done on weekdays, evening and Saturdays. Advanced colonoscopists had higher CIR and ADRs.Other units should explore the options of doing planned OOH colonoscopies to meet service demands.

References: 1 Rex, D.K., et al., Colonoscopic miss rates of adenomas determined by back-to-back colonoscopies. Gastroenterol, 1997. 112: p. 24-28. 2 Bowles, C.J.A., et al., A prospective study of colonoscopy practice in the UK today: are we adequately prepared for national colorectal cancer screening tomorrow? Gut, 2004. 53: p. 277-283. 8. 3 Gavin, D., et al., The National Colonoscopy Audit: a nationwide assessment of the quality and safety of colonoscopy in the UK. Gut, 2013. 62: p. 242-249

Disclosure: Nothing to disclose

P0211 COMPARING THE SAFETY AND EFFICACY OF COLD SNARE POLYPECTOMY FOR SMALL COLORECTAL NEOPLASMS TO EMR AND CONVENTIONAL POLYPECTOMY

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Introduction: Cold snare polypectomy (CSP) has been performed worldwide as a safe endoscopic treatment for colorectal neoplasms compared with EMR and conventional polypectomy. However, in post-cold polypectomy, it is considerably difficult to evaluate pathological examination because of failed polyp retrieval and unclear cut margin. Incomplete resection is one of the most common causes that results in local recurrence after endoscopic treatment for colorectal neoplasms. The aim of this study is to assess the safety, efficacy, bleeding risk and problems of CSP compared with EMR and conventional polypectomy for small colorectal neoplasms.

Aims & Methods: We retrospectively analyzed a total of 5,991 lesions in 3548 consecutive patients who underwent CSP, EMR or conventional polypectomy for non-pedunculated polyps up to 10 mm in size at the Akashi Medical Center, Hyogo, Japan, from May 2013 to July 2017.

When lesions were found, we used chromoendoscopy and narrow band imaging (NBI) in all cases and included a magnifying examination if magnifying endoscopy was possible to use. Endoclip was performed when the oozing did not decline even after one minute of observation in CSP, on the other hand in EMR or conventional polypectomy it depended on operator's decision. We evaluated patient characteristics, clinicopathological features of the polyps, complications, polyps retrieval, and pathological complete resection rates for neoplasm lesions. The data were statistically analyzed.

Results: CSP was performed on (n=1381; 2518polyps), EMR was performed on (n=1820; 2888polyps), conventional polypectomy was performed on (n=347; 584polyps) .Patient characteristics and clinicopathological features of the polyps did not show significant differences in three groups. Polyp size was significantly smaller in CSP group compared with the EMR group (3.89 ± 1.39vs 6.40 ± 2.04 mm, p< 0.01), and conventional polypectomy group (3.89 ± 1.39vs 5.19 ± 2.18 mm, p< 0.01). The retrieval rate for polyps was significantly lower in CSP group compared with EMR and conventional polypectomy group at (n=2035; 94.4 % vs n=2786; 99% p< 0.01), and (n=2035; 94.4 % vs n=547; 97.3% p= 0.01), respectively. Pathological complete resection rate of the neoplasm lesions was significantly lower in CSP compared with EMR at (73 % vs 86% p< 0.01), but were identical to conventional polypectomy group (73 % 76% p= 0.15). No significant difference in delayed bleeding requiring endoscopic hemostasis in CSP group compared with EMR and conventional polypectomy group at (n=1; 0.05 % vs n=6; 0.21% p= 0.12), and (n=1; 0.05 % vs n=1; 0.31% p= 0.31), respectively. The rate of using endoclip was significantly lower in CSP compared with EMR and conventional polypectomy at (n=51; 0.2 % vs n=1884; 67% p< 0.01), and (n=51; 0.2 % vs n=51; 9.1% p< 0.01), respectively.

Conclusion: CSP tended to conduct for significantly smaller lesions with lower polyp retrieval rate and lower rate of using endoclip compared with EMR and conventional polypectomy in this study. Delayed bleeding in CSP required endoscopic hemostasis was seen in only one case and perforation was not observed. Thus, CSP could be a safer and more convenient method for small colonic neoplasia compared with EMR and conventional polypectomy, On the other hand, pathological complete resection rates were significantly lower compared with EMR. Consequently, these findings highlight the importance of meticulous inspection of the remnant tumor via endoscopy after CSP to avoid unnecessary future local recurrence.

Disclosure: Nothing to disclose

P0212 USE OF ENTEROSCOPE WITHOUT THE OVERTUBE IN INCOMPLETE COLONOSCOPIES

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Introduction: Colonoscopy is the gold standard diagnostic method for colorectal cancer screening. The quality of such procedure depends on different factors, including endoscopist's skills and caecal intubation rate. Despite the progress in the endoscopy technology field, a small percentage of colonoscopies is still incomplete. The reasons for that are mostly associated to anatomic features, such as fixed, angulated, long and loopy colon, intra-abdominal adherences and female gender. To overcome such difficulties, the usefulness of scopes different from conventional colonoscope, such as paediatric colonoscope, gastroscope, single and double balloon enteroscope (SBE and DBE), has been shown in literature.

Aims & Methods: Our retrospective study aims to evaluate the caecal intubation rate using a push enteroscope (PE) without the overtube in patients who previously underwent an incomplete procedure with a standard colonoscope.

47 adult patients, mostly female (77%), who previously underwent an incomplete colonoscopy with a standard colonoscope, were retrospectively enrolled through the analysis of a dedicated database. The enteroscope used was the Olympus Enteropro Single Balloon SiF-Q180 with no overtube. Complete colonoscopy was defined as successful caecal intubation.

Results: The use of PE led to a complete procedure in 91% of patients (43 over 47). The most frequent reason (75%) for an incomplete procedure even with the use of PE was a fixed and angulated colon (3 over 4 patients).

Conclusion: Colonoscopy performed with PE was safe and no adverse events during and/or after the procedure occurred. Compared to standard colonoscope and paediatric colonoscope, PE is longer, thinner and more flexible and these features make it more suitable to complete a colonoscopy in tricky patients. Moreover, PE is a less expensive option compared to SBE and DBE (which require the overtube-balloon equipment and patient's X-ray exposure during fluoroscopic guidance) and it allows to perform operative endoscopy compared to less invasive alternatives, such as computed tomographic virtual colonoscopy and capsule endoscopy.

Our results suggest that PE is a useful and valid alternative to standard scope in difficult cases, especially those related to fixed/angulated colon and in female gender.

Disclosure: Guido Costamagna is a member of the Advisory Board of Olympus, Tokyo, Japan; the other authors have no conflict of interest to declare.

P0213 DIFFERENT RISK FACTORS FOR DELAYED POSTPOLYPECTOMY BLEEDING IN PATIENTS WITH A SINGLE POLYPECTOMY VERSUS MULTIPLE POLYPECTOMIES DURING A ONE-TIME COLONOSCOPY

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Introduction: Colorectal cancer (CRC) is a common and lethal disease. Polypectomy can prevent the development of CRC. Although polypectomy is a safe procedure, there is still 1% bleeding rate after polypectomy. During screening colonoscopy, patients may have more than one colon polyp to remove in one-time colonoscopic procedure.

However, data on the rate of delayed postpolypectomy bleeding (PPB) and risk factors for multiple polypectomies during a one-time colonoscopic procedure are limited.

Aims & Methods: The aim of the study was to evaluate the risk of delayed PPB of multiple polypectomies in a one-time colonoscopy. From Jan 2015, to Jan, 2017, patients who underwent snare polypectomy in a referral center of northern Taiwan for polyp's size between 6 and 20 millimeters (mm) were enrolled in this study. The PPB event was defined as the presentation of a bloody stool 14 days after the polypectomy and followed by repeat colonoscopic interventions. The demography of patients and the polyp characteristics were recorded. Descriptive statistics and frequency distributions were calculated. The data were analyzed by using either the Mann-Whitney U test for continuous variables or chi-square test for categorical variables. Univariate and multivariate logistic regressions were used to examine the risk factors of delay PPB. Statistical significance was defined as p value < 0.05.

Results: A total of 1188 patients were enrolled in this study. 888 (74.8%) patients underwent a single polypectomy during one-time colonoscopy, and 300 (25.2%) patients underwent ≥ 2 polypectomies during a one-time colonoscopy. There were 616 (69.4%) male patients in the single polypectomy group and 231 (77.0%) in the multiple polypectomies group. The median age in the single polypectomy group was 59 years (range: 19-96 years) and 61 years (range:20-96 years) in the multiple polypectomies group.

The mean polyp size in both groups was 8 millimeters without statistically difference. The overall delay PPB was 1.1 %. Compared to the single polypectomy group, the bleeding rate in the multiple polypectomies group was significantly higher. (3.3% vs 0.3%; p=0.02) In the univariate regression analysis for bleeding risk factors, increases in the polyp size were significantly associated with delayed PPB in the single polypectomy group. (OR: 1.3, 95% CI:1.03-1.65, p=0.02).

In the multiple polypectomies group, female was significantly associated with delayed PPB (OR: 3.7, 95% CI:1.05-12.93, p=0.04) and a history of anti-platelet/coagulant agent use was a borderline factor for delayed PPB (OR: 4.85, 95% CI:0.99-23.69, p=0.05). The patients' age, polyp location, polyp morphology, polyp pathology, prophylactic hemoclipping, and the endoscopists' experience were not found to be significant risk factors for delayed PPB in either group.

By adjusting for sex, polyp size and history of anti-platelet/coagulant agent use in the multivariate regression analysis, polyp size was still an independent factor for delayed PPB in the single polypectomy group. (OR: 1.30, 95% CI:1.02-1.65, p=0.03) Female and history of anti-platelet/coagu-

lant agent use were independent factors for delayed PPB in the multiple polypectomies group (OR: 4.07, 95% CI:1.14-14.47, p=0.03; OR: 5.54, 95% CI:1.09-27.94, p=0.03 respectively).

Conclusion: When performing ≥ 2 polypectomies during a one-time colonoscopic procedure, the rate of delayed PPB significantly increases. Polyp size was a risk factor for delayed PPB in single polypectomy. Female and history of anti-platelet/coagulant agent use were risk factors for delayed PPB in multiple polypectomies.

Disclosure: Nothing to disclose

P0214 CLINICAL AND PATHOLOGICAL CHARACTERISTICS OF ADENOMATOUS POLYPS IN LYNCH SYNDROME

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Introduction: Lynch Syndrome (LS) is an autosomal dominant disorder caused by germline mutations in DNA mismatch repair genes such as *MLH1, MLH2, MSH6* and *PMS2*, and patients with LS have an increased risk of developing colorectal cancer. While adenoma-carcinoma sequence is accelerated in patients with LS, the characteristics of adenomatous polyps in patients with LS are not precisely known.

Aims & Methods: A total of 325 consecutive adenomatous polyps in patients with LS removed by colonoscopy between June 2005 and May 2018 were retrospectively reviewed. In addition, we defined adenomatous polyps with advanced pathological features including high grade adenomas, intramucosal carcinomas, and superficial submucosal invasive carcinomas (submucosal invasion depth < 1000 μm) as index lesions and compared the prevalence and clinical characteristics of the index lesions between patients with LS and a control group. As the control group, the adenomatous polyps in patients without LS, Familial Adenomatous Polyposis, or Inflammatory Bowel Disease removed by colonoscopy between January 2015 and December 2015 at our institute were reviewed.

Results: One hundred and fifty five polyps (48%) were located in proximal colon, 114 polyps (35%) at distal colon and 56 polyps (17%) at rectum. The median polyp size was 5 mm (range 2-40 mm) and 229 polyps (71%) were non-polypoid type. The percentage of carcinomas were 1%, 7%, 69% and 86% for polyps of diameter < 5 mm, 5 ≤ X< 10 mm, 10 ≤ X< 20 mm and 20 ≤ mm, respectively.

The percentage of the index lesions was significantly higher in LS group (26%) than in the control group (15%) (P < 0.0001). The percentage of the index lesions according to the location (proximal colon, distal colon and rectum) was 32%, 33% and 41%, respectively in LS group. The mean age ± SD at the index lesions removal was significantly younger in LS group (59 ± 13 years) than in the control group (67 ± 11 years) (P < 0.0001). The median polyp size of the index lesions was significantly smaller in LS group (7 mm, range, 3-30 mm) than in the control group (10 mm, range, 1-120 mm) (P < 0.0001), which was applicable to the size of each histology including high grade adenoma, intramucosal carcinoma and superficial submucosal invasive carcinoma. Non-polypoid polyp was significantly more common macroscopic type of the index lesions in LS group (63%) than in the control group (30%) (P < 0.0001).

Conclusion: The adenomatous polyps in patients with LS, especially greater than 10 mm, showed higher degree of dysplasia than sporadic ones. The index lesions in patients with LS were smaller and more often non-polypoid morphology than sporadic ones. The percentage of index lesions was comparable at any part of the colon in patients with LS and this result suggest the adenoma-carcinoma sequence in patients with LS should be similarly accelerated between proximal and distal colon.

Disclosure: Nothing to disclose

P0215 ENDOSCOPIC ANALYSIS OF MICROSTRUCTURES OF THE COLON MUCOSA ON THE EDGE OF THE POST-RESECTION DEFECT AS A MEASURE OF PREVENTING RECURRENCE OF POLYPS AFTER A COLD POLYPECTOMY

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Introduction: To identify the residual tissue after the cold snare polypectomy, it is necessary to know an endoscopic view of the unchanged structure on the edge of the post-resection defect. This is the prevention of tumor recurrence.

Aims & Methods: To assess the usefulness of endoscopic removal of small (less than 10 mm) colon polyps with a cold snare on the basis of endoscopic microstructural analysis of the edges of the post-resection defect.

In 74 patients (22 men and 52 women) aged 28 to 84 years (59.3 ± 3.6 years), 103 colon polyps were detected. These were up to 10mm in size and no more than 5mm in height, without endoscopic signs of severe dysplasia or cancer. Most of the polyps (81/103; 78.7%) were of flat-elevated form, type 0-IIa, of which 10 (9.7%) had a depression, type 0-IIa+c; and were of polypoid form 21/103; 20.3%.

The polyps were resected with a cold snare and in all cases the edges of the defect were evaluated for the absence of residual tissue. A complete endoscopic analysis of the microstructures and the capillary vessels of the mucosa was performed on the edge of the post-resection defect, and was then compared to the histological image.

Results: The endoscopic criteria followed post cold snare resection in order to check its success were: endoscopic visualization on the edge of the post-resection defect of 1) parallel crypts and 2) the pit pattern of only type I (S. Kudo).

This was observed in 93 (90.3%) cases. In 10 (9.7%) cases, single extended modified crypts were found, with violation of their parallelism, which was a sign of residual tissue. In these cases, a combined removal technique was used - a cold snare, supplemented with biopsy forceps for the purpose of radical intervention.

During endoscopic examination of the post-resection defects in the rectum, we noted differences in the location of the crypts of the rectum in the anorectal junction and in the range of 1-2 cm proximity to it, compared to the orderly arrangement of crypts in the colon. In this area, the loss of parallelism of the crypt is determined; the irregularity of the structure giving the impression of "falling crypts" It is noted that this feature of the structure complicates the differential diagnosis of normal and residual tumor tissue.

An endoscopic assessment of the capillary network of the colon mucosa was performed, as a result of which it was determined that the possibilities of endoscopic analysis in vivo have advantages over histological examination, where it is difficult to trace the course of blood vessels. Flat-elevated polyps have capillary vessels that are small in diameter, which significantly reduces the risk of bleeding when removed by a cold snare resection when up to 10 mm in size. This was confirmed by a slight capillary leakage of blood in 101 (98.1%) cases, which stopped independently, on average, after 2-3 minutes. In 2 (1.9%) cases, due to the reception of anticoagulant therapy, the period of capillary thrombosis varied from 5 to 10 minutes. In these patients, the defects were clipped to prevent delayed bleeding.

Follow-up colonoscopies were performed on 11 (10.7%) patients: neither advanced adenomas, nor interval cancers were detected.

Conclusion: A detailed assessment of the edges of the post-resection defect of the mucosa after cold snare resection provides a reliable diagnosis of the complete success of the endoscopic intervention and the possibility of removing residual tumor tissue (if present) immediately after its completion, and therefore reduces the number of recurrence of tumors.

Disclosure: Nothing to disclose

P0216 WITHDRAWN

P0217 ARTIFICIAL INTELLIGENCE-ASSISTED POLYP DETECTION FOR COLONOSCOPY

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Introduction: A previous meta-analysis has shown that approximately 26% of neoplastic diminutive polyps are missed in single colonoscopies. We have developed a computer-aided detection (CADe) system assisted by artificial intelligence (AI) to reduce this failure and the resulting deaths from cancer. Research on CADe has been increasing in recent years, but most of it focuses on learning and analysis of still images. We think that the use of spatio-temporal data is essential for learning, improving, and evaluating AI systems. In this study, we compiled a database of many endoscopic videos and used it to develop a CADe system. We then evaluated its performance.

Aims & Methods: To develop the CADe system, we retrospectively collected colonoscopy videos from study participants who underwent colonoscopies in our institution from April 2018 to August 2018. We collected 1,089 colonoscopy videos with a total duration of 2,716,720 frames (514,240 polyp-positive frames and 2,202,480 polyp-negative frames) and constructed a new algorithm based on 3D convolutional neural networks with residual-blocks. To evaluate our system, we also retrospectively collected 96 colonoscopy videos from 96 consecutive participants between August 2018 and October 2018.The exclusion criteria were advanced colorectal cancer and inflammatory bowel disease. Expert endoscopists annotated the presence of polyps in each frame of each video, and this annotation was treated as the gold standard for the presence of polyps to determine the sensitivity and specificity.

Results: Seventy-one patients had a total of 152 polyps and 25 patients were free from polyps. The median polyp size was 4(3-5) mm, the CADe's sensitivity was 89% and the specificity was 75%. The sensitivity to polyps under 5 mm was 88%. Morphologically, the sensitivity to protruded polyps was 90% and to flat polyps was 88%. There was no significant difference between the sensitivities to protruded and flat polyps.

Conclusion: The CADe we developed by learning spatio-temporal data had a high sensitivity regardless of the size and morphology of the polyp, and may improve the adenoma detection rate.

Disclosure: Nothing to disclose

P0218 ENDOCYTOSCOPY COMBINED WITH NARROW-BAND IMAGING FOR PREDICTION OF CLINICAL RELAPSE IN PATIENTS WITH ULCERATIVE COLITIS

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Introduction: Some patients with ulcerative colitis (UC) clinically relapse in the short term despite white light endoscopic mucosal healing was achieved. We developed a novel index using endocytoscopy (EC: ×520 ultramagnifying colonoscopes providing both microvascular and crypt sharpness visualization of colorectal mucosa after application of the narrow-band imaging).

Aims & Methods: The aim of this retrospective cohort study was to evaluate clinical efficacy of endocytoscopy for prediction of future clinical relapse in patients with sustained remission. The study cohorts were including previ-

ously established UC patients in sustained corticosteroid-free (≥6 months) clinical remission (defined as partial Mayo score of ≦1) and mucosal healing (defined as Mayo endoscopic subscore of 0 or 1) undergoing endoscopic evaluation using EC between October 2016 and September 2018 at the Digestive Disease Center of the Showa University Northern Yokohama Hospital. Exclusion criterion was patients with medical history of any previous surgical colon resection. The EC images to evaluate were selected by an endoscopist (M.O.) who was blinded to clinical, histological, and endoscopic information. Another expert endoscopist (Ya. M.) evaluated the images according to endocytoscopic findings, and the cohorts were classified into either 'Healing' or 'Active' group according to endocytoscopic findings. The main outcome measure was the difference of clinical relapse-free rates compared between 2 groups. The differences of clinical relapse-free rates depending on the extent of disease (extensive colitis, left-sided colitis, and proctitis) were also investigated as sub-analysis. Cohorts were followed until the end of the study in March 2019 or until relapse. Clinical relapse was defined as the presence of rectal bleeding together with any treatment intervention.

Results: A total of 178 patients were included as the study cohorts. 6 were not completed to be followed until the end of the study. 172 patients, who were followed for 12 months on average, were analyzed. 104 being classified in the 'Healing' group, and 68 in the 'Active' group. In the follow up period, 3.8% (4/104) relapsed in the 'Healing' group, and 22.1% (15/68) in the 'Active' group. The 'Healing' group had a significantly higher clinical relapse-free rate compared with the 'Active' group (Log rank test: P< 0.01). In sub-analysis, it also revealed that the 'Healing' group had a significantly higher clinical relapse-free rate with the 'Active' group in extensive colitis, and left sided colitis (P< 0.01, and P=0.02, respectively) and not significantly in proctitis. (P=0.59).

Conclusion: Endocytoscopy has potential to predict short-term relapse in patients with clinical and endoscopic remission.

Disclosure: Nothing to disclose

P0219 ENDOSCOPIC SUBMUCOSAL DISSECTION FOR RECTAL NEOPLASIA: SAFETY AND EFFICACY IN A EUROPEAN CENTRE

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Introduction: The efficacy of endoscopic submucosal dissection (ESD) has been well documented, however Western data on colorectal ESD is limited and its role for colorectal lesions is, at present, not well defined. Nevertheless, the rectum is recognized as a particular segment and ESD may play an important role in avoiding a major surgery.

Aims & Methods: This study aims to report the feasibility, safety and effectiveness of ESD for treating premalignant and early malignant rectal lesions in a Western centre.

We conducted a prospective data analysis of all consecutive rectal lesions treated by ESD between 2013 and 2019. En bloc, pathological complete resection (R0) and curative rates, procedure time, complications and local recurrence were evaluated.

Results: Included 114 lesions from 111 patients (mean age 69,0±9,8 years old; M/F=71/40). Morphologically, lesions were laterally spreading tumour (LST) granular homogeneous (n=19), LST granular mixed (n=61), LST non-granular (n=15) and protruded lesions (n=19). Median size of the resected specimen was 50mm (13-156) and mean resection time was 107±89,1min. En bloc resection was achieved in 91,9% (102/111) of the resected lesions (3 resections were considered non-feasible). R0 resection was accomplished in 81 cases (73%) and resection was considered curative in 78 cases (70%). Complications occurred in 15 procedures (13%): 7 immediate minor bleedings, 1 immediate perforation and 7 delayed bleedings. In the resected group, asymptomatic stenosis was diagnosed in 2 patients whose resection was >90% of the rectal circumference. All complications were managed conservatively or endoscopically. Of the 78 curative resections, 53 were followed up and median follow-up time was 12 months (1-74) revealing 1 recurrence (2%).

Conclusion: To the best of our knowledge, this study represents the third largest series of rectal ESD in the West, showing that rectal ESD can achieve a high rate of en bloc and R0 resection, safely.

Disclosure: Nothing to disclose

P0220 THE ACCURACY OF WAVSTAT VERSION 4 OPTICAL BIOPSY FORCEPS IN CHARACTERIZING COLORECTAL POLYPS LESS THAN 10 MM: A PROSPECTIVE BLINDED STUDY

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Introduction: WavSTAT Version 4 (WavSTAT4) Optical biopsy (designed by SpectraScience Inc, California, USA) represents a novel means of predicting histology based on laser-induced autofluorescence spectroscopy. Potentially, this could replace standard histological assessments of colonic polyps < 10mm in size. We present our final findings following the preliminary study in 2016.

Aims & Methods: The primary aim of this study was to demonstrate the accuracy of WavSTAT4 in characterizing colorectal polyps< 10mm. The secondary aim looked at comparing the real time diagnostic performance of WavSTAT version 4 with endoscopic assessment and a combination of both. Patients attending the endoscopy unit for lower gastrointestinal endoscopy as requested by their responsible physician were approached to participate in the study. Adult patients aged above 18 years were included. Patients with known active inflammatory bowel disease or colorectal cancer were excluded from the study. Polyps < 10mm were assessed in real time by high definition white light, NBI and WavSTAT4 optical biopsy forceps. Standard techniques were used for polypectomy. Histopathological specimens were read separately by two expert GI pathologists blinded to the results of the NBI and WavSTAT4 assessments. The primary outcome measure was the negative predictive value in distinguishing adenomatous from non-adenomatous colorectal polyps. The secondary outcome measure was the accuracy of on-site recommended surveillance intervals.

Results: 136 patients participated in this study. A total of 211 polyps (199 < 10mm, 12 >10mm) were found in 79 patients (51 males, 28 females). The mean age was 65 (range 28-95 years). 50 patients were excluded from the study (no polyps in 38 patients, device failure in 8 patients, 4 polyps not retrieved). A further 7 patients were not included due to missing data. 15 polyps were not included in the final analysis due to discrepancies between the histological analysis of the two pathologists.

	WavSTAT 4 alone % (95% CI)	WLE + NBI assessment % (95% CI)	Algorithmic approach % (95% CI)
Sensitivity	93.8 (86.0-97.9)	86.2 (76.7-92.3)	93.8 (86.0-97.9)
Specificity	45.4 (35.6-55.8)	82.2 (73.3-89.0)	77.2 (67.8-85.0)
NPV	90.2 (79.3-95.7)	88.3 (81.2-92.9)	94.0 (86.9-97.4)
PPV	57.7 (53.0-62.2)	79.3 (71.4-85.4)	76.5 (69.4-82.4)
Surveillance interval (% correctly coded)	67.9	88.5	87.2
Surveillance interval (% of patients called earlier)	32.1	11.5	12.8

[Diagnostic performance of Wavstat4, Endosocpic assessment and combined algorthmic assessment for characterization of colorectal polyps less than 10mm]

WavSTAT4 had a high NPV of 90.2% and was more sensitive (93.8%) compared to endoscopic assessment (NPV 88.3%, sensitivity 86.3%). WavSTAT4 however lacked specificity and was poor for hyperplastic recto-sigmoid polyps and only accurately predicted surveillance intervals in 67.9% of patients. Due to this we implemented an algorithmic approach where pol-

yps proximal to the recto-sigmoid were classified according to WavSTAT4, whereas the endoscopic classification used only if Wavstat4 prediction was as an adenomatous polyp in the recto-sigmoid area. With this combined algorithmic approach the NPV was 94.0% which met the PIVI thresholds and improved correctly predicted surveillance intervals to 87.2% of patients.

Conclusion: This study has shown that WavSTAT4 reached the threshold to "resect and discard" however only correctly predicted surveillance intervals in 67.9% of patients. When utilizing an algorithmic approach combining WavSTAT4 and endoscopic assessment a higher NPV was achieved with 87.2% achieving accurate surveillance intervals.

Disclosure: Nothing to disclose

P0221 AN EXCLUSIVE PERFORMANCE VALIDATION ON LATERALLY SPREADING TUMOR AND SESSILE SERRATED ADENOMA IN COLONOSCOPY IMAGES AND VIDEOS OF DEEP LEARNING POLYP DETECTION SYSTEM

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Introduction: Evidences have shown that automatic polyp detection system using deep learning can achieve both high sensitivity and specificity in colonoscopy images and videos, and with real-time assistance of this CADe system, the ADR/PDR can be improved in realistic colonoscopy settings. However, the detection performance of this system on colon laterally spreading tumor and sessile serrated adenoma, which are with higher miss rate and malignancy potential, has not been specifically investigated.

Aims & Methods: A real-time automatic polyp detection system based on deep learning was validated on colonoscopy images and videos from a large-scale of consecutive patients in a previous study1, in which the system has the sensitivity and specificity both above 94%. In this study, the system was validated exclusively on laterally spreading tumor (LST) and sessile serrated adenoma (SSA). 1451 LST images from 182 patient (92(50.55%) female; age, mean(s.d.):63.21(11.52)) are collected between July 2015 and January 2019, 82 SSA videos from 26 patients (7(26.92%) female; age, mean(s.d.):50.81(10.07)) were collected between September 2018 and January 2019. The per-frame sensitivity and per-lesion sensitivity were calculated.

	LST Image Dataset	SSA Video Dataset
Data acquisition*	July2015-January2019	September2018- January 2019
Content* *	1451 images containing LST	82 colonoscopy video clips, each with a SSA appearing from the beginning until the end. 12.59 min in total and 17.99s per polyp on average
Device* * *	Olympus and Fujifilm	Olympus and Fujifilm
Patient demographics	182 patients,92(50.55%) female; age, mean(s.d.):63.21(11.52)	26 patients,7(26.92%) female; age, mean(s.d.):50.81(10.07)
Polyp histology	Total LST number 194(100%) Carcinoma 23(11.86%) SSAP 14(7.22%) Adenomatous 147(75.77%) Advanced Adenoma 135(69.59%) Hyperplastic and Inflammatory 10(5.15%)	Total SSA number42(100%) SSAP 42(100%)
Polyp location	Rectum 74(38.14%) Sigmoid colon 24(12.37%) Descending colon, including splenic flexure 10(5.15%) Transverse colon 29(14.95%) Ascending colon, including hepatic flexure 43(22.16%) Cecum 14(7.22%)	Rectum 9(21.43%) Sigmoid colon 11(26.19%) Descending colon, including splenic flexure 3(7.14%) Transverse colon 11(26.19%) Ascending colon, including hepatic flexure 7(16.67%) Cecum 1(2.38%)
Polyp size (cm)	size, mean(s.d.):2.33(1.11)	Small(≤0.5) 29(69.05%) Moderate (>0.5&<=1) 12(28.57%) Large (>1) 1(2.38%)

* All datasets were acquired from the Endoscopy Center of Sichuan Provincial People's Hospital of China. * * Resolution of images and videos are 704×576, 1,920×1,080 or 1,280×1,024. * * * Olympus EVIS LUCERA CV260 (SL)/CV290 (SL) and Fujifilm 4400/4450 HD. NA, not applicable.

[Patient demographics and polyp characteristics for the validation datasets]

Results: 1) For LST image dataset, the system achieved an overall sensitivity of 94.28% (1368/1451). the sensitivity for LST-G(H), LST-G(M), LST-NG(F), LST-NG(PD) was 94.24% (360/382), 98.41% (681/692), 86.56% (322/372) and 100% (5/5) respectively. 2) for SSA video dataset, the system achieved an overall per-frame-sensitivity of 84.10% (15883/18885). This real-time system processed 25 frames per second.

Conclusion: This study demonstrated that a local feature oriented automatic polyp detection system could detect laterally spreading tumor and sessile serrated adenoma with high sensitivity comparable with general polyps. This CADe system has a higher sensitivity on granular lesions compared to flat lesions and the per-frame sensitivity in videos for small SSAP should be further improved.

Disclosure: Nothing to disclose

P0222 CLINICAL SIGNIFICANCE OF FAMILY HISTORY OF COLORECTAL CANCER IN FIRST-DEGREE RELATIVES AS A RISK FACTOR FOR ADVANCED COLORECTAL NEOPLASIA IN ASYMPTOMATIC SCREENED POPULATIONS AGED 40 TO 54 YEARS AND 55 TO 69 YEARS

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Introduction: The clinical significance of a family history (FH) of colorectal cancer (CRC) in first-degree relatives (FDRs) as a risk factor for colorectal neoplasia is still inconclusive.[1] Several recent studies have suggested that the influence of an FH of CRC in FDRs as a risk factor in CRC screening weakens as the age of the screened population increases (≥55 years)[2]. Even for younger screened populations (< 55 years), the relationship between an FH of CRC in FDRs and the risk of colorectal neoplasia remains incompletely understood.

Aims & Methods: This study was performed to investigate the relationship between an FH of CRC in FDRs and the presence of advanced colorectal neoplasia (ACN) in asymptomatic screened individuals aged 40 to 54 and 55 to 69 years. Data from screened individuals aged 40 to 54 years (n=2,263) and 55 to 69 years (n=2,621) who underwent their first-ever screening colonoscopy at our institution from February 2004 to March 2013 were used. None of the screened individuals had an FH of hereditary CRC. Data on the following baseline characteristics of the study participants were extracted: age; sex; history of smoking, drinking, and nonsteroidal anti-inflammatory drug use; body mass index; and presence of diabetes mellitus. The relationship between the presence of FDRs with CRC and the presence of ACN was examined using the chi-square test. A multivariate logistic regression analysis incorporating all of the above-mentioned factors was also performed to calculate the odds ratio (OR) of an FH of CRC in FDRs for the presence of ACN adjusted by the other factors.

Results: Of 2,263 screened individuals aged 40 to 54 years, 249 (11.0%) had FDRs with CRC. No significant difference in the baseline characteristics was observed between these 249 individuals and the other 2,014 individuals without affected FDRs. The prevalence of ACN was significantly higher among the individuals with than without affected FDRs (5.6% vs. 1.6%, respectively; P< 0.01). Despite this significant relationship, no statistically significant association was observed between the presence of ACN and the number of affected FDRs or presence of younger affected FDRs (< 60 years). The OR of the presence of affected FDRs for ACN, which was adjusted by all other baseline characteristics, was 3.6 [95% confidence interval (CI), 1.9-6.8; P< 0.01] in the screened population aged 40 to 54 years. Among the 2,621 screened individuals aged 55 to 69 years, 291 (11.1%) had FDRs with CRC, and the prevalence of ACN was not significantly different between these 291 individuals and the other 2,330 individuals without affected FDRs (5.8% vs. 5.8%, respectively; P=0.95). The adjusted OR of the presence of affected FDRs for ACN was 1.0 (95% CI, 0.6-1.7; P=0.94). Despite this lack of a significant association, individuals with two affected FDRs (n=23) showed a significantly higher prevalence of ACN (17.4%) than those with one or no affected FDRs (5.7%) in the population aged 55 to 69 years (P=0.04). In this population, no significant association was found between the presence of affected FDRs aged < 60 years and ACN.

Conclusion: This study demonstrated the clinical significance of an FH of CRC in FDRs as a risk factor for ACN in a younger asymptomatic screened population aged 40 to 54 years. This result reemphasizes the importance of careful attention to an FH of CRC in FDRs, especially in CRC screening of younger populations. In contrast, an FH of CRC in FDRs may have a weaker impact for relatively older screened populations aged 55 to 69 years, except for those with two or more affected FDRs.

References: 1. Schoenfeld P. Gastroenterology. 2018; 155: 1298-1300. 2. Schoen RE, et al. Gastroenterology. 2015; 149: 1438-45.

Disclosure: Nothing to disclose

P0223 DIAGNOSTIC YIELD OF EARLY SURVEILLANCE AFTER INADEQUATE BOWEL PREPARATION ON SCREENING COLONOSCOPY

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Introduction: Current guidelines regarding surveillance after screening colonoscopy assume adequate bowel preparation. Management and follow-up intervals of patients with suboptimal or inadequate cleansing is unknown, with early surveillance being recommended especially after colonoscopy with poor preparation.

Aims & Methods: To determine the diagnostic yield of early repeat colonoscopy in patients with suboptimal bowel preparation in screening colonoscopy, regarding adenoma detection rate (ADR), advanced adenoma detection rate (AADR) and colorectal cancer detection rate (CRCDR). Also, to identify which factors existing on index colonoscopy are associated with the presence of advanced adenomas or colorectal cancer on repeat colonoscopy.

We performed an observational cross-sectional study by collecting data from men and women who underwent screening colonoscopy with suboptimal bowel preparation and then repeat colonoscopy within one year from May 2012 to August 2017 at Hospital General Universitario of Alicante. Adequate bowel preparation was defined as a score of 2 or 3 in every colonic segment according to the Boston Bowel Preparation Scale (BBPS). Patients with a score of 1 at any segment were considered to have a suboptimal preparation. Patients with a BBPS score of 0 at any segment or incomplete examination were excluded. Adenoma detection rate, advanced adenoma detection rate and colorectal cancer detection rate were analyzed at both index and repeat colonoscopy.

Results: Of the 2474 patients who underwent screening colonoscopy at our center during this period, 314 (12.7%) were reported to have a suboptimal preparation, with an initial adenoma detection rate of 65%, advanced adenoma detection rate of 48% and colorectal cancer detection rate of 3.8%. Of the 259 (82.5%) patients who underwent repeat colonoscopy, suboptimal cleansing persisted in 22 (9%). Among these patients, adenoma detection rate was 38'9%, advanced adenoma detection rate was 15% and no colorectal cancer was detected.

After index colonoscopy, 155 (49.4%) patients had post-polypectomy surveillance recommendation in 3 years and 159 (50.6%) in 10 years. However, after repeat colonoscopy, recommendation changed from 10 to 3 years in 15% of the patients with previous 10 years surveillance recommendation. The number of colonoscopies needed to repeat to change a surveillance recommendation was 15.

Total BBPS or presence of advanced adenoma at index colonoscopy were not associated with the presence of advanced adenoma at repeat colonoscopy. In the per-segment analysis, only the left colon was found to have a higher advanced adenoma detection rate at repeat examination in those patients with suboptimal preparation in that segment at index study (p=0'036).

Conclusion: Patients with suboptimal bowel preparation in screening colonoscopy present a high rate of advanced adenomas in repeat colonoscopy, with major changes in post-polypectomy surveillance recommendations. These findings support a recommendation for early repeat (within 1 year) colonoscopy in patients with a BBPS of 1 in any colonic segment at screening colonoscopy.

Disclosure: Nothing to disclose

P0224 ACHIEVEMENT OF EUROPEAN SOCIETY OF GASTROINTESTINAL ENDOSCOPY PERFORMANCE MEASURES: OBSERVATIONS FROM THE EUROPEAN COLONOSCOPY QUALITY INVESTIGATION QUESTIONNAIRE

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Introduction: The development of the procedure questionnaire, by the European Colonoscopy Quality Investigation (ECQI) Group, has been previously described in posters presented at United European Gastroenterology Week, 2015 and 2016.
Aims & Methods: To investigate the quality of colonoscopy in current clinical practice, through the use of online questionnaires, compared with recently published European Society of Gastrointestinal Endoscopy (ESGE) key performance measures. Data collection is an ongoing process. We analysed data collected between 2/6/16 and 30/4/18.
Results: 6445 colonoscopies were documented by 84 practitioners across 12 European countries.
Adequate bowel preparation was defined as Boston Bowel Preparation Scale score ≥6 (ESGE minimum standard ≥90%). From our data (data unavailable for 209, 3.2%), 84.2% (n = 5427) of procedures had adequate bowel cleansing.
Caecal intubation rate (ESGE minimum standard of ≥90% of all diagnostic and screening colonoscopies visualise the whole caecum, where indication exists). The caecum was the intended endpoint in 69.4% of procedures (ileum 28.1%, anastomosis 1.3%, data unavailable 1.2%). For those colonoscopies where the caecum was the intended endpoint (n = 4473), 94.7% reported reaching the caecum but only 77.5% (3281/4234) of those stated endpoint photo-documentation.
Polyp detection rate (PDR) (ESGE minimum standard ≥40% of screening and diagnostic colonoscopies performed in those aged 50 years or older). At least one polyp was detected in 40.7% (1357/3335) of qualifying procedures.
Withdrawal time from caecum to anal canal and inspection of the entire bowel mucosa at negative (no biopsy or therapy) screening or diagnostic colonoscopy (ESGE minimum standard mean 6 minutes). Of the 1150 qualifying procedures providing data, the overall mean (± SD) withdrawal time was 7.8 ± 3.1 minutes, the median withdrawal time was 7 minutes.
Conclusion: Our findings indicate that while minimum standards for PDR and withdrawal time are being met, they are not achieved for adequate bowel clearance, or photo-documentation of caecal intubation.
Disclosure: Spada C: Consultant fee from Norgine. Agrawal A, Amaro A, Hünger M, Petruzziello L Ono A, Jover R, Toth E: Consultant & advisory board participant to Norgine. Brink L: Consultancy & Advisory Board participant to Norgine, AMBU. Fischbach W: Consultancy & Advisory Board participant to Norgine; Speaking - Abbott, Bio Merieux, Falk; Advisory speaking - Aptalis, Fresenius Biotech, Pfizer; Advisory - Boehringer Ingelheim, med update. Kinnunen U: Consultant & advisory board participant to Norgine and Olympus (European NBI Expert Training Group). Riemann JF: In terms of ECQI, consultant to Norgine, otherwise no conflict of interest. Amlani B: Employee of Norgine. Koulaouzidis A: No relevant conflict of interest. Patai A: No conflict of interest. Pecere S: No conflict of interest.

P0225 THE SIGNIFICANCE OF CLOSURE OF THE MUCOSAL DEFECT AFTER COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION

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Introduction: Because of the technical difficulty of colorectal endoscopic submucosal dissection (ESD), injury to the muscularis layer or perforation might occur during the procedure. The efficacy of closure of the mucosal defect after colorectal ESD is unknown. We investigated the significance of mucosal defect closure after colorectal ESD.
Aims & Methods: We investigated 403 consecutive cases of colorectal ESD performed between January 2016 and March 2019 by an expert with an experience of >500 colorectal ESD procedures. We divided the patients into two groups; one for which mucosal defect closure was done (group C), and another for which mucosal defect closure was not performed (group N), and investigated their clinical outcomes. The closure was defined as the closure of the entire mucosal defect.
Results: Because of muscularis layer injury or perforation, 49 patients (12.2%) underwent closure of the mucosal defect and were classified into group C. Of these cases, 40 (81.6%) were closed using conventional clip and 9 (18.4%) were closed using over-the-scope clip (OTSC), respectively. The closure time was significantly shorter in conventional clip cases (6.7±3.2 vs. 22.4±7.3 min, P< 0.01) compared with OTSC cases.
On the other hand, all OTSC cases had a perforation or a widely exposed muscularis layer. One group C patient and 3 group N patients had delayed perforation (2.0% vs. 0.8%, P=0.41).
The one case in the group C patient was closed with OTSC. The clinical outcomes were not significantly different between groups, as follows: maximum temperature after the procedure (C vs. N: 37.2±0.5°C vs. 37.2±0.5°C, P=0.91), white blood cell count on postoperative day 1 (POD1) (8055±2708/µL vs. 8252±2419/µL, P=0.60), and C-reactive protein level on POD1 (1.22±1.39 vs. 1.19±1.66 mg/dL, P=0.89). However, the incidence of abdominal pain was lower in group C than in group N (16.3% vs. 17.8%, P=0.80).
Conclusion: Our results suggest that when perforation or muscularis layer injury occurs in colorectal ESD, a favorable course, similar to that of cases without such complications, can be obtained if the mucosal defect is closed.
Disclosure: Nothing to disclose

P0226 ENDOBILIARY RADIOFREQUENCY ABLATION FOR REFRACTORY BENIGN STRICTURE: A PILOT BICENTRIC STUDY

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Introduction: Endoscopic treatment of benign biliary stricture (BBS) remains challenging with 15% of recurrence ater metallic or multiple plastic stenting. We experimented endobiliary radiofrequency ablation (ERFA) with the aim to eradicate biliary fibroplasia endoscopically. We report our first experience of ERFA in the management of refractory BBS.
Aims & Methods: 8 patients with BBS (5 postoperative strictures, 2 chronic inflammatory strictures and 1 post stenting stricture) were treated from august 2014 to march 2018. All had previously unsuccessful endoscopic treatment with dilatations (1,75 [0-3]) and plastic or metallic stenting during a median of 18 months (9-48). Bipolar ERFA was delivered at power of 10 W for 90 seconds per stricture segment, followed by a 10 mm balloon dilatation without stent placement. Data were collected on technical success (ERFA delivery), clinical success (stricture resolution), adverse events and follow-up.
Results: ERFA was performed in 8 patients (7 men) with a median age of 56 years (range 20-81). All patients had stricture resolution after ERFA. No severe adverse event occurred with only a case of short abdominal mild pain. The median follow-up is 31 months.
BBS resolution without the need for further stenting was achieved in 6 patients. The 2 patients with inflammatory stricture had BBS relapse after initial resolution at 10 and 12 months, one underwent surgery, the other metallic stenting for 9 months with no further relapse at 2 years.

Conclusion: ERFA appears to be a safe and effective treatment for refractory BBS, especially for postoperative strictures. Further studies are warranted.
References: Hu B. et al. Dig Endosc. 2014 Jul;26(4):581-5.
Disclosure: Nothing to disclose

P0227 ASSESSMENT OF ERCP USING A SHORT-TYPE SINGLE-BALLOON ENTEROSCOPE FOR PATIENTS WITH SURGICALLY ALTERED GASTROINTESTINAL ANATOMY

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) in patients with surgically altered anatomy is technically challenging. We performed ERCP in such patients using a short single-balloon enteroscope (Short-SBE, Olympus), which has a 3.2-mm working channel and a 152-cm working length and for which conventional accessories are available. This study aimed to assess the efficacy and safety of ERCP using a Short-SBE in patients with surgically altered anatomy.
Aims & Methods: The present retrospective study included 144 patients (range, 32-93 years) and 236 procedures comprising Roux-en-Y reconstruction (105 patients and 141 procedures), Billroth II gastrectomy (21 patients and 40 procedures), and reconstruction by the modified Child method (18 patients and 55 procedures) performed using a Short-SBE. The success and complication rates of each procedure were evaluated.
Results: The blind end was reached in 95.3% of procedures (225/236). Of the failed procedures, five were caused by jejunum invasion. Among 225 procedures in which the blind end was reached, cholangiography was successfully performed 92.9% of procedures (209/225). Treatment was successful in 87.3% of procedures (206/236). Successfully performed therapeutic interventions included nasobiliary drainage (n = 3), plastic stent placement (n = 51), self-expandable metallic stent placement (n = 27), and stone extraction (n = 102) using endoscopic sphincterotomy (n = 5) endoscopic papillary balloon dilation (n = 11), endoscopic papillary large-balloon dilation (n = 39), and anastomosis dilation (n=22). Complications that occurred in 6.8% of procedures (16/236) included intestinal perforation (n = 1), mucosal laceration (n = 1), mild pancreatitis (n = 8), and mild cholangitis (n = 6).
Conclusion: ERCP using a short-SBE is effective and safe in patients with surgically altered anatomy.
Disclosure: Nothing to disclose

P0228 TO CUT OR NOT TO CUT - CLINICAL EFFICACY OF ENDOSCOPIC SPHINCTEROTOMY IN RECURRENT ACUTE PANCREATITIS FROM FUNCTIONAL BILIARY SPHINCTER OF ODDI DISORDER - A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Functional biliary sphincter of Oddi disorder, previously referred to as sphincter of Oddi dysfunction, is an established cause of recurrent acute pancreatitis which is defined as two or more episodes of documented acute pancreatitis per year. Data on the efficacy of endoscopic sphincterotomy in preventing future episodes of pancreatitis is limited.
Aims & Methods: We performed a systematic review and meta-analysis to evaluate the clinical efficacy of index endoscopic sphincterotomy in patients with recurrent acute pancreatitis secondary to manometrically proven functional biliary sphincter of Oddi disorder. Our goal was to assess reduction in episodes of pancreatitis following sphincterotomy, and not to assess chronic pain in these patients. We conducted a search of

several databases including PubMed, EMBASE, Google-Scholar, Scopus and Cochrane Review (from 1960 to October 2018). Random-effects model was used for analysis. Heterogeneity between study-specific estimates was calculated using Cochran Q statistical test and I^2 statistics. Publication bias was ascertained, qualitatively, by visual inspection of funnel plot and quantitatively, by the Egger test.
Results: Our initial search yielded 3201 results. After excluding non-english literature and duplicates, 1936 studies were screened and 12 met inclusion criteria. A total of 396 patients with recurrent acute pancreatitis and abnormal manometry findings were included from these studies in the final analysis. The interventions performed were as follows: endoscopic biliary sphincterotomy in 212 (53.5%), endoscopic pancreatic sphincterotomy in 19 (4.8%) and dual biliary and pancreatic sphincterotomy in 165 (41.6%) patients. Technical success ranged from 99 to 100%.The pooled estimate for clinical success following index sphincterotomy was 68.4% (95% CI 57.6-77.4; I^2=71.4%). Lone endoscopic biliary sphincterotomy was successful in 43/60 (71.6%) patients. The pooled estimate for proportion of patients with post-ERCP pancreatitis was 23.2% (95% CI 16.6-31.4; I^2=44.4%). The follow up duration ranged from 6 months (the shortest) to 120 months (the longest). There was no evidence of publication bias, based on funnel plot analysis and Egger's test.
Conclusion: Our study highlights the utility and clinical efficacy of endoscopic sphincterotomy in patients with recurrent acute pancreatitis secondary to functional biliary sphincter of Oddi disorder. We conclude that 68.4% of patients improved after endoscopic sphincterotomy and that it can be considered in patients with recurrent acute pancreatitis.
Disclosure: Nothing to disclose

P0229 WITHDRAWN

P0230 ASSESSMENT OF THE HOUSE CLASSIFICATION FOR GRADING ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY COMPLEXITY

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Introduction: In order to grade the complexity of Endoscopic Retrograde Cholangiopancreatography (ERCP) there are many scores available, the most used being the one developed by the American Society of Gastrenterology Endoscopy (ASGE).
Aims & Methods: The aim of this study was to evaluate a new classification (HOUSE) and to compare it with ASGE's. The ERCPs performed between 2015 and 2018 in our center were retrospectively reviewed. Repeated procedures in the same hospital admission and ERCPs in which cannulation was not attempted were excluded. We assessed HOUSE and ASGE classification scores, complications (pancreatitis, cholangitis, bleeding and perforation) and global technical success (GTS) - cannulation of the duct of interest, complete stone clearance and drainage of the duct of interest.
Results: A total of 900 ERCP were selected (mean age 71,6 ± 21,9 years ; 51,4% women), comprising 673 patients. According to the HOUSE classification, 765 (85%) ERCP were class 1, 86 (9,6%) class 2 and 49 (5,4%) class 3. The distribution by the ASGE classification was the following: 137 (15,2%) grade 1, 425 (47,2%) grade 2, 320 (35,6%) grade 3 and 18 (2%) grade 4. The GTS rate was significantly higher in less complex procedures according to the HOUSE (1 - 91,0%; 2 - 82,6%; 3 - 81,6%; p=0,009) and ASGE classification (1 - 98,5%; 2 - 92,7%; 3 -83,4%; 4 - 61,1%; p < 0,01). The overall complication rate was 10,0%, with an increasing complication incidence observed in more complex procedures as determined by the HOUSE (8,8%; 15,1%; 20,4%; p=0,008) and ASGE classification (5,8%; 8,2%; 13,8%; 16,7%; p=0,019). The correlation between the two scores was poor (ρ=0,239; p< 0,01).
Conclusion: Both scores accurately graded the complexity of ERCP. As complexity of procedures rises, GTS decreases while complications increase. These scores may be useful to compare technical success and complications between centers and endoscopists according to complexity as well as to stratify endoscopy training.
Disclosure: Nothing to disclose

P0231 ENDOSCOPIC TREATMENT STRATEGIES FOR BILIARY JEJUNAL ANASTOMOTIC STENOSIS

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Introduction: Although treatment by balloon endoscopy for benign biliary duct jejunal anastomotic stenosis after biliary reconstruction has been reported useful, there is currently no standardized treatment strategy. In this report, we have examined the treatment strategy and results at our facility.
Aims & Methods: We examined a total of 248 cases in 99 patients who underwent ERCP during single balloon endoscopy (SBE) with a diagnosis of cholangitis after biliary reconstruction from March 2013 to March 2019 in our hospital. After reaching the anastomotic site, direct-viewing observation was performed for diagnosis of benign or malignant disease, and biopsy was performed if malignancy was suspected.
A practical classification of endoscopic and retrograde cholangiographic appearance of hepaticojejunostomy strictures (K. Mönkemüller et al. WJG 2011; 3: 213-9) was used to evaluate the biliary-jejunal anastomotic site. The strictures were classified into Type A (small opening), B (large), C (normal), D (2 holes) and S (constriction upstream from the anastomotic site) according to endoscopic findings at the anastomosis site, and combined with the cholangiogram Type 0 (no stenosis), 1 (short stenosis), 2 (long stenosis), 3 (intrahepatic bile duct stenosis).
As a treatment strategy, only balloon dilatation was performed for Type A1 and S1, and balloon dilation plus plastic stent placement was done for A2 and S2; cases of Type B / C / D without stenosis were left untreated. In cases of stent placement, replacement was repeated every 2-3 months, and the stent was removed, if expansion was good. If endoscopic treatment was not possible, percutaneous transhepatic biliary drainage (PTBD) or EUS-guided biliary drainage (EUS-BD) was performed.
Results: The overall arrival rate to the bile duct jejunal anastomosis site was 97/99 (97.9%). Malignant recurrence at the anastomotic site was found in 15/97 (15.4%) among the achieved cases. A total of 82 benign cases were observed, and the classification of anastomotic findings was A1: 30 cases, A2: 10 cases, B / C / D: 1/30/5 cases, S1: 3 cases, S2: 1 case and complete stenosis. 2 cases showed dissection of the bile duct jejunal anastomosis. The endoscopic treatment completion rate was 80/82 (97.5%) and balloon dilation was performed in 44/80 cases (55%). Among the A1 and S1 cases, intrahepatic stones were present in 16/33 cases (48.8%). Stent placement was performed in 12/80 cases (15%), and 10 cases (83.3%) succeeded in having the stent removed. PTBD was performed in 2 cases and EUS-BD in 2 cases.
Conclusion: Balloon endoscopy enables direct observation of biliary jejunal anastomoses and is useful for diagnosis, differentiation and treatment of benign and malignant cases.
However, the classification and treatment consensus of anastomotic stenosis are still inadequate, so in the future it would be desirable to study a larger number of cases.
Disclosure: Nothing to disclose

P0232 A RETROSPECTIVE ANALYSIS TO ASSESS THE IMPORTANCE OF DOING A BILIARY SPHINCTEROTOMY AS A METHOD TO INCREASE AND SIMPLIFY CANNULATION SUCCESS RATE OF THE MAIN PANCREATIC DUCT

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Introduction: MPD cannulation is the prime requisite for any pancreatic endotherapy during an ERCP.
Lot of techniques are described for difficult bile duct cannulation, but very few for pancreatic duct cannulation. Usually in cases with chronic pancreatitis, acute on chronic pancreatitis or cases of acute pancreatitis followed by ductal leaks, the duodenum and peri ampullary region are edematous and makes MPD cannulation difficult.

We found that in difficult cases where MPD could not be cannulated easily and if we could get the wire into the CBD first, doing a wide biliary sphincterotomy improved the success of cannulation of the MPD without using any more sophisticated techniques.
Aims & Methods: Aim was to prove that doing a biliary sphincterotomy improves PD cannulation success.
Data of all cases (1206) for pancreatic ERCP from October 2008 to May 2018 in our tertiary care centre was studied.
All cases done by a single operator always using the wire guided technique. When MPD could not be cannulated in three attempts, or MPD not cannulated directly in 10 minutes or wire going in CBD first were studied
In failed MPD cannulation - we attempted to cannulate the CBD first or when wire went in CBD first inadvertently during an MPD cannulation, we did a biliary sphincterotomy wide enough to separate the biliary and pancreatic orifices and then cannulated the MPD with a cannula and a glide wire.
Results:

Number of ERP	1206
Successful direct MPD cannulation	982 (81.4%)
Difficult Cannulation	224 (18.6%)
CBD cannulated first inadvertently	199 out of 224 (88.9%)
Biliary Sphincterotomy done	199 (100%)
Successful MPD Cannulation after biliary sphincterotomy	185 (92.9%)
Failed MPD cannulation after biliary sphincterotomy	14 (7.03%)
Pancreas Divisum found	10 out of 14 failed cannulations (71.4%)
Failed MPD cannulation overall	25 out of 1206 (2.07%)

[Table 1]

Conclusion: If direct MPD cannulation is difficult, cannulating the CBD first and doing a prior biliary sphincterotomy improves the MPD cannulation success rate - from 81.4% to 92.9%.
Of those cases with failed MPD cannulation after biliary sphincterotomy, 71.4% cases had pancreas divisum which was not detected on MRCP or prior imaging.
Those who could not be cannulated at all were subjected with either EUS guided drainage or surgery.
Disclosure: Nothing to disclose

P0233 WITHDRAWN

P0234 DETECTION OF APNEA EPISODE USING NOVEL MAINSTREAM CAPNOGRAPHY SYSTEM IS FEASIBLE DURING EUS AND ERCP-RELATED PROCEDURE WITH CO_2 INSUFFLATION: A RETROSPECTIVE STUDY

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Introduction: Hypoxemia is the most frequent adverse effect of sedation during endoscopic procedures [1]. Hypoxemia can lead to unexpected cardiac arrest and/or brain injury. It has been reported that hypoxemia follows apnea during sedation, and as such, early detection of apnea might decrease hypoxemia [2]. However, the ESGE guideline recommended that capnography should be considered during non-anesthesiologist administration of Propofol in specific situations including high risk patients, intended deep sedation, and long procedures [3] A previous report revealed that the detection of $EtCO_2$ during full endoscopic procedures using the available sidestream capnometer was difficult because of blockage of the sampling tube with saliva, undetectable shallow breathing, or tachypnoea. Many previous studies reported that severe adverse events could not be prevented using the unreliable capnometer [4-6]. Thus, we developed a novel mainstream capnometer bite block system (cap-ONE

bite block, YG-227T; Nihon Kohden Corporation, Tokyo, Japan) designed to detect either nasal or oral tidal flow, with the EtCO$_2$ detector placed on the bite block without a sampling tube. The detector was not dislodged during the endoscopic procedure because the bite block was tightly fixed. A small-scale pilot study revealed the reliable detection of end-tidal EtCO$_2$ using our system [7]. This is a feasibility study for the novel mainstream capnometer system in a larger cohort.

Aims & Methods: Non-intubated patients undergoing ERCP and EUS-related procedures with CO2 insufflation under intravenous sedation with midazolam 0.25mg and pethidine 35mg were enrolled retrospectively during 2017 to 2018. EtCO2 was monitored continuously during the procedure using a mainstream capnometer system. The accuracy of total respiratory count using wave form analysis was evaluated using software (Nihon Kohden Tokyo, Japan).

Results: We enrolled 125 patients (age, 65.4±12.8; American Society of Anesthesiologists [ASA] class 1, n=81 and ASA 2, n=44; ERCP, n= 31 and EUS, n=94). Measurement of EtCO$_2$ concentration was possible from the start to the end of the procedure in all 125 cases. No measurement failure, bite block disruption, or adverse event related to the capnometer was found. Of the patients, 53.6% (67/125) had an apnoea episode. The mean time to the first apnoea episode was 9:56±1:47 min after sedation. The incidence of apnoea episode within 5 min after sedation was 52.3% (35/67). No relationship was found between the incidence of apnoea episode and comorbid diseases, smoking habit, alcohol consumption, or sleep medication addiction in the univariate analysis.

Conclusion: The detection rates of respiration and apnoea episodes were higher than those in previous reports. The novel mainstream capnometer system is reliable and feasible for use during EUS- and ERCP-related procedures even under CO$_2$ insufflation.

References: [1] Qadeer MA, Lopez AR, Dumot JA et al. Hypoxemia during moderate sedation for gastrointestinal endoscopy: causes and associations. Digestion 2011; 84: 37 [2] Lynn LA, Curry JP. Patterns of unexpected in-hospital deaths: a root cause analysis. Patient safety in surgery 2011; 5: 3 [3] Dumonceau JM, Riphaus A, Schreiber F et al. Non-anesthesiologist administration of propofol for gastrointestinal endoscopy: European Society of Gastrointestinal Endoscopy, European Society of Gastroenterology and Endoscopy Nurses and Associates Guideline--Updated June 2015. Endoscopy. 2015; 47: 1175 [4] Yamamori S, Takasaki Y, Ozaki M et al. A flow-through capnometer for obstructive sleep apnea. Journal of clinical monitoring and computing 2008; 22: 209 [5] Klare P, Reiter J, Meining A et al. Capnographic monitoring of midazolam and propofol sedation during ERCP: a randomized controlled study (EndoBreath Study). Endoscopy 2016; 48: 42 [6] Qadeer MA, Vargo JJ, Dumot JA et al. Capnographic monitoring of respiratory activity improves safety of sedation for endoscopic cholangiopancreatography and ultrasonography. Gastroenterology 2009; 136: 1568 [7] Takimoto Y, Iwasaki E, Masaoka T et al. Novel mainstream capnometer system is safe and feasible even under CO2 insufflation during ERCP-related procedure: a pilot study. BMJ Open Gastroenterol. 2019 e000266.

Disclosure: Nothing to disclose

P0235 VALUE OF PANCREATIC JUICE CYTOLOGY USING ENDOSCOPIC RETROGRADE PANCREATOGRAPHY IN PATIENTS SUSPECTED OF MALIGNANT INTRADUCTAL PAPILLARY MUCINOUS NEOPLASM

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Introduction: Pancreatic juice cytology (PJC) can provide strong evidence of malignant intraductal papillary mucinous neoplasm (IPMN), resulting in appropriate management. However, routine endoscopic retrograde pancreatography (ERP) for PJC is not recommended in IPMN patients because of the low sensitivity and the risk of post-ERP pancreatitis (PEP).
Aims & Methods: We aimed to elucidate what types of IPMN gain benefit of PJC using ERP. From April 2007 to April 2018, we reviewed medical records of 76 IPMN patients who underwent PJC using ERP in our hospital. IPMN-derived pancreatic ductal adenocarcinoma (PDAC) was suspected in 55 patients (Group A); 21 patients were suspected of having concomitant PDAC (Group B). Group A patients were further classified as having high-risk stigmata (HRS) (n=16), worrisome features (WF) (n=33), and non- WF (n=6) according to the International Consensus Guidelines 2012. We evaluated the cytology results, rate of malignant IPMN, PEP frequency and post-operative prognosis.

Results: In Group A, the rates of cytologic malignancy were as follows: non-WF, 0% (0/6); WF, 9.1% (3/33); and HRS, 56.3% (9/16). In 4 patients with HRS, PJC was negative but surgery was performed, leading to definitive diagnosis of IPMC. Finally, the rate of malignant IPMN in the patients with HRS was 81.3% (13/16). Notably, the sensitivity and accuracy of PJC in patients with WF were 100% and 100%, respectively, because the patients with negative PJC could be observed without progression. In Group B, ERP was performed in the cases with main pancreatic duct (MPD) stenosis or hypoechoic lesion that was separately detected by endoscopic ultrasound (EUS) or magnetic resonance cholangiopancreatography.The rates of cytologic malignancy in Group B was 23.8% (5/21). In 3 patients, PJC was negative but EUS-guided fine needle aspiration revealed PDAC. Therefore, the concomitant PDAC rate was 38.1% (8/21) (3, Stage 0; 4, Stage IA; 1, Stage IV). PEP frequency was 7.3% (4/55) and 23.8% (5/21) in Group A and Group B, respectively. All 9 patients were composed of branch duct (BD)-IPMN without MPD dilatation. Except for 4 patients who died of other diseases, all patients in the two groups were alive after surgery at a median follow-up of 15 months (range 2-120 months).

Conclusion: In patients suspected of IPMN-derived PDAC with WF, PCJ might have important roles in determining the appropriate treatment choice. In patients suspected of concomitant PDAC, careful follow-up examinations of the whole pancreas are needed for the early PDAC diagnosis regardless of IPMN type. Nevertheless, we should consider BD-IPMN without MPD dilatation as a risk factor of PEP.

Disclosure: Nothing to disclose

P0236 EHL FOR BILE DUCT STONES UNDER DIRECT CHOLANGIOSCOPY WITH SBE IN PATIENTS WITH SURGICALLY ALTERED ANATOMY

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Introduction: Nowadays Endoscopic treatment of Bile duct stones in patients with surgically altered anatomy have become popular with enteroscopy-ERCP. We have retrospectively investigated surgically altered patients with bile duct stones which were treated by Electrohydrolic lithotripsy(EHL) under direct single balloon enteroscopy(SBE).
Aims & Methods: We have reviewed medical records from 2009 to 2018 and finally found consecutive 159 cases of bile duct stones with surgically altered anatomy. Averaged age is 71.5y/o and male: female is 117(75%): 42(25%). The group of Roux-en-Y(R-Y) with gastrectomy were 95 cases which included gastric cancer 87cases and 8 others, R-Y without gastrectomy were 29 cases which included biliary cancer 12 cases, maljunction 8 cases, and 9 others, PD were 35 cases(53 sessions) which included pancreas cancer 20 cases, biliary cancer 7 cases and 8 others. Generally we started to treat these patients with enteroscopy-ERCP which were mainly short-type single-balloon enteroscopy(SBE). In case of large stone, we dilate the papilla by 15-18mm CRE balloon, then directly insert SBE into bile duct and crash the stones by EHL under SBE guidance.
Results: The rate of blind reach end and success rate were 88/95 cases(92.6%) and 79/81 cases(97.6%) in the Roux-en-Y(R-Y) with gastrectomy group, 28/29 cases(96.6%) and 28/28 cases(100%) in R-Y without gastrectomy, 34/35 cases(94.3%), and 33/33 cases(100%) in pancreato-duodenectomy, respectively. Totally 140/159 cases(88%) were treated by SBE which included 13 cases(8%) of EHL treatment by directly inserted SBE and remained 6 cases by surgery, 4 cases by PTBD, 2 cases by EUS-HGS, and conservative 7 cases. The adverse events were 3.1% in pancreatitis, 0.7% in bile leakage, 1.7% in perforation, and 1.1% in bleeding.
Conclusion: We concluded that EHL under direct cholangioscopy performed safely in 13/159(8%) and totally 140/159(88%) of bile duct stones were treated by enteroscopy-ERCP in surgically altered anatomy cases,
Disclosure: Nothing to disclose

P0237 WITHDRAWN

P0238 DIAGNOSTIC UTILITY OF A NEW ENDOSCOPIC SCRAPER FOR BILIARY STRICTURES

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Introduction: The endoscopic transpapillary bile duct brushing cytology and biliary forceps biopsy with endoscopic retrograde cholangiopancreatography are generally performed for pathological diagnosis of biliary strictures. The sensitivity of the conventional cytology and biopsy was reported to be 30% to 81%. The diagnosis of biliary strictures is difficult, especially of those caused by pancreatic cancer. Therefore, endoscopic transpapillary pancreatic juice cytology and endoscopic ultrasound-guided fine needle aspiration are performed for diagnosis.

Aims & Methods: The *Trefle* (Piolax Medical Devices, Yokohama, Japan) is a new device that consists of looped metallic wires to scrape and aspirate the tissue along with bile juice.The aim of the study was to compare the diagnostic performance of the new device with that of conventional cytology and biopsy. A total of 196 cases with biliary stricture underwent transpapillary biopsy and cytology between 2012 and 2018, of which 74were diagnosed using the new device.We retrospectively analyzed the diagnostic utility of the new device compared with that of conventional cytology and biopsy.

Results: The locationsof biliary strictureswereperihilar in 56 cases and distal in140. Of the 196 cases, 138 were diagnosed with a malignant stricture. Ninety-two cases had biliary cancer, whereas 46 had pancreatic cancer. The sensitivity of the new device and the conventional cytology and biopsy was 61% and 52%, respectively. Seven cases were diagnosed with malignant strictures using the new device, although they were not diagnosed during the conventional cytology and biopsy. In the cases with biliary strictures caused by pancreatic cancer, the sensitivity of the new device and the conventional cytology and biopsy was 59% and 32%, respectively.

Conclusion: Our study suggests that the new device was more useful than conventional cytology and biopsy for the pathological diagnosis of biliary strictures, especially those caused by pancreatic cancer.

Disclosure: Nothing to disclose

P0239 RADIATION EXPOSURE DOSE OF ERCP: A SINGLE-CENTER RETROSPECTIVE STUDY

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Introduction: Medical radiation provides us many benefits not only in diagnosis but also therapeutic procedure. On the other hand, its adverse effect becomes non-negligible concerns. Even a low dose exposure can affect the carcinogenesis in proportion to radiation exposure (RE) dose according to the Linear no-threshold model. Likewise, it is also important for medical staffs. Therefore, we have to recognize the proper use of medical radiation. In the field of gastroenterology, ERCP represents the major procedures under fluoroscopic guidance. However, we gastroenterologist do not know enough about the basis of RE nor how much we actually use in each ERCP.

Aims & Methods: The aim of this study is to assess the actual RE dose in ERCP and its affecting factors.

This is a retrospective, single-center cohort study of consecutive patients who underwent ERCP with the fluoroscopic unit (EXAVISTA, Hitachi..co) between Oct 2012 and Mar 2018. All ERCP procedures were categorized by disease sites into 4 types: common bile duct stone (CBDS), distal malignant biliary obstruction (DMBO), proximal malignant biliary obstruction (PMBO), and the Others. A total of 1543 ERCP procedures excluding procedures with missing data, were analyzed. We measured total fluoroscopy time (FT, sec), dose area product (DAP, mGycm^2) and air kerma (AK, mGy).

Results: The mean age was 73.9±10.8 years, and 663 patients were female (43%). 729 patients (47%) had a native papilla. ERCP procedures were performed for the purpose of treating CBDS (N=761,49%), DMBO (N=275, 18%), PMBO (N=324,21%), or other diseases (N=183, 12%).Median AKs in all case/ CBDS/ DMBO/ PMBO were 133/ 139/ 100/ 166 mGy, respectively.

In a similar fashion, median DAPs were 15.1/ 15.2/ 12.2/ 20.0 Gycm^2, and median FTs were 639/ 623/ 526/ 794 sec. Dunn's multiple comparison test revealed that PMBO showed significantly the largest DAP, AK, and FT, compared with DMBO (p< .0001/ p< .0001/ p< .0001, respectively) and, compared with CBDS (p=.0006/ p< .0001/ p< .0001, respectively). Among them, DMBO showed significantly the smallest DAP, AK and FT (p=.0015/ p=0.012/ p=.0068 than CBDS). Among all procedurs, the highest level of AK was 2.1 Gy in a PMBO case. Twelve cases (0.8%) were over 1Gy. Of them, 8 cases were PMBO including 3 cases with CBDS.

Conclusion: DAP, AK and, FT in PMBO were significantly larger than CBDS and DMBO. The disease sites significantly influenced the RD during ERCP. Some cases mainly in PMBO showed extremely high level of RE.

Disclosure: Nothing to disclose

P0240 HYDRATION WITH LACTATED RINGER'S SOLUTION COMBINED WITH RECTAL DICLOFENAC IN THE PREVENTION OF PANCREATITIS AFTER ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY

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Introduction: Pancreatitis after retrograde cholangiopancreatography (PEP) is one of the most frequent and serious complications of this exploration. It has been reported that rectal diclofenac, aggressive hydration with lactated ringer's solution alone or together with rectal indomethacin prior to exploration decreases the number of PEP.

We conducted a retrospective study in consecutive patients who underwent ERCP and were given rectal diclofenac prior to exploration or lactated ringer during and after or both interventions (lactated ringer's solution plus diclofenac) to assess whether there is reduction in the number of PEP in the treated groups.

Aims & Methods: All consecutive patients who have undergone ERCP since 2009 have been included. Until June 2012, they did not receive any type of prophylactic treatment (Group I). As of this date, rectal diclofenac 100 mg was placed before the start the exploration (Group II). Since January 2016 they were treated with intravenous infusion of lactated Ringer 200 ml / hour during the procedure and 4 hours after the procedure. In those patients in whom the pancreas was cannulated, they also received 500 ml of lactated Ringer in 30 minutes postexploration (Group III). Subsequently, from January 2017, patients received the same IV infusion of lactated Ringer during and after the exploration plus diclofenac 100 mg rectal before the procedure (Group IV). 1,896 ERCPs were included: 725 patients group I, 530 Group II, 227 Group III and 414 Group IV. The risk factors for PEP and PEP cases that were defined by consensus criteria were recorded.

Results: The average age of the patients was 70.7 years. 53.1% were male and 46.9% female. There were 65 PEP (3.4%), 3.4% of which corresponded to group II, 2.9%, to group I, 3.5% to group III and 4.3% to group IV (p, 640). 38.4% of all patients had one or more risk factors for PEP. The bivariate analysis relating the influence of the various factors under study on the likeliness of PEP development no differences were seen according to diclofenac administration status, acute hydration with lactated ringer nor with both treatments. Wirsung stent placement had no influence. PEP risk was increased by pancreatic duct cannulation and biliary sphincterotomy increased risk by a factor of 1.13 (95% CI: 0.55-2.34). In the logistic regression analysis the variable found to be significantly associated with PEP included Wirsung cannulation (with guidewire, contrast or both – OR 3,09 (95% CI: 1,45-6.58), OR 2,05 (95% CI: 0,81-5,17), and OR 4,57 (95% CI: 2.47-8.45), respectively), 83). Age younger than 75 years would increase risk by a factor of 2.35 (95% CI: 1.14-4.83). Hydratation plus diclofenac played no role in our cohort

Conclusion: In this study hydration with lactated ringer's solution combined with rectal diclofenac does not prevent the occurrence of PEP in our patients.

References: Lactated Ringer's solution in combination with rectal indomethacin for prevention of post-ERCP pancreatitis and readmission: a prospective randomized, double-blinded, placebo-controlled trial. Mok SR, Ho HC, Shah, P, Patel M,Gaughan JP, Elfant AB. Gastrointest Endosc 2017; 85: 1005-1013

Disclosure: Nothing to disclose

P0241 EVALUATION OF A NEW METAL BILIARY STENT OF 12-MM DIAMETER: A CASE CONTROL STUDY

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Introduction: : Biliary stent allows pre-operative or palliative drainage of malignant biliary stenosis, and biliary calibration in case of benign stenosis. Currently, by expert agreement, the diameter is 10-mm for metal stent. Since 2017, larger stent have been marketed in France and are approved for the biliary drainage of benign and malignant biliary stricture. These new 12-mm diameter stent could reduce the risk of recurrent biliary obstruction (RBO) and therefore increase the stent patency. The aim of our study was to compare whether the patency of 12-mm diameter stent was better than a conventional 10-mm.

Aims & Methods: From April 2017 and April 2018, 2 patients per month with benign or malignant biliary stricture were treated with metallic biliary stent, covered or uncovered, of 12-mm diametre (length 4 or 6-cm). Control patients treated with stent of 10-mm diametre were identified in our center database over the same period. These patients were paired based on age (per decade), stricture etiology (i.e., benign or malignant) and type of stent (i.e., covered or non covered). Primary endpoint was time before RBO. Secondary endpoints were technical success rate and adverse events rate (< 1 month).

Results: From April 2017 to April 2018, we included 24 patients in the 12-mm group (sex ratio 1.8/1; mean age 71 years) and 48 patients in the control group (sex ratio 1.6/1; mean age 68.8 years).
In each group, 75% of patients were treated for malignant stricture, mainly due to pancreatic adenocarcinoma. There was no statistically significant difference between the two groups in terms of sex, Karnofsky index and initial total bilirubin level. The median follow-up time was 7.49 months in the 12-mm group compared to 8.8 months in the 10-mm group (p=0.042). Technical success rate was 95.8% and 100% in the 12 and 10-mm groups respectively. The only failure was due to a stent dysfunction during the placement requiring its immediate replacement. Median time to RBO was 5.9 months in the 12-mm group vs. 8.3 months in the 10-mm group (p=0.27). In the malignant stricture subgroup, RBO occurred after 6.1 months and 17.1 months in the 12 and 10-mm group respectively (p=0.05). The adverse events rate in the month following the biliary stent placement was 25% (n=6/24) in the 12-mm group and 2% (n=1/48) in the control group without significant difference. In the 12-mm group, there were two grade II, one grade IIIa and three grade V adverse events according to the Dindo-Clavien classification. The only adverse event in the 10-mm group was grade II (acute pancreatitis). When new biliary drainage was required, it was done endoscopically in 100% of cases for both groups.

Conclusion: This case-control study does not show better permeability of 12-mm diameter metal biliary stent. This result seems to be true regardless of the etiology of biliary stricture and particularly in the group of malignant strictures. The placement of 12-mm diameter stent in benign stricture should be better evaluated. New prospective studies must be conducted to investigate the efficacy and safety of these stent.

Disclosure: Nothing to disclose

P0242 LAPARO-ENDOSCOPIC RENDEZ-VOUS MANAGEMENT OF GALLSTONES AND COMMON BILE DUCT STONES: A LARGE CASE SERIES

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Introduction: Biliary lithiasis is an endemic condition in both Western and Eastern countries, affecting 20% of the general population. In up to 20% of cases, gallstones are associated with common bile duct stones (CBDS), which are asymptomatic in up to one half of cases.
The ideal management of CBDS in the era of laparoscopic cholecystectomy is still controversial: multiple modalities have been applied with success.

The aim of our study is to evaluate the success rate, clinical results and length of hospital stay of single stage treatment of gallstones and CBDS by laparo-endoscopic rendez-vous.

Aims & Methods: From April 2000 to April 2019 a total of 495 elective patients (mean age 65 years, range 18-92, M/F 235/260) underwent single stage treatment of gallstones and CBDS by laparo-endoscopic rendez-vous technique. All patients were diagnosed preoperatively by MRCP or EUS and informed about alternative methods of treatment and potential complications related to laparo-endoscopic rendez-vous technique.

Results: Cholecystectomy and common bile duct drainage were achieved in 494 cases of 495.
The transcystic-transpapillar guidewire access was achieved in 448 of 495 (90.5%). In 46 of 495 patients (9.3%) we successfully performed intraoperative ERCP. We registered one case in which it was necessary a percutaneous drainage due to distal biliary stenosis (0.2%).
The conversion rate to an open cholecystectomy was 1.8% (9/495) because of previous abdominal surgery (7 pts) and unknown gallbladder cancer (2 pts). The mean ERCP operative time was 35 minutes (range 15-120 min). A biliary plastic stent was placed in 61 patients (12.3%) due to anatomic alteration of biliary tract (1 pt, 0.2%), not complete stone extraction (40 pts, 8%), giant lithiasis in elderly patients (17 pts, 3.4%) or biliary fistula (2 pts, 0.4%). One patient dead after the procedure for severe acute pancreatitis. Of the 495 patients who underwent laparo-endoscopic rendez-vous 6 patients (1.2%) suffered by major complications (lesions of the biliary tract=5 (1%); severe acute pancreatitis=3 (0.6%); retroperitoneal bleeding=2 (0.4%). Eleven patients (2.2%) underwent minor complications (bleeding=11). The mean length of hospitalization was 3 days.

Conclusion: Single stage treatment of gallstones and CBDS by laparo-endoscopic rendez-vous technique is a safe and effective method with low risk of postoperative pancreatitis. One-step treatment is more comfortable for patients and also shortens the mean hospital stay.

Disclosure: Nothing to disclose

P0243 ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP) IN ACUTE BILIARY PANCREATITIS (ABP)

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) plays major role in pancreaticobiliary disorders, however; its use in acute biliary pancreatitis (ABP) is a very debatable issue.
The aim of this work was to study the safety and efficacy of ERCP in ABP.

Aims & Methods: Patients presented with ABP were prospectively included and subjected to ERCP procedure after full clinical and investigational work up as per the policy of Qena university hospital. Diagnosis of AP was based on presence of deep-seated epigastric pain, at least triple-fold rise of pancreatic amylase and/or lipase, and radiologic findings of AP including edema, fluid collection or necrosis as detected by abdominal ultrasound (US) and computerized tomography (CT). Biliary aetiology of AP was confirmed by a triple-fold rise of ALT with detection of CBD stone(s) or mud in abdominal imaging.
To distinguish patients with concomitant cholangitis from those without cholangitis, the included patients were then classified into two groups: group (A) with concomitant cholangitis as defined as right upper quadrant pain, serum bilirubin ≥ 3 mg/dl and temperature ≥ 38 C, and group (B) patients without cholangitis who did not fulfill these criteria. ERCP procedures were performed by experienced ERCP endoscopist with more than 500 procedures performed.

Results: A total of 78 ABP patients were included, mean age: 40.7±13, 42 (54%) were females.
Clinical presentations on admission were; abdominal pain in 78 (100%), nausea in 55 (70.5%), jaundice in 44 (56.4%), vomiting in 43 (55 %) and fever in 35 (44.9%).
All patients were subjected to ERCP within 24 hours from the onset of pain. The cannulation technique was: wire-guided cannulation (WGC) in 56 patients (72%), transpapillary fistulotomy (TPF) in 18 (23%) and transpapil-

lary papillotomy in 4 patients (5%) with impacted stone at the papillary orifice. Definite stones were extracted in 74 patients (94%) while the rest of patients had only debris. The mean cannulation time was 13.6 minutes and the mean total procedure time was 68.4 minutes.

Our result showed a statistically significant difference among means of all biochemical parameters at baseline, 24-hours post-ERCP and at the time of discharge. The mean values of ALT, AST, ALP, total bilirubin, direct bilirubin, pancreatic amylase and lipase were: 261 U/L, 178 U/L, 252.5 U/L, 5.1 mg/dl, 3.3 mg/dl, 1013 U/L, 1404 U/L at baseline versus 180, 105, 178, 2.7, 1.7, 367, 918 one-day post-ERCP and 98, 69, 137, 1.6, 0.5, 84, 716 at discharge time.

At baseline; 18 patients had mild abdominal pain, 52 had moderate and 8 had sever while after ERCP 76 patients were pain-free, 1 patient had worsening of her pain from mild to moderate and another patient had the same moderate intensity pain. Both patients were young-age females with serum bilirubin < 3 mg/dl, BISAP score of 2 at admission, and without cholangitis. Biliary access was achieved via WGC after a relatively-long cannulation time of 17 and 23 minutes, and prolonged total procedure time of 98 and 103 minutes respectively. Both were managed medically for 5 and 7 days then were discharged.

No reported serious complications in our study.

Conclusion: In the setting of acute biliary pancreatitis, either with or without cholangitis, ERCP is safe and efficient procedure when performed by experienced hands and at the optimal time.

Disclosure: Nothing to disclose

P0244 A POPULATION-BASED ANALYSIS: WHO DOES RECTAL INDOMETHACIN IN POST-ERCP PANCREATITIS HELP?

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Introduction: Pancreatitis (PEP) post endoscopic retrograde cholangiopancreatography (ERCP) is a severe complication, with an incidence rate ranging between 1.3 – 24.4%. Many studies have shown that indomethacin effectively decreases post-ERCP pancreatitis (PEP). However, it is unclear which demographics are effected most, and the role of indomethacin in these populations. Additionally, large population-based studies reporting the effectiveness of rectal indomethacin are limited. This study aims to report populations who pose a higher than average-risk of PEP, and describe the role of indomethacin in these patients.

Aims & Methods: A population-based study was conducted using a cloud-based, HIPPA-enabled web platform called Explorys (IBM, New York) to collect aggregated de-identified electronic health records. At the time of the study, Explorys had access to over 62 million unique records. Data was obtained using ICD-9 code criteria for ERCP's, acute pancreatitis (pancreatitis within 7 days of ERCP), and inclusion of rectal indomethacin formularies. Relative risk (RR) with 95% confidence intervals (CI) in a random effect model was used for aggregated subgroup outcome data based on associated factors or patient characteristics to identify populations who may benefit most from rectal indomethacin.

	PEP [n=23,920]	PEP with Rectal Indomethacin [n=3,320]	Relative Risk [95% CI]	P
Age, n [%]				
18-65	12,150 [51]	1,920 [58]	1.11 [1.04, 1.18]	0.0011
> 65	11,630 [49]	1,390 [42]	0.68 [0.63, 0.72]	< 0.0001
Gender, n [%]				
Female	13,560 [57]	2,020 [61]	0.96 [0.90, 1.02]	0.1660
Male	10,360 [43]	1,300 [39]	0.76 [0.71, 0.81]	< 0.0001
Race, n [%]				
Caucasian	18,890 [79]	2,820 [85]	1.50 [1.37, 1.64]	< 0.0001
African-American	2,840 [12]	340 [10]	0.25 [0.22, 0.27]	< 0.0001
Hispanic	1,509 [7]	220 [7]	1.05 [0.93, 1.20]	0.4150

[Role of Rectal-Indomethacin in Post-ERCP Pancreatitis (PEP)]

Results: A total of 112,290 patients underwent ERCP, of which 23,920 (21%) developed PEP. We found a higher risk of PEP development in younger patients (18-65), African-Americans and Hispanics (P< 0.001). Rectal indomethacin decreased rates of PEP in patients > 65 [RR 0.68 (95% CI; 0.63-0.72), P< 0.0001] and African-Americans [RR 0.25 (95% CI: 0.22-0.27), P< 0.0001]. Indomethacin did not affect the risk of PEP in the younger population and Caucasians.

Conclusion: Rectal indomethacin decreases rates of post-ERCP pancreatitis in the elderly, and African-Americans. Given our study found African-Americans have higher rates of PEP, clinicians need to be aware and vigilant to provide rectal indomethacin in these populations, where benefit was greatest.

Disclosure: Nothing to disclose

P0245 ENDOSCOPIC SPHINCTEROTOMY FOLLOWED BY LARGE BALLOON DILATION IN THE EXTRACTION OF LARGE CHOLEDOCHOLITHIASIS

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Introduction: Endoscopic sphincterotomy (ES) is the standard therapy in common bile duct (CBD) stones extraction. Large stones (≥ 10 mm) or multiple stones extraction may be challenging after ES alone. Endoscopic sphincterotomy followed by large balloon dilation (ESLBD) has been described as an alternative to ES in these indications.

The aim of this study was to determine the therapeutic outcomes and safety of ESLBD compared with ES for large CBD stone extraction.

Aims & Methods: This is a retrospective study in which 323 consecutive patients who presented with choledocholithiasis >10 mm from January 2011 to December 2018 have been analyzed. In 249 ES was performed and the extraction of the stones was attempted. 74 patients were treated with ESLBD. Data for each patient and exploration were collected in an Excel sheet, and later analyzed using the IBM SPSS Statistics 20 software package. Simple statistical applications were applied in order to determine whether significant differences exist in comparison groups. We used chi-square test to compare proportions and categorical variables. Non-parametric Mann-Whitney U-test was applied in order to compare continuous variables. All comparisons were deemed to be statistically significant if P values were less than 0.05.

Results: The comparison of variables of two groups are expressed in Table 1.

VARIABLES	ES n=249	ESLBD n=74	p
Mean Age	75,81	75,82	0,828
Older than 75 Years(%)	59,3	60,8	0,893
Mean Number Stones	2,9	3,45	0,154
Size Major Stone (mm)	11,91	13,26	0,029
Male/Female (%)	52,2/47,8	50/50	0,792
Dilatation bile duct (%)	89,6	95,9	0.107
Full extraction stones (%)	68,7	69,9	0,887
Adverse Events (%)	2	0	0,593

[Comparison variables of ES and ESLBD groups]

78 (31.3%) of patients in ES group required repeat ERCP for stone clearance and in 70 large biliary dilation (LBD) was performed. In 22 (30.1%) of ESLBD group it was not possible to extract the stones and 11 had repeat LBD for complete duct clearance. Larger stone size (12.7 mm vs 16.3 mm, P < 0.001), multiple stones (3 vs 4 P < 0.06) were significant predictors of failed duct clearance at ERCP. Procedure related adverse events included 5 cases (2%) in ES group and none in ESLBD group (P< 0.593).

Conclusion: In our study ESLBD and ES clear bile stones with equal efficacy. However, ESLBD achieves the removal of larger stones in the initial ERCP with few adverse effects.

References: Endoscopic Papillary Large Balloon Dilation Versus Endoscopic Sphincterotomy for Retrieval of Large Choledocholithiasis: A Prospective

Randomized Trial. Omar MA1, Abdelshafy M2, Ahmed MY2, Rezk AG2, Taha AM2, Hussein HM2. J Laparoendosc Adv Surg Tech A. 2017 Jul;27(7):704-709.
Disclosure: Nothing to disclose

P0246 EVALUATION OF A NOVEL, NON-FLUOROSCOPIC, ALL-ARTIFICIAL MODEL FOR ENDOSCOPIC ULTRASOUND GUIDED BILIARY DRAINAGE TRAINING (TAGE-2)

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Introduction: Endoscopic ultrasound guided biliary drainage (EUS-BD) is a useful method after failed ERCP yet need expertise in performing the procedure. Hands on model for EUS-BD training has been developed to improve trainee's skill but previous models required fluoroscopy and included ex-vivo animal organs.We reported an all-synthetic interventional EUS training model (TAGE-1) and now a newer model (TAGE-2) has been developed.
Aims & Methods: This study aims to evaluate TAGE-2 model during the hands on workshop. We developed a non-fluoroscopy, all-artificial model for EUS-BD which included both hepaticogastrostomy (HGS) and choledochoduodenostomy (CDS). We launched TAGE-2 in two international EUS hands on workshops and gave a questionnaire to the participants. 10 aspects of EUS-BD was assessed scored from 1 to 4, with score 1 = poor, 2 = fair, 3 = good, 4 = excellent, by both the expert (> 300 experiences of EUS FNA) and the trainee during the workshop. The trainees were divided into a beginner (< 50 cases of EUS) and an experienced (≥50 cases of EUS FNA).
Results: The evaluation scores for EUS guided HGS and CDS are shown in table 1. Almost all items were graded as good to excellent, especially for the needle visibility, guidewire manipulation and stent deployment. However, the puncture sensation in EUS-CDS and contrast visibility in EUS-HGS are still graded fair to good by the experienced and the expert, respectively.
Conclusion: We developed a non-fluoroscopic, all-artificial model for EUS BD training which provided good training hands on for therapeutic EUS, especially for the steps and maneuverability of the instruments.

Evaluated items	HGS beginner (23)	HGS experienced (2)	HGS expert (3)	HGS overall (28)	CDS beginner (36)	CDS experienced (5)	CDS expert (4)	CDS overall (45)
Anatomical correlation	3	3	3	3	3	3	3	3
Bile duct identification	4	3	3	3	3	3	3.5	3
Needle visibility	4	3	4	4	4	4	4	4
Puncture sensation	3	3	3.5	3	3	3	2.5	3
Contrast injection	3	2.5	3.5	3	4	3	4	4
Guidewire manipulation	3	3	3	3	4	3	3	3
Tract dilation (dilation catheter)	3	3	3.5	3	4	3	4	4
Stent insertion	3	3	3.5	3	4	3.5	3	4
Overall	4	3.5	3	4	4	4	3.5	4

[Median evaluation score of TAGE-2 model for Endoscopic ultrasound guided hepaticogastrostomy (EUS-HGS) and choledochoduodenostomy (EUS-CDS).]

References: 1. Dhir V, Itoi T, Pausawasdi N, Khashab MA, et al. Evaluation of a novel, hybrid model (Mumbai EUS II) for stepwise teaching and training in EUS-guided biliary drainage and rendezvous procedures. Endosc Int Open. 2017;5(11):E1087-E95. 2. Dhir V, Itoi T, Fockens P, et al. Novel ex vivo model for hands-on teaching of and training in EUS-guided biliary drainage: creation of "Mumbai EUS" stereolithography/3D printing bile duct prototype (with videos). Gastrointest Endosc. 2015;81(2):440-6. 3. Pinyotepparatarn R, Ratanachuek T. POSTER ABSTRACTS: THERAPEUTIC: P-THER-02: A realistic, simple, inexpensive endoscopic ultrasound-guided

biliary drainage training model using three-dimensional printing bile duct and mixed gelatin material. Endoscopic Ultrasound. 2017;6(Suppl 1):S26-S.
Disclosure: Nothing to disclose

P0247 ENDOSCOPIC BAND LIGATION WITHOUT RESECTION OF SMALL SIZED SUBEPITHELIAL TUMORS: RESULTS IN SHORT-MEDIUM FOLLOW UP TERM OF A MULTICENTER PROSPECTIVE STUDY (BANDING-SET)

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Introduction: The endoscopic band ligation (EBL) without resection combined with a single-incision needle-knife (SINK) biopsy is a little reported option in the management of subepithelial tumours (SET).
Aims & Methods: The main aim was to determine the efficacy of this technique. Secondary aims: to evaluate its safety and the diagnostic yield of biopsy.
Methods: Prospective multicenter study. Inclusion criteria: SET≤15-mm, confirmed by endoscopic ultrasound (EUS). Technical success: complete EBL of the SET plus SINK biopsy. Clinical success: total disappearance of the SMT. Clinical controls: recovery at first 6 hours, calling at 48 hours and 7 days. EUS control at 4-6 weeks and 12 months. Clinical-Trials.gov register: NCT03247231.
Results: Seventy-two cases (49% of the sample calculation); EUS control 4-6 weeks n=59. Esophagus n=5, stomach n=52, duodenum n=14, rectum n=1. SET medium size: 9.6-mm (4.5-15 mm). EBL technical success: 85% (n=61/72). Clinical success at 4-6 weeks: 93% (n=55/59), overall clinical success: 79% (n=55/70). SET dependence of superficial vs deep layer subanalysis: technical success 90% vs 71%; overall clinical success 86% vs 62%. SET≤10-mm vs >10-mm: technical success 100% vs 63%; overall clinical success 98% vs 52%. Pathological diagnosis: 64% (35/55); no differences between SET-size, SET-layer, or number or biopsies. Three mild adverse events (4%): bleeding, pain, mucosal intraprocediment laceration. Incidences: epigastralgy (6h: 29%; 24-48h: 26%; 7-days: 13%; 4-6 weeks: 2%).
Conclusion: Preliminary results in the short-medium follow up term indicate that EBL of small SET, supplemented with SINK biopsy, seems to be a feasible and safe technique. The limitations of its technical and clinical success seem to be associated with the SET size and deep layers dependence.

	Superficial layer	Deep layer	SET ≤10-mm	SET >10-mm
YES technical success	46 (90%)	15 (71%)	42 (100%)	19 (63%)
NO technical success	5 (10%)	6 (29%)	0 (0%)	11 (37%)
YES clinical success	42 (95%)	13 (87%)	40 (98%)	15 (83%)
Overall NO clinical success	7 (14%)	8 (38%)	1 (2%)	14 (48%)

[Technical and clinical success subanalysis]

References: [1] Faulx AL, Kothari S, Acosta RD et al. The role of endoscopy in subepithelial lesions of the GI tract. Gastrointest Endosc 2017; 85: 1117-1132. [2] Arezzo A, Verra M, Miegge A, Morino M. Loop-and-let-go technique for a bleeding, large sessile gastric gastrointestinal stromal tumor (GIST). Endoscopy 2011; 43: E18-19. [3] Binmoeller KF, Shah JN, Bhat YM, Kane

SD. Suck-ligate-unroof-biopsy by using a detachable 20-mm loop for the diagnosis and therapy of small subepithelial tumors (with video). Gastrointest Endosc 2014; 79: 750-755. [4] Hwang JH, Konda V, Abu Dayyeh BK et al. Endoscopic mucosal resection. Gastrointest Endosc 2015; 82: 215-226. [5] Zang D, Lin Q, Shi R et al. Ligation-assisted endoscopic submucosal resection with apical mucosal incision to treat gastric subepithelial tumors originating from the muscularis propria. Endoscopy 2018; 50: 1180-1185.
Disclosure: Nothing to disclose

P0248 THE SAFETY AND THE EFFICACY OF SINGLE-SESSION ESOPHAGOGASTRODUODENOSCOPY AND ENDOSCOPIC ULTRASOUND USING NEWLY DEVELOPED ENDOSCOPE: A PROSPECTIVE INTERVENTION STUDY

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Introduction: Endoscopic ultrasound (EUS) is useful for obtaining high-resolution images of pancreaticobiliary diseases but is not readily available for a physical checkup. Recently, a new ultrasonic endoscope (EG-580UR; FUJIFILM) capable of simultaneously performing esophagogastroduodenoscopy (EGD) and EUS was developed. In this study, we evaluated the safety and efficacy of single-session EGD and EUS for the detection of upper-gastrointestinal and pancreaticobiliary diseases using this newly developed ultrasonic endoscope.
Aims & Methods: A total of 148 patients scheduled to undergo upper-gastrointestinal screening using an endoscope were prospectively included. All patients were examined using EUS together with EGD using EG-580UR. The primary endpoint was the safety of the procedures, and the secondary endpoints were the prevalence of diseases, basal imaging capability of EUS, correlation between the prevalence of pancreatic diseases and backgrounds, and procedure time. Imaging capability was scored as 0 (invisible) to 2 (sufficient visualization to evaluate the organs clearly) in each region.
Results: Intraoperative hypotension occurred as an adverse event of intravenous anesthesia in one patient, however her hypotension was reversed rapidly with the administration of ephedrine, and she recovered from anesthesia without further symptoms. The prevalence of pancreaticobiliary diseases was as written below; pancreatic cysts: 32 patients, early chronic pancreatitis: 25 patients, gallbladder polyps: 22 patients, adenomyomatosis: 9 patients, gallbladder stone: 13 patients, bile duct stone: one patient. The prevalence of upper-gastrointestinal diseases was as written below; esophagitis: 51 patients, esophageal polyp: 3 patients, chronic gastritis: 69 patients, gastric ulcer scar: oneb patient, gastric polyp: 23 patients, gastric submucosal tumor: 8 patients, duodenal ulcer scar: 8 patients, duodenal submucosal tumor: 2 patients. There were no features of malignancy of pancreaticobiliary and upper-gastrointestinal findings in any patients. Swollen abdominal lymph nodes was detected in one patient incidentally, and EUS-guided fine-needle aspiration was performed, which revealed the lesion to be follicular lymphoma. The mean EUS imaging scores of each section were 1.95 (pancreatic head and papilla), 2.0 (pancreatic body), 1.99 (pancreatic tail), and 1.89 (common bile duct and gallbladder). The age, history of diabetes mellitus, and smoking history were significantly associated with the prevalence of pancreatic diseases. Median procedure time was 21 minutes.
Conclusion: Performing EGD and EUS simultaneously using the new ultrasonic endoscope is tolerable and safe for upper-gastrointestinal and pancreaticobiliary screening.
Disclosure: Nothing to disclose

P0249 THE "TWIST-NEEDLE" - A NEW CONCEPT FOR ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE-BIOPSY

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Introduction: Endoscopic ultrasound-guided fine needle biopsy (EUS-FNB) represents a standard method for tissue acquisition of lesions adjacent to the gastrointestinal wall. 19-gauge needles acquire more tissue than needles with a smaller diameter, but are often unable to penetrate solid, rigid masses. In this study we evaluate a novel prototype that links forward movement of the needle to rotation of the needle tip.
Aims & Methods: Two needle-models that generate either a regular axial movement or a combination of axial movement with rotation of the needle tip were compared ex vivo for measurement of pressure needed to penetrate artificial tissue. Furthermore, a standard 19-gauge EUS-FNB needle was compared to a modified model ("Twist Needle") in an ex vivo model to measure the amount of tissue obtained.
Results: Pressure measurements using the rotating needle revealed that significantly less pressure is needed for penetration compared to the regular axial movement (mean ± SEM; 3.7 ± 0.3 N vs. 5.5 ± 0.3 N). Using the modified 19-gauge "Twist Needle" did not diminish tissue acquisition measured by surface amount compared to a standard needle (37 ± 5 mm² vs. 35 ± 6 mm²).
Conclusion: The method of rotation of an EUS-FNB needle tip upon forward movement requires less pressure for penetration but does not diminish tissue acquisition. Hence, the concept of our "Twist Needle" may potentially reduce some of the current limitations of standard EUS-FNB.
Disclosure: Nothing to disclose

P0250 DOES ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE BIOPSY USING A FRANSEEN NEEDLE REALLY OFFER HIGH DIAGNOSTIC ACCURACY AND POOR PUNCTURE PERFORMANCE?

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Introduction: Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) was first reported in 1992 and is now used for a wide range of lesions. This widely used non-surgical biopsy procedure provides safe, consistent results under ultrasound guidance.
A recent meta-analysis of pancreatic lesions showed that EUS-FNA was a modality producing excellent diagnostic accuracy, and EUS-FNA has now been established as an important modality for the histopathologic diagnosis of pancreatic lesions. This modality is not, however, without unresolved issues, including the need for by-lesion needle selection, the need for availability of rapid onsite evaluation (ROSE), and the need for skilled endoscopists.
New clinical applications for biopsies are on the horizon, such as genetic diagnostics and anticancer drug-sensitivity assays in addition to conventional diagnostics. Such applications will inevitably require collection of an adequate tissue volume to achieve better diagnostic accuracy. In EUS-FNA, 19-G needles are useful for histologic diagnostics, providing sufficient sample for immunostaining, but the greater puncture resistance encountered at this size increases the difficulty of the procedure. This has left users wanting smaller-gauge needles that could collect comparable volumes of tissue. In 2016, the Franseen needle emerged as a fine needle biopsy (FNB) device with the potential to provide better histologic diagnostic accuracy than conventional FNA needles. This device, however, remains under-researched.
We recently evaluated the diagnostic accuracy and utility of EUS-FNB performed with a 22-G Franseen needle for solid pancreatic lesions, comparing the results to those obtained through EUS-FNA with conventional needles.
Aims & Methods: This study aimed to investigate the diagnostic accuracy and utility of EUS-FNB performed using a Franseen needle on solid pancreatic lesions.
This study included 132 consecutive lesions sampled by EUS-FNA using a 22-G conventional needle and 93 consecutive lesions evaluated by EUS-

FNB using a 22-G Franseen needle to evaluate solid pancreatic lesions at our medical center between July 2013 and October 2018. Patient data were analyzed retrospectively.

Results: Diagnostic accuracy was significantly higher in the Franseen needle group (Group F; 91.4%, 85/93) than in the conventional needle group (Group C; 80.3%, 106/132; P=0.02). In Group F, diagnostic accuracies for pancreatic head lesions, lesions sampled by transduodenal puncture, and relatively large lesions >20 mm in diameter were 97.9% (47/48), 97.8% (45/46), and 93.3% (70/75), respectively. These values were significantly higher than in Group C (P < 0.001, 0.002, and 0.04, respectively). In terms of differentiating benign from malignant lesions, Group C showed 78.3% sensitivity (94/120), 100% specificity (12/12), 100% positive predictive value (94/94), and 31.6% negative predictive value (12/38), while Group F showed values of 89.9% (71/79), 100% (14/14), 100% (71/71), and 63.6%(14/22), respectively. Sensitivity and negative predictive value were better in Group F.

Conclusion: Using a Franseen needle for EUS-FNB of solid pancreatic lesions offers superior diagnostic accuracy to conventional FNA regardless of the lesion site.

Disclosure: Nothing to disclose

P0251 THE SENSITIVITY AND NEGATIVE PREDICTIVE VALUE OF EUS-FNA OF PANCREATIC MASSES IN PRACTICE: CAN WE RULE OUT PANCREATIC CANCER?

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Introduction: EUS-FNA is commonly performed to establish a tissue diagnosis of pancreatic cancer. Performance metrics for FNA of solid masses include diagnostic yield ≥70% and sensitivity for malignancy ≥85%.(1) These benchmarks were based on a meta-analysis of 33 studies from 1997-2009 reporting an average sensitivity of 85% but with a range among these studies of 54-95%.(2) Our previously published threshold analysis suggests that this level of sensitivity may have inadequate negative predictive value (NPV) to affect management.(3)

Aims & Methods: Objective: Review a tertiary center's clinical experience with EUS-FNA of pancreatic masses and calculate the sensitivity and NPV for pancreatic cancer.

Methods: This study was granted an IRB exemption from review. As part of our quality assurance program, all EUS-FNA procedures of solid pancreas masses from calendar years 2013 and 2014 were identified. All procedures were performed by 1 of 3 experienced endosonographers using Olympus echoendoscopes and processors and 22g or 25g FNA needles (Boston Scientific, Cook Medical) using a no suction technique. Rapid on-site evaluation for adequacy was performed by trained cytotechnicians after staining with toludine blue. Final pathology was determined by cytopathologists after review of pap stained slides and cell block material. Only cytology that was diagnostic was considered a true positive (suspicious was considered negative). Follow-up was done by chart review. False negatives had subsequent biopsy or clinical follow-up diagnostic of pancreatic cancer. True negatives ether had an alternative diagnosis established at FNA, by resection or biopsy, or adequate clinical follow-up indicative of a benign condition.

Results: 120 patients underwent EUS-FNA for pancreatic masses. Patients with a preprocedure or a pre-FNA endosonographic diagnosis of a cystic lesion without a solid mass were excluded. 102 (85%) were positive for malignancy. 18 patients with a negative cytology had median follow-up of 695 days. Of these 18, 4 were subsequently diagnosed with cancer (3 adenocarcinoma, 1 NET). The EUS-FNA was diagnostic of a benign etiology in 6 (AIP, ectopic spleen, 4 benign cystic lesions). Of the 8 without cancer and with a non-diagnostic EUS-FNA (median follow-up 830 days), 3 had surgical resections with pathology revealing benign cystic lesions, 2 had resolution of the lesion on repeat imaging, and 3 had chronic pancreatitis with no progression on at least 2 years of follow-up. The sensitivity of EUS FNA for cancer was 102/106 = 96%. The NPV was 14/18 = 78%.

Conclusion: EUS-FNA of pancreatic masses using modern techniques and rapid on-site evaluation has improved in the last 10 years. Our previously published threshold analysis indicated that if the post-test probability of cancer was ≥43% then surgery should be done.(3) With a NPV=78% and a post-test probability of 22%, a negative FNA should prompt additional testing and follow-up as opposed to proceeding with surgical resection in most cases. Given the high sensitivity for cancer in clinical practice, our results also suggest that quality benchmarks for EUS-FNA should be re-evaluated.

References: 1. Wani S, Wallace MB, Cohen J et al. Quality indicators for EUS. Gastrointest Endosc 2015;81(1):67-80. 2. Hewitt MJ, McPhail MJW, Possamai L et al. EUS-guided FNA for diagnosis of solid pancreatic neoplasms: a meta-analysis. Gastrointest Endosc 2012;75:319-31. 3. Sonnenberg A, Rodriguez SA, Faigel DO. Diagnostic ascertainment of suspicious pancreatic masses: a threshold analysis. Clin Gastro Hep 2008;6:1162-1166.

Disclosure: Nothing to disclose

P0252 THE DIAGNOSTIC ACCURACY OF ENDOSCOPIC ULTRASOUND VERSUS ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN EVALUATING COMMON BILE DUCT DILATATION OF UNDETERMINED ETIOLOGY DETECTED BY ABDOMINAL ULTRASOUND

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Introduction: The aim of the diagnostic evaluation of bile duct obstruction is to differentiate benign from malignant lesions and to stage the tumor in cases of malignancy. Endoscopic retrograde cholangiopancreatography (ERCP) helps in detecting the stricture location especially in the lower parts of biliary tract. Endoscopic ultrasound (EUS) is another modality which is safe when performed at a center with an experienced endosonographers. Isolated dilated CBD on abdominal ultrasound (US) is still in need to be probably assessed.

Aims & Methods: Our aim was to compare the accuracy of endoscopic ultrasound (EUS) to endoscopic retrograde cholangiopancreatography (ERCP) in the diagnosis of dilated common bile duct of undetermined etiology detected by abdominal ultrasound. Methods: we conducted a retrospective study on 139 patients referred to TBRI (Theodor Bilharz Research Institute) over the period of 2 years. 80 patients were included in the study and 59 were excluded due to insufficient endoscopic details. All patients with dilated CBD of indeterminate etiology by US who underwent EUS and ERCP were enrolled to compare between the accuracy of both as a diagnostic tool.

Results: Our study included 43 (53.7%) males and 37 (46.2%) females, with a mean (±SD) age of 52.01 (±12.15). The mean (±SD) of CBD diameter detected by US was 12.38 (±2.65). In comparison between ERCP and EUS in diagnosing pathological causes of CBD dilatation. EUS was statistically significant than ERCP with (p value < 0.001*). Diagnosis of CBD dilatation by EUS was as follows: 40 cases had malignant stricture, 28 cases had stones, 10 cases had benign stricture, and prominent CBD with no obstruction was in only 2 cases. While diagnosis of CBD dilatation by ERCP was as follows: 26 cases had indeterminate stricture, 24% cases had stones, another 24% cases had malignant stricture, 4 cases had prominent CBD with no obvious obstruction, and 2 cases had benign stricture.

FNA-EUS/biopsy sample was conducted on 44 cases only and the results were as follows: 36 cases had malignant stricture, 5 cases had chronic nonspecific inflammation, and 3 cases had benign non inflammatory stricture. In relation between FNA \ Biopsy sample results and pathological causes of CBD dilatation diagnosed by EUS and ERCP, there was statistically significant relation between FNA \ Biopsy sample results and findings of EUS and ERCP (with p-value< 0.001* in both), while diagnosis of CBD dilatation by EUS on those 44 cases was as follows: 36 cases (81.82 %) had malignant stricture, 6 cases (13.64%) had benign stricture and 2 cases (4.55%) had microlithiasis. While the diagnosis of CBD dilatation by ERCP was as follows: 21 cases (47.73%) had benign stricture, 19 cases (43.18%) had indeterminate stricture, 2% cases (4.55%) had stones, 1 case (2.27%) had benign stricture, and another 1 case had prominent CBD with no obvious obstruction.

	ERCP	EUS	Chi-Square		FNA / Biopsy (only 44 cases)	EUS	ERCP	Chi-Square	
	N (%)	N (%)	X2	P-value	N (%)	N (%)	N (%)	X2	P-value
Stone	24 (30%)	28 (35%)				2 (4.5%)	2 (4.5%)		FNA / Biopsy and EUS
Indeterminate stricture	26 (32.5%)	0 (0%)					19 (43.1%)	68.444	<0.001*
Benign stricture	2 (2.5%)	10 (12.5%)	36.308	< 0.001*	3 (6.8%)	6 (13.6%)	1 (2.2%)		FNA / Biopsy and ERCP
Malignant stricture	24 (30%)	40 (50%)			36 (81.8%)	36 (81.8%)	21 (47.7%)	33.868	<0.001*
Prominent CBD no obstruction	4 (5%)	2 (2.5%)					1 (2.2%)		
Chronic non-specific inflammation					5 (11.3%)				
Total	80 (100%)	80 (100%)			44 (100%)	44 (100%)	44 (100%)		

[Table (1): Descriptive data of the study]

Conclusion: Our study revealed the superiority of EUS over ERCP in diagnosing CBD dilatation of undetermined etiology detected by abdominal US.
Disclosure: Nothing to disclose

P0253 PROPHYLACTIC ENDOSCOPIC ULTRASOUND GUIDED GALLBLADDER DRAINAGE IN PATIENTS WITH UNRESECTABLE MALIGNANT BILIARY OBSTRUCTION AND CYSTIC DUCT ORIFICE INVOLVEMENT: A RANDOMIZED CONTROL TRIAL

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Introduction: Biliary self-expandable metal stents (SEMS) are a palliative therapy for malignant biliary obstruction (MBO); however, acute cholecystitis is a described adverse event. Tumor involvement to the orifice of the cystic duct (OCD) is a major predictive factor for acute cholecystitis after SEMS placement. Endoscopic ultrasound guided gallbladder drainage (EUS-GBD) have been reported for the acute cholecystitis treatment; however, the role of primary EUS-GBD for acute cholecystitis prophylaxis remains unknown.
Aims & Methods: A single-center, randomized control-trial. Primary EUS-GBD was performed using a 3.8 mm therapeutic echoendoscope and a lumen apposing metal stent (Hot Axios™ Stent and Electrocautery Enhanced Delivery System, Boston Scientific, MA) after conventional biliary drainage with SEMS. In the other arm, patients were submitted to conventional biliary drainage using SEMS without primary EUS-GBD. A sample size of 11 patients per group was estimated, considering the clinical success of EUS-GBD vs. percutaneous transhepatic gallbladder drainage (92% vs. 86%) and, a type I & II errors of 10% and 20%, respectively. Baseline characteristics were described and compared with their corresponding hypothesis testing. The primary outcome of the study was the occurrence of acute cholecystitis after randomization and assed-up to 12 months or death. Secondary endpoints were the length of hospitalization and the median relative survival. Time-to-event analysis for acute cholecystitis and relative survival were estimated through Competing Risk Analysis and Cox Regression, respectively. A p- value < 0.05 was considered statistically significant. Data analysis was performed using R.
Results: 23 patients were included: 12/23 in the primary EUS-GBD group and 11/23 in the control group. No reintervention was required in the primary EUS-GBD group; whereas, four patients from the control group developed acute cholecystitis: three patients were treated via laparoscopic cholecystectomy at the day 16, 7 and 1, after randomization. One patient in control group developed acute cholecystitis and was rejected to surgery at the day 100, being switched and treated with EUS-GBD. The median length of hospitalization in days was inferior in patients treated with primary EUS-GBD. The one-year acute cholecystitis-free survival rate was 91.7% for primary EUS-GBD compared to 36.4% in the control group (HR 0.117;

0.014-0.958, p=0.016). No difference in the median relative survival was detected among groups 2.4 months for primary EUS-GBD vs 2.8 months in the control group (HR 0.837; 0.308-2.272, p=0.727) (table 1).

	Primary EUS-GBD (n = 12)	Control group (n = 11)	p-value
Age (years), median (IQR)	63.9 (52.4 - 71.9)	71.6 (67.9 - 81.7)	0.037
Sex (female), n (%)	9 (75.0)	7 (63.6)	0.444
Primary tumor, (cholangiocarcinoma/malignant pancreas tumor)	8/4	8/3	0.555
Middle-distal common bile duct tumor obstruction, n (%)	5 (41.7)	1 (9.1)	0.112
Size of the lesion (mm), median (IQR)	27.5 (15 - 30)	23.5 (20 - 35)	1.000
Covered/Uncovered metal stent, n (%)	8/4	6/5	0.543
Hospitalization days, median (IQR)	1 (1-3)	3 (0-27)	0.054
One-year acute cholecystitis-free survival rate, n (%)	11/12 (91.7)	4/11 (36.4)	0.016
One-year relative survival rate, n (%)	8/12 (66.7)	9/11 (81.8)	0.727

[Table 1. Baseline characteristics & study outcomes per groups.]

Conclusion: Primary EUS-GBD prevent the development of acute cholecystitis after SEMS placement in patients with MBO and tumor involvement of the orifice of the cystic duct.
References: Clinical trial number: NCT03729882.
Disclosure: Nothing to disclose

P0254 ENDOSCOPIC ULTRASOUND GUIDED THERAPY IS SUPERIOR TO ENDOSCOPIC THERAPY FOR GASTRIC VARICEAL BLEEDING: A SYSTEMATIC REVIEW AND COMPARATIVE META-ANALYSIS

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Introduction: Gastric varices (GV) are less common and rupture less often than esophageal varices (EV). However, once ruptured, GV bleeding is difficult to control and carries a higher mortality than EV bleeding in the setting of portal hypertension. Treatment options include direct endoscopic (END) glue injection and endoscopic ultrasound (EUS) guided glue and/or coil injection. The role of EUS in the treatment of GV is not established.
Aims & Methods: We conducted a comprehensive search of several databases (inception to Dec 2018) to identify studies that evaluated the use of END and EUS in the treatment of GV. Our goals were to estimate and compare the pooled rates of treatment efficacy, GV obliteration, GV recurrence, early re-bleeding (< 120hrs), and late re-bleeding (>120hrs) with END and EUS. Our secondary goals were to analyze the adverse events with these two modalities in the treatment of GV.
Results: Total of 44 studies (2777 patients) were included. 26 studies (2196 patients), 8 studies (231 patients), 7 studies (303 patients), and 3 studies (47 patients) were treated with END-glue, EUS-glue, EUS-glue/coil, and EUS-coil respectively. Mean age range was between 40 and 65 years, with 68% of males. N-butyl-2-cyanoacrylate and 2-octyl-cyanoacrylate were the most commonly used glue. 28% had GOV1, 49% had GOV2, and 23% had IGV1 (Sarin classification). 63% of the patients had cirrhosis. 30% were due to alcohol, 31% due to viral hepatitis, and the rest were due to other causes. 11% of the included patients had hepatocellular carcinoma. Complete GV obliteration was significantly higher with EUS-coil/glue as compared to END-glue [(89% (95% CI 66.3-97.1, I^2=62.4) vs 57.1% (38.2-74.1, I^2=94.3), p=0.03].GV recurrence was significantly lower with EUS-coil/glue as compared to END-glue [(3.1% (95% CI 0.9-10.3, I^2=0) vs 22.6% (95% CI 13.8-34.9,

(95% CI, I2)	All EUS modalities	EUS-glue	EUS-coil	EUS-coil/glue	END-glue
Immediate treatment efficacy	93.6% (85-97.4, 59.5), p=0.17	92.3% (74-98, 54.4), p=0.44	86.2% (38.4-98.4, 6.5), p=0.99	96.5% (85.3-99.2, 61.5), p=0.1	86.4% (75.3-93, 96.1)
Complete GV obliteration	84.7% (66.8-93.8, 84.2), p=0.03	89.8% (57.4-98.3, 28.8), p=0.07	NC	89% (66.3-97.1, 62.4), p=0.03	57.1% (38.2-74.1, 94.3)
GV recurrence	6.1% (2.6-13.7, 51.4), p=0.006	12.4% (4-32.3, 18.8), p=0.29	NC	3.1% (0.9-10.3, 0), p=0.002	22.6% (13.8-34.9, 77.1)
Early rebleeding (<120 hrs)	6.8% (4.1-11.1, 13.2), p=0.43	5.9% (2.8-12, 0), p=0.83	NC	9% (4.1-18.4, 64.2), p=0.25	5.4% (4.2-6.8, 17.8)
Late rebleeding (>120hrs)	10.6% (6.3-17.3, 45.7), p=0.03	14.2% (6.6-27.9, 68.2), p=0.39	14.7% (4-42, 0), p=0.63	6.4% (2.7-14.7, 0), p=0.01	20% (14.7-26.6, 89.3)
Total adverse events	16.5% (9.7-26.9, 83.1), p=0.48	27.4% (13.8-47, 81.7), p=0.07	5.5% (0.9-26.8, 0), p=0.3	11.7% (5-25.3, 79.5), p=0.79	13% (8.5-19.5, 87.7)
Sepsis	2.5% (1.3-4.9, 0), p=0.91	2.8% (1.1-7.3, 0), p=0.65	4% (0.7-20.4, 0), p=0.53	1.7% (0.5-5.4, 0), p=0.74	2.4% (1.5-3.8, 53.6)
Distant organ embolism	4.1% (1.9-8.6, 40.6), p=0.22	3.4% (1-10.5, 0), p=0.52	4% (0.5-26.4, 0), p=0.92	4.9% (1.5-14.9, 70.8), p=0.27	2.2% (1.2-4.1, 70.9)
Fever	2.9% (1.3-6.2, 0), p=0.57	3.5% (1.1-10.5, 0), p=0.95	4% (0.5-24.9, 0), p=0.92	2% (0.5-6.9, 0), p=0.4	3.8% (2.1-6.7, 84.3)
Pain	4.3% (2.1-8.6, 29.9), p=0.3	4% (1.3-11.5, 0), p=0.51	4% (0.5-24.5, 0), p=0.68	4.7% (1.6-13.2, 67.9), p=0.36	2.7% (1.5-4.7, 73.4)
Death due to GV rebleeding	6% (3.3-10.6, 28.9), p=0.3	8.8% (3.7-19.5, 62), p=0.13	4.7% (0.9-21, 0), p=0.87	4% (1.5-10.3, 0), p=0.97	4.1% (2.7-6.2, 57.5)

EUS: endosonography, END: direct endoscopy, GV: gastric varices, All p-values are in comparison to END-glue. NC: not calculated due to limited data

[P0254 Table. Summary of pooled results.]

I²=77.1), p=0.002].Late re-bleeding was significantly lower with EUS-coil/glue as compared to END-glue [(6.4% (95% CI 2.7-14.7, I²=0) vs 20% (14.7-26.6, I²=89.30, p=0.01].The pooled rates of immediate treatment efficacy and early re-bleeding were comparable between the treatment modalities. The pooled rate of all adverse events, sepsis, distant embolism, fever, pain, and death due to GV rebleeding were similar between the groups. No difference was noted between EUS-glue and END-glue. (Table)

Conclusion: EUS guided treatment of GV with simultaneous use of coil/glue seems to give superior long term clinical benefits as compared to END-glue with comparable immediate treatment efficacy and similar risk to early-rebleeding. Well-conducted studies are warranted to further establish the role of EUS-coil/glue treatment in GV.

Disclosure: Nothing to disclose

P0255 EUS-GUIDED TISSUE ACQUISITION IN CHRONIC PANCREATITIS: DIFFERENTIAL DIAGNOSIS BETWEEN PANCREATIC CANCER AND PSEUDOTUMORAL MASSES USING EUS-FINE NEEDLE ASPIRATION OR CORE BIOPSY

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Introduction: Endoscopic Ultrasound (EUS)-guided fine needle aspiration (FNA) sensitivity for malignancy in parenchymal masses of patients with concurrent chronic pancreatitis (CP) has been reported to be unsatisfactory.

Aims & Methods: The aim of the present study was to directly compare the diagnostic accuracy of EUS-FNA and EUS-fine needle biopsy (FNB) in differentiating between inflammatory masses and malignancies in the setting of CP. We performed a retrospective analysis of prospective, multicentric databases of all subjects with pancreatic masses and clinical-radiological-endosonographic features of CP who underwent EUS-FNA or FNB.

Results: Among 1124 with CP, 210 patients (60% males, mean age 62.7 years) with CP and pancreatic masses met the inclusion criteria and were enrolled. In the FNA group (110 patients), a correct diagnosis was obtained in all but 18 cases (diagnostic accuracy 83.6%, sensitivity 69.5%, specificity 100%, PPV 100%, NPV 73.9%); by contrast, among 100 patients undergoing FNB, a correct diagnosis was obtained in all but 7 cases (diagnostic accuracy 93%, sensitivity 86.8%, specificity 100%, PPV 100%, NPV 87%) (p=0.03, 0.03, 1, 1 and 0.07, respectively). At binary logistic regression, focal pancreatitis (OR 4.9;p< 0.001), higher Ca19-9 (OR 2.3;p=0.02) and FNB (OR 2.5;p< 0.01) were the only independent factors associated with a correct diagnosis.

Conclusion: EUS-FNB is effective in the differential diagnosis between pseudotumoral masses and solid neoplasms in CP, showing higher diagnostic accuracy and sensitivity than EUS-FNA. EUS-FNB should be considered the preferred diagnostic technique for diagnosing cancer in the setting of CP.

Disclosure: Nothing to disclose

P0256 HIGH PERFORMANCE OF A NEW FRANSEEN NEEDLE FOR ENDOSCOPIC ULTRASOUND-GUIDED FINE-NEEDLE BIOPSY IN SOLID LESIONS: A MULTICENTER STUDY

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Introduction: Endoscopic ultrasound-guided fine needle aspiration (FNA) is the standard choice to samplegastrointestinal/pancreatic lesions. EUS-FNA is accurate when rapid on-site evaluation (ROSE) is performed, but ROSE is not always available. EUS- guided fine needle biopsy (EUS-FNB) can give a better chance to reach a diagnosis providing more tissue. It is not simple to use 19-gauge needles especially in transduodenal settings for risk of complications. A new needle for EUS-FNB, the Acquire needle is available from 2016. Data for pancreatic and non pancreatic solid lesions are available but these are based only on small sample size studies.

Aims & Methods: The aim of our study is to perform a retrospective evaluation of all sampling procedures performed using the 22/25 gauge Acquire needle in patients with solid lesions.We performed a retrospective analy-

sis of prospective, multicentric databases in 5 Italian Endoscopic centres, including all consecutive patients with solid lesions who underwent EUS between June 2016 and October 2018. All lesions localized at pancreas, nodes, biliary, kidney/liver masses, periduodenal/perigastric abdominal masses were enrolled in the study. Features of masses and technical details of FNB were recorded.

Results: 450 patients (60.2% males, mean age 64,3) were enrolled. EUS-FNB was performed using the 22 and 25 gauge Acquire needle. The biopsies was done transgastrically in 190 (42%)cases and transduodenally in 260 (58%) ones. A mean of 2.2 ± 0.32 passes per lesion site were performed, without any complication. A tissue core biopsy sample for histological evaluation was obtained in 438 (97%) cases. In all the cases, the specimens were useful for cytological analysis too. Acquire sensitivity, specificity and diagnostic accuracy were 98.8%,100% and 98.7% respectively

Conclusion: EUS-FNB using the 22 and the 25-gauge Acquire needle has a very high accurancy and is useful to achieve histological sample in almost all the patients

Disclosure: Nothing to disclose

P0257 EUS-GUIDED THROUGH-THE-NEEDLE MICROFORCEPS BIOPSY FOR THE DIAGNOSIS OF PANCREATIC CYSTIC LESIONS: HOW MANY SPECIMENS SHOULD BE RETRIEVED?

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Introduction: Accurate diagnosis of pancreatic cystic lesions (PCLs) is of paramount importance to guide the decision-making process and reduce the rate of inappropriate resection.

Endoscopic ultrasound (EUS)-guided through-the-needle biopsy (TTNB) has been reported to improve diagnostic yield compared with cytology [1-3]. However, TTNB technique is not yet standardized and the minimum number of visible specimen to be retrieved is unknown

Aims & Methods: The aim of this single center retrospective study was to evaluate the diagnostic yield of TTNB according to the number of macroscopically visible samples acquired.

All consecutive patients with PCLs with risk features (cyst >3 cm, thickened wall, 5-9 mm main pancreatic duct, increased size during follow-up, and mural nodules) who underwent TTNB between May 2016 and July 2018 were included. TTNB procedures were performed following an internal protocol established with the pathologists whereby the acquisition of three samples, when possible, was set as a standard. Each acquired specimen was placed separately in formalin vials.

Diagnostic yield of one, two, or three TTNB macroscopically visible specimens was analyzed and compared with fluid cytology at four levels: capability of differentiating mucinous vs nonmucinous cysts, ability to obtain a cyst-lining epithelium, definition of the grade of dysplasia, and definition of specific cyst histotype.

Results: Sixty-one patients (M/F 14/47; mean age 50.2 ± 14.7 years) were included. PCLs were located in the head, body, and tail in 18 (29.5%), 23 (37.7%), and 20 (32.8%) cases, respectively. The mean size was 40.7 ± 14.2mm. Overall, 179 TTNB specimens were evaluated (in four cases, intracystic bleeding impeded collection of the third specimen). Specimens were judged adequate for histological evaluation in 164 (91.6%) cases. A 100% histological adequacy was reached by two samples (p=0.05 versus one).

In the cytological samples, cyst epithelium was present in 27 (44.2%), the distinction between mucinous and nonmucinous cysts was possible in 30 (49.2%), the grade of dysplasia was established in 25 (41%), and a specific diagnosis of cyst type was achieved in 5 (7.9%) cases.

Compared with cytology, one TTNB specimen improved only the possibility of defining cyst histotype (p< 0.0001), whereas two specimens increased all four diagnostic categories (p< 0.003). Two specimens also increased diagnostic yield compared with one sample (p< 0.085). The collection of a third sample did not improve the value of any diagnostic level (**Table 1**). A specific diagnosis was reached in 74% of patients with two histological samples. The diagnostic reliability of TTNB compared with surgical histology was 90% (18/20 patients). The two TTNB nonconcordant cases were mucinous non-neoplastic cysts according to TTNB, resulting in mucinous cystic neoplasms with surgical histology. The rate of adverse events was 22.9% (10 cases of intracystic bleeding, 2 mild acute pancreatitis, 1 peripancreatic bleeding and 1 transitory fever).

Conclusion: Two TTNB macroscopically visible specimens allowed reaching a 100% histological adequacy and a specific diagnosis in 74% of patients. The collection of a third specimen did not add any additional information, and should be avoided in order to possibly decrease the risk of adverse events.

References: 1. Barresi L, Crinò SF, Fabbri C, et al. Endoscopic ultrasound-through-the-needle biopsy in pancreatic cystic lesions: A multicenter study. Dig Endosc. 2018 May 29 2. Kovacevic B, Karstensen JG, Havre RF, et al. Initial experience with EUS-guided microbiopsy forceps in diagnosing pancreatic cystic lesions: A multicenter feasibility study (with video). Endosc Ultrasound. 2018 Nov-Dec;7(6):383-388 3. Yang D, Trindade AJ, Yachimski P, et al. Histologic Analysis of Endoscopic Ultrasound-guided Through the Needle Microforceps Biopsies Accurately Identifies Mucinous Pancreas Cysts. Clin Gastroenterol Hepatol. 2018 Nov 21. doi: 10.1016/j.cgh.2018.11.027. [Epub ahead of print]

Disclosure: Nothing to disclose

Diagnostic level (possibility to define)	Citology N (%)	One specimen at TTNB N (%)	Two specimens at TTNB N (%)	Three specimens at TTNB N (%)	P value (citology Vs one specimen)	P value (citology Vs two specimens)	P value (one Vs two specimens)	P value (two Vs three specimens)
Histologic adequacy	na	56 (91.8)	61 (100)	61 (100)	na	na	0.05	NS
Mucinous Vs Nonmucinous	30 (49.2)	38 (62.3)	48 (78.7)	51 (83.6)	0.201	0.001	0.073	0.644
Presence of epithelial lining	27 (44.2)	32 (52.4)	44 (72.1)	48 (78.6)	0.468	0.003	0.039	0.528
Grade of dysplasia	25 (41)	31 (50.8)	42 (66.8)	46 (75.4)	0.363	0.003	0.064	0.545
Specific diagnosis	5 (7.9)	35 (57.4)	45 (73.8)	48 (78.6)	<0.0001	<0.0001	0.085	0.671

[P0257 Table:1 Histologic adequacy and four levels of diagnostic yield according to cytology and the number of retrieved specimens]

P0258 CASE SERIES OF EUS GUIDED BILIARY DRAINAGE AS A NEWLY ADOPTED TECHNIQUE FOR BILIARY OBSTRUCTION IN A TERTIARY CARE CENTER

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) is often the procedure of choice for drainage of biliary obstruction; however, this technique may not be feasible in all patients. Percutaneous transhepatic biliary drainage (PTBD) is another option but is associated with high morbidity and post procedural complications. Endoscopic ultrasound (EUS), initially a diagnostic procedure, has evolved into a therapeutic option in patients with failed ERCP. EUS can be performed immediately after attempted ERCP, thereby providing a potentially immediate solution. This project focuses on the implementation of EUS guided biliary drainage (EUS-BD) as a new technique for relieving biliary obstruction in patients with failed ERCP in a tertiary care center.

Aims & Methods: A prospective analysis of patients with biliary obstruction and failed ERCP requiring EUS-BD was conducted between November 2017 to February 2019. Indication for intervention and reason for failed ERCP were noted. Patients' clinical improvement, laboratory data, and procedural complications were documented 1 month after the procedure.

Results: Twenty-six patients (M/F, 14/12; median age 68) underwent EUS-BD. Twenty-five patients required drainage secondary to a malignancy while 1 was for choledocholithiasis. ERCP failure was due to clinical instability in 1 patient with severe aortic stenosis (4%), inaccessible papilla in 13 patients (50%), and inability to cannulate the papilla in 12 patients (46%).

The procedure was technically successful in 20 patients with the remaining 6 requiring PTBD. In patients with successful EUS-BD, there was one complication with a patient requiring ICU admission for Klebsiella bacteremia. Clinical success, in the form of reduced total bilirubin or improvement of obstructive symptoms, was noted in 100% of patients following successful EUS-BD.

Conclusion: Our study shows that EUS-BD is a technique that offers high clinical and technical success rates and low complication rates. The learning curve is short when performed in the hands of an experienced endoscopist. Furthermore, EUS-BD provides immediate solution for failed ERCP rather than investigating other therapeutic options.

Further studies are required to establish outcomes in patients with EUS-BD and comparison of this technique to potential alternative solutions such as PTBD or surgery. One limitation of this case series is the majority of cases are specific to distal biliary obstruction caused by malignancy.

Disclosure: Nothing to disclose

P0259 COMPARING MODIFIED WET SUCTION VERSUS DRY SUCTION TECHNIQUES IN EUS-FNA FOR SOLID LESIONS: A PROSPECTIVE, MULTICENTER, RANDOMIZED CONTROLLED TRIAL

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Introduction: The optima sampling techniques for endoscopic ultrasound (EUS) -guided fine-needle aspiration (FNA)are not standardized. We conducted a prospective, multicenter, randomized controlled trial comparing the modified wet suction technique (MWST) and the dry suction technique (DRST) for sampling the solid lesions in the pancreas, mediastinum and abdomen.

Aims & Methods: A total of 296 patients from 4 endoscopic centers were randomized in a ratio of 1:1 to receive either DRST or MWST as the first pass during EUS-FNA procedure. For Group A (n=134), the pass sequence was DRST - MWST - DRST - MWST versus MWST - DRST - MWST - DRST for Group B (n=135). The outcome measures were the diagnostic yield and specimen quality.

Results: We demonstrated that the MWST group had a significantly better histological diagnostic accuracy (84.85%) than DRST group (73.19%, P =0.0013). In subgroup analysis, the MWST group reached a 91.59% histological diagnostic accuracy for non-pancreatic masses and achieved a significantly superiority for all lesions >20 mm. Furthermore, the MWST provided a better specimen adequacy and less blood contamination whether it was chosen as the first pass or not.

Conclusion: In this prospective study of sampling solid masses, we found using MWST resulted in significantly better histology than DRST, especially for the masses >20 mm. Two passes of MWST provided adequate tissue for non-pancreatic lesions. The specimen quality collected by MWST was superior to DRST regardless of sequence selection bias. Trials registration: NCT02789371.

Disclosure: Nothing to disclose

	DRST group % (95% CI)	MWST group % (95% CI)	P value
Overall diagnostic accuracy			
All lesions (n=269)	89.22 (84.89-92.66)	92.94(89.19-95.69)	0.13043
Pancreatic (n=161)	86.34 (80.05-91.23)	91.30(85.84-95.16)	0.15714
Non-pancreatic (n=108)	93.52 (87.10-97.35)	95.37(89.53-98.48)	0.55245
Histological diagnostic accuracy			
All lesions (n=269)	73.19(67.05-78.74)	84.85(79.94-88.95)	0.0013*
Pancreatic (n=161)	68.84(60.41-76.45)	80.25(73.16-86.17)	0.0240*
Non-pancreatic (n=108)	79.38(69.97-86.93)	91.59(84.63-96.08)	0.0127*

[Comparison of diagnostic accuracy between DRST group and MWST group]

P0260 DOUBLE GUIDEWIRE TECHNIQUE USING A DOUBLE LUMEN CANNULA FOR INTERVENTIONAL EUS

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Introduction: There are a few reports on the use of double guidewire (DGW) technique to facilitate multiple drainage placement for EUS-guided drainage of pancreatic fluid collections (PFC). However, this technique can provide advantages other than multiple drainage placement during interventional EUS, such as scope stabilization, support for stone extraction or device insertion.

Aims & Methods: Consecutive patients who underwent interventional EUS between Feb 2012 and Apr 2019 were retrospectively reviewed. The rate and purposes of DGW technique, and clinical outcomes were evaluated. A double lumen cannula (UDLC: Uneven Double Lumen Cannula, Piolax Medical, Kanagawa, Japan) was used to achieve DGW technique. UDLC has two separate lumens (0.025" and 0.035") with a tip diameter of 3.6 Fr. DGW technique was performed as follows; Puncture using a 19-gauge FNA needle under EUS guidance, insertion of a 0.025" guidewire (GW), followed by UDLC insertion, preloaded with a 0.035" GW, over the 0.025" GW, and then, advancement of a 0.035" GW. A 0.035" stiff GW was used when multiple drainage placement is planned or when support for scope stabilization, antegrade stone extraction or device insertion is needed, while a 0.035" hydrophilic GW was used when negotiation of the stricture is necessary. After achieving DGW insertion, EUS-guided interventions were completed.

Results: During the study period, 252 interventional EUS procedures were performed: 51 pancreatic cyst drainage (PCD), 82 hepaticogastrostomy (HGS), 8 choledochoduodenostomy (CDS), 37 gallbladder drainage (GBD), 36 rendezvous (RV), 19 antegrade stone treatment (AG), 13 pancreatic duct drainage (PD) and 6 abscess drainage (AD). Among those 252 cases, DGW technique was used in 82 cases (32.5%). The reasons for DGW technique were multiple drainage placement in 61 cases (21PCD, 32 GBD, 5 HGS, 2 AD, 1 PD), scope stabilization in 10 (5 HGS, 3 PD, 1 GBD, 1 AD), support for stone removal in 4 AG, support for device insertion in 8 (4 HGS, 2 PD, 1 AG, 1 RV) and safety GW placement in 5 (3 guidewire manipulation for stricture passage and 2 stent placement). DGW technique was utilizes as a salvage technique after single guidewire procedure in 17 (20.7%) and as a primary technique in 65 (79.3%). Insertion of UDLC and DGW were

both successful in 100%. Adverse events related to DGW technique were not observed. Preplanned intervention was technically successful in 75 cases (91.5%). The reasons for preplanned procedure failure were failed multiple drainage placement in 3 and failed GW passage in 4 (3 rescue transmural drainage and 1 technical failure). Among 17 cases with salvage DGW technique, preplanned intervention was achieved only after DGW technique in 13 (76.5%).

Conclusion: DGW technique using UDLC during interventional EUS was useful for multiple drainage placement as well as support for stone removal and device insertion.

References: Seewald S, Thonke F, Ang TL, et al. One-step, simultaneous double-wire technique facilitates pancreatic pseudocyst and abscess drainage (with videos). Gastrointest Endosc. 2006 Nov;64(5):805-8. Ang TL, Teo EK, Fock KM. EUS-guided drainage of infected pancreatic pseudocyst: use of a 10F Soehendra dilator to facilitate a double-wire technique for initial transgastric access. Gastrointest Endosc. 2008 Jul;68(1):192-4. Itoi T, Itokawa F, Tsuchiya T, et al. EUS-guided pancreatic pseudocyst drainage: simultaneous placement of stents and nasocystic catheter using double-guidewire technique. Dig Endosc. 2009 Jul;21 Suppl 1:S53-6. Nakai Y, Kogure H, Koike K. Double-guidewire technique for endoscopic ultrasound-guided pancreatic duct drainage. Dig Endosc. 2019;31 Suppl 1:65-6.

Disclosure: Nothing to disclose

P0261 FOCUSSED ENDOSCOPIC ULTRASOUND RESULTS IN PATIENTS WITH UNEXPLAINED DILATATION OF COMMON BILE DUCT AND OR PANCREATIC DUCT

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Introduction: Unexplained dilation of the common bile duct (CBD) and pancreatic duct (PD) or both on abdominal imaging are amongst the most common indications for endoscopic ultrasound (EUS).

Aims & Methods: Patients referred for EUS for dilated CBD and/or PD from 2012 to 2016 for whom LFTs were available, were included in the study. CBD dilatation was defined as CBD diameter greater than 7mm at any place while PD diameter more than 4 mm in the head and 3 mm in the body and tail was considered dilated. To investigate if derangement of liver function tests (LFTs) is associated with positive findings on EUS to explain the cause for the dilated ducts.

Results: : We examined a total of 2179 EUS procedures, of which 404 patients met the study criteria. 293/404 had elevated LFTs [defined as elevation of one of these: bilirubin, ALT, ALKP or GGT] and 111/404 had normal LFTs. 74% of patients had more than one imaging modality before the EUS. EUS found a cause of dilated duct in >50% of cases in both the groups. In patients with CBD dilatation alone, elevated bilirubin was associated with finding a significant finding on EUS (p< 0.027) (66%). In those with CBD and PD dilatation, raised bilirubin (p< 0.022) and Alkaline Phosphatase (p< 0.018) were associated with positive findings (39% and 62%respectively).

Conclusion: The presence of raised bilirubin +/- concurrent ALKP rise was statistically more likely to have a cause found for the dilated duct on EUS. EUS detected undiagnosed pathology in unexplained duct dilation even in the presence of normal LFTs. We recommend early access to a diagnostic EUS in the diagnostic pathway of patients with dilated CBD and or PD.

References: Smith I, Monkemuller K, Wilcox CM. Incidentally Identified Common Bile Duct Dilatation. Journal of Clinical Gastroenterology. 2015;49(10):810-5. Malik S, Kaushik N, Khalid A, Bauer K, Brody D, Slivka A, et al. EUS yield in evaluating biliary dilatation in patients with normal serum liver enzymes. Digestive diseases and sciences. 2007;52(2):508-12.

Disclosure: Nothing to disclose

P0262 ENDOSCOPIC ULTRASOUND FEATURES ASSOCIATED WITH MALIGNANCY AND AGGRESSIVENESS OF NON-HYPOVASCULAR SOLID PANCREATIC LESIONS: RESULTS FROM A PROSPECTIVE OBSERVATIONAL STUDY

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Introduction: Non-hypovascular (i.e., isovascular or hypervascular) patterns can be observed in solid pancreatic lesions (SPLs) with different diagnoses with different prognosis and management.

Aims & Methods: The primary aim was to identify lesion features on endoscopic ultrasound (EUS) associated with malignancy/aggressiveness in this setting of patients. Secondary aims were EUS-tissue acquisition (EUS-TA) outcome and safety. In a prospective observational study we included consecutive patients with one or more non-hypovascular SPLs detected on cross-sectional imaging and referred for EUS-TA. Exclusion criteria were hypovascular pattern on contrast-harmonic EUS, concomitant chronic pancreatitis, and lesion of nonpancreatic origin. Lesion features (size, site, margins, echotexture, vascular pattern, and upstream dilation of the main pancreatic duct) were recorded. Malignancy/aggressiveness was determined by one or more of the follows: a) evidence of carcinoma at biopsy/surgical histology; b) signs of local aggressiveness (perineural invasion, lymphovascular invasion, microscopic tumor extension/infiltration or evidence of metastatic lymph nodes) at surgical specimen; c) radiologic detection of lymph nodes or distant metastases; d) tumor growth >5mm/12 months. Uni- and multivariate analyses were performed to assess the primary aim.

Results: Among 174 patients evaluated, 154 (M/F 70/84, mean age 58.7 years ± 13.1) with 161 SPLs were enrolled. SPLs were located in the head/uncinate, body, and tail in 50 (31.1%), 55 (34.1%), and 56 (34.8%) cases, respectively. Mean lesion size was 18.8 mm ± 10.6. Fifty-six lesions (34.8%) were resected and 105 (65.2%) underwent follow-up for a median period of 20 months (range 12-32 months). Overall, 40 (24.8%) lesions were defined malignant/aggressive and 121 (75.2%) benign. Irregular margins and size >20mm were independent factors associated with aggressiveness in multivariate analysis (p< 0.001, OR=5.2 and p=0.003, OR=2.1, respectively). Irregular margins and size >20mm predicted malignancy/aggressiveness with an accuracy of 81% and 74%, respectively. A subgroup analysis evaluating neuroendocrine tumors (NET) (N=92) and non-NETs (N=60) was performed (**Table 1**) revealing that in non-NET group only irregular margins were associated with malignancy/aggressiveness.

EUS-TA sensitivity, specificity and accuracy were 91.6%, 100%, and 92%, respectively. The rate of adverse events was 4%.

Conclusion: Our study demonstrated that irregular lesion margins are an independent factor useful in predicting malignancy/aggressiveness of isovascular and hypervascular SPLs. Size >20mm should be considered a warning feature only when a diagnosis of NET is confirmed. EUS-TA is safe and highly accurate in this setting and should be largely adopted for the differential diagnosis of these lesions.

Disclosure: Nothing to disclose

P0263 ENDOLUMINAL ULTRASOUND VERSUS MAGNETIC RESONANCE IMAGING IN ASSESSMENT OF RECTAL CANCER AFTER NEOADJUVANT THERAPY

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Introduction: Accurate tumor staging guides the choice of treatment modality and suggest the prognosis of rectal cancer. EUS and magnetic resonance imaging (MRI) are used indistinctly in the pretherapeutic workup of rectal cancer. Post neoadjuvant therapy interpretation of response in both MRI and EUS retains some difficulty due changes seen in the peritumoral region because of the effects of chemoradiation such as edema, inflammation, necrosis, and fibrosis lead to a hypoechoic appearance which mimics the primary tumor, leading to frequent overstaging.

Aims & Methods: To compare the performance of EUS and MRI in assessment of locoregional staging of anorectal cancer after neoadjuvant therapy. Up till now, we have twenty-eight (16 male, 12 female) were included in the study. Histopathological staging after surgery were used as reference for comparing the yield of locoregional staging for EUS and MRI. EUS and MRI were done 1 month after completion of neoadjuvant therapy.

Results: Regarding Post-Surgical T staging, there were eight patients with early tumor (T2=6 and T1=2) and twenty patients with locally advanced tumor (T3= 20 and No T4), while N staging, there were sixteen patients with negative nodes and twelve with positive nodes (N1= 7 and N2= 5). Regarding T staging; The sensitivity, specificity and accuracy of EUS (95%, 72%, 89.29%) was significantly higher than MRI (70%, 50%, 64.29%) for detecting early and locally advanced tumor. Also, EUS had a high statistical significant difference for detection of lymph nodes across MRI (sn 83.33%, sp 62.5% and acc 71.43% vs 54.55%, 52.94%, 53.57).

Conclusion: EUS appears more accurate in locoregional staging of rectal carcinoma after neoadjuvant therapy compared to MRI in rectal carcinoma.

References: Uberoi, A. S., & Bhutani, M. S. (2018). Has the role of EUS in rectal cancer staging changed in the last decade?. Endoscopic ultrasound, 7(6), 366.

Disclosure: Nothing to disclose

P0264 FEASIBILITY OF ENDOSCOPIC ULTRASOUND GUIDED BILIARY DRAINAGE FOR UNRESECTABLE MALIGNANT HILAR BILIARY STRICTURES

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Introduction: Biliary drainage is the main palliative therapeutic measure for unresectable malignant hilar biliary strictures (MHS) and survival is highly correlated to the volume of drained liver[1] Endoscopic ultrasound-guided biliary drainage (EUS-BD) has emerged as an alternative technique for primary drainage or as rescue technique after failed endoscopic retrograde cholangiography (ERCP).

Aims & Methods: The aim of this study was to demonstrate the feasibility of EUS-BD in MHS, both as the initial and rescue procedure.

This study is a single center retrospective work based on prospective data of patients included between January 2015 and September 2018 for biliary drainage of inoperable malignant hilar obstruction. For this analysis, only patients with EUS-BD drainage were included. It could be a drainage by EUS-BD alone or in combination with another technique, for initial drainage or re-intervention. Clinical characteristics of patients, stenosis and drainage were collected. The percentage of liver drained, the complication rate in the month following the procedure using Clavien-Dindo classification, the number of re-interventions, the length of hospitalisation were analyzed.

Results: Among the 139 patients of the registry, 20 patients were included (10 women and 10 men). The mean patient age was 68 years. 7 patients had an obstruction by cholangiocarcinoma and 13 by metastasis. 4 patients had type II stenosis according bismuth classification, 7 type IIIA, 2 IIIb and 7 type IV. The mean invasion of liver was 24%.

No patient had ascites or duodenal stenosis but 2 patients had a modified anatomy. EUS-hepaticogastrostomy (EUS-HGS) was the only one EUS-BD technique used. 16 patients had EUS-HGS for initial drainage: 2 EUS-HGS alone due to a right liver invasion and 14 combined with another technique : 11 combined with ERCP, 2 with Percutaneous transhepatic drainage (PCTD) and 1 with ERCP and PCTD.

The mean percentage of drained liver was 86%. The average number of stents was 2.8. The early complication rate was 31%(n=5) mainly angiocholitis (n=4) with 3 grade II and 2 grade III. The mean hospital length was 8 days.

The EUS-HGS combined with PCTD was performed in 2 patients with modified anatomy. One of this patient had a right-left drainage by hepaticogastrostomy combined without complication.

For EUS-HGS/ERCP combined drainage , 5 were performed during the same session and 6 in two sessions .Hospitalisation length was 7,4 days and 8,3 days respectively. It was mainly type IIIa (n=5) and type IV (n=5) stenosis.There was no difference between the complication rate (n=1), the number of endoscopic reintervention (n=3) and the percentage liver drainage (96% vs 97% respectively).

4 patients had EUS-HGS as re-intervention with 3 situations : One patient had rescue drainage by EUS-HGS because of pancreatitis associated with angiocholitis. Two patients had an EUS-HGS in the follow-up because of the progression of the disease (Day 183 and day 303) and 1 patient needed EUS-HGS to drain the left liver not initially drained. In the registry,11 patients had an undrained left liver due to ERCP failure or left liver atrophy. Only this patient needed additional drainage.

Conclusion: EUS-BD is a feasible and safe technique for initial drainage and for re-intervention procedures. EUS-HGS/ERCP combination seemed to be useful in cases of complex stenosis, especially type IIIa , and could be performed in one or two sessions.

References: 1.Caillol et al. Palliative endoscopic drainage of malignant stenosis of biliary confluence: Efficiency of multiple drainage approach to drain a maximum of liver segments. UEG journal, 2018.

Disclosure: Nothing to disclose

P0265 INCIDENCE AND RISK FACTORS OF ADVERSE EVENTS AFTER EUS-GUIDED FNA OR FNB FOR PANCREATIC SOLID LESIONS

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Introduction: Recently, EUS-guided fine-needle biopsy (EUS-FNB) of pancreatic solid lesions has been developed in the hopes of obtaining core tissue samples for histological evaluation. However, data with regard to the adverse events (AEs) of EUS-FNB are scarce.

Aims & Methods: We conducted a retrospective study to identify the AE rate of EUS-FNB and compare with that of EUS-FNA in patients with pancreatic solid lesions. Consecutive patients who underwent EUS-FNA/B for pancreatic solid lesions between Jan 2017 and Aug 2018 at the University of Tokyo Hospital were retrospectively studied. Inclusion criteria were patients who underwent EUS-FNA using mainly 22-gauge FNA needle (Expect, Boston Scientific Japan, Tokyo, Japan) and EUS-FNB using mainly 22-gauge FNB needle (Acquire, Boston Scientific Japan) for pancreatic solid lesions. About 10-20 strokes after application of 10-cc suction were similarly performed during EUS-FNA/B. The frequency of AEs after EUS-FNA/B of pancreatic solid lesions were compared and a multivariate logistic regression

analysis for AE rate was performed to clarify the risk factors of AE. AEs were graded according to the *ASGE lexicon's* severity grading system.
Results: A total of 221 patients were included to this study. The median age was 69 (24-91) years, and 148 patients were male. The median diameter of lesions was 20 (3-72) mm and location was in the head in 85 (38%). The median number of passes were 4 (2-8). The final diagnoses were pancreatic cancer in 122 (55%), neuroendocrine tumor in 16 (7%), autoimmune pancreatitis in 33 (15%). The rate of patients with tumor size>20mm was significantly higher in the FNB group (FNA: 39%, FNB: 67%, P< 0.01), and the rate of patients who had been punctured through the normal pancreatic parenchyma was higher in the FNA group (FNA: 69%, FNB: 42%, P< 0.01). Ten (4.5%) patients out of 221 patients had AEs (pancreatitis in 8 and pancreatic fistula in 2). Five patients had asymptomatic hyperamylasemia. The AE rates was 5.2/4.2 % in the FNA/B group and there was no statistically significant difference between these two groups. According to the *ASGE lexicon's* severity grading system, 6 cases were mild and 4 cases were moderate. The median extended length of hospital stay in patients with AEs was 3.5 (2-7) days. In one case of EUS-FNA group, endoscopic naso-pancreatic drainage was performed for moderate pancreatic fistula which had improved in 4 days. In a multivariate logistic regression analysis for AE rate, the head location of the lesions was the only statistically significant factor for AEs of EUS-FNA/B (HR 4.3, 95% CI 1.05-17.4, P=0.04). EUS-FNB (HR 1.2, 95% CI 0.31-4.85, P=0.76), the puncture through the normal pancreatic parenchyma (HR 1.3, 95% CI 0.30-5.96, P=0.71) and tumor size>20mm (HR 0.30, 95% CI 0.06-1.32, P=0.11) were not the statistically significant factors for AEs.
Conclusion: In our retrospective analysis, the total AE rate of EUS-FNA/B was 4.5%, and EUS-FNB was not the statistically significant factor for AE in patients with pancreatic solid lesions.
References: non
Disclosure: Nothing to disclose

P0266 EXPERIENCE USING RAPID ON-SITE EVALUATION OF BIOPSIES OBTAINED BY EUS- GUIDED FNA PERFORMED BY CYTOPATHOLOGY-TRAINED ENDOSCOPISTS

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Introduction: Biopsy by Fine-Needle Aspiration guided by ultrasonography (EUS-FNA) with rapid on-site evaluation (ROSE) by cytopathologists improves diagnostic capacity of the EUS. We have investigated the usefulness of ROSE performed by endoscopists with cytopathology training to assess whether the samples were adequate or not adequate.
Aims & Methods: Between March and October 2015, 49 patients with solid or cystic lesions of the gastrointestinal tract were taken to EUS-FNA. Two endoscopists with short training in cytopathology performed the ROSE and they categorized samples obtained as adequate or not adequate; the results were compared with the evaluation of a pathologist, using the same criteria to assess concordance.
Results: A high concordance of a proper reading between the endoscopist and pathologist in first EUS-FNA (EUS-FNA 1) (Kappa agreement measure 81%, sig = 0.000) and second EUS-FNA (EUS-FNA 2) (Kappa agreement measure 78%, sig = 0.001) was found.
Conclusion: Endoscopists can acquire basic skills in cytopathology to perform the ROSE, and the findings are consistent with those made by a pathologist. This strategy can contribute to obtaining adequate samples for cytopathology diagnosis and improve EUS-FNA diagnostic capacity. Basic cytopathology should be included as a subject in endosonography and endoscopy programs.
Disclosure: Nothing to disclose

P0267 ENDOSCOPIC RADIOFREQUENCY ABLATION AS FOCAL THERAPY FOR PANCREATIC METASTASIS FROM RENAL CELL CARCINOMA: A MONOCENTRIC EXPERIENCE

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Introduction: Pancreatic metastasis (PM) from renal cell carcinoma (RCC) are rare but associated with good prognosis. The usual management of PMis surgery or tyrosine kinase inhibitor (TKI) with sides effects. Endoscopic radiofrequency ablation (ERFA) is a very innovative approach to focally treat deep metastasis and could be a relevant technic to control PM from RCC.
Aims & Methods: We report a monocentric, prospective analysis for local control and toxicity in patients treated by ERFA for progressive PM from RCC. ERFA was performed under general anesthesia, with a linear EUS scope and a 19 G RFA needle; time of ablation was short (30sec to 1 mn), 1 or 2 shots were needed to ablate a 2 cm lesion.
Results: 7 pts from Paoli-Calmettes Institute (France) were recruited between May 2017 and December 2018.Median age was 72y [69-73], 4/7 female, ECOG 0-1 (100%). The median time from diagnosis to PM was 14 years [9.98-22.18], median number of PM was 2 [1-3], 5/7 was documented by histology and all were classified as progressive before ERFA. PM localizations was: head in 40%, body 40%, tail 20% and average size was 14 mm before treatment [4 - 35]. 86% of pts (6/7) had other mRCC spread, 5/7 received systemic treatment and 2 of them were on therapy at ERFA time (1 TKI, 1 Nivolumab). Two pts had ERFA as the only treatment for oligometastatic RCC. We performed 17 ERFA procedures over 14 PM. Median number of ERFA sessions was 2/patient [1-3]. With a median follow up of 18 months [4.6-35.6], 50% of treated PM displayed a complete response, 15% a partial response and 20% a stable disease at the last CT-evaluation. Only two patients were considered as progressive disease revealing 86% of PM focal control. One patient treated by TKI during procedure, developed a paraduodenal abscess 2 months after ERFA and was drained endoscopically and one with biliary prothesis developed hepatic abscesses few days after ERFA. Acute side effects like pancreatitis or life-threatening bleeding was not experienced. PM with size <20mm had the best focal control rate.
Conclusion: ERFA is feasible and displays an excellent local control for PM without any major side effect. However, TKI should be stop before the procedure to avoid complications. ERFA could be a valuable option, less morbid than pancreas resection for progressive PM.
Disclosure: Nothing to disclose

P0268 LONG-TERM OUTCOMES OF TREATMENT DECISION BASED ON THE SEVERITY OF SMALL BOWEL CAPSULE ENDOSCOPY FINDINGS IN PATIENTS WITH CROHN'S DISEASE: A SINGLE-CENTRE COHORT STUDY IN JAPAN

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Introduction: There are few reports on the impact of small bowel capsule endoscopy (SBCE) findings on clinical outcomes in patients with Crohn's disease (CD). In particular, the relevance of SBCE findings to the treatment decision in patients with CD has not been adequately evaluated. Likewise, an appropriate SBCE score to support treatment decision has not been determined.
Aims & Methods: The aim of this study was to better understand the long-term outcomes of treatment initiative based on the severity of SBCE findings and compare with the routinely used SBCE scores in patients with CD. We retrospectively compiled the data on patients with CD who underwent an initial SBCE between January 2015 and December 2017. Patients with ileostomy or colostomy, without lesions in the small intestine together with

those who received new medications within three months after SBCE were excluded. SBCE findings were evaluated using the Lewis and Capsule Endoscopy CD Activity Index (CECDAI) scores. Intervention was defined as an additional treatment involving budesonide, prednisolone, elemental diet, immunomodulators, anti-tumor necrosis factor agents or intestinal resection. The rate of treatment intervention within one year since the initial SBCE was assessed. Receiver operating characteristic (ROC) curves were constructed, and the area under the ROC curve (AUC) was calculated to determine the cut-off values for the Lewis and CECDAI scores at baseline that required treatment intervention within one year. Further, the cumulative rates of treatment intervention, following the initial SBCE, were estimated using the Kaplan-Meier method. Further, the rates of treatment intervention within one year and the cumulative rates of treatment intervention were compared using univariate analysis, stratified according to the determined cut-off value of Lewis and CECDAI scores.

Results: A total of 94 patients were included in this study (median age, 26.1 years; 22 female). The median CD activity index was 111, and the median C-reactive protein was 0.10 mg/dL. The median Lewis and CECDAI scores were 258.5 and 6.0, respectively. The rate of treatment intervention within one year was 11.7%. The ROC curve showed that the cut-off values of Lewis and CECDAI score were 645.0 (AUC = 0.803; 95% confidence interval [CI] 0.677 to 0.930; 85.5% specificity, 63.6% sensitivity) and 8.0 (AUC = 0.831; 95% CI 0.742 to 0.921; 66.3% specificity, 100.0% sensitivity), respectively. There was no significant differences between the AUC of Lewis scores and that of CECDAI scores (P = 0.705). The rates of treatment intervention within one year with Lewis score ≥645.0 and CECDAI score ≥8.0 were significantly higher than with Lewis score < 645.0 (36.8% vs. 5.3%, P = 0.001) and CECDAI score < 8.0 (28.2% vs. 0%, P < 0.001), respectively. The 1-, 2- and 3-year cumulative rates of treatment intervention were 12%, 27% and 31%, respectively. The 3-year cumulative rates of treatment intervention according to the Lewis score were < 645.0, 22% and ≥645.0, 61%, respectively (P < 0.001). Similarly, the 3-year cumulative rates of treatment intervention according to the CECDAI score were < 8.0, 15% and ≥8.0, 52%, respectively (P < 0.001).

Conclusion: Both, the Lewis and the CECDAI scores had moderate accuracy to allow decision making in the treatment of patients with CD following the initial SBCE. However, the Lewis and CECDAI scores equally predicted the therapeutic intervention. A cut-off value of Lewis score ≥645.0 and CECDAI score ≥8.0 significantly predicted the long-term outcomes of treatment intervention.

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P0269 EVALUATION OF COLON CAPSULE ENDOSCOPY IN A REAL-LIFE PROSPECTIVE COHORT SUGGESTS NEW MANAGEMENT ALGORITHMS FOR COLORECTAL NEOPLASIA IN ELDERLY PATIENTS

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Introduction: Colon capsule endoscopy (CCE) allows non-invasive exploration of colon mucosa. It has been proposed as an alternative to colonoscopy for average-risk colorectal cancer (CRC) screening patients with contraindications or unwilling to undergo colonoscopy and/or with an incomplete colonoscopy.[1,2] However relevance of CCE in a real-life practice and its short and long-term impact on clinical decisions have never been described. A prospective national cohort of CCE, the ONECC cohort, has been developed to assess these questions.

Aims & Methods: All patients that underwent a CCE (PillCam 2, MedTronics, United States) in France have been enrolled from January 2011 to May 2016 in a prospective manner in the ONECC cohort. All CCE and colonoscopy reports have been systematically collected and data analysis has been only performed on complete data. All enrolled patients had an annual phone-call during the study with a standardized questionaire until May 2017.

Results: The results of CCE in 689 patients from 14 different medical centers (7 teaching hospitals, 7 general hospitals) were analyzed. The median time of follow-up was of 3 years (0-7). The median age was of 70 years old (min 16- max 96). The main indication for CCE was represented by anaesthesia or colonoscopy contraindication (n=307; 44.6%). Bowel cleansing was considered satisfying (Excellent or Good) in 69.2% of CCE (n=477/689). CCE were considered complete in 442 cases (64.2%) and 337 examinations (48.5%) were both complete and associated with a satisfying bowel preparation. A polyp was identified in 295 CCE (42.8%) among which 189 (27.4%) were classified as significant (i.e. ≥6mm or ≥3 polyps). Following CCE, a colonoscopy was indicated in 40.5% of patient (279/689) and performed for 32.7% (225/689). The main indications to perform a colonoscopy following CCE were the diagnosis of a significant polyp on CCE (139/279; 49.8%), an incomplete examination or with unsatisfying bowel preparation (73/279; 26.1%) or the diagnosis of a non-significant polyp (30/279; 10.7%). The 2 main reasons for failure to perform colonoscopy for patients with a significant capsule were the refusal of the patient (19/52, 36.5%) and anesthesia contraindication (16/52, 30.8%). Twenty-two CCE (4,6%) were followed by the diagnosis of an advanced adenoma with high-grade dysplasia or CRC. Colonoscopy and CCE were concordant for the diagnosis of polyp with advanced dysplasia (location and size) in 84.4% of cases (27/32). Discrepancies were mainly explained by an incomplete CCE associated with a distal lesion of the sigmoid colon or rectum identified in the colonoscopy (4/5 of non concordant observations; 80%). At the end of follow-up, 115 patients were dead (16.7%) and a total of 40 advanced dysplasia were diagnosed. Performing a colonoscopy after a CCE with a significant polyp or an incomplete CCE would allow the diagnosis of 97.5% (39/40) of all advanced adenoma in the ONECC cohort.

Conclusion: In patients with a satisfying preparation and complete colonic examination a normal CCE is a reassuring result to exclude adenoma with advanced dysplasia. This real-life practice cohort shows that the decision after a positive colon capsule endoscopy takes into account patient status and the nature of capsule abnormalities in mostly old patients.

References: 1. Spada, C. et al. Colon capsule endoscopy: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy 44, 527-536 (2012). 2. Enns, R. A. et al. Clinical Practice Guidelines for the Use of Video Capsule Endoscopy. Gastroenterology 152, 497-514 (2017).

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P0270 NOMENCLATURE AND SEMANTIC DESCRIPTION OF ULCERATIVE AND INFLAMMATORY LESIONS SEEN IN CROHN'S DISEASE IN SMALL BOWEL CAPSULE ENDOSCOPY: AN INTERNATIONAL DELPHI CONSENSUS STATEMENT

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Introduction: Nomenclature and description of small bowel (SB) ulcerative and inflammatory (UI) lesions in capsule endoscopy (CE) are scarce in the medical literature. Interobserver variability in interpreting the findings remains a major limitation for the assessment of severity of mucosal lesions with a potential negative impact on clinical care, training and research regarding SBCE. Our aim is to establish a consensus on the nomenclature and the description of UI lesions seen in SBCE in Crohn's Disease (CD).

Aims & Methods: An international panel of experienced SBCE readers was formed during the 2016 UEGW meeting. A core group of 5 CE and inflammatory bowel disease (IBD) experts established an internet-based three-round Delphi consensus, but did not participate in voting process. The core group built illustrated questionnaires including various still frames of SB UI CE lesions obtained from CD patients. A group of 27 other experts was asked to rate and comment different proposals on the nomenclature and the description of the most frequent SB UI lesions. A 6-point rating scale (varying from 'strongly disagree' to 'strongly agree') was used in successive rounds. The consensus was reached when at least 80% voting members scored the statement within the 'agree' or 'strongly agree'.

Results: A 100% participation rate was obtained for all rounds. Consensual nomenclature and descriptions were reached for the seven following UI lesions: aphthoid erosion, deep ulceration, superficial ulceration, stenosis, edema, hyperemia and denudation.

Nomenclature	Description	% Nomenclature/ description
Aphthoid erosion	Diminutive loss of epithelial layering with a white center and a red halo, surrounded by normal mucosa	85.2/96.3
Deep ulceration	Frankly deep loss of tissue compared to the surrounding swollen / oedematous mucosa, with a whitish base	96.3/85.2
Superficial ulceration	Mildly depressed loss of tissue with a whitish bottom, whose features fit neither with that of aphthoid erosion nor with that of deep ulceration, as previously defined	81.5/85.2
Stenosis	Narrowing of the intestinal lumen withholding or delaying the passing of the videocapsule (therefore, to be evaluated on a video)	100.0/88.9
Edema	Enlarged / swollen / engorged villi	85.2/81.5
Hyperemia	Area of reddish villi	96.3/81.5
Denudation	Reddish (but not whitish) mucosal area where villi are absent	81.5/81.5

[International Delphi Consensus on the nomenclature and descriptions of ulcerative and inflammatory lesions seen in IBD during SBCE.]

Conclusion: Consensual nomenclature and descriptions of the most frequent SB UI lesions seen in CD in CE have been reached by an international group. These terms and descriptions are useful in daily practice, for teaching and for medical research purposes.

Disclosure: Xavier Dray has acted as a consultant for Alfasigma; Bouchara Recordati; Boston Scientific, Fujifilm, Medtronic, and Pentax

P0271 COLON CAPSULE ENDOSCOPY: AN EFFICIENT COMPLEMENT FOR INCOMPLETE COLONOSCOPIES

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Introduction: Colonoscopy is the gold standard for visualization of the colon during colorectal cancer screening. A colonoscopy is considered complete when cecum is reached. Completion rates, on some series, are described as low as 81% for mixed indications. Colon capsule endoscopy (CCE) is approved for complementing incomplete colonoscopies, with completion rates up to 90%, and it could help to detect additional relevant colonic and extracolonic findings.

Aims & Methods: To assess the value of CCE on incomplete colonoscopies: complementation rates and incremental diagnostic yields.

Retrospective, single center study, including consecutive patients that underwent CCE for incomplete colonoscopy, from April 2015 to October 2018. Our cohort was analyzed by descriptive and parametric SPSS tools.

Results: We included 55 patients submitted to CCE after an incomplete colonoscopy. Included 46 women (83.6%) with a mean age of 67 years old. CCE were complete in 64% of the patients, however, in almost 90%, we reach total colon visualization, considering both exams.

The three main indications for primary colonoscopy were colorectal carcinoma screening (49.1%), followed by positive fecal occult blood test (14.5%) and post-polipectomy surveillance (14.5%).

Significant endoscopic findings were identified in 44 (80%) CCE, namely, colon diverticula (61.8%) followed by polyps (29.1%), angiectasias (9.1%) and erosions (9.1%).

From the 16 CCE with diagnosis of colon polyps, three lesions (18.5%) had more than 10mm. Polyps were mainly found on left colon (12.7%).

Seven patients performed colonoscopy after CCE (12.7%), and in 6 (85.7%) the intended lesions were identified and treated: 5 polypectomies and 1 fulguration with argon plasma. Therefore, 87.3% of the patients won't need additional investigation after CCE.

There were no CCE retentions or other complications associated to the procedure.

Conclusion: CCE is useful and well tolerated, an important tool to be used to increase colonic diagnostic yield with direct impact on therapeutic interventions.

Disclosure: Nothing to disclose

Study characteristics			Quality indicators					Yield	
Study	Type screening	Participation, N (participation rate %)	Bowel preparation and booster regimen	Adequate bowel preparation (%)	Completion rate CCE (%)	DR CCE (%) a = Polyp b = CRC	DR OC (%) a = Polyp b = CRC	Sensitivity CCE (%) a= Polyp>5mm b=Polyp>9 mm	Specificity CCE (%) a= Polyp>5mm b= Polyp>9 mm
Groth 2012	Opportunistic, primary OC	90 (4.2)	2L PEG evening + 1L PEG morning. NaP, water	88	82	a:- b:-	a:- b:-	a:- b:-	a:- b:-
Holleran 2014	FIT based screening	62	4L PEG split dose. Sodium picosulfate	92	73	a:69 b:100	a:58 b:100	a:- b:-	a:- b:-
Suchanek 2014	Opportunistic, primary OC or FIT	225	-	90	-	a:- b:100	a:51 b:100	a:79 b:88	a:97 b:99
Rondonotti 2014	FIT based screening	50 (8.2)	2L PEG split dose + 1L water. NaP, water	70	90	a:- b:-	a:- b:-	a:88.2 b:92.8	a:87.8 b:91.7
Romero 2015	FIT based screening	53	-	-	81	a:- b:100	a:82 b:100	a:87 b:88	a:88 b:94
Rex 2015	Opportunistic, primary OC	695	4L PEG split dose. Sulfate solution, water	80	92	a:- b:75	a:- b:100	a:87 b:85	a:94 b:97
Suarez 2016	FIT based screening	88	-	82	81	a:- b:100	a:- b:100	a:- b:-	a:- b:-
Kobaek-Larsen 2017	FIT based screening	253 (17.4)	2L PEG + 3L water split dose. Moviprep, water	85	57	a:74 b:64	a:64 b:100	a:- b:87	a:- b:92
Hassan 2018	FIT based screening	203	4L PEG split dose. NaP, water, gastrografin	89	88	a:- b:-	a:- b:-	a:89.7 b:87.2	a:65.3 b:87.9
Voška 2018	Opportunistic, primary FIT	54	3L PEG evening + 1L PEG morning. NaP, water	-	-	a:- b:100	a:69 b:100	a:82 b:75	a:88 b:93
Pioche 2018	FIT based screening	19 (5.0)	Day -2: 4L PEG Day -1: 3L PEG Day 0: 1L PEG. NaP, water	74	68	a:63 b:100	a:- b:100	a:- b:-	a:- b:-

[P0271 Table 1. Overview of the 11 included studies reporting on the quality indicators and yield of CCE in a screening population.]

P0272 THE ROLE OF COLON CAPSULE ENDOSCOPY IN COLORECTAL CANCER SCREENING: A SYSTEMATIC REVIEW

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Introduction: Colorectal cancer (CRC) screening programs have been implemented in many countries in order to decrease CRC incidence and mortality. Primary colonoscopy and fecal immunochemical testing (FIT) are the most commonly used screening modalities. An alternative screening instrument is second generation colon capsule endoscopy (CCE). Although the accuracy of CCE has already been proven in several trials, information on its performance in a screening population remains scarce.

Aims & Methods: We therefore performed the first systematic review on the role of CCE as a CRC screening tool. A systematic search was conducted until November 2018 to retrieve studies from Embase, Web of Science, Medline Ovid and Cochrane Central according to the PRISMA guideline. Studies with patients participating in a population colorectal screening were included. Studies using first generation CCE were excluded.

Results: Literature search retrieved 499 studies, of these 11 studies met the inclusion criteria. The included studies focused on FIT-positive screening populations (n=7) or opportunistic screening populations (n=4). In total 1792 subjects were included. The participation rate ranged between 4.2% and 17.4% (Table 1). The polyp detection rate of CCE varied from 63% to 74%. Complete CCE led to detection of 16/17 (94%) CRCs. Sensitivity of CCE for polyps ranged between 75% and 92.8% and specificity between 65.3% and 99%. Bowel preparation was adequate in 70% to 92% and completion rate varied from 57% to 88%. No adverse events with CCE were reported in the included studies.

Conclusion: CCE is a safe and effective diagnostic tool for the detection of cancer and polyps in a screening population. Bowel preparation is adequate in most studies, but the low completion rates affect the performance of CCE. More studies are needed to determine the role of CCE as screening instrument.

Disclosure: Nothing to disclose

P0273 POLYETHYLENE GLYCOL PURGATIVES PRIOR TO SMALL BOWEL CAPSULE ENDOSCOPY IMPROVE DISTAL SMALL BOWEL VISUALISATION

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Introduction: Bowel purgatives are common practice prior to small bowel capsule endoscopy (SBCE). The use of Polyethylene glycol (PEG) laxatives is suggested to improve SB visualisation quality and diagnostic yield [Kotwal, Eur J Gastro Hep 2014]. However, this finding is not completely consistent, with other studies suggesting no clear benefit of PEG preparation over clear fluids only [Hookey, GIE 2017]. Therefore, unlike colonoscopy where the routine use of split dose bowel preparation to improve right colon cleansing has become a standard of care [Flemming, GIE 2012], the benefit and timing of purgatives prior to SBCE is unknown. We report the interim results from a clinical trial comparing the use of split dose PEG and single dose PEG against clear fluids only.

Aims & Methods: Adult patients referred for SBCE were invited to participate and subject to exclusion criteria, were randomised to control (clear fluids only), single dose PEG (2L PEG at 6am on the day of the exam) and split dose PEG (1L PEG at 7pm the day before and 6am on the day of the exam). Briefly, the mean red to green colour intensity from SBCE procedure colour bars were used to calculate a computed assessment of cleansing (CAC) scores described elsewhere [Van Weyenberg, Endoscopy 2011]. The CAC is a validated 10 point scoring system (0-10; least - most clean) used to assess small bowel visualisation quality. CAC scores are reported as mean ± SEM and student t-tests performed to compare the means.

Results: A total of 78 patients (35% male, mean age 48±2.0) were included (split n=28, single n=24 and control n=26). Intention to treat analysis show that split dose PEG preparation results in significantly greater mean CAC score in the distal quartile (5.58±0.16) of the small bowel compared to control (4.78±0.30; p=0.02). No differences in the overall, first, second and third quartile CAC score of the small bowel was found between control and PEG groups. Complete ingestion of PEG preparation occurred in 88% and 77% of single vs split dose (p=0.33). Subgroup analysis showed that amongst patients that completed preparation successfully, those randomised to both split dose (5.52±0.20; p=0.01) and single dose (5.64±0.18, p=0.003) PEG had a significantly greater mean CAC score in the distal quartile of the small bowel compared to control (4.58±0.28).

Conclusion: The use of split dose laxatives improves the visualisation quality of the distal small bowel. Initial results may suggest that the PEG dose in the morning of the procedure improves distal quartile visualisation.

References: Kotwal VS, Attar BM, Gupta S, Agarwal R. Should bowel preparation, antifoaming agents, or prokinetics be used before video capsule endoscopy? A systematic review and meta-analysis. Eur J Gastroenterol Hepatol 2014; 26(2): 137-45. Hookey L, Louw J, Wiepjes M, et al. Lack of benefit of active preparation compared with a clear fluid-only diet in small-bowel visualization for video capsule endoscopy: results of a randomized, blinded, controlled trial. Gastrointest Endosc 2017; 85(1): 187-93. Flemming JA, Vanner SJ, Hookey LC. Split-dose picosulfate, magnesium oxide, and citric acid solution markedly enhances colon cleansing before colonoscopy: a randomized, controlled trial. Gastrointest Endosc 2012; 75(3): 537-44.

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P0274 IS IT POSSIBLE TO TREAT THE ANGIODYSPLASIAS FOUND IN PATIENTS WITH OBSCURE GASTROINTESTINAL BLEEDING SUBJECTED TO SMALL BOWEL CAPSULE ENDOSCOPY?

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Introduction: Angiodysplasias of the small intestine is reported to be the most common cause of obscure gastrointestinal bleeding (OGIB). The aim of our study was to identify whether it is possible to treat the bleeding due to angiodysplasias found in patients with OGIB subjected to small bowel capsule endoscopy (SBCE).

Aims & Methods: Retrospective analysis of prospectively collected data [March 2003 - March 2019] from 5771 patients that were subjected to SBCE in our Department, which is a tertiary referral centre for this test. Among these patients, 3403 were subjected to the test for the investigation of OGIB. All these patients were referred to our Department for OGIB after a reported negative gastroduodenoscopy and a negative colonoscopy.

Results: By SBCE angiodypslasias were found in 1652 of 3403 patients (48.5%). Of these lesions 224 (13.5%) were actively bleeding at the time of testing and were localized in the proximal gastrointestinal tract (stomach or the first/second part of the duodenum) (n=12, 5.3%), the proximal jejunum (n=62, 27.6%), the distal jejunum (n=49, 21.8%), the proximal ileum (n=41, 18.3%), the distal ileum (n=42, 18.7%), and the right colon (n=18, 8.0%).

Therapeutic intervention by Argon-Plasma Coagulation (APC) cauterization was possible in 6 patients with gastric or duodenal angiodysplasias, in 7 patients with angiodysplasias in the right colon, and in 31 patients with angiodysplasias in the proximal jejunumn (using a push enteroscope), since in the remaining patients angiodysplasias were not seen during repeat endoscopy.

Therefore, in total, angiodysplasias were endoscopically treated in 44 patients (2.6%), among the 1652 initially revealed through SBCE.

Conclusion: Angiodysplasias are seen in the majority of patients with obscure gastrointestinal bleeding subjected to SBCE; however therapeutic intervention is possible only in a small minority of them, especially if double balloon endoscopy is not available.

Disclosure: Nothing to disclose

P0275 NEGATIVE SMALL BOWEL VIDEO CAPSULE ENDOSCOPY FOR OCCULT GASTROINTESTINAL BLEEDING PREDICTS A LOW RISK OF SUBSEQUENT INPATIENT ADMISSION WITH UPPER GASTROINTESTINAL BLEEDING

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Introduction: Small bowel video capsule endoscopy (SBVCE) is the investigation of choice for occult gastrointestinal bleeding (OGIB) following a negative gastroscopy and colonoscopy. Approximately 50-55% of these tests are negative, however the long-term outcome of this cohort of patients is not well described.

Aims & Methods: Aim: To assess the long-term clinical impact of a negative SBVCE in patients with OGIB.

Methods: A retrospective review of all patients who underwent SBVCE at an Australian tertiary health service between 1st January 2012- 31st December 2017 was performed. The gastrointestinal Procedure Reports database was reviewed for listed indications of 'anaemia' or 'iron deficiency'. Demographic data (including medication history) was determined by reviewing the medical record.

Primary outcome measure was hospital admission secondary to gastrointestinal bleeding within 1 year of negative SBVCE, with secondary outcome measure being further endoscopic investigation of iron deficiency anaemia or gastrointestinal bleeding within 1 year. Statistical analysis was performed using GraphPad Prism software (version 8.02).

Results: 429 cases were initially identified. 13 were excluded due to capsule retention in upper gastrointestinal tract, whilst a further 209 excluded due to either additional presence of overt gastrointestinal bleeding or a positive capsule result (Significant angioma burden, ulcers, small bowel Crohn's Disease and small bowel tumors).

207 cases were included for final assessment. 110 (53%) female, median age 61 years (range 17-91). 18 (9%) had a history of non-steroidal anti-inflammatory use, 41 (20%) reported aspirin use, 17 (8%) other antiplatelet agents and 15 (7%) were using other anticoagulation at the time of SBCE. Regarding the primary outcome measure, 7 (3%) of patients were admitted to hospital within 1 year of negative SBVCE. 11 (6%) of patients had repeat endoscopic investigation (8 patients had negative studies, 2 patients had gastric antral vascular ectasia and 1 patient had a duodenal angioma). 3/62 patients receiving antiplatelet or anticoagulant therapy were admitted to hospital compared to 4/145 not receiving these therapies. The odds ratio for readmission when on anticoagulation was 1.7 (95% confidence interval 0.44-6.8), when compared to patients not on anticoagulation - although this did not reach statistical significant (p = 0.44). No patient had multiple admissions.

Conclusion: Negative SBVCE for occult GI bleeding carries a low risk for subsequent hospital admission due to overt GI bleeding within 1 year of the study. In addition, there is a low risk of requiring further endoscopic investigations.

Disclosure: Nothing to disclose

P0276 THE NEW GENERATION OF EXPRESS VIEW IS HIGHLY ACCURATE AND IS EFFECTIVE TO REDUCE CAPSULE ENDOSCOPY READING TIME

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Introduction: Capsule Endoscopy (CE) is a first-line diagnostic test in patients with suspected small bowel bleeding (SSBB). One of the main limitation of CE is reading that might be time consuming. In order to overcome such limitation, innovative types of reading software have been developed. A new generation reading algorithm (Express-View by MiroCam) has recently released with the aim to reduce CE reading time by removing images based upon their similarity and effectively reducing the number of images for the review, without affecting the diagnostic yield. Accuracy and impact on reading time are unknown.

Aims & Methods: Primary aim was to evaluate the accuracy of the new generation Express View in patients with SSBB. Secondary objective was to evaluate the reading time with the Express View compared to standard reading. This is a per patient, interim analysis including 48 patients with SSBB prospectively enrolled in 5 centers. All patients underwent small-bowel CE (MC 1200, Intromedic, Republic of Korea). CE reading was initially performed in the standard mode according to the ESGE capsule endoscopy technical guidelines. A second reading was performed using the Express View (EV) mode by an external, blinded reader. For each lesion,

the time of visualization, nature, and relevance according to the Saurin classification were collected. For the accuracy evaluation, the Express View reading was compared to the standard reading (SR) that was considered gold standard. In case of discrepancies between SR and EV reading, accuracy parameters were re-evaluated after a consensus reading that was performed by two experienced investigators (>500 cases) and that was considered the gold standard. Reading time (gastric + small bowel) was also evaluated after selection of the first gastric, duodenal and cecal landmarks. In case of incomplete enteroscopy, the last recorded image was considered as landmark.

Results: On a total of 48 patients, 47 performed VCE examination while one patient had gastric capsule retention. Enteroscopy was complete (i.e cecal visualization) in 43 patients (91.5%). In 33 out of 47 patients (70.2%) both SR and EV mode were in agreement for type of lesion and localization, while in the remaining 14 patients (29.8%) the EV reading was discordant compared to the gold standard (i.e. SR). Sensitivity, specificity, PPV, and NPV of EV reading after the initial evaluation were 71.8%, 66.6%, 82%, 52.6%, respectively. After the consensus reading, in 12 out of 14 patients with discordant reports (n=5 SR-EV+, n=4 SR+EV-, n=3 SR+EV+ but no comparable lesions) EV was reclassified to be able to properly detect the lesion and the disagreement was considered related to a reader-misinterpretation. In the remaining 2 patients (4.2%), EV mode missed relevant lesions (1 patient with significant ileal erosions and 1 with a vascular malformation).

After consensus reading reclassification, EV mode sensitivity, specificity, NPV and PPV were 94.6%, 100%, 83.3% and 100% respectively. The mean reading time at SR and EV was 84.13 ± 53.63 min and 14.79 ± 11.2 min, respectively (p< 0.001).

Conclusion: The preliminary results of this study suggest that the new generation Express View algorithm shows excellent accuracy and significantly reduces CE reading time.

Disclosure: Nothing to disclose

P0277 COMPARISON OF SMALL-BOWEL CLEANSING BETWEEN 2 PREPARATION PROTOCOLS IN CAPSULE ENDOSCOPY (CE)

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Introduction: The European Society of Gastrointestinal Endoscopy recommends that a solution such as polyethylene glycol (PEG) should be used prior to a capsule endoscopy (CE), since it allows a better mucosal visualization and increases the diagnostic yield. However, it is still controversial which is the best enteric preparation. In the current literature, some series showed similar results between a PEG solution and a clear liquid diet on the day before the CE.

Aims & Methods: The aim of this study was to compare Brotz's enteral cleansing scales between two enteric preparation protocols in patients undergoing CE. The authors performed a retrospective single-center analysis of CE. Patients with active bleeding and whose capsule did not reach the cecum were excluded from the study. The enteric preparation protocols were (1) clear liquid diet on the previous day plus 8 hour fasting, (2) 2 liters of PEG solution plus simeticone. The CE videos were graded regarding the level of cleanliness according to 2 grading scales developed by Brotz et al previously described: a) quantitative index (QI), which grades the level of cleanliness with a score ranging from 0 to 10 and b) qualitative evaluation (QE), which grades the degree of cleanliness as excellent, good, fair and poor. The diagnostic yield between the 2 protocols was also evaluated.

Results: 110 CE were analyzed, 52.7% (n=58) were female, with a mean age of 56.1 years-old (± 18). 52.7% (n=58) of the patients had the clear liquid diet protocol and 47.3% (n=52) the PEG protocol. Sex, age and indication for CE were not significantly different between the two protocols. In addition, there were no significant differences between the PEG and the

liquid diet in relation to the QI (8.13 ± 1.56 vs. 7.47 ± 1.97, p=0.05) and the QE cleansing grades (excellent: 15.4% vs. 13.8%, good: 48.1% vs. 39.7%, reasonable: 25% vs 27.6%, poor: 11.5% vs 19%, p = 0.67). The diagnostic yield was not different between the 2 protocols (PEG: 58.8% vs Clear liquid diet: 55.2%, p=0.7).

Conclusion: The use of a PEG solution did not show to affect the small-bowel cleansing in CE when evaluated by QI and QE Brotz scales, and did not affect the diagnostic yield of CE.

Disclosure: Nothing to disclose

P0278 COMPARING THE EFFICACY AND SAFETY OF METAL VERSUS PLASTIC STENTS IN PREOPERATIVE BILIARY DRAINAGE

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Introduction: There is conflicting evidence regarding whether routine preoperative biliary drainage (PBD) should be performed if clinically warranted prior to a pylorus-preserving pancreaticoduodenectomy (PPP) for resectable pancreatic head cancer. In addition, there are limited studies that investigated whether PBD with metal or plastic biliary stents have differing impacts on PBD-related complication rates, post PPP surgical outcomes, and healthcare resource utilisation.

Aims & Methods: An Australian multicentre retrospective cohort study was conducted which included patients who underwent PBD prior to PPP from 2010 to 2019. Patients included received PBD based on one or more of: cholangitis defined by revised Tokyo guidelines, level of total bilirubin ≥40 μmol/L, expected time to operation ≥7 days, or receiving neoadjuvant chemotherapy.

The aim of this study was to compare PBD with fully covered self-expandable metal stent (FCSEMS) compared to plastic stents in terms of the rate of endoscopic reintervention, stent related complication and surgical complications in patients with resectable pancreatic head cancer who later underwent a PPD.

Results: 106 patients underwent PBD. 32 patients (30.19%) received a FCSEMS versus 74 (69.81%) with plastic). The mean age was 66.75 ± 9.79 years, 47.17% were male and the baseline bilirubin was 184.91 ± 113.59 μmol/L. Both FCSEMS and plastic effectively reduced bilirubin (Δ140.04 ± 113.04 μmol/L from baseline) with no difference between the FCSEMS arm and the plastic arm (Δ134.56 ± 108.35 μmol/L vs Δ152.19 ± 123.74 μmol/L, p-value:0.47).

There was no difference in the PBD complication rates in the FCSEMS and plastic stent groups respectively: readmission (p-value=0.40), pancreatitis (p-value=0.25), cholangitis (p-value=0.35), haemorrhage (p-value=0.51), stent occlusion without cholangitis (p-value=0.09), and reintervention with either ERCP or PTC (p-value=0.21). There were no cases of stent related perforation. There was also no difference in the post-operative complication rates including surgical or biliary leaks, infection, haemorrhage or return to theatre in the FCSEMS and plastic stent groups.

On multivariate logistic regression analysis, the stent type was not an independent risk factor of endoscopic or post-operative complication or death. On multivariate linear regression analysis, the stent type was not an independent risk factor for increased length of stay for those readmitted for a stent related complication. The resection histopathology showed pancreatic adenocarcinoma (69.81%), neuroendocrine (2.83%), autoimmune pancreatitis (0.94%) and other primary malignancy (26.42%).

Conclusion: Both FCSEMS and plastic PBD stents were comparable in normalising bilirubin pre-PPP. There were no statistically significant difference in pre or post-operative complications or healthcare resource utilisation between the two groups apart from the increased upfront cost of the FCSEMS. The cost benefit in using plastic stents in preference to FCSEMS may be an important consideration where there are clinical indications for PBD or long wait times for surgical management of resectable pancreatic head cancer.

Disclosure: Nothing to disclose

P0279 EUS-GUIDED TRANSJEJUNAL DRAINAGE WITH FORWARD-VIEWING ECHOENDOSCOPE IN THE PATIENTS WITH ALTERED ANATOMY

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Introduction: Forward-viewing echoendoscope (FV-ES) was originally designed for therapeutic procedures, particularly for pseudocyst drainage. The advantage of FV-ES is that it enables the axial application of force during needle insertion and accessory device deployment. Although other big advantage of FV-ES is its easier manipulation throughout the GI tract due to forward viewing, a wider angulation rage, and short length of the hard tip, there are few reports on EUS-guided transjejunal anastomotic drainage for the patients with altered anatomy. The advantages of this technique are that we can approach both biliary systems and it is a 1-step procedure (no need for Rendezvous method) and it is not performed through the abdominal cavity.
Aims & Methods: We evaluated the feasibility of the EUS-guided choledochojejunostomy (EUS-CJS) and pancreaticojejunostomy (EUS-PJS) with FV-ES (TGF-UC260J; Olympus, Tokyo, Japan) for the patients with surgically altered anatomy from Feb 2015 through Mar 2019 in our institution, retrospectively.
Results: A total of 7 cases with surgically altered anatomy were received transjejunal anastomotic drainage with FV-ES. All of them were after pancreaticoduodenectomy with modified Child reconstruction. The indication for drainage was complete stricture of the hepaticojejunal anastomosis in 6 cases and the pancreaticojejunal anastomosis in one case. The success rate of reaching the target site at afferent limb is 100% (7/7) and median reaching time was 6 min (4-17). EUS-CJS and bile duct stent placement was succeeded in 66.7% (4/6). Erroneous puncture of unintended bile duct in one case and impossibility to pass by mechanical dilatation device in one case, in which cautery dilation catheter was not applied due to major vessels close to the puncture site on EUS. Both were rescued by percutaneous transhepatic biliary drainage. EUS-PJS and pancreatic duct stent placement was succeeded in one case (1/1). No adverse events related to the procedure were happened such as sever bile or pancreatic juice leakage.
Conclusion: EUS-CJS and PJS with FV-ES is feasible in the patients with modified Child's reconstruction after pancreaticoduodenectomy and they can be safe and effective method in case of complete stricture of the anastomotic site.
Disclosure: Nothing to disclose

P0280 DOUBLE STENTING HAS BETTER OUTCOMES THAN DOUBLE SURGICAL BYPASS IN THE CASE OF COMBINED MALIGNANT DUODENAL AND BILIARY OBSTRUCTION: A META-ANALYSIS AND A SYSTEMATIC REVIEW

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Introduction: Data about efficacy of palliative double stenting of malignant duodenal and biliary obstruction are limited.
Aims & Methods: Systematic literature search was performed to assess feasibility and optimal method of double stenting of malignant duodenal and biliary obstruction compared to surgical double bypass in terms of technical and clinical success, adverse events, reinterventions, and sur-

vival. Seventy-two retrospective and 8 prospective studies published until July 2018 were enrolled. Event rates with 95% confidence intervals were calculated.
Results: Technical and clinical success rates of double stenting were 97% (95-99%) and 92% (89-95%), respectively. Clinical success of endoscopic biliary stenting was higher than that of surgery (97% [94-99%] vs 86% [78-92%]) in an older population (67.9 years [67.0-68.9 years] vs 63.7 years [62.3-65.0 years]). Double stenting was associated with less adverse events (13% [8-19%] vs 28% [19-38%]) but more frequent need for reintervention (21% [16-27%] vs 10% [4-19%]) than double bypass. No significant difference was found between technical and clinical success and reintervention rate of endoscopic retrograde cholangiopancreatography (ERCP), percutaneous transhepatic drainage (PTD) and endoscopic ultrasound guided biliary drainage (EUS-BD). ERCP was associated with the least adverse events (3% [1-6%]), followed by PTD (10% [0-37%]) and EUS-BD (23% [15-33%]).
Conclusion: Substantially high technical and clinical success can be achieved with double stenting also in elderly. ERCP is recommended as first choice for biliary stenting as part of double stenting. Prospective comparative studies with well-defined outcomes and cohorts are needed.
Disclosure: Nothing to disclose

P0281 EFFICACY AND SAFETY OF ENDOSCOPIC DRAINAGE OF PERIPANCREATIC FLUID COLLECTIONS: A RETROSPECTIVE MULTI-CENTRIC EUROPEAN STUDY

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Introduction: Endoscopic ultrasound (EUS)-guided drainage is considered the gold standard for the treatment of symptomatic peripancreatic fluid collections (PFCs). Both lumen-apposing metal stents (LAMS) and double pigtail plastic stents (DPPS) can be deployed once access in the collection is achieved.
Aims & Methods: In this retrospective study we aimed to evaluate the efficacy and safety of EUS-guided drainage of PFCs. Data from consecutive patients undergoing drainage in 8 European centers were retrospectively retrieved. Characteristics of PFC, type of stent, technical success (successful stent deployment), clinical success (satisfactory drainage), rate of early adverse events, drainage duration and complications on stent removal were evaluated.
Results: 96 patients [69 men (72%), 57.8±12.8yrs] underwent drainage from 2016 to 02.2019. A pancreatic pseudocyst (PC) and a walled-off necrosis (WON) was drained in 62 and 34 patients, respectively. LAMS were used in 76 (79.2%) patients; DPPS in 20 (20.8%) of them. In 75 patients (78.1%) PFC was located in the body or tail of the pancreas with a mean diameter of 12±5cm. In 86 cases (89.6%) the transgastric approach was used to access the PFC. For all above characteristics no difference was detected between PC and WON (p>0.1). Among LAMS, the 15mm diameter was chosen in 57 (75%) of the cases. Overall, 30 DPPS were used [median 2(1-3)]; the most common diameters were 10Fr (15/30, 50%) and 7Fr (12/30, 40%). A successful deployment was possible in 92 (95.8%) of the cases with no difference regarding either the PFC type (p=0.13) or the type of stent (p=1). Clinical success was achieved in 88 (92%) of the patients; PC had better response than WON (62/62 vs. 6/32, p=0.001, respectively). Type of stent did not affect the rate of clinical success (p=0.61).

An early complication was evident in 16 (16.8%) of the cases. The most common adverse event was bleeding (n=5, 5.2%) followed by obstruction of the stent causing inflammatory reaction (n=4, 4.2%), perforation (n=3, 3.1%) and migration necessitating stent replacement (n=3, 3.1%). More complications were noted in the LAMS group (n=14, 18.7%) compared to DPTS group (n=2, 10%) but this difference did not reach statistical significance (p=0.51). PFC type was also not related to the rate of early complications [9/62, 14.5% vs. 7/33, 21.2% for PC and WON, respectively (p=0.41)]. 10/16 adverse events were handled conservative while 6 patients received further intervention to treat the adverse event. All 5 bleeding episodes were recorded in the LAMS group with 4 patients undergoing embolization. All but one patients recovered completely. The mean duration of drainage was 61.1±67 days, but was significantly longer for the DPTS group compared to that of LAMS [98.5±47.7 vs. 54±68.2; p=0.007, respectively]. In LAMS group, stent removal was intended in all cases while in the DPPS group 4 cases received indwelling stent placement. On stent removal 9 (11.8%) complications were recorded in the LAMS group compared to none in the DPPS. Buried stent syndrome (n=6, 7.9%) was the most common complication on stent removal followed by bleeding (n=3, 3.9%). PFC type did not affect the complication rate on removal.

Conclusion: EUS-guided drainage of PFCs using LAMS or DPPS is associated with high percentages of technical and clinical success. Early adverse events are similar between the two types of drainage and not affected by the type of collection. Drainage using LAMS is of shorter duration, but severe complications occur more frequently on stent removal, regardless of the type of PFC.

Disclosure: Nothing to disclose

P0282 SHORT-TERM OUTCOMES OF ENDOSCOPIC RADIOFREQUENCY ABLATION FOR UNRESECTABLE MALIGNANT HILAR BILIARY OBSTRUCTION

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Introduction: Inoperable biliary cancer with hilar biliary stenosis has a poor prognosis and requires multiple drainage of complicated stenoses. Radiofrequency ablation (RFA) for the bile duct was recently reported to be effective in ensuring the long-term stent patency and affording a good prognosis. Many reports on biliary RFA have been retrospective studies of distal biliary obstruction including a variety of etiologies, such as a pancreatic cancer, biliary cancer, and metastasis of the lymph node and other organ cancers.

Aims & Methods: We prospectively evaluated the feasibility and short-term outcomes of endoscopic biliary RFA for malignant hilar biliary obstruction (MHBO) caused by biliary cancer. The primary outcomes of the study were the technical success of RFA with the bilateral placement of a self-expandable metallic stent (SEMS) and complications within 30 days after the procedures. Bilateral biliary stenting for MHBO was performed by the partial stent-in-stent method using a thin delivery system of the SEMS after RFA.

Results: Twelve patients (10 men; 70.8 ± 6.0 years of age) were enrolled in the study between May 2017 and March 2019. Hilar bile duct cancer was diagnosed in 11 patients (92%), while 1 had gallbladder cancer (8%). The Bismuth classification of biliary stenosis was III and IV in 7 (58%) and 5 (42%). The mean stricture length was 39.1 ± 14.6 mm. Before RFA, all patients underwent biliary drainage once in 2 patients (17%), twice in 9 patients (75%), and 3 times in 1 patient (8%). The technical success rate for RFA with SEMS placement was 100%. The mean number of ablations was 5.4 ± 1.1. Post-procedural adverse events occurred in 4 patients (33%; 3 with fever and 1 with cholecystitis). The patients with a fever improved immediately with conservative treatment. The case of cholecystitis required percutaneous aspiration of the gallbladder three days after the procedure and was suspected to have been influenced by the SEMS placement, as the stent was placed across the cystic duct without ablation of the duct.

Conclusion: The short-term outcomes of RFA for MHBO were suitable. Further preoperative studies are needed to confirm the efficacy of RFA with bilateral placement of a SEMS for MHBO.

Disclosure: Nothing to disclose

P0283 REINTERVENTION FOR STENT OCCLUSION AFTER PLACEMENT OF MULTIPLE SELF-EXPANDABLE METALLIC STENTS FOR MALIGNANT HILAR BILIARY OBSTRUCTION

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Introduction: Endoscopic reintervention for stent occlusions following the placement of multiple self-expandable metallic stents (SEMS) for malignant hilar biliary obstruction (MHBO) is challenging, and the appropriate drainage method have not yet been clarified. We aimed to clarify a suitable reintervention method for stent occlusions following placement of multiple SMES for MHBO.

Aims & Methods: Between October 2017 and March 2019, 41 patients with MHBO underwent reintervention for stent occlusion after placement of multiple SEMS. We retrospectively evaluated the technical and functional success rates of the reintervention, and the time to recurrent biliary obstruction (RBO). The treatment strategy of reintervention was the first choice via ERCP, and EUS-BD was performed/co-administered in cases when transpapillary drainage was insufficient.

Results: Re-intervention was performed in 41 of 118 cases (34.7%) that were indwelled with multiple SEMS for hilar region stenosis. The median age of the patients was 59 ± 11.5 years, and the patients comprised of 27 men and 17 women. Etiologies included cholangiocarcinoma in 17 cases, gallbladder cancer in 6, pancreatic cancer in 5, and others in 13. Bismuth classification were type II in 15 patients (36.6%), type III in 17 patients (41.5%), and type IV in 9 patients (21.9%). Regarding the methods used for the placement of the initial SEMS, 28 cases (68.2%) underwent SBS and 13 cases (31.7%) underwent PSIS. In 24 (58.5%) and 17 (41.5%) cases, 2 and 3 areas were drained.

As a result, the technical and functional success rates of re-intervention were 82.9% (34/41) and 90.2% (37/41), respectively. In SBS group, the technical and functional success rates were 82.2% (23/28) and 92.3% (26/28), and in PSIS group, these were 84.6% (11/13) and 92.3% (12/13). In dranage for 2 areas group, the technical and functional success rates were 79.2% (19/24) and 91.7% (22/24), and in dranage for 3 areas group, these were 88.2% (15/17) and 94.1% (16/17). ERCP was performed in 25 cases, EUS-BD (all EUS-HGS) in 13, and ERCP+ EUS-BD in 3 (EUS-HGS in 2, EUS-HDS in 1). Stent for re-intervention was used Plastic stents(PS) for 3 cases, PS + SEMS for 2, and SEMS for 36. The median time to RBO was 109 days. The time to RBO tended to be longer in the EUS-BD group compared to that of the ERCP group (116 days vs. 78 days; long-rank test, p = 0.076). There was no significant difference in examination time (72.2 vs. 79.4, p = 0.52). In the ERCP group, mild acute pancreatitis was observed in 3 cases (12%). In the EUS-BD group, the stent straying into the gastric wall was observed in 1 patient (postoperative 59 days), intraabdominal abscess (CT-CAE v5.0 grade 3) in 1, and hemorrhage from the puncture site (CTCAE v5.0 grade 2) in 1.

Conclusion: When considering reintervention for MHBO, EUS-BD has a long patent period and can be used as a new reintervention method.

Disclosure: Nothing to disclose

P0284 ENDOSCOPIC TREATMENT OF ACUTE CHOLECYSTITIS IN POOR SURGICAL CANDIDATES IS COST-EFFECTIVE

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Introduction: Endoscopic gallbladder drainage is an alternative to percutaneous gallbladder drainage (PGBD) to treat acute cholecystitis in poor surgical candidates. Treatment is achieved through retrograde transpapillary gallbladder drainage (ERC-GBD) or endosonographic gallbladder drainage (EUS-GBD), and offers similar success rates with less adverse events. No cost-effectiveness analysis has compared these three strategies.

Aims & Methods: We aim to compare the clinical and cost determinants of three treatment alternatives for acute cholecystitis in subjects who were deemed poor surgical candidates for cholecystectomy.

A cost-effectiveness analysis compared three strategies: PGBD, ERC-GBD and EUS-GBD. A decision tree was created comparing clinical outcomes during the first three months after hospitalization. All subjects included were considered poor surgical candidates based on comorbidities, and subsequently managed with bowel rest, intravenous fluids and antibiotics without improvement.

Effectiveness was a composite of length of hospitalization plus additional hospital care due to adverse events or readmissions (measured in hospital days). Costs of care were obtained from the National Inpatient Sample and published literature. Outcomes estimates (e.g. procedure complications and readmissions) were obtained from published literature. Primary analysis was performed from the health care perspective.

Cost-effectiveness was compared to the national average cost of one hospital bed *per diem* as reference. One-way sensitivity analyses and Monte Carlo simulations were generated to evaluate effect modifying variables.

Results: Analysis of a hypothetical cohort of patients considered poor candidates for cholecystectomy showed that the cost effectiveness of endoscopic therapies was superior to PGBD. Compared to PGBD, ERC-GBD was a cost-saving strategy and EUS-GBD was cost effective, requiring $1,312 per hospitalization day averted. Both interventions were acceptable under the cost of one-hospital-bed per diem ($2,338 national average). Compared to ERC-GBD, EUS-GBD required spending $8,950 more per hospitalization day averted.

Sensitivity analyses showed that our model was notably affected by LAMS price, length of stay for patients managed conservatively, and length of stay for patients requiring laparoscopic cholecystectomy. Cost effectiveness was minimally affected by variations in technical success rates of endoscopic procedures. One-way sensitivity analysis showed that a decrease of LAMS price (to $780) could potentially make EUS-GBD the dominant strategy.

The Monte Carlo simulation included a variable range of therapeutic success rates. ERC-GBD was cost effective in the majority of simulation trials, and was under the cost of one hospitalization day. ERC-GBD ceased being cost effective when willingness to pay for a new intervention was greater than $10,000. ERC-GBD remained more cost effective than EUS-GBD in the Monte Carlo simulation.

Analysis from a societal perspective added $6,264 for PGBD, $4,659 for ERC-GBD, and $4,543 for EUS-GBD over 3 months. Loss of productivity days represented approximately 60% of the additional costs. Cost-effectiveness results did not change from the primary analysis; EUS-GBD remained cost effective, with $762 per hospital day averted compared to PGBD.

Conclusion: Endoscopic treatment for acute cholecystitis is cost-effective compared to PGBD, favoring ERC-GBD over EUS-GBD. Further efforts are needed to make endoscopic treatments available in more medical centers, reduce equipment costs and shorten inpatient care.

Disclosure: Nothing to disclose

P0285 VALUE OF PERCUTANEOUS CT-GUIDED MICROWAVE ABLATION IN TREATMENT OF INOPERABLE COLORECTAL PULMONARY METASTASES

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Introduction: Image-guided percutaneous thermal ablation can be used for treatment of non-operable primary and metastatic lung tumors. These techniques are based on heating effect on the tissue around a percutaneous applicator causing coagulative necrosis of the tumor cells. Microwave ablation (MWA) is a commonly used locoregional interventional procedure in treatment of pulmonary tumors with satisfactory outcome.

Aims & Methods: To study the efficacy of MWA in treatment of colorectal pulmonary metastases.

Patients and methods: A total of 47 patients (22 men and 25 women; mean [± SD] age, 63.8 ± 14.6 years; range, 30-91 years) with 68 inoperable lung metastases of colorectal origin (Mean tumor size15 ± 9.0 mm) were treated with MWA under guidance of CT-Fluoroscopy using conscious sedation according to the guidelines from November 2008 to October 2017.

Diagnosis of lung metastases relied on chest CT with contrast (Somatom Sensation 64; Siemens, Erlangen, Germany with scanning parameter: 5-mm collimation, 30 mAs, and 120 kVand 5-mm section thickness) and lung biopsy.

Follow-up post ablation by chest CT was done after 24 hours, three months, six months, one year and every 6 months onwards to determine treatment response. Patients were either adequately ablated (no residual tumor activity) or had local progression (residual tumor activity). Local progression was considered when the lesion became of larger size or expressed morphological changes in its shape such as protrusion or, irregular, scattered, nodular or eccentric focus arising from the margin in addition to denovo lesion showing contrast uptake. Survival rates were calculated from the time of the first ablation session, with the use of Kaplan-Meier and log-rank tests. Changes in the size and volume of the ablated lesions were measured using the Kruskal-Wallis method.

Results: Forty four lesions (64.7%) showed complete response to treatment and 24 lesions (35.3%) had local progression (residual activity). The median time to local tumor progression was 7.6 months. The median survival was 31.5 months for patient underwent MWA according to the Kaplan-Meier test. The overall survival rate at 1, 2, and 4 years was 83.5%, 68.2%, and 16.5%, respectively.

The progression-free survival rate at 1, 2, 3, and 4 years was 53.9%, 28.8%, 10.0%, and 1.0%, respectively.

Successful tumor ablation was significantly more frequent for lesions with a maximal axial diameter of 3 cm or smaller than for lesions greater than 3 cm in maximal axial diameter (P =.0001). There were no deaths during the procedure and the mortality rate within 6 months after ablation was 0%. Early postablation complications included pneumothorax (10.3%), pain (8.8%), hydroneumothorax (5.8 %), pulmonary hemorrhage (5.8%) and postablation syndrome (2.9%). An intercostal chest tube was applied in one (14.2%) of the 7 sessions with pneumothorax. No significant long term complications were seen.

Conclusion: Pulmonary CT-guided microwave ablation therapy for management of pulmonary metastases of colorectal origin is safe and effective minimally invasive option and can improve local tumor control and survival rate in patients who are not candidate for surgical resection. The efficacy of the ablation is determined by the size and location of the tumor in relation to the hilar structures.

Disclosure: Nothing to disclose

P0286 APPARENT DIFFUSION COEFFICIENT IN EVALUATING EARLY TREATMENT RESPONSE AFTER CT-GUIDED MICROWAVE ABLATION FOR INOPERABLE COLORECTAL PULMONARY METASTASES

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Introduction: Microwave ablation (MWA) is a commonly used locoregional thermal ablation technique in treatment of primary and secondary pulmonary tumors. There is growing evidence that apparent diffusion coefficient (ADC) value can be used in evaluating early MWA therapeutic efficacy in treatment of pulmonary tumors and thus represent a reliable predictor of tumor recurrence after treatment.

Aims & Methods: To determine the early treatment response of lung MWA in patients with colorectal pulmonary metastases using ADC value.

Patients and methods: A total of 47 patients (22 men and 25 women; mean [± SD] age, 63.8 ± 14.6 years; range, 30-91 years) with 68 lung lesions of colorectal origin were retrospectively included, and were treated with MWA according to the guidelines during the period from November 2008 to October 2017.

All lesions were evaluated by diffusion weighted imaging (DWI) and ADC value measurement before and 24 hours after MWA. DWI was obtained using axial a single-shot echoplanar imaging with two *b*-values (50,400, 800 mm²/s) using 3 tesla MRI machine. Quantitative ADC maps were calculated using commercially available software and an imaging workstation.

Diagnosis of lung tumors relied on chest CT and/or MRI with contrast. Follow-up post ablation by chest CT and/or MRI with ADC value measurement

was done after 24 hours, three, six months, one year and every 6 months onwards to determine responsive cases (no residual tumoral activity) and local progression cases with residual tumor activity. Local progression was considered when the lesion became of larger size or expressed morphological changes in its shape such as protrusion or, irregular, scattered, nodular or eccentric focus arising from the margin in addition to denovo lesion showing contrast uptake. Immediate changes in ADC values were compared to the net response based on CT and/or MRI follow-up.

Results: Forty four lesions (64.7%) responded to ablation and twenty four lesions (35.3%) had shown local progression (residual tumor activity). ADC values were significantly higher in lesions that responded to MWA than in non-responding lesions.

The mean ADC value before treatment was $0.8 \pm 0.2 \times 10^{-3}$ mm2/s (mean $\pm$ SD), while after treatment it was $1.7 \pm 0.3 \times 10^{-3}$ mm2/s with a statistically significant difference ($P = 0.001$) for the responsive group .

The mean ADC of the local progression group before treatment was $0.7 \pm 0.2 \times 10^3$ mm²/s , and increased after treatment to reach $1.4 \pm 0.3 \times 10^3$ mm²/s with a statistically significant difference ($P = 0.001$).

The mean ADC value before treatment didn't show significant difference between responding ($0.8 \pm 0.2 \times 10^{-3}$ mm2/s) and local progression group($0.7 \pm 0.2 \times 10^3$ mm²/s; P = 0.857).

There is statically significant difference in mean ADC value between responsive group (was $1.7 \pm 0.3 \times 10^{-3}$ mm2/s) and local progression group ($1.4 \pm 0.3 \times 10^3$ mm²/s) after ablation ($P = 0.001$)

A cut-off ADC value (1.42) has been suggested as a reference point to predict the response after ablation with 66.67 % Sensitivity, 84.21% Specificity, 66.7% PPV& 84.2% NPV.

Conclusion: ADC value calculated from DWI performed 24 hours post treatment is a good quantitative measurement for early prediction of the therapeutic efficacy of MWA in treatment of patients with inoperable lung metastases of colorectal origin and can be used as good alternative to CT imaging in early immediate post ablation follow-up before morphological changes in tumor become detectable on conventional CT and/or MRI.

Disclosure: Nothing to disclose

P0287 ROLE OF COMBINED PALLIATIVE LOCAL THERMAL ABLATION AND TRANSARTERIAL CHEMOEMBOLIZATION IN IRRESCETABLE INTRAHEPATIC CHOLANGIOCARCINOMA IN TERMS OF LOCAL TUMOR CONTROL AND OVERALL SURVIVAL

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Introduction: Intrahepatic cholangiocarcinoma (ICC) constitutes around 30% of all hepatic malignant neoplasms and considered the second most common primary malignant hepatic tumor following hepatocellular carcinoma. ICC is often diagnosed at an advanced stage; associated with poor prognostic outcomes and 5-year survival less than 5%.

conventional transarterial chemoembolization (TACE) have been recently applied in cases of ICC. Microwave and radiofrequency are minimal invasive procedures have also been proved to be effective safe therapeutic modalities in case of various hepatic tumors including HCC and liver deposits aiming to decrease tumor burden by inducing local coagulative necrosis; still their therapeutic value in case of ICC not clearly defined.In the last 10 years, we implemented TACE, local thermal ablative methods, and combined treatment protocols as minimal invasive palliative procedures aiming to limit the disease process and improve survival rates.

Aims & Methods: To assess the combined role of local thermal ablation and transarterial-chemoembolization in cases of irresectable intrahepatic choloangiocarcinoma.

Methods & Materials: Retrospective analysis for 32 patients with CCC from Januar 2007 till December 2017, in which 11 males (34.4 %) and 21 (65.6 %) females with mean age 59.2 years (25-86) with either irresectable (22/32, 68.8%) or recurrent lesions (10/32, 31.3%) managed by at least three sessions of TACE (3-26, mean 9) with local thermal ablation for overall 73 lesions with mean size 21 mm (10-74) with either laser (9/73, 12.3%), radiofrequency (8/73, 11%) or microwave (56/73, 76.7%) devices. Follow

up using contrast enhanced MRI to evaluate local tumor control based on modified Response Evaluation Criteria for Solid Tumors (mRECIST) and the survival was evaluated using Kaplan-Meier method.

Results: The mean and median survival was 42.5 and 28 months (CI: 27.3-57.6 and 15.3-40.7 respectively). The initial local tumor response following 3 TACE was stable (10%), partial response (80%), progressive (10%) and complete remission (0%) and final effect was 13.3%, 16.7%, 63.3% and 6.7% respectively. Local lesion response following thermal ablation was complete resolution of the targeted lesion in 47/73 lesions (64.4%) and incomplete response at the rest. 6.2% (2/30) patients developed local complication following thermal ablation.

Significant correlation has been found between the size of the targeted lesion and the response with better results at diameter ranging from 10-50 mm. However no significant correlation was found between the device type and the ablation outcome.

Conclusion: Combined targeted local liver therapy has a potentiality to provide safe therapeutic option for irresectable or recurrent cholangiocarcinoma and may affect the overall patients' survival as well.

Disclosure: Nothing to disclose

P0288 ENDOVASCULAR PRESSURE MEASUREMENTS TO ASSESS THE FUNCTIONAL SEVERITY OF MESENTERIC ARTERY STENOSIS IN PATIENTS SUSPECTED OF HAVING CHRONIC MESENTERIC ISCHEMIA

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Introduction: Chronic mesenteric ischemia (CMI) is an invalidating disease causing severe complaints of postprandial abdominal pain and weight loss. CMI is most often caused by stenosis of one or more mesenteric arteries, a frequent finding in the general population with a prevalence rising to up to 67% in patients >80 years of age(1). The abundant collateral mesenteric circulation protects the bowel against ischemia, creating a diagnostic challenge since CMI only occurs when the collateral circulation is insufficient. Revascularization is performed after multidisciplinary group discussion amongst gastroenterologists, vascular surgeons and interventional radiologists of the patient's history, radiological imaging and result of a functional test. Treatment decisions are especially challenging in patients with a single vessel mesenteric stenosis, since 27% does not experience an improvement of symptoms after successful revascularization(2). An assessment of hemodynamic significance of a stenosis to determine clinical relevance and support treatment decision could be of great value in these patients. Endovascular pressure measurements to assess the severity and clinical relevance of a stenosis have been validated in coronary and renal arteries and are widely used to guide treatment decision in clinical practice(3,4). No conclusive data on clinical applicability of pressure measurements in the mesenteric arteries exist.

Aims & Methods: The aim of this single center, retrospective cohort study was to identify clinically significant mesenteric stenosis by correlating mesenteric pressure measurements with clinical success after stenting of the celiac artery (CA) or superior mesenteric artery (SMA). All consecutive patients planned for endovascular mesenteric artery treatment with pressure measurements between April 2015 and May 2017 were included. Pressure measurements were performed before and after intra-arterial administration of a vasodilator (nitroglycerin). For both series of measurements the pressure gradient over the stenosis and the pressure distal to the stenosis divided by the aortic pressure (Pd/Pa) were calculated. Clinical success was defined as an improvement of symptoms and or weight gain.

Results: In total 41 endovascular mesenteric procedures with pressure measurements were performed in 37 patients (mean age 67.7±10.8 years, 62% female). The measured Pd/Pa without vasodilator in patients with an isolated CA or SMA stenosis or an inferior mesenteric artery and either CA or SMA stenosis(N=24), significantly differed between patients with clinical success after stenting (N=18), median 0.885 (IQR 0.735-0.904) versus patients without clinical success 0.923 (0.897-0.958), p=0.040. After administration of a vasodilator differences increased further with a Pd/Pa of 0.703 (0.598-0.769) in patients with clinical success and 0.827 (0.818-

0.906) in patients without, p=0.009. The pressure gradient showed similar differences, without vasodilator 17.5 (11.0-29.0) vs. 8.0 (4.0-15.0), p=0.047 and after vasodilator 36.0 (21.0-40.0) vs. 20.0 (9.0-21.0), p=0.041. A Pd/Pa after vasodilator with a cut-off ≤0.8 proved to be the best predictor of clinical success with a sensitivity of 86% and specificity of 83% (AUC=0.869).

Conclusion: Endovascular pressure measurements seem a promising tool to assess the clinical relevance of mesenteric artery stenoses and hence may be helpful in making treatment decisions. Pressure measurements in a larger cohort are needed to verify the results of this study.

References: 1. Mensink PB, Moons LM, Kuipers EJ. Chronic gastrointestinal ischaemia: shifting paradigms. Gut. 2011;60(5):722-37. 2. van Dijk LJD, Moons LMG, van Noord D, Moelker A, Verhagen HJM, Bruno MJ, et al. Persistent symptom relief after revascularization in patients with single-artery chronic mesenteric ischemia. J Vasc Surg. 2018. 3. Aboyans V, Ricco JB, Bartelink MEL, Bjorck M, Brodmann M, Cohnert T, et al. Editor's Choice - 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS). Eur J Vasc Endovasc Surg. 2018;55(3):305-68. 4. Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. EuroIntervention. 2019;14(14):1435-534.

Disclosure: Nothing to disclose

P0289 DESTRUCTION OF VASCULAR BED IN ABLATED ZONE AS A RESULT OF IRREVERSIBLE ELECTROPORATION OF PANCREATIC CANCER

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Introduction: Irreversible Electroporation (IRE) of the pancreas is an increasingly used method for unresectable pancreatic cancer that can be used in cytoreduction followed by surgical treatment and shows promising results in palliative care.

IRE is an ablative technique where electric pulses cause damage the cell membrane leading to apoptosis. It is claimed that IRE is not causing thermal effect comparing to radiofrequency and microwave ablation.

The early assessment of signal intensity changes after IRE could provide information on actual processes occurring in the ablation zone.

Aims & Methods: The study aims to assess the MR (Magnetic Resonance) images performed before and up to 7 days after IRE to evaluate the early post IRE changes in signal intensities in the ablation zone with a special emphasis on thermal effect and vascularization in the ablated zone.

We retrospectively analyzed the MRI studies of 24 patients (10 F, 14M, aged 35-71) with unresectable pancreatic cancer during or shortly after chemotherapy. IRE was performed under general anesthesia percutaneously or during open surgery with the use of 4-6 electrodes (AngioDynamics) placed in pairs at a maximum distance of 20mm between each other, 90 pulses of 90us (maximum 1500V/cm) were delivered per pair of electrodes. The MR images were performed on 1,5T and 3T scanners one day before IRE procedure, on the 1st and 7th day after. The standard protocol for pancreas was performed including T1-weighted images (T1W), T2-weighted images (T2W), Diffusion Weighted Images (DWI), ADC (Apparent Diffusion Coefficient) maps, Dynamic Contrast Enhancement (DCE) images with subtraction series. The qualitative and quantitative assessment of the obtained images was performed.

Results: The signal intensity in the ablated zone on T1 Fat Saturation (Fat-Sat) after contrast media administration with subtraction was in the range 0-6,25 (Mean 2,03, SD 1,83). The ADC values after IRE were significantly higher compared to pre IRE measurements. These trends were found likewise on different MR scanners (1,5, 3T).

The signs of thermal effect, e.g., areas of electrodes placement were found in 83,3% of patients. They were seen as small, hypointense zones close to electrodes on T1-weighted fat saturation contrasted enhanced images in the coronal plane.

Conclusion: Lower (close to zero) SI values in the ablated zones on T1 FatSat images after contrast media aministration images with subtraction proves that vascular bed within the ablation zone was completely damaged. The

growth of ADC values after IRE is the effect of cellular water displacement to intercellular space what is a sign of cytolysis. IRE can create a thermal effect on exposed tissues.

Disclosure: Nothing to disclose

P0290 WITHDRAWN

Surgery I
10:30-17:00 / Poster Exhibition - Hall 7

P0291 THE FEASIBILITY AND CLINICAL OUTCOMES OF ENDOSCOPIC FULL THICKNESS RESECTION ASSISTED LAPAROSCOPIC SURGERY FOR DUODENAL NEUROENDOCRINE NEOPLASMS

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Introduction: The duodenal neuroendocrine tumors (dNETs) are arising from the cell of the mucosal layer and often small and confined to the superficial layer. Surgery and endoscopic resection are both considered appropriate; however, there are critical hurdles to both modalities in real practice. Laparoscopic surgery has a difficulty to determine precise tumor location, and endoscopic resection has high risks for bleeding, perforation, and incompleteness. In our study, we compared the treatment outcomes of endoscopic full-thickness resection assisted laparoscopic surgery (EFTRLS).

Aims & Methods: The electronic medical record database was reviewed at a university hospital (Yeouido St. Mary's Hospital), Seoul, Korea. A total of 33 patients were found to be diagnosed during the last 10 years, from June 2008 to Dec 2018.

Results: Among the 35 patients with dNETs, 12 were excluded, follow-up loss (3), transfer-out (2), treatment refusal (2), invisible after forceps biopsy (2), poorly differentiated histology (2), and the presence of metastatic lesion (1). Twenty-three patients who showed well-differentiated histology, less than 2 mitosis per 10 HPF and less than 3% of Ki-67 index, underwent excision of tumors. Sixteen were treated with endoscopic resection, 3 with surgery only and 4 with EFTRLS. Resection margin involvement was none in the EFTRLS group compare to other single modality groups (0% [0/4 cases] vs 19% [3/16 endoscopic resection] vs 33% [1/3 surgery only]). One endoscopically treated patient had a macroscopic residual tumor and needed additional surgery. Two patients of endoscopic resection group experienced perforation and underwent surgery. Tumor recurrence and metastasis were not reported during the study period in all patients.

Conclusion: EFTRLS provides a precise and secure safety margin of tumor resection and abolishes the risk of uncontrolled bleeding and perforation. EFTRLS has the advantage in the oncological completeness and patient safety over either endoscopic resection alone or surgery alone.

Disclosure: Nothing to disclose

P0292 CLINICAL VALUE OF PER-ORAL ENDOSCOPIC MYOTOMY (POEM) FOR ACHALASIA (AC)

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Introduction: Achalasia (AC) is a clinically rare disease of lower esophageal inflammatory changes and myenteric plexus injury has been treated by medication, surgical and endoscopic methods. During the pathological process, the lower esophageal sphincter (LES) contracts, leading to food retention, and esophageal peristalsis, constriction and expansion. Clinical symptoms include dysphagia, food reflux, nausea, vomiting, chest pain,

and severe malnutrition. The drug and surgical treatments have many disadvantages such as, easy-to-relapse, high cost and complications, and the patient's intolerance. Contrary to the above-mentioned methods, the Peroral endoscopic myotomy POEM, a new endoscopic treatment of AC has been affirmed with the short-term efficacy. However, there are few reports on long-term efficacy of POEM. The study aims to evaluate the short-term, medium- and long-term effects of POEM analyzing the clinical data of 59 patients with AC in the second hospital from 2012 to 2018.

Aims & Methods:
Objective: To explore the short-term and long-term clinical efficacy of peroral endoscopic myotomy (POEM) and its postoperative complications in the treatment of achalasia (AC).

Methods: The retrospective clinical study of 59 patients who underwent POEM was conducted from Jan. 2012-April 2018 in the Endoscopy Center of Lanzhou University Second Hospital. The short-term and long-term clinical efficacy, complications and changes in the clinical manifestations was comparatively analyzed according to the Eckardt scoring system before and after achalasia (AC) management by POEM.

Results: All the 59 patients underwent 100% successful POEM, in which the disorder duration ranges from 4-380 months. The follow-up times were 6-89 months, respectively. The pre-operative and post-operative Eckardt score was 6.45±1.63, 0.52±0.56 (P<0.05), respectively. The patients, who were follow-up 12 month, mean Eckardt score was 0.61. Post-operative weight gain was 9.92±5.97kg). The post-operative complications were observed in 5 cases (8.4%) and 1 case (1.69%) was successfully treated conservatively, whereas 23 cases (38.9%) presented with gastro-esophageal reflux.

Conclusion: The short-term and long-term clinical efficacy of POEM is safe and effective in the treatment of achalasia (AC).

Disclosure: Nothing to disclose

P0293 TREATMENT STRATEGY FOR LAPAROSCOPIC HIATAL HERNIA REPAIR

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Introduction: Based on the anatomy-function-pathology (AFP) classification, the recurrence rate of A2 and A3 hiatal hernia after laparoscopic fundoplication (LF) is higher than A1, a mesh is used to reinforce the esophageal hiatus.
Aims & Methods: The aim of this study is to report the surgical outcomes and treatment strategies in our institution. The subjects were 509 patients (mean age 55.2±16.6 years, 209 women) who underwent primary LF for hiatal hernia from January 1995 to November 2018. These patients were divided into the 3 groups by A factor of AFP classification (A1:A2:A3=285:148:76). We assessed the patients' background, pathological condition, surgical outcome, recurrence rate and changes in surgical procedure.
Results: The median age (years) of the patients in each group was A1:A2:A3=46:63:74 and the size of the hernia increased in proportion to the age (p< 0.001). Female ratio was significantly higher in A3 (p< 0.001). Preoperative reflux esophagitis was severe in A2 (p< 0.001) and operation time (min) became longer by the hernia size (A1:A2:A3=135:165:191, p< 0.001), but the amount of bleeding was minimum in each group (p=0.753). The incident rate (%) of intraoperative complications in A3 was significantly higher (A1:A2:A3=9:8:23, p=0.005). The recurrence rate of hiatal hernia after LF was 13% (68/509), and the recurrence rate (%) was increased by the hernia size (A1:A2:A3=12:18:24, p=0.043). Therefore, we introduced reinforcement of the hiatus using mesh since February 2011 for cases with A2 and A3, from 75 years old and above, BMI 28 or more. After that, the recurrence rate of A2 markedly decreased to 3% (1/37, p=0.001), but that of A3 was still high (8/34=24%) and no effect was obtained by mesh reinforcement (p=1).
Conclusion: Mesh reinforcement decreased the recurrence rate of A2 patient. Further improvement is necessary for A3 patients, and now the fixation of the anterior wall of the stomach and the abdominal wall is added.
Disclosure: Nothing to disclose

P0294 A SINGLE CENTER EVALUATION ON IMPLEMENTATION OF SELECTIVE PATHOLOGIC EXAMINATION OF THE GALLBLADDER

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Introduction: Historically, all gallbladders are send for histopathologic examination following cholecystectomy to exclude presence of malignancy. Several hospitals switched to a selective histopathologic (Sel-HP) policy to reduce unnecessary pathological workload. Our aim was to evaluate the evolution of a Sel-HP policy and determine safety and cost reduction.
Aims & Methods: A single center retrospective study was conducted from January 2012 to December 2017 in a teaching hospital in the Netherlands. All gallbladders were macroscopically examined by the surgeon or resident. Consequently, they decided which cases required additional histopathologic evaluation. We reviewed the number of gallbladders send for pathologic examination. To identify missed GBC we reviewed the Netherlands Comprehensive Cancer Organisation (IKNL) registry to detect GBC in patients of whom the gallbladder was not send for histopathology.
Results: Out of the 2271 patients, 1083 (47.7%) were selected for additional histopathology to assess the presence of malignancy. Percentage of gallbladders selected for histopathologic examination decreased from 83% in the first year to 38% in the last year. Six (0.26%) gallbladder cancers (GBC) were discovered, 7 times (0.31%) a low grade dysplasia and 3 times (0.13%) an intestinal metaplasia of the gallbladder. During follow-up, no patient was found to have GBC recurrence after Sel-HP. Our policy implementation reduced medical cost and saved over €65 000.
Conclusion: The strategy of a Sel-HP policy decreased the number of referred gallbladders to the department of pathology by roughly 60%, while no GBC cases were missed and therefore appears to be safe and leads to significant cost reduction.
Disclosure: Nothing to disclose

P0295 IMPACT OF COMPLICATIONS ON OUTCOMES AFTER PANCREATODUODENECTOMY: ANALYSIS OF A NATIONWIDE AUDIT

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Introduction: Pancreatoduodenectomy is a high-risk surgical procedure, after which one complication may provoke a sequence of adverse outcomes. To improve quality of care after pancreatoduodenectomy, initiatives are required to mitigate the impact of separate complications. To allow prioritization of such initiatives, the aim of this study was to quantify the attribution of individual complications to postoperative mortality, organ failure, prolonged hospital stay and unplanned readmissions after pancreatoduodenectomy in a national cohort.
Aims & Methods: Data from all consecutive patients undergoing pancreatoduodenectomy from January 2014 to December 2017 were extracted from the mandatory nationwide Dutch Pancreatic Cancer Audit.

Using a modified Poisson regression model, adjusted risk ratios were calculated for the association of each of the individual complications (i.e. postoperative pancreatic fistula, postpancreatectomy hemorrhage, bile leakage, delayed gastric emptying, wound infection and pneumonia) with each of the study outcomes (i.e. in-hospital mortality, organ failure, prolonged hospital stay and unplanned readmission). Complications were defined according to the International Study Group of Pancreatic Surgery. Prolonged hospital stay was defined as exceeding the 75th percentile in this cohort (i.e. longer than 18 days).

Risk adjusted population attributable fractions (PAF) were calculated for each complication-outcome pair while adjusting for patient- and treatment related factors and the presence of other complications in individual patients. The PAF represents the percentage of an outcome that could be prevented in a theoretical scenario where a specific complication would be eliminated completely and is therefore particularly useful in prioritizing quality improvement initiatives.

Results: Overall, 2620 patients were analyzed. A total of 1672 patients (63.8%) experienced complications after pancreatoduodenectomy, leading to an in-hospital mortality of 3.6% (95 patients), organ failure in 7.6% (198 patients), and an unplanned readmission of 16.2% (427 patients). Postoperative pancreatic fistula and postpancreatectomy hemorrhage had the greatest independent impact on both mortality and organ failure.

Complete elimination of these complications would lead to a 25.7% [95% CI 13.4-37.9%] and 32.8% [95% CI 21.9-43.8%] decrease in mortality and a 21.8% [95% CI 12.9-30.6%] and 22.1% [95% CI 15.0-29.1%] decrease in organ failure, respectively. Delayed gastric emptying had the greatest independent impact on prolonged hospital stay (risk adjusted PAF 27.6% [23.5-31.8%]).

The reasons of unplanned readmission remained largely unexplained in this analysis. The impact of other evaluated complications on the study outcomes was relatively small.

Conclusion: Interventions to improve clinical outcome after pancreatic resection may have the greatest effect when focused on prevention and treatment of postoperative pancreatic fistula and postpancreatectomy hemorrhage, because these complications have the most impact on both mortality and organ failure. To reduce prolonged hospital stay, initiatives to decrease delayed gastric emptying should be explored.

Disclosure: Nothing to disclose

P0296 THE IMPACT OF OUT-OF-HOURS LAPAROSCOPIC CHOLECYSTECTOMY IN ACUTE CHOLECYSTITIS

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Introduction: A way to avoid the delay of surgery for patients with acute cholecystitis is to perform laparoscopic cholecystectomy 24/7. Existing data on the safety of out-of-hours operations are conflicting and large studies regarding this are few.

Aims & Methods: The aim of this study was to investigate if out-of-hours laparoscopic cholecystectomy is associated with a higher rate of complications.

We used the Swedish Registry of Gallstone Surgery and Endoscopic Retrograde Cholangiopancreatography (GallRiks). Data from patients registered for laparoscopic cholecystectomy due to acute cholecystitis, between 2006-2017 was collected. Out-of-hours surgery was defined as starting 7 pm – 7 am on weekdays or any time during weekends (Friday 7 pm - Monday 7 am). A multivariate logistic regression analysis was performed to assess the risk of complications, with time of procedure as independent variable.

We also analyzed the rate of conversion to open surgery and rate of procedures exceeding 120 minutes. Adjustments were made for sex, age, BMI and ASA score.

Results: Altogether 13165 procedures were included in the analysis. The adjusted Odds Ratio (OR) for complications, comparing the out-of-hours procedures compared to daytime surgery, was 1.14 (95% CI 1.01-1.27, p=0.03). OR for conversion to open surgery was 2.07 (1.89-2.27, p< 0.001) and OR for operative time exceeding 120 minutes was 0.50 (0.46-0.54, p< 0.001).

Conclusion: We found a small increased risk of per-/postoperative complications comparing out-of-hours surgery to daytime surgery. The conversion rate was significantly higher in the out-of-hours group. The operative time was significantly lower when surgery was performed out-of-hours.

Disclosure: Nothing to disclose

P0297 RISK FACTORS FOR PROLONGED POSTOPERATIVE ILEUS IN COLORECTAL SURGERY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Prolonged postoperative ileus (PPOI) represents a frequent complication following colorectal surgery, affecting approximately 10%-15% of these patients(1).

Aims & Methods: This systematic review and meta-analysis aimed to evaluate the perioperative risk factors for PPOI.

Study conducted in accordance with the PRISMA Statement. Pubmed, Embase, Scielo and LILACS databases were searched from inception to November 2018 for studies that evaluated primary clinical data regarding the analysis of risk factors for PPOI after colorectal surgery. Heterogeneity was assessed with the I[2] measure of inconsistency. The Newcastle-Ottawa scale was used for bias assessment within studies, and the Grading of Recommendations Assessment, Development an Evaluation (GRADE) approach was used for quality assessment of evidence on outcome levels. According to the AMSTAR 2 tool, this meta-analysis was ranked with a high methodological quality.

Results: Fifty-six studies were included, of which forty-two were assessed in the meta-analysis, comprising a total of 131,034 patients that underwent colorectal surgery from 1997 to 2017. From these, 25838 (19.71%) developed PPOI. Significant risk factors for PPOI development were male sex (OR 1.56;95%CI 1.25-1.94), age (MD 3.17;95%CI 1.63-4.71), cardiac comorbidities (OR 1.65;95%CI 1.24-2.20), previous abdominal surgery (OR 1.44; 95%CI 1.19, 1.75) and open approach (OR 2.47;95%CI 1.77-3.44). Included studies evidenced a moderate heterogeneity. The quality of evidence was regarded as low-moderate according to the GRADE approach.

Conclusion: Multiple factors as demographic characteristics, past medical history and type of approach can increase the risk of developing PPOI in colorectal surgery patients. The knowledge of these will allow a more accurate assessment of PPOI risk in order to take measures to decrease its impact in this population.

References: 1.) Wolthuis AM, et al. Incidence of prolonged postoperative ileus after colorectal surgery: a systematic review and meta-analysis. Colorectal Dis. 2016;18(1):O1-9.

Disclosure: Nothing to disclose

P0298 THE "TIME-OF-DAY" EFFECT ON 30-DAY MORTALITY FOR ELECTIVE ABDOMINAL SURGERY

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Introduction: Emphasis on systematic approaches to patient safety has led to many studies demonstrating worse outcomes in the absence of supporting staff, especially during the night. This so called "time-of-day" effect has shown conflicting results based on the hospital setting, type of surgery, supporting system, or country studied.

Aims & Methods: The purpose of this study was to investigate the time-of-day effect on 30-day mortality for elective abdominal surgery patients in a tertiary care center. All patients receiving elective abdominal surgery between May 2003 and Feb. 2018 at Seoul National University Bundang Hospital were included in the study. Patients were evaluated by the starting time of the surgery received and grouped into first- surgery and non-first-surgery. To reduce the effects of confounding variables an inverse

probability treatment weighting (IPTW) propensity score analysis was done utilizing 51 variables. These variables included baseline characteristics (age, BMI, ASA class, residential and education status, alcohol and smoking status), baseline vital signs and lab results (blood pressure, pulse rate, body temperature, blood cell count, liver function tests, electrolyte tests), surgery type (minimal invasive surgery, cancer vs. non-cancer operation, anesthesia type), whether the patient underwent post-operative ICU care, and operation year. The primary outcome was 30-day mortality.

Results: Out of a total of 66,606 patients receiving abdominal surgery, 58,649 (88.1%) were elective procedures. There was a total of 110 (0.19%) 30-day mortalities (first-surgery: 20/15,285, 0.13%; non-first-surgery: 90/43,364, 0.21%). There were more cancer surgeries in the first-surgery group, and the patients were of older age and higher ASA class. The two groups were well rounded in the IPTW adjusted population. Undergoing first-surgery was found to be protective against 30-day mortality (Relative risk (first vs. non-first) = 0.58 95%CI[0.35-0.96], P = 0.033). In the numbers-needed-to-treat analysis, the calculated absolute difference was 0.088% and translated to 1 additional mortality for every 1,142 patients treated.

Conclusion: Receiving the first surgery may be protective for 30-day mortality in elective abdominal surgeries. Further large-scale population studies are needed to evaluate these findings.

Disclosure: Nothing to disclose

P0299 CLINICAL IMPACT OF BACTERIAL CONTAMINATION OF INTRA-ABDOMINAL DISCHARGE ON THE INCIDENCE OF PANCREATIC FISTULA AFTER PANCREATICODUODENECTOMY

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Introduction: Pancreatoduodenectomy (PD) is one of the most technically demanding operations, and thus, a challenge for surgeons. Postoperative pancreatic fistula (POPF) is the most severe postoperative complication of pancreatic surgery, and is recorded in 6-16% of patients. Some studies have shown that bacterial contamination in abdominal discharge is associated with the development of pancreatic fistula after PD. Moreover, we previously found that retrograde infections can be prevented and the incidence and severity of pancreatic fistulae reduced by using a closed drainage system following PD [1]. In another study, we showed that infection with Pseudomonas aeruginosa during the perioperative period in PD activates pancreatic juice secretion and induces the progression of pancreatic fistulae to higher grade fistulae [2]. However, thus far, the clinical relationship between POPF and the bacterial strain involved remains unclear. Therefore, this study was performed to assess the relationship between POPF following PD and the bacterial strain involved in a clinical setting.

Aims & Methods: The data for 82 consecutive patients who had undergone PD at Fukuoka University Hospital between January 2009 and July 2014 were retrospectively analysed to review patient characteristics and perioperative and postoperative parameters. We compared the clinicopathologic features between patients with bacterial contamination of drainage fluid and those without bacterial contamination of drainage fluid. We also examined the relationship between POPF and bacterial contamination of drainage fluid, according to bacterial strain.

Results: In total, 82 patients who underwent PD were divided into 2 groups: 57 patients to the bacterial contamination negative group and 25 patients to the bacterial contamination positive group. The incidence of preoperative cholangitis was significantly higher in the bacterial contamination positive group (p=0.014). The incidence of Grade B/C POPF was significantly higher in the bacterial contamination positive group than in the bacterial contamination negative group (44.0% vs. 0.0%; p< 0.001). Soft gland texture and bacterial contamination of intra-abdominal discharge were found to be risk factors for POPF (odds ratio: 9.00; odds ratio: 43.94, respectively). The incidence of Grade B/C POPF was significantly higher in patients harbouring Pseudomonas aeruginosa than in patients harbouring bacteria other than Pseudomonas aeruginosa (p=0.005).

Conclusion: Our findings suggest that bacterial contamination of intra-abdominal discharge plays an important role in the risk for the development of pancreatic fistulae. Therefore, bacterial infection control is very important in the perioperative PD period. Herein, all cases involving Pseu-

domonas aeruginosa isolation progressed to POPF. These results suggest that Pseudomonas aeruginosa is related to POPFs. The results are consistent with our previous vitro research [2]. Therefore, such cases should be handled with extreme caution.

References: 1. Kato D, Sasaki T, Yamashita K, et al. Drain selection reduces pancreatic fistulae risk: a propensity-score matched study. Hepatogastroenterology 2015; 62: 485-492. 2. Yamashita K, Sasaki T, Itoh R, et al. Pancreatic fistulae secondary to trypsinogen activation by Pseudomonas aeruginosa infection after pancreatoduodenectomy. J Hepatobiliary Pancreat Sci 2015; 22: 454-462.

Disclosure: Nothing to disclose

P0300 ENDOSCOPIC VACUUM THERAPY (EVT) FOR TREATMENT OF ANASTOMOTIC DEHISCENCE AFTER COLORECTAL SURGERY

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Introduction: Management of anastomotic dehiscence after colorectal surgery is a severe complication. EVT (Endoscopic Vacuum Therapy) is a promising therapeutic approach, being able to reduce both morbidity and mortality.

Aims & Methods: The primary endpoint of this series was to analyze efficacy and feasibility of EVT in the management of anastomotic leakage after colorectal surgery. This is a prospective single center study evaluating consecutive patients referred for EVT for anastomotic dehiscence. Patients were excluded in case of small cavity (i.e. < 1 cm) or circumferential anastomotic defect. All patients were treated with the same EVT. A preliminary endoscopic evaluation was performed in order to define size and shape of dehiscence. Then, the sponge was modeled to fit the cavity and advanced through a 12 mm overtube into the dehiscence. After removal of the overtube, the sponge was connected to a suction bottle at a 150 mmHg negative vacuum. After a mean 3-days interval, the sponge was removed and replaced until healing process was achieved (i.e cavity < 1 cm covered by granulating tissue). In order to maintain the healing process, further endoscopic curettages were performed until full resolution of the cavity (disappearance of anastomotic leakage at endoscopy). Treatment failure was defined as persistence of cavity during follow up and/or no sign of tissue granulation and/or infection signs. Procedures were performed under conscious sedation, according to our internal safety protocol and ASA score. All patients signed the informed consent.

Results: 14 patients with low colorectal anastomosis dehiscence were evaluated between October 2017 and April 2019: 2 were excluded (< 1 cm defect) and treated with pig tail drainage. 12 patients (M=11; F=1) (median age of 70 y.o. - R 40-86) were included. Indications for EVT were Hartmann's stump insufficiency (n=6), anastomotic leakage after Laparoscopic Total Mesorectal Excision (Lap-TME) (n=3) and anastomotic dehiscence after Trans-anal Total Mesorectal Excision (TaTME) (n=3). A total of 169 sponges were placed in 12 patients with a median number of 12,5 (R 4-31) per patient. Overall, full resolution was achieved in 6 patients in a median time of 97 days (range, 15-160). 4 patients had an initial healing process followed by a subsequent deterioration requiring EVT reinsertion: 1 patient finally had a full resolution of the cavity, a treatment failure was observed in 1, while the remaining 2 patients died during EVT for neoplastic progression (n=1) and septic complications (n=1). The remaining 2 patients had a treatment failure. No EVT-related complications were observed.

Conclusion: EVT seems to be a feasible and safe treatment with a high success rate in patients with large colorectal anastomotic dehiscence. It represents a minimally invasive alternative to surgical re-treatment.

Disclosure: Nothing to disclose

P0301 ENDOSCOPIC MANAGEMENT OF BARIATRIC SURGERY COMPLICATIONS: LONG-TERM RESULTS OF 830 CONSECUTIVE PATIENTS IN A SINGLE CENTER EXPERIENCE

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Introduction: Surgery is the gold standard treatment of morbid obesity and its related co-morbidities. However early or late surgical related adverse events(AE) occurs in 4 to 25% of patients requiring, in most cases, re-interventions. Endoscopy is an effective treatment especially if it is performed soon after occurrence of AE. However a comprehensive evaluation of long-term results and need for revisional surgery after endoscopic management is lacking.
Aims & Methods: The aim of this study is to report overall results and long-term outcomes of patients underwent to endoscopic management for AE following bariatric surgery in a tertiary interventional endoscopic center. From January2013 to April2019, 830 consecutive patients(640F), average age 44(17 - 72), underwent upper GI endoscopy for suspected AE following obesity surgery.
651 patients underwent Sleeve Gastrectomy, 167 gastric-by-pass(98 Roux-en-Y and 69 Omega)(GBP)and 12 had lap-band. 168 patients presented an AE after revisional bariatric surgery.
358 patients were addressed for sepsis due to supposed leak(extravasation of medium contrast).
226 patients presented dysphagia due to GI stenosis.
201 subjects presented fistula(abnormal communication between two re-epithelized structures or skin due to previous placement of surgical drainage).
28 patients had a perigastric intra-abdominal collection.
12 patients had partial intragastric migration of gastric band.
5 presented weight regain following GBP for enlargement of G-J anastomosis. Endoscopic management according to the different type of AE were one or an association of the following: endoscopic internal drainage, septotomy, stenting with Lumen apposed metal stent, Argon plasma coagulation(APC) anastomotic remodeling and trans-oral lap band ablation.
Clinical success was defined as follows: leak and fistula: no medium contrast extravasation, no chemistry tests alterations no need for prolonged antibiotics therapy. Stricture: adequate passage of medium contrast at swallow study or easy crossing of the stricture with a standard gastroscope. Lap band migration:uneventful removal. Loss of excess weight after G-J anastomotic remodeling with APC. Long term clinical success was considered after a minimum follow up of more than 18 months.
Results: 89 patients underwent endoscopy after one week from index surgery(5,13 ± 1,92days), 451 between 8 and 42days(19,63 ± 9,17), 93 patients between 43 and 91days(60,34 ± 13,07) and 197 after more than 91days(854,93 ± 1170,37). Overall mean period was of 223days(0-2100) from index surgery.
70 patients(8.4%) presented normal findings at upper endoscopy.
An average of 6 endoscopic sessions(1-31) were needed to achieve AE resolution in 72%(598) of patients. At long follow up (more than 18 months) 16%(96 out 598) of patients healed were lost whereas. 8%(66) are still under treatment.
Overall mortality was of 0,6%(5 out 830) whereas overall AE related to endoscopic treatment was of 2%(15)namely bleeding, stent migration with/or perforation. 3 patients with perforation required emergency surgery.
11.%(91 patients) underwent revisional surgery either for endoscopic treatment failure or poor quality of life after an average of 331days(15 - 1400).
Conclusion: According to this large case series endoscopy plays a pivotal role in the management of AE following bariatric surgery guaranteeing good results with low morbidity and mortality rates avoiding emergency surgery in 65% of cases. However several endoscopic sessions are needed. Long-term follow up showed that 11% of patients require, revisional surgery, either in case of endoscopic clinical success.
Disclosure: Nothing to disclose

P0302 HEALTH-RELATED QUALITY OF LIFE FOLLOWING HYBRID MINIMALLY INVASIVE VS. OPEN ESOPHAGECTOMY FOR PATIENTS WITH ESOPHAGEAL CANCER, ANALYSIS OF A MULTICENTER, OPEN-LABEL, RANDOMIZED PHASE III CONTROLLED TRIAL, THE MIRO TRIAL

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Introduction: Hybrid minimally invasive esophagectomy (HMIE) has been shown to reduce major postoperative complications compared with open esophagectomy (OE) for esophageal cancer.
Aims & Methods: The aim of this study was to compare short- and long-term health-related quality-of-life (HRQOL) following HMIE and OE within a randomized controlled trial.
We performed a multicentre, open-label, randomised controlled trial at 13 study centres between 2009 and 2012. Patients aged 18-75 years old with resectable cancers of the middle or lower third of the oesophagus were randomized to undergo either transthoracic OE or HMIE. Patients were followed-up every six months for three years postoperatively and global health assessed with EORTC-QLQC30 and esophageal symptoms assessed with EORTC-OES18.
Results: The short-term reduction in global HRQOL at 30-days specifically role functioning (-33.33 (HMIE) vs. -46.3 (OE); P=0.0407) and social functioning (-16.88 (HMIE) vs. -35.74 (OE); P=0.0003) was less substantial in the HMIE group. At two years, social functioning had improved following HMIE to beyond baseline (+5.37) but remained reduced in the OE group (-8.33) (P=0.0303). At two years, increases in pain were similarly reduced in the HMIE compared with the OE group (+6.94 (HMIE) vs. +14.05 (OE); P=0.018. However at three-years there were no statistical significant differences between treatment groups in changes from baseline HRQOL.
Conclusion: HMIE reduces the short-term adverse effects upon global health from esophagectomy compared to an open approach, with some persistence of these improvements up to two years. This HRQOL effect may be mediated by a reduction in postoperative complications following HMIE.
Disclosure: Nothing to disclose

P0303 WITHDRAWN

P0304 FIVE YEAR AUDIT OF ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) IN DAILY CLINICAL PRACTICE

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Introduction: ESD provides a modern endoscopic resection technique with a high rate of en bloc resections for lesions in the upper and lower gastrointestinal tract (GIT). It is recommended for high grade dysplasia (HGD) or superficial early cancer and other lesions with a diameter > 10 mm where common snare resection is difficult to perform.
Aims & Methods: Our aim was to report our experience and results of ESD in the GIT in daily clinical practice over a five year period in a Swiss private hospital. Therefore we retrospectively analysed 302 ESD cases (cs) of 268 patients (pts) that have had at least one ESD resection. All ESD were performed by one experienced endoscopist (PN).
Results: In the last 5 years 302 ESD in 268 pts were performed and now analysed (136 f, mean age 64.4). Further surgery after ESD was needed in 27 cs (9%). Of these, 19 cs (6.3%) were ESD-related: 15 (5%) ESD were not

completed due to technical problems (missing lifting sign, difficult anatomical situations, difficult pts conditions), 4 due to severe adverse event (SAE). 8 (2.6%) were not ESD-related: 6 due to unfavourable histology, 2 recurrences. Major SAE occurred in 15 cs (5%) and consisted of perforation (9 cs, 3%), delayed bleeding (4 cs 1.3%) or infection (2 cs, 0.7%).

From the further analysis 18 (6%) cs with a not completed ESD were excluded.

Of these 18, 13 had subsequent surgical resections, 2 had a second ESD in the follow up and 2 snare resections were performed. 1 needed no further resection.

The definitive study population consisted of the remaining 284 ESD-cs in 254 pts. The median lesion size was 3 cm (0.8-8), median intervention time was 14 min (5-111).

Follow-up was performed according to current guidelines and took place between 1 and 59 months after ESD. So far, local recurrence was found in 11 cs (3.9%).

Esophagus: 23 ESD (8%) were performed (1x surgery due to unfavourable histology (histo)): 2 showed an adenocarcinoma. 9 showed Barret's mucosa, of which 6 had HGD. 2 showed superficial squamous cell carcinoma pT1a. In 10 other benign lesions were found.

Stomach: 76 ESD (27%) were performed (3x surgery: 1 due to unfavourable histo, 1 delayed perforation, 1 recurrence). 4 GIST. 11 hyperplastic polyps. 11 ectopic pancreatic tissue (1 combined with a hamartoma). 7 inflammatory fibroid polyps (Vanêk's Tumour). 3 NET. 1 solitary nodal malign lymphoma. 39 other benign lesions.

Duodenum: 14 ESD (5%) were performed (no further surgery). 4 adenoma, of which 1 with HGD. 1 NET. 1 Peutz-Jeghers Polyp. 8 other benign lesions.

Colon above sigmoid: 79 ESD (28%) were performed (4x surgery: 2 due to delayed perforation, 1 unfavourable histo, 1 technical reasons). 1 had no histo (lost). 68 showed adenoma, of which 3 with HGD. 10 other benigne lesions.

Sigma: 23 ESD (8%) were performed (1x surgery due to delayed perforation). 1 adenocarcinoma pT1 which was successfully treated by ESD. 21 adenoma, of which 6 with HGD. 1 retention "juvenile" polyp.

Rectum: 69 ESD (24% of all ESD) were performed, (4x surgery: 3 due to unfavourable histo, 1 due to recurrence). 5 showed adenocarcinoma. 1 showed squamous cell dysplasia AIN III. 48 adenoma, of which 19 showed HGD. 15 other benign lesions.

Conclusion: ESD is a safe technique in daily clinical practice if performed by experienced endoscopists. With a high rate of successfully treated HGD and carcinoma it appears to be a favourable choice of treatment for such lesions.

Disclosure: Nothing to disclose

P0305 A CASE-MATCHED STUDY ON EUS-GUIDED DRAINAGE OF WALLED-OFF NECROSIS USING 20MM VS 15MM LUMEN APPOSING METAL STENTS: IS BIGGER BETTER?

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Introduction: EUS-guided placement of lumen apposing metal stents (LAMS) for the drainage of walled-off necrosis (WON) has gained popularity due to ease of placement, wide bore and anti-migration properties. Traditionally, the 10mm and 15mm diameter LAMS have been used. The 20mm diameter LAMS was recently introduced and provides 300% and 78% greater cross-sectional area as compared to the 10mm and 15mm stents, respectively. Therefore, it is plausible that the 20mm stent may result in improved efficacy. Nonetheless, the larger flanges may theoretically increase risk of adverse events (AEs) (e.g. bleeding). It is currently unknown how the 20mm and 15mm LAMS compare in terms of efficacy and safety.

Aims & Methods: To compare the 15 mm and 20 mm LAMS for the treatment of symptomatic WON in terms of technical success, clinical success and AEs. This was a retrospective comparative study at 21 centers (16 US, 4 Europe, 1 South America) between 04/14 and 10/18. Adult patients with WON who underwent EUS-guided drainage with 15 mm or 20 mm LAMS were identified. Patients with 20mm LAMS were matched to those with 15mm LAMS by age, gender, and route of LAMS insertion (trans-gastric vs trans-duodenal) with a ratio of 1:2. Univariable analysis was performed to compare technical success, clinical success and AE rates between the two groups.

Results: A total of 306 patients (31% F; mean age 55.1 yr) underwent EUS-guided WON (mean size 107mm) drainage (204 with 15 mm LAMS; 102 with 20 mm LAMS). The most common etiology of WON was gallstone pancreatitis (39.2%), most common indication for drainage was abdominal pain (54.9%), and most common location was pancreas body (53.9%). Baseline characteristics of patients and WON in both groups were equivalent. The technical success of LAMS placement of the 15mm and 20mm stents were similar (100%). At 6-month follow-up, the rate of clinical success with resolution of WON was similar in the two groups (92.1% vs 91.6%; p 0.85). The mean number of endoscopic necrosectomy sessions required for WON resolution was lower in the 20mm LAMS group compared with the 15mm LAMS group (0.8% vs 1.5%, p < 0.001). The need for additional intervention for WON resolution, including nasocystic drainage and percutaneous drainage, was not significantly different (Table 1).
A total of 31 (15.2%) AEs events developed in patients with 15mm LAMS and 22 (21.6%) AEs developed patients with 20mm LAMS (mild AE 2% vs 2%, moderate AE 13.2% vs 17.6%, p=0.30, severe AE 0% vs 2%; p 0.11, p=0.11, 15 mm and 20 mm, respectively) and were comparable without significant difference (3.4% vs. 4.9% with bleeding, 1.5% vs. 1% with infection, 4.4% vs. 4.9% with stent occlusion; 6.4% vs. 6.9% with stent migration; p 0.61).
Conclusion: The 20mm LAMS carries similar efficacy and safety profile to the 15mm stent, while requiring significantly less necrosectomy sessions.

	Total (N=306)	20 mm LAMS (N=102)	15 mm LAMS (N=204)	p-value
Technical Success, n (%)	306 (100)	102 (100)	204 (100)	
Clinical Success, n (%)	281 (91.8)	94 (92.1)	187 (91.6)	0.85
Total number of direct endoscopic necrostomy	1.8 (8.2)	1.3 (0.8)	2.1 (1.5)	<0.001
WON recurrence requiring intervention, n(%)	25 (8.2)	8 (7.9)	17 (8.4)	0.22
Surgical necrostomy	1 (0.3)	1(0.9)	0	0.24
Endoscopic stent placement	18 (5.8)	6 (5.8)	12 (5.8)	0
Percutaneous catheter placement	6 (1.9)	1 (0.9)	5 (2.4)	0.38
Length of hospital stay (days), mean (SD)	12.5 (25)	15.4 (27.6)	10.9 (23.2)	0.13
Follow-up duration	5.8	2.7 (SD, 2.6)	7.3 (SD 9.5)	<0.001

[Clinical Outcomes of WON drainage using 20mm LAMS vs 15mm LAMS]

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P0306 PANCREATIC DUCT SPHINCTEROTOMY: A VALUABLE TECHNIQUE APPLIED TO DIFFICULT COMMON BILE DUCT CANNULATION

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Introduction: Pancreatic duct sphincterotomy, a technique referred also as transpancreatic precut sphincterotomy, has been used to access difficult cannulation of CBD with an immediate success rate of 60-90%[1]. The aim of this study is to present a single center's experience of such technique along with its success rate, indications and identified complications.
Aims & Methods: Eighty three patients who underwent endoscopic retrograde cholangiopancreatography using pancreatic duct sphincterotomy technique to access the CBD was retrieved from the endoscopy unit's patient's record from January 2014 to December 2018. Only 72 were retrospectively analyzed due to the unavailability of charts. Pancreatic duct sphincterotomy was used on cannulations that were deemed difficult and when initial standard technique failed.

Results: The success rate of CBD cannulation was 96.4%, while failed access to CBD was only 3.6%. A periampullary diverticulum, an anatomic obstacle to sphincterotomy, was noted among 27% of successfully cannulated patients. Procedure-related complications was 18% in which bleeding (mild: 2.7%, moderate:4.1%) and pancreatitis (mild:8.3%, moderate:4.2%) were the only ones identified while 81.9% did not have any complications.
Conclusion: Pancreatic duct sphincterotomy is an effective technique for difficult bile duct cannulation with minimal mild to moderate bleeding and pancreatitis as the only procedure-related complication.
Disclosure: Nothing to disclose

IBD I
10:30-17:00 / Poster Exhibition - Hall 7

P0307 SACRAL NERVE STIMULATION INHIBITS THE MAPK/NF-κB SIGNALING PATHWAY AND PROMOTES TREG -TH1/TH17 CELL BALANCE AND SELF-RENEWAL OF ENTERIC NERVOUS SYSTEM IN TNBS-INDUCED INFLAMMATION IN RATS

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Introduction: The IBD includes Crohn's disease (CD) and ulcerative colitis (UC). The common characteristic of IBD is chronic relapsing of inflammation of the gastrointestinal tract. It is thought that IBD results from an aberrant and continuing immune response to the microbes in the gut, catalyzed by the genetic susceptibility of the individual.2,4,6-trinitrobenzene sulfonic acid (TNBS) is known to induce inflammation through triggering the MAPK/NF-κB pathway and activation of T helper cells. Recently, sacral nerve stimulation (SNS) was reported to exert an anti-inflammatory effect on TNBS-induced colitis.
The aim of this study was to investigate whether the SNS anti-inflammatory effect was mediated via the MAPK/NF-κB signaling pathway and/or balancing Th1/17-Treg cells. Meanwhile, we also explored if SNS could alter self-renewal of neurons in myenteric plexus.
Aims & Methods: Forty male Sprague-Dawley (SD) rats were implanted wire electrodes unilaterally at sacral nerve (S3). One week later, the rats were administrated with TNBS intra-rectally. Five days later, 20 of the rats were treated with SNS 1 hour daily for 10 days with the optimized parameters derived from previous studies and the other 20 rats were treated with sham-SNS (exactly the same setting but SNS at 0mA). Additional 20 rats were treated with intra-rectal injection of saline, serving as controls. Animal behaviors and various inflammatory factors were assessed by the disease activity index (DAI), macroscopic score, microscopic score, fluorescence-activated cell sorter and western blot. Longitudinal muscle myenteric plexus (LMMP) was studied by immunohistochemistry.
Results: 1) Compared with saline group, the TNBS treatment substantially induced inflammation, increased the percentage of Th1 cells (4.71% ± 1.18% vs. 8.87% ± 2.32%, P=0.03), Th17 cells (8.78% ± 1.95% vs. 12.35% ± 1.61%, P=0.02) and Treg cells (10.15% ± 3.57% vs. 15.73% ± 2.81%, P=0.04); it also increased p-ERK/ERK by 3.3 folds (P< 0.01) and p-JNK/JNK by 21.7 folds (P< 0.001) and increased nuclear translation of NF-κB p65 by 4.5 folds (P< 0.01); 2) compared to sham-SNS, SNS significantly decreased DAI (area under the curve: 64.3 ± 3.8 vs. 49.5 ± 3.2, P< 0.01), microscopic scores (4.6 ± 1.1 vs. 2.7 ± 0.8, P=0.04) and macroscopic scores (5.85 ± 0.9 vs. 2.55 ± 0.6, P=0.03) and normalized the colon length(16.05 ± 1.6 cm vs. 14.33 ± 1.3 cm, P< 0.05); 3) in colon tissues, compared with sham-SNS, SNS reduced the percentage of Th1 cells (8.87 ± 2.32% to 5.40 ± 1.39%, P=0.04) and Th17 cells (12.35 ± 1.61% to 9.75 ± 1.17%, P=0.04) but increased Treg cells (15.73 ± 2.81% to 20.15 ± 2.24%, P=0.03); 4) SNS reduced the percentage of the phosphorylation of MAPKs compared to Sham-SNS (p-ERK/ERK: 22.5%, P=0.03; p-JNK/JNK: 25.6%, P=0.04) and prevented the nuclear translocation of NF-κB p65 by 41.7% (P=0.02, vs. sham-SNS); 5) the percentage of choline acetyltransferase (ChAT) neurons were decreased by TNBS but reversed by SNS (19.06±2.07% to 25.68±3.56%, P=0.02). The percentage of

nitric oxide synthase (NOS) neurons was increased by TNBS but decreased by SNS (17.21 ± 1.27% to 13.34 ± 1.63%, *P*=0.03).
Conclusion: SNS is effective in inhibiting colon inflammation through the inhibition of the MAPK/NF-κB pathway, balancing of Th1/Th17-Treg cells, and also improving the LMMP neuronal self-renewal and regeneration.
Disclosure: Nothing to disclose

P0308 BERBERINE IMPROVED EXPERIMENTAL CHRONIC COLITIS VIA REGULATING INTERFERON-γ AND IL-17A PRODUCING LAMINA PROPRIA CD4⁺T CELLS THROUGH AMPK ACTIVATION

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Introduction: A herbal medicine, berberine (BBR), which is used as an anti-diarrhea medicine in Japan, is known as an AMPK activator to show various kinds of action such as diabetes control and anti-tumor response. Recently, BBR has been reported to elicit anti-inflammatory response of CD4⁺ T cells resulting in improvement of experimental chronic inflammatory diseases such as multiple sclerosis and may be of potential therapeutic utility in the treatment of immune-mediated diseases. Inflammatory bowel disease (IBD) is also immune-mediated diseases characterized by a chronic inflammation of the gastrointestinal tract. Inflammatory lamina propria (LP) CD4⁺ T cells are acknowledged as critical factors in the pathogenesis of IBD. Some reports showed the anti-inflammatory response of BBR against experimental colitis models, however, detailed analysis of BBR against LP CD4⁺ T cells including anti-inflammatory mechanisms have not been performed.
Aims & Methods: To investigate the effect of BBR against LP CD4⁺ T cells of IBD, we conducted a T cell transfer model of chronic colitis in which SCID mice were injected with CD4⁺CD45RB^high T cells resulting in T cell mediated colitis. The excised colitic LP CD4⁺T cells were used for *in vitro* experiments (1) and the chronic colitis model mice were used for *in vivo* experiments (2).
(1) In *in vitro* experiments, we stimulated colitic LP CD4⁺ T cells by PMA/Ionomycin to induce interferon (IFN)-γ and interleukin (IL)-17A production. With this model, we investigated the effect of BBR connecting AMPK pathway and immune system activation. To investigate the effect of AMPK activation on immune system, AMPK agonist AICAR and antagonist Compound C were added to the culture.
(2) In *in vivo* experiments, the colitic mice were fed with BBR and subjected to the mechanism investigation.
Results: (1) When colitic LP CD4⁺T cells were cultured with BBR, the frequency of IFN-γ and IL-17A producing cells reduced and the activation of AMPK was induced by Western blotting (WB). When colitic LP CD4⁺T cells were cultured with AMPK agonist, (AICAR) or antagonist, Compound C (C.C), AICAR significantly suppressed and C.C significantly increased inductions of IFN-γ and IL-17A producing cells frequency. WB analysis showed AICAR significantly activated and C.C significantly inactivated AMPK activities. Metabolic assay showed BBR suppressed oxidative phosphorylation (OXPHOS) and ATP production in colitic LP CD4⁺T cells.
(2) The BBR fed mice showed reduced severity of colitis with significant reduction of IFN-γ and IL-17A producing cells frequency. This effect was induced by AMPK activations of colitic LP CD4⁺T cells.
Conclusion: BBR elicited anti-inflammatory response in colitic LP CD4⁺T cells via AMPK activation possibly induced by OXPHOS inhibition. AMPK activation of LP CD4⁺T cells could be a new therapeutic target of IBD and BBR might be a good candidate.
Disclosure: Nothing to disclose

P0309 FREE FATTY ACID RECEPTOR TYPE 4 LIGANDS ALLEVIATE INTESTINAL INFLAMMATION IN MICE

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Introduction: Diet is considered an important pathological trigger in inflammatory bowel diseases (IBD), as feeding habits can affect intestinal permeability and efficient clearance of bacterial antigens, consequently influencing the immune system. Moreover, high incidence of IBD was reported in western, developed countries which is likely related to the increasing environmental pollution, as well as "westernization" of the populations' diet and lifestyle (e.g. diet rich in animal fat and protein and low in fiber), all of which significantly affect individuals' immune response. Free Fatty Acid receptors (FFARs), expressed on the intestinal epithelial cells, belong to the family of luminal-facing receptors that are responsive to nutrients (nutrient-sensing receptors). They are possibly involved in the maintenance of gut function and implicated in IBD.
Aims & Methods: The objective of this study was to test the anti-inflammatory activity of synthetic agonists of FFARs in mouse models of colitis. Therapeutic activity of GW9508 (FFAR1 agonist), 4-CMTB (FFAR2 agonist), AR420626 (FFAR3 agonist) and GSK137647 (FFAR4 agonist) was investigated in two models of semi-chronic colitis: induced by trinitrobenzenesulfonic acid (TNBS) mimicking Crohns disease as well as induced by DSS that recapitulates ulcerative colitis in humans. Body weight, macroscopic score, ulcer score, colon length, weight and thickness, as well as myeloperoxidase (MPO) activity were recorded. Expression of FFAR1, 2, 3 and 4 in the colon was compared between control and colitic animals.
Results: We found that expression of FFAR1 is significantly elevated while FFAR2 reduced in the inflamed colon. Systemic administration of GSK137647 (FFAR4 agonist; 1 mg/kg, twice daily) attenuated both TNBS-induced and DSS-induced colitis in mice, as indicated by significantly reduced body weight loss as well as macroscopic parameters and MPO activity. The action of GSK137647 was blocked by pretreatment with selective FFAR4 antagonist AH 7614 (5 mg/kg, twice daily).
Conclusion: This is the first investigation evaluating the anti-inflammatory activity of FFAR agonists and showing that pharmacological intervention targeting FFAR4, which is a sensor of medium and long chain fatty acids, attenuates intestinal inflammation. Further experiments evaluating the signaling pathways triggered by FFAR4 stimulation are pending.
Disclosure: Nothing to disclose

P0310 STUDY OF THE PROTEOMIC PROFILE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE, ITS CORRELATION WITH DIAGNOSIS AND DISEASE ACTIVITY

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Introduction: : Inflammatory bowel disease (IBD) consists of 2 main disorders: ulcerative colitis (UC) and Crohn's disease (CD). IBD is characterized by chronic, uncontrolled inflammation of the intestinal mucosa. Although major advances have improved the understanding of the multifactorial influence of genetic, environmental, microbial, and inflammatory determinants of IBD, the etiology of the disease still confusing. The diagnosis is based on a combination of disease history, colonscopy, inflammatory biomarkers, radiological and histological evaluation.Most biomarkers used are not disease specificand not reliable, but reflect generalized inflammation.
Aims & Methods: The aim of the work is to identify serum proteomic profiles of IBD cases and correlating this profile with the other diagnostic markers and activity of the disease.We performed a study with 101serum samples collected from patients classified in 3 groups (31 Crohn's, 37 ulcerative colitis, 33 healthy controls) according to accredited criteria. They were subjected to: complete history taking, thorough clinical examination, Lab investigations (routine, fecalcalprotectin, ANCA, ASCA), endoscopy (upper, lower), histopathology, imaging were done. plasma proteomic pattern of IBD patients and control subjects was determined using matrix-assisted

laser desorption/ionization (MALDI) TOF MS analysis, all serum samples were subjected to solid-phase extraction (SPE). We analyzed the spectra obtained from all the samples using ClinProTool.

Results: There was a statistical significant difference of the serum proteome profiles of UC group in comparison to health volunteers, Also there was a statistical significant difference of the serum proteome profiles of crohn's group in comparison to health volunteers, we used Support Neural Network (SNN), Genetic algorithms (GA) to analyse proteomic profile of UC and CD cases versus control cases respectively. (64, 76) signals were identified by the ClinProt software with a statistically different area for UC, Crohn's disease respectively. There was a statistical significant difference between active versus inactive UC group and Crohn's disease group.

Conclusion: Advances in mass spectrometry and bioinformatics have allowed capturing and selecting the signal of thousands of small, low molecular weight peptides.The pattern of these peptides holds the promise of distinguishing disease states and providing clinically important information such as prognosis, response to therapy, or even targets of therapy.

Disclosure: Nothing to disclose

P0311 ST2+/IL-33 RESPONSIVE CELLS PROMOTE TUMORIGENESIS IN COLITIS-ASSOCIATED COLORECTAL CANCER

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Introduction: It is now well-established that IL-33 and its receptor, ST2, are important factors in the pathogenesis of IBD. Emerging evidence also suggests its critical role in epithelial proliferation and the potential contribution to inflammation-driven tumorigenesis that can lead to colorectal cancer (CRC).

Aims & Methods: The aim of our study was to characterize the precise contribution of IL-33/ST2 axis in the azoxymethane (AOM)/dextran sodium sulfate (DSS) model of colitis-associated CRC. C57/BL6 wild-type (WT), IL-33 KO, ST2 KO and CD73 KO mice were given a single dose of AOM (7.4 mg/kg) followed by two cycles of 3% DSS for 7d in drinking water. Disease Activity Index (DAI), as well as endoscopic and histological evaluation of colons were performed. IHC, immunofluorescence (IF) and qPCR were done on full-thickness colons for IL-33 and ST2 localization and identification, as well as mRNA expression, respectively. FACS analysis was performed on cell suspensions from resected, isolated polyps and qPCR for Vimentin, Desmin, αSMA, CD34, CD31, CD73 was completed on sorted cells in order to functionally characterize ST2+/IL-33 responsive cells.

Results: IL-33, ST2L, and sST2 mRNA transcripts were dramatically elevated in AOM/DSS-treated WT mice vs. controls. IHC of treated WT mice revealed localization of IL-33 to the colonic epithelium and to cells within the LP morphologically consistent with tissue macrophages. ST2 staining was localized to the intestinal epithelium in tissues immediately adjacent to tumors, while within the tumors themselves, ST2+ cells displayed a spindle/fibroblast-like morphology with a unique distribution throughout the polyps. Little to no staining for both IL-33 and ST2 was present in controls. Using IF, ST2 co-localized with αSMA in polyps; however, ST2 staining was not exclusive for αSMA+ cells. FACS analysis showed a distinct population of CD45+ hematopoietic cells consisting of CD3/CD8+ cytotoxic T cells (CTLs), CD19+ B-lymphocytes, CD11b+CD11c- and CD11b+CD11c+ myeloid cells. ST2 was mainly expressed by CTLs, and CD11b+CD11c- and CD11b+CD11c+ myeloid cells. Non-hematopoietic cells (CD45-) also expressed ST2. At qPCR, CD45-ST2+ and CD45+ST2+ expressed significantly elevated levels of CD73 *vs.* ST2- cells. AOM/DSS treatment in IL-33, ST2 KO and CD73KO mice resulted in a significant decreased polyp number and size *vs.* WT, with colonoscopy revealing the development of protruding lesions with abnormal

vascular patterns, suggesting pre-tumorous lesions in WT mice, while all KO mice showed their absence with a more impressive mucosal inflammation, likely due to reduced epithelial proliferation and repair caused by the deficiency of IL-33 signaling.

Conclusion: Our results suggest that the IL-33/ST2 axis promotes tumorigenesis in colitis-associated CRC through the activation of CD73.

Disclosure: Nothing to disclose

P0312 REGULATION OF INTESTINAL EPITHELIAL HOMEOSTASIS BY THE IBD RISK GENE CCNY

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Introduction: Inflammatory bowel diseases (IBD) are recurring inflammatory disorders characterized by chronic dysregulation of the intestinal epithelium. The etiology of IBD is still unknown. CCNY, encoding Cyclin Y, has previously been identified as a putative risk gene in Crohn's disease and Ulcerative Colitis[1]; however, the function of CCNY in the gut is unknown. We have shown that Cyclin Y is a critical activator of the Wnt/beta-catenin signalling pathway, which controls stemness and proliferation in intestinal epithelia[2]. We thus investigated whether CCNY regulates epithelial homeostasis and wound repair in the gut.

Aims & Methods: To address the role of CCNY in intestinal epithelia, we used a RNA interference based loss-of-function approach in model cell lines HEK 293T, SW48 and HCT 116 cells. Wnt signalling activity was assayed by a Topflash luciferase reporter assay following siRNA-mediated depletion of CCNY in model cell lines. In addition, we generated transgenic mice with deletion of Ccny specifically in intestinal epithelial cells. These animals were subjected to the dextran sulphate sodium (DSS) model of intestinal injury (acute, 5 days of DSS) and repair (recovery, 5 days of DSS followed by 5 days of plain drinking water), which mimics human Inflammatory Bowel Diseases[3]. In addition to the *in vitro* experiments, we determined daily colitis progression and epithelial homeostasis in mice using an established disease activity index, histopathological analyses (haematoxylin-eosin staining, crypt length measure) and proliferation markers. Animal were weighed daily.

Results: In contrast to non-intestinal model epithelial cells, loss-of-function of CCNY did not reduce Wnt signalling activity in intestinal HCT116 and SW48 cell lines. Accordingly, CCNY depletion did not impair epithelial proliferation or stemness *in vitro*. Ccny mutant mice did not present any changes compared to controls regarding proliferation, crypt length or histopathology. Moreover, markers of Wnt activity and cell proliferation were unchanged in Ccny mutant mice compared to their littermate controls, and we observed no changes in disease activity indexor weight loss of the animals during both acute intestinal inflammation or after recovery.

Conclusion: Our results thus far suggest that IBD risk gene CCNY is dispensable for intestinal epithelial homeostasis. The apparent uncoupling of Cyclin Y from Wnt signalling in the gut is the subject of ongoing investigation in our lab. In addition, we continue to investigate the possible contribution of CCNY to epithelial regeneration following colitis.

References: 1 Franke A. et al., Sequence variants in IL10, ARPC2 and multiple other loci contribute to ulcerative colitis susceptibility, Nat Genet. 2008 Nov;40 (11):1319-23. doi: 10.1038/ng.221 2 Koch S. et al., Post-transcriptional Wnt Signaling Governs Epididymal Sperm Maturation, Cell. 2015 Nov 19;163(5):1225-1236. doi: 10.1016/j.cell.2015.10.029 3 Wirtz S. et al., Chemically induced mouse models of acute and chronic intestinal inflammation, Nat Protoc. 2017 Jul;12(7):1295-1309. doi: 10.1038/nprot.2017.044

Disclosure: Nothing to disclose

P0313 NOTCH SIGNALING ROLE IN THE PENETRATING BEHAVIOR IN CROHN'S DISEASE

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Introduction: Fibrosis and fistula development constitute the main complications associated to Crohn's disease. Notch signalling has been implicated in lung, kidney, liver and cardiac fibrosis and in various disease conditions such as scleroderma.

Aims & Methods: We aim to analyse here the pattern of NOTCH ligands, receptors and effectors expression in surgical resections from stenotic and fistulizing CD patients and to determine the potential role of these ligands in favouring fistula and fibrosis. CD patients (n= 52) were categorized according to Montreal classification (age at diagnosis, location and behaviour). mRNA was isolated from resections of patients presenting a stricturing (B2, n=26) or a penetrating (B3, n=15) behaviour or from unaffected mucosa of patients with colorectal cancer (control, n=15). The expression of Notch ligands, receptors, and effectors (HES1 and MATH1) was determined by RT-PCR or WB. The dates are showed as mRNA expression of NOTCH ligands and receptors vs. the housekeeping gene β-ACTIN in intestinal mucosa and values correspond to mean ΔCT (CT target - CT housekeeping) ± SEM. Significant differences vs the respective Non-IBD patients are shown by *$P< 0.05$ or **$P< 0.05$ and vs B2 CD patients by #$P< 0.05$. Correlations between data were analysed using Pearson's correlation coefficient (*$p < 0.05$).

Results: The expression of NOTCH3 and NOTCH4 receptors was significantly higher in intestinal samples from B3 CD patients (14. 8±0.3**#, and 9.6±0.9**#, respectively) than in controls (17.4±0.2, and 13.4±0.3, respectively) or B2 CD patients (16.0±0.3*, and 11.5±0,3*, respectively), but only NOTCH3 expression was up-regulated in crypts in the penetrating group (Control:14.5±0.5; B2: 15.3±0.5; B3: 12.4±0.3*#). The fistulizing group presented a generalized overexpression of NOTCH ligands (JAG2, DLL3 and DLL4) compared with controls and among them, only DLL3 expression was up-regulated in the penetrating group (Control: 0.39±0.05 A.U.; B2: 0.31±0.04 A.U.; and B3:0.81±0.18*# A.U.). Similar levels of HES1 and MATH1 mRNA expression were detected between different groups while protein levels of HES1 were higher in the fistulising group than in control or stenotic groups (3.4±0.1 A.U*#, 2.8±0.2 A.U and 2.0±0.1 A.U, respectively). The expression of DLL3 significantly correlated with FSP1 (r=0.77, P=0.04*), DESMIN (r=0.80, P=0.03*), and SNAIL1 (r=0.59, P< 0.04*), only in intestinal tissue from the fistulizing CD group.

Conclusion: Activation of the Notch signalling pathway is detected in Crohn's disease patients with a penetrating (B3) behaviour compared with those with a structuring (B2) phenotype and it may be involved in fistula development over fibrosis.

Disclosure: Nothig to disclosure

P0314 MICROBIAL METAGENOMIC SIGNATURES REVEAL DYSBIOTIC DIFFERENCES AND SIMILARITIES BETWEEN INFLAMMATORY BOWEL DISEASES

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Introduction: The etiology of inflammatory bowel diseases (IBD) including Crohn's disease (CD) and ulcerative colitis (UC) involves an aberrant immune response towards the gut microbiome in genetically susceptible individuals. Approximately 25% of patients with UC may undergo total large bowel resection (proctocolectomy) followed by creation of a reservoir ("pouch") from the normal small bowel. Most will develop de-novo inflammation of the previously normal small bowel comprising the pouch (pouchitis). Pouchitis may be a model for the development of intestinal inflammation with features resembling CD.

Aims & Methods: To compare the microbiome and its functions across different phenotypes of IBD, faecal samples were obtained from patients with a pouch, diagnosed according to accepted criteria and inflammatory biomarkers were detected. Shotgun metagenomics was applied and microbiome data was analyzed using specifically designed bioinformatics pipelines. Outcomes were compared to metagenomic data from two independent cohorts, PRISM and LifeLines DEEP-NLIBD both comprised of CD and UC patients and healthy-controls.

Results: Samples from 78 patients with a pouch (40 normal pouch, 38 pouchitis) were analysed and compared to data of 88 patients with CD 76 with UC and 56 healthy controls. PCoA analysis based on bacterial species and enzymes profiles showed substantial overlap between patients with a normal pouch, pouchitis and CD. Taxonomic and functional variation correlated (Spearman r=0.5, P< 0.05) with inflammation (faecal calprotectin) and samples were stratified according to phenotype, from healthy controls to UC, CD, patients with a normal pouch and pouchitis (highest inflammation). Area under the curve of 0.9 (mean) was achieved for three IBD phenotypes classifier and was the highest for patients with a pouch. Most of the misclassified pouch patients' samples were labelled as CD. Escherichia coli and several Streptococcus and Veillonella species were significantly more abundant in IBD phenotypes compared to healthy controls, while patients with a pouch, especially with pouchitis presented the highest levels (median relative abundance of E. coli: 13% compared to 4% in CD, 2.7% in UC and 0.3% in healthy, P=4x10-18). In contrast, beneficial bacteria such as Eubacterium rectale, Roseburia inulinivorans, Faecalibacterium prausnitzii, Ruminococcus bromii and Bacteroides species were depleted in patients with a pouch, especially in pouchitis (E. rectale: 1.2%, 6.9%, 5.5%, and 10.8%; R. bromii: 0.13%, 1.2%, 2.3% and 4.2%; F. prausnitzii: 2.7%, 3.3%,, 7.3% and 6.5% in pouch, CD, UC, and healthy controls, respectively, P< 0.05). Microbial enzymes related to protection against oxidative stress: glutathione-disulfide reductase, peroxiredoxin and nitric-oxide dioxygenase were enriched in patients with a pouch. Moreover, numerous metabolic pathways were associated with IBD phenotypes. Specifically: heme biosynthesis with a pouch, CD and UC; NAD salvage with a pouch, aromatic amino-acid biosynthesis and starch degradation with healthy controls (lowest in patients with a pouch).

Conclusion: Major metabolic and microbial signatures common to IBD patients as well as several that are phenotype-specific were identified. Robust bacterial taxonomic and functional overlap supports resemblance between a pouch and CD. Oxidative stress and virulence pathways are associated with IBD, specifically with pouch, while beneficial metabolic pathways are decreased. Patients with pouchitis harbour a distinct signature characterized by intensified dysbiosis.

Disclosure: Nothing to disclose

P0315 THERAPEUTIC EFFECT OF AUTOPHAGY MODULATION IN INTESTINAL FIBROSIS

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Introduction: Intestinal fibrosis is a common complication of Crohn's Disease (CD) patients characterized by an obstruction of the intestinal lumen which requires surgery. Several single nucleotide polymorphisms in autophagy-related genes associated to CD have been identified. Although autophagy is impaired in CD patients, the relevance of autophagy in intestinal fibrosis is still not well elucidated.

Aims & Methods: We aim to analyze the effect of pharmacological modulation of autophagy in the development of murine intestinal fibrosis. Murine intestinal fibrosis was induced using the heterotopic transplant model. Segments of 1cm colon from mice were subcutaneously transplanted into the neck of a recipient mice and collected after 7 days. Recipient mice were treated with a daily injection of 3-MA (10mg/kg) or rapamycin (1.25 mg/kg). Expression of intestinal inflammation, fibrosis and EMT markers were analyzed by qPCR and protein levels of autophagy markers by Western Blot. Collagen layer was evaluated by Sirius Red Staining. Intestinal resections from CD patients were obtained and expression

of p62, Col1a1, α-SMA, Snail1 and Snail2 was analyzed by qPCR. Results are expressed as fold induction (mean±SEM, n≥5). Statistical analysis was performed with one-way ANOVA followed by Newman-Keuls test. Correlations were analyzed with the Spearman coefficient.

Results: Intestinal grafts 7 days after surgery exhibited a reduced autophagic flux since higher levels of p62 and lower levels of phospho-MTOR and LC3 were detected compared with intestinal grafts at day 0. The inhibition of autophagy by 3-MA and the activation of autophagy by rapamycin were also confirmed by WesternBlot. As shown in Table 1, grafts obtained 7 days after surgery from 3-MA-treated mice exhibited a significant increase in the expression of proinflammatory, profibrotic and EMT genes and a significant thicker collagen layer after Sirius Red Staining. Of interest, grafts 7 days after transplantation obtained from rapamycin-treated mice showed a significant reduction in the expression of proinflammatory, profibrotic and EMT genes and a significant reduction in the thickness of the collagen layer after Sirius Red Staining. In intestinal resections from CD patients, the expression of p62 positively correlates with the expression of Col1a1 ($r_{Spearman}$=0.6098, P=0.004), α-sma ($r_{Spearman}$=0.5168, P=0.041), Snail1 ($r_{Spearman}$=0.4112, P=0.0003) and Snail2 ($r_{Spearman}$=0.4410, P=0.0009).

	TNF-α	IL-1β	COX-2	Col1a1	Col3a1	Col4a1	Snail1	Snail2	Itgb6
Graft day 0	1.1 ±0.2	1.6 ±0.8	1.1 ±0.2	1.2 ±0.4	2.6 ±1.9	1.1 ±0.3	1.0 ±0.1	1.0 ±0.1	1.1 ±0.2
Graft day 7	50.5 ±7.5	243.7 ±35.9	103.1 ±22.3	41.3 ±9.3	166.9 ±61.4	2.7 ±0.8	11.6 ±1.5	3.7 ±0.7	2.7 ±0.4
Graft day 7 + 3-MA	102.9 ±22.9	425.4 ±84.9	174.5 ±46.2	74.2 ±9.2	2005.0 ±1229.0	11.7 ±1.7	21.1 ±4.6	7.3 ±1.8	7.7 ±1.9
Graft day 7 + Rap	24.1 ±6.2	132.8 ±33.5	36.2 ±9.3	9.5 ±1.9	40.6 ±17.9	4.1 ±1.1	7.5 ±1.3	1.8 ±0.5	1.9 ±0.5

[Table 1: Expression of proinflammatory, profibrotic and EMT genes in intestinal grafts analyzed by qPCR.]

Conclusion: Pharmacological modulation of autophagy modulates intestinal inflammation and fibrosis since the inhibition of autophagy exacerbates intestinal inflammation and fibrosis whereas an autophagy activation reduces the intestinal fibrosis. In addition, in intestinal resections from CD patients the expression of autophagy markers correlates with the expression of pro-fibrotic and pro-EMT genes, which led us to suggest that pharmacological modulation of autophagy might be a new therapeutic option for intestinal fibrosis.

Disclosure: Nothing to disclose

P0316 TOBACCO ALKALOID ASSESSMENT IN ACUTE AND RECOVERY DSS-INDUCED COLITIS FULL HUMAN IMMUNE SYSTEM HU-MOUSE MODEL

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Introduction: Cigarette Smoke (CS) contains many compounds that exert biological effects, increasing the risk of cardiovascular and pulmonary diseases as well as carcinogenesis in exposed individuals. Moreover, smoking in Crohn's Disease patients is associated with greater disease activity, increased requirement for immunosuppressant, and early post-operative recurrence.

However, epidemiological and clinical evidence from robust case-controlled studies points to an inverse association between smoking and the onset and development of ulcerative colitis (UC). The biological mechanisms responsible of the underlined smoking effects on UC progression remain largely elusive. Several studies have demonstrated the anti-inflammatory action of cholinergic agonists, such as the main tobacco alkaloid, nicotine.

However, contrasting results have been observed in clinical and non-clinical studies addressing the role of nicotine in UC, opening new questions on the molecular mechanisms at the base of the intrinsic nicotinic anti-inflammatory activity and the possible involvement of other tobacco alkaloids in the observed reduced severity of UC.

In the present study, we aimed to investigate the potential anti-inflammatory activity of nicotine and another tobacco alkaloid (PMI001) in a full human immune system Hu-Mouse colitis model.

Aims & Methods: NOD/Shi-scid/IL-2Rγ null immunodeficient mice were engrafted with functional cord blood-derived human CD34+ hematopoietic stem cells. During the 14 weeks following cell injection, the engrafted human stem cells developed fully functional human dendritic cells, granulocytes, NK cells, macrophages, and monocytes as well as B and T lymphocytes. After complete maturation, mice were treated with nicotine or PMI001 for two weeks. Colitis was induced by adding 3% dextran sulfate sodium (DSS) over seven days, and mouse necropsy was performed after DSS treatment (acute model) or five days after DSS removal (recovery model). Disease-specific endpoint analysis (global clinical score, colon length, body weight loss, diarrhea, rectal bleeding), immune-phenotyping, colon histopathological assessment, and colon transcriptomics were performed.

Results: Data analysis revealed that nicotine significantly reduces all the associated acute colitis symptoms (diarrhea, rectal bleeding, and body weight loss) and improves colitis-specific endpoints (colon length, global clinical score). Moreover, histopathological analysis confirmed a significant reduction of colon inflammation, tissue damage, and mononuclear cell infiltration upon nicotine treatment. Finally, nicotine significantly improved the survival of mice; no mortality was observed compared to the vehicle group. The tobacco alkaloid PMI001 showed a similar, although generally weaker, effectiveness trend. Further molecular analyses are ongoing to investigate the molecular mechanisms implicated in the disease progression.

Conclusion: The risks of smoking far outweigh any possible benefit, thus smoking cessation must be considered as a first step toward well-being and healthy status. However, tobacco constituents, such as nicotine or other alkaloids, may exert positive effects in the context of UC, thus representing molecules to further investigate. Using a full human immune system mouse models, the current study enabled the investigation of possible molecular mechanisms responsible for the attenuation of UC by tobacco alkaloids, providing therapeutic opportunities for the treatment of the various pathological conditions with an inflammatory component.

Disclosure: The research described in this abstract was sponsored by Philip Morris International.

P0317 EXPERIMENTAL TNBS COLITIS MODEL IN CYNOMOLGUS MACAQUES ASSESSED LONGITUDINALLY BY COLONOSCOPY, HISTOPATHOLOGY AND PET/CT: A PILOT STUDY

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Introduction: We have developed and longitudinally characterized a non-human primate (NHP) macaque model of chemical colitis for the purpose of testing efficacy of mucosal healing therapies in a highly translational model.

Aims & Methods: Disease induction and progression was assessed by clinically relevant modalities, including white light colonoscopy, histopathology, and positron emission tomography/computed tomography (PET/CT). Utilizing four cynomolgus macaques, colitis was initiated and maintained with endoscopic application of the hapten 2,4,6-trinitrobenzenesulfonic acid (TNBS) on Day 0 (100mg), D7 (50mg), and D14 (50mg), and mucosal health was assessed and scored by colonoscopy at baseline (14 days before D0), D7, D14, D17, D21, D28, and D48. Histopathology from colonoscopy guided mucosal pinch biopsies was performed at baseline, D17, D28, and D42 and quantified using a modified Geboes score. To assess colonic mucosal inflammation non-invasively, we quantified maximum standardized uptake value (SUV-max) signals of the radio-ligand, 18F-fluorodeoxyglucose ([18F]FDG), a glucose metabolism marker, in two cynomolgus macaques at baseline, D17, D21, D28, and D42. To account for background signal, SUV-max values were collected from PET images that had been gated relative to the baseline PET image for each subject.

Results: Colonoscopy revealed ulcers, mucosal friability, luminal narrowing, and mucosal edema, which were significantly increased in severity relative to baseline (mean score=0.25) on D14 (mean score=6.6, *p=0.029*), D17 (mean score=8.3, *p< 0.005*) and D21 (mean score=7.3, *p< 0.054*); however, mucosal changes assessed by colonoscopy were not significantly different on D28 (mean score=5.08, *p=0.174*) or D42 (mean score 2.25, *p=0.478*). Histological evaluation demonstrated epithelial changes com-

pared to baseline (mean score=0) including ulceration, loss of goblet cells, and epithelial hyperplasia, which were observed on D17 (mean score=5, *p=0.005*) and D28 (mean score=2, *p=0.120*). Inflammatory changes included increased numbers of neutrophils and eosinophils and increased occurrence of intra-epithelial leukocytes, which were observed on D17 (mean score=2.5, *p=0.060*) and D28 (mean score=2.5, *p=0.041*). By D42, epithelial and inflammatory changes had resolved. TNBS application increased [¹⁸F] FDG, SUV-max signal on D17 by 6-fold and on D21 by 3-fold compared to baseline; however, SUV-max was not increased compared to baseline at D28 and D42.

Conclusion: The pathological features and feasibility for longitudinal and clinically relevant assessment demonstrate the translational strength of this NHP, TNBS colitis model. Further, the duration of significant, quantifiable pathology should provide a window for the immediate evaluation of therapeutic interventions, targeting mucosal healing and inflammation.

Disclosure: The design, study conduct, and financial support for the study were provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the publication. Dr. Anthony Slavin was a scientist at AbbVie at the time of the study. All other authors are AbbVie employees.

P0318 SPECIFIC FAECAL MICROBIOME FEATURES IN HEALTHY INDIVIDUALS WITH HIGHER RISK OF CROHN'S DISEASE ONSET

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Introduction: Crohn's disease (CD) is a multi-factorial disorder and familial aggregation of CD has long been recognized. In first-degree relatives of patients suffering from IBD, the relative risk for disease onset can be up to 5-fold higher than that in unaffected families[1]. The interplay between impaired host genetics, defective immune system components and altered gut microbiome composition is often pointed out as the main drivers of CD pathogenesis.

Aims & Methods: We included 112 individuals comprising adult CD patients in clinical remission (n=33; time to diagnosis < 2 years), their healthy first degree relatives (HFDR; n=46) and matched healthy controls (HC; n=33). Our objectives were to identify microbial features within the microbiota composition of HFDR that were discriminant from CD and HC and to correlate them to host inflammatory markers such as faecal calprotectin. The faecal microbiota composition, diversity and estimated loads were assessed by 16S rRNA gene sequencing and quantitative PCR. Other CD-associated biomarkers (serum IgG and IgA ASCA and faecal calprotectin) and Adherent-Invasive *Escherichia coli* (AIEC) detection in stool samples and their respective phylotyping/invasiveness classification) were evaluated.

Results: Estimated bacterial loads were similar between the different groups (CD=9.8, HC=10.2, HFDR=10; log10 CFU/g). Microbial diversity was not lower in CD or HFDR (CD=0.91, HC=0.90 and HFDR=0.93; Simpson index). Microbiota richness (number of observed OTUs) was higher in HFDR

(227.6) individuals as compared to CD (181.7) and HC (205.4) (p=0.01) . Eight bacterial genera displayed significantly different abundances across the groups. CD microbiome was characterized by higher abundances of *Bacteroides* and *Intestinibacter* and lower abundances of *Faecalibacterium and Odoribacter* than HC and HFDR microbiomes. The microbiota composition of HFDR harboured specific microbial features such as higher representation of *Coprococcus*, *Gemmiger* and *Clostridium* IV and an almost undetectable presence of *Haemophilus*. At the species level *Coprococcus catus*, *Coprococcus comes*, *Gemmiger formicilis*, *Eubacterium siraeum* and *Clostridium leptum* were significantly more abundant in the microbiota of HFDR as compared to CD and HC. *E. coli* strains isolated from CD patients and HFDR presented higher invasion ability to intestinal epithelial cells compared to *E. coli* strains isolated from HC. AIEC strains are mostly distributed among B2 phylogroup. No association was found between these microbiota features and ASCA measurements as well as fecal calprotectin levels.

Conclusion: Our study depicts the presence of specific microbial features within the microbiota of healthy individuals with higher risk of CD onset. Healthy relatives of CD patients exhibited higher microbiota richness and higher abundances of numerous bacterial taxa than CD patients but also healthy controls. These specific microbial features (mostly bacteria known to produce short-chain fatty acids, such as butyrate or formate) may counterbalance potential host impairments such as genetic predisposition. Furthermore, healthy relatives harbour more invasive *E. coli* strains than healthy controls. Since healthy relatives microbiome differ from that of healthy individuals, therapeutic approaches focusing on bacteria specifically associated with healthy relatives microbiome may be more appropriate to correct the microbiota dysbiosis in CD.

References: 1: Ramos G.P. and Papadakis K.A., Mayo Clinic Proceedings, 2019.

Disclosure: Nothing to disclose

P0319 PATIENTS WITH CROHN'S DISEASE EXHIBIT A DYSREGULATED LYMPHOCYTE RESPONSE TO CORTICOSTEROIDS: IMPLICATIONS IN STRESS-INDUCED DISEASE AGGRAVATION AND FAILURE OF THERAPY

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Introduction: Crohn's disease (CD) is a chronic inflammatory bowel disease engendering both psychological and physiological stresses. Our previous studies demonstrated that prolonged stress and chronic inflammation cause dysregulation of glucocorticoid (GC) signaling in different immune subsets, with consequent reduced sensitivity to GCs, so-called steroid resistance, and a shift towards a more aggressive immune response. The present study aims to identify and characterize patterns of steroid resistance in adult CD patients.

Aims & Methods: We analyzed leukocyte subset distribution, functionality and their responsiveness to GCs using peripheral blood mononuclear cells (PBMCs) isolated from CD patients (mean age 35 years, mild-moderate disease activity with a Harvey-Bradshaw Index in the range 6-15) and from age- and sex-matched healthy controls. PBMCs underwent stimulation with anti-CD3 without or with methylprednisolone (MP, 1-10,000 ng/ml) followed by measuring secreted levels of IL-2 (24 hours), IL-10 (48 hours), IFN-γ (48 hours), and IL-17 (72 hours) with ELISA. In addition, PBMCs were activated with PMA/ionomycin for 6 hours and analyzed for cytokine production with flow cytometry. Finally, non-activated PBMCs were analyzed for lymphocyte subsets such as naïve, exhausted, regulatory (Tregs) and effector memory T cells.

Results: MP in increasing doses caused a progressive reduction of PBMC cytokine production; the effect was less in CD (n=8) than in controls (n=8). For IL2 and IL10 the difference became statistically significant at MP 1000 ng/ml (Table). MP in increasing doses caused a progressive reduction of TNFα producing cells in the CD8 population. The effect was less pronounced in CD (n=4) than controls (n=4). The difference became statis-

tically significant at MP 10000 and 100000 ng/ml (Table). Non-activated PBMCs analyzed for lymphocyte subsets such as naïve, exhausted, regulatory (Tregs) and effector memory T cells did not demonstrated differences between CD (n=4) and controls (n=4).

Fold of steriod sensitivity decrease in CD patients							
	MP, ng/ml	1	10	100	1000	10000	100000
IL2 production	mean (p)	1.040 (0.63)	1.306 (0.15)	1.587 (0.07)	2.391 (0.049)	2.2105 (0.049)	
Il1 production	mean (p)	1.191 (0.28)	1.328 (0.19)	1.379 (0.36)	1.462 (0.05)	1.341 (0.11)	
Fold of steroid resistance in CD patients							
relative TNFα production by CD8	average(p)	1.129 (0.57)	1.905 (0.14)	1.241 (0.41)	1.049 (0.64)	8.445 (0.03)	3.031 (0.01)

[Cytokine production after MP stimulation]

Conclusion: In CD patients certain immune cell subsets demonstrated a loss of steroid sensitivity. This may be indicative of a dysregulated hypothalamus-pituitary-adrenal (HPA) axis, which phenomenon may contribute to the disease process itself and moreover augur an inadequate response to corticosteroid therapy.
Disclosure: Nothing to disclose

P0320 ACTIVATION OF ARYL HYDROCARBON RECEPTOR ATTENUATES INTESTINAL INFLAMMATION BY ENHANCING IRF4 MEDIATED MACROPHAGE M2 POLARIZATION

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Introduction: Inflammatory bowel diseases (IBDs) are characterized by a functional dysregulation of immune cells, among which macrophages play an indisputable role. Macrophages could undergo opposite polarization under different conditions thus exerting pro-/anti-inflammatory effects. Aryl hydrocarbon receptor (AhR), a ligand-dependent transcription factor, is implicated in intestinal inflammation by regulating both innate and adaptive immune response, but the relationship between AhR and macrophages in inflammatory bowel diseases has not been investigated.
Aims & Methods: We investigated the distribution of macrophages in colonic tissue of patients with active IBDs and assessed the effects of AhR activation in trinitrobenzenesulfonic acid (TNBS)-induced colitis in mice and on the polarization of bone marrow derived macrophages (BMDMs). Macrophage IRF4 expression was measured and IRF4 siRNA was used to explore the potential mechanism behind AhR mediated macrophage polarization.
Results: Compared with normal controls, there are fewer M2 macrophages in colonic tissue of patients with active IBDs. Experimentally, intra-colonic administration of 6-formylindolo [3,2-b] carbazole (FICZ), an AhR agonist, protected against TNBS-induced colitis ,manifested by less frequency of diarrhea and bloody stool and less weight loss. This protection was associated with the increase of M2 macrophages and the release of IL-10 in the intestine. *In vitro*, FICZ enhanced the expression of M2 related hallmarks like Ym-1, Fizz1 and CD206, and increased the production of anti-inflammatory mediators. Furthermore, FICZ mediated M2 polarization was accompanied by an induction of IRF4 expression, and IRF4 silencing using siRNA significantly impaired M2 polarization.
Conclusion: In conclusion, AhR activation reduces the severity of colitis and the inflammatory process via enhancing macrophage M2 polarization, and this effect could be mediated by the induction of IRF4 expression. These findings provide insight into the mechanisms of colonic inflammation and could lead to new therapeutic strategies for IBDs.
Disclosure: Nothing to disclose

P0321 PLASMA CONCENTRATION OF LIPOPROTEIN (A) AND ITS RELATIONSHIP WITH INFLAMMATION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Inflammatory bowel disease (IBD) patients have increased risk of cardiovascular disease (CVD). Dyslipidemia is a confirmed risk factor for CVD. The purposes of this retrospective study were to examine the lipid and lipoprotein profiles in patients with IBD, investigate the relationship between disease severity and lipid and lipoprotein profiles, and also analyze influence factors.
Aims & Methods: Three hundred seven consecutive Crohn's disease (CD) patients and 235 consecutive ulcerative colitis (UC) patients were included in this retrospective study. We retrieved patients' clinical and laboratory parameters from their medical records. The control group (n=167) comprised clinically healthy subjects from the same geographic region as the IBD study group. Total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and lipoprotein (a) (Lp (a)) levels were analyzed in relation to disease activity. Tukey's post-hoc test, Mann-Whitney U test, and Pearson's or Spearman's coefficient were used in the statistical analyses.
Results: Compared to the controls, patients with CD and UC had lower TC, TG, HDL-C, and LDL-C levels. This lipid pattern was more prominent in patients with CD than in those with UC. Furthermore, TC, HDL-C, and LDL-C levels were negatively associated with the Crohn's Disease Activity Index (CDAI) and Mayo scores. Additionally, patients with CD had higher Lp (a) levels than in those with UC and the controls. Patients with active CD had higher Lp (a) concentrations than those with inactive CD, and the Lp (a) levels were positively associated with the CDAI, C-reactive protein level (CRP), and erythrocyte sedimentation rate (ESR).
Conclusion: Lower TC, TG, HDL-C, and LDL-C levels are demonstrated in patients with IBD (particular CD) compared to normal controls and are negatively correlated with the disease activity. Conversely, higher Lp (a) concentrations are observed in patients with CD, and they are positively correlated with CDAI. Inflammation may induce dyslipidemia in IBD. Furthermore, a more efficient method for diagnosing and treating dyslipidemia is warranted in patients with IBD.
Disclosure: Nothing to disclose

P0322 REDUCED CDX2 EXPRESSION IN ILEOCOLONIC BIOPSIES FROM PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: The caudal-related homeobox transcription factor 2 (CDX2) plays an important role in intestinal epithelial differentiation, proliferation, migration, and adhesion. Coskun and colleagues previously reported that CDX2 was downregulated in ulcerative colitis, showed that TNF-areduces CDX2 mRNA and protein levels in cultured Caco-2 colon epithelial cells, in a dose-dependent manner, and this effect was significantly reduced by adding the anti-TNF-a drug infliximab to the culture medium (Biochim. Biophys. Acta. 2011;1812:283-9).
Aims & Methods: The aim of this study was to determine whether CDX2 is reduced in Crohn's disease (CD) and whether CDX2 levels are affected by anti-TNF-a treatment.
Sections of formalin-fixed paraffin-embedded ileocolonic biopsy tissues from 6 biologics-naiive patients with Crohn's disease (CD), 16 patients with CD treated with anti-TNF-a (CD-T), 7 biologics-naiive patients with ulcerative colitis (UC), and 7 biopsies without significant distortion or active inflammation (controls), were stained by immunohistochemistry (IHC) for CDX2. The inflammation activity was scored on a scale from 0 (no activity) to 3 (erosion/ulceration) using a modified Riley Histological Activity

Score (HAS). The level of CDX2 expression was determined using the image analysis software OTMIAS; the expression levels of CDX2 are given in OTMIAS Units (OU). Statistical analysis was performed using Prism statistical analysis software.

Results: There was no significant correlation between CDX2 levels and (HAS). Compared to the control group (mean 21.13), CDX2 expression was reduced in CD (mean 5.2, p = 0.0147) and in CD-T (mean 8.137, p = 0.0176). CDX2 expression was also reduced in UC, but this was not statistically significant (mean 11.89, p = 0.1625). Biopsies from CD-T patients had only slightly higher mean CDX2 expression (8.137) compared to CD (5.2, p = 0.4797).

Conclusion: CDX2 levels in ileocolonic epithelial cells are significantly reduced in biopsies from patients with CD compared to controls, confirming what has been previously reported in UC. However, treatment with anti-TNF-adid not significantly impact the levels of CDX2 expression in CD suggesting that other inflammatory mediators may be involved in CDX2 downregulation, in addition to TNF-a. Lack of correlation between CDX2 levels and HAS suggests that CDX2 downregulation may be more related to the chronic inflammation than a direct response to acute inflammation.

Disclosure: Mamoun Younes: President of, and owns significant shares in, Olive Tree Media, LLC, the maker of the quantitative image analysis software OTMIAS used in this study. All other authors: No conflicts.

P0323 THE ANTI-INFLAMMATORY EFFECTS OF NICLOSAMIDE ON CYTOKINES PRODUCED BY PBMCS DERIVED FROM IBD PATIENTS

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Introduction: Despite considerable progress in IBD therapies, at least half of the treated patients fail to reach remission. Monoclonal antibody therapies are associated with immunogenicity. Niclosamide is a salicylide which has been used as an anti-helminthic drug and minimally absorbed from the gastrointestinal tract. It has been shown to have anti-inflammatory properties and is currently repurposed for use in head and neck cancer. We aimed to study its effects on immune cells *ex vivo* and potential for repurposing in IBD.

Aims & Methods: Peripheral blood mononuclear cells (PBMCs) from the bloods of 6 IBD patients were cultured with or without stimulation with 0.5μg/ml antiCD3 (clone OKT3). Niclosamide was prepared in dimethyl sulfoxide (DMSO) and diluted into culture medium at 0.25mM and 0.5mM. Effect of niclosamide upon cell survival and T cell activation was measured at 1 day by flow cytometry analysis of activation markers CD69, CD25 and CTLA-4. At six days, cells were re-stimulated with PMA and ionomycin in the presence of Brefeldin A and expression of cytokines IL-17A, TNFα, IFNγ and IL-2 measured by flow cytometry. Data was analysed by Flowjo and significance tested by Friedman Analysis.

Results: Niclosamide was not toxic to cells at the concentrations tested and did not alter the frequencies of CD4+ and CD8+ T cells, CD19+ B cells or CD14+ monocytes in unstimulated cells. However, niclosamide reduced CD4 and CD8 T cell activation indicated by a significant decrease in the frequency of CD4+ cells expressing CTLA-4 and CD25 and CD69 and CD25 by CD8+ cells. This resulted in a significant decrease in T cell number at six days *(P=0.0120)*. Furthermore, it significantly inhibited expression of pro-inflammatory cytokines IL-17, IFNγ, TNFα and IL-2 by CD4 and CD8+ T cells.

Conclusion: Niclosamide has a strong anti-inflammatory effect on T cells from IBD patients with no significant cell toxicity seen at concentrations used. The significant reduction in cytokine levels known to be involved in IBD make it a potential drug that could be used in IBD.

Disclosure: Nothing to disclose

P0324 PROTEOMIC MARKERS OF RESPONSE TO ANTI-TNF DRUGS IN CROHN'S DISEASE

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Introduction:
Therapy with anti-TNF has improved notably the management of Crohn's disease (CD). However, 25-40% of patients treated with these drugs lose response long-term. In addition, these treatments are expensive and not without risk of adverse events. Therefore, it is essential to identify reliable markers that will select those patients who can benefit of anti-TNF drugs, thus improving their efficacy and safety.

Aims & Methods: A consecutive cohort of CD patients, who were naïve to anti-TNF therapy, were enrolled and followed up during 12 months. Demographic, analytical, nutritional and physiopathology were recorded. Patients were stratified according to clinical response as follows: a) Non-primary response (NPR) at 12 weeks post-treatment; b) loss of response (LR) within 12 months; c) sustained clinical response (SCR). In addition, plasma samples were collected previously to anti-TNF treatment and further analysed by SWATH proteomics, in order to identify potential biomarkers of response to anti-TNF. Anova or Kruskal-Wallis tests were used for analysis, according to data distribution. Functional pathways of identified biomarkers was analysed by DAVID Bioinformatics Resources 6.7.

Results: 54 CD patients were included. 77.3% showed a SCR. However, 4.5% of patients had NPR and 18.2 % LR. Patients with recent diagnosis of CD (< 12 months) were less likely to achieve SCD. Indeed, the interval from diagnosis to anti-TNF therapy was shorter in patients NPR (0± 0) as compared with LR (9.9 ± 5.9 years) and SCR (6.32±8.0 years) (p=0.04).We have identified as NPR factors, the early use of antiTNF during the first year of diagnosis (NPR: 0±0 vs LR: 9.9±5.9 and SCR: 6.32±8.0) (p=0.043). Increased blood leucocytes count before treatment was also associated with NPR (NPR: 13.7±2.1 vs LR: 8.4±2.3 and SCR: 7.6±2.9) (p=0.018). In addition, we have identified the overweight as a factor of losing response during the first year of treatment (BMI: NPR: 24.5± 7.5, LR: 27.6± 4.6 vs SCR: 23.4± 3.6) (p=0.036). As potential biomarkers of primary response we have identified 18 proteins upregulated, related to hemostasis and metabolism of carbohydrates, all of them with p≤0.009 and a fold change ≥ 2.4. 17 of these proteins are regulated by acetylation.
In addition, 4 proteins were potential biomarkers of loss of response (p≤0.05 and fold change from 0.5 - 1.4). 2 of them related to lipids metabolism.

Conclusion: Early need for anti-TNF and increased blood leucocytes count, probably related to a more severe disease, are associated with NPR. Overweight is associated with secondary loss of response to anti-TNF. In addition, hemostasis, metabolism of carbohydrates and lipids may be involved in the response to anti-TNF in CD.

Disclosure: Nothing to disclose

P0325 THE EFFECT OF PAI-1 ON ENDOPLASMIC RETICULUM STRESS IN RATS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Studies have shown that long-term, severe endoplasmic reticulum stress (ERS) exceeds regulatory capacity of cells, and activation of the unfolded protein response (UPR) will cause a large number of unfolded and misfolded proteins to deposit in the endoplasmic reticulum. Induction of apoptosis leads to an immune response that causes an immune imbalance. Among them, cytokines TNF-α, IL-1, IL-6, IFN-γ and BIP play a key role in the pathogenesis of IBD. Plasminogen Activator Inhibitor 1 (PAI-1) is an irreversible inhibitor of tissue-type Plasminogen Activator (tPA) and urokinase Plasminogen Activator (uPA).

Studies have shown that PAI-1 is involved in the inflammatory process of IBD [4], but the relationship between its specific gene expression and the involvement of related cytokines in the ERS process is still unclear.

Aims & Methods: In this study, we will investigate the effect of PAI-1 gene on ERS in rats with inflammatory bowel disease.

12 Wistar normal rats were randomly divided into 2 groups: Control group(n=6) and IBD group(n=6); 12 PAI-1 knock out rats were randomly divided into 2 groups: Knock out PAI-1 control group(n=6) and Knockout PAI-1+IBD group(n=6). The model of IBD was induced by 2,4,6-trinitrobenzene sulfonic acid (TNBS)/absolute ethanol; The pathological grade was evaluated using HE staining; The gene transcriptional levels of PAI-1, IL-6, IFN-γ, BIP were measured by Quantitative Real-time PCR (qRT-PCR); The protein expression levels of PAI-1, IL-6, IL-10, IFN-γ, BIP, p-IRE1α, p-JNK, JNK were measured by western blot.

Results: 1.Pathological examinations showed severe changes of colonic tissue and inflammation in IBD rats whereas relieved symptoms were found in PAI-1 knock out rats with IBD.

2. Compared with the control group, the transcription levels of the inflammation-related factors IL-6, IL-10, IFN-γ and BIP in the colon tissue of rats in the IBD group were significantly up-regulated ($p< 0.01$), and the transcription level of PAI-1 gene was significantly up-regulated ($p< 0.01$). Compared with the IBD group, the transcription levels of PAI-1, IL-6, IL-10, IFN-γ and BIP genes in Knock out PAI-1+IBD group were significantly down-regulated (p>0.01).

3. Compared with the Control group, the PAI-1 protein expression in the colon tissue of the IBD group was significantly increased, and the protein expression levels of PAI-1, IL-6, IL-10, IFN-γ, BIP, p-IRE1α, p-JNK, JNK were Significantly up-regulated. Compared with Knockout PAI-1 control group, there was no significant difference in PAI-1 protein expression of Knock out PAI-1+IBD group, the protein expression levels of PAI-1, IL-6, IL-10, IFN-γ, BIP, p-IRE1α, p-JNK, JNK of Knock out PAI-1+IBD group were significantly up-regulated. Compared with the IBD group, the protein expression levels of PAI-1, IL-6, IL-10, IFN-γ, BIP, p-IRE1α, p-JNK, JNK were significantly down-regulated in the Knock out PAI-1+IBD group.

Conclusion: This study explored the interaction of PAI-1 in inflammatory response and endoplasmic reticulum stress. It is concluded that the expression of PAI-1 gene is positively correlated with tissue inflammation and endoplasmic reticulum stress in IBD rats, which may promote the development of inflammatory bowel disease.

References: [1] Engel MA,Neurath MF. New pathophysiological insights and modern treatment of IBD [J].Gastroenterology,2010,45(6):571-583. [2] Corazzari M, Rapino F, Ciccosanti F, et al. Oncogenic BRAF induces chronic ER stress condition resulting in increased basal autophagy and apoptotic resistance of cutaneous melanoma[J]. Cell Death & Differentiation, 2015, 22(6):946-958. [3]Abdel Salam AG,Ata HM,Aalman TM,et al.Potential therapeutic utility of mesenchymal stem cells in inflammatory bowel disease in mice [J].Int Immunopharmacol,2014,22(2):515-521. [4] Shaghaghi, Z; Bonyadi, M; Somi, MH; et al.Association of plasminogen activator inhibitor-1 gene polymorphism with inflammatory bowel disease in Iranian Azeri Turkish patients.[J].Saudi J Gastroenterol.2014,20(1):54-58. [5]Iba T, Thachil J. Clinical significance of measuring plasminogen activatorinhibitor-1 in sepsis[J]. J Intensive Care. 2017,5:56. [6]Ole D. Laerum, Martin Illemann, Arne Skarstein,et al. Crohn's Disease But Not Chronic Ulcerative Colitis Induces the Expression of PAI-1 in Enteric Neurons[J]. Am J Gastroenterol. 2008,103(9):2350-2358. 2015,24(3):253-256. [9]Richardson CE,Kooistra T,Kim DH.An essential role for XBP-1 inhostprotection against immune activation in C.elegans[J].Nature,2010,463(7284):1092-1095. [10]Sano R , Reed J C . ER stress-induced cell death mechanisms[J]. Biochimica et Biophysica Acta (BBA) - Molecular Cell Research, 2013, 1833(12):3460-3470.
Disclosure: Nothing to disclose

P0326 COMBINING ABSOLUTE QUANTIFICATION OF FECAL BACTERIA WITH METAGENOMIC SEQUENCING DATA IMPROVES THE CHARACTERIZATION OF THE GUT MICROBIOME OF PATIENTS WITH CROHN'S DISEASE

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Introduction: Evidence for the role of the gut microbiota in the development and progression of Crohn's disease (CD) is increasing. So far, gut microbiome studies in patients with CD have focused on characterising the changes in bacterial abundances. Clinical, environmental factors and inflammation can influence not only the microbial composition in the gut but also its total bacterial biomass. However, the total number of bacteria in a sample is rarely considered when investigating the relation between microbiome and gastrointestinal diseases.

Aims & Methods: We hypothesize that combining sequencing data with absolute quantification of the gut microbiota (e.g. the number of bacteria per gram of feces) provides better insight in disease heterogeneity and improves the accuracy of gut microbiome studies in diseases such as IBD. We collected 140 fecal samples from a cohort of 70 patients with CD, taken at two time points with an interval of three weeks. Microbial densities were calculated by fluorescence in situ hybridization. Microbiota composition was estimated by shotgun metagenomic sequencing. Phenotypic data, such as medication use and surgery, was obtained from clinical records. PERMANOVA analysis was used to estimate the explained variance of each phenotype on the microbiome composition. Differences between disease phenotypes and microbial loads were calculated using a Wilcoxon-test. To estimate the confounding effect of absolute bacterial quantification, metagenome-wide associations were then recalculated adjusting for bacterial cell counts.

Results: Patients with CD showed a large variation in gut bacterial densities, which is independent of disease activity, measured as the level of fecal calprotectin (rho=0.05, P=0.53). Differences in microbial loads explained most of the variation in microbiome composition between samples (R2=10%, P = 0.0001). Higher densities were related with an increased compositional abundance of beneficial bacteria, such as *F.prausnitzii* and *R.intestinalis*, while lower microbial loads were associated with an expansion of potentially pathogenic bacteria such as *E.coli* and *R.gnavus*. Patients with intestinal resections showed lower microbial loads (P= $5.94E^{-06}$), although the latest resection occurred, on average, 11 years before sample collection. Interestingly, by using the concentration of DNA extracted in combination with the bacterial richness per sample we can capture ~40% of the variation in the number of bacteria per gram of fecal material. Correcting for bacterial densities in the microbe-trait associations allowed us to increase the specificity of microbiome-wide association studies and therefore pinpoint relevant species in CD sub-phenotypes, such as the association between *F.prausnitzii* and clinical resections in the ileum.

Conclusion: The number of bacteria in the gut of patients with CD show a large variation between individuals. Lower microbial densities are correlated with the expansion of pathogenic bacteria and associated with intestinal resection. For specific conditions or sub-phenotypes in the context of IBD, adding bacterial quantification to metagenomics sequence data reveals potential false positive and false negative findings. The differences in bacterial loads should be considered when exploring the gut microbiota of patients with CD, both as a separate major indicator of gut health and as correction factor for microbe-phenotype association.

Disclosure: Nothing to disclose

P0327 AUTOPHAGY INDUCTION OF INTESTINAL EPITHELIUM ALLEVIATE COLITIS IN DSS MODEL MICE

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Introduction: Crohn's disease (CD) and ulcerative colitis, generally known as inflammatory bowel disease (IBD), are chronic, relapsing and refractory disorders of the intestine. The pathogeneses of IBD is still not clear. Autophagy is a required system to maintain cellular homeostasis by disassembling unnecessary or dysfunctional components in the cytoplasm, and plays an important role in recovery from inflammation and bacterial infection of intestinal epithelium. Involvement of autophagy-related genes such as Atg16L1, NOD2 and LRRK2 has also been reported in the onset of CD. Therefore, we investigate the effect of autophagy induction on the alleviation of colonic inflammation.
Aims & Methods: The modulators of autophagy were screened by *in vitro* screening assay from compound library derived from food and herbal medicine. Autophagy induction was examined using autolysosome formation in MEF cell line. The modulator of autophagy screened by *in vitro* assay was administrated to the acute dextran sulfate sodium (DSS)-induced colitis model mice and the effect was evaluated by weight reduction, colon length and histopathological examination.
Results: From screening assay, 3 compounds showed autophagy induction and relieving colitis. The administration of one compounds derived from herbal medicine (named SO) significantly prevent weight loss, colonic shortening and infiltration of inflammatory cells. SO induced autophagosome formation in Caco2 (human intestinal epithelium cell line) by concentration dependency. Western blotting assay showed the expression of representative autophagy marker LC3 was high in the epithelium and enhanced by administration of SO. Immunohistological examination showed high expression of LC3- II in the intestinal epithelium after administration of SO in colitis model mice.
Conclusion: We identified 3 autophagy modulators which has effects of autophagy induction and relieving colitis. SO which has high activity for inducting autophagy induced the effect of alleviation colitis through autophagy induction of intestinal epithelium.
Disclosure: Nothing to disclose

P0328 WHOLE BLOOD ACTB, B2M, AND GAPDH EXPRESSION REFLECTS ACTIVITY OF INFLAMMATORY BOWEL DISEASE, ADVANCEMENT OF COLORECTAL CANCER, AND CORRELATES WITH CIRCULATING INFLAMMATORY AND ANGIOGENIC FACTORS: RELEVANCE FOR REAL TIME QUANTITATIVE PCR

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Introduction: Inflammatory bowel disease (IBD) and colorectal cancer (CRC) evoke response from circulating immune cells and analyzing gene expression patterns in whole blood, owing to its availability, might be advantageous over more relevant but less accessible bowel tissues. The effect of bowel inflammation and cancer on the expression of the most popular internal controls: ACTB, GAPDH, and B2M in whole blood is unknown, although at least GAPDH occurred to be tightly regulated and suspected of supporting cancer growth, challenging its suitability as reference.
Aims & Methods: We designed our present study to find and validate optimal reference genes for whole blood transcriptom studies involving patients with CRC and IBD, active and non-active (1), and to examine and compare the effect, if any, bowel cancer and inflammation might have on the expression of popular HKG in whole blood (2).Stability of ACTB, B2M, GAPDH, HPRT1, SDHA, and TBP expression in blood from controls, colorectal cancer, and active inflammatory bowel disease patients was evaluated in RT-qPCR using NormFinder, geNorm, BestKeeper, and comparative ΔCt method and validated by comparison with absolute quantification of IL1β and CCL4.
Results: HPRT1, SDHA and TBP were superior normalizers for whole blood in CRC and IBD. The highest variability was in active IBD. B2M was significantly lower in CRC but higher in IBD. GAPDH was higher in CRC and IBD. ACTB and GAPDH corresponded with CRC advancement (ρ=0.52 and ρ=0.53) and with clinical activity in Crohn's disease (ρ=0.44 and ρ=0.57) and ulcerative colitis (GAPDH: ρ=0.72). ACTB, B2M, and GAPDH correlated with circulating inflammatory/angiogenic indices, differently in IBD and CRC. In IBD, ACTB positively correlated with CRP, B2M with FGF2 and MIP1α, and GAPDH with CRP, IL1β, IL4, IL8, IL12, G-CSF, and TNFα. In CRC, ACTB positively correlated with IL1β, IL6, IL8, FGF2, G-CSF, GMCSF, MIP1α, and TNFα and GAPDH with IL1β, IL6, FGF2, G-CSF, GM-CSF, MIP1α, and TNFα, and B2M negatively with FGF2, G-CSF, and TNFα.
Conclusion: The expression of frequently used normalizers for whole blood transcriptomic analysis, that is, GAPDH, ACTB, and B2M, is directionally affected by bowel inflammation and cancer, rendering them unsuitable as reference in CRC and IBD. The expression of HPRT1, SDHA and TBP was stable across CRC and IBD patients allowing for their recommendation as normalizers in studies involving both groups of patients.
Disclosure: Nothing to disclose

P0329 ACETYLCHOLINE-PRODUCING T-CELLS CONTRIBUTE TO INNATE IMMUNE DRIVEN COLITIS BUT ARE REDUNDANT IN T-CELL DRIVEN COLITIS

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Introduction: Clinical trials suggest that vagus nerve stimulation presents an alternative approach to classical immune suppression in Crohn's disease. T-cells capable of producing acetylcholine (ChAT[+] T-cells) in the spleen are essential mediators of the anti-inflammatory effect of vagus nerve stimulation. Besides the spleen, ChAT[+] T-cells are found abundantly in Peyer's patches of the small intestine. However, the role of ChAT[+] T-cells in colitis pathogenesis is unknown.
Aims & Methods: The aim of this study was to investigate the role of ChAT^{+} T-cells in experimental models of colitis. We made use of CD4[cre]ChAT^{fl/fl} mice (CD4ChAT^{-/-} mice), lacking ChAT expression specifically in CD4^{+} T-cells. Littermates (ChAT^{fl/fl} mice) served as controls. We used three experimental colitis models: 1) Acute dextran sulphate sodium (DSS)-induced colitis: 7 days of 2% DSS in the drinking water; 2) A resolution model of DSS-induced colitis: 5 days of 2% DSS in the drinking water followed by 7 days without DSS; 3) T-cell transfer colitis using CD4^{+}CD45RB^{high} T-cells as donor cells. Outcome measures included bodyweight loss, endoscopy and histology score, colon weight and intestinal cytokine levels.
Results: In acute DSS-induced colitis, CD4ChAT^{-/-} mice showed attenuated colitis and lower intestinal inflammatory cytokine levels compared to ChAT^{fl/fl} mice. In contrast, in the resolution model of DSS-induced colitis, CD4ChAT^{-/-} mice showed a worsened colitis recovery and augmented colonic histological inflammation scores and inflammatory cytokine levels as compared to ChAT^{fl/fl} mice. In the T-cell transfer model, T-cells from CD4ChAT^{-/-} mice induced a similar level of colitis compared with ChAT^{fl/fl} T-cells.
Conclusion: Our results indicate that ChAT[+] T-cells aggravate the acute innate immune response upon mucosal barrier disruption in a DSS-induced colitis model, while they are supporting the later resolution process of this innate immune driven colitis. Surprisingly, ChAT expression in T-cells seems redundant in the context of T-cell driven colitis.

References: Rosas-Ballina et al. Acetylcholine-synthesizing T cells relay neural signals in a vagus nerve circuit. Science (New York, NY) 334: 98-101, 2011. Dhawan S et al. Acetylcholine-producing T cells in the intestine regulate antimicrobial peptide expression and microbial diversity. Am J Physiol Gastrointest Liver Physiol 311: G920-G933, 2016.
Disclosure: Nothing to disclose

P0330 FREE FATTY ACID RECEPTOR AGONISTS AFFECT COLONIC EPITHELIAL ION TRANSPORT IN MOUSE COLON

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Introduction: The family of Free Fatty Acid Receptors (FFARs), specific G protein-coupled receptors consist of four members: FFAR1-4, where each responds to different chain length fatty acids (FAs). It was reported that FFAR ligands may reduce inflammatory states, thus FFARs have become a potential new target in inflammatory bowel disease (IBD). IBD is a heterogeneous disorder characterized by chronic, relapsing, inflammation in the gastrointestinal tract, consisting of ulcerative colitis (UC) and Crohn's disease (CD). Neither CD nor UC are fatal diseases but both are debilitating with a wide range of symptoms. One of IBD symptoms is secretory diarrhea, which occurs when secretion of water and electrolytes into the intestinal lumen exceeds its absorption. The movement of fluid between the intestinal lumen and blood is driven by the active transport of ions, thus restoration of this process in IBD patients could be beneficial as the chronicity of symptoms leads to decrease in patient's quality of life.
Aims & Methods: The aim of this study was to evaluate the effects of FFAR1-4 agonists on epithelial ion transport in isolated mouse colon stimulated by Forskolin (FSK) and Veratridine (VER) and compare between groups comprising healthy control and 3% Dextran Sulfate Sodium (DSS)-treated mice.
Male c57 mice were randomly divided into healthy control group and group treated with 3% DSS in drinking water. Epithelial ion transport was examined using Ussing Chambers. Changes in ion flux were determined on the basis of short-circuit current (ΔIsc) in isolated mouse colon exposed to FFAR1-4 and stimulated with FSK or VER.
Results: ΔIsc values were reduced in inflamed tissues as compared to controls in all colon samples stimulated with FSK. Incubtion of healthy tissue with FFAR1 and FFAR2 agonists caused significant ($p < 0.05$) reduction of ΔIsc induced by FSK. On the other hand, FFAR3 agonist caused significant ΔIsc decrease in inflamed colon tissue stimulated with FSK. FFAR1 and FFAR2 agonists lowered, but FFAR3 and FFAR4 agonists increased ion transport in control tissues stimulated with VER. Incubation of DSS-treated mouse colon tissue with FFAR1, 2 and 4 agonists diminished ΔIsc caused by VER.
Conclusion: FFAR agonists differentially affect the ion transport in healthy and inflamed colon tissue. The varying effects depend not only on the receptor but also on the modulator of ion flux (FOR or VER). These differences may be explained by the activation of various intracellular pathways by FFAR agonists, which need further investigation.
To summarize, we suggest that it is possible to develop treatment in a form of specialized diet enriched with specific FFAR ligands which could ameliorate symptoms of IBD associated with disrupted transport across intestinal epithelium.
Disclosure: Nothing to disclose

P0331 MOLECULAR RESPONSE TO USTEKINUMAB IN MODERATE-TO-SEVERE ULCERATIVE COLITIS BY SERUM PROTEIN AND COLON TRANSCRIPTOMIC ANALYSIS: RESULTS FROM THE UNIFI PHASE 3 MAINTENANCE STUDY

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Introduction: The cytokines IL-12 and IL-23 are elevated in ulcerative colitis (UC), and genetic association suggests that they play causative roles in the disease. Ustekinumab (UST), an anti-IL-12p40 monoclonal antibody that binds both cytokines, is an effective therapy for moderate-to-severe UC. We previously observed a partial normalization of UC disease signatures in colonic biopsy gene expression and serum protein levels following UST induction therapy.[1] However, the molecular effects of maintenance UST therapy in UC patients are unknown.
Aims & Methods: We evaluated the molecular effects of UST in the UNIFI Phase 3 maintenance study of UST in moderate-to-severe UC (n=961). Subjects in response to UST 8 weeks after intravenous induction were randomized to receive maintenance treatment with subcutaneous placebo, UST 90 mg every 8 (q8w) weeks, or UST 90 mg every 12 weeks (q12w). Colonic biopsy mRNA and serum samples from the first ~60% of patients treated in the UNIFI phase 3 induction study[2] were analyzed, with equal representation of patients with or without a history of biologic therapy failure (Table 1). Biopsy and serum samples from healthy subjects were analyzed as controls.
Results: At Week 44 after the start of maintenance therapy, the expression of colonic genes dysregulated in UC was altered towards normal levels in all treatment groups, with the greatest improvements among those receiving UST and those in clinical remission ($p < 0.05$ for maintenance Week 44 versus start of maintenance). No dose effect was observed between q8w and q12w UST treatment arms, and no significant improvements in disease signature occurred in non-responders to placebo or UST. Ustekinumab maintenance therapy magnified the normalization of serum proteins following UST induction; among subjects receiving q8w UST who were in remission at Week 44, the proteins IFNγ, IL-17A, MMP3, and SAA reached concentrations comparable to those seen in healthy controls. Similar trends occurred in subjects in remission following q12w UST and to a lesser degree among UST-treated subjects not in remission at Week 44. Among subjects receiving placebo maintenance therapy who were in remission at Week 44, the disease-associated serum proteins that decreased following UST induction were not further reduced during maintenance. As previously observed in the induction studies, UST maintenance did not reduce serum TNF levels.
Conclusion: UST maintenance therapy suppressed IL-12 and IL-23-related serum proteins and promoted normalization of the UC disease transcriptomic profile. These results provide insight into the molecular mechanisms associated with the efficacy of UST maintenance therapy.

	Biopsy mRNA (550 UC and 18 healthy cntl)	Serum Protein (574 UC and 50 healthy cntl)
Analytes	Affymetrix HG U133 PM arrays	12 serum markers: • Matrix metalloproteinases: MMP-1,3,9 • Cytokines and cytokine receptors: IFNγ, IL-17A, IL-22, IL-10, IL-2R, TNFα, TNFR1 • Acute Phase Reactant: SAA Inflammatory marker: NGAL
Methods	Generalized linear model (GLM) & Gene Set Variation Analysis	GLM
Time points	Screening, induction Week 8 (maintenance Week 0), and maintenance Week 44	-
Significance cutoffs	|fold change| > 1.5x and p < 0.05	-

[Table 1. Biopsy mRNA and serum protein assessments in UNIFI]

References: 1.K Li, et al. Molecular Response to Ustekinumab in Moderate-to-severe Ulcerative Colitis by Serum Protein and Biopsy Gene Expression Analysis: Results from the UNIFI Phase 3 Induction Study. Presented at ECCO 2019, March 6-9, 2019, Copenhagen, DK.

2.BE Sands, et al. Safety and Efficacy of Ustekinumab Induction Therapy in Patients with Moderate to Severe Ulcerative Colitis: Results from the Phase 3 UNIFI Study. Presented at ACG 2018, October 9, 2018, Philadelphia, PA, USA.
Disclosure: Drs.Li, Yang, Hayden, Strawn, Wadman, Bhagat, Marano, and Friedman are all employees of Janssen Research & Development, LLC

P0332 EFFECTS OF MATRIX METALLOPROTEINASE (MMP)-7, MMP-13 AND CATHEPSIN G ON THE INTEGRITY AND FUNCTION OF ANTI-TUMOUR NECROSIS FACTOR (TNF)-α AND ANTI-INTEGRIN BIOLOGIC AGENTS

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Introduction: Biologic therapy is highly effective in inflammatory bowel disease (IBD), however a significant proportion of patients fail to respond, and mechanisms underlying primary non-responsiveness are unclear. We have previously observed that proteolytic degradation by MMP (matrix metalloproteinase)-3 and MMP-12, which are up-regulated in IBD inflamed mucosa, may contribute to primary non-responsiveness to anti-tumour necrosis factor (TNF)-α agents in IBD.[1] We hereby investigated the effect of other proteases on the integrity and function of anti-TNF-α and anti-integrin agents.
Aims & Methods: We co-incubated increasing concentrations of activated recombinant human MMP-7, MMP-13, and Cathepsin G with the anti-TNF-α agents Infliximab, Adalimumab, and Etanercept, or with the anti-integrin agent Vedolizumab, and we subsequently analysed the cleavage reaction products by Western blotting. Using a reporter cell line, we evaluated the effect of recombinant human proteases on the ability of anti-TNF-α agents to neutralise soluble TNF-α.
Results: Infliximab, Adalimumab and Vedolizumab were not degraded by MMP-7, MMP-13, or Cathepsin G. Etanercept was degraded in a concentration-dependent manner by MMP-7 and MMP-13, but not by Cathepsin G. Degradation by MMP-7 and MMP-13 did not significantly impair the ability of Etanercept to neutralise soluble TNF-α.
Conclusion: Despite being known to cleave immunoglobulins,[2] MMP-7 and MMP-13 do not appear to impair the integrity and function of Infliximab and Adalimumab. In keeping with our previous findings, Etanercept appears to be highly susceptible to the action of proteases.
References: 1. Biancheri P, et al. Gastroenterology 2015;149:1564-74. 2. Brezski RJ, et al. MAbs 2010;2:212-20.
Disclosure: Nothing to disclose

P0333 EFFECT OF CO-MORBIDITIES IN CROHN'S DISEASE ASSOCIATED URINARY METABOLIC PROFILES

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Introduction: Distinct metabolic signatures have been detected in urine that differentiate Crohn's disease (CD) from controls in multiple studies, with consistent discriminatory metabolites derived from bacteria and co-bacterial pathways (1). Multiple other diseases have also been found to affect the urinary metabolome, and many of these relate to changes in bacterial associated metabolites (2).
Aims & Methods: The aim of this study was to examine whether the same metabolite changes that have been previously shown are present in a real life cohort of CD patients, and if these patients could be distinguished from controls despite the presence of co-morbidities. Nuclear magnetic resonance (^{1}H NMR) spectroscopy was used to acquire urinary metabolic data from 74 CD patients and 100 controls. 19 of the CD group and 48 of the controls had at least one significant co-morbidity (diabetes, asthma, hypertension). Multivariate analysis was performed using OPLSDA. Univariate analysis was also performed to assess whether bacterial associated metabolites, as demonstrated in previous studies (1), were significantly different in CD patients compared to controls. These metabolites were hippurate, alanine, citrate, P-cresol, phenyacetylglutamine (PAGn), and dimethylglycine (DMG).
Results: OPLSDA analysis showed statistically significant separation between CD patients and controls irrespective of the presence of co-morbidities. Model 1 compares CD patients to healthy controls (H). Models 2 and 3 include CD patients with at least one other co-morbidity (CDWC), and Model 3 includes non-CD patients with another co-morbidity in the control group (C).
Univariate analysis showed that the bacterial associated metabolites hippurate, citrate, P-cresol, DMG, and PAGn changed with statistical significance between CD groups and controls irrespective of the presence of co-morbidities.
Conclusion: The pattern of change in discriminating metabolites appear to be preserved in models separating CD from controls when patients with co-morbidities are included in the models, and these groups can be significantly separated with multivariate analysis. It is likely the effect of microbial disturbance is still measurable with this technique in a real world cohort.

Model		n	R2X	Q2	P value CV-ANOVA	Metabolites driving model in CD
1	CD : H	106 (54 : 52)	0.085	0.231	0.014	hippurate↓ alanine↓ citrate↓ P.cresol↓ PAGn↑ DMG↓ leucine↓ aspartate↓
2	CDWC : H	128 (74 : 54)	0.100	0.175	0.057	hippurate↓ alanine↓ citrate↓ P.cresol↓ PAGn↑ DMG↓
3	CDWC : C	174 (74 : 100)	0.037	0.093	<0.001	hippurate↓ alanine↓ citrate↓ P.cresol↑ PAGn↑ DMG↓ sucrose↑

[Table 1. - OPLSDA Models of CD groups vs controls]

References: (1) Williams, 2009. AJG). (2) Lu, 2013. Front. Med.
Disclosure: Nothing to disclose

P0334 THE IMPACT OF ULCERATIVE COLITIS ON QUALITY OF LIFE AND PRODUCTIVITY ACROSS EUROPE, A BURDEN OF ILLNESS STUDY

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Introduction: Ulcerative Colitis (UC) has a significant impact on quality of life, ability to work and making career choices and often a negative psychosocial impact on patients' lives. The wider implications to psychosocial well-being and activities of daily living challenge existing paradigms which are currently limited to clinical "remission" and regard surgery in some instances as being "curative". There is an urgent need for studies assessing health-related quality of life (HRQoL) even as modern biological therapies redefine our perceptions of disease control.
The Living with Ulcerative Colitis: Identifying the socioeconomic burden in Europe (LUCID) study was a descriptive, retrospective, cross-sectional, European (France, Germany, Italy, Spain, United Kingdom, Denmark, Norway,

Poland, Romania and Turkey), multi-site bottom-up prevalence-based Burden of Illness research study carried out by HCD Economics and the University of Chester in partnership with Crohn's and Colitis UK.

Aims & Methods: The aim of this study was to explore the impact of UC on patients' HRQoL and productivity. Patients were recruited through Gastro-enterologists (surveyed between August 2018 – February 2019) and split into two population cohorts; Arm 1: Patients with moderate or severe UC status at initiation of documentation period (12 months prior the index date) and Arm 2: Patients with moderate or severe UC that achieved mild UC or remission at initiation of documentation period. Each patient was invited to complete a public patient involvement and engagement (PPIE) form. The PPIE included patient reported outcome measures (PROMs) to capture intangible costs using the work productivity and impairment (WPAI) questionnaire, which quantifies work time missed, work impairment and activity impairment, and HRQoL using the EQ5D. The EQ5D produces a utility score of the patients current HRQoL from five domains, with 1 denoting perfect health and 0 denoting death.

Results: 1,658 patients completed the PPIE form. Of these patients, 9 patients did not have their UC status recorded so could not be assigned to an arm. Out of these patients, 1,001 patients (60.7%) were categorised into arm 1 with 648 patients (39.3%) categorised into arm 2. 994 patients from arm 1 and 638 patients from arm 2 completed the EQ5D with a mean score of 0.81 (0.17 SD) and 0.86 (0.16 SD) respectively. The mean WPAI scores for arm 1 (n=602) were 0.11 (0.25 SD) for work time missed (absenteeism), 0.24 (0.21 SD) for impairment (presenteeism), 0.28 (0.24 SD) for work impairment and 0.27 (0.24 SD) for activity impairment. The mean WPAI scores for arm 2 (n=368) were 0.01 (0.19 SD) for work time missed (absenteeism), 0.24 (0.18 SD) for impairment (presenteeism), 0.2 (0.21 SD) for work impairment and 0.18 (0.2 SD) for activity impairment.

Conclusion: Our preliminary results show that UC has implications on HRQoL and work productivity for all patients with UC, ranging from those in remission or mild disease to those with moderate or severe UC, underpinning the need for more holistic and inclusive definitions of care and disease control. Further analysis, to understand the impact of ulcerative colitis on patients, is ongoing to address this important and unmet need.

References: Rubin, D. T., Siegel, C. A., Kane, S. V., Binion, D. G., Panaccione, R., Dubinsky, M. C., ... Hopper, J. (2009). Impact of ulcerative colitis from patients' and physicians' perspectives: Results from the UC: NORMAL survey. Inflammatory Bowel Diseases, 15(4), 581-588. https://doi.org/10.1002/ibd.20793

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P0335 RISK OF REOCCURRENCE OF PERIANAL FISTULAS IN PATIENTS WITH CROHN'S DISEASE IN THE UNITED STATES – A RETROSPECTIVE CLAIMS DATABASE STUDY

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Introduction: Perianal fistulas (PAF) in patients with Crohn's disease (CD) are associated with morbidity and impaired quality of life. Limited data is available on the risk of PAF among patients with CD and long-term PAF relapse rates.

Aims & Methods: To describe characteristics of patients with CD and PAF, and rates of PAF reoccurrence (a proxy for disease relapse including both relapse of previous fistula and development of new fistula). A retrospective cohort study on US adult patients with CD identified in an US administrative claims database (2001-2018) was conducted. Patients with PAF were identified using diagnosis or procedure codes in medical claims. A PAF episode, starting from the first PAF occurrence, was defined as consecutive PAF-related codes ≤120 days of each other. PAF reoccurrence was defined as a new PAF-related code occurring after a PAF-free period of ≥180 days (proxy for remission) following the end of the first PAF episode. Time from the 180-day PAF-free period to PAF reoccurrence was estimated using KM analyses. A similar analysis was conducted in CD patients with a PAF-free period of ≥360 days.

Results: 5,482 patients with a PAF-free period of ≥180 days after their first PAF episode were included (CD-PAF cohort; mean age=43.8 years and proportion of males=51.8%). Over a mean follow-up duration of 2.6 years, 28.8% had a PAF reoccurrence. Estimated rates of PAF reoccurrence in these CD-PAF patients were 23.7%, 32.0%, 42.1% and 47.8% at 1, 2, 5, and 10 years, respectively (Table 1).

In the 12 months before first PAF occurrence, 70.8% of CD-PAF patients received non-biologic therapies: corticosteroids (46.5%), antibiotics (44.4%), aminosalicylates (5-ASA) (32.5%) and immunomodulators (IMDs)/immunosuppressants (IMs) (21.1%); 25.3% used ≥1 biologic therapy; and 19.2% had ≥1 CD-related surgery. In the 4 months after first PAF occurrence, 66.5% of CD-PAF patients received non-biologic therapies: antibiotics (39.6%), corticosteroids (30.3%), 5-ASA (27.4%) and IMDs/IMs (22.1%); 31.8% used ≥1 biologic therapy; and 47.2% had ≥1 CD-related surgery.

In patients with a longer PAF-free period of ≥360 days (CD-PAF360 cohort), a numerically lower proportion had a PAF reoccurrence (20.5%) and estimated rates of reoccurrence were numerically lower at every time point (32.6% at 5 years and 39.4% at 10 years) vs the CD-PAF cohort.

Cohort (N)	Duration of follow-up, mean [a]	Patients with PAF reoccurrence, N (%)	KM analyses	3 months	6 months	1 year	2 years	5 years	10 years
CD-PAF (N=5,482)	2.6 years	1,578 (28.8%)	KM rates [b,c]	10.0%	16.0%	23.7%	32.0%	42.1%	47.8%
CD-PAF (N=5,482)	2.6 years	1,578 (28.8%)	Patients at risk, N	4,478	3,771	2,824	1,702	494	85
CD-PAF360 (N=3,764)	2.7 years	771 (20.5%)	KM rates [b,c]	5.2%	9.2%	14.5%	21.7%	32.6%	39.4%
CD-PAF360 (N=3,764)	2.7 years	771 (20.5%)	Patients at risk, N	3,236	2,824	2,162	1,360	422	67

[a] Duration of follow-up starts from the end of the PAF-free period following the first PAF episode

[b] KM rates of PAF reoccurrence from the end of the PAF-free period of 180 days (CD-PAF) or 360 days (CD-PAF360) following the first PAF episode. KM rates are estimated at given time points and represent cumulative incidence accounting for right censoring

[c] Similar findings were observed in the sensitivity analysis defining a PAF episode as all consecutive PAF within 180 days of each other (vs. 120 days)

[Table 1. Kaplan-Meier rates of reoccurrence of perianal fistulas among patients with Crohn's disease]

Conclusion: In this retrospective US claim database analysis, the 5-year and 10-year rates of PAF reoccurrence following PAF remission of ≥180 days were 42.1% and 47.8% among patients with CD, respectively. Patients achieving longer-term remission (≥360 days) had numerically lower rates of PAF reoccurrence. Future studies should examine the impact of disease severity and treatment on long-term rates of PAF reoccurrence.

Disclosure: HP, TL, KDN, GO and SC-H are employees of Takeda. DLV and DS are employees of Analysis Group, Inc., which has received consulting fees from Takeda.

P0336 EPIDEMIOLOGY, CLINICAL CHARACTERISTICS, EVOLUTION AND TREATMENTS IN NEWLY DIAGNOSED INFLAMMATORY BOWEL DISEASE (IBD): RESULTS FROM THE NATIONWIDE EPIDEMIBD STUDY OF GETECCU

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Introduction: Updated data on the incidence, evolution and treatment strategies used in IBD management in South Europe is needed. This is the largest study on the recent epidemiology of IBD in Spain.
Aims & Methods:
i) To assess the incidence of IBD in Spain;
ii) to describe the main epidemiological and clinical characteristics of patients at diagnosis and the evolution of the disease; and iii) to explore the use of treatments in the biological era.
Prospective and population-based nationwide registry. Adult patients diagnosed with IBD ¾Crohn's disease (CD), ulcerative colitis (UC) or IBD unclassified (IBD-U)¾ during 2017 in the 17 Spanish regions were included and will be followed-up for 5 years after diagnosis. Treatment was grouped into 5 categories: mesalazine (oral or topical), steroids (intravenous, oral or topical), immunomodulators (thiopurines, methotrexate or cyclosporine), biologics (anti-TNF, vedolizumab or ustekinumab) and surgery. Cumulative incidence of exposure to each of the studied treatments was estimated by Kaplan-Meier curves.
Results: 3,627 incident cases of IBD diagnosed during 2017 from 108 centres covering over 22 millions of adult inhabitants (about 50% of the Spanish population) comprise the study cohort.
The overall incidence (per 100.000 person-years) of IBD was 16: 7.5 for CD, 8 for UC, and 0.5 for IBD-U. 46% of patients had CD and 50% UC. Diagnosis delayed was significantly longer in CD than in UC (5 vs. 2 months, p< 0.01). The proportion of patients with symptoms at diagnosis was higher in UC (94 vs. 89%, p< 0.01).
On the opposite, the proportion of patients with family history of the disease (18 vs. 13%, p< 0.01), smoking habit (38 vs. 12%, p< 0.01) and extraintestinal manifestations (12.5 vs. 6%, p< 0.01) were significantly higher in CD than in UC. At diagnosis, 18% of CD patients had structuring or fistulising behaviour and 64% of UC patients had pancolitis or left-sided colitis. 27% of patients were hospitalized during a median follow-up of 10 months (35% of CD and 22% of UC patients, p< 0.01).
During follow-up, 33 (2.4%) CD patients progressed to a more severe phenotype, and 2 (0.01%) UC patients to more extensive involvement. The cumulative incidences of the different treatments are shown in table 1.
Conclusion: The incidence of IBD in Spain is relatively high and similar to figures reported in Northern Europe. IBD patients require the use of substantial diagnostic and therapeutic resources, which are higher in CD than in CU. One third of patients are hospitalized in the first year after diagnosis and over 5% undergo surgery. Our results highlight the high burden of IBD as well as the important challenges faced by health-care systems to manage this costly and complex disease.

Treatments	Cumulative incidence of exposure to treatments (%)					
	6 months			12 months		
	UC	CD	p	UC	CD	p
Mesalazine (%)	89	36	<0.01	99	40	<0.01
Steroids (%)	35	70	<0.01	40	75	<0.01
Immunomodulators (%)	7	38	<0.01	11	50	<0.01
Biologics (%)	7	13	<0.01	11	31	<0.01
Surgery (%)	1	8	<0.01	2	11	<0.01

[Table 1. Cumulative incidences of exposure to different therapeutic options in Crohn's disease (CD) and ulcerative colitis (UC) patients]

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P0337 WITHDRAWN

P0338 TIME TRENDS OF CROHN'S DISEASE IN CATALONIA FROM 2011 TO 2017. INCREASING USE OF BIOLOGICS CORRELATES WITH A DECREASE IN SURGICAL REQUIREMENTS. A POPULATION-BASED STUDY IN CATALONIA

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Introduction: Data from clinical trials suggest that biological drugs might improve the outcomes in Crohn disease (CD) by reducing the need for surgery or hospitalization. Data on the trends in biological drugs use and outcomes in CD patients are scarce.
Aims & Methods: The aim of this study was to valuate the time-trends of the prescription of biological drugs and other treatments for Crohn's disease (CD), and its relationship with outcomes as surgery and hospitalization in Catalonian population.
All patients with CD included in the Catalan Health Surveillance System (including data on more than 7.5 million individuals) from 2011 to 2017 were identified. The exposures to different IBD treatments was retrieved from the electronic dispensation records. Time trends for surgery and hospitalization were also described and correlated with treatment. The statistical analysis was carried out using the statistical package R, version 3.4.3.
Results: The use of salicylates, corticosteroids and immunosuppressant treatment decreased from 2011 to 2017 from 28.8% to 17.1%, 15.8% to 13.7%, and 32.9 to 29.6%, respectively. Biological treatments increased from 15.0% to 18.7%. Adalimumab was the most prescribed (1604 patients, 52% of all biologics in 2017). Ostomy rates per 1000 patients/year decreased from 13.2 in 2011 to 9.8 in 2017. Corresponding figures for surgical resection decreased from 24.1 to 18.0. The rate of the CD-related hospitalizations per 1000 patients/year decreased from a 92.7 to a 72.2.
Conclusion: Use of biological drugs increased from 15.0% to 18.7% from 2011 to 2017. During the same periods we observed an improvement in the outcomes of CD
patients.
Disclosure: Nothing to disclose

P0339 PREVALENCE OF INFLAMMATORY BOWEL DISEASE (IBD) IN A COLORECTAL CANCER POPULATION SCREENING PROGRAM

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Introduction: in general, IBD are diagnosed in subjects with gastrointestinal symptoms, despite this a diagnostic delay is often observed. However IBD may also be present in asymptomatic subjects. In these cases, diagnosis may be further delayed, incidentally done or missed.

Aims & Methods: we analyzed an electronic database of a regional colorectal cancer population screening program offered to subjects from 50 to 70 years old with faecal occult blood. From 1 September 2013 to 31 August 2018, among subjects who underwent colonoscopy in a single hospital, we identified subjects with endoscopic findings suggestive of IBD. Of these, we retrieved histological findings as well as information on other examinations and possible therapeutic decisions.

Results: 3972 subjects undergoing to colonoscopy were enrolled. In 46 (1.16%) subjects (24 men, mean age ± SD 60.3 ± 6.8 years) endoscopic findings suggestive of IBD were present: 35 of CD and 11 of UC; none of these subjects were taking oral anticoagulants or NSAIDs and reported gastrointestinal symptoms. After a median follow-up of 12 months (range 2-58), a definitive diagnosis of IBD was done in 13 subjects (0.33%). Of these, 3 already underwent to colonoscopy in the context of the same program and 1 showed familiarity for IBD. Nine were diagnosed with CD (7 men, 60.0 ± 6.6 years) and 4 with UC (3 men, 59.1 ± 6.9 years). In CD population, 4 patients showed colonic, 4 ileal and 1 ileo-colonic location; 1 was treated with steroids and then with vedolizumab, 1 with steroids and then with azathioprine, 1 with 5-ASA, 1 with Budesonide, while 5 did not receive any therapy. In UC population, 2 patients showed extension limited to rectum and 2 to rectum and sigmoid colon; all patients started therapy with 5-ASA, 1with systemic steroids and Vedolizumab.

Conclusion: prevalence of IBD in a colorectal cancer population screening program is 0.33%. IBD diagnosis can be missed in asymptomatic subjects, but only 1 out of 4 subjects with endoscopic findings suggestive of IBD is eventually diagnosed as affected by CD or UC.

Disclosure: Nothing to disclose

P0340 GUT MICROBIOME OF PATIENTS WITH ULCERATIVE COLITIS

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Introduction: The etiology of inflammatory bowel diseases (IBD), including ulcerative colitis (UC), has not been established. The role of microbiota in the development of intestinal wall inflammation is still unclear. Can dysbiosis be one of the causes of the disease, or is it a consequence of it? We still do not know.

Aims & Methods: Our study was prospective aimed to evaluate the composition of the gut transient and mucosal microbiome in various forms of UC by real-time polymerase chain reaction (RT-PCR). None of patients had received antibiotics or probiotics previously. Stool samples and mucosal biopsies were collected for each participant immediately frozen until analysis. 70 patients with UC were included. The median age was 40±14.4 years (range 18-69). 43 were female (61.4%), 27 - male (38.6%). Duration of the disease was 7.22±6.9 years (range 0.5-38). Extensive colitis was diagnosed in 78.6% cases (n=55), left-sided colitis - 21.4% (n=15). Acute UC was found in 3 (4.3%) patients, relapsing course of the disease in 29 (41.4%) and remitting course in 38 (54.3%) patients. The activity of the UC (Truelove-Witts classification) was variable: mild - 38 (54.3%), moderate - 14 (20%) and clinical remission - 18 (25.7%). PCR diagnostics of stud-

ied samples was carried out using a DT-96 amplificator (DNA-Technology, Russia). The non-parametric Mann-Whitney test was performed to calculate the confidence.

Results: Using RT-PCR, the following bacterial phylotypes were isolated: *Firmicutes, Bacteroidetes, Actinobacteria, Euryarchaeota, Fusobacteriaceae, Verrucomicrobia,* and *Proteobacteria.* When comparing the microbial composition in stool samples and mucosal biopsies of the affected parts of the intestine in left-sided UC were revealed the following differences. The total bacterial mass of biopsies (4.736) is less compared to the total bacterial mass of fecal samples (7.240) (p< 0.05). In stool samples the concentration of *Methanobrevibacter spp* (p< 0.05), *Fusobacteriaceae* (p< 0.05), *Akkermansia muciniphila* (p=0.0441), *Staphylococcus spp* (p=0.0002), *Anaerococcuscus spp* (p=0.0308), *Helicobacter spp* (p < 0.05), *Bdelovibrio* (p=0.0017), *Suterella wadsworthensis* (p=0.0295), *Pseudomonas spp* (p< 0.05), *Campylobacter spp* (p< 0.05), *Mageebacillus indolicus* (p< 0.05), *Clostridium leptum gr-* (p=0.0025) was significantly less. The number of *Lactobacillus spp* is reduced in the biopsy compared to stool samples (p=0.0434). The difference in the microbes' concentration in stool samples and biopsies from unaffected sections in left-sided UC is similar to the above data (p< 0.05).

The content of *Clostridium leptum gr-* is significantly reduced in the inflamed part of the intestine (p=0.03). In patients with extensive UC, when comparing stool samples and biopsies, a significant decrease in the concentration of 15 species in stool samples (p< 0.05) was found. The number of *Lactobacillus spp* is reduced in the biopsies compared to stool samples (p< 0.05).

Conclusion: In any form of UC, stool samples significantly reduced microbes' concentration in types *Euryarchaeota, Fusobacteriaceae, Verrucomicrobia,* and *Proteobacteria.* The content of *Lactobacillus spp* in the affected areas of the intestine has been reduced. Transient microbiota differs in composition from the mucosal and does not reflect the real microbial diversity of mucosal microbiome. Its definition in routine practice is not diagnostically significant. The composition of mucosal microbiota of the right and left sections of large intestine in left-sided UC was not significantly different.

Disclosure: Nothing to disclose

P0341 ASSESSMENT OF ENDOTHELIAL FUNCTION AND CARDIOVASCULAR RISK IN COEXISTING INFLAMMATORY BOWEL DISEASE AND EXTRAINTESTINAL MANIFESTATIONS:PRELIMINARY DATA OF A PROSPECTIVE STUDY

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Introduction: Inflammatory bowel diseases (IBD) can be considered as systemic conditions for the possible involvement of extraintestinal manifestations (EIMs). Previous studies showed that patients with IBD in an active phase have an increased cardiovascular (CV) risk compared to healthy controls. Flow-mediated dilation (FMD) of brachial artery and carotid intima-media thickness (IMT) are ultrasound, validated techniques, which assess endothelial function and atherosclerosis. We aimed to assess CV risk in IBD patients with EIMs in order to evaluate a possible influence of extraintestinal inflammatory activity.

Aims & Methods: We enrolled 56 consecutive subjects with an established diagnosis of IBD associated with EIMs and 20 patients with IBD without EIMs as control group. The first group was subsequently divided into 4 subgroups on the bases of disease activity (patients with both active or inactive IBD and EIMs, patients with intestinal symptoms and no signs of EIM and vice versa). Patients were screened for common CV risk factors and underwent FMD and IMT evaluation.

We performed Kruskal-Wallis test, followed by Dunn's post-hoc test for multiple comparisons for analysis of continuous variables. Spearman's test was used for correlation analysis.

Results: FMD and IMT values showed no statistically significant difference in any group (P=0.64 and P=0.65) nor when we considered only the presence of active or inactive EIM (control group vs active or vs inactive EIM, P=0.44 and P=0.29). FMD showed no correlation with patients' and disease characteristics, while IMT correlated with BMI (p< 0.0001).

Conclusion: Our study showed no difference in CV risk in IBD patients with a concomitant EIM. However, it cannot address definite conclusions , since the lack of statistically significant differences is probably due to the small sample size. Therefore, we should obtain a clear picture about the possible relationship between CV risk and EIM in IBD only when the results will involve an adequate sample size.
Disclosure: Nothing to disclose

P0342 INADEQUATE FERTILITY AND PREGNANCY KNOWLEDGE IS RELATED TO VOLUNTARY CHILDLESSNESS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE IN SERBIA-RESULTS FROM TWO REFERRAL CENTERS

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Introduction: Inflammatory bowel diseases (IBD) are frequently diagnosed in individuals who are in the reproductive period. Lack of fertility and pregnancy-related knowledge leads to subsequent voluntary childlessness, although pregnancy outcome is favorable in the majority of IBD patients that plan pregnancy when the disease is in remission.
Aims & Methods: The aim of the study was to investigate specific reproductive knowledge in patients with IBD. In this study 165 female IBD patients (aged 20 to 74) treated in the Clinic for Gastroenterology and Hepatology Clinical center of Serbia and Clinical center of Vojvodina completed a standardized questionnaire consisting of demographic characteristics, pregnancy, and abortion data, IBD phenotype and therapy. Disease-related pregnancy knowledge was assessed using Crohn's and colitis pregnancy knowledge score (CCPKnow). CCPKnow consists of 18 questions and scores lower than 7 are considered poor. Patients were divided according to the diagnosis into the group with ulcerative colitis (UC) and Crohn's disease (CD). These two groups were further stratified according to the occurrence of pregnancy after IBD diagnosis.
Results: We analyzed data from 165 IBD patients (73 UC, 92 CD). In UC group 23 (31.5%) and in CD group 32 (34.9%) were childless. After IBD was diagnosed a total of 48 pregnancies occurred. In 17 UC patients, there were 24 pregnancies while in CD patients a total of 18 women had 24 pregnancies. Statistically, a significant difference was shown in UC patients when the average number of children was compared between groups with and without pregnancy after IBD diagnosis (2.05 vs.0.94, p< 0.001). The average age at diagnosis in UC patients who gave birth after IBD diagnosis was 24±6 compared to 37±13years in the group who did not give birth after IBD diagnosis (p< 0.001). Average CCPKnow score surprisingly did not differ between the two groups (6.82 vs. 5.76 p>0.05). CD patients who were pregnant after diagnosis were significantly younger (p< 0.001) compared to those who did not (21±7 vs 33±12, respectively) and they had an average of 1.5 children compared to 0.96 in those who did not have children after IBD was diagnosed (p< 0.05). The CCPKnow score was higher in patients that had children after IBD diagnosis although the difference did not reach statistical significance (7.61 vs. 5.31, p=0.051). The average number of children in mothers on biological therapy was 1.0 on infliximab (IFX) and 0.96 on adalimumab (ADA).
Conclusion: : Our study confirmed that voluntary childlessness is common in female patients with IBD. The CCPKnow score is extremely low in the examined population and is not related to the decision to have children after IBD diagnosis. Patients who had children after IBD was diagnosed were significantly younger at diagnosis and had more children than those who remained childless after IBD was diagnosed. There is an urgent need to improve pregnancy and fertility-related knowledge in IBD patients in Serbia.
Disclosure: Nothing to disclose

P0343 ASSOCIATION OF VITAMIN D STATUS WITH IRON DEFICIENCY AND HEPCIDIN SERUM EXPRESSION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Vitamin D deficiency and iron deficiency are common comorbidities in inflammatory bowel disease (IBD) and linked to complications like osteoporosis and anemia, respectively[1]. There is emerging evidence that active vitamin D may enhance intestinal iron absorption and prevent iron deficiency and iron deficiency anemia by direct suppression of hepcidin mRNA transcription[2,3].
Aims & Methods: To investigate a potential influence of vitamin D status on iron metabolism, iron deficiency and iron deficiency anemia in IBD, 25-hydroxyvitamin D levels, 1,25-dihydroxyvitamin D levels, hepcidin serum concentrations, biochemical markers of iron status (serum iron, ferritin, transferrin, transferrin saturation) and hemoglobin levels were measured in 104 adult patients with IBD (67 patients with Crohn's disease [CD] and 37 patients with ulcerative colitis [UC]). Multivariate logistic and linear regression models included age, gender, body mass index, smoking status, disease activity and C-reactive protein levels as covariables when assessing the association of vitamin D levels with iron deficiency, iron deficiency anemia, hemoglobin levels and biochemical markers of iron status. Patients, who were substituted with iron during the last 30 days, were excluded from the study. For iron substitutions dating back longer than 30 days (up to three months), a corresponding categorical covariable was introduced in a multivariate confirmatory model. For categorical considerations, vitamin D deficiency was defined as 25-OH-vitamin D < 20 ng/ml. Iron deficiency and iron deficiency anemia in IBD were defined according to ECCO guidelines.
Results: In multivariate logistic regression models controlling for age, gender, body mass index, smoking status, disease activity and C-reactive protein levels, lower 25-hydroxyvitamin D levels were significantly associated with iron deficiency in patients with IBD (β [SE] = - 0.064 [0.030], P = 0.029). In multivariate linear regression models, vitamin D deficiency was significantly associated with decreased levels of ferritin (β [SE] = 0.25 [0.11], P = 0.024) and transferrin saturation (β [SE] = 8.41 [4.07], P = 0.044) in IBD. IBD patients with lower 25-hydroxyvitamin D levels exhibited significantly lower serum iron levels (β [SE] = 0.94 [0.42], P = 0.029) and ferritin levels (β [SE] = 0.013 [0.0059], P = 0.037). Moreover, multivariate linear regression models showed a significant negative association of higher 1,25-dihydroxyvitamin D : 25-hydroxyvitamin D ratios with lower hepcidin serum levels in IBD (β [SE] = - 4.31 [1.67], P = 0.012). For CD, multivariate linear logistic regression analysis revealed a significant association of increased concentrations of active 1,25-dihydroxyvitamin D with higher transferrin saturation levels (β [SE] = 0.43 [0.18], P = 0.027). In CD patients, there was a significant positive correlation of 25-hydroxyvitamin D levels with iron (Kendalls Tau 0.17, P < 0.05), ferritin (Kendalls Tau 0.18, P < 0.05) and transferrin saturation (Kendalls Tau 0.21, P < 0.05). Furthermore, levels of active 1,25-dihydroxyvitamin D correlated positively with transferrin saturation in patients with CD (Kendalls Tau 0.21, P < 0.05).
Conclusion: Vitamin D deficiency in IBD patients correlates significantly with parameters indicating iron deficiency. An optimized vitamin D status may ameliorate iron deficiency in IBD, potentially by downregulation of hepcidin serum expression, suggesting a beneficial role for vitamin D substitution. Further interventional studies are warranted to prove this hypothesis.
References: 1. Hwang, C., Ross, V. & Mahadevan, U. Micronutrient deficiencies in inflammatory bowel disease: from A to zinc. Inflamm Bowel Dis 18, 1961-1981. 2. Moran-Lev, H., et al. Vitamin D Decreases Hepcidin and Inflammatory Markers in Newly Diagnosed Inflammatory Bowel Disease Pediatric Patients- A Prospective Study. J Crohns Colitis (2019). 3. Smith, E.M. & Tangpricha, V. Vitamin D and anemia: insights into an emerging association. Curr Opin Endocrinol Diabetes Obes 22, 432-438 (2015).
Disclosure: Nothing to disclose

P0344 NEUROCOGNITIVE DEFICITS IN ADULT INFLAMMATORY BOWEL DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: People with inflammatory bowel disease (IBD) are exposed to multiple risk factors for cognitive impairment, including inflammation, nutritional deficiencies, depression, pain and vascular damage. Furthermore, reduced productivity and subjective cognitive difficulties are highly prevalent in people with IBD. To date, however, the presence of neurocognitive deficits in people with IBD has not been systematically evaluated.

Aims & Methods: Using a PRISMA systematic review and meta-analysis, we tested for domain-specific neurocognitive deficits in people with IBD compared to healthy controls. We systematically searched EMBASE, Web of Knowledge, Medline, CINAHL, PsycINFO and grey literature from inception to 31 December 2018 for cross-sectional- and longitudinal studies comparing cognitive function in adults with IBD versus healthy controls. According to DSM-5 classification, cognitive measures were stratified by domains of executive function (including working memory), attention, perceptual-motor, learning and recall, language, social cognition, as well as premorbid IQ. For any cognitive domain reported by 3 or more studies, we performed random-effects meta-analysis using STATA 15.0 to calculate the standardised mean difference (SMD) between IBD and control groups; higher scores reflected better performance. Where a single study used multiple measures within a single domain, we averaged the effect sizes. Between-study heterogeneity was assessed using the I^2 statistic; publication bias estimated using Egger's intercept test; and study quality assessed using the IBD-modified Newcastle-Ottawa scale. For significant findings, we used Monte-Carlo permutation tests for meta-regression to test the following potential moderators of cognitive impairment: age, sex (% female), IBD disease duration, depressive symptoms (% of maximum questionnaire score) and years of formal education.

Results: Of 8287 articles screened, 11 were included, of which 3-, 6-, and 1 were of high, moderate and low quality respectively. All studies were cross-sectional; none specifically recruited older adults; and 6-, 1-, and 4 recruited populations with Crohn's disease, ulcerative colitis and mixed IBD respectively. The sample (n=674 people) had mean age 39.9 years and 60.2% were female. Despite no difference between groups in premorbid IQ (p=0.13), the IBD group showed deficits compared to healthy controls in attention (pooled effect size (ES) = -0.40 [95% confidence interval -0.69 to -0.10], p=0.009, I^2=4.3%) and executive function (pooled ES = -0.38 [-0.70 to -0.07], p=0.017, I^2=20.3%), including specifically in working memory (pooled ES = 0.73 [-1.09 to -0.37], p< 0.001, I^2=0%). By contrast, deficits in learning and recall were inconsistent (pooled ES = -0.50 [-1.08 to 0.08], p=0.089, I^2=72.8%) and data for other cognitive domains insufficient for meta-analysis. There was no evidence of publication bias. Although there were no significant moderators of cognitive impairment, power of meta-regression was limited by low between-study heterogeneity.

Conclusion: Despite comparable premorbid IQ, people with IBD show small-to-moderate deficits in attention and overall executive function, including large deficits in working memory. Such deficits may impact adversely on productivity. Longitudinal studies are required to test the course of neurocognitive deficits - including specifically in older adults - whilst testing the biological and psychological pathways that can be modified to improve cognitive function in people with IBD.

Disclosure: Nothing to disclose

P0345 THE CHANGING PATTERN OF INFLAMMATORY BOWEL DISEASE INCIDENCE IN NORTHERN FRANCE: A CONTINUING INCREASE IN THE YOUNG WOMEN (1988-2014)

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Introduction: Inflammatory Bowel Disease (IBD) incidence rates seem to be stabilised in adults in industrialised countries unlike in the paediatric population.

Aims & Methods: The aim of this study was to describe changes in incidence and phenotypic presentation of adult-onset IBD in northern France during a 27-year period. All adult-onset IBD patients (≥ 17 years at IBD diagnosis) were issued from the EPIMAD population-based IBD registry in France between 1988 and 2014. Standardized incidence rates were calculated for Crohn's Disease (CD) and Ulcerative Colitis (UC) in the whole population, and separately according to age and gender. Digestive location was defined according to the Montreal classification.

Results: 17,686 incident IBD cases were recorded including 10,206 CD (58%), 6,839 UC (39%) and 640 IBD unclassified (IBDU) (4%). Median age at diagnosis was lower in CD (28 years, interquartile range (IQR) [22-40]) than in UC (36, IQR[27-49]) (p<0.0001). Age at diagnosis was stable in time for both diseases (p=0.37 in CD and p=0.52 in UC). Females were younger at diagnosis than men, especially in UC : respectively 28 IQR[21-39] vs 29 IQR[22-40] in CD (p<0.0001) and 33 IQR[26-45] vs 39 IQR[28-51] (p<0.0001) in UC. The proportion of females were significantly higher in CD (females/males = 1.36) conversely to UC (females/males = 0.84) (P<0.0001). Sex ratio was stable over time in CD (p=0.28) and changed in UC with an inversion from 0.70 in 1988-1990 to 1.10 in 2012-2014 (p=0.001). Median time between onset of symptoms and IBD diagnosis was consistently 3 months IQR[1-6]. Mean annual incidence was $13.5/10^5$ 95% Confidence Interval (95%CI) [13.3 - 13.7] for IBD overall, $7.5/10^5$ 95%CI[7.4 - 7.7] for CD, $5.4/10^5$ 95%CI[5.3 - 5.6] for UC and $0.51/10^5$ 95%CI[0.46 - 0.55] for IBDU. From 1988-1990 to 2012-2014, a continuous increase in incidence of CD was observed while that of UC stayed stable: for CD from 5.5 to $7.9/10^5$ (+44%, p< 0.0001) and for UC at $5.4/10^5$. The most important increase of IBD incidence rate was in young women (17-39 years): average percent change of +1.9% per year in CD (p< 0.0001) and +1.7% per year in UC (p< 0.0001). In CD, over time, pure colonic location (L2) decreased from 41% (1988-1990) to 25% (2012-2014), while pure ileal (L1) and ileo-colonic (L3) locations increased from 20% to 26% and from 39% to 49%, respectively (p< 0.0001). During the same period, explorations of the small bowel increased from 76% to 86%. In UC, proctitis (E1) and left sided colitis (E2) represented 38% and 37% of the locations.

Conclusion: In this French population-based study, CD incidence increases continuously during a 27-year period, especially CD with ileal involvement, while UC incidence remains stable. These results highlight the difference in immunopathology between each CD phenotype. Moreover, CD and UC incidence rates rise mostly in young women (17-39 years), suggesting that one or more strong environmental factors may predispose the women to IBD.

Disclosure: Nothing to disclose

P0346 INFLAMMATORY BOWEL DISEASE IS ASSOCIATED WITH A HIGHER RISK OF RENAL CANCER

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Introduction: Inflammatory bowel disease (IBD) including ulcerative colitis (UC) and Crohn's disease (CD) has been implicated as a precursor to extra-intestinal cancers. Recent studies have shown an increased risk of renal cancer.

The aim of our study is to conduct a population-based study to explore the risk of renal cancer in IBD, and evaluate the role of IBD associated medications.

Aims & Methods: A population-based study was conducted using a cloud-based, HIPPA-enabled web platform called Explorys (IBM, New York) to collect aggregated de-identified electronic health records. At the time of the study, Explorys had access to over 62 million unique records. Data was obtained using ICD-9 code criteria for Crohn's disease, ulcerative colitis, and malignant neoplasm of the kidney. Each cohort was further evaluated for baseline patient characteristics and usage of IBD-associated medications, including corticosteroids, biologics, and immunomodulators. All-cause mortality was also reported. Comparisons were reported for relative risks (RR) with 95% confidence intervals (CI) in a random effect model.

Results: Renal cancer was more common in patients with both UC [RR 3.51 (95% CI: 3.29-3.74), P< 0.0001] and CD [RR 3.45 (95% CI: 3.25-3.66), P< 0.0001] vs. the general population. Patients over the age of 65, males, and Caucasians with CD had an increased risk of renal cancer. Patients over the age of 65, males, Caucasians and African-Americans with UC had an increased risk of renal cancer. In patients with CD, subsequent renal cancer had an increased risk in the setting of corticosteroids [RR 2.45 (95% CI: 2.12-2.82), P< 0.001], biologics [RR 1.86 (95% CI: 1.65-2.10), P< 0.001], and immunomodulators [RR 1.37 (95% CI: 1.19-1.58), P< 0.001]. In patients with UC, renal cancer risk was elevated in patients on corticosteroids [RR 2.24 (95% CI: 1.92-2.62), P< 0.001], biologics [RR 1.61 (95% CI: 1.41-1.83), P< 0.0001] and immunomodulators [RR 1.44 (95% CI: 1.20-1.72), P< 0.001]. All-cause mortality was higher in patients with renal cancer in patients with CD [RR 3.91 (95% CI: 3.35-4.56), P< 0.0001] and UC [RR 3.55 (95% CI: 3.01- 4.19), P< 0.0001].

Conclusion: Risk of renal cancer is higher in patients with ulcerative colitis and Crohn's Disease. All-cause mortality risk is significantly higher in patients with UC and CD with renal cancer.

Disclosure: Nothing to disclose

P0347 PHENOTYPIC CHARACTERISTICS OF ULCERATIVE COLITIS IN LATIN AMERICANS VERSUS HISPANICS FROM THE UNITED STATES: A SYSTEMATIC REVIEW WITH META-ANALYSIS

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Introduction: Latin America has been experiencing a rise in the prevalence and incidence of inflammatory bowel disease. Environmental and dietary changes may be contributing to this rise. Ulcerative colitis (UC) is more common than Crohn's disease in Latin America, but it is unclear whether the phenotype seen in Latin America is similar to the one seen in Hispanics residing in the United States (U.S.), two locations with distinct environmental and dietary exposures. In addition, it is yet to be determined whether there are major differences in the phenotype of ulcerative colitis across Latin America.

Aims & Methods: We conducted a systematic review with meta-analysis of population-based studies to compare the phenotypic characteristics of UC in Latin America with UC in Hispanic-Americans in the U.S. We also aimed to compare phenotype of UC across Latin American countries. Phenotype was defined using the Montreal classification. A systematic search was conducted using MEDLINE and EMBASE. Google Scholar was used to search for unpublished data.

Inclusion criteria:

(i) studies describing the phenotype of UC in Latin America and Hispanics in the U.S.

(ii) age equal to or greater than 18 years.

Exclusion criteria:

(i) prevalence or incidence studies not describing phenotype.

A random effects model was chosen "a priori" for analysis of pooled proportions.

Results: A total of 4,627 studies were screened. There were 34 studies from 9 countries in Latin America and 7 studies from Hispanics in the U.S. This included 4,082 patients with UC from Latin America and 390 Hispanic patients with UC in the U.S.

The predominant phenotype in Latin America was proctitis (E1) with a pooled proportion of 0.37 (95% CI 0.28-0.45, I^2 98.2%), as compared with 0.08 (95% CI 0.05-0.11, I^2 18%), p=0.003, in the U.S. Extensive colitis (E3) was present in two-thirds of Hispanics in the U.S. as compared with only one-third of Latin Americans, p<0.001. There was no difference in the prevalence of left-sided colitis (E2) in Latin America and the U.S, with nearly one-third of patients showing this phenotype in both regions, p=0.82. Among the Latin American countries, Cuba and Puerto Rico had the highest frequency of proctitis with nearly two-thirds of patients showing this phenotype. Left-sided colitis was more frequent in Colombia (0.39, 95% CI 0.34-0.45) and Peru (0.36, 95% CI 0.29-0.44), whereas, extensive colitis was more frequent in Argentina (0.67, 95% CI 0.59-0.75) and Mexico (0.54, 95% CI 0.51-0.57).

Variables	Countries of Origin	N	Prevalence	95 % Confidence Interval		I Squared	ES P Value (%)	Meta regression p value
E1: Proctitis	Latin America	33	0.37	0.28	0.45	98.2		0.003
	Hispanic Americans	6	0.08	0.05	0.11	18.06		
E2: Left-sided colitis	Latin America	30	0.27	0.23	0.32	91.11		0.815
	Hispanic Americans	5	0.26	0.15	0.38	82.01		
E3: Extensive Colitis	Latin America	34	0.38	0.32	0.44	95.26		<0.001
	Hispanic Americans	6	0.64	0.52	0.77	84.01		

[Phenotypic Characteristics of Ulcerative Colitis in Hispanics from Latin America versus the United States]

Conclusion: The phenotype of UC varies between Latin America and the U.S. Proctitis was more frequent in Latin America, whereas, extensive colitis was the predominant phenotype in Hispanics from the U.S. This may suggest that Hispanics that develop UC in the U.S. have a more aggressive form of the disease. In Latin America, Cubans and Puerto Ricans have a milder form of UC as compared with Argentinians and Mexicans who are more likely to have extensive disease. Further research is warranted to determine underlying genetic, environmental and dietary factors which may account for these differences.

Disclosure: Nothing to disclose

P0348 TREFOIL FACTOR 3 IS HIGHLY PREDICTIVE OF COMPLETE MUCOSAL HEALING INDEPENDENTLY AND IN COMBINATION WITH C-REACTIVE PROTEIN IN PATIENTS WITH ULCERATIVE COLITIS

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Introduction: Trefoil factors (TFFs) include a family of three mucin-associated peptides secreted by goblet cells in the intestinal mucosa. They have a key role in maintaining mucosal barrier integrity and are up-regulated at the site of mucosal damage. It has recently been suggested that serum levels of TFF3 can predict disease activity and reflect mucosal healing (MH) in ulcerative colitis (UC) patients with minimal disease activity. However, its potential to predict complete MH independently or in combination with other biomarkers has never been addressed.

Aims & Methods: In the current study we aimed to evaluate the role of trefoil factor 3 (TFF3) as a marker for complete MH in patients with UC. 116 consecutive UC patients were enrolled. TFF3 levels were measured by ELISA and were compared to clinical activity, assessed by Lichtiger Index, fecal calprotectin (FCP) and C-reactive protein (CRP) levels. Colonoscopy was performed in all the patients and the findings were graded according to Mayo endoscopic score (EMS) and UC endoscopic index of severity (UCEIS).

Results: TFF3 levels were significantly correlated with Lichtiger Index (r = 0.736, p < 0.001), EMS (r = 0.811, p < 0.001), UCEIS (r = 0.820, p < 0.001), FCP (r = 0.696, p < 0.001) and CRP (r=0.405, p < 0.001). The TFF3 cut-off level of 6.74 ng/ml indicated complete MH (EMS = 0; UCEIS =0) with a sensitivity and specificity of 0.879 and 0.869, respectively (area under the curve (AUC), 0.927; 95% confidence interval, 0.877-0.976). The DeLong's test revealed no significant difference between the AUC of TFF3+CRP and the AUC of FCP (Z = 1.717, p = 0.086), AUC of TFF3+FCP (Z = 1.908, p = 0.056), and AUC of TFF3+CRP+FCPP (Z = 1.915, p = 0.056). However, the AUC of TFF3+CRP showed significant difference with the AUC of TFF3 (Z = 2.210, p = 0.027) and the AUC of CRP (Z = 3.145, p = 0.002) for predicting complete MH.

Conclusion: TFF3 levels correlated significantly with clinical activity, endoscopic indices, CRP and FCP. TFF3 is highly predictive marker of complete MH independently and in combination with CRP in patients with UC

Disclosure: Nothing to disclose

P0349 THE Y-ECCO/CLINCOM 2019 SURVEY ON POSTOPERATIVE CROHN'S DISEASE RECURRENCE SUGGESTS OVERTREATMENT WITH PROPHYLACTIC BIOLOGICAL THERAPY

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Introduction: Prevention of post-operative recurrence (POR) is a controversial field in Crohn's disease. Despite evidence for some clinical risk factors favoring POR (previous ileocolonic resections, extensive resection, penetrating disease, active smoking), there is no total agreement among guidelines[1-2] on initiation of postoperative prophylactic therapy, preferred drug as well as on the modality and timing of POR assessments.

Aims & Methods: Our aim was to obtain an international perspective on the current adopted therapies and strategies (immediate postoperative prophylaxis versus endoscopy-driven) with regard to prevention of POR. A 11-question anonymous survey was proposed to all gastroenterologists participating at various ECCO pre-meeting workshops in March 2019.

Results: Data from 168 participants were collected (participation rate 24%). Median gastroenterology experience was 8 years [IQR 4-14 years], 65% junior (≤10 years of practice), 35% senior (>10 years). The majority were European (67%), while the remainder were representatives of 19 countries across all five continents. Most participants (60%) were working in an academic hospital.

Post-operative endoscopic evaluation to assess POR was routinely performed within 12 months by 87% of respondents. This was the same for patients who do or do not receive immediate postoperative prophylactic therapy. After a first endoscopy without POR, 89% of physicians reported following up patients with a combination of clinical examination, lab test and fecal calprotectin, and 45% considered endoscopy as a routine assessment modality. Comparison between young and senior gastroenterologists did not show any statistical difference (p>0.05).

Most respondents (60%) reported starting medical prophylaxis against POR in naïve patients if 1 or more risk factors are present, while 16% of respondents would prescribe immunoprophylaxis even in patients without risk factors. Only 20% of participants reported that they would wait for endoscopic proof of recurrence (Rutgeerts score ≥i2) before starting immunomodulators. Data were similar between young and senior gastroenterologists (p>0.05).

In regard to the class of drug, the number of POR risk factors lead the majority (59%) to prescribe biologics over immunosuppressants. Among biologics, 98% of respondents having access to anti-TNF reported a routine use of them in this setting, while 62% and 56% of physicians with access to vedolizumab and ustekinumab respectively prescribed these drugs for POR prophylaxis.

In the specific clinical context of perianal disease, fistulizing phenotype or concomitant colonic disease, most of the participants reported adopting an immediate POR prophylaxis in 98%, 85% and 88% of cases, respectively. Conversely, a significant number of respondents were more prone to an endoscopy-driven treatment in the elderly (42%) and in long-standing disease after failure of thiopurines (51%). No significant difference (p>0.05) in post-operative approach was registered in these scenarios between young and experienced gastroenterologists.

Conclusion: Clinicians are well aware of the risk of POR in Crohn's disease and tight endoscopic control within twelve months is often proposed. After a first ileocolonoscopy without POR, most respondents reported relying on fecal calprotectin for routine monitoring. The surprisingly high rate of immediate postoperative prophylactic therapy with biologics, even in the absence of clear endoscopic recurrence or clinical risk factors for POR, highlights the need for a randomized trial comparing immediate prophylaxis with endoscopy-driven therapy.

References: [1] Paolo Gionchetti, Axel Dignass, Silvio Danese, et al., on behalf of ECCO; 3rd European Evidence-based Consensus on the Diagnosis and Management of Crohn's Disease 2016: Part 2: Surgical Management and Special Situations, Journal of Crohn's and Colitis, Volume 11, Issue 2, 1 February 2017, Pages 135-149 [2] Nguyen GC, Loftus EV Jr, Hirano I, et al., AGA Institute Clinical Guidelines Committee. American Gastroenterological Association Institute Guideline on the Management of Crohn's Disease After Surgical Resection. Gastroenterology. 2017 Jan;152(1):271-275

Disclosure: Nothing to disclose

P0350 INTERLEUKINS LEVELS: ARE WE ON THE ROAD TO TAILORED THERAPY IN INFLAMMATORY BOWEL DISEASE?

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Introduction: There is a rising interest in identifying easy to dose disease markers to predict response to therapy in inflammatory bowel disease (IBD) patients.

Several markers have been studied, but none of them has been validated.

Aims & Methods: The aim of our study was to understand the role of inflammatory interleukins in predicting the response to immunosuppressive or biological therapy. A monocentric prospective study was conducted. Forty IBD patients who needed to start immunosuppressive or biological drugs were included. For each patient serological levels of interleukin (IL)1-B, IL4, IL6, IL8, Il10, IL12p70, IL17, IFN-gamma, TNF-alfa, TGF-beta-1 were dosed at the time of enrollment (T0) and after three months of immunosuppressive or biological therapy (T3). To dose these cytokines, multiplex Bio-Plex® system was used.

Results: Among the 40 enrolled patients, 32 (80%) were suffering from Crohn's disease (CD) and 8 from Ulcerative Colitis (UC); the mean age was 46.6 years (18-79 years).

IL1-B T0 was detectable only in CD patients (mean value 0.05 pg/ml), with no difference due to illness localization.

Serological T0 TNF-a levels correlated with pre-treatment endoscopic activity: among patients with moderate or severe endoscopical activity median value was 20.94 pg/ml while among mild activity or remission group median value was 13 pg/ml (p=0,034).

T0 IL8 levels correlated both with pre-treatment fecal calprotectin (p=0,03; r= 0.437) and endoscopic activity (median value 28,07 pg/ml for moderate to severe activity vs 5,79 pg/ml median value for mild activity/remission; p=0,023)

T0 TGF-b1 levels were significantly lower in CD patients than in UC patients (p = 0.0076).

Low levels of IL6 at T0 (< =0.54 pg/ml) predicted a negativization of fecal calprotectin after three months of adalimumab (ADA) administration (area under the curve [AUC] = 0.89; p=0,001; sensitivity = 72.7%; specificity = 100%). Low levels (median value = 0.54 pg/ml) of T0 IL6 correlated with a higher probability to response to azathioprine (AZA) too (p = 0.049). T0 IL6 >=0.9 pg/ml correlated with higher response to vedolizumab (VEDO).

Patients who responded to AZA had undetectable T0 serological levels of IFN-g, while the ones who did not respond had a median IFN-g level of 0.11 pg/ml (p = 0.043).

T0 serological levels of TGF-b1 correlated with response to AZA (< 4.7 pg/ml) and to ADA (>6.57 pg/ml) (p = 0.027).

Low IL12p70 levels predicted a better response to therapy at all (p = 0.0095), but not for each drug separately.

T0 IL8 levels predicted response to vedolizumab therapy: at ROC curve analysis we observed for >6,6 pg/ml levels of IL8 a response to VEDO in all patients (AUC = 1; sensitivity 100%; specificity 100%; p=0.0001).

Conclusion: IFN-g and TGF-b1 may be useful to identify AZA responders and IL8 and IL6 levels could be good predictors of response to both biological and immunosuppressive drugs. Our study is a first step for tailored therapy in IBD patients.

Disclosure: Nothing to disclose

P0351 MEASURING INFLIXIMAB DRUG LEVELS CONSISTENTLY: ALIGNMENT TO THE 1ST INTERNATIONAL STANDARD MATERIAL (NIBSC 16/170) USING IDKMONITOR® INFLIXIMAB DRUG LEVEL ELISA LEADS TO AN INCREASE IN THE MEASURED INFLIXIMAB CONCENTRATION

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Introduction: Measuring the concentration of infliximab drug levels in IBD patients is widely practiced. Variability between assays has previously been a problem as inconsistent results are obtained between different laboratories, depending on the methodology and manufacturer used.

Introduction of the 1st International Standard infliximab material (NIBSC 16/170) should allow for alignment of the methods for measuring infliximab, and ultimately more consistent results between laboratories.

Immundiagnostik has aligned the IDKmonitor® Infliximab drug level ELISA by re-calibrating with the International Standard infliximab material (NIBSC 16/170). The impact of this change upon clinical results is explored.

Aims & Methods: The aim of this work is to determine the change in the measured concentration of infliximab using the IDKmonitor® Infliximab drug level ELISA kit before and after alignment with the 1st International Standard infliximab (NIBSC 16/170).

Serum samples received through the routine infliximab monitoring service (n=80) were measured using the IDKmonitor® Infliximab drug level ELISA, using kits manufactured before and after calibration with the 1st International Standard infliximab (NIBSC 16/170). Regression and correlation results were obtained.

Results: Regression analysis of results before and after the calibration provide are good ($R2 = 0.99$). Correlation of the data shows that when aligned to the 1st International Standard infliximab (NIBSC 16/170), the measured concentration of infliximab is higher than that obtained with the kit manufactured before the calibration (i.e. post calibration result = 1.35x pre-calibration result + 0.81).

Conclusion: International standardisation of infliximab drug level concentrations is now possible due to the introduction of the 1st International standard infliximab. This is a step change towards consistency of measuring infliximab drug levels.

However, clinicians who are using this test for monitoring need to be aware of this change and consider patient results carefully in the light of this information.

Disclosure: Nothing to disclose

P0352 LEVELS OF SERUM FREE THIOLS ARE SUPERIOR TO FECAL CALPROTECTIN IN PREDICTING ENDOSCOPIC DISEASE ACTIVITY IN INFLAMMATORY BOWEL DISEASE

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Introduction: Oxidative stress is considered to play a pivotal role in the pathogenesis of Inflammatory Bowel Diseases (IBD). Serum free thiol groups (R-SH) reliably reflect systemic oxidative stress, since they are readily oxidized by reactive species. Endoscopic examination is the gold standard to determine disease activity in IBD. In clinical practice, fecal calprotectin (FC) levels are most widely used as surrogate marker for endoscopically proven disease activity.

However, its diagnostic accuracy and applicability are still subject to de-

bate. Systemic biomarkers for disease activity are urgently sought to improve disease activity monitoring and to avoid repeated endoscopic examination.

Aims & Methods: In this study, we aimed to establish concentrations of serum free thiols in IBD and assessed their potential utility as a discriminating biomarker for different grades of endoscopic disease activity. Serum free thiol concentrations were measured in 78 IBD patients (31 patients with Crohn's disease (CD) and 47 patients with ulcerative colitis (UC)) and 50 healthy controls, adjusted for serum albumin. Albumin-adjusted serum free thiols were analyzed for associations with clinical and biochemical disease parameters. Endoscopic disease activity was assessed by the Simple Endoscopic Score for CD (SES-CD) and Mayo endoscopic subscore for UC, that were merged to create an IBD composite endoscopy score. Non-parametric ROC estimation with cross-validated areas under the curves (AUCs) was used to assess the discriminative value of serum free thiols regarding the degree of endoscopic disease activity (n=54) and to compare this to fecal calprotectin (n=28) in patients for which those data were available.

Results: Mean serum free thiol concentrations were significantly decreased in both CD and UC as compared to healthy controls (19.4±3.1 and 17.8±3.4 vs. 21.1±1.9 µmol/g of albumin, $P < 0.001$). Albumin-adjusted serum free thiols significantly inversely associated with age ($r = -0.49$, $P < 0.01$), platelet counts ($r = -0.29$, $P < 0.01$) and fecal calprotectin levels ($r = -0.32$, $P < 0.05$). Patients with severe endoscopic disease activity demonstrated significantly lower serum free thiol concentrations compared to patients having mild disease activity (16.2±3.1 vs. 20.4±3.4 µmol/g of albumin, $P < 0.01$). Finally, serum free thiols highly accurately discriminated between mild and moderate-to-severe disease activity, better than fecal calprotectin (FC) levels (AUC=0.87, $P < 0.001$ vs. AUC=0.76, $P < 0.05$, respectively). After cross-validation, serum free thiols maintained their predictive accuracy (AUC=0.89, $P < 0.001$).

Conclusion: Serum free thiols are reduced in IBD as compared to healthy controls and strongly correlate with the degree of endoscopic disease activity. Quantifying systemic redox status in IBD may be a promising, minimally invasive strategy to monitor IBD disease activity. Future studies are warranted to further explore free thiols as potential biomarker for IBD disease activity in larger, prospective patient cohorts and serially assess their predictive value in relation to disease course and therapeutic interventions.

Disclosure: Nothing to disclose

P0353 VALIDATION OF NOVEL FECAL INFLAMMATORY MARKER FOR ASSESSMENT OF INFLAMMATORY BOWEL DISEASE ACTIVITY

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Introduction: Diagnosis of inflammatory bowel disease (IBD) require combination of patient history and physical examination in association with laboratory, endoscopic, histologic, and radiographic investigations. Although ileocolonoscopy is the preferred method of diagnosis, assessing disease extent, activity and follow up after therapy but repeated endoscopy is neither practical nor feasible, being invasive, time consuming, and not always well tolerated or accepted.

Therefore, employment of non-invasive biomarkers is needed. No single marker is ideal. Many studies focus on fecal calprotectin (FC) in IBD and confirm its value in diagnosis, disease activity evaluation, effect evaluation, and relapse monitor.

Neopterin, is a metabolite of cyclic guanosine monophosphate that is released by activated T lymphocytes and macrophages after induction by interferon γ. Neopterin release from activated macrophages may provide, at least theoretically by its intrinsic mechanism of release, an advantage over calprotectin which is not secreted and represents a neutrophil-derived protein.

Aims & Methods: ts specificity and sensitivity to To investigate the relation between fecal neopterin (fNeo) excretion and IBD clinical and endoscopic activity indices and compare its specificity to that of fecal calprotectin.

60 patients were included: 30 patients with ulcerative colitis (UC) (15 clinically in remission, 15 active) and 30 patients with Crohn's disease (CD) (15 clinically in remission, 15 active) and 20 healthy control subjects.

FC and fNeo were detected in stool samples by enzyme-linked immuno-sorbent assay (ELISA).

The following indices were calculated at enrollment: for Crohn's disease the Crohn's disease activity index (CDAI) and simple endoscopic score for Crohn's disease (SES-CD); for ulcerative colitis, Simple Clinical Colitis Activity Index (SCCAI) and ulcerative colitis endoscopic index of severity (UCEIS).

Results: Among UC patients, fNeo was higher in those with either clinically active or inactive disease than in control subjects (P=0.001, P=0.040 ; for active and inactive disease vs. controls respectively) but there was no significant difference between both UC groups (P=0.225). For CD patients, fNeo concentration was higher in those with active disease than in those with inactive diseas (P< 0.001) or healthy controls (P=0.001). Nonsignificant trends toward greater fecal neopterin concentration were observed with increased colonic disease involvement. Neopterin was not found to be significantly correlated with all laboratory tests done (Heamoglobin, platelets, white blood cells, ESR, CRP, serum albumin, fecal calprotectin). fNeo was significantly correlated with CDAI (r=0.604, P< 0.001) , SES-CD (r=0.600, P< 0.001) in CD patients but not with SCCAI, UCEIS in UC patients. fNeo was found to have comparable sensitivity and overall accuracy to FC in predicting endoscopic disease activity in CD patients but less in UC and combing both stool tests together increases the sensitivity and specificity of either alone.

Conclusion: Stool neopterin could be used to assess disease activity in CD but not in UC patients as it correlates positively with disease activity indices in CD but not in UC. Thus its measurement represents a novel reliable biomarker useful to detect and monitor the severity of mucosal affection in CD patients more than UC.

Disclosure: Nothing to disclose

P0354 CLINICAL FEATURES, THERAPEUTIC REQUIREMENTS AND EVOLUTION OF PATIENTS WITH CROHN'S DISEASE AND UPPER DIGESTIVE TRACT INVOLVEMENT (CROHNEX STUDY)

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Introduction: Patients with upper (L4) and diffuse (L1 + L4) Crohn's disease (CD) may have a more aggressive and refractory disease course. However, evidence on this particular sub-type of patients is scarce. Clinical guidelines do not offer specific protocols on how to manage them.

Aims & Methods: To identify the clinical characteristics, therapeutic requirements and complications that are independently associated with an upper digestive tract CD involvement.

Retrospective study of cases and controls matched (1: 2) by sex and age in patients with CD (L4 or L1 + L4: cases; L1 or L3: controls) of the ENEIDA database (49 hospitals). The small intestine was evaluated with radiologic and/or endoscopic examination, and complex perianal disease was excluded. Clinical variables: pattern, severity, anaemia; Complications: stenosis, fistula, abscess, perforation and digestive bleeding; Therapeutic requirements: use of antiTNF, second line biologic drug, 1 or more biological treatment, iv iron, blood transfusions, enteral nutrition, endoscopic/radiological treatments, surgeries and hospitalisations were investigated. A logistic regression analysis with those significant variables in univariate analysis (SPSS) was performed.

Results: 941 cases and 1882 controls were identified. Multivariate analysis showed that cases were independently associated to a stricturing pattern at disease diagnose (OR: 1.3 (95% CI: 1-1.6), p = 0.028), anaemia due to iron loss (OR: 1.9 (95% CI: 1.3-2.7), p < 0.002), more extensive involvement (> 30cm) (OR: 2.7 (95% CI: 2.2-3.3), p < 0.0001), and the use of anti-TNF

during follow-up (OR 1.3 CI 95% 1-1.6 p = 0.033). In contrast, they exhibit fewer abscesses (OR: 0.6 (95% CI: 0.5-0.9), p = 0.001) and have less familial history of inflammatory bowel disease (OR 0.7 CI 95% 0.6 -0.9 p = 0.008).

Conclusion: In the most extensive series of upper digestive tract involvement in CD, it is shown that they present a more evolved disease at CD diagnosis, suggesting that these patients may be diagnosed late on time. Consequently, they are more refractory to treatments, requiring more frequently anti-TNF treatment. Chronic anaemia due to iron loss in the absence of endoscopic findings should be suspicious of upper CD involvement. Diagnostic and specific treatment strategy for these patients must be considered including signs that allow a high rate of suspicion and a rapid therapeutic escalation.

Disclosure: Nothing to disclose

P0355 LONGTERM OUTCOMES OF STEROID RESPONSIVE AND NON RESPONSIVE PATIENTS WITH ACUTE SEVERE ULCERATIVE COLITIS

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Introduction: Up to onethird of patients with acute severe ulcerative colitis (ASUC) will fail intravenous steroid (IVS) treatment, requiring rescue therapy with cyclosporin (Cys), infliximab (IFX), or colectomy. Even with the best available therapy, over 1/3 of these patients will still require surgery. Long-term outcomes of steroid responsive (SR) patients have seldom been studied. We hypothesize that this subgroup of patients also presents an unfavorable short and long term prognosis.

Aims & Methods: We hypothesize that SR patients also presents an unfavorable short and long term prognosis.

Retrospective multicenter study including patients fulfilling Truelove and Witts criteria for ASUC. Response to IVS was determined by the attending physician between the 3rd and 5th day of admission. Patients were then classified as steroid nonresponders (SNR) or SR. A cohort of consecutive patients admitted with a flare of Ulcerative colitis but without criteria for ASUC served as a control group (CG). Endpoints included the need for biologics, surgery or both in the 5 years following discharge.

Results: 253 patients were included, 170 (67.2%) with ASUC (SNR: 47, SR: 123) and 83 controls. 53.4% were male with median age of 33 (18-80). Although SR patients presented lower surgical rates than SNR patients (13.9% vs 53.2%, P< 0.001) they were substantially higher than in the CG (0%, P< 0.001). Of note, 70.6% of surgeries in SR patients occurred within one year after discharge. Furthermore, 40.6% of SR patients were subsequently readmitted with a flare of colitis requiring biologics or surgery in 44.0% and 28.0% of cases, respectively. Concerning treatment escalation, SR patients required less biologic therapy than SNR (36.7% vs 91.5%, P< 0.001) but more so than patients in the CG (18.1%, P< 0.001). Likewise, a composite endpoint of any unfavorable outcome was more common in SR patients than in the CG (44.9% vs 18.1%, P< 0.001). Time to event analysis showed that SR patients reached an unfavorable outcome sooner than the CG (logrank test P< 0.001).

Conclusion: Patients with ASUC present an unfavorable prognosis, even after an adequate response to IVS. Early therapy intensification should strongly be considered in these patients as almost half develop unfavorable outcomes.

Disclosure: Nothing to disclose

P0356 A PROACTIVE INFLIXIMAB DRUG MONITORING STRATEGY IMPROVES OUTCOMES IN PATIENTS WITH CROHN'S DISEASE

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Introduction: There is increasing evidence supporting the use of therapeutic drug monitoring (TDM) of anti-TNF therapies in Crohn's disease (CD) following loss of response. However, the potential benefit of proactive TDM is still unknown [1-4].

Aims & Methods: To study the pharmacokinetics and clinical benefits associated with a proactive TDM strategy in CD.

Patients completing Infliximab (IFX) induction were assigned to a proactive TDM protocol (pTDM). Before the 4th infusion and before every 2 infusions, IFX drug levels and anti-drug antibodies were measured using a drug sensitive assay (Theradiag®, Lisa Tracker). Treatment was proactively escalated aiming at a trough level of 3-7 ug/ml. A retrospective cohort of patients treated with IFX but without TDM was used as a control group (noTDM). Endpoints included the need for IBD-related surgery and hospitalization, treatment discontinuation, and mucosal healing (absence of ulceration in non-operated patients or Rutgeerts score < i2 in operated patients) at 2 years of follow-up. Patients with major bowel surgery, drug holiday and primary IFX non-response were excluded.

Results: 185 patients were included in the study (35 in the pTDM and 150 in the noTDM group); Baseline characteristics were non-significant between groups. A median (range) of 3 (1-7) drug/anti-drug measurements were collected in the pTDM group over the 2-year period. The median (range) IFX trough levels and anti-drug antibodies were 5.80 µg/ml (0.03-16.4) and 0 U/mL (0-200.0), respectively. Pharmacokinetic analysis showed a significant correlation between IFX trough levels and C-reactive protein (ρ= -0.197, P= 0.01), fecal calprotectin (ρ= -0.344, P= 0.004) and anti-drug antibodies (ρ= -0.220, P= 0.003). Higher trough levels were associated with higher rates of mucosal healing (7.25 µg/ml (1.9-14) vs 2.9 µg/ml (0.03-7); P= 0.02, AUROC= 0.83), magnetic resonance enterography normalization (7.25 µg/ml (3.75-14) vs 2.14 µg/ml (0.03-7); P< 0.001, AUROC= 0.92) and transmural healing (7.5 µg/ml (3.75-14) vs 2.6 µg/ml (0.03-7.66); P= 0.015, AUROC= 0.88).

After 2 years of follow-up, pTDM patients presented higher rates of treatment escalation (74.3% vs 20.7%, P< 0.001) and mucosal healing (77.1% vs 46.7%, P= 0.01), but similar rates of hospitalization (P= 0.534), surgery (P= 0.241) and treatment discontinuation (P= 0.212). pTDM patients were less likely to reach any of the former outcomes (66.0% vs 45.7%, P= 0.033). In regression analysis only proactive TDM (OR 0.44 95%CI 1.52-8.54; P= 0.04) and immunomodulation (OR 0.35 95%CI 1.17-4.63; P= 0.016) were independently associated with mucosal healing. Immunomodulation did not influence IFX trough levels (P= 0.456) and anti-drug antibodies (P= 0.150), and was not associated with improved rates of mucosal healing (P= 0.182) in the pTDM group.

Conclusion: Higher IFX trough levels were associated with lower inflammatory biomarkers and higher rates of endoscopic and radiologic healing. In comparison with a cohort under conventional management, proactive TDM was unable to show a difference in the rates of surgery, hospitalization and treatment discontinuation but significantly improved the rates of mucosal healing at 2-years. As several studies have shown that mucosal healing reduces the rates of surgery and hospitalization in the long-term, we hypothesize that a longer follow-up would significantly improve our results.

In conclusion, improved IFX pharmacokinetics were associated with better disease control. Proactive TDM was associated with higher rates of mucosal healing than a conventional non-TDM based management.

References: 1- Vande Casteele N, Ferrante M, Van Assche G, et al. Trough concentrations of infliximab guide dosing for patients with inflammatory bowel disease. Gastroenterology. 2015 Jun;148(7):1320-9.e3. 2- D'Haens G, Vermeire S, Lambrecht G, et al. Increasing Infliximab Dose Based on Symptoms, Biomarkers, and Serum Drug Concentrations Does Not Increase Clinical, Endoscopic, and Corticosteroid-Free Remission in Patients With Active Luminal Crohn's Disease. Gastroenterology. 2018 Apr;154(5):1343-1351.e1. 3- Papamichael K, Chachu KA, Vajravelu RK, Vaughn BP, Ni J, Osterman MT, Cheifetz AS. Improved Long-term Outcomes of Patients With Inflammatory Bowel Disease Receiving Proactive Compared With Reactive Monitoring of Serum Concentrations of Infliximab. Clin Gastroenterol Hepatol. 2017 Oct;15(10):1580-1588.e3. 4- Papamichael K, Vajravelu RK, Vaughn BP, Osterman MT, Cheifetz AS. Proactive Infliximab Monitoring Following Reactive Testing is Associated With Better Clinical Outcomes Than Reactive Testing Alone in Patients With Inflammatory Bowel Disease. J Crohns Colitis. 2018 Jun 28;12(7):804-810

Disclosure: Nothing to disclose

P0357 A NEW INSIGHT OF LIQUID BIOPSY FOR IBD-ASSOCIATED NEOPLASIA

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Introduction: IBD-associated cancer and high grade dysplasia (HGD) are sometimes difficult to diagnose, because the patients with IBD-associated cancer do not have any characteristic symptoms and the tumor cannot be detected easily because of their inflammatory background. To overcome the weakness of the current methods for the diagnosis of IBD-associated cancer and HGD, we tried to develop "liquid biopsy" with blood based on the concept of non-invasive diagnostic method with circulating tumor DNA.

Aims & Methods: Ten patients with IBD-associated cancer and HGD were enrolled in this study. Tumors and paired non-tumor tissues obtained from 10 patients were analyzed for mutations of 48 oncogenes (Cancer panel; Haloplex, Agilent Technology) using next generation sequencing (NGS; Illumina, San Diego, CA, USA). Blood from 10 patients was also analyzed for the mutations with droplet digital PCR (ddPCR; BioRad, Hercules, CA, USA). Each sample was obtained prior to the treatment. As negative controls, 10 tissues and blood samples of IBD patients without neoplasia were analyzed for mutations of the 48 oncogenes in the same way.

Results: The median (range) age was 49 (34-83) years and the male/female ratio was 0.67 (4/6). Of the 10 cases, 7 were IBD-associated cancer and 3 were IBD-associated HGD. Five, three, and two patients were diagnosed as stage 0 (which contained HGD), stage I, and stage III, respectively. We set the cut-off value at 5% for rare mutation rate based on the results of control samples to avoid false positive. Seven of 10 (70%) tumor tissue samples were positive for the mutations. TP53, KRAS, and PIK3CA mutations were detected in 5/10 (50%), 1/10 (10%) and 1/10 (10%) respectively. The frequency of the amino acid changes in each gene were as follows: TP53 (20.9%; R136H), TP53 (25.0%; C110W), TP53 (8.5%; H140Q), TP53 (31.1%; R150W), TP53 (12.8%; R141H), KRAS (40.0%; G12V) and PIK3CA (34.1%; R88Q). In these seven patients, the same mutations were detected in all blood samples. On the other hand, blood samples of the remaining 3 patients without the mutations in tissue did not show any mutations either. Concordance rate with mutations between tissue and blood was 100%. Blood analysis for the mutations indicated that sensitivity, specificity, positive predictive value (PPV) and negative predict value (NPV) were 70%, 100%, 100% and 76.9%, respectively. None of negative control samples showed any mutations.

Conclusion: Mutations in tumor could be detected in blood using digital PCR with high PPV (100%). Liquid biopsy with blood may help us to diagnose IBD-associated cancer and HGD non-invasively.

Disclosure: Nothing to disclose

P0358 USEFULNESS OF LEUCINE-RICH ALPHA-2-GLYCOPROTEIN (LRG) TO MONITOR THE EFFICACY OF ADALIMUMAB TREATMENT IN PATIENTS WITH ULCERATIVE COLITIS (PLANET STUDY)

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Introduction: Leucine-rich alpha-2 glycoprotein (LRG) is an acute phase protein induced by various inflammatory cytokines. Naka *et al.* has recently reported that LRG is an effective biomarker for inflammatory diseases, such as inflammatory bowel diseases (IBD). In this study, we prospectively measured serum LRG in patients with ulcerative colitis (UC), who were treated with adalimumab. We also analyzed the correlation of serum LRG with other disease activity markers.
Aims & Methods: This is a multicenter prospective observational study [Predictor and Biomarker; LRG (leucine rich alpha-2 glycoprotein) for Inflammatory Bowel Disease Treatment with Adalimumab: PLANET study (UMIN000019958)]. Active UC patients with Mayo score of 6 or more were recruited for the standard adalimumab treatment. Serum LRG levels were measured by latex turbidimetric immunoassay before and at 12, 24 and 52 weeks after the initiation of adalimumab. Partial Mayo score (PMS), fecal calprotectin (fCP) and C-reactive protein (CRP) were evaluated at the same time point, and severity of colonic inflammation was evaluated by Mayo endoscopic subscore (MES) and Ulcerative Colitis Endoscopic Index of Severity (UCEIS) at 12 and 52 weeks. This study was funded by Eisai Co., Ltd.
Results: Forty-seven patients with UC (27 males, 20 females; age 40.6 ± 14.4; disease duration 6.9 ± 6.7 years; left-side colitis 16 cases, total colitis 30 cases, right-side/segmental colonic type 1 case) were registered.
The serum LRG level was 23.6 ± 10.4 μg/ml before the treatment (n = 46), and was decreased to 13.9 ± 5.5 μg/ml at 12 weeks (n = 37), 12.5 ± 5.0 μg/ml at 24 weeks (n = 31), and 13.1 ± 5.0 μg/ ml at 52 weeks (n = 27).
The levels of LRG and CRP were significantly correlated with pre-treatment PMS, MES and UCEIS (PMS, r = 0.503; MES, r = 0.534; UCEIS, r = 0.394 for LRG: PMS, r = 0.440; MES, r = 0.538; UCEIS, r = 0.365 for CRP).
In addition, LRG and fCP were significantly correlated with MES (LRG, r = 0.429; fCP, r = 0.448) and UCEIS (LRG, r =0.608; fCP, r = 0.512) at 12 weeks. LRG and fCP were significantly correlated with PMS at 52 weeks (LRG, r = 0. 398; fCP, r = 0.494).
At week 52, however, fCP was the only parameter, which was significantly correlated with UCEIS (r = 0.640). When serial data were put into an analysis, LRG was the best correlated with PMS and UCEIS (PMS, r = 0.408; UCEIS, r = 0.301).
Conclusion: LRG is a novel serum biomarker which can reflect disease activity possibly better than CRP and fCP in UC patients with adalimumab treatment.
Disclosure: HI: AbbVie, EA Pharma, EisaiMitsubishi Tanabe Pharma, Mochida pharmaceutical, Kyorin pharmaceutical, Janssen, Zeria pharmaceutical, Takeda pharmaceutical,, Sekisui Medical. AbbVie, Kissei, Nippon Kayaku; SS: Abbvie, Tanabe Mitsubishi, Janssen Pharmaceutical; KM: EA Pharma, Thermo Fisher Scientific,Sekisui Medical, Alfresa Pharma; SK:Abbvie, Tanabe Mitsubishi, Janssen; TK: Kyorin, Abbvie, Eli Lilly, Pfizer Inc., Janssen, Takeda Pharmaceutical, Medtronic, Gilead Sciences Inc., Alfresa Pharma Corporation and Celltrion; MM: Tanabe Mitsubishi, Abbvie, JIMRO, EA Pharma, Kyorin, Mochida, Nippon Kayaku; SH:Tanabe Mitsubishi, Eiken Chemical; TT: Mitsubishi Tanabe , AbbVie, Mochida pharmaceutical, Takeda pharmaceutical; MT: Abbvie, Tanabe Mitsubishi, Janssen Pharmaceutical, EA Pharma, Nippon Kayaku, Kyorin; TK: EA Pharma, Sekisui Medical, Thermo Fisher Scientific

P0359 CHROMOENDOSCOPY TO DETECT NEW DYSPLASIA IN THE SURVEILLANCE OF INFLAMMATORY BOWEL DISEASE WITH PREVIOUS DYSPLASIA

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Introduction: Inflammatory bowel disease (IBD) patients are in higher risk of developing colorectal cancer (CRC) than general population. Studies show that surveillance with chromoendoscopy (CE) detects a higher number of dysplastic lesions, allowing their endoscopic resection and therefore preventing CRC. It also saves costs by avoiding non-targeted biopsies. We aimed to assess the endoscopic results from follow-up CE in IBD patients with diagnose of dysplasia.
Aims & Methods: We carried out a retrospective data collection from IBD patients who have had dysplastic lesions in surveillance chromoendoscopy, which were performed in our hospital from January 2013 to November 2018. Demographic and clinical data were assessed at the time of the first CE, as well as endoscopic findings in this CE and in the first follow-up CE.
Results: 320 chromoendoscopies were performed, all of them using Indigo Carmine 0.2% and spray catheter Olympus.
41 patients show dysplastic lesions in the initial CE. Most of them were male (75.5%), with median age 58 years old (23.8-77.4) and familiar history of colorectal cancer was found on 26.7% of them. Ulcerative colitis was more frequent than Crohn's disease (84%), most patients had extensive colitis (79%) and an average age of evolution of the disease of 16 years. 17% were in treatment with biological drugs, 23.7% with immunomodulators and 80% with salicylates, at an average dose of 2.33 g/d. 12 patients (30%) had already had dysplasia in previous colonoscopies, all of them were visible lesions and they were treated endoscopically.
In the initial chromoendoscopy, an average of 2.89 dysplastic lesions with an average size of 8 mm was detected, 76.9% were flat lesions (0-IIa or 0-IIb from Paris classification) and 86% were completely removed endoscopically. Most of them were located distal to the splenic flexure (72%). 80% were tubular adenomas with low grade dysplasia (LGD); there were 2 cases of high grade dysplasia (HGD) and one case of adenocarcinoma.
At this time we have performed 25 follow-up CE and new dysplasic lesions were found in 39% of them, with an average of 3.25 lesions, < 10 mm in size, 75% in distal location. 50% of the visible lesions were tubular adenomas LGD, 12.5% serrated adenomas LGD and 12.5% hyperplasic.
In our analysis we found that those patients with flat lesions 0-IIa in the baseline chromoendoscopy have more frequent dysplastic lesions in the revision compared to those with lesions 0Is (78.6% vs 0%, p=0.035). Bowel cleanliness also influenced the number of lesions detected, as we found that those patients whose Boston was < 8 in the baseline CE have a greater number of lesions in the next CE (16 vs. 8; p=0.005)
Conclusion: Surveillance with chromoendoscopy in IBD patients with previous dysplastic lesions detects new dysplasia in 30% of cases. Low grade dysplasia was the most frequent histology within the removed lesions. Finding higher number of lesions, 0-IIa lesions or worse bowel preparation (Boston < 8) in the first chromoendoscopy predicts having a higher number of lesions on the follow-up in our sample.
Disclosure: Nothing to disclose

P0360 HIGH INFLIXIMAB EXPOSURE INCREASES THE RISK OF INFECTION

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Introduction: Infliximab (IFX) increases the risk of infection in patients with inflammatory bowel diseases (IBD), but the relationship between drug ex-

posure, mostly estimated by the trough level of IFX (TLI), and infections remains controversial. The present study aimedtoassess factors associated with infection among IFX-treated patients, including pharmacokinetic data.

Aims & Methods: All IBD patients receiving the IFXmaintenance regimen from November 2016 to April 2017 were screened and prospectively followed. Patients during induction phase of treatment at baseline or who interrupted the treatment during the study period were excluded. Clinical and biological data, infectious events and the TLI were collected at each infusion visit.IFX exposure was estimated by the area under the curve (AUC) of the drug concentration using pharmacokinetic modelling,andthen the individual exposure over the 6-month period was estimated by the sum of the AUC (ΣAUC). Independent risk factors of infection were identified by logistic regression.

Results: Among the 288 patients treated with infliximab during the study period, 209 patients were included: 102 men (49%), mean ($\pm$SD) age 39 ($\pm$14) years old, 159 Crohn's disease (76%). A total of 54 (26%) patients received a combination therapy. The mean TLI was 5.46 mg/Land the mean ΣAUC was 3938 ($\pm$1427) mg.d/L, corresponding to a mean period of IFX exposure of 24.7 ($\pm$3.5) weeks.A total of 215 infections were collected from 640 infusionvisits (63 [29%]bacterial infections, 143 [67%]viral infections and 9 [4%] fungal infections).At least one infection occurred in 123 patients (59%), more than one infection in 64 patients (30 %), and 46 patients (22%) received antibiotics. Three factors were independently associated with infection after a multivariate analysis: smoking (OR=2.05, p=0.046), IBD flare-up (OR=2.71, p=0.0060) and a high ΣAUC of IFX (>3234 mg.d/L) (OR=2.02, p=0.02). The ΣAUC was higher in patients with infection than in patients without infection (p=0.04) and correlated with the numberof infections (p=0.04). The trough concentration of IFX alonewas not associated with infection.

Conclusion: Almost two-thirds of patients treated with IFX developed an infectionover the 6-month follow-up,and this risk was individually related to increasedcumulative drug exposure. These results encourage starting therapeutic de-escalation for patients in remission, guided by drug monitoring.

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P0361 USEFULNESS OF CAPSULE ENDOSCOPY IN PATIENTS WITH CROHN'S DISEASE IN REMISSION

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Introduction: No biomarkers can effectively predict the clinical prognosis of Crohn's disease (CD) in remission. Capsule endoscopy (CE) is known as a direct examination that can detect minute lesions of the mucous membrane. However, the consensus on the relevance of CE findings and the subsequent course of disease remains to be determined.

Aims & Methods: CE was performed after the patency capsule (PC) procedure to verify the patency of the small intestinal tract in patients with CD in remission, and the relationship between CE findings and prediction of clinical prognosis was evaluated.

A total of 45 patients with small intestine type and small intestine-colon type CD in remission phase underwent CE after the PC procedure from October 2010 to December 2017 (27 men, 18 women; average age, 34.9 years). All patients had CD activity index (CDAI) of < 150 (average, 92.7). Patients were divided into "active group" with small or longitudinal ulcers detected by CE and "non-active group" without ulcer, and the relationship between the two groups was examined according to disease duration, CDAI value, and C-reactive protein (CRP) value. In addition, occurrence of "exacerbation" requiring change or strengthening of treatment was determined, and its relationship with CE findings was evaluated.

Results: Among the 45 patients, 35 (77.8%) were confirmed to have patent small intestines by PC and subsequently underwent CE. Incidents of capsule retention in the small intestine were not observed. Among the

35 patients who underwent CE, 12 (34.3%) were included in the "active group" and 23 (65.7%) in the "non-active group." The disease durations were 82.8 and 142.1 months and the CDAI values were 100.8 and 88.3 in the "active group" and "non-active group," respectively, without significant differences. CRP values were 1.04 and 0.53, respectively, which were significantly higher in the "active group" than those in the "non-active group" (p < 0.05). "Exacerbation" occurred in 6 (50%) and 2 (8.7%) patients, respectively, which was significantly higher in the "active group" than those in the "non-active group" (p < 0.01).

Conclusion: CE was safely performed in 77.8% of patients with CD in remission after performing the PC procedure. The CRP value was significantly associated with the active phase of the small intestinal mucosa as detected by CE. Exacerbation rate was significantly higher in the "active group" than those in the "non-active group." CD in remission may be exacerbated even in clinical remission when an active phase of small intestinal mucosa is detected by CE, and thus, the treatment should be strengthened. These findings suggested that CE is a useful examination procedure to predict the clinical prognosis in patients with CD in remission.

Disclosure: Nothing to disclose

P0362 DEMOGRAPHIC FEATURES OF ULCERATIVE COLITIS PATIENTS AS PREDICTORS OF RESPONSE TO ADSORPTIVE GRANULOMONOCYTAPHERESIS AS REMISSION INDUCTION THERAPY: A RETROSPECTIVE ASSESSMENT OF TREATMENT OUTCOMES

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Introduction: Inflammatory bowel disease (IBD) is associated with elevated myeloid lineage leucocytes, which show activation behaviour[1] including the CD14+CD16+DR++ phenotype known as proinflammatory monocytes and a major source of tumour necrosis factor-α.[2] Accordingly selective depletion of myeloid leucocytes by granulomonocytapheresis (GMA) with an Adacolumn is expected to promote remission and enhance drug efficacy. However, hitherto studies in IBD have reported contrasting efficacy outcomes, ranging from an 85%[3] to statistically insignificant.[4] Patients' demographic features should guide to select responder patients.

Aims & Methods: In ulcerative colitis patients, we were interested to identify relevant demographic features, which potentially could indicate a favourable response to GMA. Therefore, in a retrospective setting, we looked at the baseline clinical and endoscopic features of responders and non-responders to adsorptive GMA in 146 consecutive ulcerative colitis patients who had undergone GMA as remission induction therapy, 74 steroid naive, 70 steroid dependent, and 2 steroid refractory. Patients had received up to an 11 GMA sessions over 10 weeks. At entry and week 12, patients were clinically and endoscopically evaluated, allowing each patient to serve as her or his own control. Clinical activity index (CAI) ≤4 was defined as remission. Biopsies from endoscopically detectable inflamed mucosa were processed to see the impact of GMA on leucocytes within the mucosa.

Results: At entry, the average CAI was 12.8, range 10-17. Ninety-four patients (64.1%) had responded to GMA, 53 of 74 steroid naïve (71.6%), 40 of 70 steroid dependent (57.1%), and 1 of the 2 steroid refractory cases. On average remission was sustained for 8.6 months in steroid naïve patients and for 10.4 months in steroid dependent cohort. Mucosal biopsies revealed that infiltrating leucocytes were mostly neutrophils and monocytes. There was a marked reduction of infiltrating leucocytes in the biopsies from the responder patients. Patients with extensive deep UC lesions together with loss of the mucosal tissue at the lesions were non-responders. Patients with the first UC episode were identified as the best responders (100%), followed by steroid naive patients. Further, a short duration of active UC prior to GMA marked a patient as a likely responder.

Conclusion: Patients who responded well to GMA attained a favourable long-term clinical course. GMA was more effective if applied immediately after a relapse than after a lag time. In general, GMA is favoured by patients for its safety profile and for being a non-drug remission induction option. Patients with extensive deep ulcers, with long duration of UC refractory to multiple pharmacologics are unlikely to benefit from GMA. In therapeutic settings, knowing baseline features, which may identify responder patients should help to avoid futile use of medical resources.

References: 1. McCarthy DA, et al. Peripheral blood neutrophils in inflammatory bowel disease: morphological evidence of in vivo activation in ac-

tive disease. Clin Exp Immunol 1991; 86: 489-93. 2. Belge KU, et al. The proinflammatory CD14+CD16+DR++ monocytes are a major source of TNF. J Immunol 2002;168:3536-42 3. Cohen RD. Treating ulcerative colitis without medications - look mom, no drugs. Gastroenterology 2005;128:235-36. 4. Sands BE, et al. A randomized, double-blind, sham-controlled study of granulocyte/monocyte apheresis for active ulcerative colitis. Gastroenterology 2008;135:400-09.

Disclosure: Nothing to disclose

P0363 USEFULNESS OF SERUM LEUCINE-RICH ALPHA-2-GLYCOPROTEIN (LRG) FOR MONITORING THE EFFICACY OF ADALIMUMAB TREATMENT IN PATIENTS WITH CROHN'S DISEASE (PLANET STUDY)

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Introduction: Leucine-rich alpha-2 glycoprotein (LRG) is an acute phase protein induced by various inflammatory cytokines. Naka T. *et al.* has recently reported that the serum level of LRG is an effective biomarker to reflect the activity of chronic inflammatory diseases, such as inflammatory bowel disease. In the present study, we prospectively analyzed the levels of serum LRG in patients with Crohn's disease (CD) who were treated with adalimumab. We also analyzed the correlation of LRG levels with conventional disease activity markers.

Aims & Methods: This is a multicenter prospective observational study [Predictor and biomarker; LRG (leucine rich alpha-2 glycoprotein) for inflammatory bowel diseasetreatment with Adalimumab: PLANET study (UMIN000019958)]. Active CD patients with Crohn's disease activity index (CDAI) score of 220 or more were recruited for the standard adalimumab therapy. Serum LRG levels were measured by latex turbidimetric immunoassay before and at 12, 24 and 52 weeks after adalimumab treatment. CDAI score,C-reactive protein (CRP) and fecal calprotectin (fCP) levels were evaluated at the same time point, and the severity of intestinal inflammation was evaluated by Simple endoscopic score for Crohn's disease (SES-CD) before and at 24 and 52 weeks after adalimumab treatment.

Results: Thirty-four patients with CD (24 males, 10 females; age 29.5 ± 14.0; disease duration 4.5 ± 6.6 years; ileocolitis 27 cases, ileitis 3 cases, colitis 4 cases) were registered. The serum LRG level was 32.5 ± 13.6 µg/ml before treatment (n = 34), and it decreased to 17.3 ± 9.4 µg/ml at 12 week (n = 33), 18.7 ± 11.7 µg/ml at 24 week (n = 31), and 15.8 ± 8.1 µg/ ml at 52 week (n = 28).

LRG levels were significantly correlated with CDAI at 12, 24 and 52 weeks (12 week, r = 0.440; 24 week, r = 0.743; 52 week, r = 0.554). CRP levels were significantly correlated with CDAI before treatment, and at 24 and 52 weeks (pre, r = 0.375; 24 week, r = 0.622; 52 week, r = 0.597). fCP was correlated with CDAI only at 52 week (r = 0.600).

In addition, LRG was significantly correlated with SES-CD before treatment (r = 0.391). LRG, CRP and fCP were significantly correlated with SES-CD at 24 week (LRG, r = 0.563; CRP; r= 0.470, fCP, r = 0.659), and LRG (r = 0.697) and fCP (r = 0.593) were significantly correlated with SES-CD at 52 weeks. When serial data were put into an analysis, LRG was the most highly correlated with CDAI and SES-CD (CDAI, r = 0.660; SES-CD, r = 0.636).

Conclusion: LRG is a novel serum biomarker for CD, which specially represents endoscopic activity of the disease. LRG may be superior to CRP and fCP for monitoring CD under adalimumab treatment.

P0364 MANAGEMENT OF INFLAMMATORY BOWEL DISEASE PATIENTS IN THE EMERGENCY DEPARTMENT: A FRENCH NATIONAL CONSENSUS

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Introduction: Inflammatory bowel diseases (IBD) are conditions of unpredictable evolution. Despite recent therapeutic progress, particularly since the arrival of biologics, visits to the emergency department (ED) by IBD patients remain frequent and two-thirds of the ED visits lead to hospital admission.

There are currently no guidelines on the actions to be taken when an IBD patient visits the ED: urgent CT scan, hospitalization, or discharge. Certain situations can sometimes lead to unnecessary hospitalizations or, on the contrary, to an inappropriate discharge. The aim of this study was to define criteria to help in the decision-making process in IBD patients visiting ED.

Aims & Methods: To address this problem, after a systematic literature review, a Delphi consensus on the actions to be taken when an IBD patient visits the ED was organized in France. Three experts (2 gastroenterologists and 1 emergency physician) built an initial list of criteria which, if met, could lead either to an emergency CT scan prescription or to a hospitalization. An Internet-based two-round Delphi consensus was constructed and a panel of 119 healthcare professionals (68 gastroenterologists, 42 emergency physicians and 9 nurses) were asked to rate each criterion according to a 4-point rating scale (from 'strongly agree' to 'strongly disagree') and to propose additional criteria. Consensus was reached for one criterion when at least 75% of voting members scored the statements 'strongly agree' or 'agree'.

After the first round a national web conference was organized to present and discuss the results and to build the list of criteria for the second round. The first round took place between 21st November and 5th December 2018 and the second round between 19th December 2018 and 15th January 2019.

Results: 86 healthcare professionals took part in the first round of voting and 58 in the second round. For both Crohn's disease and ulcerative colitis, consensus was reached on '*IV morphine titration*, '*fever*', '*vomiting*', '*laboratory-confirmed signs of dehydration*', '*anoperineal abscess*', '*haemodynamic instability*' as criteria for hospitalisation. The criteria '*suspect abdomen*', '*bowel resection in the past 30 days*' and '*bowel obstruction*' reached consensus both for hospitalization and emergency CT scan. Regarding biological criteria, consensus was reached on '*haemoglobin < 9*

g/dL or decrease of ≥ 2 g/dL' and '*acute renal failure*' as criteria in favour of hospitalization and '*very high CRP*' for an emergency CT scan. The final checklist is presented in Table 1.

Conclusion: A French group of experts reached a multidisciplinary consensus on a list of clinical and biological criteria which could be used in daily practice when an IBD patient is admitted to the ED. It is hoped that the use of this list will improve management of IBD patients visiting ED. Future studies will be conducted to evaluate the use and the impact of this new tool.

Criteria for immediate hospitalisation	
Clinical criteria	• Suspect abdomen • IV morphine titration • Fever • Vomiting • Laboratory-confirmed signs of dehydration • Bowel resection in the past 30 days • Anoperineal abscess • Bowel obstruction • Haemodynamic instability
Laboratory criteria	• Haemoglobin <9 g/dL or decrease of ≥ 2 g/dL • Acute renal failure
Criteria for emergency CT scan	
Clinical criteria	• Suspect abdomen • Bowel resection in the past 30 days • Bowel obstruction
Laboratory criteria	• Very high CRP

[Final checklist]

P0365 HEPATOBILIARY MANIFESTATIONS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Hepatobiliary manifestations in IBD (chronic inflammatory bowel diseases) are common. The most common is steatosis and the most specific is primary sclerosing cholangitis (PSC).
Aims & Methods: The objectives of the study are: to evaluate the frequency of these anomalies, and enumerate the different etiologies as well as their consequences on the management of IBD.This is a 26-year retrospective study [1990 -2016], which includes patients with IBD who presented with at least one biological and / or morphological hepatobiliary abnormality.
Results: Out of 1157 patients followed up, 109 patients had at least one liver anomaly, being an incidence of 9.42%. The average age of our patients was 37 years with extremes [13 years, 69 years], the female sex was predominant [68 women, 41 men] with a sex F / H ratio of 1.6. Crohn's disease was the predominant type of IBD (93 cases of Crohn's, 13 cases of UC, 3 cases of indeterminate colitis). Clinically, 89% of patients were asymptomatic. The biological assessment found cytolysis in 37% of cases, cholestasis in 21%, both in 6% of cases and normal in 36% of cases. Abdominal ultrasound was performed for all patients . Magnetic resonance cholangiopancreatography was performed in 15.6% of cases (17 cases) and found: an aspect suggestive of sclerosing cholangitis in 8 cases and normal in 9 cases. Puncture Biopsy of the liver was performed in 28.45% of cases (27 cases). The etiologies were as follows: hepatocellular toxicity in 30,25% (33 cases) (24 cases under thiopurines , 6 cases under methotrexate (MTX), 3 cases under salicylic agent and one case under anti bacillary), a steatosis in 26.21% (27 cases), an infectious origin in 15.6% (17 cases) (16 cases of viral hepatitis B or C, 1 case of hepatic abscess), primary sclerosing cholangitis (PSC) in 9.18% (10 cases), vesicular lithiasis (VL) in 11.9% (13 cases), autoimmune hepatitis type I in 2.75% (3 cases), hepatic angioma in 3.66% of cases (4 cases).), 1 case (0.91%) of liver metastasis of adeno-

carcinoma in the retained rectum after colectomy for ulcerative colitis and undetermined origin in 5.42% (6 cases) . transitory anormalies were noted in 6.42% of cases (7 cases). 13 cases of our patients associate 2 anomalies at the same time. Therapeutic drug hepatotoxicity led to the decrease of the dose in 42.4% (14 cases) and to stop definetely the medicament in question in 57.58% (19 cases) with either a therapeutic abstention in asymptomatic patients or a change to another therapeutic molecule: from one purine agent to another or to MTX, MTX or salicylic to a purinic agent. PSC cases were treated by ursodeoxycholic acid. The cases of steatosis improved once the disease stabilized. Treatment of autoimmune hepatitis was similar to that of IBD combined with corticosteroid therapy followed by azathiopirine. The case of liver metastasis was followed by surgical resection followed by chemotherapy. For the other patients a specific treatment was applied. The evolution was good in all patients.
Conclusion: Hepatobiliary manifestations in patients with IBD are frequent , the incidence in our study is 9.42%. as it's showed it range from benign diseases and side effects of the treatement to malignant disorders . Early diagnosis by a monitoring of liver function at regular intervals is important because of the therapeutic implications for the overall management of patients . Additionally, we should not forget the search for common causes of liver disease as well as for the general population.
Disclosure: Nothing to disclose

P0366 THE INTRA-INDIVIDUAL VARIABILITY OF FECAL CALPROTECTIN IN PATIENTS WITH GI-SYMPTOMS

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Introduction: Levels of faecal calprotectin (FC) are used to distinguish between functional and organic gastrointestinal disease. In routine clinical practice, we have observed intra-patient variability in FC measurements made during a short time period. This may indicate that the detection assay is not as reliable as originally presumed. To evaluate this variability more closely, we retrospectively analysed FC measurement data from a selected patient cohort.
Aims & Methods: Our aim was to systematically assess the variability in the levels of FC measured within a defined period of time in patients with either a functional or organic gastrointestinal disorder. We searched our electronic patient database for all patients with a gastrointestinal disorder, independent of diagnosis, who had at least three FC measurements made within a 10-day period.
Results: Of 404 patients who fulfilled the search criteria and were included in the study analysis, there were 284 women (70%) with a mean age (range) of 45.8 (11 to 90 years). Based on the commonly recommended cut-off value of 50 µg/g for most European countries, 144 patients (35.6%) had three values below the cut-off level and 150 (37.1%) had all three values above the cut-off. Therefore, 110 patients (28.1%) showed a variability in FC levels, which included values considered normal as well as pathological. The range analysis for this patient group showed: 48 patients(43.6%) with the range < 50 µg/g; 33 (30%) within 50-99 µg/g; 11 (10%) within 100-199 µg/g; 9 (8.2%) within 200-500 µg/g; and 8 pts (7.3%) with values > 500 µg/g. Large variability was also seen in a sub-analysis of three patient groups categorised either with an organic disease (232, 57.4%), functional disease (153, 37.9%) or uncertain diagnosis (19, 4.7%). In patients with an organic disease, 66 (28.4%) had FC values below and above the cut-off, whereas there were 30 (19.6%) and 11 (58%) patients with normal and pathological values in the groups defined with a functional disease and uncertain diagnosis, respectively. Further analysis showed variability in patients with three elevated values: 21 (14%) in the range < 50 µg/g; 25 (16.7%) within 50-99 µg/g; 33 (22%) within 100-199 µg/g; 38 (25.3%) within 200-499 µg/g; 19 (12.7%) within 500-1000 µg/g; and 14 (9.3%) with levels > 1000 µg/g. When the cut-off was increased to 100 µg/g, 92 patients (22.6%) had values below and above the cut-off. By applying a cut-off of 150 µg/g, the number of patients with both normal and pathological values decreased to 62 (15.4%). Age and gender did not have any significant influence on the data analysis.
Conclusion: We were able to show a relevant variability in FC values measured in our patients. More than one quarter of the patients (28%) had levels of FC deemed both normal and pathological within the sampling time

period. The range for patients with all three measured values above the cut-off of 50 µg/g was relatively large, which creates significant difficulties in analysing the results. By applying a higher cut-off of 100 or 150 µg/g, the number of patients with normal and elevated values was reduced, which suggests that a higher cut-off may be more pertinent. Our analysis also raises the question of whether a single measurement is sufficient to form the basis for clinical decision. We suggest that, as with occult blood, three measurements could be performed. All three values in conjunction with a clear picture of patient symptoms should enable the clinician to determine further treatment procedures. To clearly define recommendations for clinical practice, a large prospective study is needed.

Disclosure: Nothing to disclose

P0367 ARE WE CHOOSING WISELY IN INFLAMMATORY BOWEL DISEASE CARE? THE IG-IBD CHOOSING WISELY CAMPAIGN

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Introduction: Since it started in 2012 in the USA, the Choosing Wisely campaign promoted by the American Board of Internal Medicine has rapidly spread all over the world, involving all medical subspecialties. The campaign aims at promoting the clinician-patient relationship, identifying procedures, tests, and treatments that are commonly used in routine practice, but necessity of which should be questioned or discussed. The Canadian inflammatory bowel disease (IBD) Network has recently carried out the first choosing wisely campaign for IBD. However, it was carried out with a top-down approach, involving only 14 expert gastroenterologists. A choosing wisely campaign conducted in a broader scientific community could promote a more rationale, clinically-oriented, management for patients suffering from IBD.

Aims & Methods: Between May 2018 and March 2019 we carried out the choosing wisely campaign involving regular members of the Italian Group for the Study of IBD (IG-IBD). Modified Delphi process was applied. All IG-IBD members were asked to submit through SurveyMonkey five statements starting with "Do not..." addressing any management strategy, procedure, or treatment the necessity of which should be questioned or discussed. As a second step, all the proposed recommendations were evaluated by a group of seven senior members and three young members (panellists) who prioritised each item, giving a score from 1 to 10 (1=lowest priority, 10=maximum priority). The ten recommendations with the highest score were prioritised again by all IG-IBD members with the same scoring system. The top five list of the IG-IBD choosing wisely campaign was identified.

Results: Overall, 101 members (mean age 42±12; 62 males), working in both academic (57%) and non-academic (43%) hospitals, participated in the campaign. Most participants were gastroenterologists (92%), followed by internists (4%), surgeons (2%), and paediatricians (2%). In the second step, before selecting the top ten recommendations, panellists merged together and rephrased similar statements, and consensus was reached after discussion through email. The top five "Do not..." recommendations are as follow: 1. Do not use corticosteroids for maintenance therapy, or without a clear indication (score 9.08); 2. Do not forget venous thromboembolism prophylaxis in hospitalised patients with active disease (score 8.9); 3. Do not treat perianal Crohn's disease with biologics without prior surgical evaluation (score 8.66); 4. Do not discontinue IBD-related medications during pregnancy unless specifically indicated (score 8.63); 5. Do not delay surgery (8.4).

Conclusion: The IG-IBD promoted a choosing wisely campaign with a bottom-up approach, thus reflecting the most compelling, but yet unmet, needs in the care of IBD across Italy. Despite the growing number of guidelines, uncertainties still exist in day-by-day clinical practice. We therefore envisage that the top five recommendations will be a useful tool for enhancing patient-doctor relationship and provide a better care, especially among non-IBD experts.

References: 1. Nguyen GC et al. Modified Delphi process for the development of choosing wisely for inflammatory bowel disease. Inflamm Bowel Dis 2017;23:858-865. 2. Montano N et al. The Italian Society of Internal Medicine choosing wisely campaign. Intern Emerg Med 2016;11:1125-1130.

Disclosure: Nothing to disclose

P0368 OPPORTUNISTIC INFECTION IN PATIENTS WITH INFLAMMATORY DISEASE USING BIOLOGICAL THERAPY. (PROSPECTIVE STUDY)

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Introduction: Infection by clostridium difficile has been related in patients who were in hospital and making use of antibiotics therapy.
Up till now , such an infection has not been seen in patients making use of biological and without history preview of hospitalization or antibiotic and who are in remission.

Aims & Methods: We investigated the incidence of parasitosis as well as clostridium difficile in the faeces of patients with inflammatory bowel disease during the course of three years of monotherapy with TNF inhibitors (infliximab and adalimumab) or thiopurines (azathioprine)Prospective study with patients in follow-up at a referral center of inflammatory bowel diseases , who were in remission (endoscopic and clinical), with no previous hospitalisation or use of antibiotics, but undergoing treatment with biological therapy for at least six months. The results were compared with those of patients with inflammatory disease not using immunosuppressive agents.

Results: Of the total sample of 329 (212 Crohn's disease, 117 ulcerative colitis) patients undergoing biological therapy, 81.13% tested positive for clostridium B versus 18.87% of those only taking immunosuppressants (p< 0.0001) OR 4.956 CI 1.96-8.39, demonstrating that patients on TNF inhibitors were four times more likely to be affected by clostridium (p=0.0002). In contrast, no positivity was observed for parasitosis.
No predominance was observed among the biologics (adalimumab/infliximab), p=0.79.

Conclusion: Patients undergoing biological therapy are more susceptible to becoming infected with clostridium, and not only those hospitalised or receiving antibiotics. This study points to the importance of clostridium research in this specific group of patients.

Disclosure: Nothing to disclose

P0369 CONFOCAL LASER ENDOMICROSCOPY REVEALS DIFFERENTIAL RESPONSE IN PATIENTS WITH ACTIVE ULCERATIVE COLITIS UNDERGOING ANTI-INTEGRIN COMPARED TO ANTI-TNF-ALPHA THERAPY

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Introduction: Endoscopic quantification of inflammation in ulcerative colitis (UC) is limited to superficial criteria. Mucosal healing is only validated after 8 weeks of treatment and therefore cannot predict early therapy response in UC patients undergoing biological therapy with either anti-integrin or anti-TNF-alpha antibodies. Confocal Laserendomicroscopy (CLE) allows real-time visualisation of dynamic changes of the mucosal anatomy and might therefore be a reliable tool for an exact quantification of inflammation in UC.

Aims & Methods: To evaluate CLE for dynamic quantification of the level of inflammation in UC patients undergoing biological therapy (Vedolizumab (VDO) or Infliximab (IFX)) as a marker for early therapy response.

90 patients (54m) with active UC were recruited for probe based CLE (Cellvizio) in the sigmoid colon before and 2/4/6/14 weeks(wk) after initiation of therapy with IFX (46 patients) or VDO (44 patients). The following CLE criteria were quantified: Mucosal barrier dysfunction, vascular alteration, changes of crypt architecture, inflammatory cell infiltrate. Data were correlated to endoscopic Mayo scores and histological activity indices. Data are presented as mean±SD.

Results: Response to therapy (defined as clinical remission at wk 14) was achieved in 73.9% (30/46) of IFX patients and 70.5% (31/44) of VDO patients. At baseline, fluorescin accumulated in the mucosa after 8.9±6.1sec. In patients with later response to both therapies time to accumulation significantly decelerated within 2 wk to 14.8±5.2sec compared to patients without response (9.6±5.4sec.; p=0.03). Capillary diameters were dilated up to 16.3±3.2µm prior to initiation of biological therapies. In case of therapy response a reduction in the capillary diameter of 20.2% (13.65±3.2µm, p=0.001) was observed within the first two weeks of treatment.

Crypts were significantly enlarged up to an outer diameter of 114.1±21.2µm at baseline and showed a significant shrinkage in response to therapy (92.9±12.3µm; p=0.01). Endoscopic Mayo score revealed no significant differences at wk 2 between responders and non-responders.

In patients not responding to biological therapy pCLE criteria did not show significant changes after 2 wk of treatment.

Though both therapy groups exhibited significant changes of pCLE criteria between response and non-response patients, changes were markedly higher in the IFX group compared to the VDO groups after 2 wk of treatment. Thereafter, no significant changes were observed between the groups.

Conclusion: Dynamic pCLE criteria allow a reliable quantification of the level of inflammation in UC. The assessed criteria proved to be predictive for therapy response already after 2 wk of treatment and preceded mucosal healing by far. Of note, dynamic, intramucosal changes occur significantly earlier in patients undergoing IFX therapy compared to VDO.

Disclosure: Nothing to disclose

P0370 ASSESSMENT OF IBD-DISK IN A PROSPECTIVE MULTICENTER COHORT OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: The IBD-disk is a 10-item visual tool assessing the disease burden in patients with inflammatory bowel diseases (IBD) with no validation to date. In a cohort of patients with IBD, we aimed to determine the correlation between the IBD-disk and each of its components with the daily-life IBD burden.

Aims & Methods: A one-week cross-sectional cohort study has been conducted in 42 tertiary centers in France and Belgium affiliated to the GETAID in November 2019 recruiting all consecutive outpatients with IBD. Patients fulfilled a self-administered anonymous standardized questionnaire collecting data on patients', IBD and treatment characteristics. Patients were asked to complete each component of the IBD-disk on 10-point Likert scales (0 = no burden ; 10 = maximal burden) assessing abdominal pain, body image, education and work, emotions, energy, interpersonal interactions, joint pain, regulating defecation, sexual functions, and sleep) ranging from 0 to 100 as well as a 10-point Likert scale assessing the daily-life IBD burden. The objective of the study was to determine the correlation between the IBD-disk score and the daily-life IBD burden, using Pearson's correlation coefficient.

Secondary objectives were to determine the correlation between each component of the IBD-disk score and the daily-life IBD burden. A multivariate linear regression was carried out to investigate the effect of each IBD-disk score component on daily life IBD burden scale. In addition, we evaluated completion rate as well as patient satisfaction for IBD-disk.

Results: A total of 2011 outpatients with IBD responded to the survey (930 men; median age 40.0 (29.0-52.0) yrs; median IBD duration 10.5 (4.5-18.5) yrs; 67.8% of patients with Crohn's disease). Patient global assessment of clinical remission was noted in 49.9%. Completion of the IBD-disk was complete in 1484 (73.8%) cases and partial (>5 items) in 220 (10.9%). It was considered as easy to complete by 88.4% of patients. The mean IBD-disk score was 39.0 ± 23.2. After removing 29 outliers, a significant correlation was found between IBD-disk score and daily-life IBD burden scale (r=0.65, p< 0.001).

A significant correlation was found between 5 IBD-disk score components (abdominal pain, regulating defecation, education/work, emotions and energy) and daily-life IBD burden (r>0.50). Based on multivariate linear regression analysis, we build a modified 5-item IBD-disk score (education and work x3 + regulating defecation x2 + abdominal pain + energy + emotions) ranging from 0 to 80 with the highest correlation with daily-life IBD burden (r=0.68, p< 0.001).

The receiver operating characteristic (ROC)- curves analysis indicated a good performance to predict the absence of clinical remission (AUROC 0.70 95%CI[0.66-0.72], p< 0.001) and a significant daily-life IBD burden (0.82 [0.80-0.84], p< 0.001) with an optimal cut-off above 30.

Subgroup analysis of patients in clinical remission revealed a significant burden (score >5) in many dimension of burden: body image (33%), education/work (34%), emotions (40%), energy (55%), interpersonal interactions (17%), sexual functions (23%), and sleep (47%).

Conclusion: The IBD-disk had a good completion rate and demonstrated a close correlation with daily-life IBD burden in a large multicentre cohort of IBD patients. Our results suggest that the IBD-disk could be a valuable tool in routine practice to assess daily-life IBD burden. Although a simplified 5-item IBD-disk demonstrated better performance to assess IBD burden, the overall score, the IBD-disk allows to explore all dimensions of IBD burden.

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P0371 INCIDENCE AND SIGNIFICANCE OF FATIGUE IN PATIENTS WITH IBD

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Introduction: Fatigue is common in IBD patients, even in clinical remission and adversely affects the quality of life. For this reason, it has been suggested to use fatigue questionnaires as PROs (patient reported outcomes). We aimed to study the degree of fatigue in IBD patients and identify factors that are positively or negatively related to its presence.

Aims & Methods: Patients with IBD (men: 48.7%, Crohn's Disease: 65.8%, age: 39.7yrs median, 18.1-72 yrs range), with a regular f-up in our Department completed the Fatigue Severity Scale, IBD Fatigue self assessment 1 & 2, short IBDQ and Short Health Scale upon consensus. Two groups of patients were studied: Group A, patients attended the IBD outpatient clinic (111 patients / 127 questionnaires) and Group B, patients attended the infusion center for biological therapy (45 patients / 256 questionnaires). The SPSS-23 statistical program was used to identify correlations between fatigue and various clinical-laboratory parameters of patients.

Results: Problematic fatigue (FSS> 36) was reported by 45.9% of patients. No difference was observed between Crohn's disease and Ulcerative Colitis or between the two groups of patients. There were statistically significant correlations between fatigue and disease activity (R = 0.452, *P*

<0.001), HGB (R = -0.318, *P* < 0.001) and albumin (R = -0.172, *P* = 0.039). Fatigue was significantly associated with quality of life based on the short IBDQ and SHS questionnaires (R = -0.544, *P* < 0.001 and R = 0.426, *P* < 0.001 respectively). There was also a statistically significant relationship of both fatigue and quality of life with parameters such as female sex (*P* < 0.01), arthralgia (*P* < 0.05) and biological agent treatment (*P* < 0.05). Sequential measurements showed that the quality of life and fatigue rate were consistently maintained in patients with remission under biological therapy.

Conclusion: In the group of IBD patients we studied, a significant correlation with various clinical characteristics was observed. The presence of fatigue is a factor associated with poor quality of life for patients.

Disclosure: Nothing to disclose

P0372 INTER-OBSERVER AGREEMENT OF ULCERATIVE COLITIS "EXTENDED MAYO ENDOSCOPIC SCORE (EMES)" WITHIN A MULTICENTER INFLAMMATORY BOWEL DISEASE (IBD) TEAM WORK

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Introduction: Ulcerative colitis (UC) endoscopic scores decode and translate mucosal damage and into a numeric value to reach inter/intra-observer standardization and variability reduction. At this regard, we elaborated a new UC endoscopic score i.e. the "Extended Mayo Endoscopic Score (EMES)". In this study, we evaluated its inter-observer agreement within a multicenter IBD endoscopy experts team and compared EMES concordance with that of Mayo score.

Aims & Methods: Sixteen UC consecutive patients underwent follow-up colonoscopy. Sixteen videos were recorded during instrument withdrawal phase. They were anonymously loaded on a web platform realized by SEM web-service, FORMEDICA Scientific Learning srl, Lecce, Italy. Thirteen endoscopists were allowed to access by a personal account in order to evaluate UC activity using both Mayo and EMES scores from April to May 2018. EMES has the peculiarity to depict in every colon segment (ascending, transverse, descending, sigmoid and rectum) the following features: erythema (0: absent, 1: mild, 2: moderate, 3: severe); vascular pattern (0: normal, 1: reduction, 2: disappearance); erosions (0: absent, 1: from 1 to 5, 2: 6 to 10, 3:>10); ulcers (0: absent, 1: from 1 to 5, 2: 6 to 10, 3:>10).
The weighted Fleiss' kappa (k) with 95% confidence interval (CI) and the p-value defined the Interrater agreement for global EMES, for every colon segment EMES and for Mayo score. Agreement was considered poor if k< 0; slight for k=0-0.2; fair for k=0.21-0.4; moderate for k=0.41-0.6; substantial dor k=0.61-0.8; almost perfect for k=0.81-1. STATA MP14 software was used.

Results: The interobserver agreement degree of EMES score was moderate even if statistically significant (k= 0.56; 95% CI= 0.46 - 0.67; p< 0.001). Every colon segment showed the following agreement degrees: ascending (k= 0.46; 95% CI= 0.32 - 0.60; p< 0.001); transverse (k= 0.48; 95% CI= 0.29 - 0.67; p< 0.001); descending (k= 0.49; 95% CI= 0.35 - 0.64; p< 0.001); sigmoid (k= 0.52; 95% CI= 0.39 - 0.65; p< 0.001); rectum (k= 0.55; 95% CI= 0.42 - 0.69; p< 0.001) (figure 1). Mayo score result was similar to EMES global agreement (k= 0.53; 95% CI= 0.39 - 0.66; p= 0.001).

Conclusion: EMES and Mayo score showed a moderate, but significant global agreement. Despite the evidence of the need of a further improve-

ment of the agreement for both scores, this study suggested that EMES could be a feasible diagnostic tool for disease activity assessment and tailored therapy.

Disclosure: Nothing to disclose

P0373 SOMATIC DISTRESS SYMPTOMS ARE ASSOCIATED WITH HIGHER DISEASE ACTIVITY IN CROHN'S PATIENTS

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Introduction: Patients with Crohn's disease (CD) struggle continuously with chronic somatic symptoms that could bring about emotional distress. Previous studies have mostly focused on the symptoms of depression and anxiety [1]. The present study evaluates a possible role of somatic distress (previously termed somatization) due to perceived bodily sensations (e.g., numbness, dizziness, chest pain), in addition to depression and anxiety, in exacerbating disease activity among adult patients with CD.

Aims & Methods: A cross-sectional analysis was performed on unselected CD patients (age >18years) attending for routine follow-up at a teaching hospital. Clinical disease activity was assessed by the Harvey-Bradshaw Index (HBI) [2]. Anxiety, depression and somatic distress symptoms were measured using the self-report Brief Symptom Inventory questionnaire [3]. Socio-economic status (SES) was self-declared on a Likert scale [4]. Path analysis models tested the contribution of depression, anxiety and somatic distress to disease activity, in the whole cohort and across socio-demographic groups.

Results: The cohort was composed of 494 CD patients, mean age 38.0 ±13.8 yr., women 58%. Declared SES was: bad 20%, medium 50%, high 30%. Among the three dimensions of distress symptoms, somatic distress was the only significant predictor of increased HBI for the entire sample (Table). The effect of somatic distress on HBI was stronger in men than women, but there were no gender differences in the effects of depression or anxiety on HBI. The effect of somatic distress on HBI was stronger for individuals with low SES (vs. medium SES) and for patients who had recently endured a stressful life event (vs. those who did not). In contrast, no such differences were found in the effect of depression or anxiety on HBI across these subgroups.

Conclusion: Somatic distress is more strongly related than depression and anxiety to disease activity in CD. The association between somatic distress and HBI was especially strong for men, for patients with a recent stressful life event and for patients with low SES. We suggest that screening for emotional distress arising from perceived bodily sensations should be part of CD care. Further investigation will determine whether somatic distress symptoms are causal for elevated markers of inflammation, and whether psychological interventions designed to manage somatic distress could improve outcomes for IBD patients.

	All	Gender		SES			Stressful life event	
		Men	Women	Low	Medium	High	No	Yes
β Somatic distress	0.65***	0.91***	0.52***	0.91***	0.48***	0.67***	0.32	.072***
β Depression	0.11	0.20	0.06	-0.15	0.14	0.47	0.29	0.05
β Anxiety	-0.23	-0.53**	-0.11	-0.17	-0.15	-0.74	-0.28	-0.22

*[Effect of somatic distress, depression and anxiety on HBI: Summary of path coefficients across socio-demographic groups (** p<.01, *** p<.001)]*

References: 1. Mikocka-Walus A, Knowles SR, Keefer L, et al. Controversies revisited: A systematic review of the comorbidity of depression and anxiety with inflammatory bowel diseases. Inflamm Bowel Dis 2016; 22(3):752-62. 2. Bennebroek Evertsz, F. B., Hoeks, C. C., Nieuwkerk, P. T., et al. Development of the patient Harvey Bradshaw index and a comparison with a clini-

cian based Harvey Bradshaw index assessment of Crohn's disease activity. J Clin Gastroenterol 2013; 47: 850- 856. 3. Derogatis, L. R., & Melisaratos, N. The brief symptom inventory: An introductory report. Psychol Med 1983; 13: 595-605. 4. Slonim-Nevo V, Sarid O, Friger M, Schwartz D, Chernin E, Shahar I, Sergienko R, Vardi H, Rosenthal A, Mushkalo A, Dizengof V, Ben-Yakov G, Abu-Freha N, Munteanu D, Gaspar N, Eidelman L, Segal A, Fich A, Greenberg D, Odes S; Israeli IBD Research Nucleus (IIRN). Effect of psychosocial stressors on patients with Crohn's disease: threatening life experiences and family relations. Eur J Gastroenterol Hepatol. 2016; 28:1073-1081.
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P0374 MINDFULNESS-BASED COGNITIVE INTERVENTION IMPROVES WORK PRODUCTIVITY AND ACTIVITY IMPAIRMENT AMONG CROHN'S DISEASE PATIENTS. A RANDOMIZED CONTROLLED TRIAL

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Introduction: Crohn's Disease (CD) is a chronic debilitating inflammatory intestinal disease causing lifetime medical problems. It was shown to affect patients' ability to work and perform everyday leisure activities. We assessed whether a specifically designed Cognitive Behavioral Mindfulness Intervention (CBMI) as an add-on treatment, could improve work productivity and leisure activities in CD patients.
Aims & Methods: Unselected adult CD patients with mild to moderate disease activity (4< HBI < 16) attending for routine follow-up at the outpatients' department of a university-affiliated tertiary hospital were enrolled consecutively into a prospective randomized controlled study. Patients were randomized to CBMI (Intervention group) or were wait-listed (Control group). CBMI was taught to Intervention group patients by trained therapists, using SKYPE in weekly hour-long sessions over an 8-week period. Medical details were collected by study physician and medical treatment was uninterrupted. Patients' clinical status was scored by the Harvey Bradshaw Index (HBI). Treating physicians were blinded to randomization. Patients completed the Work Productivity and Activity Impairment (WPAI) Questionnaire, which assesses their ability to work and perform leisure activities in the previous week while coping with their disease. The WPAI generates four scores: Absenteeism - missed work d\t CD; Presenteeism - reduced on-the-job effectiveness; Work productivity loss -overall work impairment; Activity Impairment - degree CD affected regular leisure activities. HBI and WPAI were again completed three months from baseline.
Results: The cohort consisted of 41 patients, 20 in the Intervention Group (IG) and 21 in the Control Group (CG). Of the IG and CG patients 65% and 62% were female, the mean (SD) age was 36 (14.4) and 34 (10.8) years, mean (SD) disease duration was 9.7 (10.1) and 9.7 (8.9) years, 10% and 14.3% were smokers, baseline mean HBI was 9.14 and 8.5, and employment rates were 71.4% and 85.0% respectively. Three months from baseline HBI decreased by 3.35 in the IG vs 1.95 in the CG. Absenteeism decreased from 25.4% to 4.6% in the IG (P=0.06) and increased from 15.1% to 21.8% in the CG (P=0.55). Presenteeism decreased from 52.1% to 24.3% in the IG (P=0.027) and from 43.3% to 38.0% in the CG (P=0.63). Work productivity loss decreased from 57.0% to 26.9 % in the IG (P=0.021) and from 49.8% to 45.2% in the CG (P=0.46). Activity impairment decreased from 47.0% to 29.0% in the IG (P=0.018) and from 51.9% to 48.6% in the CG (P=0.51).
Conclusion: Work productivity is significantly improved by a specifically designed CBMI. This intervention should be added to the treatment options for better outcomes in CD.
Disclosure: Nothing to disclose

P0375 EVALUATION OF THE DIAGNOSTIC VALUE OF FECAL CALPROTECTIN IN THE MANAGEMENT OF CROHN'S DISEASE: MOROCCAN EXPERIENCE

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Introduction: To limit the repetition of colonoscopies, which are not appreciated by patients, non-invasive tools have been developed. Among them, fecal calprotectin is the non-invasive reference biomarker for assessing endoscopic activity in Crohn's disease (CD).
Aims & Methods: The objective of our study is to evaluate the performance of fecal calprotectin for the detection of endoscopic activity in patients with Crohn's disease .This is a single-center retrospective study that includes patients with CD. Inclusion criteria: Patient with both fecal calprotectin and ileocoloscopy. Fecal calprotectin was measured by ELISA and expressed in mg / kg. Criterion of judgment : Endoscopic remission: CDEIS < 6 and Rutgeert score < i2. Statistical analysis was performed using Medcalc V9 software. The diagnostic evaluation of (calpro) was performed by the ROC curve. For each value, the sensitivity (Se), the specificity (Spe), the positive predictive value (VPP) and the negative predictive value (VPN) were determined. The best threshold value of (calpro) corresponds to the value having a better sensitivity for a better specificity.
Results: A total of 70 patients were included in this study. There are 54 women and 16 men; the couple calprotectin-fecal-ileocoloscopy was performed 90 times. According to the Montreal classification: the localization is distributed as follows: L1 = 17.8%, L2 = 20% , L3 = 62.2% and the phenotype is distributed as follows: B1 = 50%, B2 = 37.8%, B3 = 12 , 2%. Clinically: 76.6% were asymptomatic. The analysis of the area under the curve ROC revealed a diagnostic value estimated at 70% (confidence interval [0.589 - 0.788]). The best detection threshold for the endoscopic activity was 150 mg / kg. This threshold demonstrated the following performances: Se = 72.97%, Spe = 71.70%, VPP = 64.3%, VPN = 79.2%. If we take operated patients separately, the analysis of area under ROC curve found an estimated diagnostic value of 72% (confidence interval [0.544 - 0.859]). The best detection threshold for endoscopic activity was 127 mg / kg . This threshold demonstrated the following performance: Se = Se = 66.67%, Spe = 78.57%, VPP = 82.4%, VPN = 61.1%.
Conclusion: Measurement of fecal calprotectin have a diagnostic value acceptable for the diagnosis and monitoring of endoscopic remission in patients with Crohn's disease. In our study, the optimal threshold was 150 mg / kg and 127 mg/kg in operated patients. This threshold value presented a better sensitivity for a better specificity.
Disclosure: Nothing to disclose

P0376 ARTIFICIAL NEURAL NETWORK AS AN ASSISTANT IN THE DIFFERENTIAL DIAGNOSIS BETWEEN ULCERATIVE COLITIS AND CROHN'S DISEASE

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Introduction: Due to the lack of a "gold standard" in the diagnosis of IBD, the differential diagnosis between ulcerative colitis (UC) and Crohn's disease (CD) can be difficult. The complexity of the short-term diagnosis, but its extreme necessity, the lack of uniform criteria for diagnosis, but at the same time high social and medical significance, require the development of new algorithms and methods for identifying and differentiating the forms of IBD.
Aims & Methods: We have created an artificial neural network (ANN) of the multilayer perceptron type using the Neural Network Toolbox application from the MATLAB application package. Three types of images were used to train the ANN: the norm of the endoscopic picture of the colon, the endoscopic pictures of UC and CD. The first stage is the training of an

artificial neural network to distinguish the presence or absence of pathology (29 images of the "normal colon", 14 images of the CD, and 15 ‑ UC). The second stage is the training of the network in the task of differentiating IBD. The network was trained on an array of 124 images (62 images of each class of pathologies). Each image was previously converted to grayscale mode, and then into a matrix of pixels. A vector with the number of elements equal to the size of the image was fed to the input of the perceptron.

Results: To solve the problem of identifying pathology, a perceptron was built with 32,2784 input neurons, 10 hidden neurons and 2 output neurons, which represent the conclusion that the image belongs to one of two classes: norm or pathology. To solve the problem of differentiating CD and UC, a perceptron was created with 364500 input neurons (this value was determined by the image resolution) and 2 output neurons, representing the conclusion that the image belongs to one of two classes: ulcerative colitis or Crohn's disease. ANN studied no more than three times, because then there was a decrease in accuracy.

The best result in the differentiation of pathologies was shown by a neural network of the type MP 364500: 364500-20-2: 2, the overall recognition accuracy of which was 96.8%. However, on the control sample, the accuracy was 84.2%.

The effectiveness of the created artificial neural network in relation to the differentiation of the forms of IBD (UC / CD) can be judged by the criteria: specificity (Sp) 78.2%, sensitivity (Se) 93.1%, accuracy (Ac) 85.7%.

Conclusion: At present, it is planned to further refine the models obtained in order to increase the reliability of their estimates. In particular, it is planned to train the network on a larger array of endoscopic images, including those with higher resolution, as well as the use of other types of networks, in particular, the radial basis function. The resulting ANN can be used to solve the problems of classifying endoscopic images of the intestine for the presence of IBD, as well as to differentiate between Crohn's disease and ulcerative colitis.

Disclosure: Nothing to disclose

P0377 SUBOPTIMAL ADHERENCE TO VACCINATION IN PREGNANT PATIENTS WITH INFLAMMATORY BOWEL DISEASE ON BIOLOGICS

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Introduction: Inflammatory bowel disease (IBD) affects 0.7% of the Canadian population[1]. Studies have suggested that preventative health services are received at a significantly lower rate for IBD patients than the general population[2]. Further, many IBD patients are young, female and of childbearing age. Recent data has demonstrated that despite having multiple health care providers, post partum individuals with IBD have suboptimal health care maintenance rates, with lower self-reported rates of vaccination[3]. We determined adherence to vaccination in pregnant women with IBD by linking a provincial database to a dedicated IBD pregnancy registry.

Aims & Methods: To determine the proportion of pregnant women with IBD on biologics who received key vaccines, which included Hepatitis A and B, pneumococcal vaccines 13 and 23, the diphtheria, tetanus and acellular pertussis (dTap) vaccine, human papilloma virus (HPV) vaccine, and the hemophilus influenza (HiB) vaccine. Adherence was based on serological documentation of immunity and/or electronic public health provincial vaccination records.

Results: Records of 115 IBD patients who were pregnant and on a biologic in the study period of 2012-2018 were reviewed. The median age of patients studied was 32 years (IQR 6). Of these patients, 23% had ulcerative colitis (UC), 2% had indeterminate colitis, and 75% had Crohn's disease (CD). 87% were on an anti TNF-alpha biologic (infliximab, adalimumab or golimumab), 7% were on vedolizumab and 6% on ustekinumab. Our results show that 70% had either serological evidence of immunity or registry reported vaccination to Hepatitis B. 37% had serological or registry reported evidence of Hepatitis A vaccination. With the pneumococcal vaccine, 2% had records of the Prevnar 13 vaccine with 35% having received the Pneumovax 23 vaccine. When it came to the dTap vaccine, 78% had evidence of vaccination. The recorded rate of a complete HPV vaccine was 4% while exposure to the hemophilus influenza (HiB) vaccine was 14%.

Conclusion: Our study suggests deficiencies in rates of vaccination in the pregnant IBD population on biologics, particularly hepatitis A, the pneu-

mococcal vaccines, HPV and HiB vaccines. These results will serve as a starting point for establishing determinants of suboptimal adherence within the studied population. Ultimately, targeted education programs can be developed.

References: [1] The Impact of Inflammatory Bowel Disease in Canada. 2018 Final Report and Recommendations. [2] Selby L, Kane S, Wilson J, et al. Receipt of preventive health services by IBD patients is significantly lower than by primary care patients. Inflamm Bowel Dis. 2008;14:253-258. [3] Mao EJ, Sheibani S, Martin C, Bloomfeld RS, Isaacs K, Saha S, Mahadevan U. Preventive Health Care Among Postpartum Women With Inflammatory Bowel Disease: Results From the PIANO Registry. Inflamm Bowel Dis. 2019 Mar 14;25(4):797-802.

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P0378 RELATION BETWEEN 6-THIOGUANINE NUCLEOTIDES AND RED CELL MEAN CORPUSCULAR VOLUME, WHITE BLOOD CELL, NEUTROPHIL AND LYMPHOCYTE COUNT IN PATIENTS TREATED WITH AZATHIOPURINE AND 6-MERCAPTUPURINE

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Introduction: Inflammatory bowel disease (IBD) is caused by dysregulated immune responses, thus thiopurine drugs, 6-mercaptopurine (6-MP) and prodrug Azathioprine (AZA) are indicated in refractory and steroid-dependent patients. Due to narrow therapeutic ranges, risks of myelosuppression and liver toxicity, these drugs require therapeutic monitoring of metabolites. The 6-Thioguanine nucleotide (6-TGN) metabolite is predominant during therapeutic efficacy (235-460 pmol/8x10^{8} erythrocytes), whereas 6-Methylmercaptopurine (6-MMP) correlates with toxicity. Monitoring is associated with significant laboratory costs and a more cost-effective surrogate marker is desirable. As thiopurines cause lymphopenia and increased mean corpuscular volume (MCV), it has been postulated that these may be clinically useful in determining 6-TGN levels, and thus therapeutic efficacy of immunomodulatory treatment.

Aims & Methods: To investigate the correlation between 6-TGN levels in relation to MCV, white blood cell count (WBC), neutrophil and lymphocyte count in patients treated with thiopurines.

We retrospectively analysed an electronic database of IBD and non-IBD patients from 2008 to 2017 who were treated with thiopurines (either 6-MP or AZA) in a regional Australian hospital. A total of 931 laboratory results were consecutively obtained, with some patients having repeated blood tests. Pearsons correlation was performed between 6-TGN and MCV levels. Laboratory results were grouped with those < 235 pmol/8x10^{8} erythrocytes (below therapeutic level, n=403) and those ≥235 pmol/8x10^{8} erythrocytes (above therapeutic level, n=528). Unpaired t-test was used to compare the MCV, WBC, neutrophil and lymphocyte levels of these two groups. The value of these surrogate markers to distinguish shunters (6-TGN < 260, 6-MMP > 5700) vs. non-shunters (6-TGN ≥ 260, 6-MMP ≤5700) was also assessed.

Results: Results showed that a positive statistically significant correlation existed between 6-TGN and MCV levels (r=0.3219, p< 0.0001) within our dataset. The odds ratio of therapeutic levels of 6-TGN (≥235 pmol/8x10^{8} erythrocytes) found in patients with MCV ≥92 fl was 2.79 (95% CI 2.13, 3.67) (p< 0.0001), compared to patients with MCV < 92 fl. Patients above therapeutic 6-TGN level had a mean MCV of 92.66 fl, compared to MCV 89.1 fl (p< 00001) in patients below therapeutic 6-TGN (< 235 pmol/8x10^{8} erythrocytes). Therapeutic patients also had a mean WBC of 6.59 x10^{9}/L (p=0.0012), neutrophil count of 4.37 x10^{9}/L (p=0.0211) and lymphocyte count of 1.53 x10^{9}/L (p=0.033), which were statistically lower levels than non-therapeutic patients at 7.16 x10^{9}/L, 4.73 x10^{9}/L and 1.64 x10^{9}/L respectively. The mean MCV (95 fl) and WBC (5.915 x10^{9}/L) of shunters was statistically different to the mean MCV (90.91 fl) and WBC (6.885) of non-shunters (p=0.0001 and p=0.0131 respectively). The mean neutrophil and lymphocyte count between shunters and non-shunters was non-significant.

Conclusion: The results from this study show that there is a statistically significant correlation between 6-TGN and MCV levels. Patients with above therapeutic 6-TGN levels have statistically higher MCV levels and statisti-

cally lower levels of WBC, neutrophils and lymphocytes. Further, there are statistically significant odds that patients managed on thiopurines with MCV ≥92 fl have a therapeutic 6-TGN level. This indicates that it may be possible to use these markers as surrogates for expensive 6-TGN levels in patients treated with thiopurines. Further, this study suggests that shunters have a statistically higher mean MCV and WBC.
Disclosure: Nothing to disclose

P0379 BAMBOO JOINT-LIKE APPEARANCE IN STOMACH - AN ENDOSCOPIC BIOMARKER OF CROHN'S DISEASE. A PROSPECTIVE CASE CONTROL STUDY

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Introduction: Crohn's disease (CD) is a chronic inflammatory condition that typically involves the ileocecal region; but the whole gastrointestinal (GI) tract can be affected. Lesions in the upper GI tract are increasingly diagnosed. It was suggested that lesions in the stomach, with a bamboo joint-like appearance (BJA) might be an endoscopic biomarker for CD. However, the reported prevalence of upper GI tract involvement in CD varies greatly and diagnostic significance of BJA remains to be defined. A majority of European studies were retrospective and did not refer to the presence of BJA in stomach.
Aims & Methods: Our aim was to investigate the prevalence, characteristic and clinical importance of upper gastrointestinal involvement in a patients with CD, with special focus on the lesion named bamboo joint like appearance. A prospective, case control study was conducted. 144 patients were included into the study, 72 with CD (37 female, 35 male) and 72 gender and age matched non IBD controls. The endoscopy was performed by experienced physician using a high definition endoscope with narrow band imaging.
Results: The upper gastrointestinal tract was involved in 43 out of 72 (59.7 %) patients with CD. Most commonly stomach was affected (n=37; 51.4 %), followed by duodenum (n=21; 29.2%) and esophagus (n=9; 12.5 %). 16 (22.2%) of CD patients had BJA in proximal part of gastric body or/and fundus . BJA was present irrespectively of the patient's sex, age, location of the disease, and medications taken. BJA was absent in control group (statistically significant difference with study group, p=0.00025).
Conclusion: The upper gastrointestinal involvement in Crohn's disease is common phenomenon. The most commonly affected area is the stomach with a specific lesion for CD, the bamboo joint like appearance. This finding may help to identify individuals at high risk for CD using only gastro-duodenoscopy.
References: 1.Yokota K, Saito Y, Einami K, Ayabe T, Shibata Y, Tanabe H, et al. A bamboo joint-like appearance of the gastric body and cardia: possible association with Crohn's disease. Gastrointest Endosc. 1997;46(3):268-72. 2. Kuriyama M, Kato J, Morimoto N, Fujimoto T, Okada H, Yamamoto K. Specific gastroduodenoscopic findings in Crohn's disease: Comparison with findings in patients with ulcerative colitis and gastroesophageal reflux disease. Dig Liver Dis. 2008;40(6):468-75. 3.Horjus Talabur Horje CS, Meijer J, Rovers L, van Lochem EG, Groenen MJ, Wahab PJ. Prevalence of Upper Gastrointestinal Lesions at Primary Diagnosis in Adults with Inflammatory Bowel Disease. Inflamm Bowel Dis. 2016;22(8):1896-901. 4.Greuter T, Piller A, Fournier N, Safroneeva E, Straumann A, Biedermann L, et al. Upper Gastrointestinal Tract Involvement in Crohn's Disease: Frequency, Risk Factors, and Disease Course. J Crohns Colitis. 2018;12(12):1399-409.
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P0380 *POINT-OF-CARE* TESTING SYSTEM FOR FECAL CALPROTECTIN DETECTION IN THE TELEMONITORING OF PATIENTS WITH INFLAMMATORY BOWEL DISEASES

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Introduction: Telemedicine refers to the professional monitoring of patients and the transmission of medical information remotely via information technologies. The first Czech study of the remote monitoring of IBD patients called "IBD Assistant" was launched at the IBD Clinical & Research Centre ISCARE IVF in 2018. The inclusion criteria for the study were as follows: (1) a diagnosis of Crohn's disease or ulcerative colitis, (2) remission of the disease verified by endoscopy conducted during the 12 months prior to the start of the study, (3) age > 18 years, (4) user-level computer literacy with the possibility of regular use of an online smartphone, and (5) the subject's own email address.
The exclusion criteria were (1) lacking knowledge of the Czech language, (2) a diagnosis of IBD within the 3 months preceding the start of the study, (3) pregnancy, (4) ongoing biological treatment, and (5) hospitalisation in the preceding 3 months due to exacerbation of IBD symptoms. In addition to monitoring the patients' subjective complaints, the occurrence of defined clinical signs and treatment adherence, the best-known and most widely used biomarker of gut inflammation - fecal calprotectin (FC) measurement - were integral parts of the project.
Aims & Methods: Quality assessment of the home-based CalproSmart (CALPRO, Norway) FC test in the telemonitoring of patients with inflammatory bowel disease (IBD).
One hundred FC values were compared. The first data set was measured by patients using the home-based CalproSmart test, and the second data set was obtained using standard fluoroimmunoassay (FIA) in a clinical laboratory. The principle of CalproSmart measurement is lateral flow analysis. Its measurement range is 70-1,500 µg/g. Expert measurements were conducted by using the ELiA Calprotectin Phadia (Thermo Fisher Scientific, USA) diagnostic kit. The measurement range of the analysis is 0-6,000 µg/g.
Results: Spearman's correlation coefficient r = 0.895 (p = 0.0004) and weighted Cohen's kappa 0.835 indicate good correlation of two data sets measured by different measurement systems; see Table 1.

		LFA (CalproSmart)		
		LOW	MODERATE	HIGH
	LOW	53	6	0
FIA (Phadia)	MODERATE	2	32	1
	HIGH	0	1	5

FIA - fluoroimmunoassay; LFA - laminar flow analysis; LOW - concentrations of fecal calprotectin up to 200 µg/g; MODERATE - concentrations of fecal calprotectin between 201 and 500 µg/g; HIGH - concentrations of fecal calprotectin over 500 µg/g; Unweighted kappa = 0.814; Weighted kappa = 0.835; Standard error of kappa = 0.055; 95% confidence interval: from 0.706 to 0.923; The strength of agreement is considered „very good."

[Table 1. LFA and FIA performance results in terms of Cohen's kappa coefficient]

Conclusion: The home-based FC test CalproSmart is well-suited to qualitative FC analysis in the telemonitoring of patients with IBD. It cannot replace standard laboratory FC measurements, but such performance is not required for the home-based kit.
Disclosure: Nothing to disclose

P0381 SERUM TROUGH SB5 LEVELS: A COMPARISON OF TWO DIFFERENT IMMUNOASSAYS FOR THE MONITORING OF BIOSIMILAR ADALIMUMAB TREATMENT IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: SB5 is a biosimilar monoclonal antibody adalimumab for the treatment of patients with inflammatory bowel disease (IBD). Only minor differences in clinically inactive components are allowable in biosimilars compared to reference products. However, even a small difference in the molecular structure can lead to different behavior of the biosimilar drug in analytical systems for the detection of serum drug trough levels.

Aims & Methods: Although monitoring of adalimumab serum trough levels hold an important significance in treatment modalities and clinical outcome during the treatment, no data about monitoring of drug serum trough levels in IBD patients treated with SB5 are present to date. Therefore, we would like to compare recombinant human TNFa -based (rhTNFa) ELISA kit for the adalimumab trough levels detection with results obtained from the system based on the monoclonal antibody towards an original adalimumab.

Sixty-two IBD serum samples from patients on maintenance treatment with SB5 (40 mg subcutaneously every two weeks) were analyzed. Sera form IBD Blood Bank established according to the Ethics Committee of *ISCARE* (Nr 2015/Ia) were used. SB5 trough levels were measured by the standard enzyme immunoassay (ADALIMUMAB ELISA ImmunoGuide, REF: IG-AA103) based on recombinant human TNFa (rh TNFa). Moreover, the same serum samples were analyzed by RIDAScreen ADM Monitoring (R-Biopharm, REF: G09043) based on the highly specific monoclonal antibody towards original adalimumab MA-ADM40D8 isolated and characterized at the KU Leuven.

Data were analyzed by Statistica 13.3. (TIBCO). The strength and direction of association between two variables were assessed by Spearman's rank order correlation coefficient. The Kruskal-H test was used for comparing two cohorts of concentration values.

Results: Of 62 serum samples, 54 were patients with Crohn's disease and 8 patients with ulcerative colitis, 36 were women and 26 were men, median age was 41.5 years. Excellent quantitative agreement was observed between adalimumab trough levels measured by rhTNFa-based, and monoclonal antibody-based kits, r = 0.804, P < 0.0001. Non-parametric Kruskal Wallis test have shown that medians of trough levels concentrations in two data groups are not different, p = 0.363.

Conclusion: rh-TNFa-based ELISA kit and monoclonal antibody-based ELISA kit for measuring SB5 trough levels showed similar overall performance. and were in very good mutual quantitative agreement. This would provide valuable information on the possibility of using these assays as monitoring tools during treatment with biosimilar adalimumab.

Disclosure: Nothing to disclose

P0382 WITHDRAWN

P0383 FACTORS CONTRIBUTING TO INDETERMINATE INTERFERON-γ RELEASE ASSAY RESULTS IN INFLAMMATORY BOWEL DISEASE PATIENTS UNDERGOING PRE-BIOLOGIC TUBERCULOSIS SCREENING

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Introduction: IFN-γ release assays (IGRA) are routinely used in patients with Inflammatory Bowel Disease (IBD) prior to initiation of biologic monoclonal antibody treatment to screen for latent tuberculosis (TB) in-fection. IGRA results are often indeterminate, resulting in the need for repeat testing and a potential delay in commencing appropriate management. Disease activity and corticosteroid treatment have previously been shown to be associated with indeterminate IGRA results. We hypothesise that there is a positive correlation between systemic inflammation and indeterminate IGRA results.

Aims & Methods: We performed a case-control study of 268 IBD (5 IBDU, 48 UC, 215 CD) patients who underwent pre-biologic IGRA testing at our tertiary IBD referral centre. We compared various phenotypic, disease activity and treatment characteristics of patients who had a determinate IGRA with those who had an indeterminate IGRA results. Biochemical disease activity was evaluated using CRP, platelet count and albumin measured within one week of IGRA testing. We also aimed to assess whether treatment setting (inpatient vs outpatient) affected IGRA results. The Mann-Whitney U and Chi-Square tests were used to compare the two groups.

Results: Of the 268 included patients, 42 (16%) had an indeterminate IGRA and the remaining 226 (84%) were determinate: 215 negative, 11 positive (table 1).

We observed that a significantly higher proportion of patients with an indeterminate IGRA results were on corticosteroid therapy (50% vs 15.5%, p< 0.0001) and were inpatients (52% vs 5%, p=<0.0001) at the time of testing. We also found that patients with an indeterminate result had a higher median CRP (25 vs 5mg/L, p=<0.0001) and platelet count (412 vs 330x10⁹/L, p=<0.0001) as well as a lower albumin (35 vs 44g/L, p=<0.0001). There was no significant difference in the proportion of patients in each group who were receiving immunomodulators at the time of testing (55% indeterminate IGRA vs 61% determinate IGRA, p=0.48).

	Indeterminate IGRA (n=42)	Determinate IGRA (n=226)	p
Characteristic			
IBD phenotype, UC:CD:IBDU	15:24:3	33:191:2	
Use of immunomodulators	23 (55%)	137 (61%)	0.48
Use of steroids	21(50%)	35 (16%)	<0.0001
Treatment setting- inpatient	22 (52%)	12 (5%)	<0.0001
Disease activity			
Median CRP (mg/L)	25	5	<0.0001
Median albumin (g/L)	35	44	<0.0001
Median platelet count (x109/L)	412	330	<0.0001

[Table 1. Univariate analyses of associations with an indeterminate IGRA result]

Conclusion: Our results demonstrate that patients with more active IBD are significantly more likely to have an indeterminate IGRA test than those with less active disease. IGRA testing may be of limited diagnostic utility in the context of hospitalised patients and those receiving corticosteroids. These factors should be taken into account by clinicians when considering how to manage patients with indeterminate IGRA requiring escalation to a biologic. In patients with factors known to contribute to indeterminate IGRA testing, low risk of TB and a normal chest radiograph, clinicians may decide to proceed with biologic treatment rather than delay. If possible, IGRA testing should be carried out prior to the initiation of corticosteroid therapy.
Disclosure: Nothing to disclose

P0384 ADHERENCE TO THERAPY INFLAMMATORY BOWEL DISEASE OBSERVED IN MOSCOW CLINICAL SCIENTIFIC CENTER

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Introduction: Inflammatory bowel diseases (IBD) are chronic autoimmune inflammatory diseases with intestinal lesions and external manifestations. The concept of permanent life-long medication is the cornerstone in the treatment of IBD. Depending on the dosage regimen prescribed, the patient is injected with a dose and an interval between doses.

Aims & Methods: To assess adherence to the treatment of diseases in patients with Crohn (CD) and ulcerative colitis (UC), observed in the department of inflammatory bowel disease.

Materials and methods. The study included 55 (45.8%) men and 65 (54.2%) women older than 18 years, 70 (58.3%) patients with UC, 50 (41.7%) with CD, who attend treatment and examination in the department of inflammatory bowel diseases. Patient adherence to therapy is evaluated using the Moriska-Green test, the results of which all patients were divided into two groups: the first group – patients with low adherence treatment (LAT); the second group – patients with high adherence to treatment (HAT).

Results: It was shown that patients with high adherence to therapy were 78 (65.0%) versus 42 (35.0%), respectively (p <0.001). In the group of patients with HAT, women predominate – 26 (61.9%) versus 16 (30.1%) men (p <0.001). In the group of HAT, patients with CD 30 (71.4%) also prevail against 12 (28.6%) patients with UC (p <0.001). It was established that in the group of HAT, patients receiving 5-aminosalicylic acid preparations (5-ASA) 23 (54.8%) and biological preparations (BP) – 15 (35.7%) predominate. In the LAT group, patients with the necessary immunosuppressors and glucocorticosteroids prevail – 54 (69.3%), against patients receiving 5-ASA and BP – 24 (30.7%) (p <0.001). The frequency of exacerbations of diseases was higher in the LAT group – 52 (66.6%), versus 13 (30.9%) in the HAT group (p <0.001). The frequency of surgical interventions in patients with CD was higher in the LAT group – 15 (75.0%) versus 5 (16.6%) in the HAT group (p <0.001). A significant difference between the groups was noted when it was possible to obtain drugs in the preferential provision (38.5%) in the HAT group versus 40 (51.3%) LAT groups (p <0.001). It was shown that the patient has no age, no educational and socio-economic status.

Conclusion: Among patients with IBD, examined in the department of inflammatory bowel diseases, 65% have a low commitment to taking prescribed medications. Low adherence of treatment is associated with factors such as the use of systemic immunosuppressants and glucocorticosteroids in therapy, complications during CD, the frequency of exacerbations of IBD. Female sex is reliably associated with high adherence to treatment, the presence of drugs in the preferential provision.

Disclosure: Nothing to disclose

P0385 PRELIMINARY ANALYSIS OF UTILISATION AND CLINICAL RESULTS FROM THE NHS SCOTLAND THERAPEUTIC DRUG MONITORING SERVICE FOR BIOLOGIC MEDICINES

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Introduction: Anti-tumour necrosis factor α (anti-TNFα) drugs infliximab (IFX) and adalimumab (ADL) are effective treatments for inflammatory bowel disease (IBD) and have greatly improved outcomes for many individuals. However, treatment effects are not universally favourable with primary non-response (PNR) to treatment occurring in up to 30% and secondary loss of response (SLR) in up to 46% of IFX and ADL treated IBD cohorts (1,2).Therapeutic drug level and anti-drug antibody monitoring (TDM) has emerged as a useful tool for optimising the effectiveness of these drugs, identifying individuals who may benefit from dose or treatment frequency adjustments to regain control of disease after relapse, or even to prevent PNR or SLR.

Aims & Methods: Ensuring safe and effective use of biologic medicines has been identified as a key priority for NHS Scotland. Inequity and inconsistency of access to TDM across the nation was recognised as a barrier to delivering best practice and so a nationally commissioned TDM service was established in January 2018 to support clinical practice, providing universal access to TDM for IBD services across Scotland. A service webpage was developed to provide guidance on testing strategies and interpretation of TDM results (3). Preliminary data and initial clinical observations from the first year of the service have now been collated. Data collection and analysis of results regarding usage and clinical impact of the service were identified as key outcome measures to assess service success and sustainability.

An automated search of clinical data and test results recorded within the clinical biochemistry electronic results management system was conducted to identify all TDM tests performed between 01/01/2018 and 31/12/2018. Outcomes for descriptive analysis included the number of samples received and processed, overall testing population, service utilisation by Health Board, and the number and results of TDM tests performed per patient. TDM results were interpreted according to published guidance on the service webpage and comparison was made with previously published data (4).

Results: 3609 specimens were received for testing, from 13 of the 14 Scottish Health Boards. 3561 drug level (DL) tests were performed; 1786 IFX, 1775 ADL. 2717 total antidrug anti-body (TABT) tests and 681 free antidrug anti-body tests (FABT) were performed according to service protocol. 2791 individuals had one or more TDM tests during the 12-month period, of whom 541 were tested twice or more (range 2-5).

		INFLIXIMAB	ADALIMUMAB	
Drug level by category	Supratherapeutic DL > 8mcg/ml	546 (30.6%)	708 (39.9%)	Supratherapeutic DL > 10 mcg/ml
	Therapeutic DL ≥3<8.1mcg/ml	738 (41.3%)	636 (35.8%)	Therapeutic DL ≥5<10.1 mcg/ml
	Sub-therapeutic DL < 3mcg/ml	502 (28.1%)	431 (24.3%)	Sub-therapeutic DL < 5 mcg/ml
TABT by category	Negative (<10 AU/ml)	791 (54.2%)	905 (71.9%)	Negative (<10 AU/ml)
	Positive (>10 AU/ml)	668 (45.8%)	353 (28.1%)	Positive (>10 AU/ml)
FABT by category	Negative (< 5AU/ml)	376 (82.8%)	176 (77.6%)	Negative (<10 AU/ml)
	Positive (> 5 AU/ml)	78 (17.2%)	51 (22.4%)	Positive (>10 AU/ml)

[Table 1 - IFX & ADL DL, TABT and FABT results by category as defined in service guidance (AU/ml = Arbitrary Units/ml)]

Conclusion: TDM has been enthusiastically embraced with rapid uptake of testing in IBD. It is estimated that > 50% of individuals treated with IFX or ADL have been tested at least once in the first year. DL results were found to be similar to previously published data, as were rates of antibody positivity. The large volume of data generated by the service may provide additional evidence regarding the utility of TDM in predicting clinical response. Next steps are to conduct a comparative effectiveness analysis where proactive vs reactive TDM testing strategies will be compared, with the primary outcome measure being the proportions of patients with SLR.

References: 1. Ben-Horin S and Chowers Y. Review article: loss of response to anti-TNF treatments in Crohn's disease. Alimentary Pharmacology & Therapeutics, 33: 987-995. doi:10.1111/j.1365-2036.2011.0461. 2. Osterman MT, Haynes K, Delzell E, et al. Comparative effectiveness of infliximab and adalimumab for Crohn's disease. Clin Gastroenterol Hepatol 2014;12:811-817 3. Scottish Biologic Therapeutic Drug Monitoring Service https://www.nhsggc.org.uk/about-us/professional-support-sites/biochemistry/biological-therapy-monitoring/ 4. Kennedy NA, Heap GA, Green HD et al. Predictors of anti-TNF treatment failure in anti-TNF-naive patients with active luminal Crohn's disease: a prospective, multicentre, cohort study. Lancet Gastroenterology and Hepatology (2019). https://doi.org/10.1016/S2468-1253(19)30012-3.

P0386 IMPACT OF BASELINE CORTICOSTEROID THERAPY ON TOFACITINIB INDUCTION EFFICACY AND INFECTION RISK IN PATIENTS WITH ULCERATIVE COLITIS: DATA FROM GLOBAL CLINICAL TRIALS

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Introduction: Tofacitinib is an oral, small molecule Janus kinase inhibitor for the treatment of ulcerative colitis (UC). Oral corticosteroids are an acknowledged induction therapy, but are associated with side effects including infections.[1]

Aims & Methods: We evaluated induction efficacy and infection risk with tofacitinib 10 mg twice daily (BID) treatment based on baseline corticosteroid use in tofacitinib UC induction studies. Remission (total Mayo score ≤2, no individual subscore >1, rectal bleeding subscore 0), mucosal healing (Mayo endoscopic subscore ≤1) and clinical response (decrease from baseline total Mayo score of ≥3 points and ≥30%, and decrease in rectal bleeding subscore of ≥1 point or absolute rectal bleeding subscore of 0 or 1) were evaluated in two 8-week, Phase 3 tofacitinib induction studies (OCTAVE Induction 1 & 2; NCT01465763 & NCT01458951; pooled data). Induction studies allowed stably dosed corticosteroids (25 mg/day maximum). Efficacy and safety data were summarised by oral corticosteroid use at induction baseline (BLC-Yes/No). Infections of interest included herpes zoster (HZ), serious infections (SIs), and adjudicated opportunistic infections (OIs).

Results: Of 1139 patients (placebo: n=234; 10 mg BID: n=905) in OCTAVE Induction 1 & 2, 525 (46.1%) were on corticosteroids at baseline (< 15 mg daily dose: 32.8%; ≥15 mg daily dose: 67.2%). A statistically significant treatment effect of tofacitinib 10 mg BID vs placebo was observed for remission, mucosal healing and clinical response at Week 8, for both subgroups of patients with and without baseline oral corticosteroid use (Table). Differences vs placebo were numerically greater for patients not receiving oral corticosteroids at baseline. In OCTAVE Induction 1 & 2, infections of interest occurred with similar frequency among both subgroups of patients: the proportion of placebo-treated patients with HZ was 0.8% for BLC-No vs 0.0% for BLC-Yes; and 0.2% for BLC-No vs 1.0% for BLC-Yes with 10 mg BID. The proportion of placebo-treated patients with SIs was 0.0% for BLC-No vs 0.0% for BLC-Yes; and 1.0% for BLC-No vs 0.2% for BLC-Yes with 10 mg BID. The proportion of placebo-treated patients with OIs was 0.0% for BLC-No vs 0.0% for BLC-Yes; and 0.2% for BLC-No vs 0.5% for BLC-Yes with 10 mg BID.

% (n/N)	Placebo (N=234)	Tofacitinib 10 mg BID (N=905)	Difference from placebo (95% CI)
Remission - oral CS use at baseline (No)	5.0 (6/121)	18.1 (89/493)	13.1** (7.9, 18.2)
Remission - oral CS use at baseline (Yes)	7.1 (8/113)	17.0 (70/412)	9.9** (4.0, 15.9)
Mucosal healing - oral CS use at baseline (No)	7.4 (9/121)	28.2 (139/493)	20.8*** (14.6, 26.9)
Mucosal healing - oral CS use at baseline (Yes)	20.4 (23/113)	32.0 (132/412)	11.7* (3.0, 20.4)
Clinical response - oral CS use at baseline (No)	26.4 (32/121)	54.0 (266/493)	27.5*** (18.5, 36.5)
Clinical response - oral CS use at baseline (Yes)	35.4 (40/113)	61.9 (255/412)	26.5*** (16.5, 36.5)

Data are FAS, NRI, central read endoscopy. 95% CI for differences from placebo are based on the normal approximation for the difference in binomial proportions
*p<0.05; **p<0.01; ***p<0.0001 vs placebo based on Cochran-Mantel-Haenszel chi-square test
BID, twice daily; CI, confidence interval; CS, corticosteroid; FAS, full analysis set; N, number of patients in treatment group; n, number of patients with efficacy response; NRI, non-responder imputation

[Table. Summary of efficacy at Week 8 in OCTAVE Induction 1 and 2 by oral CS use at baseline (yes/no)]

Conclusion: Tofacitinib demonstrated significant induction efficacy vs placebo for both subgroups of patients with and without baseline corticosteroid use. Proportions of HZ, SIs and OIs in OCTAVE Induction 1 & 2 were generally similar for both subgroups of patients with and without baseline corticosteroid use; however, the relatively small number of events and short duration of follow-up (8 weeks) are limitations of this analysis.

References: 1. Rubin DT et al. Am J Gastroenterol 2019; 114: 384-413.

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P0387 LIVING WITH ULCERATIVE COLITIS IN GERMANY: ESTIMATING THE FREQUENCY AND EXTENT OF DOSE ESCALATIONS AMONG PATIENTS WITH MODERATE TO SEVERE ULCERATIVE COLITIS

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Introduction: Treatment options for inducing/maintaining clinical remission in moderate to severe ulcerative colitis (UC) include biologic therapies. Yet, in some patients, biologics are less effective over time due to immunogenicity and fail to maintain remission. Hence, dose escalations (dose intensifications or more frequent dosing) may be considered. Previous studies assessing dose escalations in biologic therapies have mainly focused on one biologic, predominantly adalimumab (ADA) or infliximab (INF); therefore, there is a need for data relating to other biologic therapies and also for comparative data.

Aims & Methods: This study aimed to estimate the frequency and extent of dose escalations in patients with UC in Germany initiated on biologic therapy. A retrospective, longitudinal cohort design was employed utilising de-identified German statutory health insurance (SHI) claims data within the Health Risk Institute database. Adult patients (18+ years of age) with UC (ICD-10 K51) but without Crohn's disease (ICD-10 K50) were indexed (Jan 2013-Dec 2015) on biologic therapy initiation (ADA, golimumab [GOL], INF or vedolizumab [VED]) with a 24-month follow-up. Patients had to be continuously insured by SHI and have no record of biologic therapy in the prior 12 months.

Daily doses (in milligrams [mg]) were calculated as a quotient of dose prescribed and duration between prescriptions/administrations (in days). Dose escalations were defined as an increase in daily dose of ≥50% compared with the recommended maintenance daily dose (ADA = 2.86, GOL = 3.57, INF = 6.25 [70 kg assumed], VED = 5.36) following induction period. De-escalations were defined as a daily dose equal to or below the recommended maintenance daily dose. Time to dose escalation (from start of maintenance) and subsequent de-escalation were calculated.

Results: In total, 304 patients were identified (mean age 42.9 years, 56.3% male), and 56% of patients had sufficient data to assess dose escalations. Of those, over half (59%) of patients received a dose escalation, occurring after a mean of 58.5 days (see Table). A significant difference (P< 0.0001) in the frequency of dose escalations was observed across index biologics, with 73% of patients initiated on ADA receiving a dose escalation. Patients initiated on INF were escalated, on average, to over four times the

recommended dose. Patients initiated on VED were escalated to double the recommended dose. Two-fifths (41%) of patients who received a dose escalation received a subsequent de-escalation.

Conclusion: A large proportion of patients required dose escalations to manage their UC. The prevalence and timing of dose escalations differed significantly between biologic therapies, with the largest proportion of dose escalations observed for ADA. These data suggest that many patients may require dose escalations to achieve and maintain remission when being treated with current biologic therapies. Further advanced treatment options that remain effective for this patient population without the need for dose escalations may be warranted.

Outcomes	Total (n=169)	ADA (n=49)	GOL (n=27)	INF (n=75)	VED (n=18)
Dose escalation, n (%)[a]	99 (59)	36 (73)	5 (19)	49 (65)	9 (50)
Time to escalation (days), mean (SD)[b]	58.5 (106.4)	17.0 (30.1)	82.2 (115.8)	80.5 (118.0)	91.2 (179.5)
Dose at escalation (mg/day), mean (SD)	N/A	8.1 (5.6)	13.1 (7.7)	27.3 (41.4)	9.8 (0.9)
- % increase relative to maintenance dose[c]	N/A	182%	268%	336%	83%
Subsequent de-escalation, n (%)[d]	41/99 (41)	11/36 (31)	<5	26/49 (53)	<5
Time to de-escalation (days), mean (SD)	75.7 (104.7)	31.8 (32.2)	-	102.5 (122.7)	-
Dose at de-escalation (mg/day), mean (SD)	N/A	2.2 (0.5)	-	5.2 (0.7)	-
- % of maintenance dose[c]	N/A	77%	-	84%	-

[a]P<0.0001; [b]P=0.0316; [c]Recommended maintenance dose: ADA = 40 mg/2 weeks, GOL = 100 mg/4 weeks, INF = 5 mg/kg/8 weeks, and VED = 300 mg/8 weeks; [d]P=0.0386 (ADA vs INF only)
-, data not presented as sample size <5 (due to data protection requirements applied by board of SHIs); ADA, adalimumab; GOL, golimumab; INF, infliximab; N/A, not applicable; SD, standard deviation; SHI, statutory health insurance; VED, vedolizumab

[Table. Dose escalations and de-escalations by index biologic therapy]

P0388 LIVING WITH ULCERATIVE COLITIS IN GERMANY: EXPLORING CONCOMITANT STEROID AND IMMUNOSUPPRESSANT USE AMONG PATIENTS WITH MODERATE TO SEVERE ULCERATIVE COLITIS

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Introduction: Biologic therapies for the treatment of moderate to severe ulcerative colitis (UC) provide relevant options for achieving clinical remission. Yet, in some patients, they do not induce and/or maintain clinical response or remission as monotherapy. Thus, concomitant treatment with steroids and/or immunosuppressants (IMs) is required. Given the long-term safety profile associated with these therapies, it is important to understand concomitant steroid/IM use in this patient population to determine how biologics are being used in combination with other therapies to achieve response/remission in UC.

Aims & Methods: This study explores the concomitant use of steroids and IMs in patients with UC in Germany initiated on biologic therapy. A retrospective, longitudinal cohort design was employed utilising de-identified German statutory health insurance (SHI) claims data within the Health Risk Institute database. Adult patients (18+ years of age) with UC (ICD-10 K51) but without Crohn's disease (ICD-10 K50) were indexed (Jan 2013-Dec 2015) on biologic therapy initiation (adalimumab [ADA], golimumab [GOL], infliximab [INF] or vedolizumab [VED]) with a 24-month follow-up (FU). Patients had to be continuously insured by SHI and have no record of biologic therapy in the prior 12 months (baseline). Steroid use (oral only) and IM use were observed in the FU period and stratified by whether steroids/IMs had been received prior to biologic initiation or not (ie newly initiated). Descriptive statistics are reported and Chi-squared or Fisher's exact tests were used to assess statistical significance of outcomes across index biologics.

Results: In total, 304 patients were identified (mean age 42.9 years, 56.3% male). Only a quarter of patients (26%) did not require any treatment with steroids in the FU period (see Table). Prednisolone was the most frequently observed steroid (88%) among steroid users. Approximately two-fifths of patients (41%) received treatment with IMs in the FU period, with azathioprine being the most frequently observed IM (77%). Most IM users (72%) had received an IM in the baseline period, whilst 28% newly initiated an IM following biologic initiation.

Conclusion: Steroid use was high following biologic initiation, with only a quarter of patients being steroid-free. Over a quarter of IM users were newly initiated on IM treatment following biologic initiation. These data suggest that control with biologic monotherapy is often insufficient treatment, highlighting the need for further advanced treatment options for this patient population.

Outcomes, n (%)	Total (n=304)	ADA (n=125)	GOL (n=47)	INF (n=114)	VED (n=18)
Steroid users	224 (74)	98 (78)	36 (77)	78 (68)	12 (67)
Prednisolone[a]	197 (88)	88 (90)	31 (86)	69 (88)	9 (75)
Prednisone[a]	47 (21)	23 (23)	6 (17)	17 (22)	<5
Budesonide[a,b]	45 (20)	17 (17)	10 (28)	11 (14)	7 (58)
Methylprednisolone[a]	<5	<5	0	<5	0
Hydrocortisone[a]	<5	<5	0	<5	0
Newly initiated steroid in FU[a]	24 (11)	11 (11)	<5	7 (9)	<5
IM users	126 (41)	59 (47)	17 (36)	46 (40)	<5
Azathioprine[c]	97 (77)	41 (69)	12 (71)	40 (87)	<5
Methotrexate[c]	20 (16)	14 (24)	<5	<5	0
Mercaptopurine[c]	14 (11)	8 (14)	<5	<5	0
Tacrolimus[c]	5 (4)	<5	<5	<5	0
Newly initiated IM in FU[c]	35 (28)	13 (22)	<5	17 (37)	-

[a]Of all steroid users; [b]P=0.0049; [c]Of all IM users
-, data not presented as sample size <5 (due to data protection requirements applied by board of SHIs); ADA, adalimumab; FU, follow-up; GOL, golimumab; IM, immunosuppressant; INF, infliximab; SHI, statutory health insurance; VED, vedolizumab

[Table. Concomitant steroid and IM use by index biologic therapy]

P0389 FAECAL CALPROTECTIN LEVELS, C-REACTIVE PROTEIN LEVELS AND PARTIAL MAYO SCORE AS EARLY PREDICTORS OF CLINICAL AND ENDOSCOPIC OUTCOMES IN ADULT PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS TREATED WITH TOFACITINIB IN A PHASE 2 STUDY

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Introduction: Tofacitinib is an oral, small molecule Janus kinase inhibitor for the treatment of ulcerative colitis (UC). Faecal calprotectin (FCP) levels were shown to correlate with clinical and endoscopic outcomes at Week 8 in patients with moderately to severely active UC receiving tofacitinib in a Phase 2 study.[1]

Aims & Methods: In these post-hoc analyses, we aimed to determine if FCP levels, C-reactive protein (CRP) levels or partial Mayo score (PMS) can be early predictors of clinical or endoscopic outcomes in a Phase 2, randomised, double-blind, placebo-controlled, parallel group, multicentre study (NCT00787202).[2] FCP levels and PMS at baseline, Week 2 and Week 4, and CRP levels at baseline and Week 4, were analysed based on whether patients with moderately to severely active UC treated with tofacitinib 10 mg twice daily (BID) had clinical response, clinical remission, mucosal healing or endoscopic remission at Week 8. Univariate logistic regression analyses were performed to evaluate if FCP levels (log transformed), CRP levels (log transformed) or PMS were associated with clinical and endoscopic outcomes.

Results: In patients treated with tofacitinib 10 mg BID (N=28), numerically greater decreases from baseline were observed in FCP levels and PMS at Weeks 2 and 4 in patients who achieved clinical response, clinical remission, mucosal healing and endoscopic remission at Week 8 vs those who did not achieve these clinical or endoscopic outcomes. FCP levels at Week 2 were decreased by >50% from baseline in patients who achieved endoscopic remission. Furthermore, numerically greater decreases from baseline were observed in CRP levels at Week 4 in patients who achieved clinical response and mucosal healing at Week 8 vs those who did not achieve these clinical or endoscopic outcomes (Table).

Tofacitinib 10 mg BID (N=28)								
	FCP, geometric mean (SD)			CRP, geometric mean (SD)			PMS, mean (SD)	
	Baseline	Week 2	Week 4	Baseline	Week 4	Baseline	Week 2	Week 4
Clinical response[b]								
Yes (N=19)	350.3(7.2)	221.8(5.7)	195.0(5.0)[d]	4.7(5.5)[e]	1.1(5.2)	5.4(1.5)	2.6(1.8)[f]	1.8(1.5)[d]
No (N=9)	352.4(4.4)[c]	443.3(6.8)	502.8(1.6)	4.6(3.2)	2.7(5.4)	5.6(1.6)	4.0(2.5)	3.8(2.3)
Clinical remission[g]								
Yes (N=15)	317.1(8.6)	214.0(6.2)	203.0(5.5)[i]	3.7(5.5)[i]	0.8(4.3)	5.0(1.9)	1.8(1.7)[h]	1.4(1.4)[i]
No (N=13)	398.3(3.9)[h]	373.5(5.8)	360.8(2.6)	6.1(3.7)	3.1(5.4)	6.0(0.8)	4.2(1.8)	3.6(2.0)
Mucosal healing[k]								
Yes (N=19)	341.0(7.5)	257.0(6.5)	221.4(4.5)[d]	5.3(5.3)[e]	1.2(5.5)	5.3(1.8)	2.4(2.1)[f]	1.9(1.7)[d]
No (N=9)	375.7(3.9)[c]	324.9(5.6)	395.5(3.0)	3.8(3.4)	2.3(5.2)	5.9(0.6)	4.2(1.9)	3.6(2.2)
Endoscopic remission[l]								
Yes (N=9)	815.7(5.3)	385.9(5.2)	444.5(4.0)[m]	3.8(6.7)[c]	0.9(4.8)	5.8(1.5)	2.3(2.0)[c]	1.5(1.7)[c]
No (N=19)	230.1(5.9)[c]	236.9(6.5)	225.4(4.0)	5.2(4.0)	1.9(5.6)	5.3(1.6)	3.5(2.2)[d]	2.9(2.0)[e]

[a]FAS, observed case; [b]Clinical response was defined as a decrease from baseline total Mayo score of ≥3 points and ≥30%, plus a decrease in rectal bleeding subscore of ≥1 point or an absolute rectal bleeding subscore of 0 or 1; [c]N=8; [d]N=17; [e]N=18; [f]N=16; [g]Clinical remission was defined as a total Mayo score of ≤2, with no individual subscore >1; [h]N=12; [i]N=13; [j]N=14; [k]Mucosal healing was defined as a Mayo endoscopic subscore of 0 or 1; [l]Endoscopic remission was defined as a Mayo flexible proctosigmoidoscopy subscore of 0; [m]N=7

BID, twice daily; CRP, C-reactive protein; FAS, full analysis set; FCP, faecal calprotectin; N, number of patients in the analysis population; PMS, Partial Mayo Score; SD, standard deviation

[Table. FCP levels, CRP levels and PMS in patients treated with tofacitinib 10 mg BID, by Week 8 efficacy endpoints[a]]

In patients treated with tofacitinib 10 mg BID, logistic regression results showed that PMS at Week 2 (odds ratio [OR] [95% confidence interval (CI)] 0.496 [0.288, 0.856]; p=0.0117) and Week 4 (OR [95% CI] 0.463 [0.251, 0.853]; p=0.0135), and CRP levels at Week 4 (OR [95% CI] 0.582 [0.342,

0.990]; p=0.0460), were significantly associated with clinical remission at Week 8. In addition, PMS at Week 4 (OR [95% CI] 0.572 [0.345, 0.948]; p=0.0302) was significantly associated with clinical response at Week 8.

Conclusion: These post-hoc analyses of a Phase 2 study showed that decreases as early as Week 2 in FCP levels and PMS, and as early as Week 4 in CRP levels, may be predictors of improved clinical and endoscopic outcomes in patients with moderately to severely active UC treated with tofacitinib 10 mg BID, although definitive conclusions cannot be drawn due to low patient numbers.

References: 1. Sandborn WJ et al. Gastroenterology 2016; 150: 96-102. 2. Sandborn WJ et al. N Engl J Med 2012; 367: 616-624.

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P0390 LABORATORY PARAMETERS RELATED TO MONITORING IN PATIENTS WITH ULCERATIVE COLITIS TREATED WITH TOFACITINIB FOR UP TO 3 YEARS IN THE OCTAVE OPEN-LABEL, LONG-TERM EXTENSION STUDY

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Introduction: Tofacitinib is an oral, small molecule Janus kinase inhibitor for the treatment of ulcerative colitis (UC). Monitoring of liver enzymes, lipids, absolute neutrophil count (ANC), absolute lymphocyte count (ALC) and haemoglobin (Hg) is recommended in patients (pts) with UC treated with tofacitinib.[1]

Aims & Methods: We investigated the changes in laboratory parameters in pts with moderately to severely active UC treated with tofacitinib in OCTAVE Open, an ongoing Phase 3, open-label, long-term extension (OLE) study (NCT01470612; data as of Sep 2018, database not locked). Pts who had completed or demonstrated treatment failure in the OCTAVE Sustain maintenance study, or those who were non-responders after completing OCTAVE Induction 1 or 2, were eligible for inclusion in the OLE study. Pts who were in remission at the end of OCTAVE Sustain were assigned to tofacitinib 5 mg BID; all other pts were assigned to tofacitinib 10 mg BID in the OLE study. Changes from baseline values in the OLE study for liver enzymes, lipids, ANC, ALC and Hg at Month 36 were evaluated (observed data). The proportions of pts with laboratory values meeting protocol criteria for discontinuation (two sequential: aspartate aminotransferase [AST] or alanine aminotransferase [ALT] elevations ≥3× upper limit of normal [ULN] with ≥1 total bilirubin value ≥2× ULN or signs or symptoms consistent with hepatic injury; AST or ALT elevations ≥5× ULN; ANC < 750/ mm³; ALC < 500/mm³; or Hg < 8.0 g/dL or >30% decrease from baseline) were assessed. The proportions of pts with investigator-defined hyperlipidaemia treatment-emergent adverse events (TEAEs), and with a change in lipid-lowering agent (LLA), were also reported.

Results: Changes from OLE study baseline in liver enzymes, lipids, ANC, ALC and Hg at Month 36 in pts treated with tofacitinib 5 and 10 mg twice daily (BID) are presented in the Table. With regard to meeting protocol criteria for discontinuation, 2.9% and 1.0% of pts treated with tofacitinib 5 and 10 mg BID, respectively, met the criteria for liver enzyme elevations; 0.6% and 1.4% of pts treated with tofacitinib 5 and 10 mg BID, respectively, met the criteria for ALC; 0 and 0.1% of pts treated with tofacitinib 5 and 10 mg BID, respectively, met the criteria for ANC; and 0 and 1.4% of pts treated with tofacitinib 5 and 10 mg BID, respectively, met the criteria for Hg. Hyperlipidaemia TEAEs were experienced by 1.7% of pts treated with tofacitinib 5 mg BID and 1.2% of pts treated with tofacitinib 10 mg BID. Furthermore, 8.0% and 6.6% of pts treated with tofacitinib 5 and

10 mg BID, respectively, had a new LLA added, and 2.3% and 1.7% of pts treated with tofacitinib 5 and 10 mg BID, respectively, had their LLA dose increased.

Conclusion: No major changes from OLE study baseline were observed in the laboratory parameters recommended for monitoring in pts treated with tofacitinib up to Month 36. In addition, the proportions of pts meeting protocol criteria for discontinuation for liver enzymes, ANC, ALC or Hg, with hyperlipidaemia TEAEs or with a change in LLA, were evaluated and were low in both tofacitinib treatment groups. Due to the dose assignment in the OLE study, the pt populations in the treatment arms differ in terms of their baseline remission status.

	Tofacitinib 5 mg BID		Tofacitinib 10 mg BID	
	N	Mean (SD)	N	Mean (SD)
Liver enzymes				
ALT (IU/L)	79	5.32 (20.57)	296	7.47 (18.54)
AST (IU/L)	79	5.10 (26.02)	295	7.51 (14.86)
	83	-5.88 (36.85)	314	20.76 (43.76)
Lipids				
Cholesterol (mg/dL)	83	-2.44 (9.48)	314	6.69 (16.46)
HDL cholesterol (mg/dL)				
LDL cholesterol (mg/dL)	81	-4.06 (32.23)	312	11.90 (36.43)
Triglycerides (mg/dL)				
	82	3.31 (62.14)	314	11.91 (61.54)
Blood cells				
Hg (g/dL)	79	0.17 (0.98)	295	0.99 (1.64)
ALC (10³/mm³)	79	-0.23 (0.50)	289	-0.54 (0.66)
ANC (10³/mm³)	79	0.01 (1.83)	289	-1.02 (2.37)

Data are as of Sep 2018, database not locked
ALC, absolute lymphocyte count; ALT, alanine aminotransferase; ANC, absolute neutrophil count; AST, aspartate aminotransferase; BID, twice daily; HDL, high-density lipoprotein; Hg, haemoglobin; LDL, low-density lipoprotein; N, number of patients with non-missing data; OLE, open-label, long-term extension; pts, patients; SD, standard deviation; UC, ulcerative colitis

[Table. Change from OLE study baseline in clinical laboratory parameters at Month 36 in pts with UC treated with tofacitinib (observed data)]

References: 1. European Medicines Agency. 2018. Xeljanz (tofacitinib citrate) – summary of product characteristics. Available at: https://www.medicines.org.uk/emc/medicine/33167.

P0391 ITEM-LEVEL IMPROVEMENTS IN INFLAMMATORY BOWEL DISEASE QUESTIONNAIRE SCORES IN PATIENTS WITH ULCERATIVE COLITIS TREATED WITH TOFACITINIB INDUCTION THERAPY

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Introduction: Tofacitinib is an oral, small molecule Janus kinase inhibitor for the treatment of ulcerative colitis (UC). The effect of tofacitinib treatment on Inflammatory Bowel Disease Questionnaire (IBDQ) domains has been reported in patients with UC in OCTAVE Induction 1 & 2 and OCTAVE Sustain, with significant improvements observed in all domains vs placebo.[1] However, the effect of tofacitinib on the individual items within each IBDQ domain has not been analysed previously.

Aims & Methods: We examined the effect of induction treatment with tofacitinib 10 mg twice daily (BID) on individual IBDQ items in adults with moderate to severe UC. Data were pooled from OCTAVE Induction 1 & 2 (NCT01465763 & NCT01458951), which were identical, randomised, 8-week, double-blind, Phase 3 studies.[2] The IBDQ was self-administered by patients at baseline, Week 4 and Week 8, and has four domains, with individual items within each domain. The IBDQ domains are bowel symptoms (10 items), systemic symptoms (5 items), emotional function (12 items) and social function (5 items), with higher scores indicating better health-related quality of life (HRQoL).[1,3] Change from baseline in IBDQ items was analysed for tofacitinib 10 mg BID vs placebo using a linear mixed-effects model, with treatment, study, prior tumour necrosis factor inhibitor treatment, corticosteroid use at baseline, geographical region, week, treatment by week interaction, and baseline score as fixed effects, and patients as a random effect. No multiplicity adjustment was performed for this ad-hoc analysis.

Results: Significant improvements (p< 0.05) were observed in all IBDQ items with tofacitinib 10 mg BID vs placebo at Weeks 4 and 8. The largest treatment differences within each domain were reported as follows: 'bowel movements been loose' at Weeks 4 and 8, and 'problem with rectal bleeding' at Week 8 (all 1.1), for the bowel symptoms domain; 'getting a good night's sleep' at Week 4 (0.8) and Week 8 (0.9), for the systemic symptoms domain; 'fear of not finding a washroom' at Week 4 (0.6) and Week 8 (0.8), and 'felt embarrassed' and 'felt angry' at Week 4 (both 0.6), for the emotional function domain; and 'avoid attending events' at Week 4 (0.8) and Week 8 (1.0), and 'difficulty doing leisure/sports' at Week 8 (1.0), for the social function domain (Table).

Conclusion: Tofacitinib treatment resulted in improvements vs placebo in all bowel-related symptoms, systemic symptoms, emotional functioning and social functioning IBDQ items, highlighting the broad impact of tofacitinib on all aspects of HRQoL. The greatest numerical improvements across all items were reported for 'bowel movements been loose' and 'problem with rectal bleeding'. This analysis provides an informative and useful perspective on which components of the IBDQ domains are the most improved following tofacitinib induction therapy, which may help to facilitate patient-physician dialogue.

IBDQ item, LSM (SE)	Week 4		Week 8	
	Placebo (N=231)	Tofacitinib 10 mg BID (N=881)	Placebo (N=218)	Tofacitinib 10 mg BID (N=849)
Bowel symptoms				
Bowel movement frequency[a]	1.1 (0.1)	2.1 (0.1)[†]	1.3 (0.1)	2.2 (0.1)[†]
Bowel movements been loose	0.7 (0.1)	1.8 (0.1)[†]	1.0 (0.1)	2.1 (0.1)[†]
Problem with rectal bleeding[b]	1.3 (0.1)	2.3 (0.1)[†]	1.6 (0.1)	2.7 (0.1)[†]
Systemic symptoms				
Feeling fatigued or tired	0.7 (0.1)	1.1 (0.1)[†]	0.8 (0.1)	1.4 (0.1)[†]
Felt generally unwell[c]	0.9 (0.1)	1.4 (0.1)[†]	1.0 (0.1)	1.6 (0.1)[†]
Getting a good night's sleep	0.7 (0.1)	1.5 (0.1)[†]	0.8 (0.1)	1.7 (0.1)[†]
Emotional function				
Fear of not finding a washroom	0.9 (0.1)	1.4 (0.1)[†]	0.9 (0.1)	1.7 (0.1)[†]
Felt embarrassed[b]	0.7 (0.1)	1.4 (0.1)[†]	0.9 (0.1)	1.6 (0.1)[†]
Felt angry[b]	0.4 (0.1)	1.1 (0.0)[†]	0.5 (0.1)	1.1 (0.1)[†]
Social function				
Delay/cancel social engagements[c]	0.8 (0.1)	1.4 (0.1)[†]	0.8 (0.1)	1.5 (0.1)[†]
Difficulty doing leisure/sports[d]	0.9 (0.1)	1.6 (0.1)[†]	1.0 (0.1)	2.0 (0.1)[†]
Avoid attending events[c]	0.5 (0.1)	1.3 (0.1)[†]	0.5 (0.1)	1.5 (0.1)[†]

[†]p<0.0001 vs placebo
[a]Week 4: placebo N=227, tofacitinib 10 mg BID N=862; Week 8: placebo N=213, tofacitinib 10 mg BID N=832; [b]Week 4: tofacitinib 10 mg BID N=879; Week 8: tofacitinib 10 mg BID N=848; [c]Week 4: tofacitinib 10 mg BID N=880; Week 8: tofacitinib 10 mg BID N=848; [d]Week 4: tofacitinib 10 mg BID N=880
BID, twice daily; IBDQ, Inflammatory Bowel Disease Questionnaire; LSM, least squares mean; N, number of patients evaluated; SE, standard error

[Table. Change from baseline for the IBDQ items with the top three largest treatment differences in each domain (full analysis set, observed case)]

References: 1. Panés J et al. J Crohns Colitis 2018; 12: 145-156.
2. Sandborn WJ et al. N Engl J Med 2017; 376: 1723-1736.
3. Guyatt GH et al. J Clin Epidemiol 1989; 42: 403-408.

P0392 CLINICAL COURSE AND DIETARY PATTERNS AMONG PATIENTS INCORPORATING THE AUTOIMMUNE PROTOCOL FOR MANAGEMENT OF INFLAMMATORY BOWEL DISEASE

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Introduction: Elimination diets, including the autoimmune protocol (AIP), may improve symptoms among patients with inflammatory bowel disease (IBD), but limited data exist on diet efficacy and utilization.
Aims & Methods: The aim of our study was to examine clinical course and dietary patterns of patients with IBD utilizing AIP. We conducted an anonymous online survey sent through electronic newsletters and support groups utilizing AIP. The survey assessed demographics, IBD disease activity and medication use, including use of steroids and immunosuppression (biologics and/or immunomodulators). Participants were asked about AIP utilization and food group reintroductions. Symptom measures of abdominal pain, stool frequency, and rectal bleeding were compared at baseline (BL, prior to starting AIP), week 6 (after starting AIP), and present, separately for Crohn's disease (CD) and ulcerative colitis (UC).
Results: There were 78 respondents who attempted AIP for management of IBD. Mean age was 39.4 years (SD 11.4), with mean IBD duration 13.2 yrs (SD 11.4), 78% prior steroid exposure, and 35% currently on immunosuppression. Seventy-three percent perceived achieving clinical remission due to AIP, but this was more common among patients not on immunosuppression (76% vs. 24% on immunosuppression, p< 0.001). After starting AIP, 32% reported being able to discontinue steroids. AIP was initiated according to protocol by 73%, while 27% modified it.
Compared to BL, 6 weeks after starting AIP more patients with CD reported no abdominal pain (47% vs BL 17%, P = 0.01), normal stool frequency (53% vs BL 30%, P < 0.01), and no rectal bleeding (90% vs 43%, P = 0.057). Similarly, more patients with UC reported no abdominal pain (60% vs BL 14%, P < 0.01), normal stool frequency (47% vs BL 14%, P < 0.01), and no rectal bleeding (63% vs 30%, P < 0.01) 6 weeks after starting AIP, compared to BL.
Food group reintroductions were started within 0-4 weeks of starting AIP among 8%, while 23% reintroduced within 5-8 weeks, 24% within 2-6 months, 23% within 6-12 months, and 13% after 12 months. Although success of food group reintroductions varied, this did not appear to affect symptom improvement, with majority of patients with IBD reporting no abdominal pain (80%), no rectal bleeding (72%), and normal stool frequency (64%) at present.
Conclusion: In this retrospective study, patients utilizing AIP for management of IBD report clinical benefit, with reduction of steroid use and improvement in IBD symptoms, including with food group reintroduction.
Disclosure: Dr. Konijeti has previously received honoraria from Takeda, Abbvie, Janssen, and Pfizer.

P0393 TOFACITINIB FOR THE TREATMENT OF ULCERATIVE COLITIS: AN UPDATE ON THE ANALYSIS OF MALIGNANCY RATES FROM THE UC CLINICAL PROGRAMME

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Introduction: Tofacitinib is an oral, small molecule Janus kinase inhibitor for the treatment of ulcerative colitis (UC). The safety of tofacitinib for the treatment of moderate to severe UC was evaluated in a randomised, placebo-controlled induction Phase (P) 2 study (NCT00787202),[1] 2 induction P3 studies (NCT01465763; NCT01458951), 1 maintenance P3 study (NCT01458574),[2] and an ongoing, open-label, long-term extension (OLE) study (NCT01470612).[3] Here, we present an update on the integrated analysis of adjudicated malignancies observed in the UC clinical development programme, as of Sep 2018.
Aims & Methods: Patients (pts) who received placebo, tofacitinib 5 or 10 mg twice daily (BID) were analysed as 3 cohorts: Induction (P2/P3 induction studies, N=1220), Maintenance (P3 maintenance study, N=592) and Overall (pts receiving tofacitinib 5 or 10 mg BID in P2, P3 or ongoing OLE studies, N=1157). Proportions and incidence rates (IRs; unique pts with events per 100 pt-years [PY] of exposure) were evaluated for malignancies (excluding non-melanoma skin cancer [NMSC]) and NMSC. For Overall Cohort analysis, pts were categorised based on the average daily dose of tofacitinib: predominant dose (PD) tofacitinib 5 mg BID (average total daily dose < 15 mg) and PD tofacitinib 10 mg BID (average total daily dose ≥15 mg). For P3 studies, an independent adjudication committee reviewed all potential malignancies. Overall Cohort data are as of Sep 2018.

	Induction Cohort[a]		Maintenance Cohort[a]			Overall Cohort
	Placebo (N=282; 44.8 PY)	Tofacitinib 10 mg BID (N=938; 156.2 PY)	Placebo (N=198; 100.4 PY)	Tofacitinib 5 mg BID (N=198; 146.2 PY)	Tofacitinib 10 mg BID (N=196; 154.3 PY)	Tofacitinib All (N=1157; 2403.6 PY)
Age (years), mean (SD)	41.4 (14.4)	41.3 (13.8)	43.4 (14.0)	41.9 (13.7)	43.0 (14.4)	41.3 (13.9)
Prior TNFi failure, n (%)	124 (53.0)[b]	465 (51.4)[c]	89 (44.9)	83 (41.9)	92 (46.9)	583 (51.9)[d]
Prior immunosuppressant failure, n (%)	158 (67.5)[b]	661 (73.0)[c]	129 (65.2)	143 (72.2)	141 (71.9)	813 (72.3)[d]
Prior immunosuppressant treatment, n (%)	160 (68.4)[b]	683 (75.5)[b]	134 (67.7)	149 (75.3)	144 (73.5)	838 (74.6)[d]
Disease duration (years), mean (SD)	8.2 (6.8)	8.2 (7.0)	8.8 (7.5)	8.3 (7.2)	8.7 (7.0)	8.2 (7.0)
Malignancies (excluding NMSC), n (%), IR [95% CI][e,f,g]	0 (0.0)	0 (0.0)	1 (0.5), 0.97 [0.02, 5.39]	0 (0.0), 0.00 [0.00, 2.48]	0 (0.0), 0.00 [0.00, 2.35]	17 (1.5), 0.69 [0.40, 1.11]
NMSC, n (%), IR [95% CI][e,f]	0 (0.0)	2 (0.2)	1 (0.5), 0.97 [0.02, 5.40]	0 (0.0), 0.00 [0.00, 2.48]	3 (1.5), 1.91 [0.39, 5.59]	19 (1.7),[h] 0.78 [0.47, 1.22]

Data are as of Sep 2018 for the Overall Cohort (OLE study database not locked)
[a]As per the SCS analysis convention, only events occurring within 28 days after the last dose are included in this Table for calculation of proportion and IR; [b]N=234; [c]N=905; [d]N=1124; [e]Data for the Induction Cohort are shown as n (%), due to the short duration (8 weeks) of the induction studies; [f]Adjudicated data do not include data from the P2 Study (A3921063; NCT00787202); [g]One case of breast cancer in the Maintenance Cohort (placebo arm); in the Overall Cohort, 17 malignancy events (excluding NMSC), including two cases of cervical cancer, breast cancer and adenocarcinoma of the colon, and one case each of hepatic angiosarcoma, cholangiocarcinoma, leiomyosarcoma, diffuse large B-cell lymphoma, Epstein-Barr virus-associated lymphoma, malignant melanoma, renal cell carcinoma, lung cancer, invasive ductal breast carcinoma, essential thrombocythemia, acute myeloid leukaemia, plus secondary malignancies in the liver and peritoneum; [h]Of the 19 Overall Cohort pts with NMSC, most (17/19) had prior immunosuppressant failure, most (15/19) had prior treatment failure with TNFi, and seven had prior NMSC
BID, twice daily; CI, confidence interval; IR, incidence rate (patients with events per 100 patient-years of exposure); N, number of patients in the treatment group; n, number of patients in a specified category; NMSC, non-melanoma skin cancer; OLE, open-label, long-term extension; P, Phase; pts, patients; PY, patient-years; SCS, summary of clinical safety; SD, standard deviation; TNFi, tumour necrosis factor inhibitors

[Table. Demographics and summary of incidence of malignancies (all causality) among pts in the Induction, Maintenance and Overall Cohorts]

Results: The Overall Cohort comprised 1157 pts with 2404 PY of tofacitinib exposure and up to 6.1 years of treatment (median 623 days) who received ≥1 dose of tofacitinib 5 or 10 mg BID (Table). There were no pts with malignancy events (excluding NMSC) in the Induction Cohort, 1 pt with a malignancy event (excluding NMSC; placebo, breast cancer) in the Maintenance Cohort, and 17 pts with malignancy events (excluding NMSC) in the Overall Cohort (IR 0.69; 95% confidence interval [CI] 0.40, 1.11). There was no clustering of malignancy events (excluding NMSC) in the Overall Cohort (Table). Of the 17 pts with malignancy events (excluding NMSC), 3 had received a PD of tofacitinib 5 mg BID (IR 0.49; 95% CI 0.10, 1.45) and 14 a PD of tofacitinib 10 mg BID (IR 0.75; 95% CI 0.41, 1.27).

NMSC was reported in 2 (0.2%) tofacitinib-treated Induction Cohort pts, 4 Maintenance Cohort pts (3 tofacitinib 10 mg BID; IR 1.91; 95% CI 0.39, 5.59; and 1 placebo-treated pt; IR 0.97; 95% CI 0.02, 5.40) and 19 Overall Cohort pts (IR 0.78; 95% CI 0.47, 1.22; 4 had received a PD of tofacitinib 5 mg BID and 15 a PD of tofacitinib 10 mg BID).

Conclusion: In the UC clinical programme, malignancies (including NMSC) were observed with tofacitinib treatment. There was no clustering of types of malignancy (excluding NMSC). The IR of malignancies (excluding NMSC) reported here is similar to that previously reported (IR 0.7; 95% CI 0.3, 1.2),[4] suggesting no treatment duration impact on the IR of malignancies (excluding NMSC). The IRs for malignancies (NMSC, and excluding NMSC) were similar to those reported for tofacitinib in pts with rheumatoid arthritis[5] and in pts with UC treated with biologics.[6,7]

References: 1. Sandborn WJ et al. N Engl J Med 2012; 367: 616-624.
2. Sandborn WJ et al. N Engl J Med 2017; 376: 1723-1736.
3. Lichtenstein GR et al. Am J Gastroenterol 2018; 113: Abstract 571.
4. Sandborn WJ et al. Clin Gastroenterol Hepatol 2018: Epub ahead of print.
5. Cohen SB et al. Ann Rheum Dis 2017; 76: 1253-1262.
6. Sandborn WJ et al. Gastroenterology 2012; 142: 257-265.e253.
7. Sandborn WJ et al. Gastroenterology 2014; 146: 96-109.e101.

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P0394 PREDICTORS OF DELAYED RESPONSE TO TOFACITINIB: RESULTS OF THE OCTAVE OPEN STUDY FOR DELAYED RESPONDERS

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Introduction: Tofacitinib is an oral, small molecule Janus kinase inhibitor for the treatment of ulcerative colitis (UC). The efficacy and safety of tofacitinib was shown in 3 Phase 3, randomised, placebo-controlled trials in patients (pts) with moderately to severely active UC.[1] Pts who received tofacitinib 10 mg twice daily (BID) for 8 weeks in OCTAVE Induction 1 & 2 (NCT01465763 & NCT01458951) and did not achieve clinical response could enter an ongoing, Phase 3, multicentre, open-label, long-term extension (OLE) study (NCT01470612)[2] and receive tofacitinib 10 mg BID. Long-term maintenance data for up to 3 years of treatment in the OLE study for those who achieved clinical response with an additional 8 weeks of tofacitinib treatment (ie delayed responders) have been previously reported.[3]

Aims & Methods: We evaluated potential predictors of delayed response, ie a clinical response (≥3-point and ≥30% decrease from induction study baseline total Mayo score, plus ≥1-point decrease in rectal bleeding subscore [RBS] or absolute RBS ≤1) after 16 weeks of tofacitinib 10 mg BID (8 weeks induction plus an additional 8 weeks in the OLE study). Potential predictors evaluated included characteristics at baseline of OCTAVE Induction 1 & 2 and the OLE study, and at Month 1 of the OLE study. Pts were analysed as 3 subgroups: induction responders (pts who demonstrated clinical response after 8 weeks of tofacitinib 10 mg BID); delayed responders; and complete non-responders (pts who did not respond to 16 weeks of treatment with tofacitinib 10 mg BID).

	Induction responders[a] (N=521)	Delayed responders[b] (N=148)	Complete non-responders[c] (N=106)
Prior TNFi failure at OCTAVE Induction baseline, n (%)	237 (45.5)	85 (57.4)	66 (62.3)
Total Mayo score - OCTAVE Induction baseline, mean (SD) - Mean change from OCTAVE Induction baseline to OCTAVE Induction Week 8 (SD)	8.8 (1.4) -5.6 (1.7)	9.1 (1.4) -1.0 (1.2)	9.2 (1.3) -0.4 (1.1)
PMS - OLE study Month 1, mean (SD) - Mean change in PMS from OLE baseline to OLE Month 1 (SD)	N/A N/A	2.9 (1.7)[d] -2.4 (1.7)[d]	5.2 (1.7)[e] -0.9 (1.6)[e]
Mayo endoscopic subscore - OCTAVE Induction baseline, mean (SD) - Mean change from OCTAVE Induction baseline to OCTAVE Induction Week 8 (SD)	2.6 (0.5) -1.0 (0.9)	2.6 (0.5) 0.1 (0.5)	2.7 (0.5) 0.1 (0.5)
Mayo stool frequency subscore - OLE study baseline, mean (SD) - OLE study Month 1, mean (SD) [mean change from OCTAVE Induction baseline (SD)]	N/A N/A	2.2 (0.8) 1.4 (0.9) [-1.2 (0.9)][f]	2.5 (0.7) 2.4 (0.8) [-0.3 (0.7)][e]
Mayo rectal bleeding subscore - OLE study baseline, mean (SD) - OLE study Month 1, mean (SD) [mean change from OCTAVE Induction baseline (SD)]	N/A N/A	1.1 (0.8) 0.5 (0.7) [-1.1 (0.7)][f]	1.2 (0.7) 1.1 (0.7) [-0.4 (0.8)][e]
C-reactive protein (mg/L) - OCTAVE Induction baseline, mean (SD) - Mean change from OCTAVE Induction baseline to OCTAVE Induction Week 8 (SD) - OLE study baseline, mean (SD)	10.0 (16.6)[g] -7.3 (16.4)[h] N/A	10.8 (16.2)[i] -2.2 (18.8)[i] 8.3 (15.4)	14.6 (26.9) -3.4 (29.4)[j] 11.2 (18.4)

OCTAVE Induction data are pooled data from OCTAVE Induction 1 and 2
[a]Pts who demonstrated a clinical response following 8 weeks of tofacitinib 10 mg BID in OCTAVE Induction; [b]Pts who demonstrated a clinical response following 16 weeks of tofacitinib 10 mg BID; [c]Pts who did not demonstrate a clinical response following 16 weeks of tofacitinib 10 mg BID; [d]N=143; [e]N=104; [f]N=144; [g]N=511; [h]N=510; [i]N=146; [j]N=105
BID, twice daily; FAS, full analysis set; N, number of patients in the analysis population; n, number of patients in the category; N/A, not applicable; OLE, open-label, long-term extension; PMS, partial Mayo score; pts, patients; SD, standard deviation; TNFi, tumour necrosis factor inhibitor

[Table. Characteristics of induction responders, delayed responders and complete non-responders (FAS, observed case)]

Results: Characteristics at baseline of OCTAVE Induction 1 & 2 were generally similar between the 3 subgroups (Table). The proportion of pts with prior tumour necrosis factor inhibitor (TNFi) failure was numerically higher among complete non-responders than that among delayed responders (Table). Induction baseline mean C-reactive protein (CRP) was numerically higher in complete non-responders compared with induction responders and delayed responders (Table). A similar trend was observed at baseline of the OLE study; mean CRP value was numerically lower for delayed responders than complete non-responders (Table). At Month 1 of the OLE study, stool frequency subscore (SFS) and RBS were numerically lower in delayed responders compared with complete non-responders, and the reduction in partial Mayo score (PMS) from baseline of the OLE study was greater for delayed responders than complete non-responders (Table).

Conclusion: Numerically higher proportions of complete non-responders and delayed responders had prior TNFi failure vs induction responders. In pts with UC, changes in SFS, RBS and PMS during extended induction treatment with tofacitinib may be indicative of the likelihood of clinical response. Extended treatment with tofacitinib 10 mg BID beyond the initial 8-week induction period may be associated with clinical response in a subset of pts with UC who do not respond initially. This ad hoc analysis is limited by the small sample size and further evaluation is needed to confirm the findings.

References: 1. Sandborn WJ et al. N Engl J Med 2017; 376: 1723-1736.
2. Lichtenstein GR et al. Am J Gastroenterol 2018; 113 (Suppl 1): Abstract 571.
3. Rubin DT et al. J Crohns Colitis 2019; 13 (Suppl 1): Abstract DOP43.

P0395 A MULTICENTRIC STUDY ON THE EFFECTIVENESS OF ANTI-TNF AGENTS IN SYMPTOMATIC STRICTURING CROHN'S DISEASE

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Introduction: Approximately one half of the patients with Crohn's disease may develop intestinal strictures during their lifetime. The effectiveness of the currently approved drugs in these stricturing complications remains barely known. Our aim was to determine the effectiveness of anti-TNF therapy for symptomatic stenosis in Crohn's disease patients.
Aims & Methods: We included adult patients with symptomatic stricturing Crohn's disease receiving their first-line anti-TNF therapy. Strictures were defined as constant luminal narrowing with pre-stenotic dilatation. We excluded those patients with previous anti-TNF exposure, surgery or endoscopic therapy of the stenosis. The effectiveness of the anti-TNF agent

was defined as a composite outcome combining the persistence of the treatment and without dose or frequency intensification, with no new immunomodulators, surgery or endoscopic therapy during follow-up.
Results: A total of 262 patients from 32 IBD Units in Spain were included. The main characteristics of the cohort are summarized in Table 1. The median number of stenosis per patient was 1 (range 1-9). One hundred-forty one patients (54%) received infliximab and 121 (46%) adalimumab. The treatment was considered to be effective in 81% and 60% of patients after 6 and 12 months, respectively, while this outcome was fulfilled by 21% after a median follow-up of 40 months (IQR, 19-85). There were no radiological findings at baseline associated with the effectiveness or the rate of surgery. During follow-up, anti-TNF therapy required a dose or frequency adjustment in 39% of patients, 12% required a new immunomodulator or endoscopic therapy in 4%. The proportion of subjects requiring surgery was 15% after 1 year, and 21% after 2 years, with an overall rate of surgery of 32%. In the multivariate analysis, infliximab was associated with a higher rate of surgery as compared to adalimumab (OR 1.78; 95% CI, 1,025-3,09). The anti-TNF agent was discontinued in 131 patients (50%) after a median of 16 months (IQR, 7.5-37), mainly due to an absence or loss of response (56%). A total of 88 subjects (34%) required a switch to a new biologic drug (72% to a second anti-TNF, 24% to ustekinumab and to 5% to vedolizumab).
Conclusion: Anti-TNF agents are effective in approximately 20% of patients with Crohn's disease complicated with symptomatic strictures, avoiding surgery in a relatively high proportion of cases.

Characteristic	Infliximab N = 141	Adalimumab N = 121	All N = 262	p value
Age at diagnosis, years Median (IQR)	33 (25-47)	33 (23-46)	33 (25-46)	0.92
Sex, female N (%)	72 (51)	67 (55)	139 (53)	0.48
Disease duration, months Median (IQR)	1.6 (0-59)	2.9 (0-83)	2.2 (0-71)	0.38
Perianal disease, N (%)	19 (13)	16 (13)	35 (13)	0.55
Concomitant thiopurines, N (%)	98 (69)	24 (65)	165 (63)	0.003
Baseline CRP, mg/L Median (IQR)	5.3 (1.0-11.9)	3.9 (0.7-10-7)	5.3 (1.0-15)	0.26
Number of stenosis per patient Median (IQR)	1 (1-2) range 1-8	1 (1-2) range 1-9	1 (1-2) range 1-9	0.43

[Patient characteristics]

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P0396 CLINICAL EFFECTIVENESS OF GOLIMUMAB IN ULCERATIVE COLITIS: A PROSPECTIVE MULTICENTRE STUDY BASED ON THE SWEDISH NATIONAL QUALITY REGISTRY FOR IBD, SWIBREG

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Introduction: Clinical trials have demonstrated that golimumab is effective in anti-TNF naïve patients with ulcerative colitis.
Aims & Methods: The aim of this prospective, multicentre cohort study was to assess the clinical effectiveness of golimumab in a real world setting. All patients with moderate-to-severe ulcerative colitis, defined as Mayo endoscopic subscore ≥2 who initiated golimumab between June 2014 and

June 2017 at 16 Swedish hospitals were eligible for inclusion after written consent. Clinical characteristics, treatment, clinical, biochemical, endoscopic activity and quality of life measures were recorded at baseline and prospectively, using an electronic Case Report Form, integrated with the Swedish National Quality Registry for IBD (SWIBREG). Primary objective was clinical effectiveness at 12 weeks and 52 weeks, i.e. clinical response (defined as a decrease in Mayo score by ≥3 points or 30% from baseline) and remission (defined as a score of ≤2 with no individual subscores >1.) Continuous data are presented as median (interquartile range). Differences between baseline and follow-up were assessed by Wilcoxon-signed rank test.
Results: 50 patients were included during the three-year study period. At study entry, 24/50 (48%) were on concomitant treatment with immunomodulators, 16/50 (32%) on oral corticosteroids and 27/50 (54%) on 5-ASA (table 1). In total, 35/50 (70%) had previously been exposed to at least one TNF-antagonist. The 12 and 52-week drug continuation rates were 37/50 (74%) and 23/50 (46%), respectively. The 12-week clinical response rate was 14/50 (28%), the remission rate, 8/50 (16%) and the corresponding figures at week 52 were 13/50 (26%) and 10/50 (20%). Among patients who continued golimumab, the median Mayo score decreased from 7 (6-9) at baseline to 1 (0-5) at 52 weeks (p< 0.01) and the median faecal calprotectin decreased from 862 (335-1759) µg/g to 90 (34-169) µg/g (p< 0.01). Consistently, quality of life improved in golimumab treated patients, with a significant reduction of the overall short health scale (SHS) score (p< 0.01).

Median age yr. (IQR)	41 (28-53)
Sex female no. (%)	25 (50)
Median disease duration yr. (IQR)	5 (2-11)
Extent no. (%)	
Proctitis (E1)	5 (10)
Left-sided colitis (E2)	19 (38)
Extensive colitis (E3)	26 (52)
Previous medications no. (%)	
Immunomodulators	46 (92)
Anti-TNF therapy	35 (70)

[Table 1. Baseline clinical and demographical characteristics of patients with ulcerative colitis]

Conclusion: In this prospective cohort study, golimumab-treated patients, in Swedish clinical practice, represented a treatment refractory patient-group, in which 70% previously were exposed to anti-TNF. Despite this, our results confirm that golimubab is an effective therapy in UC.
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DB has nothing to disclose.
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LN has nothing to disclose.
AK works at MSD Sweden.
HH has received consultant/lecture fees from AbbVie, Janssen, Takeda, Pfizer, Vifor Pharma, Tillotts and Ferring.
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PK has received lecture fees from Ferring, Jansen, Takeda and Otsuka.
HS has received consultant/lecture fees from Fering, Takeda, Pfizer, Tillotts, Janssen and Abbvie.
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P0397 LUPUS-LIKE REACTIONS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE TREATED WITH ANTI-TNFS ARE RARE BUT INSIDIOUS ADVERSE EVENTS: DATA FROM A LARGE SINGLE-CENTER COHORT

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Introduction: The occurrence of lupus-like reactions (LLRs) may complicate the management of patients with inflammatory bowel disease (IBD) treated with anti-TNFs. However, very few data on the incidence, predictors, and clinical outcomes of LLRs have been reported.
Aims & Methods: We aimed to describe all these features in a large cohort of IBD patients treated with anti-TNF drugs. All records of consecutive patients who started a treatment with an anti-TNF from January 2006 to June 2018 were retrospectively reviewed. Patients were defined as having LLR by the presence of immunologic abnormalities (positivity for ANA and/or anti-ds-DNA), along with clinical features that included at least two of the following: arthralgia, fatigue, fever, cutaneous manifestations, or serositis, which had a clear temporal association with exposure to the anti-TNFs, and resolved without recurrence once the drug was discontinued. Univariable and multiple Cox proportional hazard models were used to estimate the association between all variables at baseline and occurrence of LLRs.
Results: 760 patients (1059 total treatments with anti-TNFs) were included. Participants contributed a total of 2863.5 person-years of follow-up, during which 16 cases of LLRs (2.1% of patients) were reported, with an incidence rate of 5.6 per 1000 person-years. Female gender and being former smokers were more prevalent in the LLR group (75.0% versus 44.1%, p= 0.02; and 18.8% versus 5.4%, p=0.037, respectively), with a hazard ratio of 3.86 (95% CI: 1.21-12.38; p=0.023) and 4.42 (95% CI: 1.20-16.24; p=0.025), respectively, at Cox regression analysis adjusted for possible confounders. LLRs occurred after a mean of 12.0 ± 9.7 months of therapy with anti-TNFs. Antinuclear antibodies were universally positive, and 10 out 16 (62.5%) patients had also anti-ds-DNA. Arthropathy was the most frequent symptom (87.5%), followed by fatigue (81.2%), and fever (31.2%). Three cases presented with a concomitant autoimmune hepatitis-like syndrome. The diagnosis of LLR was further confirmed by a re-challenge with the culprit agent in half of the cases. All LLRs resolved following discontinuation of the drug after a mean of 8.1 ± 4.2 weeks, even if 10 patients required corticosteroids for the control of symptoms. Five patients (31.2%) were switched to a second anti-TNFs, and one of them developed a second LLR.
Conclusion: In this very large cohort of patients treated with anti-TNFs, LLRs were rare adverse events, more common in women and former smokers. Clinical features are non-specific and insidious. All LLRs resolved following discontinuation of the drug, but the use of corticosteroids was required in most of the cases.
Disclosure: FSM served as advisory board member or received lecture grants from for AbbVie, Biogen, MSD, Takeda Pharmaceuticals. AO served as advisory board member for AbbVie, MSD, Takeda Pharmaceuticals, and received lecture grants from AbbVie, MSD, Sofar, Chiesi, and Takeda Pharmaceuticals.

P0398 EFFECTIVENESS AND SAFETY OF USTEKINUMAB FOR THE TREATMENT OF CROHN'S DISEASE IN REAL-LIFE STUDIES: A META-ANALYSIS

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Introduction: The real-life value of ustekinumab in Crohn's disease is under evaluation.
Aims & Methods: The aim of this single-arm meta-analysis was to estimate the effectiveness and safety of ustekinumab in real-life observational studies. PubMed Central/Medline and Embase, as well as reference lists of articles, were systematically searched through December 2018. Only real-life observational studies were included.
Results: Seven studies comprising 597 patients met the inclusion criteria. Almost all patients had been previously exposed to anti-TNFs. Ustekinumab was administered subcutaneously at induction in all studies except one. The pooled estimates rates of clinical response and remission at in-

duction were 72% (95% CI: 53-86%; range: 39-100%; I²=92%) and 42% (95% CI: 20-68%; range: 15-84%; I²=92%), respectively. At maintenance, the pooled estimates rates of clinical response, clinical remission, endoscopic response, and endoscopic remission were 69% (95% CI: 56-79%; range: 48-89%; I²=86%), 47% (95% CI: 25-70%; range: 28-73%; I²=93%), 60% (95% CI: 53-67%; range: 55-77%; I²=0%), and 24% (95% CI: 19-31%; range: 15-31%; I²=0%), respectively. The pooled estimate of incidence rates of total adverse events and infections were 15.3 (95% CI: 8.7-26.8; range: 7.2-34; I²=89%) and 3.7 (95% CI: 2.0-6.9; range: 2.2-9.0; I²=60%) per 100 persons-years, respectively.
Conclusion: Cumulative analysis of data from real-life studies confirmed that ustekinumab holds the potential to deserve a relevant role in the management of patients with Crohn's disease with a reassuring safety profile. Furthermore, its clinical effectiveness at induction seems to be higher in real-life observational studies compared with randomized controlled trials.
Disclosure: FSM served as advisory board member or received lecture grants from for AbbVie, Biogen, MSD, Takeda Pharmaceuticals. AO served as advisory board member for AbbVie, MSD, Takeda Pharmaceuticals, and received lecture grants from AbbVie, MSD, Sofar, Chiesi, and Takeda Pharmaceuticals.

P0399 LONG-TERM EFFECT OF RISANKIZUMAB ON IMPROVED AND SUSTAINED HEALTH-RELATED QUALITY OF LIFE OVER 3 YEARS IN PATIENTS WITH MODERATE TO SEVERE CROHN'S DISEASE: INTERIM ANALYSIS OF A PHASE 2 OPEN-LABEL EXTENSION STUDY

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Introduction: The clinical and endoscopic efficacy of risankizumab (RZB), an IL-23 inhibitor, in patients with moderate to severe Crohn's disease (CD) have been reported in the phase 2 trials of induction[1] and maintenance phases over 52 weeks.[2] Longer term outcomes were assessed from an ongoing open-label extension (OLE) study (NCT02513459).
Aims & Methods: This study aims to evaluate the long-term effects of RZB on health-related quality of life (HRQoL) measured by the Inflammatory Bowel Disease Questionnaire (IBDQ) for up to 3 years from the ongoing phase 2 OLE study. Patients who achieved clinical response (decrease from baseline [BL] in CD Activity Index [CDAI] ≥100) without remission (CDAI < 150) after Period 2 (Week 26) or clinical response and/or remission after Period 3 (Week 52) of the preceding study[1,2] were enrolled to receive open-label RZB 180 mg subcutaneous (SC) injections every 8 weeks for up to 216 weeks. Patients who lost clinical response or remission after completion of the preceding study were re-induced with open-label RZB 600 mg intravenous (IV) infusions at Weeks 0, 4 and 8. Patients could only receive subsequent RZB 180 mg SC maintenance treatment if they achieved response and/or remission following re-induction treatment. Percentages of patients with IBDQ response per minimal clinical important difference (MCID: increase in IBDQ total score from the induction BL ≥16); IBDQ remission (IBDQ total score ≥170); and mean change from induction BL in IBDQ total, domain, and selected individual scores were calculated at Weeks 0, 24, 48, 72 and 96 with a data cut-off date of February 4, 2019. Results were reported as observed, and additional non-responder imputation was applied for remission/response data.
Results: A total of 65 adults with CD were enrolled, including 4 patients who were re-induced. At BL of the preceding study, median (range) age 34 (19-67) years and median disease duration 10 (2-38) years; 60 (92%) patients were previously exposed to tumour necrosis factor antagonists. Over 96 weeks of OLE therapy with RZB, >90% achieved IBDQ response and >58% of patients achieved IBDQ remission (Table, as observed). Mean change from induction BL to Week 0 of the OLE study was 62.5 points for IBDQ total score and this improvement was maintained over 96 weeks. This maintenance effect was also observed across all four IBDQ domains, with a mean change per individual item scores improved by approximately 2 points (Table). Individual items with the greatest improvement at Week

96 from Induction BL were abdominal pain (2.7 points), abdominal cramps (2.7 points), bowel movement frequency (2.4 points), number of loose bowel movements (2.5 points), feeling unwell (2.8 points), quality of sleep (2.3 points) and fatigue (1.9 points).

Outcome	Week 0	Week 24	Week 48	Week 72	Week 96
N (as observed)	64	65	60	52	51
IBDQ response (increase of IBDQ total score ≥16 from the Induction Baseline), n/N (%)					
As observed	60/64 (93.8)	59/65 (90.8)	57/60 (95.0)	47/52 (90.4)	47/51 (92.2)
NRI	60/65 (92.3)	59/65 (90.8)	57/65 (87.7)	47/65 (72.3)	47/65 (72.3)
IBDQ remission (IBDQ total score ≥170), n/N (%)					
As observed	40/64 (62.5)	38/65 (58.5)	42/60 (70.0)	36/52 (69.2)	37/51 (72.5)
NRI	40/65 (61.5)	38/65 (58.5)	42/65 (64.6)	36/65 (55.4)	37/65 (56.9)
Total IBDQ score, mean change ± SD (mean change per item)*	62.5 ± 38.8 (1.95)	58.7 ± 35.6 (1.83)	64.1 ± 33.1 (2.00)	63.8 ± 43.4 (1.99)	62.4 ± 39.2 (1.95)
IBDQ bowel symptom domain, mean change ± SD (mean change per item)*	20.4 ± 11.7 (2.04)	18.3 ± 11.6 (1.83)	20.5 ± 10.7 (2.05)	20.5 ± 12.8 (2.05)	19.1 ± 13.1 (1.91)
IBDQ systemic symptom domain, mean change ± SD (mean change per item)*	11.0 ± 8.2 (2.20)	10.6 ± 7.7 (2.12)	11.7 ± 7.5 (2.34)	11.3 ± 9.0 (2.26)	10.6 ± 8.6 (2.12)
IBDQ social function domain, mean change ± SD (mean change per item)*	9.9 ± 6.7 (1.98)	9.1 ± 6.4 (1.82)	9.6 ± 6.1 (1.92)	10.1 ± 7.5 (2.02)	10.3 ± 5.8 (2.06)
IBDQ emotional function domain, mean change ± SD (mean change per item)*	21.1 ± 16.8 (1.76)	20.8 ± 15.6 (1.73)	22.3 ± 15.0 (1.86)	21.9 ± 18.3 (1.83)	22.4 ± 17.1 (1.87)

*Total number of items in IBDQ is 32: 10 items in bowel symptom domain, 5 items in systemic symptom domain, 5 items in social domain, and 12 items in emotional domain.

[Table. IBDQ response, IBDQ remission and mean change in IBDQ total and domain scores from induction BL]

Conclusion: In patients with moderate to severe CD responding to RZB, improvements in HRQoL as measured by IBDQ were maintained over 3 years with RZB treatment. Bowel symptoms as well as patients' sleep quality and fatigue were found to have the greatest improvement with RZB therapy.

References: 1. Feagan BG, et al. Lancet. 2017;389:1699-1709. 2. Feagan BG, et al. Lancet Gastroenterol Hepatol. 2018;3:671-80.

P0400 EFFICACY AND SAFETY OF USTEKINUMAB USING ENDOVENOUS INDUCTION IN CROHN'S DISEASE: REAL-WORLD CLINICAL SETTING FROM A MULTICENTER OBSERVATIONAL STUDY

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Introduction: Randomized clinical trials have confirmed that biological therapy with ustekinumab (UST- amonoclonal antibody targeting interleukins12 and 23) is an effective treatment to induce and maintenance of remission in Crohn's disease (CD). UST using intravenous (ıv) induction in CD was approved in Spain in june 2017 and limited data on the efficacy and safety of this drug in clinical practice are available.

Aims & Methods:

Aim: To assess the efficacy and safety of UST, using iv induction, in a real world clinical setting.

Methods: A retrospective multicenter cohort study was performed on IBD patients receiving iv induction dose ofUST between june 2017 and june 2018 in five tertiary hospitals from Canary Islands (Spain). Efficacy was defined as clinical remission (HBI ≤4) at 8 weeks and 3,6 and 12 months and steroid withdrawal at 3and 12 months. We examined previous use of anti-TNF agents, need of surgery, rate of treatment discontinuation and adverse effects during UST treatment.

Results: A total of 47 CD patients (22M/25F; mean age 29 ±11 years; A2 85.1%, L3 59.6%/ B1 44.7%/p 44.7%) were included. Mean time from diagnosis to use of UST was 224 ± 323 months and 17.4% of patients were naive to anti-TNF and 43% had received 3 previous biological treatment. UST was indicated for induction of remission in 47,7% patients. Remission was achieved in 51.6% and 42% of patients at 8 weeks and 12 months, respectively. Steroid withdrawal was obtained in 80% of patients at 3 month of UST treatment. Escalation treatment by administrating UST every 8 weeks was indicated in 80% of casesand 91% received combination treatment with inmunosupresans (80% azathioprine). Number of previous anti-TNF agents , uso of steroids when starting UST and combination treatment with inmunosupresant did not reach stadistical significance to associate with clinical response to UST. The mean time of use of UST was 6.7± 3 months . Biological treatment discontinuation occurred in 30 % of patients predominantly owing to lack or loss of response. Surgery was underwent in 5 patients (10%). No adverse effects were reported and only one infection (infectious colitis) (2,1%) during follow-up.

Conclusion: UST is a safe treatment for IBD patients but the efficacy of UST might be distorted due to the complex profile of IBD patients in which we use in routine clinical practice.

Disclosure: Nothing to disclose

P0401 LONG-TERM OUTCOMES OF INFLIXIMAB THERAPY FOR PATIENTS WITH CROHN'S DISEASE AT DIFFERENT TIMES OF INITIATION OF INFLIXIMAB ADMINISTRATION: A SINGLE-CENTRE COHORT STUDY IN JAPAN

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Introduction: In Japan, infliximab was first approved for patients with Crohn's disease as an induction therapy in 2002. Subsequently, it was approved for maintenance therapy and dose escalation in 2007 and 2011, respectively. However, the comparative long-term effectiveness of infliximab treatments in patients with Crohn's disease at different times of initiation of infliximab administration is not fully established.
Aims & Methods: The aim of this study was to compare the rates of dose escalation of infliximab, intestinal resection and retention of infliximab among patients with Crohn's disease at different times of initiation of infliximab administration. Data for 338 patients with luminal Crohn's disease who were treated at our hospital with infliximab (5 mg/kg) for ≥14 weeks between January 2003 and May 2017 were retrospectively reviewed. The cumulative rate of the dose escalation of infliximab from 5 mg/kg to 10 mg/kg, the rate of intestinal resection and the rate of retention of infliximab following the initial infliximab administration were estimated using the Kaplan-Meier method. Patients were categorised into three groups according to the time of initiation of the infliximab therapy [A, 2003-2006 (n = 83); B, 2007-2010 (n = 146) and C, 2011-2017 (n = 109)]. Patient characteristics and the rates of dose escalation of infliximab, intestinal resection and retention of infliximab were compared among the three groups. Prognostic factors related to the outcomes were evaluated using the log-rank test.
Results: Of the 338 patients (median age, 29.7 years; 85 females), the median duration of the disease at initiation of infliximab therapy was 4.3 years. Of the total patients, 201 patients had ileocolitis, 75 had ileitis and 62 had colitis. In addition, 145 patients were diagnosed with non-stricturing, non-penetrating disease, 145 with stricturing disease and 48 with penetrating disease. Perianal disease was diagnosed in 156 patients. The median C-reactive protein was 1.01 mg/dL. Prior to initiation of the infliximab therapy, 108 patients had undergone at least one intestinal resection and 11 had been previously exposed to adalimumab. Concomitant treatment with immunomodulators (azathioprine or 6-mercaptopurine) and prednisolone was administered to 248 and 36 patients respectively. The 1-, 3-, 5- and 10-year cumulative rates of dose escalation of infliximab, intestinal resection and retention of infliximab in all 338 patients were 16.2%, 33.7%, 42.3% and 52.2%, 3.4%, 9.8%, 13.8% and 21.3% and 98.2%, 93.5%, 89.8% and 80.1%, respectively. Patients in group C had significantly shorter disease durations (P = 0.029) and higher rates of concomitant treatment with immunomodulators (P < 0.001) than those in group A. The 5-year cumulative rates of dose escalation of infliximab, intestinal resection and retention of infliximab were 54.2%, 17.1% and 88.5% in group A; 46.8%, 16.6% and 89.1% in group B and 27.3%, 6.5% and 92.2% in group C, respectively. The rates of dose escalation of infliximab (P < 0.001) and intestinal resection (P = 0.043) in group C were significantly lower than those in groups A and B.
Conclusion: The rates of dose escalation of infliximab and intestinal resection of patients with Crohn's disease who were administered infliximab after 2011 were lower than those of patients who were administered infliximab before 2010. Early induction of infliximab and a combined therapy with infliximab and immunomodulators in the 2011-2017 period may have contributed to the reduction in the rates of dose escalation of infliximab and intestinal resection.

P0402 ASSESSMENT OF PATIENTS' PREFERENCE FOR A NEW AUTO-INJECTION PEN COMPARED WITH THE PREFILLED SYRINGE FOR SELF-ADMINISTRATION OF ADALIMUMAB IN PATIENTS WITH CROHN'S DISEASE: A PROSPECTIVE COHORT STUDY

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Introduction: In Japan, a new auto-injection pen for self-administration of adalimumab, which differs in shape from the conventional auto-injection pen used worldwide, has been available since June 2018. This pen is filled with the same drug solution and fitted with the same 29-gauge needle as the prefilled syringe. However, there are no data comparing the new pen and the syringe in terms of preference among patients with Crohn's disease (CD). We report the results from the Comparison of Preference for New Auto-injection Pen Versus Prefilled Syringe in CD Patients Receiving Adalimumab Treatment (COMFORT).
Aims & Methods: The COMFORT study was to assess the patients' preference for the new pen in comparison with that of the syringe of adalimumab using a questionnaire survey. This study was a prospective cohort study conducted at a single centre in Japan. Patients with CD who agreed to switch from the adalimumab syringe to the new pen between September 2018 and January 2019 were enrolled. The inclusion criteria were as follows: 1) patients who were self-injecting 40 mg/0.4 mL of adalimumab using a syringe every other week, 2) those who were treated with adalimumab for ≥6 weeks and had ≥1 self-injections with a syringe and 3) those whose date of consent was within 2 weeks from the last date of self-injection with the syringe. The first questionnaire survey was conducted within 2 weeks from the last date of self-injection using the syringe, and the patient's impressions of the syringe during the final self-injection were assessed. All patients were instructed by a nurse on how to use the pen after the first survey was completed. The second and third surveys were conducted within 1 h after the first and seventh self-injection using the pen, and the patients' impressions of the pen were then investigated. Pain at the injection site was assessed using the visual analogue scale (VAS). In all surveys, VAS scores and the overall patients' satisfaction were examined. In the second and third surveys, pain, administration time, safe operability, simplicity, convenience and overall assessment were investigated to determine the patients' preference for the pen, syringe or neither.
Results: A total of 81 patients (median age, 33.6 years; female, 33.3%) were included in this study. All patients responded to the first survey, while 73 and 64 patients responded to the second and third surveys, respectively. The mean VAS score significantly decreased from 28.2 during the first survey to 16.7 (P < 0.001) and 19.1 (P = 0.003) during the second and third surveys, respectively. The proportion of patients who were satisfied increased sequentially from 66.7% in the first survey to 78.6% and 85.2% in the second and third surveys. The proportion of patients who reported that the pen was generally better than the syringe significantly increased from 69.9% in the second survey to 83.9% in the third survey (P = 0.012). Similarly, the proportion of patients who reported that the pen caused milder pain, took less time to administer, had safer operability, was simpler and more convenient to use than the syringe increased from 61.6%, 82.2%, 76.7%, 83.6% and 69.9% in the second survey to 71.4%, 87.3%, 85.7%, 88.9% and 79.4% in the third survey, respectively.
Conclusion: The new pen for self-administration of adalimumab caused less pain than the syringe. Further, approximately 70% of patients answered that the new pen was generally better than the syringe at the first self-injection. In addition, the proportion of patients who preferred the new pen was higher at the seventh self-injection than at the first self-injection.

P0403 LONG-TERM EFFICACY AND SAFETY OF ETRASIMOD FOR ULCERATIVE COLITIS: RESULTS FROM THE OPEN-LABEL EXTENSION OF THE OASIS STUDY

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Introduction: The efficacy of etrasimod, a once-daily, oral, selective, sphingosine-1-phosphate receptor modulator as induction therapy in adult patients with moderate to severe ulcerative colitis (UC) was previously demonstrated in the 12-week phase 2, randomised, placebo-controlled, double-blind (DB), OASIS study (NCT02447302). This open-label extension (OLE) study (NCT02536404) subsequently evaluated for an additional 34 weeks the safety and efficacy of etrasimod in achieving and maintaining response and/or remission in patients who completed OASIS.

Aims & Methods: All patients completing the OASIS DB study were eligible to enrol in the OLE and receive etrasimod 2 mg QD for up to 46 weeks from the DB baseline, irrespective of their response or treatment during the DB study. Efficacy was summarized in the modified intent-to-treat (mITT) population evaluable cohort, which included patients with required assessments who received etrasimod 2 mg throughout the OLE. Patients in the treat-through (TT) group received etrasimod 2 mg in both the DB and OLE studies. Endpoints were clinical remission (endoscopic score ≤1 [with absence of friability], rectal bleeding [RB] 0, and stool frequency [SF] score ≤1 with ≥1 point decrease from DB baseline), clinical response (clinical remission or decrease in 3-component Mayo Clinic score [endoscopy findings, RB, or SF] of ≥2 points and ≥30% decrease from DB baseline, with either a RB decrease of ≥1 or RB score of ≤1), and endoscopic improvement (subscore ≤1). All statistics are descriptive. End of treatment (EOT) was the last observation for each patient, occurring at week 46 (week 34 of OLE) for study completers or at last visit for patients who discontinued or had missing data.

	By previous treatment group in DB study			
	DB Study: Any treatment	DB Study: Etrasimod 1 mg	DB Study: Etrasimod 2 mg	DB Study: Placebo
	OLE: Etrasimod 2 mg	OLE: Etrasimod 2 mg	OLE: Etrasimod 2 mg	OLE: Etrasimod 2 mg
	(N = 105)	(N = 35)	(N = 31)	(N = 39)
Patients with clinical response, %				
n	94	33	28	33
Week 12 (end of DB study)	40.4	39.4	57.1	27.3
End of treatment	70.2	75.8	64.3	69.7
Patients with clinical remission, %				
n	94	33	28	33
Week 12 (end of DB study)	21.3	9.1	50.0	9.1
End of treatment	35.1	33.3	39.3	33.3
Patients with endoscopic improvement, %				
n	96	34	29	33
Week 12 (end of DB study)	26.0	14.7	51.7	15.2
End of treatment	44.8	50.0	41.4	42.4

[Key efficacy endpoints for patients in the OLE etrasimod 2-mg group (mITT evaluable cohort)]

Results: 118 patients (84% of DB completers) entered the OLE; 112 patients (safety population) received etrasimod 2 mg at any point in the OLE, of whom 105 patients (evaluable cohort) received etrasimod 2 mg throughout the OLE and 92 patients (82% of OLE enrollers) completed the OLE. At EOT, 70% of patients had a clinical response, an increase from 40% at week 12 (Table). Clinical response at EOT was seen in 87% (33/38) and 81% (13/16), respectively, of week-12 responders who received OLE etrasimod 2 mg or were in the 2-mg TT group; clinical remission at EOT was seen in 60% (12/20) and 64% (9/14), respectively, of week-12 remitters who received OLE etrasimod 2 mg or were in the 2-mg TT group. Median lymphocyte

reduction from the DB baseline was 44.6% at week 12 with etrasimod 2 mg and 42.9% at EOT in the 2-mg TT group. Of patients who received etrasimod 2 mg at any point during the OLE, 60% (67/112) experienced ≥1 TEAE (most of mild or moderate severity) and 9% (10/112) discontinued study drug due to a TEAE (worsening UC, atrial fibrillation, or headache). Of the 14 serious TEAEs reported in 7 patients, only 1 was considered treatment-related (worsening UC). The impact on heart rate and atrioventricular (AV) conduction was minimal, with no study discontinuations related to bradycardia or AV block.

Conclusion: Etrasimod 2 mg demonstrated sustained clinical response, clinical remission, and endoscopic improvement at the end of the OLE compared with the end of induction therapy. Etrasimod demonstrated a favourable long-term safety profile, with most AEs of mild to moderate severity; no new safety findings were reported.

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P0404 NONCLINICAL SAFETY ASSESSMENT OF LC51-0255, AN ORAL SPHINGOSINE-1-PHOSPHATE 1 RECEPTOR (S1P1) MODULATOR WITH A FAVORABLE PROFILE

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Introduction: LC51-0255 is a highly selective and potent S1P1 modulator under the clinical development for the treatment of Ulcerative Colitis (UC). The objective of this study was to evaluate the safety of LC51-0255 in nonclinical toxicity studies with rats and monkeys.

Aims & Methods: GLP toxicity studies were conducted in Sprague-Dawley rats and Cynomolgus monkeys. LC51-0255 was orally administered in 0.5% methylcellulose for up to 26 weeks in rats and 39 weeks in monkeys.

Results: LC51-0255 was evaluated for 4-, 13- and 26-week repeated oral dosing toxicity in Sprague-Dawley rats. The no-observed-adverse-effect-level (NOAEL) of LC51-0255 was 3 mg/kg/day in the toxicity studies in rats. Due to immunosuppressive nature of pharmacological effects of LC51-0255, low leukocyte and lymphocyte counts were observed, and changes in organ weight and histopathology from lymphoid tissues were mainly observed from 10 mg/kg/day groups. But those changes showed a tendency of recovery at the end of each recovery period of the studies. Although there were no functional abnormalities, toxicity target organs from the rat studies were considered to be liver and lung, based on the changes in organ weight and histopathology.

In toxicokinetic analysis in rats, the values of C_{max} and AUC_{0-24} of LC51-0255 increased in a dose proportional manner throughout the studies, and no clear sex-related differences were noted. Estimated human safety margins based on AUC_{0-24} were over 20-fold and over 30-fold for male and female rats, respectively.

To evaluate the systemic toxicity of orally administered LC51-0255 on Cynomolgus monkeys, 4-, 13- and 39-week toxicity studies were examined. The NOAEL of LC51-0255 was 3 mg/kg/day throughout the toxicity studies in monkeys. Similar to the rat toxicity studies, low leukocyte and lymphocyte counts were observed due to immunosuppressive effects of LC51-0255. In the spleen, organ weight loss and atrophy were observed. But those changes showed a tendency of recovery at the end of each recovery period of the studies.

Clinical signs including diarrhea and soft stool were mainly observed from 10 mg/kg/day groups. But those signs were considered to be related to the physicality of the test article formulation and toxicologically insignificant. Although there were no functional abnormalities, toxicity target organs from monkey toxicity studies were considered to be liver and lung, based on the changes in organ weight and histopathology.

In toxicokinetic analysis in monkeys, the values of C_{max} and AUC_{0-24} of LC51-0255 increased in dose proportional manner on the Day 1 of dosing throughout the studies. But accumulation ratio of LC51-0255 showed a tendency to decrease with increasing dose. From 3 mg/kg/day, the mean values of C_{max} and AUC_{0-24} showed similar values throughout the dosing period. Estimated human safety margins based on AUC_{0-24} were over 20-fold and over 30-fold for male and female monkeys, respectively.

Conclusion: LC51-0255 is a potent S1P1 modulator with high selectivity at S1P1 receptor versus the other S1P receptors

Nonclinical safety of LC51-0255 was assessed for genotoxicity, safety pharmacology, general toxicity and reproductive/developmental toxicity studies, and there were no specific safety concerns. Most of findings are related to its pharmacological activity as a S1P1 modulator.

These safety assessments support the continuing development of LC51-0255 for Ulcerative Colitis and other potential autoimmune disorders.

Disclosure: Nothing to disclose

P0405 LONG-TERM BUDESONIDE TREATMENT AND RISK OF OSTEOPOROTIC FRACTURES IN PATIENTS WITH MICROSCOPIC COLITIS

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Introduction: Budesonide is a well-established treatment of microscopic colitis (MC). Due to a substantial first-pass metabolism of oral budesonide the systemic bioavailability is low compared to other oral corticosteroids. This may lead to a decreased risk of adverse effects normally related to long-term use of corticosteroids. Due to a high risk of relapse long-term treatment of MC is often necessary. However, adverse effects related to long-term use of budesonide are of concern.

Aims & Methods: The aim was to determine whether use of oral budesonide is associated with risk of osteoporotic fractures in patients with MC. Based on data from the Danish nationwide health registries, we conducted a case-control study nested within patients with a histologically verified diagnosis of MC from 2004 to 2012. Cases were individuals with a first-occurrence of a fracture likely caused by osteoporosis i.e.,fracture of hip (ICD-10: S72), wrist (S525) or spine (S220 & 320). Controls were patients with MC without fractures matched according to age, gender and type of MC. Cases were matched to controls by risk set sampling in a ratio of 1:3. We estimated odds ratios (ORs) for the association between ever use of budesonide and any osteoporotic related fractures, and for hip-, wrist and spinal fractures independently. Further, we investigated dose-response associations and associations for subgroups at suspected high or low risk of fractures. Potential confounding was adjusted for by risk set sampling and regressionanalyses

Results: Among 10,652 patients with a diagnosis of MC we identified 485 cases with a first occurrence of an osteoporotic fracture as defined above. The majority were women (86%) and the median age was 78 years. After adjustment for confounding, a modestly increased adjusted OR was observed for the overall association between use of budesonide and osteoporotic fractures (OR 1.39, CI: 1.09-1.76). Stratification by type of fracture revealed the highest risk of spinal fractures (2.15, CI: 1.09-4.25), followed

hip-, and wrist fractures (OR 1.34 (CI: 0.94-1.93) and OR 1.26 (CI: 0.87-1.83), respectively). No dose-response association was evident (OR for doubling of cumulative dose 1.03 (CI: 0.91-1.16). When addressing differences across subgroups, we generally found moderately increased ORs (1.28-1.97).

	Cases Exposed/ unexposed	Controls Exposed/ unexposed	Crude odds ratio 95% CI	Adjusted* odds ratio 95% CI
No use	120 / 365	460 / 976	1.00 (Ref)	1.00 (Ref)
Spinal fracture	54 / 14	128 / 74	2.29 (1.19 – 4.42)	2.15 (1.09 – 4.25)
Wrist fracture	141 / 51	386 / 181	1.29 (0.90 – 1.86)	1.26 (0.87 – 1.83)
Hip fracture	170 / 55	462 / 205	1.37 (0.97 – 1.93)	1.34 (0.94 – 1.93)

[The association between budesonide use and types of osteoporotic fractures.]

Cases: MC-patients with an osteoporotic fracture; Controls: MC-patients without fractures; matched according to age, gender and type of MC.
Adjusted for all comorbid conditions and co-prescribed medication.
CI = 95% confidence interval; DDD = Defined daily dose

Conclusion: A moderate increased risk risk of osteoporotic fractures related to use of oral budesonide among individuals with MC was found. However, no dose-response association could be demonstrated. Based on present study we suggest using bone densitometry to periodically assess bone mineral density in MC patients on long-term oral budesonide to maintain clinical remission.

References: 1. Bonderup OK, Hansen JB, Birket-Smith L, Vestergaard V, Teglbjaerg PS, Fallingborg J. Budesonide treatment of collagenous colitis: a randomised, double-blind, placebo controlled trial with morphometric analysis. Gut 2003;52 (2):248-51. 2. Bonderup OK, Hansen JB, Teglbjrg PS, Christensen A, Fallingborg JF. Long-term budesonide treatment of collagenous colitis: a randomised, double-blind, placebocontrolled trial. Gut 2009;58(1):68-72.

P0406 SAFETY AND IMMUNE MODULATORY PROPERTIES OF LC51-0255, AN ORAL, SELECTIVE SPHINGOSINE 1-PHOSPHATE 1 (S1P1) RECEPTOR MODULATOR, IN HEALTHY VOLUNTEERS

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Introduction: LC51-0255 is a potent, selective, and orally available sphingosine-1-phosphate 1 (S1P1) receptor agonist which exerts anti-inflammatory effect. Once it is bound to S1P1 receptor, it is internalized from the cell membrane and is introduced to receptor degradation pathway, leading to the capture of immune cells in the secondary lymph node. We herein present the phase 1 clinical study results of LC51-0255 as a potential treatment of auto-immune diseases such as ulcerative colitis (UC).

Aims & Methods: A dose blocked-randomized, double-blind, placebo-controlled, single and multiple dosing, dose-escalation phase 1 clinical study was conducted to investigate the safety, tolerability, pharmacokinetic/pharmacodynamic (PK/PD) characteristics and food effect on the bioavailability of LC51-0255 after oral administration in healthy male volunteers. Eligible subjects were healthy male, 19 - 45 years of age with BMI 18.0 - 27.0 kg/m2. In the single ascending dose (SAD) study, 50 subjects (n=10/dose group) were randomly assigned, in 4:1 ratio, to receive either LC51-0255 (0.25 - 4 mg) or placebo, and the food effect was evaluated in LC51-0255 2 mg dose group. In the multiple-ascending dose (MAD) study, 40 subjects (n=10/dose group) were randomized (4:1) to receive either LC51-0255 (0.25 - 1.5 mg) or placebo once daily for 21 days. Safety and tolerability assessment included adverse events (AE), electrocardiogram (ECG), laboratory tests, and Holter monitoring. Blood samples were collected to evaluate the PK and PD of LC51-0255.

Results: There was no serious adverse event in SAD study. Decreased heart rate (bradycardia) was the most common AE, and one case of asymptomatic 2nd degree atrioventricular block occurred after single administration of LC51-0255 4 mg, both of which are well-known AEs in the same class of S1P agonists. These AEs were well tolerated and resolved within study period without any intervention. No clinically significant QT prolongation was reported in ECG and Holter monitoring. In present, MAD study is ongoing. Systemic exposure of LC51-0255 increased dose-dependently after a single dose, in dose range of 0.25 to 4 mg, with the mean area under the plasma concentration time curves (AUC) ranging from 127.72 to 2498.99 μg·h/L. There was no apparent effect of food on the systemic exposure of LC51-0255. The peak plasma concentration of LC51-0255 was observed at 3 – 4 hours after oral administration and the mean elimination half-life was 70-130 hours, making it suitable for once daily administration. The fraction excreted into urine was less than 0.1% across all dose levels, indicating that the renal excretion is not the major route of elimination.

The absolute lymphocyte count (ALC), a PD biomarker, decreased dose-dependently with the mean maximum change from baseline of ALC ranging from 34 to 77%. These results showed that the pharmacodynamics of LC51-0255 was consistent with expected pharmacology. All dose levels reached its maximum pharmacodynamic effect at 6 hours post administration except for 4 mg (10 hours). Reduced ALC levels were recovered to normal range during the study period.

Conclusion: Overall, LC51-0255 was well tolerated at all doses tested in this study. Systemic exposure increased dose-dependently and PK profile was favorable for once daily administration. ALC displayed a dose-dependent reduction, showing the potential of LC51-0255 as an effective treatment for UC. These findings support further evaluation of LC51-0255 in phase 2 clinical studies to determine the safe and efficacious dose in UC patients.

Disclosure: Nothing to disclose

P0407 DEFINING MEANINGFUL ATTRIBUTES FOR THE TREATMENT OF IBD FROM PATIENTS' PERSPECTIVE

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Introduction: Crohn's disease (CD) and ulcerative colitis (UC) are chronic, debilitating inflammatory bowel diseases (IBD). Medications used in the treatment of IBD include aminosalicylates, glucocorticoids, immunomodulators, biologics, and small molecules, with each class having distinct characteristics a patient may consider. Research into patient preferences in IBD indicates that values regarding medical treatment may vary depending on the clinical disease phenotype.[1-4] The development of a comprehensive descriptive system addressing all the meaningful aspects related to the management of IBD conditions is of utmost importance to enable a rigorous analysis of patients' preferences.

Aims & Methods: We present a descriptive system that includes the most relevant attributes for IBD treatment decision making, focusing on the patient perspective.

A three-step approach was used to develop the descriptive system. First, a literature review was performed and an initial list of attributes was developed and classified within domains and categories. Second, a focus group meeting was conducted with eight patient representatives and nine gastroenterologists. Using feedback elicited from the focus group meeting, the research team constructed an initial draft of the descriptive system, including a subset of domains and attributes. Third, all participants of the focus group meeting participated in two-rounds of structured online interviews. The structured interviews were used to refine the wording used for naming and defining each attribute and the levels of those attributes in the initial descriptive system.

Results: We identified 32 eligible publications and a list of 127 attributes grouped into 7 domains (effectiveness, side-effects, health related quality of life [HRQoL], well-being, available evidence, administration/convenience, and other) was developed. This list was discussed in the focus group meeting and a draft of the descriptive system containing 16 relevant attributes was constructed.

The same attributes were defined for UC and CD while taking into consideration that the relative weights for each disease may differ. During the first round of interviews, patients ranked all attributes included in the descriptive system and based on the second round of interviews, the final descriptive system containing a total of 3 domains, 10 attributes, and their corresponding levels was developed (Table).

Domain	Attribute name/Descriptor
Efficacy	Abdominal pain (8 levels) Other disease-related pain (8 levels) Bowel urgency (4 levels) Fatigue (4 levels)
Complications/Risk	Risk of cancer and serious infections within the next 10 years (3 levels) Risk of mild to moderate complications (4 levels) Aesthetic complications related to treatment (3 levels)
Health related quality of life	Emotional status (3 levels) Sexual life (3 levels) Social life and relationships (3 levels)

[Table. Final list of attributes]

Conclusion: This qualitative research shows which attributes within the domains of efficacy, complications/risk, and HRQoL patients value most when making treatment decisions. We developed a descriptive system that outlines the IBD treatments by means of the 10 most relevant attributes, which should be considered by physicians and nurses when discussing treatment options with a patient. These attributes will be weighted in a future study based on patient preferences.

References:
1. Bewtra M, Kilambi V, Fairchild AO, Siegel CA, Lewis JD, Johnson FR. Patient preferences for surgical versus medical therapy for ulcerative colitis. Inflamm Bowel Dis. 2014 Jan;20(1):103-14. doi: 10.1097/01.MIB.0000437498.14804.50.
2. Almario CV, Keller MS, Chen M, Lasch K, Ursos L, Shklovskaya J, Melmed GY, Spiegel BMR. Optimizing Selection of Biologics in Inflammatory Bowel Disease: Development of an Online Patient Decision Aid Using Conjoint Analysis. Am J Gastroenterol. 2018 Jan;113(1):58-71. doi: 10.1038/ajg.2017.470. Epub 2017 Dec 5.
3. Casellas F, Herrera-de Guise C, Robles V, Navarro E, Borruel N. Patient preferences for inflammatory bowel disease treatment objectives. Dig Liver Dis. 2017 Feb;49(2):152-156. doi: 10.1016/j.dld.2016.09.009.
4. van Deen WK, Nguyen D, Duran NE, Kane E, van Oijen MG, Hommes DW. Value redefined for inflammatory bowel disease patients: a choice-based conjoint analysis of patients' preferences. Qual Life Res. 2017 Feb;26(2):455-465. doi: 10.1007/s11136- 016-1398-z. Epub 2016 Aug 31.

P0408 WITHDRAWN

P0409 EFFICACY OF EARLY ANTI-TUMOR NECROSIS FACTOR TREATMENT IN ADULT AND PEDIATRIC PATIENTS WITH CROHN'S DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: There is an increasing body of evidence supporting earlier use of anti-tumor necrosis factor (anti-TNF) agents to improve outcomes and change the natural course of Crohn's disease (CD). The objective of this study was to perform a meta-analysis to assess the impact of early anti-TNF use in the treatment of CD.
Aims & Methods: The PubMed and Embase databases were searched for English language papers and conference abstracts published through 31 December 2017. Studies were selected for inclusion if patients initiated anti-TNFs within 2 years of a CD diagnosis or if anti-TNFs were used before or with immunosuppressants (top-down) in clinical trials and retrospective observational studies based on PRISMA guidelines. Random-effects meta-analyses were conducted to compare clinical remission (including steroid-free remission), disease relapse and endoscopic healing rates with early anti-TNF treatment (< 2 years of disease duration or top-down treatment strategy) to late/conventional treatment (defined as biologic use after >2 years of disease duration or conventional step-up treatment strategy in recently diagnosed patients).
Results: A total of 3,061 records were identified, of which 39 references met the selection criteria for systematic review. The meta-analysis included 14 studies that reported comparative remission, relapse and endoscopic healing rates for early vs late/conventional anti-TNF treatment. Early vs. late/conventional anti-TNF use was more likely to result in clinical remission or steroid-free remission, with an odds-ratio (OR) of 2.11 (95% CI: 1.66-2.68, n=2,113, P< 0.001). The positive results were observed in both adult (OR 1.97 at week 26 [95% CI: 1.53-2.53, n=803, P< 0.001]) and pediatric subgroups (OR 3.07 at week 52 [95% CI: 1.59-5.94, n=217, P< 0.001]). Conversely, early treatment with anti-TNFs was associated with reduced risk of relapse compared to late/conventional treatment, with an OR of 0.31 (95% CI: 0.14-0.68, n=596, P=0.003). A subgroup analysis for adults was not feasible, however in the pediatric patient subgroup, the OR for relapse with early treatment was 0.18 (95% CI: 0.07-0.43, n=105, P< 0.001). Early anti-TNF treatment was also more likely to result in endoscopic heal-

ing compared to late/conventional treatment (OR 2.06 [95% CI: 1.35-3.15, n=454, P< 0.001]). A subgroup analysis for pediatrics was not feasible, but in the adult patient subgroup, the OR for endoscopic healing with early treatment was 2.21 (95% CI: 1.34-3.64, n=424, P=0.002).

	Early anti-TNF Treatment[a]			Late/conventional Treatment[a]			Odds Ratio (95% CI)	P value
	Total (n)	Events (n)	Event rate	Total (n)	Events (n)	Event rate		
Clinical Remission[b]	524	341	65.1%	1589	610	38.4%	2.11 (1.66, 2.68)	<0.001
Disease Relapse[c]	123	32	26.0%	473	227	48.0%	0.31 (0.14, 0.68)	0.003
Endoscopic Healing[d]	200	108	54.0%	254	92	36.2%	2.06 (1.35, 3.15)	<0.001

[a] Early treatment is defined as anti-TNF use <2 years of disease duration or top-down treatment strategy; late/conventional treatment is defined as anti-TNF use after >2 years of disease duration or conventional step-up treatment strategy [b] Definition of clinical remission: 3 studies used CDAI<150; 1 study used CDAI<150 plus no bowel resection and no steroid use; 2 studies used PCDAI≤10; 1 study used corticosteroid free remission [c] Definition of disease relapse: 1 study used increase in CDAI≥70 and an absolute CDAI>220; 3 studies used PCDAI>10 [d] Definition of endoscopic healing: 2 studies used SES-CD=0; 1 study used CDEIS<4 and absence of deep ulcers; 1 study used absence of any mucosal ulcers (including aphthous ulcers); 1 study used absence of mucosal ulceration; 1 study used disappearance of ulcerations, multiple erosions, bleeding and friability (grade 0 or 1) CDAI: Crohn's Disease Activity Index; PCDAI: Pediatric Crohn's Disease Activity Index; SES-CD: Simple Endoscopic Score for Crohn's Disease; CDEIS: Crohn's Disease Endoscopic Index of Severity

Table. Results of meta-analysis on clinical remission, relapse and endoscopic healing with early anti-TNF treatment versus late or conventional treatment in Crohn's disease

Conclusion: Early use of anti-TNF in CD patients is associated with improved outcomes in clinical remission, disease relapse, and endoscopic healing compared to late/conventional treatment.

P0410 ST-0529 IN MODERATE TO SEVERE ACTIVE ULCERATIVE COLITIS: LESSONS LEARNED AND PERSPECTIVES

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Introduction: There is an unmet need for safe and effective treatment options for patients with moderate to severe ulcerative colitis (UC) who have intolerance to, experience an inadequate response to, or relapse of the current recommended treatments. Many patients experience infusion or injection site reactions with biologic therapies, and immunomodulators increase malignancy risk, highlighting the need for new safe oral alternatives. Although cyclosporine (CsA) has similar safety and efficacy to infliximab for acute severe UC management, its use is limited due to its serious systemic side effects (SSE). Sublimity has developed ST-0529, an oral formulation of CsA with a diffusion-controlled mechanism of release that delivers CsA directly to diseased tissue of the ileum and colon, thereby reducing systemic absorption, and potentially minimising the risk of SSE and the need for extensive drug monitoring.

Aims & Methods: Two phase 1 and one phase 2 studies have been completed with ST-0529.[1] Phase 1 results showed that ST-0529 (dose range 37.5-150 mg) achieves similar or higher colonic tissue concentrations of CsA and significantly lowers systemic CsA levels compared to continuous IV CsA in healthy subjects.[2],[3] Phase 2a pilot results confirmed safety of ST-0529 75 mg once-daily in patients with mild or moderate UC after 4 weeks of treatment and showed a numerical increase in rates of remission and response with ST-0529 compared to placebo, although not statistically significant. Post-hoc analysis found that compared to placebo, patients with moderate disease (35% vs 17%, *p*=0.0499) and moderate disease taking concomitant 5-aminosalicylate and/or steroids without immunosuppressives (47.8% vs 17.9%, *p*=0.026) did significantly better on ST-0529.[4] To further investigate ST-0529 in UC, a phase 2b, multicentre, randomised, double-blind, placebo-controlled, parallel-group study will evaluate efficacy, safety and tolerability of ST-0529 in achieving clinical remission in subjects with moderate to severe UC. This study will also characterise the pharmacokinetic (PK) and pharmacodynamic (PD) profile of ST-0529 as well as its impact on quality of life in subjects with UC. Key inclusion criteria will include a diagnosis of histologically confirmed moderate to severe UC for ≥3 months defined as 3-Component Mayo Score (Mayo) of 5-9. Approximately 280 subjects are planned to be enrolled (40 are targeted for participation in a PK sub-study), randomised 1:1:1:1 (dosage regimen in table 1). Randomisation will be stratified according to disease severity as assessed by Mayo, prior treatment with anti-TNF therapy and corticosteroid use. The primary efficacy outcome will be clinical remission at week 12, defined as stool frequency subscore ≤1 associated with a decrease ≥1-point, rectal bleeding subscore 0, and an endoscopic subscore ≤1 using Mayo. Rectal bleeding and stool frequency subscores will be calculated from data collected in subject diaries and endoscopic subscore provided by a central reader.

Results:

	ST-0529 Dosage 1 (n=70)	ST-0529 Dosage 2 (n=70)	ST-0529 Dosage 3 (n=70)	Placebo (n=70)
Dosage regimen	18.75 mg twice-daily, oral (capsule)	37.5 mg twice-daily, oral (capsule)	75 mg twice-daily, oral (capsule)	To match ST-0529 dose twice-daily, oral (capsule)
Treatment duration	12 weeks			
PK sub-study	Whole blood samples being collected at Week 2 at 0 (pre-dose), and at 2, 4, 6, and 8 hours post-dose (n=40)			

[Table 1: Phase 2b trial overview - Test product (ST-0529) and comparator (placebo)]

Conclusion: Orally administered ST-0529 represents a novel approach to attaining therapeutically relevant tissue concentrations of CsA in the colon and may offer an alternative for inadequate clinical response to traditional therapies. The results from this trial will help identify the appropriate dose(s) of ST-0529 for use in phase 3 clinical studies.

References: [1]O'Donoghue D, Bloom S, Coulter I. Colon targeted, low systemic absorption soluble ciclosporin in ulcerative colitis. *Gut.* 2013;62(Suppl 2):A1.3-A2. doi:10.1136/gutjnl-2013-305143.3.
[2]Colombel J, Coulter I, Hall J, Rosa M, McDonald B, Cullen A. P053 Targeted release oral cyclosporine formulation as a potential new therapy for ulcerative colitis. *Gastroenterology.* 2019;156(3):S37-S38. doi:10.1053/j.gastro.2019.01.109.
[3]Colombel J, Coulter I, Hall J, Rosa M, McDonald B, Cullen A. P053 Targeted release oral cyclosporine formulation as a potential new therapy for ulcerative colitis. *Inflamm Bowel Dis.* 2019;25(Suppl 1):S26-S26. doi:10.1093/ibd/izy393.059.
[4]Bloom S, Iqbal T, Nwokolo C et al. OP16 A randomised, multi-centre, double-blind, placebo-controlled study of a targeted release oral cyclosporine formulation in the treatment of mild-to-moderate ulcerative colitis: efficacy results. *Journal of Crohn's and Colitis.* 2019;13(Suppl 1):S011-S011. doi:10.1093/ecco-jcc/jjy222.015.

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P0411 HUMAN ADIPOSE MESENCHYMAL STEM CELLS MODULATE MYELOID CELLS TOWARDS AN ANTI-INFLAMMATORY AND REPARATIVE PHENOTYPE: ROLE OF IL-6 AND PGE2

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Introduction: Mesenchymal stem cells (MSCs) are the focus of intensive efforts directed towards developing cell-based therapies in immunologic disorders.[1,2] MSCs have been shown to activate the endogenous immune regulatory system of the recipient to induce a therapeutic effect.[1,2] Darvadstrocel (DVS) is an expanded, allogeneic, adipose-derived MSC (ASC) therapy approved in Europe[5,6] and Israel for the management of treatment-refractory complex perianal fistula (CPAF) in patients with inactive or mildly active Crohn's disease (CD)[3,4]. DVS has been shown to have long-term success rates comparable with existing medical and surgical therapies for CPAF.[3,4]
The mechanism of action of DVS is only partially understood.[3,4] It has been suggested that MSCs can modulate phenotype and function of monocytes via prostaglandin E2 (PGE2) and interleukin 6 (IL-6) during their differentiation to macrophages (Mphs) and dendritic cells.[7,8,9]

Aims & Methods: To characterise the modulatory effect of DVS on human myeloid cells *in vitro*.
Freshly isolated human monocytes from peripheral blood were differentiated *in vitro* towards M0 Mphs, M1 pro-inflammatory Mphs, M2 anti-inflammatory Mphs or mature dendritic cells (mDCs) in the presence or absence of DVS in non-contact conditions. The phenotype and function of the differentiated Mphs and dendritic cells were determined by flow cytometry, and their secretome (sets of secreted proteins) was assessed by Olink technology (a proteomic analysis system based on the Proximity Extension Assay). The role of the soluble factors PGE2 and IL-6 was investigated using neutralisation assays.

Results: The co-culture of monocytes in the presence of DVS during their differentiation to Mphs or mDCs resulted in polarisation towards an anti-inflammatory and phagocytic phenotype. This was characterised by an increased expression of phagocytic receptors and modulation of surface chemokine receptors, a reduced expression of co-stimulatory and activation molecules, and a decrease in the amount of cell debris present. Additionally, the morphology of M1 and M2 Mphs was modulated when differentiated in the presence of DVS. DVS promoted an elevation of secreted factors with anti-inflammatory, reparative and antimicrobial functions. DVS appeared, therefore, to be able to modulate monocyte cells towards an anti-inflammatory and reparative phenotype through secretion of soluble factors. Chemical inhibition of PGE2 with indomethacin resulted in complete neutralisation of the modulatory effect of DVS on mDC phenotype, whereas inhibition of IL-6 resulted in only a minor reduction of DVS-mediated modulation. The data indicate that PGE2 and IL-6 are the main soluble factors responsible for this modulatory effect.

Conclusion: The results demonstrate a mechanism of the DVS-mediated induction of anti-inflammatory and reparative phenotypes that potentially modulates monocyte/Mph/mDC differentiation. The modulatory effects of DVS on human myeloid cells are mediated by PGE2, and to a lesser extent, IL-6 examined on mDCs.

References: 1. Uccelli A, Prockop DJ. Curr Opin Immunol 2010;22:768-774. 2. English K, Wood KJ. Cold Spring Harb Perspect Med 2013;3:a015560. 3. Panés J, et al. Lancet 2016;388:1281-1290. 4. Panés J, et al. Gastroenterology 2018;154:1334-1342.e4. 5. European Medicines Agency (EMA) Committee For Medicinal Products For Human Use. Alofisel, INN-darvadstrocel EPAR Annex I Summary of Product Characteristics. (2018). http://www.ema.europa.eu. Accessed: April 2019. 6. Swiss Agency for Therapeutic Products. www.swissmedic.ch. Accessed: April 2019. 7. Kondo M, et al. Arthritis Rheumatol 2015;67:1250-1260. 8. Hwa Ko, J, et al. Proc Natl Acad Sci USA 2016;113:158-163. 9. Prockop DJ, Youn Oh J. Mol Ther 2012;20:14-20.

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P0412 INCIDENCE OF VENOUS THROMBOEMBOLIC EVENTS IN PATIENTS WITH ULCERATIVE COLITIS TREATED WITH TOFACITINIB IN THE ULCERATIVE COLITIS CLINICAL DEVELOPMENT PROGRAMME

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Introduction: Tofacitinib is an oral, small molecule Janus kinase inhibitor for the treatment of ulcerative colitis (UC). The safety of tofacitinib for the treatment of moderate to severe UC was evaluated in a randomised, placebo-controlled Phase (P) 2 induction study (NCT00787202),[1] 2 induction P3 studies (NCT01465763; NCT01458951), 1 maintenance P3 study (NCT01458574),[2] and an ongoing, open-label, long-term extension (OLE) study (NCT01470612).[3] A safety signal for pulmonary embolism (PE) was seen in the tofacitinib 10 mg twice daily (BID) arm of an FDA post-marketing requirement study in rheumatoid arthritis designed to evaluate the long-term risk of major cardiovascular events and malignancy. Patients (pts) eligible for this ongoing, open-label, safety-endpoint-driven study had to be ≥50 years of age, have ≥1 cardiovascular risk factor and be on a stable dose of methotrexate. UC is a known risk factor for deep vein thrombosis (DVT) and PE, with reported incidence rates ranging from 0.07 to 0.30 and 0.04 to 0.20, respectively.[4,5] Here, we report the incidence of DVT and PE in the tofacitinib UC clinical programme, as of Sep 2018.

Aims & Methods: Pts who received placebo, tofacitinib 5 or 10 mg BID were analysed in three cohorts: Induction (P2/P3 induction studies, N=1220), Maintenance (P3 maintenance study, N=592) and Overall (pts receiving tofacitinib 5 or 10 mg BID in P2, P3 or ongoing OLE studies, N=1157). DVT and PE events were identified using preferred terms in the Standardised Medical Dictionary for Regulatory Activities query 'embolic and thrombotic events, venous' and incidence rates (unique pts with events per 100 pt-years [PY] of exposure) were evaluated. For Overall Cohort analysis, pts were categorised based on the average daily dose of tofacitinib: predominant dose (PD) tofacitinib 5 mg BID (average total daily dose < 15 mg) and PD tofacitinib 10 mg BID (average total daily dose ≥15 mg).

	Induction Cohort (8 weeks)[a]		Maintenance Cohort (52 weeks)[a]			Overall Cohort (≤6.1 years)[a,b]		
	Placebo (N=282; 44.8 PY)	Tofacitinib 10 mg BID (N=938; 156.2 PY)	Placebo (N=198; 100.4 PY)	Tofacitinib 5 mg BID (N=198; 146.2 PY)	Tofacitinib 10 mg BID (N=196; 154.3 PY)	PD Tofacitinib 5 mg BID (N=197; 595.5 PY)	PD Tofacitinib 10 mg BID (N=960; 1801.1 PY)	Tofacitinib All (N=1157; 2403.6 PY)
DVT, n (%), IR [95% CI]	1 (0.4), 1.99 [0.05, 11.07]	0 (0.0), 0.00 [0.00, 2.22]	1 (0.5), 0.97 [0.02, 5.39]	0 (0.0), 0.00 [0.00, 2.48]	0 (0.0), 0.00 [0.00, 2.35]	0 (0.0), 0.00 [0.00, 0.61]	1 (0.1),[c] 0.05 [0.00, 0.30]	1 (0.1), 0.04 [0.00, 0.23]
PE, n (%), IR [95% CI]	1 (0.4), 1.98 [0.05, 11.04]	0 (0.0), 0.00 [0.00, 2.22]	1 (0.5), 0.98 [0.02, 5.44]	0 (0.0), 0.00 [0.00, 2.48]	0 (0.0), 0.00 [0.00, 2.35]	0 (0.0), 0.00 [0.00, 0.61]	4 (0.4),[d] 0.21 [0.06, 0.55]	4 (0.3), 0.16 [0.04, 0.41]

For Overall Cohort analysis, pts were categorised based on the average daily dose of tofacitinib (placebo exposure was not included): PD tofacitinib 5 mg BID (average total daily dose <15 mg) and PD tofacitinib 10 mg BID (average total daily dose ≥15 mg)
[a]Excluding events occurring after 28 days from the last dose of the corresponding cohort; [b]Data are as of Sep 2018 (OLE study database not locked); [c]DVT event occurred in 1 pt (58 years of age at DVT event) 1149 days following the first dose of tofacitinib; [d]PE events occurred in 1 pt (25 years of age at PE event) with prior DVT and PE, 216 days following the first dose of tofacitinib; 1 pt (57 years of age at PE event) with prior phlebothrombosis and stroke, 236 days following the first dose of tofacitinib; 1 pt (70 years of age at PE event) with cholangiocarcinoma and metastases to the peritoneum, 383 days following the first dose of tofacitinib; and 1 pt (21 years of age at PE event) who was receiving oral contraceptives for dysfunctional uterine bleeding, 569 days following the first dose of tofacitinib
BID, twice daily; CI, confidence interval; DVT, deep vein thrombosis; IR, incidence rate; N, number of patients; n, unique number of patients with a particular adverse event; OLE, open-label, long-term extension; PD, predominant dose; PE, pulmonary embolism; pts, patients; PY, patient-years

[Table. Incidence rates (unique pts with event per 100 PY of exposure) of DVT and PE among pts in the Induction, Maintenance and Overall Cohorts]

Results: The Overall Cohort comprised 1157 pts who received ≥1 dose of tofacitinib 5 or 10 mg BID, with 2404 PY of tofacitinib exposure and up to a maximum of 6.1 years of treatment. Results for DVT and PE are shown in the Table. In the Induction and Maintenance Cohorts, 2 pts had DVT and 2 had PE; all had received placebo in the study. In the Overall Cohort, there was 1 pt with DVT and 4 pts with PE; all 5 pts had received PD of tofacitinib 10 mg BID and all events occurred during the OLE study. Pts with PE had the following notable medical history: 1 with prior DVT and PE, 1 with phlebothrombosis and stroke, 1 was receiving oral contraceptives for dysfunctional uterine bleeding, and 1 had cholangiocarcinoma and metastases to the peritoneum, and PE was the cause of death. The pt with DVT was diagnosed following a long-haul flight and management of an infected leg wound sustained in a recent motorbike accident.

Conclusion: In this post-hoc analysis of pts from the OCTAVE programme, during tofacitinib exposure, 4 pts had PE and 1 pt had DVT. All of the events in pts taking tofacitinib occurred during the OLE study in pts treated with PD of tofacitinib 10 mg BID (83% of pts in the Overall Cohort received a PD of tofacitinib 10 mg BID) and with risk factors for thrombotic events. This post-hoc analysis is limited by small sample size and limited drug exposure, and further study is needed.

References:
1. Sandborn WJ et al. N Engl J Med 2012; 367: 616-624.
2. Sandborn WJ et al. N Engl J Med 2017; 376: 1723-1736.
3. Lichtenstein GR et al. Am J Gastroenterol 2018; 113 (Suppl 1): Abstract 571.
4. Weng MT et al. Inflamm Bowel Dis 2018; 24: 1791-1800.
5. Bernstein CN et al. Thromb Haemost 2001; 85: 430-434.

P0413 CLINICAL REMISSION DEMONSTRATED WITH ORAL OZANIMOD IN THE OVERALL POPULATION AND ACROSS MULTIPLE SUBGROUPS OF PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS IN THE TOUCHSTONE TRIAL

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Introduction: Ozanimod is an oral immunomodulator that selectively targets $S1P_1$ and $S1P_5$. TOUCHSTONE, a randomised, double-blind, placebo-controlled phase 2 trial that evaluated patients with moderately to severely active ulcerative colitis (UC) showed significantly higher rates of clinical remission, clinical response, and endoscopic mucosal healing (Mayo endoscopic subscale score of 0/1) at Weeks 8 and 32 in patients assigned to ozanimod 1 mg compared to those who received placebo (Sandborn *NEJM* 2016). The objective of this analysis was to assess clinical remission at Week 32 across subgroups of interest.

Aims & Methods: Patients were randomised 1:1:1 and received ozanimod 1 mg, ozanimod 0.5 mg, or placebo. Mayo score, based on stool frequency, rectal bleeding, mucosal appearance at endoscopy, and physician rating of disease activity, was calculated at baseline, end of induction (Week 8), and end of maintenance (Week 32). Clinical remission was defined as total Mayo score ≤2, with no subscore >1. A post hoc sub-group analysis evaluated clinical remission rates at Week 32 according to baseline Mayo score, years since UC diagnosis, and body mass index (BMI).

Results: A total of 197 patients were randomised and received ozanimod 1 mg (n=67), 0.5 mg (n=65), or placebo (n=65), with 103 (52.3%) entering a maintenance period based on response criteria (ozanimod 1 mg, n=42; 0.5 mg, n=36; placebo, n=25), and 91 (88.3%) completing the study. Differences in the proportion of patients in clinical remission with ozanimod 1 mg versus placebo by subgroup illustrate that the treatment effect favoured ozanimod 1 mg in every subgroup analysed (Table).

The 95% confidence intervals for the treatment difference between ozanimod 1 mg and placebo exclude 0 for the overall population and subgroups of baseline Mayo score >8, years since UC diagnosis >6, and BMI <25 kg/m².

	Treatment Difference in Week 32 Remission Rate (Ozanimod 1mg vs placebo)	95% Confidence Limits	
		Lower	Upper
Clinical Remission at Week 32			
Overall	16.23%	4.67%	27.80%*
Baseline Mayo score (≤8)	14.35%	-4.20%	32.89%
Baseline Mayo score (>8)	18.18%	5.02%	31.34%*
Years of UC diagnosis at baseline (≤6)	12.90%	-0.07%	25.87%
Years of UC diagnosis at baseline (>6)	23.48%	1.10%	45.87%*
BMI at baseline (≥25 kg/m²)	15.44%	-2.10%	32.98%
BMI at baseline (<25 kg/m²)	16.82%	1.41%	32.23%*

BMI: body mass index; ITT: intent-to-treat; NRI: non-responder imputation; UC: ulcerative colitis. *P<0.05.

[Clinical Remission at Week 32 by Subgroup of Interest (ITT, NRI)]

Conclusion: In the TOUCHSTONE trial, ozanimod therapy was consistently more efficacious than placebo for induction of clinical remission across a wide range of patient subtypes including those with relatively long disease duration and high disease activity.

References: Sandborn WJ, Feagan BG, Wolf DC, D'Haens G, et al. Ozanimod induction and maintenance treatment for ulcerative colitis. N Engl J Med. 2016;374(18):1754-1762.

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P0414 LONG-TERM EFFICACY AND SAFETY OF UPADACITINIB TREATMENT IN PATIENTS WITH CROHN'S DISEASE: ONE-YEAR RESULTS OF THE ONGOING PHASE 2 CELEST OPEN-LABEL EXTENSION STUDY

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Introduction: Upadacitinib (UPA), an oral selective Janus kinase 1 inhibitor, demonstrated clinical and endoscopic efficacy and a favourable safety profile as induction and maintenance treatment in patients with moderate to severe Crohn's disease (CD).[1,2]

Aims & Methods: To report the 1-year efficacy and safety results of UPA long-term treatment in the ongoing CELEST open-label extension (OLE) study.

Patients who completed the 52-week CELEST study[2], either receiving double-blind or open-label rescue treatment during CELEST, were enrolled to receive the once daily (QD) UPA modified release formulation for up to 8 years; patients on double-blind therapy received 15 mg QD and those on open-label rescue therapy received 30 mg QD. Clinical remission 2.8/1.0, enhanced clinical response, CD activity index (CDAI) remission, CDAI response 70, endoscopic remission, endoscopic response 50%, Inflammatory Bowel Disease Questionnaire (IBDQ) remission, and change from baseline (BL) in C-reactive protein and faecal calprotectin, as defined in the table, were analysed at Week 0 to Month 12 (Table).

Missing data were imputed via last observation carried forward; observed-case analysis was done for the endoscopic endpoints. Adverse events (AEs) were collected throughout the study up to 30 days after the last UPA dose.

Results: Of 107 patients enrolled, 76 received 15 mg QD and 31 received 30 mg QD, with median (range) age of 40 (19, 76) years and disease duration 10.4 (1.4, 47.4) years. At Week 0, the mean (SD) UPA exposure was 303.0 (108.8) days. Overall, the number of patients with clinical remission, clinical response, endoscopic remission, endoscopic response, and reporting IBDQ remission was maintained from Week 0 to Month 12 (Table).

Incidences of AEs were 75.0% and 83.9% for UPA 15 and 30 mg QD groups, respectively. AEs leading to discontinuation of study drug were 6.6% in the UPA 15 mg and 19.4% in the UPA 30 mg QD groups. Serious AEs occurred in patients receiving UPA 15 mg QD (10.5%) and UPA 30 mg QD (12.9%).

The most frequently reported serious AE (4.7%) and AE leading to study drug discontinuation (4.7%) was CD. One case of serious infection was reported in each of the UPA treatment groups. Herpes zoster was reported in patients receiving UPA 15 mg QD (1.3%, n=1) and UPA 30 mg QD (6.5%, n=2). One case of malignancy (basal cell carcinoma) occurred in the UPA 15 mg QD group and one case of latent tuberculosis in the UPA 30 mg group.

No cases of opportunistic infection, thromboembolic event, or death were reported.

Conclusion: The 1-year efficacy of UPA observed after induction and maintenance was sustained in patients with CD. No new safety signals were identified.

References:
1. Sandborn WJ, et al. Gastroenterology. 2017;152(5 Suppl 1):S1308-S1309.
2. Panes J et al. Journal of Crohn's and Colitis. 2018; 12(S1):S238-S239.

Efficacy endpoints	UPA 15 mg QD	UPA 30 mg QD
Clinical remission 2.8/1.0, n/N (%)[a]		
Week 0	40/71 (56.3)	16/28 (57.1)
Month 12	38/60 (63.3)	16/28 (57.1)
Enhanced clinical response, n/N (%)[a]		
Week 0	59/76 (77.6)	24/31 (77.4)
Month 12	51/63 (81.0)	23/31 (74.2)
CDAI remission, n/N (%)[a]		
Week 0	49/76 (64.5)	20/31 (64.5)
Month 12	41/63 (65.1)	18/31 (58.1)
Endoscopic remission, n/N (%)[b]		
Week 0	20/69 (29.0)	7/28 (25.0)
Month 12	22/43 (51.2)	10/20 (50.0)
Endoscopic response 50%, n/N (%)[b]		
Week 0	39/69 (56.5)	15/28 (53.6)
Month 12	29/43 (67.4)	15/20 (75.0)
IBDQ remission, n/N (%)[a]		
Week 0	43/76 (56.6)	15/28 (53.6)
Month 12	41/62 (66.1)	14/30 (46.7)
Change in hs-CRP from baseline to Month 12, mg/L, Median (range)[a]		
Week 0	-4.2 (-88.4, 169.0)	-9.9 (-93.6, 61.4)
Month 12	-2.710 (-81.0, 33.3)	-7.2 (-93.7, 135.0)
Change in FCP from baseline to Month 12, mcg/g, Median (range)[a]		
Week 0	-680.0 (-9560, 2621)	-438.5 (-6770, 5391)
Month 12	-650.0 (-9590, 7971)	-615.0 (-7549, 3800)

[a]Last observation carried forward analysis; [b]Observed cases analysis; [c]Baseline (BL) of the CELEST study

For the LOCF analysis, any missing data was mainly due to (1) discontinuation, (2) missing visit (3) loss of data due to technical reason, e.g., ePro malfunction. During the study, subjects who met the criteria for inadequate response were allowed to dose escalate from 15 mg QD to 30 mg QD. In the 15 mg QD group, these subjects (N=15) were removed from the 15 mg QD analysis after dose escalation visit.

UPA=upadacitinib; QD=once daily; CDAI=Crohn's disease activity index; CR=CDAI response; IBDQ= Inflammatory Bowel Disease Questionnaire; hs-CRP=high sensitivity C-reactive protein; FCP=faecal calprotectin

Clinical remission 2.8/1.0: very soft/liquid stool frequency (SF) ≤2.8 and abdominal pain (AP) score ≤1.0, both not worse than BL in patients with SF≥4 or AP score ≥2.0 at BL of CELEST study
Enhanced clinical response: ≥60% reduction from BL in SF or ≥35% reduction from BL in AP and both not worse than BL of CELEST study
CDAI remission: CDAI <150
Endoscopic remission: Simplified Endoscopic Score for CD (SES-CD) ≤ 4 and at least 2-point reduction from BL of CELEST study and no subscore >1
Endoscopic response 50%: SES-CD reduction >50% from BL of CELEST study or endoscopic remission
IBDQ remission: IBDQ ≥170

[Clinical and endoscopic endpoints at Week 0 and Month 12 in the CELEST OLE study]

Disclosure:
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P0415 THERAPEUTIC INTENSIFICATION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE - A COMPARISON OF DIFFERENT BIOLOGIC THERAPIES

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Introduction: The loss of response to biologic therapies in Inflammatory Bowel Disease (IBD) is common. Treatment intensification may be helpful in regaining response in up to 1/3 of patients. To date, there have been no studies comparing the need for escalation between different biological therapies.
Aims & Methods: To compare the need and predictors of therapy escalation in Crohn's Disease (CD) and Ulcerative Colitis (UC). This was a retrospective cohort single center study including patients under maintenance therapy with Infliximab (IFX), Adalimumab (ADA), Golimumab (GLB) or Vedolizumab (VDZ). Patients with at least 2 years of follow-up were included. Non-responders and patients with treatment interruption prior to the need of escalation were excluded.
Results: 344 patients were included: 258 with CD and 86 with UC; 51,7% were male with mean age of 43,6±13 years. IFX: 229 (180 CD, 49 UC), ADA: 74 (62 CD, 12 UC), GLB: 14 (all UC) and VDZ: 27 (16 CD, 11 UC). In general, the need for treatment escalation was superior in UC (Log Rank test, p=0.001). In UC, therapeutic escalation in GLB patients was less frequent than IFX patients (p=0.035). For CD we could not find a difference in the need of escalation between drugs. In multivariate analysis age, gender, localization and behavior of the disease and combo therapy weren't predictors of the need of drug escalation during the two years of follow-up, independently of the biologic therapy used.
Conclusion: Therapeutic intensification is more frequent and occurs earlier in patients with UC, regardless of the treatment used.
Disclosure: Nothing to disclose

P0416 USTEKINUMAB MAINTAINED CLINICALLY MEANINGFUL IMPROVEMENT IN HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH MODERATE TO SEVERE CROHN'S DISEASE: RESULTS FROM THE IM-UNITI LONG-TERM EXTENSION

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Introduction: The IM-UNITI study evaluated the safety and efficacy of subcutaneous (SC) ustekinumab (UST) maintenance therapy in patients with moderately to severely active Crohn's disease (CD) who completed induc-

tion treatment with UST. Previously, we reported the effects of UST on health-related quality of life (HRQoL) through Wk44. Here, we evaluated HRQoL through Wk140 in patients who entered the long-term extension of the IM-UNITI study.

Aims & Methods: Patients who completed the safety and efficacy evaluation at Wk44 of the maintenance study were eligible to continue their regimen in the extension study (placebo [PBO], UST 90 mg q12w, or UST 90 mg q8w). All patients who were treated in the extension study were included in this analysis of Inflammatory Bowel Disease Questionnaire (IBDQ) and SF-36 data according to the treatment they received during the extension study. The IBDQ is a 32-item questionnaire with 4 dimensions: bowel symptoms, systemic symptoms, emotional function, and social function. The total score ranges from 32 to 224, higher scores indicate better quality of life, and a change ≥16 points was defined as clinically meaningful. For SF-36, a change ≥5 points was defined as clinically meaningful.

Results: For patients who entered the extension, mean total IBDQ scores and SF-36 scores at maintenance baseline were comparable across treatment groups (Table). Patients who received UST maintained the improvement in IBDQ and SF-36 that was achieved by maintenance baseline through Wk140, and those who received PBO generally worsened. Through Wk140, 26.5% of patients receiving PBO, 61.5% of patients receiving UST 90 mg q12w, and 59.3% of patients receiving UST 90 mg q8w had ≥16-point improvements from induction baseline in IBDQ score. In addition, 10.9%, 51.6%, and 54.2%, respectively, had ≥5-point improvements in SF-36 physical component summary scores, and 8.7%, 43.8%, and 43.7%, respectively, had ≥5-point improvements in SF-36 mental component summary scores during the same period.

Conclusion: In patients who entered the long-term extension of the IM-UNITI study, those who received SC UST maintenance generally maintained improvements in IBDQ and SF-36 scores that were achieved through IV induction, and those who received PBO gradually lost these improvements.

Outcome	Placebo SC	Ustekinumab 90 mg SC q12w	Ustekinumab 90 mg SC q8w
Patients who entered the long-term extension, n	151	213	354
IBDQ maintenance baseline score, mean (standard deviation)	165.0 (32.04)	148.0 (36.15)	151.8 (36.61)
IBDQ change from baseline to Week 140, mean (standard deviation)	0.8 (37.12)	19.2 (40.65)	17.6 (40.36)
SF-36 physical component maintenance baseline score, mean (standard deviation)	45.85 (7.200)	43.65 (8.189)	43.77 (8.291)
SF-36 physical component change from baseline to Week 140, mean (standard deviation)	1.19 (8.091)	3.52 (8.378)	3.90 (8.132)
SF-36 mental component maintenance baseline score, mean (standard deviation)	46.29 (10.765)	42.51 (11.466)	43.82 (11.253)
SF-36 mental component change from baseline to Week 140, mean (standard deviation)	-0.30 (11.126)	3.76 (10.712)	1.95 (11.784)

*Patients who had prohibited CD-related surgery or discontinued study agent due to lack of efficacy or due to an adverse event of worsening CD before week 140 had their induction baseline value carried forward or were considered not to have achieved the ≥16- or ≥5-point improvement. Patients who had insufficient data at week 140 had their last value carried forward.

[Table: Inflammatory Bowel Disease Questionnaire (IBDQ) and SF-36 scores through Week 140 in patients who entered the long-term extension study]*

Disclosure: Drs. Sands,Targan, Sandborn, and Feagan are investigators for Janssen Research & Development, LLC Dr. Han is an employee of Janssen Global Services, LLC Dr. Zou is an employee of Janssen Research & Development, LLC Dr. Gasink is an employee of Janssen Scientific Affairs, LLC

P0417 HIGH PLATELET COUNT PREDICTS A RAPID RESPONSE TO ADALIMUMAB AND A FAVOURABLE SHORT-TERM OUTCOME IN PATIENTS WITH ULCERATIVE COLITIS: A MULTI-CENTRE RETROSPECTIVE COHORT STUDY

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Introduction: In the real-world settings, few studies have focused on the short-term effectiveness of adalimumab (ADA) therapy in patients with ulcerative colitis (UC). In particular, determination of demographic features of patients with UC who rapidly respond to ADA are relevant clinical issues, but are currently unknown. We report results from our Adalimumab Multi-centre Cohort Study on Effectiveness in Patients with Ulcerative Colitis (ADVENTURE).

Aims & Methods: In the ADVENTURE study, our major interests were to investigate the short-term effectiveness of ADA therapy in patients with UC and understand the relevant prognostic factors. This was a retrospective, multi-centre, cohort study involving seven institutes in Japan, compiling data from patients with UC who had received at least one induction dose of 160 mg of ADA between June 2013 and May 2017. Patients had to have a Lichtiger clinical activity index (CAI) score of ≥5 at the initial ADA administration. The CAI scores were analysed at baseline, at 2 and 12 weeks after the initial ADA administration. Remission was defined as CAI score ≤4, while response was defined as a decrease of ≥50% relative to baseline. Rapid responder was defined as a patient who achieved response at 2 weeks. The related prognostic factors in rapid responders were determined using univariate and multivariate logistic regression analyses. Receiver operating characteristic (ROC) curves were also constructed, and the area under the ROC curve (AUC) was calculated to determine the cut-off value for the prognostic factors of rapid response. Additionally, we looked at the rate of remission at 12 weeks in rapid responders, stratified by the identified prognostic factors.

Results: A total of 91 patients were included in this study (median age, 37.9 years; 37 female), and median duration of UC was 3.3 years. At baseline, the median CAI score was 9, and the median platelet count was 300×10^9/L. Prior to initiation of ADA therapy, 32 patients had previously been exposed to infliximab (IFX). Of the 91 patients, 37.4% and 45.1% achieved response at 2 weeks and remission at 12 weeks. Among these 34 rapid responders, 82.4% (28 of 34) achieved remission at 12 weeks. Multivariate logistic regression analysis identified a higher platelet count as an independent prognostic factor for a higher rate of rapid response. Likewise, ROC curve showed that a platelet count cut-off value ≥312 × 10^9/L (AUC = 0.725; 95% confidence interval, 0.614-0.836) was associated with a rapid response (73.7% specificity, 70.6% sensitivity). In the univariate analysis, the rate of rapid response with platelet count ≥312 × 10^9/L (61.5%) was significantly higher than with platelet count < 312 × 10^9/L (19.2%) (P< 0.001).

Further, patients with platelet count ≥312 × 10^9/L showed significantly more rapid responses in both IFX-naive (61.5% vs. 27.3%, P = 0.016) and IFX-exposed patients (61.5% vs. 5.3%, P = 0.001), while the proportion of rapid responders in IFX-exposed patients with platelet count < 312 × 10^9/L was only 5.3%. Similarly, 5.3% of the IFX-exposed patients with platelet count < 312 × 10^9/L achieved remission at 12 weeks.

Conclusion: Approximately 40% of patients with UC showed a rapid response to ADA therapy after 2 weeks. Up to an 80% of the rapid responders also achieved remission at 12 weeks. The rate of rapid response was significantly higher in patients with platelet count ≥312 × 10^9/L. However, in this study we found that both rapid response and remission at 12 weeks were difficult to attain, especially in the IFX-exposed patients with a platelet count of < 312 × 10^9/L.

P0418 ASSESSING THE LEVEL OF UNMET NEED AMONGST ULCERATIVE COLITIS PATIENTS IN THE UNITED STATES AND EUROPE

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Introduction: To assess the level of unmet need within Ulcerative Colitis (UC) patients currently prescribed biologic treatment and patients prescribed conventional treatments in Europe and the USA.
Aims & Methods: This is a real-world survey of treating Gastroenterologists and their consulting UC patients conducted in 2017 after the introduction of vedolizumab to the UC market. Patients were included from France, Germany, Italy, Spain, the United Kingdom and the United States of America. Physicians completed patient record forms for the next seven eligible adult patients diagnosed with UC. Patient record forms contained details on patient demographics, clinical factors, satisfaction with control of condition and details on current treatment received. Only patients with a diagnosis of moderate-to-severe disease severity were included in the analysis. Patients currently receiving biologic treatment with a duration over 3 months allowing time for response to treatment where compared to patients receiving conventional treatments.
Results: A total of n=1714 patients from the EU and n=619 from the US were included in the analysis. In the EU n=522 / US n=182 of UC patients were currently receiving biologic treatment and EU n= 1049 / US n=389 were currently receiving conventional treatment. Physicians reported in the EU 34% / US 42% of biologic patients were not currently in remission, EU 44% / US 57% for conventional patients. 36% of biologic patients in the EU and 51% in the US had experienced in the last 12 months or were currently experiencing a flare, 36% EU and 28% US for conventional patients. In the EU 71% / US 75% of biologic patients currently experienced symptoms, suffering a mean EU 3.2 / US 3.3 symptoms. For conventional patients EU 77% / US 85%. Patients with symptoms suffered a mean of EU 3.8 / US 3.3 symptoms.
Conclusion: A high proportion of UC patients receiving conventional treatments were not classed as currently being in remission by their physician, were currently experiencing symptoms and had currently or had suffered from a flare in the last 12 months. This was similar for patients who were currently receiving biologic treatment despite the introduction of vedolizumab to the market.
Disclosure: Jim Kershaw and James Lucas are consultants for Janssen Beerse, Belgium Dominik Naessens is an employee of Janssen Global, Beerse, Belgium

P0419 IBD BIOSIMILAR TO BIOSIMILAR INFLIXIMAB SWITCHING STUDY: PRELIMINARY RESULTS

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Introduction: Biosimilar infliximab products have become part of routine clinical care for patients with IBD. As part of the regulatory process, the European Medicines Agency compare a biosimilar product with the originator molecule but do not compare biosimilar products with each other. The introduction of multiple biosimilar products into clinical practice means that patients maybe asked to transition from one biosimilar product to another. Whilst Remicade™, CT-P13 and SB2 have been compared in a laboratory setting[1], there is a paucity of clinical outcome data, as well as data on the patient experience of this process. The aim of this study is to assess the outcome of transitioning a cohort of IBD patients from CT-P13 to SB2 in a real world setting.
Aims & Methods: IBD patients treated with CT-P13 6 or 8 weekly at a dose of 5mg/kg at Southampton General Hospital were approached to participate in the study. After giving informed consent, at their next routine infliximab infusion they were transitioned to SB2. Demographics, disease history, disease activity scores (mHBI or partial Mayo), IBD Control PROM[2], adverse events and FBC, UE, CRP, and LFTs were collected at baseline and week 16/18 (depending on the infusion regime). A historical cohort of CT-P13 patients was used to assess drug persistence. SAS was used to conduct the analysis. Data is presented as mean +/-standard deviation. t-Test was performed to compare outcomes at week 0 and week 16/18.
Results: 133/144 patients approached (105 CD, 28 UC) participated in the study with a mean duration of disease of 9.64+/-8.96 yrs and had been treated with infliximab for 2.96 +/-2.72 years. 89/133 were on immunomodulators. The mean mHBI and partial Mayo scores at week 0 vs week 16/18 were 3.13 +/- 3.31 vs 3.15 +/- 3.17 (p=0.32) and 1.53+/-1.75 vs 0.91+/-1.64 (p=0.15) respectively. The overall disease control component of the IBD control PROM at week 0 and week 16/18 for CD and UC were 74.99 +/- 23.4 vs 78.09 +/- 19.27 (p=0.66) and 76.22 +/-23.80 vs 81.57 +/-21.21 (p=0.49) respectively. The treatment specific components of the IBD-Control PROM (Q1b, 3f, 4a, 4b and 4c) showed no significant differences between Week 0 and Week 16/18. 7 patients stopped treatment due to therapeutic failure, 6 due to adverse drug reactions, 2 withdrew consent, 2 were lost to follow up and 1 for other reasons. There was no significant difference in drug persistence between a historical CT-P13 treated patient cohort and the SB2 treated patients in this study.
Conclusion: The advent of multiple biosimilar infliximab molecules means patients maybe asked to consider transitioning from one biosimilar to another biosimilar. There are considerably challenges to demonstrate the safety of interchangeability of multiple switches between different biosimilar products. This study has set out examine the outcomes of transitioning from one biosimilar to another biosimilar in a real world cohort of patients. This data suggests that there does not appear to be a detrimental effect on patient outcomes as assessed by disease activity, the treatment specific domains of the IBD-control PROM and drug persistence for at least 4 months. Further longer term data is required in multiple large cohorts of patients to confirm this finding as well as examine the outcomes of multiple switches between biosimilar products.
References: 1. Lee et al MABS 2017 9:6, 968-977 2. Bodger et al Gut 2014 63(7):1092-102 2. Bodger et al Gut 2014 63(7):1092-102
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P0420 OPTIMIZATION OF DOSES OF THIOPURINIC DRUGS (AZATIOPRINE AND MERCAPTOPURINE) IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE UNDER TREATMENT COMBINED WITH ANTI-TNF ALPHA (INFLIXIMAB/ADALIMUMAB)

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Introduction: The combination of Anti-TNF drugs with thiopurinic drugs in the treatment of IBD, has shown greater clinical efficacy[1], serum drug levels in therapeutic range in a higher proportion of patients, and less antibody formation, than monotherapy with Anti-TNF[2,3]. However, the dose of the thiopurinic drug in combined treatments has not been clearly established. Some authors consider that this dose could be lower than that used in monotherapy[4](2.5 mg/kg/day).

Aims & Methods: A retrospective study was performed, selecting all patients with established diagnosis of IBD in follow-up at the IBD Unit of the Hospital La Paz, from 2006 to 2018, who were on combined maintenance treatment with azathioprine and Anti-TNF. 91 patients were recruited for treatment with infliximab and 52 for treatment with adalimumab. Two groups of patients were established for both infliximab and adalimumab, one with the standard dose (2-2.5 mg/kg) and one with a lower dose (less than 2 mg/kg). The main objectives are to evaluate the clinical and pharmacokinetic response: through the measurement of the levels of the biological drug and the formation of anti-drug antibodies(ADA) ,as well as the loss of clinical response (defined as the need to intensify or change the treatment). As secondary variables, PCR and fecal calprotectin are determined.

Results: In the adalimumab group, there are no statistically significant differences in remission rates, response without remission , or failure depending on the dose of thiopurines (adequate or low). If we join response and remission in the same group (efficacy versus failure), the low dose group and the standard dose group also showed no statistically significant differences. There are no differences between PCR and calproctectin levels among patients with optimal doses of thiopurines and low doses. The last determinations of mean adalimumab levels were not significantly different between groups. No ADA formation was detected.

In the infliximab group, there is no statistically significant difference in remission, response or failure rates depending on the dose of thiopurines (adequate or low). If we compare efficacy vs failure, there are no statistically significant differences depending on the dose of thiopourins. There are no differences between the levels of PCR and fecal calprotectin, nor in the formation of ADA; nor in the last two determinations of mean infliximab levels among patients with optimal doses of thiopurines vs lower doses. If we consider pharmacokinetic failure (infliximab levels < 1000 ug/ml and/or ADA), there were also no statistically significant differences(p=0.063).

Conclusion: Consistent with the findings of other studies, there are no differences in the pharmacokinetic characteristics or in the responses of patients with the biologic treatment combined with thiopurine a standard dose with respect to the group with low dose (< 2 mg/kg). The use of a lower dose of Azathioprine can provide a better tolerance of the drug, a better safety profile, and lower economic cost.

References: 1.-Yarur AJ, Jain A, Sussman DA, Barkin JS, Quintero MA, Princen F, et al. The association of tissue anti-TNF drug levels with serological and endoscopic disease activity in inflammatory bowel disease: The ATLAS study. Gut. 2015. Epub ahead of print 2.-Maser EA, Villela R, Silverberg MS, Greenberg GR. Association of trough serum infliximab to clinical outcome after scheduled maintenance treatment for Crohn's disease. Clin Gastroenterol Hepatol. 2006;4:1248---54 3.- Colombel JF, Sandborn WJ, Reinisch W, Mantzaris GJ, Kornbluth A, Rachmilewitz D, et al; SONIC Study Group. Infliximab, azathioprine, or combination therapy for Crohn's disease. N Engl J Med. 2010;362:1383-95. -4. Roblin X, Boschetti G, Williet N, et al. Azathioprine dose reduction in inflammatory bowel disease patients on combination therapy: an open-label, prospective and randomised clinical trial.

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P0421 META-ANALYSIS: DEEP REMISSION IN IBD WITH ANTI-TNF AGENTS

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Introduction: Clinical remission and mucosal healing have been therapeutic targets in the treatment of inflammatory bowel disease (IBD). However emerging paradigms suggest deep remission (DR) as an impactful and achievable goal of therapy. Although there is no consensus on the definition of deep remission, many authors consider clinical remission with mucosal healing with or without additional criteria as deep remission. Achieving deep remission may positively impact the long-term trajectory of disease. This meta-analysis aims to determine the rate of deep remission with anti-TNF agents, the oldest and most utilized biologics therapy.

Aims & Methods: Using the search terms ("inflammatory bowel diseases" OR "IBD" OR "crohn*" OR "ulcerative colitis" OR "UC" OR "colitis") AND ("mucosal healing" OR "deep remission" OR "complete remission" OR "full remission" OR "endoscopic remission"), 7,514 articles and abstracts were identified between Pubmed and EMBASE on October 1, 2018. Inclusion criteria were adult IBD patients treated with anti-TNF medications, with report of achieving deep remission defined as at least clinical remission and mucosal healing or endoscopic remission. Exclusion criteria were studies focusing on pediatric patients, reporting < 10 patients, and non-

	Infliximab (n=91)	Adalimumab (n=52)	Infliximab (2-2,5 mg/kg) (n=45)	Infliximab (<2mg/kg) (n=46)	P value	Adalimumab (2-2,5 mg/kg) (=36)	Adalimumab (<2 mg/kg) (n=16)	P value
Crohn Disease / Ulcerative Colitis (n, %)	75 (82,6%)/16 (17,4%)	50 (96,2%)/2 (3,84%)	37(82,2%) /8 (17,7%)	38(82,6%) /8 (17,4%)		36 (100%) /0 (0%)	14 (87,5%)/2 (12,5%)	
Combined treatment time (months) (mean,range)	36 (8-127)	37 (7-116)	37 (8-125)	35 (8-124)	0,105	40(7-67)	33(7-116)	0,231
Serum levels mg/ml (mean, SD) (ultimate determination)	2906 (3183)	7500 (4639)	2316 (2735)	3484 (3500)	0,08	7571.417(5817,9)	8001,6 (5021,744)	0,4
Serum levels mg/ml (mean, SD) (penultimate determination)	2594 (2398)	7797 (4519)	2186 (1842)	2994,63 (2803)	0,108	7827.45 (4051,1)	8470.7(6572,1)	0,34
Fecal Calprotectin (mean, SD)	195,68 (275)	122 (141)	185 (185,9)	237 (354,6)	0,408	147.92 (228,5)	164.9 (229,6)	0,41
C-reactive protein (mean, SD))	18,67 (119,7)	4,3 (10,4)	8,10 (19,2)	29,01 (167,3)	0,52	5.71 (12,30)	2.57 (3,7)	0,188
Response to treatment (remission/ response / failure) (n,%)	37(40,7%)/14 (15,4%)/40 (43,96%)	32 (61,5%) /10(19,2%)/10 (19,2%)	18(40,9%) /4 (8,9%) /23 (51,5%)	19(41,3%) /10 (21,7%)/17 (37%)	p=0,174	23(66,6%)/6 (15,38%)/7 (17,95%)	9 (56,25%)/4(25%)/3 (18,25%)	0,83
Effectiveness/faulure (n,%)	51 (56%)/40 (44%)	32(76,19%)/10 (23,8%)	22 (48,9%) /23 (51,1%)	29(63,1%) /17 (36,9%)	0,175	29 (81,8%)/7 (18,2)	13(80,6%)/3 (19,4%)	0,951
Anti-drug antibody formation (yes/ no) (n, %)	83 (91,2%)/8 (8,79%)	0/0 (0%)	42(91,3 %)/4(8,7%)	41(91,1%)/4 (8,8%)	0,974	0/0 (0%)	0/0 (0%)	

[P0420Table 1. Results of the study according to the doses of thiopurines]

English publications. Publications were independently reviewed for inclusion by two authors. A third author reviewed studies not agreed upon. Statistical analysis was performed using OpenMetaAnalyst.

Results: 14 peer-reviewed manuscripts, two of which were randomized control trials, with 1248 total cases were included. Most patients were treated with infliximab (IFX) or adalimumab (ADA). Length of follow-up ranged from 10 to 138 weeks. Overall, 37.7% (509/1248, CI 0.267-0.488) of patients achieved deep remission with anti-TNF medications. Rates of DR ranged from 7% to 63%. There was significant heterogeneity (I^2=94.82%, P< 0.001). In sub-analysis, 37.1% of patients with CD and 50.3% with UC achieved deep remission. 40.1% of patients on ADA and 41.1% on IFX achieved deep remission. Two studies (Magro 2016, Kaymak 2018) with histologic remission as a criteria reported only 10.1% (13/129) rate of deep remission combined.

Studies	Estimate (95% CI)	Deep Remission/ Treated	CD	UC	Studies	Estimate (95% CI)	Deep Remission/ Treated	CD	UC
De Vos et al. 2013	0.345 (0.245, 0.445)	30/87		30/87	Colombel et al. 2015	0.455 (0.371, 0.540)	61/134	61/134	
Molander et al. 2013	0.484 (0.422, 0.546)	122/252	79/183	43/69	Zhang et al. 2016	0.557 (0.447, 0.667)	44/79	44/79	
Dai et al. 2014	0.556 (0.489, 0.622)	120/216	62/109	58/107	Borje et al. 2016	0.625 (0.388, 0.862)	10/16		10/16
Colombel et al. 2014	0.194 (0.095, 0.292)	12/62	12/62		Zittan et al. 2016	0.483 (0.357, 0.610)	29/60	29/60	
Kopylov et al. 2015	0.143 (0, 0.326)	2/14	2/14		Magro et al. 2016	0.250 (0.060, 0.440)	5/20		5/20
Echarii et al. 2015	0.375 (0.225, 0.525)	15/40	15/40		Kaymak et al. 2018	0.073 (0.024, 0.122)	8/109	8/109	
Yu et al. 2015	0.189 (0.114, 0.263)	20/106	20/106		Munoz-Villafranca et al. 2018	0.585 (0.452, 0.718)	31/53		31/53
Overall	0.377 (0.267, 0.488)	509/1248	332/896	177/352					

[Studies Reporting Rates of Deep Remission with Anti-TNF Agents]

Conclusion: This study systematically reviewed the effect of Anti-TNF agents on achieving deep remission. Anti-TNF agents achieved deep remission in IBD in 37.7% of patients, with rates similar between adalimumab and infliximab. Unfortunately, a lack of available trials precludes the comparison of IFX and ADA in UC and CD. A limitation is the heterogeneity amongst studies, including reported findings, variable definitions of deep remission, length of follow up, and concomitant medications such as immunomodulators. Future studies comparing anti-TNF agents to newer biologics with other mechanisms of action may elucidate the best treatment approach for achieving deep remission.

Disclosure: Nothing to disclose

P0422 A LARGE POOLED SAFETY ANALYSIS OF 3 POST-MARKETING STUDIES CONDUCTED IN INFLAMMATORY BOWEL DISEASE PATIENTS TREATED WITH BIOSIMILAR INFLIXIMAB (CT-P13)

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Introduction: CT-P13 (biosimilar infliximab) has well established its place in the treatment of rheumatoid diseases and Inflammatory Bowel Disease (IBD) in the European Union (EU) since gaining marketing authorisation in 2013. However, real-world safety data of patients with Crohn's Disease (CD) and Ulcerative Colitis (UC) receiving infliximab biosimilar in the EU are limited. This analysis presents a pooled analysis of available UC and CD safety data from 3 open-label post-marketing studies.

Aims & Methods: The primary objective of the analysis was to evaluate adverse events of special interest (AESIs) in patients with IBD in a real-world setting. Safety data from the Pfizer CONNECT-IBD study (13 EU countries), the Celltrion CT-P13 4.3 registry (5 EU countries) and Celltrion CT-P13 KO-

REA PMS were collected up to the data cut-off date of 27 December 2017. Descriptive analyses are presented for the safety population (≥1 dose of CT-P13). Overall, 2813 patients were included in the safety analysis of which 2,215 patients (78.7%) were from the EU.

Results: A total of 999 UC and 1814 CD patients were included in the safety population. Mean age was 41.6 and 35.8 years and the mean treatment duration of CT-P13 was 264.6 and 266.4 days in UC and CD patients, respectively. EU patients constituted 76.0% (759 patients) of the UC and 80.3% (1456 patients) of the CD population. Thus, the results of this analysis can be considered representative of real-world CT-P13 (biosimilar infliximab) safety data from the EU. Overall, 27.43% and 27.78% of UC and CD patients, respectively, experienced at least 1 treatment-emergent adverse event (TEAE) and 10.01% and 10.92% of UC and CD patients, respectively, experienced at least 1 treatment-emergent serious adverse event (TESAE). A total of 8.81% and 5.68% patients discontinued treatment due to TEAEs in UC and CD patients respectively. Three deaths (attributed to sudden heart death, sepsis and unknown cause, 1 each) were reported among the UC patients and 1 death attributed to rupture of aneurysm of the abdominal aorta was reported among the CD patients.

Incidences of AESIs are included in Table 1 and are aligned with the known safety profile of the reference product as described in the literature and Summary of Product Characteristics (SmPC)

([1, 2, 3, 4, 5]). More specifically, active TB was reported in 2 patients (0.20%) and 4 patients (0.22%) in the UC and CD population, respectively. Of the 6 patients, 1 patient was from Portugal and the remaining 5 patients were from Korea. Incidences of active TB and serious infections including TB were within the range of the reference values from observational studies of the reference product (incidence of active TB: 0.7% and 1.18%; incidence of serious infection: 8.16% and 7.3%) ([1, 2, 3]).

AESI	UC (N = 999)	CD (N = 1814)
Serious Infection including TB	24 (2.40%)	40 (2.21%)
Active TB	2 (0.20%)	4 (0.22%)
Serum sickness	1 (0.10%)	0
Haematologic reactions	4 (0.40%)	23 (1.27%)
Systemic lupus erythematosus/ lupus-like syndrome	1 (0.10%)	3 (0.17%)
Non-haematologic malignancy	5 (0.50%)	7 (0.39%)
Hepatobiliary event	4 (0.40%)	7 (0.39%)
Intestinal or perianal abscess	NA	31 (1.71%)

[Table 1. Incidence of AESIs]

Conclusion: Incidence of AESIs, including active TB and serious infection, among IBD patients treated with CT-P13 in the 3 post-marketing studies were low and consistent with the known safety profile of infliximab. The pooled safety analysis suggests a favourable benefit-risk balance and safety profile for IBD patients treated with CT-P13 in EU.

References: 1. Delabaye I, De Keyser F. 74-week follow-up of safety of infliximab in patients with refractory rheumatoid arthritis. Arthritis Res Ther. 2010;12(3):R121. 2. Vander Cruyssen B, Durez P, Westhovens R, De Keyser F. Seven-year follow-up of infliximab therapy in rheumatoid arthritis patients with severe long-standing refractory disease: attrition rate and evolution of disease activity. Arthritis Res Ther. 2010;12(3):R77 3. D'Haens G, Reinisch W, Colombel J-F, Panes J, Ghosh S, Prantera C, et al. Five-year Safety Data From ENCORE, a European Observational Safety Registry for Adults With Crohn's Disease Treated With Infliximab [Remicade(R)] or Conventional Therapy. J Crohns Colitis. 2017 Jun 1;11(6):680-9. 4. Remicade EU product information https://www.ema.europa.eu/documents/product-information/remicade-epar-product-information_en.pdf (last accessed 22 Dec 2018) 5. Yoneno K, Hisamatsu T, Matsuoka K, Okamoto S, Takayama T, Ichikawa R, et al. Risk and Management of Intra-Abdominal Abscess in Crohn's Disease Treated with Infliximab. Digestion. 2014;89(3):201-208

P0423 COGNITIVE BEHAVIORAL INTERVENTION DECREASES PSYCHOLOGICAL STRESS AND DISEASE ACTIVITY IN ADULTS WITH CROHN'S DISEASE: PRELIMINARY RESULTS OF A RANDOMIZED CONTROLLED TRIAL

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Introduction: Psychological stress in Crohn's disease (CD) triggered symptomatic activity independently of calprotectin levels (Targownik 2015). Patients with active CD had significantly more stress than those in remission (Sarid 2018). We examine whether cognitive behavioral intervention (CBI) can reduce psychological stress as well as disease symptoms in CD.

Aims & Methods: Unselected adults (≥18 years) with active CD attending routine follow-up at a university hospital were randomized to enter a stress reduction CBI program combining cognitive behavioral and mindfulness techniques, or act as controls. CBI was taught by trained social workers in 8 on-line sessions, delivered one-to-one for 1 hour weekly over 8 weeks. Home practice twice daily with feedback to an application was required. Disease activity was measured by Harvey-Bradshaw Index (HBI) and psychological stress by the Brief Symptom Inventory (BSI), at entry and at 3 months follow-up. The BSI assesses 53 symptoms in categories of Somatization, Obsessive-Compulsive, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation and Psychoticism. Combining the category scores yields the Global Severity Index (GSI). BSI range is 0-4; a higher score indicates more stress.

Results: The cohort comprised 41 patients: mean age 35 years, BMI 22.7, disease duration 5.5 years, 63.4% female, 78% with higher education, 88% non-smokers. Median HBI was 8.0 (range 5-16). Twenty patients were taught CBI and 21 were controls. There were no differences in age, gender, education, smoking habit and disease severity between the groups. In CBI patients there was a large reduction of HBI at 3 months, and significant decreases in all category scores except anxiety and paranoid ideation. In controls the drop of HBI was minor, and category scores were unchanged or increased. The GSI score decreased significantly in CBI, but there was no significant change in controls. See Table (Wilcoxon signed-ranks test, entry vs. 3 months. *p< .05, **p< .01).

	CBI		Controls	
	Entry	3 months	Entry	3 Months
HBI	8.0	4.0**	8.0	7.0*
Somatization	1.2	0.8*	1.1	1.3
Obsessive -Compulsive	1.1	0.8*	1.8	2.1
Interpersonal sensitivity	1.0	0.4*	1.5	1.5
Depression	1.1	0.5*	1.5	1.5
Anxiety	1.1	0.8	1.7	1.7
Hostility	0.6	0.4*	0.8	0.8
Phobic anxiety	0.4	0.2*	0.8	0.8
Paranoid ideation	1.0	0.6	1.0	1.4
Psychoticism	0.9	0.2**	0.6	1.0
GSI	1.0	0.6*	1.2	1.4

[Table 1: Median HBI and BSI values in patients taught CBI versus controls]

Conclusion: Patients taught CBI demonstrated significant less psychological stress and diminished disease activity, whereas control subjects exhibited no improvement in stress measures and little change of disease activity. These findings may imply a role for psychological stress impacting disease activity in CD patients.

Disclosure: Nothing to disclose

P0424 EFFECTIVENESS AND SAFETY OF ENDOSCOPIC BALLOON DILATION OF COLORECTAL STRICTURES IN CROHN'S DISEASE

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Introduction: Endoscopic balloon dilation (EBD) is widely used to manage Crohn's disease (CD) ileal stricture. However, data of EBD on inflammatory bowel diseases (IBD) colorectal strictures are scarce.

Aims & Methods: We performed a retrospective study in 9 tertiary centers, including all consecutive IBD patients who underwent EBD for native or anastomotic colorectal stricture between 1999 and 2018. Outcomes were rate of technical success defined by a passable stricture at the end of the EBD, clinical success defined by a passable and asymptomatic stricture and colonic resection at the end of follow-up. Factors associated with EBD success were also investigated by logistic regression.

Results: Fifty-seven patients (25 women, median age: 36 years, InterQuartile Range, 31-48) were included. All patients had CD and 42 (74%) had symptomatic stricture. Regarding the 60 strictures, 52 (87%) were native and the most frequent location was left colon (27%). 39 (65%) measured less than 5 cm, 57 (95%) were non-passable by the scope and 35 (58%) ulcerated.

Among the 161 EBD performed (median number of dilatations per strictures: 1, IQR 1-3), technical success was observed in 123 (76%) EBD. One perforation occurred (0.6% per EDB and 2% per patient). After a median follow-up of 4.3 years [IQR 2.0-8.4], 24 patients (42%) underwent colonic resection, 9 (16%) had symptomatic strictures non-passable by the scope, 11 (19%) had asymptomatic non-passable strictures and 13 (23%) had asymptomatic strictures passable by the scope.

One colon lymphoma and one colorectal cancer were diagnosed (3.5% of patients), respectively on endoscopic biopsies and at the time of surgery. None factor was associated with technical, clinical success, or surgery including therapeutic modification.

Conclusion: EBD of CD-associated colorectal strictures is feasible, efficient and safe as more than 50% of patients avoid surgery.

Disclosure: Nothing to disclose

P0425 BARRIERS AND FACILITATORS IN CONDUCTING THERAPEUTIC TRIALS IN INFLAMMATORY BOWEL DISEASE: A MONOCENTRIC ITALIAN SURVEY

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Introduction: Anti-TNF agents and other currently available biologic drugs represent a valid therapeutic option for inflammatory bowel diseases (IBD). However, these treatments are not effective in all patients, and moreover the initial response diminishes over time. So, clinical therapeutic trials are a fundamental tool for identifying new categories of drugs useful for

ensuring clinical benefit in patients with IBD. However, a number of difficulties, still not clearly investigated, may affect the recruitment of patients in large clinical trials.

Aims & Methods: The aim of this survey was to assess patients' perceptions regarding their willingness to take part in clinical therapeutic trials in a local resident group of IBD patients from Southern Italy. Consecutive patients with Crohn's disease (CD) and ulcerative colitis (UC) were recruited to complete a self-administered, locally validated, questionnaire dealing with their knowledge about clinical trials and attitude towards participation . Patients also completed the Short Inflammatory Bowel Disease Questionnaire (S-IBDQ) to investigate their quality of life (QoL). Demographic and clinical data were recorded.

Results: Of the 132 patients who completed the survey, 38 (29%) had CD and 94 (71%) UC; 57% were male, the mean age was 47.8 (range 16-82) years and 75 (57%) had a long-standing disease (> 10 years). Sixty (45%) patients displayed active disease, 30 (23%) were currently on biologic therapy while 21 (16%) underwent surgery. More than half (65%) showed a poor QoL according to S-IBDQ. Sixty-six per cent were married or cohabiting, 20% had a family history of IBD, and 78% had a high school diploma.

Although few (16%) patients have previously participated in clinical research, 67% claimed their willingness to take part in a clinical therapeutic trial for IBD. Overall, 43% feared taking placebo, 88% would refuse if the drug had never been tested on humans, 24% were poor inclined to frequent visits, 76% were more prone to participate when the medical staff was always the same. Monetary remuneration and gastroenterologist conditioning were a motivation for participation in 34 (26%) and 27 (20%) patients, respectively.

Using multivariate analysis, the chance of taking placebo was the only significant risk factor for denying participation in a clinical trial [adjusted odd ratio (OR) 12.46, 95% confidence interval (CI) 7.81-50.73, p=0.000)] while monetary remuneration (OR:5.46, 95% CI:1.21-18.67, p=0.03) and having the same medical staff (OR:8.46, 95% CI:2.08-20.13, p=0.02) were predictive factors of willingness to participate. Age, gender, type and duration of disease, current biologic therapy, prior participation, poor QoL, marital status, level of education, and previous surgery did not affect the decision to take part.

Conclusion: In a native local resident series of IBD patients more than half of the patients were willing to participate in a clinical therapeutic trial. Placebo represented a barrier to enrollment while the presence of an established medical staff and monetary compensation could be facilitative . Clinicians should pay attention to understanding the critical issues affecting enrollment in clinical IBD therapeutic trials , in order to improve their quality and optimize their management.

Disclosure: Nothing to disclose

P0426 LONG-TERM FOLLOW-UP OF SWITCHING FROM ORIGINAL INFLIXIMAB TO INFLIXIMAB BIOSIMILAR. REAL WORLD DATA

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Introduction: Several studies have reported positive outcomes for efficacy measures in inflammatory bowel disease patients treated with CT-P13, an infliximab biosimilar. Still, data from follow-up periods longer than 1 year are scarce. Here, we assessed the long term data of effectiveness, loss of response, safety and immunogenicity of switching from infliximab to CT-P13 in patients with inflammatory bowel disease.

Aims & Methods: This was a prospective single-center observational study in patients with moderate to severe Crohn's disease (CD) and ulcerative colitis (UC) switched from infliximab original to infliximab biosimilar (CT-P13) since March 2015 and followed up to 24 months. Montreal classification status and previous/concomitant therapies were recorded (Table1). The efficacy endpoint was the change in the Harvey-Bradshaw for CD and partial Mayo score for UC. Clinical Remission was considered HB≤ 4 and

partial Mayo score was ≤ 2. Changes in C-reactive protein, infliximab-drug levels, and antidrug antibodies were collected during followed up. All adverse events (AEs) were monitored.

Results:

Characteristics		n(%)	CI (95%)
Sex	Men // Women	51(51) // 49(49)	40.7; 61.3 // 38.7; 59.3
Age (years, range)	CD // UC	40.5 (18-77) // 44.0 (37-53)	
Smoking status: Never // Previous // Current		68 (68) // 18 (18) // 14 (14)	58.4; 77.6 // 9.9; 26.0 // 6.7; 21.3
CD patients (n=64)			
Age at diagnosis: A1, A2, A3 // Location at diagnosis: L1,L2,L3,L3+L4 // Disease behavior: B1,B2,B3 // Perianal disease	A1 (<17) // A2 (17-40) // A3 (>40) // L1 (ileal) // L2 (colonic) // L3 (ileocolonic) // L3+L4 (upper gastrointestinal tract) // B1 (nonstricturing, nonpenetrating) // B2 (stricturing) // B3 (penetrating) // Yes	8 (12.5) // 46 (71.9) // 10 (25.6) // 16 (25) // 27 (42.2) // 18 (28.2) // 3 (4.7) // 39 (60.9) // 12 (18.8) // 13 (20.3) // 28 (43.8)	3.6; 21.4 // 60.1; 83.7 // 5.9; 25.3 // 13.6; 36.4 // 29.3; 55.1 // 16.3; 39.9 // 0.9; 13.1 // 48.2; 73.7 // 8.4; 29.1 // 9.7; 30.9 // 30.8; 56.7
UC patients (n=36)			
Extent (UC): E1, E2, E3 // Severity: S1, S2, S3 // Extraintestinal manifestations	E1 (proctitis) // E2 (left-sided colitis) // E3 (pancolitis) // S1 (mild) // S2 (moderate) // S3 (severe) // Yes	13 (36.1) // 11 (30.6) // 12 (33.3) // 13 (36) // 17 (47.2) // 6 (16.7) // 10 (27.7)	19.9; 53.2 // 14.1; 46.9 // 15.5; 50.1 // 19.9; 53.2 // 29.5; 64.9 // 3.1; 30.2 // 11.8; 43.8
Prior medication exposure: Thiopurines // Methotrexate // Concomitant medication use: Thiopurines // Methotrexate // Steroids	CD // UC // CD // UC // CD // UC // CD // UC // CD // UC	33 (51.6) // 19 (52.8) // 20 (31.3) // 5 (13.9) // 27 (42.2) // 13 (36.1) // 14 (21.8) // 3 (8.3) // 10 (15.6) // 5 (13.9)	38.5; 64.6 // 29.7; 17.7 // 19.1; 43.4 // 4.7; 29.5 // 29.3; 55.1 // 19.0; 53.2 // 10.9; 32.8 // 1.8; 22.5 // 5.9; 25.3 // 4.7; 29.5
Time using Remicade (months) // Time global using infliximab (months)		58 (37-80) median (IQR) // 81 (63-107) median (IQR)	

[Table 1. Baseline demographics/clinical characteristics]

100 patients were included (64 CD, 36 UC). Most of them (72%) remained on CTP-13 and 28% of patients discontinued the therapy due to loss of response, adverse events or remission/mucosa healing. Remission at 18 and 24 months occurred in 69.9% and 68.5% of patients, respectively. Global remission in patients with Crohn's disease was: 79.7%, 67.7%, 67.7% and 65.6% to basal remission, 12 months, 18 months and 24 months, respectively. Global remission in patients with Ulcerative Colitis was: 75.0%, 74.2%, 74.2% and 74.2% to basal remission, 12 months, 18 months and 24 months, respectively. 22% of patients received a dose increase, with remission being reached in 60% of them. HB score, partial Mayo score, C-reactive protein and infliximab-drug levels did not show significant changes. AEs were reported in 14% of patients.

Conclusion: Most of the patients switching from infliximab original maintained CT-P13 at 2 years of follow-up with a good profile of effectiveness and safety.

Disclosure: Nothing to disclose

P0427 PATIENTS' PERCEPTIONS AND UNMET NEEDS IN INFLAMMATORY BOWEL DISEASES: A MONOCENTRIC ITALIAN SURVEY

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Introduction: Inflammatory bowel diseases (IBD) significantly impact the patient's quality of life (QoL) and clinicians should be aware of patients' perspectives and needs in the everyday life.

Aims & Methods: The aim of this survey was to assess patients' perceptions regarding their QoL, quality of care, and satisfaction in a local resident series of IBD patients from Southern Italy. Consecutive patients with

Crohn's disease (CD) and ulcerative colitis (UC) were recruited. The survey consisted of the following self-administered questionnaires: the Short Inflammatory Bowel Disease Questionnaire (S-IBDQ), the Hospital Anxiety and Depression Scale (HADS), the Brief Illness Perception Questionnaire (B-IPQ) and a questionnaire dealing with impact of IBD on patients' life locally validated. Demographic and clinical characteristics were recorded. Multivariate logistic regression analysis (MVA) was performed to assess association between variables.

Results: Of the 120 IBD patients who completed the survey, 34 (28%) had CD and 86 (72%) had UC, 73 (60%) were male, the median age was 44 years (range 18-80), the mean body mass index (BMI) was 23.7±3.2, and the mean disease duration was 14±11 years. Seventy-four (62%) per cent were married or cohabiting, 25 (20%) had a family history of IBD, and 90 (75%) had a high school diploma. Overall, 77 (64%) had poor QoL as assessed by S-IBDQ, 61 (51%) had HADS positive for anxiety/depression, the mean illness perception score was significantly high, and 46 (38%) claimed a poor sleep quality. Of 51 and 31 patients who experienced biologics agents and surgery, 63% and 74% were satisfied, respectively. Participation in therapeutic clinical would be accepted from 92% patients. Only 44 (37%) patients considered themselves satisfied with the relationship with the family doctor, while 97 (81%) trusted their gastroenterologist. Independent risk factors (adjusted odd ratio, 95% confidence interval) for low S-IBDQ were a poor sleep quality (5.88, CI 1.8-20.2), a positive HADS (6.31, CI 1.93-20.6) and a high illness perception (1.13, CI 1.05-1.2). At MVA, age, gender, BMI, type and duration of disease, biologic therapy, surgery, marital status, and level of education did not affect S-IBDQ score.

Conclusion: In a local resident setting of IBD patients from Southern Italy, more than half reported a low QoL. This was significantly associated with anxiety/depression, high illness perception and poor sleep quality. Biologics and surgery are well accepted from IBD patients and their willingness in participating to clinical trials claimed. Relationship with family doctors should be improved.

Disclosure: Nothing to disclose

P0428 SAFETY AND TOLERABILITY OF BIOLOGIC AGENTS IN INFLAMMATORY BOWEL DISEASE: A RETROSPECTIVE STUDY IN A TERTIARY REFERRAL CENTER

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Introduction: Inflammatory bowel diseases (IBD), which include Crohn's Disease (CD) and Ulcerative Colitis (UC), are chronic conditions with a remitting-relapsing course. The main therapeutic goal in IBD patients is to induce and maintain long-term remission. Besides conventional therapy, biologic agents are widely and increasingly used. Such drugs, however, may arise safety issues due to increased risk of infections, severe infusion reactions and cancer. Therefore, we aimed to evaluate safety and tolerability of biologic drugs.

Aims & Methods: We retrospectively reviewed patients followed at our tertiary referral center from 1999 and 2018 and treated with biologics in order to assess the prevalence of adverse events (AE), their characteristics and predictors. We used t-test or chi-squared test for univariate analysis. We draw Kaplan-Meier curves and used Cox regression for multivariate analysis and to calculate Hazard Ratio (HR) and 95% confidence intervals (CI).

Results: Three hundred sixty patients were recruited (61.7% CD). They underwent 538 biologic courses overall. Male/female ratio was 209/151 and mean age was 37.2±14.5. Eighty patients (14.9%) experienced an AE, mostly infusion reactions (77.5%). Additionally, we recorded 4 severe infections and one case of melanoma. AEs were significantly more frequent in UC patients compared to CD patients (19% versus 12.3%, p=0.03). UC patients with AE had more severe partial Mayo (3.6±3.1 versus 2.3±3.0, p< 0.001) and full Mayo score (4.9±4.1 versus 3.3±4.1, p< 0.001) and extraintestinal manifestations were less common (21.2% versus 33%, p=0.04). Finally, AEs were more commonly related to infliximab (67.5% versus 41% for other biologic agents, p< 0.001).

However, at multivariate analysis, none of the following factors was independently associated to AE: UC (HR=1.6, 95% CI 0.8-3.3 p=0.17), partial Mayo (HR=1.3 , 95% CI 0.9-1.7 p=0.14), full Mayo (HR=0.9 95% CI 0.7-1.2,

p=0.66), extraintestinal manifestations (HR=0.7 95% CI 0.4-1.2, p=0.14) or type of biologic drug (p=0.45). More details are listed in table 1.

Conclusion: On the basis of our data, the most common AEs of biological therapies were hypersensitivity reactions Although there are not single predictors of AE, probably many factors are likely to influence each other and to contribute to AE onset. Further studies are needed to assess long term safety.

Disclosure: Nothing to disclose

	Univariate		Multivariate	
	HR (95% CI)	p	HR (95% CI)	p
Disease • Crohn • RCU	1 (reference) 1.7 (1.1-2.7)	0.03	1 (reference) 1.6 (0.8-3.3)	0.17
Partial Mayo	1.1 (1.0-1.2)	<0.001	1.3 (0.9-1.7)	0.14
Full Mayo	1.1 (1.0-1.2)	0.001	0.9 (0.7-1.2)	0.66
Extraintestinal manifestations	0.6 (0.3-1)	0.04	0.7 (0.4-1.2)	0.14
Biologic • infliximab • adalimumab • vedolizumab • golimumab	1 (reference) 0.5 (0.3-0.8) 0.02 (0.003-0.2) 0.8 (0.2-2.8)	<0.001	1 (reference) 0.9 (0.3-2.9) 0.5 (0.2-2.0) 0.8 (0.1-7.6)	0.45

[Table 1]

P0429 EFFICACY AND SAFETY OF USTEKINUMAB IN PATIENTS WITH MODERATE TO SEVERE CROHN'S DISEASE: A REAL WORLD STUDY IN BRAZIL

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Introduction: Ustekinumab (UST) is a fully human monoclonal antibody against IL-12/23 approved in Brazil for the treatment of moderate-to-severe Crohn's disease(CD) in November 2017. UST has demonstrated its efficacy in induction and maintenance therapy for patients with CD. Real world data regarding the efficacy and safety of UST in this population is lacking in our country. We hereby report our experience with UST in patients with moderate to severe CD.

Aims & Methods: A retrospective chart review and a prospective study were performed including patients from eleven IBD referral centers with moderately to severely active CD starting on UST (IV infusions followed by scheduled subcutaneous [SC] injections) between November 2017 and March2019. We accessed clinical response and remission (based on Harvey-Bradshaw index [HBI]), fecal calproprotectin (FC) and C-reactive protein (CRP) levels. Clinical response and clinical remission were defined by HBI decrease ≥ 3 and HBI ≤ 3, respectively. Clinical remission was accessed in weeks 0, 8, 16, 24, 32, 40, 48 and 56. CRP levels were evaluated in weeks 0, 8, 16, 24, 32, 40 and 48. FC levels were evaluated in weeks 0, 8, 16 and 40.

Results: One-hundred and fifty-one patients were treated with UST during the study period. The mean age was 38.2 years, disease duration was 10.8 years, 57.6% had previous surgeries, 45.0% had perianal disease, 49.3% had anaemia, 55.7% were female, 15.9% were smokers. The majority of patients were treated with 90mg every 8 weeks (97.4%) during mainte-

nance. The majority of patients was previously exposed to biological therapy (87.6%). Of these, 16 patients were naïve, 38 were previously exposed to one biologic, 63 exposed to two biologics and 9 exposed to three biologics. Previous biological therapies included infliximab (n=93), adalimumab (n=88), vedolizumab (n=11) and certolizumab pegol (n=8). Mean HBI at baseline was 10.1 and 73.5% of patients had HBI higher than 3 at baseline. At baseline mean CRP was 22.7 mg/L and mean FC was 1243.3 mg/kg. At week 8, 80.2% of patients achieved clinical response and 44.9% achieved clinical remission. Clinical remission was observed in 57.4% (week 16), in 60.7% (week 24), in 69.8% (week 32), in 75.0% (week 40), in 63.8% (week 48) and in 72.0% (week 56) of patients. CRP decreased to 15.1mg/L at week 8, followed by a significant decrease until week 48 (8.1 mg/L). Sixty-three percent of the patients showed a decreased in the FC levels from baseline until week 40. However, the mean FC at week 40 was 1201.0mg/Kg, exhibiting a decrease of 42.3mg/Kg from baseline. Adverse events occurred in 28.6% of patients. Twelve patients stopped UST, three due to pregnancy, five due to a lack of response and four due to others. No new safety signals were observed.

Conclusion: UST therapy was successful for inducing and maintenance of clinical remission and improving laboratory biomarkers of disease activity in patients with moderate-to-severe CD and who were refractory to anti-TNF therapy. Both UST induction and maintenance regimens until week 56 were overall well tolerated. These results support a favorable safety and efficacy profile.

Disclosure: Nothing to disclose

P0430 EFFECTIVENESS AND SAFETY OF REFERENCE INFLIXIMAB AND BIOSIMILAR IN ULCERATIVE COLITIS: A FRENCH REAL-LIFE EQUIVALENCE STUDY

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Introduction: CT-P13, a biosimilar of the reference product infliximab, has been approved for the treatment of ulcerative colitis on the basis of the results of trials conducted in patients with spondyloarthritis and rheumatoid arthritis.

Aims & Methods: The objective wasto compare the effectiveness and safety of CT-P13 and the reference productin infliximab-naive patients with ulcerative colitis.

A comparative real-life equivalence cohort study was conducted using the French nationwide health administrative database. Infliximab-naive patients with ulcerative colitisover 15 years of age who started infliximab with no other indications for infliximab were included. The primary outcome was a composite endpoint (death, ulcerative colitis-related surgery, all-cause hospitalization and reimbursement for other biologics). Equivalence was defined as a 95% confidence interval (CI) of the hazard ratio (HR) of CT-P13 versusthe reference product, in a multivariable marginal Cox model situated within prespecified margins of [0.80 to 1.25].

Results: 3,112 patients were included between January 1, 2015 and June 30, 2017: 1,434 received the reference product, 1,678 received CT-P13. Overall, 710 patients in the reference productgroup and 743 patients in the CT-P13 group met the composite endpoint. In multivariable analysis of the primary outcome, CT-P13 was equivalent to the reference product(HR 1.04; 95%CI: 0.94-1.15). The number of serious infections was lower in the CT-P13 group (HR 0.65; 95%CI: 0.48-0.88). There was no difference in the incidence of solid or hematologic malignancy (HR 0.81; 95%CI: 0.41-1.60).

Conclusion: The effectiveness of CT-P13 is equivalent and the risk of serious infectionscould be lower than that of the reference product for infliximab-naive patients with ulcerative colitis.

Disclosure: Dr. Meyer, Mr. Drouin, Dr. Weill and Prof. Coste declared no conflict of interest. Dr. Rudant reports personal fees from CNAM during the conduct of the study. Prof. Franck Carbonnel received board or lecture fees from Enterome, MSD, BMS, Janssen, Pfizer, Abbvie, Mayoly Spindler, Takeda, Pileje.

P0431 SAFETY AND EFFECTIVENESS OF GRANULOCYTE AND MONOCYTE ADSORPTIVE APHERESIS IN ELDERLY PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A MULTICENTRE COHORT STUDY

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Introduction: There are few studies on the usefulness of granulocyte and monocyte adsorptive apheresis (GMA) in elderly patients with inflammatory bowel disease (IBD). We report the result of the "Post-marketing surveillance study on the safety and response of GMA treatment in patients with Crohn's disease or ulcerative colitis with at least one special situation who received Adacolumn (PARTICULAR)".

Aims & Methods: The aim of this study is to investigate the safety and effectiveness of GMA in elderly patients with IBD who participated in the PARTICULAR study. This retrospective, multicentre cohort study included patients with ulcerative colitis (UC) or Crohn's disease (CD) who had at least one special situation feature and who had received GMA therapy in medical institutions of Japan between November 2013 and March 2017. Patients with at least one special situation, including elderly patients, patients with anaemia and patients on multiple immunosuppressants (IMs) were enrolled. Patients ≤64 years were excluded from this study. GMA was performed using Adacolumn (JIMRO, Takasaki, Japan). Each patients received up to a maximum of 11 sessions. All adverse events (AEs) were recorded during the observation time interval. The safety of GMA was assessed in all patients. The effectiveness of GMA was assessed in patients with UC with a partial Mayo (pMayo) score of ≥3. Remission was defined as a pMayo score of ≤2, while response was defined as a decrease in the pMayo score by ≥2 points and by ≥30% decrease relative to that at baseline plus all 3 sub-scores ≤1. Patients receiving concomitant treatment with infliximab, adalimumab or calcineurin inhibitors were excluded from the effectiveness assessment.

Results: A total of 125 patients (118 UC, 7 CD) from 93 institutions were included. The median age was 72.0 years. Fifty-one patients did not have any special situation, and 74 had one or more special situations. The incidence rate of AEs was 11.2% in all patients. The incidence rate of AEs was significantly lower in patients without any special situation (3.9%) than in those with one or more special situations (16%). The incidence rate of AEs with the special situation subgroups were: 21.9% (7/32) in anaemic patients, 22.7% (5/22) in patients on multiple IMs, 25.0% (4/16) in patients with diabetes mellitus, 25.0% (4/16) in patients with ischaemic heart disease/arrhythmia, 20.0% (2/10) in hypertensive patients, 16.7% (1/6) in patients with dyslipidemia, 25.0% (1/4) in patients with liver dysfunction and 33.3% (1/3) patients with renal dysfunction. A univariate analysis found the occurrence of AEs significantly higher in patients with anaemia, on multiple IMs, diabetes mellitus and ischaemic heart disease/arrhythmia than in patients without any special situation. Anaemia and multiple IMs were also identified as independent predictors for a higher incidence of AEs. The effectiveness of GMA was assessed in 92 patients with UC, showing response and remission rates of 72.8% and 48.9%, respectively. The response and remission rates were slightly higher in patients without any special situation (81.0%, 52.4%) than in those with one or more special situations (66.0%, 46.0%).

Conclusion: A rather low incidence rate of AEs (3.9%) was identified in elderly IBD patients treated with GMA, and not displaying any special situation, while the incidence of AEs was significantly higher in patients with one or more special situation (16%), which could be attributed to anaemia or multiple IMs. Remission and response was achieved by GMA in approximately 50% and 70% of the elderly UC patients, respectively.

Disclosure: Hiroki Tanaka has received lecture fees from JIMRO Co. Ltd., AbbVie GK, EA Pharma Co. Ltd., Mochida Pharmaceutical Co. Ltd., Kyorin Pharmaceutical Co. Ltd. and Mitsubishi Tanabe Pharma Corporation. Taro

P0432 SAFETY OF GRANULOCYTE AND MONOCYTE ADSORPTIVE APHERESIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE UNDERGOING CONCOMITANT TREATMENT WITH IMMUNOSUPPRESSANT MEDICATIONS: A MULTICENTRE COHORT STUDY

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Introduction: Few studies have assessed the safety of granulocyte and monocyte adsorptive apheresis (GMA) in patients with inflammatory bowel disease (IBD) undergoing concomitant treatment with multiple immunosuppressant medications. To address this research gap, we investigated adverse events (AEs) associated with GMA in patients with IBD treated with multiple immunosuppressants who participated in the "Post-marketing surveillance study on the safety and response of GMA treatment in patients with Crohn's disease or ulcerative colitis with at least one special situation who received Adacolumn (PARTICULAR)".
Aims & Methods: The aim of this study is to investigate the safety of GMA in patients with IBD treated with multiple immunosuppressants who participated in the PARTICULAR study. This retrospective, multicentre cohort study included patients with ulcerative colitis (UC) or Crohn's disease (CD) who had at least one special situation feature and who had received GMA therapy in medical institutions of Japan between November 2013 and March 2017. Patients with at least one special situation, including elderly patients, patients with anaemia and patients on multiple immunosuppressants were enrolled. GMA was performed using Adacolumn (JIMRO, Takasaki, Japan). Each patients received up to a maximum of 11 sessions. All adverse events (AEs) were recorded during the observation time interval. In addition, feasibility problems (FPs) including difficulty in achieving blood access, technical problems related to the system operation during the operation of the GMA column were recorded. Any AE for which the causality of GMA could not be ruled out was classified as adverse device effect (ADE). The safety of GMA was assessed in all patients. The incidence of AEs was investigated relative to the number and type of immunosuppressants using univariate and multivariate logistic regression analyses.
Results: A total of 437 patients (368 UC, 69 CD; 45.5% female) from 93 institutions were included. Of these, 140, 169, 101 and 27 patients received none, 1, 2 and ≥3 immunosuppressants, respectively. Concomitant prednisolone, immunomodulators, anti-tumor necrosis factor agents and calcineurin inhibitors were administered in 189, 151, 89 and 24 patients, respectively. Among all patients, AEs, ADEs and FPs were observed in 50 (11.4%), 11 (2.5%) and 71 (16.2%) patients, respectively. AEs in ≥1% of patients included headache in 10 patients (2.3%), nausea/vomiting in 9 (2.1%) and fever in 6 (1.4%). The rates of AE in patients receiving none, 1, 2 and ≥3 immunosuppressant medications were 7.9%, 11.8%, 11.9% and 25.9%, respectively. In multivariate logistic regression analysis, anaemia and concomitant immunosuppressants were independently associated with the incidence of AEs. Particularly, a higher number of concomitant immunosuppressants showed an increasing trend with odds ratios related to AEs. In contrast, concomitant prednisolone were associated with a reduced risk of AEs. Nausea/vomiting and headache were the most common AEs in patients on multiple immunosuppressant medications (5.6% and 3.2%, respectively).
Conclusion: Concomitant treatment with immunosuppressants was independently associated with the incidence of AEs such as nausea/vomiting and headache in patients with IBD receiving GMA. As the number of concomitant immunosuppressants increased, the incidence of AEs also increased. However, our data also suggest that GMA is safe in patients with IBD receiving prednisolone.

P0433 SAFETY AND EFFECTIVENESS OF RETREATMENT WITH GRANULOCYTE AND MONOCYTE ADSORPTIVE APHERESIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES: A MULTICENTRE COHORT STUDY

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Introduction: There are few treatment options that can be applied repeatedly as remission induction therapy for patients with inflammatory bowel disease (IBD). Granulocyte and monocyte adsorptive apheresis (GMA) is a treatment option for patients with IBD, which can be applied repeatedly as remission induction therapy. Nonetheless, currently, there is no report on the safety and efficacy of repeated treatment with GMA in patients with IBD. We report the result of the "Post-marketing surveillance study on the safety and response of GMA treatment in patients with Crohn's disease or ulcerative colitis with at least one special situation who received Adacolumn (PARTICULAR)".
Aims & Methods: The aim of this study was to assess the safety and effectiveness of retreatment with GMA in patients with IBD who participated in the PARTICULAR study. Our retrospective, multicentre cohort study included patients with ulcerative colitis (UC) or Crohn's disease (CD) who had at least one special situation feature and who had received GMA therapy at 93 medical institutions of Japan between November 2013 and March 2017. Patients with at least one special situation, including elderly patients, patients with anaemia and patients on multiple immunosuppressants were enrolled. Patients who received GMA for the first time were excluded. GMA was performed using Adacolumn (JIMRO, Takasaki, Japan). Each patients received up to a maximum of 11 sessions. All adverse events (AEs) were recorded during the observation time interval. In addition, feasibility problems (FPs) during the operation of the GMA column were recorded. The safety of GMA was assessed in all patients. The effectiveness of GMA was assessed in patients with UC with a partial Mayo (pMayo) score of ≥3. Remission was defined as a pMayo score of ≤2, while response was defined as a decrease in the pMayo score by ≥2 points and by ≥30% decrease relative to that at baseline plus all 3 sub-scores ≤1.
Results: A total of 131 patients who received GMA retreatment (109 UC, 22 CD; 51.9% female) with a median age 41.0 years were included. Among all patients, 81 did not have any special situation, while 50 had at least one special situation, including 17 elderly, 18 with anemia and 24 on multiple immunosuppressants. AEs and FPs were observed in 9.9% and 8%, respectively. The FPs rate (3.7%) in the GMA retreated patients without any special situation was significantly lower than the rate (16.0%) in patients with at least one special situation (P=0.021). The rates of AEs and FPs in the elderly, patients with anaemia and those on multiple immunosuppressants were 17.6% and 23.5%, 22.2% and 16.7% and 12.5% and 8.3%, respectively. The effectiveness of GMA retreatment was assessed in 78 patients with UC. Remission and response rates were 41.0% and 55.1%, respectively. There were no significant differences in the rates of remission (43.4% vs. 36.0%) and response (56.6% vs. 52.0%) between patients without any special situation and those with at least one special situation. Remission and response rates in 11 elderly, 8 with anemia and 8 on multiple immunosuppressants were 36.4% and 63.6%, 37.5% and 50.0% and 25.0% and 37.5%, respectively.
Conclusion: Relatively low rates of AEs and FPs and favourable response and remission rates were observed in patients who received GMA retreatment. The rate of FPs in patients who received GMA retreatment without any special situation was significantly lower than those with special situation. Although the rate of FPs in the elderly was relatively high, approximately 60% of the elderly patients achieved response by receiving GMA retreatment.

Pharma Co. Ltd., Mochida Pharmaceutical Co. Ltd., Kyorin Pharmaceutical Co. Ltd. and Mitsubishi Tanabe Pharma Corporation. Eiji Hosoi is employee of JIMRO Co. Ltd. All other authors have nothing to disclose.

P0434 REAL LIFE EFFECTIVENESS OF VEDOLIZUMAB IN PATIENTS WITH IBD: A SINGLE CENTER EXPERIENCE

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Introduction: Vedolizumab is a fully humanized monoclonal antibody that selective binds the α4β7 integrin, recently approved for the treatment of patients with Inflammatory Bowel Diseases (IBD). It acts blocking the migration of circulating T-lymphocytes into inflamed gastro-intestinal tissue.
Aims & Methods: Here we present a real-life experience with patients affected with IBD treated with Vedolizumab.
All consecutive patients observed at a single Center (Gastroenterology Department of "Casa Sollievo della Sofferenza" Hospital) treated with Vedolizumab from September 2016 were included. Demographic and clinical data (age at disease diagnosis, disease location and duration, behavior, and previous therapies) were collected. We also collect clinical activity before and during therapy with Vedolizumab and concomitant medications. The clinical response to induction (valued by means of Harvey Bradshaw index and partial Mayo score for Crohn's disease and Ulcerative Colitis patients respectively) was assessed after 3 months of therapy. Persistence of therapy with Vedolizumab was also evaluated.
Results: A total of 68 patients (30 Crohn's Disease (CD) and 38 Ulcerative Colitis (UC)) were included. Thirty-eight patients were male (55.8%), and the mean disease duration was 10.2±7.3 years and 11.8±6.8 years for CD and UC respectively. The majority of patients had moderate activity when started Vedolizumab (90% and 86.8% of those with CD and UC, respectively). Fifty-two patients (76.5%) had been treated with Anti TNF alpha before Vedolizumab. Clinical response after three months of therapy was achieved in 22 CD patients (73%) and 33 UC patients (87%). Fifteen patients (11 CD and 4 UC) definitively discontinued Vedolizumab (9 for primary non response, 1 for intolerance, and five for loss of response after a mean of 25±2.9 months of therapy - range 21-30). Fifty-two patients (76.4%) are on-going in treatment with a mean persistence of therapy of 12.2±7,3 months (range 1 - 33). No significant differences for clinical response rate were found between patients naïve vs previous treated with anti TNF alpha (87% vs 83%, p=1.0), short (≤ 2 years) vs long disease duration (75% vs 83%, p=0.6), older (≥ 65 years) vs younger patients (70% vs 85%, p=0.1), and disease behavior for Crohn's disease (66.6% of patients with B1 responded to Vedolizumab vs 80% both for B2 and B3, p=0.3).
Conclusion: Vedolizumab was effective in patients with IBD (both CD and UC), irrespective of previous anti TNF alpha therapy, age of patients, disease duration and disease behavior in Crohn's disease.
Disclosure: Nothing to disclose

P0435 SPACING THE ADMINISTRATION INTERVAL OF ANTI-TNF AGENTS: A VALID STRATEGY FOR PATIENTS WITH INFLAMMATORY BOWEL DISEASE?

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Introduction: Patients with psoriasis and rheumatologic diseases are eventually treated with biological agents using treatment schedules with more spaced administrations than those approved in data sheet. These schedules are cheaper, and they even might reduce the risk of adverse events. However, they are scarcely used in inflammatory bowel disease (IBD).
Aims & Methods:
Aim: To describe the clinical outcomes of IBD patients treated with anti-TNF agents by means of a spacing schedule (administration interval greater than 8 weeks for infliximab or 2 weeks for adalimumab).

Methods: Using the local databases from two referral centers, all the patients with IBD who were in clinical remission at the time they were moved to a spaced schedule with infliximab or adalimumab, were identified. Patients with ostomy or ileoanal pouch, indication of anti-TNF therapy for perianal disease, or adverse events as the main cause for spaced schedule, were excluded. The spaced schedule was considered successful if, at the end of the follow-up, the patient remained in clinical remission with the same spaced schedule or without biological therapy and if no return to the conventional schedule, dose-escalation, change to another biological agent, a course of systemic corticosteroids or surgery were required.
Results: 85 patients were included (58 Crohn's disease, 27 ulcerative colitis/IBD unclassified). 60 were treated with infliximab (49 every 10 weeks and 11 every 12 weeks) and 25 with adalimumab every 3 weeks. Before the spaced schedule, 38% of patients had previous courses of anti-TNF, and 7% required dose-escalation. The spaced schedule was initiated after the median of 25 months of anti-TNF treatment (IQR 14-49). Baseline C-reactive protein (CRP) was available in all patients (95% with CRP< 5mg/L). Baseline faecal calprotectin was available in 31% of patients (100% < 250 µg/g). Morphological assessment of disease activity (colonoscopy, MRI enterography) within 6 months before the spaced schedule was available in 48% of patients (3% and 17% with endoscopic and RMI activity, respectively). 64% were on combination therapy with an immunosuppressant at the beginning of the anti-TNF. The median time on spaced schedule was 15 months (IQR 12-25). 37% of patients returned to a conventional schedule and 9% required dose-escalation. In 16 patients (19%) the anti-TNF was stopped because of sustained remission (9/22). 12 patients had available trough infliximab levels before the spaced schedule (median: 2.8 µg/mL [IQR, 1.12-4.30]) and 21 patients after two spaced doses (median: 1.6 µg/mL ([IQR, 0.5-3.5]). 10 patients had available trough infliximab levels before and after the spaced schedule; with a significant decrease in drugs levels (p=0.007). At the end of follow-up, 50 out of 85 patients (59%) met the success criteria of the spaced schedule. A longer time (> 5 years) from IBD diagnosis to the introduction of anti-TNF treatment (RR 2.1 [IC 95% 1.1 - 4.3]; p=0.034) and a baseline CRP >2mg/L prior to spacing (RR 3.2 [IC 95% 1.4 - 7.5]; p=0.008), were the only independent predictive factors of the failure of the spacing strategy.
Conclusion: Anti-TNF administration at longer intervals than those provided in the data sheet of the drug can be a convenient and cheaper alternative, particularly effective in patients in whom anti-TNF treatment was early initiated (within 5 years from disease diagnosis) and once deep remission has been achieved.
Disclosure: Laura Núñez has received educational grants from Janssen; Míriam Mañosa has served as a speaker and has received research or educational funding from MSD, AbbVie, Takeda, Janssen, Ferring, and Pfizer; Francisco Mesonero has served as a speaker for Janssen, MSD, Takeda y Abbvie; Fiorella Cañete has served as a speaker or has received educational grants from Takeda, Janssen, MSD, and Ferring; Margalida Calafat has served as a speaker for Takeda, Janssen, Faes Farma and MSD; Antonio López-Sanromán has served as a speaker, a consultant and an advisory member for or has received research funding from MSD, Abbvie, Pfizer, Takeda, Janssen, Ferring, Faes Farma, Shire Pharmaceuticals, Dr. Falk Pharma, Tillotts Pharma, Chiesi, Gebro Pharma, and Vifor Pharma; Eugeni Domènech has served as a speaker or has received research or educational funding or advisory fees from MSD, AbbVie, Takeda, Kern Pharma, Pfizer, Janssen, Celgene, Adacyte Therapeutics, Otsuka Pharmaceuticals, Ferring, Shire Pharmaceuticals, Tillots Pharma, Thermofisher, Grifols, and Gebro. All the remaining authors declared no conflicts of interest.

P0436 SURGERY AND HOSPITALIZATION RATES IN INFLAMMATORY BOWEL DISEASE PATIENTS IN THE QUÉBEC PROVINCIAL DATABASE FROM 1996 - 2015

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Introduction: Inflammatory bowel diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), are associated with high healthcare expenditures related to medications, hospitalisations, and surgeries. Our aim was to analyse disease outcomes and treatment algorithms in newly diagnosed IBD patients in Québec over the past 2 decades, comparing periods before and after routine public reimbursement of biologics.

Aims & Methods: Overall, 34644 newly diagnosed IBD patients (CD: 20644 or 59.5%; M:F CD: 3:4, UC: 1:1; CD < 40 years old: 46% vs. UC< 40 years old: 35%) were identified from the population-based health insurance database of Québec from 1996 to 2015. The primary and secondary outcomes included time to and probability of first hospitalisation and first major surgery, and medication exposures. Prescription data were collected from the public prescription database (RAMQ).

Results: Probability of major surgery increased after 2010 in CD (at 5 years after diagnosis: before and after 2010: 8% (SD: 0.2%) vs. 15% (0.6%); p< 0.0001) and UC patients (6% (0.2%) vs. 10% (0.6%); p< 0.0001). Hospitalisations rates remained unchanged, but were higher in CD compared with UC (p< 0.0001). IBD patients on biologicals had overall lower probability of hospitalisations compared with other drug types (overall 5 years probability for all IBD patients using 5-ASA: 37% (0.6%); biologicals: 31% (1.8%), p< 0.0001). Biologicals were more commonly prescribed in CD after 2010 (4% (0.2%) vs. 16% (0.6%), p< 0.0001), especially in patients less than 40 years old at diagnosis. Thiopurine exposure increased in IBD patients after 2010 (CD: 21% (0.4%) vs. 24% (0.6%) p< 0.0001; UC: 13% (0.4%) vs. 16% (0.7%), p< 0.0001), while methotrexate use remained overall low (overall 5 years probability in CD: 4% (0.1%); UC: 1% (0.1%); p < 0.0001). Corticosteroid exposure was unchanged before and after 2010 (CD: 31% (0.4%) vs. 30% (0.7%) p=0.46; UC: 31% (0.5%) vs. 34% (0.9%); p=0.03). 5-ASA use was higher in UC (40% (0.4%), p < 0.001), while in CD it became lower after 2010 (33% (0.4%) vs. 21% (0.6%), p< 0.0001).

Conclusion: The probability of first hospitalizations remained unchanged whilst the probability of first major surgery was increased despite the higher and earlier use of biologicals therapies in IBD in this large population-based inception cohort from Québec. Overall, there was a slight increase in the use of thiopurines and methotrexate, while the use of corticosteroids was unchanged.

Disclosure: Nothing to disclose

P0437 ANALYSIS OF UC COLECTOMY RATES IN PRE- AND POST- BIOLOGIC ERA IN LOTHIAN, SCOTLAND

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Introduction: The use of biologic therapy for UC in the UK has lagged significantly behind that of Crohn's disease because of restricted guidance from NICE (NICE Clinical Guideline 166, June 2013). Following approvals of anti-TNF and vedolizumab for UC in early 2015 there has been a significant increase in prescribing. The aim of this study was to describe trends in colectomy rates for UC over time spanning the pre- and post-biologic era.

Aims & Methods: All patients (adult and paediatric) with a diagnosis of UC who received maintenance biologic treatment and/or underwent a colectomy in Lothian between 1st January 2005 and 31st December 2018 were identified by interrogating multiple clinical and administrative databases.

Patient phenotype, prescribing and surgical data including complications were extracted by manual review of the EHR. Operations were classified by extent of resection and by time interval from diagnosis to colectomy (early within 6 months vs established after 6 months from diagnosis). Linear regression and segmental regression assuming poisson variance were used to identify temporal changes (statistical joinpoints) in the trend of biologic prescription and colectomy rates. Biologic prescription and colectomy rates were described per 100 UC patients, with yearly prevalence data obtained from the Lothian IBD Registry (Jones et al, ECCO 2019).

Results: A total of 175 patients were treated with maintenance biologic therapy during the study (Table 1). Rates of initiation of maintenance biologic therapy increased from 0.05 per 100 UC patients in 2005 to 1.26 in 2018 (p< 0.001). For the whole study period the biologic prescription annual percentage change (APC) was 30.4% (14.5-48.6% 95% CI). Rates of prescription of infliximab as rescue therapy remained at a steady state throughout the study.

A total of 448 colectomies for UC were performed during the study period (Table 1). Colectomy rates per 100 UC patients fell throughout the study period; from 1.47 colectomies per 100 UC patients in 2005 to 0.44 in 2018 (p< 0.001). There was a significant inflection point in the rate of change with a statistical joinpoint identified in 2014. The colectomy rate APC was -4.1% per year from 2005 to 2014 and -18.9% from 2014 to 2018 (p=0.019). There was no increase in complications in patients treated with biologics pre-operatively.

Year	UC Prevalence	Colectomies	1st Biologic prescriptions	Year	Population	Colectomies	1st Biologic prescriptions
2005	2152	32	1	2012	3164	30	2
2006	2289	35	0	2013	3279	34	5
2007	2445	33	0	2014	3415	40	13
2008	2548	32	1	2015	3566	26	32
2009	2727	36	2	2016	3678	26	28
2010	2881	46	1	2017	3798	24	39
2011	3003	37	2	2018	3876	17	49

[Table 1 UC colectomy and first maintenance biologic prescription numbers per year]

Conclusion: The increase in biologic prescribing for UC has been parallelled by a significant reduction in colectomy rates without increased postoperative complications. This is the first population based study that shows a reduction in colectomy rates in parallel with increased use of biologics for UC.

References: Jones G et al, ECCO 2019, DOP87. Multi-parameter datasets are required to identify the true prevalence of IBD: The Lothian IBD Registry (LIBDR)

Disclosure: PJ has received travel support from Takeda. NP has received consultancy fees from Takeda and speaker fees and travel support from AbbVie, Takeda and Norgine. IDA has received consultancy fees from Vifor and travel support from Shire. CWL has received research support from AbbVie and Shire, consultancy fees from AbbVie, Pfizer, Dr. Falk, Hospira, MSD, Pharmacosmos, Takeda and Vifor, and speaker fees and travel support from AbbVie, Pfizer, Dr. Falk, Ferring, Hospira, MSD, Shire, Takeda and Warner-Chilcott. GRJ, KK and ML have no personal interests to declare.

P0438 WITHDRAWN

P0439 RISK OF LATE POST-OPERATIVE RECURRENCE OF CROHN'S DISEASE IN ENDOSCOPIC REMISSION AFTER ILEOCAECAL RESECTION: A 10-YEAR MULTICENTER EXPERIENCE

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Introduction: The Rutgeerts' score (RS) grades the severity of signs of endoscopic Crohn's disease (CD) recurrence in the postoperative patient after ileocolonic resection. Although the International Organization for the

Study of Inflammatory Bowel Disease (IOBD) agreed that a RS< i2 reflects endoscopic remission, the risk of late post-operative disease recurrence in these patients remains unclear.

Aims & Methods: We performed a multicenter, retrospective cohort study to evaluate the risk of late post-operative CD recurrence in patients who are in endoscopic remission after ileocaecal resection. All CD patients that underwent an ileocolonic resection with curative intent between 2006-2016 were screened for eligibility in three large-volume IBD centres. Only those who had no signs of endoscopic recurrence (defined as RS< i2) at baseline assessment between month 3 and 18 after surgery were included. Post-operative recurrence during follow-up was defined as a composite endpoint of at least one of the following: clinical recurrence (i.e. new or worsening IBD-related abdominal pain and/or diarrhea), IBD related hospitalization, development of bowel damage (i.e. new intra-abdominal fistulae, abscesses and/or strictures), the need for endoscopic balloon dilatation of the anastomosis, and the need for redo-surgery. Time to disease recurrence was estimated by Kaplan-Meier analysis, and cox regression analysis was used to identify potential risk factors for recurrence.

Results: A total number of 86 patients (n=55 female; n=27 active smokers) were included. Median (IQR) time between CD diagnosis and ileocolonic resection was 6.1 (0.9-19.4) years. Seventeen (19.8%) patients had undergone previous surgery, while the majority (n=55, 64%) had received treatment with immunomodulators and/or biologicals before ileocolonic resection. Median (IQR) time between surgery and baseline endoscopy was 7 (5.7-9.5) months and forty (46.5%) patients received therapy with immunomodulators and/or biologicals in this period. Median (IQR) follow-up time after baseline endoscopy was 3.5 (1.6-5.3) years. Based on the composite endpoint, late post-operative CD recurrence was seen in 35 (40.7%) patients (Table 1). Recurrence status was comparable between patients with RS of i0 (20/55) or i1 (15/31) at baseline endoscopy (p=0.28), and independent whether or not patients had received medical therapy between surgery and baseline endoscopy (16/40 with therapy vs. 19/46 without therapy; p=0.9). Median (IQR) time to disease recurrence was 14.2 (6.3-26.1) months. No risk factor for late post-operative CD recurrence could be identified after bivariate cox regression analysis.

Conclusion: This is the first study looking at the risk of late post-operative CD recurrence after ileocaecal resection with curative intent. It was seen in up to 40% of patients despite initial endoscopic remission, and continuous follow-up of this population remains therefore warranted.

Outcome parameter	Yes	No
Clinical recurrence, % (n)	36 (31)	64 (55)
IBD-related hospitalization, % (n)	15.1 (13)	84.9 (73)
Need for endoscopic balloon dilatation, % (n)	4.7 (4)	95.3 (82)
New intra-abdominal bowel damage, % (n)	16.3 (14)	83.7 (72)
Need for IBD-related surgery, % (n)	3.5 (3)	96.5 (83)
Composite endpoint, % (n)	40.7 (35)	59.3 (51)

[Risk of late post-operative CD recurrence]

P0440 ASSESSMENT OF THE NEED FOR THE FIRST INTESTINAL RESECTION IN PATIENTS WITH CROHN'S DISEASE FOLLOWING DIAGNOSIS: A SINGLE-CENTRE COHORT STUDY IN JAPAN

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Introduction: Studies on the natural history of Crohn's disease (CD) show that up to 50% of CD patients require their first intestinal resection within 10 years of diagnosis. In recent years, immunomodulators (IM) and anti-tumour necrosis factor (TNF) agents have become available and used to treat CD worldwide, but currently, there is inadequate information regarding the need when the first intestinal resection should be undertaken.

Aims & Methods: The aim of this study was to investigate the time when the first intestinal resection becomes necessary after the diagnosis of CD and understand the relevant prognostic factors including concomitant administration of IM or anti-TNF agents. We retrospectively compiled and reviewed the data on patients with CD who had been treated at our hospital between January 2010 and December 2012. Patients who were diagnosed with CD prior to 1989 and had undergone intestinal resection before the diagnosed of CD were excluded. All patients were followed until the initial intestinal resection was done or until March 2019. Patients who were lost to follow-up were censored. Patients were divided into two groups according to the year of CD diagnosis (Group A, 1990-2001; Group B, 2002-2012). Between groups A and B, patients' demographic variables were compared using univariate analysis. Further, the cumulative rates of the initial intestinal resection following the diagnosis of CD in the two groups were evaluated using the Kaplan-Meier method together with the log-rank test.

Results: A total of 291 patients, median age, 21.7 years; 93 female were available for evaluation. At the diagnosis of CD, 157 patients had ileocolitis, 84 had ileitis and 50 had colitis. Two-hundred and two patients were diagnosed with non-stricturing, non-penetrating disease, 75 with stricturing disease and 14 with penetrating disease. Perianal disease was diagnosed in 159 patients. During the observation period, concomitant prednisolone, IM (azathioprine or 6-mercaptopurine) and anti-TNF agents (infliximab or adalimumab) were administered to 72, 162 and 177 patients, respectively. Among the 291 patients, 125 were assigned to Group A and 166 to Group B. The proportion of the patients diagnosed with non-stricturing, non-penetrating disease, stricturing disease and penetrating disease were 60%, 33% and 7% in Group A and 77%, 20% and 3% in Group B, respectively indicating that the number of patients with non-stricturing, non-penetrating disease in Group B significantly increased compared to Group A, while patients with stricturing and penetrating disease decreased compared with Group A (P = 0.008). Patients who had received concomitant treatment with prednisolone were significant lower in Group B than in Group A (19% vs. 34%, P = 0.007), while patients on concomitant IM or anti-TNF agents were significantly higher in Group B than in Group A (IM: 66% vs. 42%, P < 0.001; anti-TNF agents: 78% vs. 44%, P < 0.001). Further, the cumulative rates of 1, 5, 10 and 15 years intestinal resection were 16%, 29%, 47% and 57% in Group A and 8%, 15%, 21% and 24% in Group B, respectively showing that the cumulative rates of intestinal resection in Group B were significantly lower than in Group A (P < 0.001).

Conclusion: This study showed a significant reduction in the rates of initial intestinal resection in patients with CD diagnosed during 2002-2012 than those diagnosed during 1990-2001. It is assumed that a decrease in patients with stricturing and penetrating disease and an increase in IM and anti-TNF agents use may have contributed to the decrease in the intestinal resection rate beyond 2001.

P0441 TRANSANAL CLOSE RECTAL DISSECTION (TACRD) PROCTECTOMY: A NEW ROAD TO AN OLD DESTINATION

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Introduction: Total mesorectal excision (TME) is the gold standard resectional strategy for rectal cancer. In benign diseases so called close rectal dissection (CRD), has been traditionally advocated to minimize damage to pelvic neural plexuses and complications reducing dead space, compared to TME. In daily practice laparoscopic CRD has never spread because affects a worse visualization, a chopsticks conflict and a more difficult hemostasis. Transanal approach bottom to up to the pelvis (taCRD) could allow a better visualization and an easily and safer hemostatic control.
Aims & Methods: Aim of the study was to evaluate safety and feasibility of TaCRD proctectomy in our inflammatory bowel diseases (IBD) cohort. From January 2016 to December 2018 prospective colorectal disease database maintained at IRCCS Sacred Heart - Don Calabria Hospital of Negrar was required to identify patients underwent taCRD proctectomy for IBD). Transanal platform of choice was Gel Point Path™. We analyzed all clinical and operative data.
Results: Nineteen patients (median age 43,6 ± 11,4, male/female 13/6, median BMI 22,3 ± 3), 16 with ulcerative colitis (UC) and 3 with Crohn's disease (CD). TaCRD proctectomy was always performed when dysplasia or cancer are not suspected. In 9 cases an ileal pouch-anal anastomosis (ta-IPAA) (47,3%) was done. Operative time was 85 min (±21) in 89,1 % of patients. Dissection was properly carried on with radiofrequency plus hook in 69,4 % of cases. The main intraoperative problem was smoke evacuation in 15,7 % of cases; No bleeding was experienced neither chopstich conflict that led to conversion to abdominal approch. During postoperative course we experienced 2 complication (10,4 %); one bleeding that has been no need of blood transfusion (Clavien-Dindo I) and one collection, successfully treated with antibiotics (Clavien Dindo II). In our series taIPAA creation did not affect further complications .
Conclusion: Our experience confirmed that TaCRD is feasible and safe with proper indication. It allows a less rate of complication even when performed as the road to pouch creation. A next step will be the evaluation of functional results compared with laparoscopic TME and TaTME.
Disclosure: Nothing to disclose

P0442 LAPAROSCOPIC INTRAOPERATIVE ULTRASOUND IN PATIENTS WITH CROHN'S DISEASE: A FEASIBILITY STUDY

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Introduction: Transabdominal bowel ultrasound (BUS) is being increasingly adopted for diagnosing and monitoring of patients with Crohn's disease (CD), due to its wide availability and readiness. Specifically, BUS has been reported to accurately evaluate CD extension, activity and to detect presence of CD-related complications. Moreover, ultrasound elastography has been recently demonstrated able to quantify bowel wall fibrosis. No study has so far assessed feasibility and usefulness of laparoscopic bowel ultrasound during CD-related surgery.
Aims & Methods: The aim of the study is to assess the feasibility and usefulness of laparoscopic bowel ultrasound during CD-related surgery. Consecutive CD patients undergoing their first laparoscopic surgery were enrolled. Intraoperative laparoscopic ultrasound was performed in the first stage of surgical intervention by a dedicated surgeon expert in CD-related surgery. A dedicated 5-10 Mhz US laparoscopic transducer with a flexible tip and a depth of 4-10 centimeters was used for all examinations.
Results: Between March 2016 and March 2017 10 CD patients were enrolled. Intraoperative US was feasible in all patients (i.e. intraoperative US study of CD-affected tract), and no procedure-related complication was reported. Mean US execution time was 25 minutes (range 15-40 minutes). Median follow-up following surgery was 29 months (range 24-36). In all patients,

intraoperative US was helpful for CD surgical management (Table). During post-operative follow-up, 1 patient experienced a grade I complication according to Clavien-Dindo while 1 patient experienced a grade IIIa complication. No patient underwent a second bowel resection at the end of follow-up

Pts (n)	Intraoperative laparoscopic ultrasound-related advantage
2	Suggesting not to perform bowel resection
1	Helping to rule out CD diagnosis
2	Clarification of intestinal and mesenteric morphology
3	Identification of the exact location of CD-related complications (fistula and abscesses)
1	Identification and characterization of concomitant lesions
4	Clarification of imaging discrepancies
8	Exact definition of bowel resection margin

[Table 1]

Conclusion: Results of the present study demonstrate that laparoscopic intraoperative ultrasound is feasible and safe in patients with Crohn's disease. Our preliminary data seem to suggest that this technique may be helpful for CD surgical management, even if these results should be confirmed in a prospective study.
Disclosure: Nothing to disclose

P0443 COLECTOMY RATES AND POSTOPERATIVE COMPLICATIONS IN PATIENTS WITH ULCERATIVE COLITIS REGISTERED IN A TERTIARY CENTER

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Introduction: According to disease duration, surgical intervention rate in patients with UC varies from 4.9% to 15.6%.[1] The standard procedure is proctocolectomy with ieal pouch, its curative goal being limited by the postoperative complications, which occurs in 30% of the cases[2].
Aims & Methods: The purpose of our study was to asses the colectomy rates and the main postoperative complications in patients with UC admitted in a Tertiary Gastroenterology Center - Fundeni Clinical Institute, Bucharest, Romania - during January 2012 - March 2019. Among 592 of patients with UC admitted in our clinic during the mentioned period, 111 patients (18%) with severe disease, we retrospectively analysed the data from 28 patients (4.7%) who underwent surgical intervention. We extracted the data using our hospital information system. The mean age at diagnosis was 38 years. Disease extension, surgical indication, intervention type, postoperative and long-term complications with their specific treatment were analysed.
Results: The main indications for the surgery intervention were severe, medically unresponsive flare (69.2%), the presence of dysplasia/adenocarcinoma (11.54%), toxic megacolon (7.69%), stenosis (7.69%) and abcess (3.85%). The most common intervention was the restaurative procedure (53.85%), followed by proctocolectomy with a permanent ileostomy (19.23%), hemicolectomy (15.38%) and total colectomy with ileorectal anastomosis (11.54%).The progression of disease extension was observed in 30.77% of the patients, being strongly correlated to the medical intractability (p< 0.001). Postoperatively, the most frequent complications were the local and systemic infections (50.00%), haemorrhage (18.75%), early stomal complications (12.50%), anastomotic leak (6.25%), eventration (6.25%) and fistulas (6.25%). 52.63% of the interventions were performed laparoscopically; the laparotomic procedures and also the urgent surgeries (23.08%) were associated with more frequent infectious complications (p< 0.001). Pouch-related complications (pouchitis, stenosis, pouch failure and irritable pouch syndrome) were the most common long-term complications - 41.67%, with a response rate to the medical treatment of 50.00%.
Conclusion: The data regarding the colectomy rate registered in our clinic is similar to those mentioned in the literature. The timing and surgical approach have an essential role in the postoperative evolution.
References: 1. "Long-Term Colectomy Rates in Patients with Ulcerative Colitis Treated with Infliximab: A Single Canadian Tertiary Care Centre's Experience." Journal of Crohn's and Colitis, vol. 9, no. suppl 1, 2015, doi:10.1093/

ecco-jcc/jju027.659. 2. Kühn, Florian, and Ernst Klar. "Surgical Principles in the Treatment of Ulcerative Colitis." Viszeralmedizin vol. 31,4 (2015): 246-50. doi:10.1159/000438894
Disclosure: Nothing to disclose

Other Lower GI Disorders I

10:30-17:00 / Poster Exhibition - Hall 7

P0444 FECAL CALPROTECTIN LEVELS ARE ELEVATED IN TRANSTHYRETIN AMYLOIDOSIS PATIENTS WITH GASTROINTESTINAL MANIFESTATIONS

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Introduction: Transthyretin amyloid (ATTR) amyloidosis is a rare systemic disorder characterized by amyloid deposits formed by misfolded monomers of transthyretin (TTR). Gastrointestinal (GI) manifestations are common in ATTR amyloidosis, however their pathogenesis is not fully elucidated.
Aims & Methods: In the current study, we aimed to evaluate the diagnostic role of fecal calprotectin (FC) in ATTR patients with GI manifestations and to evaluate the role of intestinal inflammation in the pathogenesis of the disease. We recruited 21 consecutive ATTR amyloidosis patients and 42 sex and age-matched healthy controls. Presence of GI symptoms and severity of peripheral neuropathy had been evaluated. Colonoscopy and FC assessment were performed in all subjects.
Results: Mean levels of FC in ATTR amyloidosis patients 184 μg/g (30-430) were significantly higher then those of controls 40 μg/g (30-70), p< 0.001. ROC curve analysis indicated a FC cut-off level of 71 μg/g differentiates ATTR amyloidosis with GI manifestations from healthy subjects with 91% sensitivity, 100% specificity, 100% positive predictive value, 95% negative predictive value and 97% overall accuracy. FC values were significantly associated with the presence of neutrophilic granulocytes infiltration in the colonic mucosa (p=0.002), with the presence of amyloid deposits in rectal mucosa (p=0.007) and the presence of diarrhea (p=0.046).
Conclusion: FC levels are elevated in patients with ATTR amyloidosis with GI manifestations, which suggests an inflammatory component in the pathogenesis of the disease. The presence of elevated FC concentrations could help gastroenterologists to include ATTR amyloidosis in their diagnostic work-up
Disclosure: Nothing to disclose

P0445 PRELIMINARY DATA ON ORAL AND FECAL MICROBIOTA IN PATIENTS AFFECTED BY LYNCH SYNDROME

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Introduction: Microbiota alterations seem to play an associated role in colorectal cancer (CRC) pathogenesis. Bacteroides, Fusobacterium, Salmonella, Escherichia and Campylobacter have been widely studied, demonstrating their promoting role on inflammatory environment, production of molecules affecting DNA stability and alteration of proliferative responses. Few projects are ongoing on microbiota alterations in patients affected by Lynch Syndrome (LS).
Aims & Methods: Our aim was the characterization of oral and fecal microbiota in LS patients compared with healthy normal controls. We analized oral and fecal microbiota of 17 LS patients: 12 patients were MSH2 mutation carriers, 3 MLH1 mutation carriers, 2 MSH6 mutation carriers. 11 underwent on emicolectomy and one proctocolectomy for CRC, besides one gastric cancer, one endometrial cancer and one duodenal cancer. Total DNA was purified from fecal samples and oral washes. The V3-V4 region of the 16s rRNA gene was amplified. Purified DNA was quantified and libraries were diluted and mixed for pooling with unique molecular tags. Sequences with high quality score and length >250bp were used for the taxonomic analysis with QIIME software.
Results: Oral wash microbiota of Lynch patients and 41 matched normal healthy controls were analyzed. Alpha diversity was statistically different between the two groups, with a lower observed otus/chao1 index in Lynch patients compared to controls. The unweighted beta diversity was able to distinguish the two populations. At the genus level, taxonomic analysis of oral wash samples showed a statistically significant increase of *Veillonella* (17% vs 11%) and a decrease of *Neisseria* (10% vs 17%) and *Prevotella* (3% vs 5%) in Lynch patients compared to control subjects. Fecal microbiota of Lynch patients and 21 matched normal healthy controls were analyzed. No statistically significant differences were observed neither in alpha diversity and nor in beta diversity between the two groups. Taxonomic analysis of fecal samples identified a statistically significant increase of Bifidobacteriaceae in Lynch patients compared to controls (2% vs 0%) and a slight increase of Enterobacteriaceae in Lynch samples (1% vs 0%).
Conclusion: An increase of *Veillonella* and a decrease of *Neisseria* was observed in oral wash samples of Lynch patients. In fecal samples of Lynch patients we observed an increase of Bifidobacteriaceae. These associations were described in sporadic colorectal cancer and Crohn's disease (CD) too. Further study on larger groups of patients are needed to confirm or revoke these results.
Disclosure: Nothing to disclose

P0446 SERUM METABOLITE PROFILES IN ACUTE RADIATION ENTERITIS: AN ANIMAL MODEL STUDY

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Introduction: Acute radiation enteritis (ARE), a complication with radiotherapy for pelvic and abdominal tumors, seriously undermines the life quality, even shortens the life span of survivors. Untargeted metabolomics analysis may help find the diagnostic biomarkers, metabolic mechanism and intervention strategies for ARE.

Aims & Methods: ARE rat model was established through single abdominal irradiation with a gamma-ray dose of 10 Gy. The fecal condition of each rat was recorded. H&E staining was employed to evaluate the change in intestinal structure at four days after radiation. Serum from 15 ARE models and 10 controls were collected for untargeted metabolomics detection by ultra-high-performance liquid chromatography/quadrupole-time-of-flight-mass spectrometry (UHPLC-Q-TOF/MS). Variable importance for the projection (VIP) was calculated in Orthogonal partial least squares discrimination analysis (OPLS-DA) which worked together with heat map to categorize samples and screen metabolites. Significantly differentially expressed metabolites (VIP > 1 and P < 0.05) between ARE group and control group were identified. At last, Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis was employed to explore the metabolomic pathways affected by abdominal irradiation.

Results: At two days after radiation, ARE rats showed obvious diarrhea, while the control rats continued to defecate normally. H&E staining revealed a dramatic destruction in the intestinal villi of irradiated animals, which confirmed the occurrence of ARE. Based on the metabolomics data, 6044 positive peaks and 4241 negative peaks were extracted from each sample. In OPLS-DA, the explanation rate for Y variable (R2Y) and prediction ability (Q2) (0.998 and 0.788 in positive ion mode, 0.997 and 0.866 in negative ion mode) confirmed the stability and reliability of the model. The heat map for cluster analysis showed satisfactory discriminatory power between ARE rats and controls. Further analysis identified 66 significantly differentially expressed metabolites, ten of which changed by more than three folds and might be biomarkers for ARE. KEGG pathway enrichment analysis indicated that the differentially expressed metabolites were involved in multiple different pathways, including central metabolism in cancer, mineral absorption, protein digestion and absorption, aminoacyl-tRNA biosynthesis, ABC transporters, pyrimidine metabolism.

Conclusion: Ten metabolites, with more than three folds change in expression, may serve as useful biomarkers for ARE. The pathways through which abdominal irradiation disrupts metabolic activity of intestinal cells may provide a clue for elucidating ARE physiopathology.

Disclosure: The authors declare no conflict of interest

P0447 LOSS OF THE MICROBIALLY REGULATED HEXOKINASE 2 IN INTESTINAL EPITHELIAL CELLS PROTECTS FROM ACUTE COLITIS

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Introduction: Hexokinases (HK) are a group of five isoenzymes, which catalyze the first step of glycolysis and thereby limit its pace. HK activity is tightly linked to immune responses[1] and HK2 also functions as a pattern recognition receptor sensing a bacterial cell wall component and thereby mediates a pro-inflammatory response[2].

Aims & Methods: Our goal was to examine the function of HK2 for host-microbiota-interactions and intestinal inflammation. To that end, we generated mice lacking *Hk2* specifically in intestinal epithelial cells (*Hk2*-ΔIEC) and tested their susceptibility to acute inflammation using the dextran sodium sulfate (DSS) colitis model. In parallel we stimulated epithelial cell lines and gnotobiotic mice with bacterial strains and metabolites to identify bacterial agents that may modulate *Hk2* expression and thereby intestinal inflammation.

Results: Under unchallenged conditions *Hk2*-ΔIEC mice did not exhibit a major metabolic or inflammatory phenotype, whereas loss of HK2 in the intestinal epithelium was protective during acute inflammation. We found that the normal microbiota strongly regulates HK2 expression and activity. Additionally, we identified individual bacteria and metabolites that repress *Hk2* expression in intestinal epithelial cells and gnotobiotic mice. We currently test whether supplementation with these bacterial factors protects from intestinal inflammation.

Conclusion: Our data identified the microbiome as a central regulator of HK2 and glycolysis and thereby as a potential therapeutic target for acute inflammatory conditions.

References: 1 Perrin-Cocon et al. "Toll-like Receptor 4-Induced Glycolytic Burst in Human Monocyte-Derived Dendritic Cells Results from p38-Dependent Stabilization of HIF-1α and Increased Hexokinase II Expression.", J

Immunol, 201 (5) 1510-1521, September 01, 2018 2 Wolf et al. "Hexokinase Is an Innate Immune Receptor for the Detection of Bacterial Peptidoglycan.", Cell 166, 624-636, July 28, 2016

Disclosure: Nothing to disclose

P0448 IMPACT OF THE DIETARY POLYACETYLENIC FALCARINOL AND FALCARINDIOL ON INFLAMMATION AND COLORECTAL CANCER: A MECHANISTIC STUDY IN A PRIMED RAT MODEL

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Introduction: Colorectal cancer (CRC) development is a multistep process, from normal epithelial cells via inflammation to aberrant crypt foci (ACF) and progressive adenoma stages, to carcinomas and then metastatic disease [1, 2]. In order to reduce the incidence and consequences of CRC, effective prevention and treatment strategies need to be identified. Due to the long precancerous stage of identifiable disease, dietary intervention may exert favorable effect on polyp formation and/or inhibition of adenomas transformation to CRC. Recent findings indicate that long-term consumption of a diet rich in vegetables may prevent the development of CRC [3].

For the prevention of CRC by dietary measures, vegetables such as carrots are highly interesting due to their content of the bioactive polyacetylenic falcarinol (FaOH) and falcarindiol (FaDOH) [4]. FaOH and FaDOH have shown many interesting bioactivities including anti-inflammatory and cytotoxic activity [4-6]as well as antineoplastic effect in animal models [7, 8]. In this study, we demonstrate that FaOH and FaDOH prevent the development of early neoplastic lesions in the colorectal intestine in a dose-response relationship corresponding to the logarithmic of the concentration of the contents of FaOH and FaDOH in the diet. Furthermore, the results presented also demonstrate that FaOH and FaDOH have an effect on inflammatory markers and they seem to act as selective COX-2 inhibitors, which appears to be their main mechanism of action in relation to colon cancer prophylactics.

Aims & Methods: The gene expression of seven inflammatory markers COX-1, COX-2, NFκβ1, IL1β, IL6, PPARγ and TNFα in tissue from biopsies was analyzed by means of Real-time quantitative PCR (RT-qPCR). The biopsies include neoplastic tissue from the control group, receiving standard rat diet (SRD) without the supplement of FaOH and FaDOH and size matched neoplastic tissue from the test group receiving SRD supplemented with 7 µg FaOH g-1 feed and 7 µg. Prior to the RT-qPCR, RNA from the tissue was extracted using QIAzol and EconoSpin column purification where after it was converted into complementary DNA.

Results: The expression level of seven different inflammatory and cancer biomarkers COX-1, COX-2, TNFα, IL-6, NF-κβ, IL-1β, and PPARgamma2, were examined in both neoplastic and healthy tissue from biopsies obtained from rats receiving either SRD or SRD supplemented with FaOH and FaDOH.

Upregulation of most biomarkers, except COX-1, TNFα, and IL-1β, was observed in neoplastic tissue compared to normal tissue. Contrary, a significant downregulation in expression levels were detected in five of the seven biomarkers when comparing biopsies of neoplastic tissue from rats receiving a SRD with biopsies of neoplastic tissue from rats receiving the FaOH and FaDOH as a food supplement. A significant downregulation in the expression of TNFα, IL-6, NF-κβ, PPARγ2 and COX-2 was detected. The qRT-PCR analyses showed no significant difference in the expression level in healthy tissue for all biomarkers when the rats received FaOH and FaDOH as a food supplement compared to rates receiving SRD.

Conclusion: Collectively, the results of the present study shows that FaOH and FaDOH in combination has a chemopreventive effect on CRC in a cancer primed rat model and that this effect is due to their inhibitory effect on key biomarkers in the NF-κB signaling pathway and in particular the downstream target COX-2. The present study therefore opens up for precise dietary advices to prevent this disease and to develop new selectively COX-2 inhibitors with no or only minor side effects.

References: 1. Vogelstein and Kinzler, The multistep nature of cancer. Trends Genet, 1993. 9(4): p. 138-41. 2. Lucas et al., Microbiota, Inflammation and Colorectal Cancer. Int J Mol Sci, 2017. 18(6). 3. Leenders et al., Subtypes of

fruit and vegetables, variety in consumption and risk of colon and rectal cancer in the European Prospective Investigation into Cancer and Nutrition. Int J Cancer, 2015. 137(11): p. 2705-14. 4. Waluga et al., Pharmacological and dietary factors in prevention of colorectal cancer. J Physiol Pharmacol, 2018. 69(3). 5. Christensen and Brandt, Bioactive polyacetylenes in food plants of the Apiaceae family: occurrence, bioactivity and analysis. J Pharm Biomed Anal, 2006. 41(3): p. 683-93. 6. Metzger et al., Purple carrot (Daucus carota L.) polyacetylenes decrease lipopolysaccharide-induced expression of inflammatory proteins in macrophage and endothelial cells. J Agric Food Chem, 2008. 56(10): p. 3554-60. 7. Kobaek-Larsen et al., Inhibitory effects of feeding with carrots or (-)-falcarinol on development of azoxymethane-induced preneoplastic lesions in the rat colon. J Agric Food Chem, 2005. 53(5): p. 1823-7. 8. Kobaek-Larsen et al., Dietary polyacetylenes, falcarinol and falcarindiol, isolated from carrots prevents the formation of neoplastic lesions in the colon of azoxymethane-induced rats. Food Funct., 2017.

Disclosure: Nothing to disclose

P0449 IMMUNOTHERAPY INDUCED COLITIS: A SINGLE CENTER EXPERIENCE

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Introduction: Immunotherapy has significantly improved the traditionally poor prognosis of several malignant diseases including metastatic melanoma and Non Small Cell Lung Cancer (NSCLC), while their efficacy in a number of other tumor types is vigorously studied. Immune check point inhibition can lead to activation of autoreactive T-cells resulting in a new spectrum of side effects called immune-related adverse events (IRAEs). Gastrointestinal manifestations are common complications of immunotherapy, being often the cause of treatment discontinuation.

Aims & Methods: We retrospectively assessed 9 patients (5 males, mean age: 65.4 years) admitted to the Gastroenterology Department, because of gastrointestinal symptoms while being on therapy with immune checkpoint inhibitors for NSCLC (7 patients) and metastatic melanoma (2 patients). Two patients were treated with ipilimumab, 6 with nivolumab, and one with a combination treatment.

Results: Diarrhoea was the most common symptom, followed by abdominal pain, fever and nausea. The mean time of symptom occurrence was 17 weeks after initiation of immunotherapy (8-27 weeks). The colonoscopy findings in 6 patients were consistent with colitis with continuous inflammation pattern (mucosal erythema, ulcerations, loss of subepithelial vascular pattern and friable mucosa), while 3 patients had normal endoscopic findings. Cryptitis, and crypt abscesses were common pathological findings. Granulomas were not detected. Hospitalization was required for three patients as they met the Truelove-Witts criteria for acute severe colitis. CRP levels were elevated in 8 cases (mean 7.3 mg/dl, 3.9 - 10.6) and returned to normal after the treatment. The albumin levels were decreased in 7 patients (mean 3.3 g/dl, 2.6 - 3.9). Seven patients were treated with corticosteroids and one patient received salvage therapy with infliximab after failure of steroid treatment. Time to symptom resolution was noted to be variable (ranging from 1 day to 4 weeks).

Conclusion: Given the constantly expanding use of immune checkpoint inhibitors, it is important for the gastroenterologists to be familiar with the gastrointestinal IRAEs. Steroids comprise the first line of treatment, but salvage therapy with infliximab may be necessary in case of a steroid treatment failure. The role of alternative biologics, mainly vedolizumab is being studied. Long-term management of immune related colitis and the effect of infliximab on the malignant disease have to be further evaluated.

Disclosure: Nothing to disclose

P0450 LOSS OF PTPN2 IN EITHER DENDRITIC CELLS OR T CELLS RESULTS IN REDUCED TUMOR BURDEN IN THE ORTHOTOPIC COLON TUMOUR MOUSE MODEL

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Introduction: In the recent years, protein tyrosine phosphatase non-receptor type 2 (PTPN2) has emerged as a potential cancer immunotherapy target. Our previous data demonstrate that loss of PTPN2 in dendritic cells (DC) or in T cells results in reduced tumour burden in the azoxymethane (AOM)-dextran sodium sulphate (DSS) induced model of colitis-associated colorectal carcinoma (CRC). However the role of PTPN2 in inflammation independent CRC pathogenesis has not yet been determined. Here, we show that tissue-specific deletion of PTPN2 in DCs or T cells results in reduced tumour load in the orthotopic cecum injection mouse model of CRC.

Aims & Methods: Tumours were induced in mice specifically lacking PTPN2 in either DCs (PTPN2fl/fl-CD11cCre) or T cells (PTPN2fl/fl-CD4Cre) and their WT littermate controls by injecting MC38 tumour cells into the mouse caecum. Immune cells in spleen, mesenteric lymph nodes (mLN), tumour (T) and tumour-adjacent normal tissue (non-T) were analysed using flow cytometry and immunohistochemistry.

Results: Although tumour burden varied between individuals, PTPN2fl/f-CD11cCre and PTPN2fl/fl-CD4Cre mice had clearly less and smaller tumours compared to their littermate controls. In turn, PTPN2-deficient mice exhibited significantly increased levels of CD44+ effector/memory CD4+ and CD8+ T cells in spleen and mLN, indicating enhanced T cell activation. Additionally, we observed increased granzyme B expression in the spleen from PTPN2fl/fl-CD4Cre mice compared to their littermate controls, suggesting increased cytotoxic/anti-tumour activity of PTPN2-deficient CD8+ T cells. Furthermore, expression of regulatory T cells was decreased in PTPN2-deficient mice, showing lower effector/memory T cells suppression in PTPN2fl/f-CD11cCre and PTPN2fl/f-CD4Cre mice compared to their littermate controls. Finally, PTPN2-deficient mice presented increased levels of the checkpoint marker PD-1 on T cells in the spleen, further displaying highly increased immune response.

Conclusion: Our results demonstrate an important *in vivo* role for PTPN2 in the pathogenesis of inflammation independent CRC. Loss of PTPN2 in either DCs or T cells exerts anti-tumour effects and ultimately results in lower colon tumour burden. This effect is likely mediated via promoting anti-cancer immune responses by modulating T cell activation, cytotoxicity and immune checkpoint molecules expression.

Disclosure: Nothing to disclose

P0451 CHARACTERIZATION OF A NEW BACTERIAL LIGAND FOR PPARγ

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Introduction: Data from clinical research suggest that certain probiotic bacterial strains have the potential to modulate colonic inflammation in patients with inflammatory bowel diseases. Nonetheless, this data differs considerably among studies due to the probiotic bacterial strains used and the poor knowledge of their mechanisms of action.

Aims & Methods: The aim of our study was to better characterize the mechanisms of the anti-inflammatory activity of Escherichia coli Nissle 1917 (EcN), a probiotic used for the treatment of multiple intestinal disorders. Lipids were extracted from pathogenic *Escherichia coli* (E. coli) strains UTI, Nu14, SP15, CFT, NC101, from an asymptomatic E. coli ABU, from a commensal E. coli M1/5 and from the probiotic EcN. Llipid extracts were analyzed by liquid chromatography coupled to high resolution mass spectrometry for identification and by liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS) for quantification. To assess the passage of 3-hydroxyoctadecaenoic acid (C18-3OH) across the intestinal barrier, we used caco2 cells

differentiated in transwell and colon biopsies in Ussing chambers. Time-resolved fluorescence resonance energy transfer (TR-FRET)-based competitive binding assay was performed to assess the C18-3OH agonist properties for the peroxisome proliferator activated receptor gamma (PPARγ). Mice received an oral administration of C18-3OH and were injected with a PPARγ antagonist (GW9662, IP). Concentration of C18-3OH and mRNA expression of genes dependent on the PPARγ activation (*Fiaf* and *Lfabp)* were quantified in mouse colons. In order to test the impact of the C18-3OH on colitis, mice have been submitted to DSS-induced colitis model and to oral administration of C18-3OH. Intensity of colitis was determined by the quantification macroscopic and microscopic scores, paracellular permeability, pro-inflammatory and pro-resolving lipids and mRNA expression of protein implicated in barrier functions (Zo1, Occludin, Muc2, ...), chemokines (Cxcl1, Cxcl2,...) and cytokines (IL6, IL1β, ...).

Results: In EcN, we identified and quantified free long chain fatty acids (LCFA) from 8 to 18 carbons hydroxylated on the 3rd carbon. The concentration of C18-3OH was increased in EcN compared to other E. coli strains. This bacterial lipid was not able to cross caco2 cells in transwell or tissue in Ussing chambers but penetrated the cells. The C18-3OH bonded the receptor-binding site of PPARγ. Oral administration of C18-3OH increased its concentration in the colon and increased *Fiaf* and *Lfabp* mRNA expression; treatment with a PPARγ antagonist inhibited these effects. C18-3OH treatment to mice with DSS-induced colitis significantly decreased paracellular permeability, colon thickness, macroscopic and microscopic scores and pro-inflammatory lipid concentration compared to DSS-treated mice. In addition, the C18-3OH decreased *Reg3γ, Zo1, Cxcl1 and Cxcl2* mRNA expression.

Conclusion: The bacterial lipids C18-3OH is a agonist of PPARγ. It could therefore represent a new mechanism of probiotics anti-inflammatory activities.

Disclosure: Nothing to disclose

P0452 GASTROINTESTINAL AND LIVER IMMUNE-RELATED ADVERSE EVENTS INDUCED BY INMUNE CHECKPOINT INHIBITOR: A DESCRIPTIVE OBSERVATIONAL STUDY

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Introduction: Immune checkpoint inhibitors (ICIs), such as anti-CTLA-4 and anti-PD-1 antibodies, are effective against several malignancies. They are associated with gastrointestinal and liver immune-related adverse events (GI-IrAEs and LI-IrAEs), which may be severe and lead to ICI discontinuation.

Aims & Methods: The aim of this study is to evaluate real-world data about the efficacy and gastrointestinal and liver toxicity of ICIs in several cancers among patients who have progressed on one or more prior lines of chemotherapy.

Methods: All patients with advanced cancers who received at least 1 molecular-targeted therapy after the failure of chemotherapy between May 2015 and September 2018 at our center were retrospectively assessed. Information about efficacy and toxicity was collected and analyzed. The grade of irAEs was defined based on the Common Terminology Criteria for Adverse Event (CTCAE) version 4.0.

Results: 132 patients who had received ICIs were included, 32% female, with mean age 66.3 (SD 10.4) years. Primary tumors were as follows: 86 (65.6%) non-small cell lung cancer; 30 (22.9%) melanoma; 12 (9.16%) kidney cancer; and 3 (2.29%) others tumors. ICIs therapy included atezolizumab (N=13), nivolumab (N=82), pembrolizumab (N=28), durvalumab (N=2), ipilimumab (N=1) and combined programmed cell death protein 1/cytotoxic T-lymphocyte-associated protein 4 antibodies (N=6). 19.6% of evaluable patients achieved a response. 51 (38.6%) patients developed any IrAEs. GI-IrAEs were observed in 17 (12.9%) patients: 9 grade 1, 6 grade 2 and 2 grade 3. 8 out 17 (47%) needed steroids and 1 patient needed surgery due to colonic perforation. 4 of 6 patients with combined treatment suffered from GI-IrAEs. No more treatment-related discontinuations or deaths occurred because of GI-IrAEs. LI-IrAEs were observed in 4 patients (3.03%), which all consisted of mild grade hepatitis (grade 1 and 2). 50% patients needed steroids and 1 patient stopped treatment. Any patient with combined treatment suffered from Li-IrAEs. IrAEs were no related with age or sex. IrAEs development did not predict response.

Conclusion: GI-IrAEs are among the most commonly encounter IrAEs, mainly with combination treatment. LI-IrAEs are rare. Both are potentially life-threatening events. Their management in a multidisciplinary approach will help to reduce morbidity and therapy interruptions.
Disclosure: Nothing to disclose

P0453 TOXIN A AND B COMBINED WITH GLUTAMATE DEHYDROGENASE IMMUNOASSAYS CAN SAVE TOXIGENIC CULTURE FOR THE DIAGNOSIS OF *CLOSTRIDIOIDES DIFFICILE* INFECTION

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Introduction: *Clostridioides difficile* infection (CDI) in adults is an important nosocomial intestinal infectious disease, which can be life-threatening. An efficient diagnosis of CDI is needed both for patient safety and for hospital cost saving. The stool toxin enzyme immunoassay (EIA) is a major method of laboratory rapid testing, however, its sensitivity is inadequate. On the other hand, the sensitivity of toxigenic culture (TC) or nucleic acid amplification test (NAAT) is excellent, however, it costs much and may overdiagnose CDI. The glutamate dehydrogenase (GDH) EIA is also reported as high sensitivity, but the significance compared with TC is not clear.

Aims & Methods: We performed a single-center prospective study to examine the effectiveness of EIAs detecting toxin A/B and GDH (C.DIFF QUIK CHEK, Alere), compared with selective anaerobic culture (cycloserin-cefoxitin mannitol agar; CCMA-EX, Nissui) as the reference method (TC). During the period from August 2012 to December 2013, the hospitalized patients with unexplained and newly onset watery diarrhea (defined as more than 3 stools/day) were included in the study. All the stool specimen was simultaneously tested by EIA and TC. For the positive selective culture plate, all the colonies in a single plate were picked up and suspended at once in saline, then applied to the toxin A/B EIAs. In this study, CDI was defined as positive with TC (both selective culture and toxin EIA).

Results: A consecutive 447 stool specimens were tested. Toxin A/B EIAs were positive for 62 samples (13.9%), and all of them were also positive with GDH and TC. Among the 385 specimens that were negative with toxin A/B EIAs, 35 samples (9.1%) were positive with GDH and also with TC. Twenty (57.1%) out of those 35 culture positive specimens were positive with toxin tests. There was no specimen that was positive in selective culture while the GDH test was negative. Accordingly, the prevalence of CDI was 18.3% in this study. The sensitivity of the rapid test only for toxin A/B was 75.6%, while the combination of GDH test resulted in the positive predictive value of 84.5% and the negative predictive value of 100%. This study also proved the GDH EIA to be equivalent to TC.

Conclusion: Our study indicated that the two-step combination of TC for the GDH negative stool samples is not needed. The combination rapid test for *Clostridioides difficile* GDH and toxins is useful that could save unnecessary TC costs. In accordance with the study, we have established the algorithms for CDI test (Figure 1). Patients positive with GDH while negative for toxin EIAs could be placed on preemptive contact precautions and could also be treated empirically until the results of TC are revealed. During the period from January 2014 to December 2018, 1442 stool specimens were tested, and 216 cases (15.0%) were diagnosed as CDI, without any nosocomial outbreak incident.

Disclosure: Nothing to disclose

P0454 EFFICACY OF MULTIPLEX STOOL PCR ASSAY FOR DETECTION OF ENTEROPATHOGENIC BACTERIA IN PATIENTS WITH ACUTE INFECTIOUS DIARRHEA

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Introduction: Bacterial infections are important cause of acute infectious diarrhea. Conventional stool culture and microscopic examination are time consuming and often lack sensitivity and specificity. Recently, there has been substantial development of multiplex molecular assays for the detection and identification of pathogens responsible for causing diarrhea.

Aims & Methods: In this study, we evaluated the efficacy of multiplex stool polymerase chain reaction (PCR) test in patients with acute infectious diarrhea. A total of 250 admitted patients with acute infectious diarrhea were recruited in Kangdong Sacred Heart Hospital from January 2016 to December 2018. Multiplex PCR detected 7 enteropathogenic bacteria including Salmonella, Campylobacter, Shigella, Escherichia coli O157:H7, Aeromonas, Vibrio, Clostridium difficile. We reviewed clinical and laboratory findings by stool multiplex PCR test and compared with those by stool culture.

Results: Mean age was 49.7±20.5 years and hospital stay was 7±10.5 days. Multiplex stool PCR test detected much more enteropathogens compared with stool culture (61.2% vs. 5.2%). Of culture-positive specimens, 4% of those were the same pathogens detected in multiplex PCR test. Stool multiplex PCR detected 88 Campylobacter, 46 E. Coli H7, 16 Clostridium, 11 Salmonella, 5 Aeromonas, 4 Shigella and 4 Vibrio. Campylobacter was the most common pathogen in stool PCR (88/250, 35.2%) and culture (4/10, 40%). Stool PCR-positive patients presented more fever >38°C [72/153 (47.1%) vs. 33/97 (34%), P=0.04] and higher C-reactive protein (CRP) at admission [100.9±79mg/L vs. 65.1±83mg/L, P=0.001] compared with PCR-negative patients.

Conclusion: Multiplex stool PCR test showed superior sensitivity to conventional culture for detection of pathogens in acute infectious diarrhea. Stool PCR result may be useful to predict clinical severity of infectious diarrhea.

Disclosure: Nothing to disclose

P0455 PROBIOTICS FOR THE PREVENTION OF CLOSTRIDIUM DIFFICILE INFECTION AMONG PATIENTS UNDERGOING ANTIBIOTIC THERAPY- PRELIMINARY RESULTS

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Introduction: *Clostridium difficile infection (CDI)*, is the leading cause of antibiotic-associated diarrhea (AAD), a disease which increased in incidence and severity over the last years. Antibiotics exposure is considered the most significant risk factor for *CDI among eldery and hospitalized patients*. Probiotics have been proposed for the prevention and treatment of a variety of gastrointestinal conditions, but guidelines do not recommend probiotic use for prevention of CDI (1). *The aim* of this study is to evaluate the efficacy of probiotics in preventing CDI.

Aims & Methods: We performed an unblinded, randomized, prospective study (October 2018- March 2019), in which 140 patients admitted in our department, who fulfilled the inclusion criteria and received antibiotics, regardless the indications, were included. Four arms of study were created: three probiotics and one group placebo. The patients received probiotics in less than 24 hours from the first antibiotic dose, during the treatment and 7 days after, according to their dose indication. Strains such as Lactobacillus, Clostridium Butiricum, Bacilus Mesentericus, Bifidobacterium and Streptococcus faecalis were used. Primary and secondary outcomes were frequency of AAD and CDI and adverse events.

Results: Out of 140 patients, 54 female and 86 male, mean age 63±12 years, mean hospitalization days 7.5±6.1. 35.5%(50/140) were on placebo and 64%(90/140) received probiotics. 16.4% received prophylaxis antibiotics. Among those with infection, the most frequent was urinary infection 28.2%. Other risk factors for CDI accounted were: use of proton pomp inhibitors 18.5%(26/140) patients, 46.4%(65/140) patients with age >65 years, liver cirrhosis 47.1%(66/140) patients.

13.5%(19/140) of patients developed antibiotic-associated diarrhea, 30%(15/50) patients from the placebo group and 4.4%(4/90) patients on probiotics (*p*< 0.0001). Out of 140 patients, 4.2%(6/140) were confirmed with CDI, 10%(5/50) patients from placebo group and only 1.1% (1/90) patient on probiotics (*p*=0.013). Patients exposed to antibiotics, without taking probiotics had a higher risk of CDI: OR=9.8 CI 95% (1.12-87) *p*=0.039. None of the patients reported adverse events.

Conclusion: The rate of antibiotic-associated diarrhea and CDI was significantly lower in the probiotics group, but further studies are requiered in order to determine the optimal strain.

References: Christine SM Lau and Ronald S Chamberlain. Probiotics are effective at preventing Clostridium difficile-associated diarrhea: a systematic review and meta-analysis. Int J Gen Med. 2016; 9: 27-37.Published online 2016 Feb 22. doi: 10.2147/IJGM.S98280

Disclosure: Nothing to disclose

P0456 EARLY CONTRAST-ENHANCED CT BEFORE COLONOSCOPY SIGNIFICANTLY IMPROVES THE RATES OF IDENTIFYING THE RESPONSIBLE DIVERTICULUM CAUSING COLONIC DIVERTICULAR BLEEDING AND ENDOSCOPIC HEMOSTASIS

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Introduction: Colonoscopy for colonic diverticular bleeding (CDB) within 24 hours after hematochezia is useful to make a diagnose and perform therapeutic intervention, but it has problems due to the necessity of pre-treatment and a low CDB identification rate. Intravenous contrast material-enhanced computed tomography (CT) before colonoscopy contributes to improvement of the rate of identifying stigmata of recent hemorrhage (SRH) compared with that by colonoscopy alone, but the timing of CT to improve the colonoscopic hemostatic rate has remained unclear.

Aims & Methods: We assessed the usefulness of performing contrast-enhanced CT early after the first hematochezia (within 6 hours) for CDB patients retrospectively. A diverticulum with active hemorrhage, blood clots, and an exposed hemorrhagic vessel was defined as the diverticulum responsible for CDB. The subjects were 146 CDB patients who visited our hospital between January 2012 and January 2018 and were examined by contrast-enhanced CT and then colonoscopy within 24 hours. For analysis, the Mann-Whitney U-test and chi-square test were used. Patients examined by contrast-enhanced CT within 6 hours and after 6 hours were designated as an early CT group (69 patients (47 %)) and elective CT group (77 patients (53%)), respectively. The treatment effectiveness of contrast-enhanced CT early after the onset of CDB was investigated.

Results: Ninety-nine patients (67.8%) were male and the mean age was 72 years old (37-96 years old). There was no difference in the characteristics between the early and elective CT groups. The extravasation-positive rate significantly improved in the early CT group compared with that in the elective CT group (49 vs. 27%, respectively; P=0.006). In addition, the colonoscopic hemostatic rate significantly improved in the early CT group compared with that in the elective CT group (32 vs. 13%, respectively; P=0.006). No adverse event after contrast-enhanced CT, such as contrast-induced nephropathy, occurred.

Conclusion: Early contrast-enhanced CT after the onset of CDB significantly improved the responsible diverticulum identification rate and colonoscopic hemostatic rate in the early CT group. By performing contrast-enhanced CT in the early phase, extravasation positivity served as an index to apply hemostasis to the responsible diverticulum, suggesting that the responsible diverticulum was safely and accurately identified by contrast-enhanced CT performed early after hematochezia, which significantly contributed to colonoscopic control of hemorrhage.

Disclosure: Nothing to disclose

P0457 BLOOD GROUP O IS AN INDEPENDENT RISK FACTOR FOR DELAYED POST-PROCEDURAL BLEEDING AFTER ENDOSCOPIC RESECTION FOR COLORECTAL TUMORS: A MULTI-CENTER CASE-CONTROL STUDY

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Introduction: Delayed post-procedural bleeding (DPPB) is a common adverse event after endoscopic resection (ER) for colorectal tumors and occasionally requires additional interventions. Recently, O blood group of ABO blood group system has been reported as a risk factor for various bleeding events, but the relationship with DPPB has yet to be investigated. This study aimed to evaluate if the O blood group would be relevant to DPPB.

Aims & Methods: This was a case-control study comparing cases who did and did not developed DPPB who underwent colorectal ER at four university hospitals between January 2014 and December 2017. We enrolled the consecutive patients who underwent colorectal ER using any of the following ER techniques (EMR, ESD, cold snare/forceps polypectomy, and hot snare/forceps polypectomy) during the study period. We excluded the patients whose ABO blood group was unidentified or who underwent procedures without interrupting antithrombotic agents. We reviewed medical records and the endoscopy database which included the following information: 1) ABO blood group, 2) age, 3) sex, 4) daily use of anti-platelets/coagulants, 5) size of resected tumors, 6) the number of resected tumors, 7) procedure. The control group consisted of all the patients who completed the treatment without DPPB. DPPB was defined as the occurrence of hematochezia or melena requiring blood transfusion or hemostatic intervention with colonoscopy, surgery, or radiology up to 28 days after endoscopic resection. Univariate and multivariate logistic regression analysis were performed to determine the risk factor for colorectal DPPB using the independent variables including ABO blood group.

Results: Among 10,253 consecutive patients who underwent colorectal ER, 1,628 patients (15.9%) were excluded according to the criteria for unidentified blood group (n=1,604) and/or continued antithrombotic agents (n=25). A total of 8,625 patients who met the eligibility criteria were enrolled in the analysis. Of the 8,625 patients, 6,111 (70.9%) were male; the age was 66.3 years ±11.4 (mean ± SD); the median number of tumors resected per patient was 2 (IQR, 1-3); the number of cases with a large lesion (≥20 mm) was 1,158 (13.4%). In total, 237 (2.75%) patients developed DPPB (the case group); 8,625 patients did not (the control group). In univariate analysis, O blood group was significantly related to increased risk of DPPB (odds ratio [OR], 1.57; 95% confidence interval [CI], 1.21-2.04; P=0.00079) equivalent to other known risk factors: younger age (< 60 years) (OR, 1.71; 95% CI, 1.31-2.24; P=0.000097), sex (male) (OR, 1.83; 95% CI, 1.32-2.55; P=0.00034), the number of tumors (OR, 1.44; 95% CI, 1.10-1.89; P=0.0088), tumor-size>2cm (OR, 1.90; 95% CI, 1.39-2.59; P=0.000057). In multivariate logistic regression analysis, O blood group remained as an independent risk factor for DPPB (adjusted OR, 1.57; 95% CI, 1.20-2.04; P=0.0009) (Table 1).

		Coefficient (β)	Standard error	Wald	Adjusted OR	95% CI	P-value
Age	< 60 years	0.626	0.143	4.39	1.87	1.41 - 2.47	0.000011
Sex	Male	0.565	0.171	3.31	1.76	1.26 - 2.46	0.00092
Use of antithrombotic agents	Yes	0.402	0.163	2.47	1.49	1.09 - 2.06	0.013
Blood group	O	0.448	0.135	3.32	1.57	1.20 - 2.04	0.00091
Number of polyps	≥ 2	0.448	0.147	3.05	1.57	1.17 - 2.09	0.0023
Tumor-size	≥ 20mm	0.577	0.193	2.99	1.78	1.22 - 2.60	0.0028
Procedure	ESD	0.490	0.302	1.63	1.63	0.90 - 2.95	0.104

[Table 1 : Multivariate analysis of risk factors for DPPB based on ABO blood group and other known factors]

Conclusion: The patients with O blood group were associated with an increased risk of DPPB. The pre-operative screening of ABO blood group may improve the preoperative risk assessment.

Disclosure: Nothing to disclose

P0458 EFFECTIVENESS OF TRANSCATHETER ARTERIAL EMBOLIZATION FOR COLONIC DIVERTICULAR BLEEDING

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Introduction: Colonic diverticular bleeding is the most common cause of acute severe lower gastrointestinal bleeding. Recently, it has been increasing with the aging of the population and the widespread use of antithrombotic drugs. Although it stops spontaneously in many cases, a small number of patients experience re-bleeding or shock. Persistent or acute massive bleeding with hemodynamic disorders sometimes requires an in-

terventional treatment. Persistent bleeding or acute massive of presenting with hemodynamic disorders requires an interventional treatment. In our institution, we perform transcatheter arterial embolization (TAE) for cases in which bleeding points are not able to be detected and cannot be treated successfully by endoscopic procedures.

Aims & Methods: The aim of this study is to evaluate the effectiveness of TAE for colonic diverticular bleeding.

The subjects are 21 patients who were diagnosed as colonic diverticular bleeding and were performed endovascular treatment in our institution from January 2006 to December 2018. We retrospectively evaluated patient characteristics and clinical outcomes, including success rates of hemostasis, transfusion requirement, early rebleeding, and complications.

Results: In all 21 patients, endoscopic hemostasis was difficult and early rebleeding developed. The median time of endoscopic procedures before TAE was 2 times. The hemostasis by arterial embolization was successful in 15 patients (71.4%), while the bleeding points could not be identified in 6 patients. In 11 cases (52.3%), an extravasation image was observed by angiography, and in all cases, hemostasis was succeeded by TAE.

In 4 cases no extravasation was found by angiography, but TAE was performed because an approximate bleeding point could be identified by CT and endoscopic findings. After TAE, no recurrence of bleeding were observed. In 2 patients (9.5%) intestinal ischemia was observed as adverse event and operation was performed.

Conclusion: TAE is effective treatment for colonic diverticular bleeding in which endoscopic hemostasis is not successful, or in massive bleeding.

Disclosure: Nothing to disclose

P0459 UTILITY OF SHOCK INDEX FOR RISK STRATIFICATION IN ACUTE LOWER GASTROINTESTINAL BLEEDING

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Introduction: Although the incidence of acute lower gastrointestinal bleeding (LGB) is increasing, the predictors of outcomes are not as well studied and defined as for acute upper gastrointestinal bleeding. Several risk scores have been developed over the past years in order to early stratify patients according to the risk of complications. The shock index (SI) score (heart rate divided by systolic blood pressure) is a simple tool that can provide an assessment of hemodynamic status.

Aims & Methods: The aim of this study was compare the utility of Shock Index (SI) for predicting outcomes: a) Transfusion, b) Treatment (endoscopic, vascular embolization or surgery), c) Clinical intervention (transfusion and treatment), d) Rebleeding, e) Readmission and f) Mortality in patients with LGB between scores used for risk prediction in upper gastrointestinal bleeding (Glasgow- Blachford Score (GBS) and Pre-endoscopic Rockall) and in LGB (Oakland, Strate, Velayos and Newman scores).

International Classification of Diseases, 9 Revision, Clinical Modification codes for admission diagnosis were used to identify retrospectively a cohort of patients with acute LGB from January 2013 to December 2017 hospitalized to a tertiary care, university-affiliated hospital. Data were extracted from the electronic clinical records of the Hospital. Area under the receiver operating characteristic (AUROC) curve were calculated for SI and the different risk scores for each outcomes. AUROCs were compared with the DeLong method by using STATA 14.1 software (StataCorp.2015).

Results: A total of 406 consecutive patients admitted with LGB were identified. Median age was 76.6 years (range 23-97), 277 (68.1%) of patients were older than 70 years, 219(53.8%) were men. Six (1.5%) died, 36 (8.8%) rebleeding, 20 (4.95) needed readmission, 110 (27%) needed transfusion, 52 (12.5%) needed treatment (48 endoscopic, 4 vascular embolization, 0 surgery). The most common source bleeding was diverticular 115 (28.3%). SI was not useful to predict any outcome (AUROC < 0.6). The SI was similar to the acute LGB scores for prediction rebleeding or readmission. The GBS and Oakland score was the best for predicting transfusion, need clinical intervention. All the risk scores were more accurate for determining need transfusion than need treatment or clinical intervention.

SCORE	TRANSFU-SION	TREATMENT	CLINICAL INTERVEN-TION	REBLEEDING	READMIS-SION	DEATH
SHOCK INDEX	0.58 (0.51-0.64)	0.49 (0.40-0.57)	0.55 (0.49-0.61)	0.58 (0.48-0.69)	0.57 (0.45-0.69)	0.58 (0.38-0.77)
GLASGOW-BLATCHFORD	0.89 (0.85-0.92)	0.65 (0.56-0.73)	0.82 (0.78-0.87)	0.72 (0.63-0.81)	0.70 (0.58-0.82)	0.76 (0.49-1.00)
PRE ENDOSC ROCKALL	0.70 (065-0.76)	0.56 (0.49-0.64)	0.68 (0.62-0.73)	0.68 (0.60-0.76)	0.63 (0.51-0.75)	0.82 (0.58-1.00)
OAKLAND	0.89 (0.85-0.93)	0.63 (0.55-0.72)	0.82 (0.77-0.86)	0.74 (0.65-0.83)	0.71 (0.59-0.83)	0.78 (0.63-0.93)
STRATE	0.67 (0.62-0.73)	0.60 (0.52-0.67)	0.65 (0.60-0.71)	0.67 (0.59-0.76)	0.70 (0.59-0.81)	0.56 (0.31-0.80)
VELAYOS	0.78 (0.74-0.82)	0.65 (0.57-0.73)	0.74 (0.70-0.79)	0.68 (0.60-0.76)	0.68 (0.57-0.79)	0.80 (0.67-0.92)
NEWMAN	0.78 (0.73-0.82)	0.64 (0.56-0.71)	0.75 (0.70-0.79)	0.68 (0.60-0.75)	0.67 (0.55-0.79)	0.78 (0.63-0.92)

[Table 1: AUROC and IC 95 % for shock index and risk scores]

Conclusion: SI was not useful to predict any outcome. Both Oakland Score and GBS were superior for predicting transfusion or clinical intervention. The GBS may be and useful tool for risk stratification in LGB. If can be used for as common score for predicting need of clinical intervention in upper and lower gastrointestinal bleeding. More precise prognostic scales are needed in LGB.

References: Tapaskar N, Jones B, mei S, Sengupta N. Comparaison of clinical prediction tools and identification of risk factors for adverse outcomes in acute lower gastrointestinal bleeding. Gastrointest Endosc. 2019 May;89(5). Ratra A, Rassameehiran S, Parupudi S, Nugent K. Utility of the Shock Index and Other Risk-Scoring Tools in Patients with Gastrointestinal Bleeding. South Med J. 2016 Mar;109(3):178-84.

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P0460 EFFECT OF WEEKEND HOSPITAL ADMISSION ON LOWER GASTROINTESTINAL BLEEDING OUTCOMES

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Introduction: "Weekend effect" refers to worse outcomes among patients presenting to the hospital on weekends. Many different processes are required in the management of patients with acute lower gastrointestinal bleeding (LGB). The availability of some of these procedures may be reduced on weekend. The weekend effect closely reflect the organizational level and performances of healthcare services under "off-hour" conditions, it can identify the possible deficiencies in functioning and the need for improvements. At present, it is not known whether there is a weekend effect in LGB.

Aims & Methods: The primary aim of this study is to investigate whether adverse outcomes for patients admitted with LGB differ depending on weekend versus weekday admission. The secondary aim was to determine whether any such differences are mediated by the timing of colonoscopy. International Classification of Diseases, 9th Revision, Clinical Modification codes for admission diagnosis were used to identify retrospectively a cohort of patients with acute LGB from January 2013 to December 2017 hospitalized to in a tertiary care, university-affiliated hospital. Data were extracted from the electronic clinical records of the Hospital. Time of admission was recorded defining weekend as midnight Friday to midnight Sunday. Hospital admissions on holydays no weekend were excluded. We used definition for adverse outcomes as the composite outcome: a) Transfusion, b) Treatment (endoscopic, vascular embolization or surgery), c) Clinical intervention (transfusion and treatment), d) Re-bleeding and f) Mortality in patients with LGB.

Our center has endoscopy available 24 hours a day, 7 days a week.

For discrete variables we tested for significant differences between groups with X2 tests If 25 %or more of cells had expected values less than 5; the

Fisher exact test was used.. For continuous variables we used t-test (two-tailed). P values < 0.05 were considered statistically significant. Statistical analysis was performed using STATA 14.1 software (StataCorp.2015).

Results: A total of 452 consecutive patients admitted with LGB were identified. Of these 348 (73.9%) were admitted during the weekday and 104 (23.1%) during the weekend. Compared to patients admitted on a weekday, weekend admissions had similar adverse outcomes, need transfusion similar, treatment or need clinical intervention and had similar re-bleeding and mortality in patients with LGB.

Results are resumed in Table 1.

	WEEKEND 104 (23%)	WEEKDAY 348 (73.9%)	P value
Age(years) (mean± sd)	72.1 (±14.6)	73.4 (± 13.8)	0.39
Gender (Female) (%)	47 (45.2)	167 (48)	0.62
Heart rate (mean ± sd) / Systolic blood pressure (mean±sd)	84.52(±17.2)/ 133 (±24.9	82.6 (±18) / 133.1(±25.7)	0.41 / 0.93
Antiplatelet /Anticoagulant	21(20.2) / 39(37.5)	74 (21.3) / 127(36.5)	0.84 / 0.82
Hemoglobin (gr/dl) mean (±sd)	120 (±26.5)	118 (±29.7)	0.59
Length of hospital stay (days) (mean ±sd)	8.38 (±7.7)	7.8 (±6.9)	0.6
Time to colonosocpy (days) (mean ±sd)	4.6 (±3.2)	4.5 (±2.6)	0.5
Adverse outcome (%)	33(31.7)	123(35.4)	0.49
Transfusion (%)	25 (24.0)	102 (29.3)	0.29
Treatment (%)	9 (8.7)	52 (14.9)	0.10
Clinical Intervention (%)	30 (28.8)	124 (35.6)	0.2
Rebleeding (%)	11 (10.6)	30 (8.6)	0.54
Severe Bleeding (%)	29 (27.9)	109 (31.3)	0.50
Death (%)	3 (0.9)	3 (2,9)	0.14

[Table 1: Characteristics and results of patients admitted for LGB on weekend and weekday]

Conclusion: The outcomes for patients admitted with acute lower gastrointestinal bleeding (LGB) no differ depending on weekend versus weekday admission. The timing of colonoscopy no differ on weekday versus weekend. This study was limited by being a single institution study, which could lead to a sampling bias. Our findings should be reevaluated in other healthcare systems under the same socioeconomic conditions.

References: Gupta A, Agarwal R, Ananthakrishnan AN. "Weekend Effect" in Patients With Upper Gastrointestinal Hemorrhage: A Systematic Review and Meta-analysis. Am J Gastroenterol. 2018 Jan;113(1):13-21.

Disclosure: Nothing to disclose

P0461 COMPLEX ANTITHROMBOTIC THERAPY IN PATIENTS WITH ACUTE LOWER GASTROINTESTINAL BLEEDING: CLINICAL OUTCOMES

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Introduction: The use of multiple antithrombotic medications, including anticoagulants and antiplatelet agents have been on the rise. When prescribed in dual or triple combinations, these regimens are considered complex antithrombotic therapies (CAT). CAT is frequent in patients with acute lower gastrointestinal bleeding (LGB). However, there is little data on the clinical course of patients undergoing CAT.

Aims & Methods: The aim os this study was to analyze the relationship of CAT (dual treatment: antiplatelet - anticcoagulant or antiplatelet - antiplatelet) and the adverse outcomes on patients with LGB.

International Classification of Diseases, 9th Revision, Clinical Modification codes for admission diagnosis were used to identify retrospectively

a cohort of patients with acute LGB from January 2013 to December 2017 hospitalized to in a tertiary care, university-affiliated hospital. Data were extracted from the electronic clinical records of the Hospital. The primary outcome studied was severe LGIB as defined
(1) continued bleeding in the first 24 hours of admission (transfusion ≥2 units of packed red blood cells and/or a decrease in hematocrit ≥20%) and/or
(2) recurrent bleeding after 24 hours of clinical stability (rectal bleeding accompanied by a further decrease in hematocrit ≥20% and/or additional blood transfusions and/or readmission for LGIB .Secondary outcomes included:
a) Re-bleeding,
b) Transfusion requirements,
c) Treatment (endoscopy, interventional radiology or surgery),
d) Readmission and
e) Death.
Re-bleeding was defined as
(1) clinically significant recurrent bleeding requiring repeat endoscopic or radiographic procedures (after initial colonoscopy) or
(2) additional blood transfusion requirements or
(3) a further decrease inhematocrit of 20% or more after a 24-hour period of stability after initial presentation.
For discrete variables we tested for significant differences between groups with X2 tests If 25 %or more of cells had expected values less than 5; the Fisher exact test was used. P values < 0.05 were considered statistically significant. Differences in outcomes were expressed in odds ratio (OR) with 95% confidence intervals (95%CI). Statistical analysis was performed using STATA 14.1 software (StataCorp.2015)
Results: A total of 471consecutive patients admitted with LGB were identified 417 (88.5 %) in not CAT group versus 54 (11.5%) in CAT group . Mean age was 76.8 years in CAT group versus 72.6 in not CAT group, 203 (48.7%) were men in not CAT group and 42 (77.8 %) in patients using CAT. The most common source bleeding was diverticular 114 (27.3%) in not CAT group and ischemic colitis 13 (24.1%) in CAT group. Outcomes of patients admitted for lgb (with CAT treatment versus without CAT treatment) are show in Table 1.

	WITH CAT 54 (11.5%)	WITHOUT CAT 417 (88.5%)	OR (95%IC)
SEVERE LGB	24 (44.4)	115 (27.8)	2.1 (1.18- 3.75)
TRANSFUSION	23 (42.6)	105 (25.2)	2.21 (1.23 - 3.95)
REBLEEDING	8 (14.3)	34 (8.2)	1.96 (0.86 - 4.49)
TREATMENT	10 (18.5)	50 (12)	1.67 (0.79 - 3.52)
READMISSION	8 (14.3)	12 (2.9)	5.87 (2.28 - 15.1)
DEATH	0 (0)	6 (1.4)	2.1 (1.18 - 3.75)

[Table 1: Outcomes of patients admitted for LGB (with CAT treatment versus without CAT treatment)]

Conclusion: Patients in CAT have a higher frequency of severe LGB ; transfusion and readmission compared to patients without CAT. No difference was found between them for re-bleeding, need for treatment and death.
References: Abraham NS, Hartman C, Richardson P, Castillo D, Street RL, Naik AD. Risk of Lower and Upper Gastrointestinal Bleeding, Transfusions, and Hospitalizations with Complex Antithrombotic Therapy in Elderly Patients. Circulation. 2013 Oct 22;128(17):1869-77.
Disclosure: Nothing to disclose

P0462 EPIDEMIOLOGY AND TIME TRENDS OF LOWER GASTROINTESTINAL BLEEDING – A POPULATION BASED COHORT STUDY OVER MORE THAN 30 YEARS

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Introduction: Gastrointestinal bleedings (GIBs) are acute events which are potentially severe but not always life threatening and often can be safely treated. There have been numerous studies reporting on the rates of GIBs associated with use of drugs mostly focusing on upper GIBs and data regarding lower GIBs (lGIBs) in the general population is limited

Aims & Methods: The aim of this study was to evaluate the incidence rates of lGIBs and the trends overtime in the general population of Finland. Data from participants of prospectively conducted population-based FINRISK health examination surveys was utilized for this study. FINRISK enrolled persons aged 25-74 years, recruited by random sampling from the population register, stratified by 10-year age group, sex and study area. The total number of participants in each survey was approximately 6000-8000. The participation rate in 1972 survey was >90% with a gradually declining trend to 57% in men and 67% in women in 2012. The follow-up took place using record linkage to the country-wide electronic health registers which included hospital discharge register and causes of death register. With the help of these national registers, the coverage of the follow-up was 100% for persons living in Finland. The follow-up period was from the enrollment up to the onset of an lGIB leading to hospitalization, death due to any cause, or end of the follow-up period which was December 31st, 2016. Participants with a history of GIBs before the baseline were excluded from the analyses. Incidence rates, recurrence rates (events recorded were >30 days apart), cause-specific mortality rates and 28-day case-fatality rates for lGIBs were calculated with 95% confidence intervals (CIs). The time-trends in event rates were calculated using a log-linear poison regression model adjusting for baseline age, gender, region, and the year of enrollment. Age standardization was conducted using weights from the European standard population
Results: A total of 71,068 participants were included in the study and they experienced 1750 incident lGIBs. The median age of participants experiencing lGIBs was 49.9 years and among the ones without GIBs it was 45.4 years. The age standardized incidence rates for lGIBs in males and females were 1.58 and 1.29 per 1000 py, respectively. Among men, there was a slight increase in the early 1990's but after that a constant decline ending at the level of about one-third of those in the late 1980's (ref. period). Among women, there was a steady decline over the years ending up to less than 15% of the rates in the late 1980's by the end of the study period in 2012-16. Among incident lGIBs, the recurrence rates of lGIBs in males and females were 11.4 and 11.1 per 1000 py, respectively. There was a substantial random variation in the proportion of recurrent lGIBs but in general an increasing trend was observed. Cause-specific mortality rates for lGIBs were the lowest in the study with 24 deaths. Cause-specific mortality rates in males and females were 0.01 and 0.03 per 1000 py, respectively. The 28 day case-fatality rates in males and females were 0.7% and 1.7%, respectively. Trends overtime of cause-specific mortality rates and case-fatality rates due to lGIBs could not be calculated due to the low number of cases
Conclusion: Overall, the age-standardized incidence rates of lGIBs are higher in males than in females. The rates of lGIBs have significantly decreased since the late 1980's. The mortality rates due to lGIBs were in general low but tended to be higher in females compared to males
Disclosure: Pareen Vora is an employee at Bayer AG, Berlin Germany; Gunnar Brobert is an employee at Bayer AB, Solna, Sweden; Veikko Salomaa has participated in a conference trip sponsored by Novo Nordisk and received a honorarium for participating in an advisory board meeting (unrelated to the present study). Veikko Salomaa and Arto Pietilä has ongoing research collaboration with Bayer AG.

P0463 PROSPECTIVE EVALUATION OF GASTROINTESTINAL BLEEDING IN PATIENTS UNDER DIRECT ORAL ANTICOAGULANT THERAPY: A REAL-WORLD STUDY

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Introduction: Gastrointestinal bleeding (GIB) is a common adverse event associated to anticoagulant therapy. Pivotal clinical trials have shown that compared to warfarin, direct oral anticoagulants (DOACs) have a similar efficacy to prevent thromboembolic complications, but with higher rates of GIB. However, real-world studies are needed to assess the risk and severity of GIB in patients under direct oral anticoagulant therapy.

Aims & Methods: We aimed to analyse the severity of GIB with DOACs, compared to vitamin K antagonists (VKAs) in patients admitted to the emergency department with GIB who were under anticoagulant therapy. Patients under anticoagulant therapy admitted to the emergency department with GIB were prospectively recruited from July 2016 to January 2018. Inclusion criteria were patients with non-valvular atrial fibrillation (NVAF) or thromboembolic disease treated with DOACs, and patients with AF of any cause, mechanical heart valve or thromboembolic disease treated with VKAs. Patients under heparin therapy were excluded. Clinical presentation, the need for blood transfusion, length of hospital stay, and results of endoscopic and radiologic studies were recorded. Severity of the bleeding episode was defined though the International Society of Hemostasis and Thrombosis (ISTH) scale. Patients were followed up until discharge or death.

Results: Throughout the study, a total of 208 events of GIB were documented in 178 patients: 119 events under AVKs, and 89 events under DOACs (Apixaban=36, Rivaroxaban=29, Dabigatran=19 Edoxaban=5). Female sex was more prevalent in both groups (54% in the VKA group and 59% in the DOAC group). Mean age in both groups was similar (VKAs: 78.6±0.9 years, DOACs: 80.2±0.7 years, p= ns). CHADsVASC score and previous history of GIB were similar in both groups, although a higher prevalence of chronic kidney disease in the AVK group was observed (p= 0.009) while a higher prevalence of chronic cerebrovascular disease was seen in the DOAC group (p= 0.024). Concomitant anti-platelet therapy was 16% in the VKA group, and 24.7% in the DOAC group (p= ns). Clinical presentation was lower GIB in 52.9% of the VKA group patients and 53.9% in the DOAC group (p=ns). According to ISTH, major bleeding was the most frequent in both groups (VKAs: 77.3%, DOACs: 82%; p=ns). Mean hemoglobin on admission was 10±0.5 g/dL in the VKA group, and 10.1± 1 g/dL in the DOAC group (p=ns). Decrease of hemoglobin compared to last known value was 2.7±0.2 g/dL in the VKA group, and 3±0.2 g/dL in the DOAC group (p=ns). The mean number of packed red blood cells transfused was similar in both groups (2.26 ± 0.23 in VKA group, and 2.30 ± 0.28 in DOAC group (p=ns). No differences were observed in the length of hospital stay between groups.

Conclusion: Gastrointestinal bleeding severity is similar in patients taking DOACs when compared to patients under VKAs therapy. Future studies with a higher number of patients are needed to confirm our data.

Disclosure: Nothing to disclose

P0464 SILENCING OF MBD2 AND EZH2 INHIBIT THE PROLIFERATION OF COLORECTAL CARCINOMA CELLS BY RESCUING THE TRANSCRIPTION OF SFRP

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Introduction: The Secreted frizzled related proteins (SFRPs) is an extracellular inhibitors of wnt pathway signaling and was found to be underexpressed in the early stage of colorectal tumorigenesis due to hypermethylation of the promoter. MBD2 and EZH2 are core members of MBD and PCG protein families respectively, which have been known as crucial proteins of epigenetic regulation.

Aims & Methods: The aim of this study is to figure out the potential role of MBD2 and EZH2 proteins in colorectal cancer (CRC) and its effects on the transcription of SFRP. The mRNA expression of SFRPs in CRC and adjacent noncancerous tissues are analyzed by bioinformatics. Real-time quantitative polymerase chain reaction (qRT-PCR) and western blot were used to detect the expression of MBD2, EZH2 and SFRPs in CRC cell lines and human normal intestinal mucosa cell NCM460. We knockdown of MBD2 and EZH2 using small interfering RNA (siRNA) to clear its role in the regulation of SFRPs gene expression. The function of MBD2 and EZH2 in cell proliferation, cycle, apoptosis and invasion was examined in CRC cell lines.

Results: The mRNA expression level of SFRPs was significantly decreased in CRC tissues and cell lines compared to adjacent tissues and NCM460 (P< 0.05). However, the mRNA level of EZH2 and MBD2 were highly expressed in CRC cell lines (P< 0.05). In SW480 cell, interference with MBD2 could reactivate the expression of SFRP1 (P< 0.05), but interference with EZH2 could not reactivate it (P>0.05); Interference with EZH2 could reactivate the expression of SFRP2, SFRP4 and SFRP5 (P < 0.05), but interference with MBD2 could not activate it. In HCT116 cell, interference with MBD2

could reactivate the expression of SFRP1 (P< 0.05), but interference with EZH2 could not reactivate it (P>0.05). However, in SW480 and HCT116 cells, interfering with MBD2 and EZH2 at the same time was more effective than interfering one of them alone in restoring the expression of SFRP1, SFRP2, SFRP4 and SFRP5 genes (P < 0.05). We found that compared with interfering with MBD2 or EZH2 alone, interfering with MBD2 and EZH2 together could significantly inhibit the proliferation, migration and invasion of CRC cells. Flow cytometry analysis showed that simultaneous interference with MBD2 and EZH2 in SW480 cell was more effective than interfering with MBD2 or EZH2 alone in blocking cell cycle and causing more cells to stagnate in S phase (P < 0.05); however, in HCT116, compared with interfering with MBD2 or EZH2 alone, more cells stagnated in G0/G1 phase when interfering with MBD2 and EZH2 at the same time (P < 0.05). In addition, compared with interfering with MBD2 or EZH2 alone, interfering with MBD2 and EZH2 in SW480 and HCT116 cells together could remarkably increase apoptosis (P < 0.05).

Conclusion: Compared with silencing MBD2 or EZH2 alone, silencing MBD2 and EZH2 can inhibit the proliferation of CRC cells by restoring the expression of SFRP more effectively. MBD2 and EZH2 may be potential therapeutic targets for colorectal tumors, however, the regulatory mechanism of SFRP remains to be further studied in the future.

Disclosure: Nothing to disclose

P0465 SILYMARIN, BOSWELLIC ACID, CURCUMIN AND MALTODEXTRIN ENRICHED DIETETIC FORMULATION REDUCES THE GROWTH OF INHERITED INTESTINAL POLYPS IN AN ANIMAL MODEL

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Introduction: Colorectal cancer (CRC) is the conclusive result of a multi-step phenomenon that, in most cases, goes through the adenoma-carcinoma sequence pathway. Some substances of plant origin have been reported to exert an effect in reducing intestinal neoplasm development, especially in animal models. In detail, silymarin, a phytoestrogen compound derived from milk thistle (*Silybum marianum*) may decrease intestinal carcinogenesis through both anti-oxidant and estrogen receptor-beta agonist properties. Previous studies have shown that silymarin is able to hamper intestinal carcinoma (IC) development in Apc[Min/+] mice and familial adenomatous polyposis patients with ileal pouch-anal anastomosis. *Boswellia serrata* is a plant with anti-inflammatory properties. Interestingly, boswellic acids, especially Acetyl-11-Keto-beta-Boswellic Acid (AKBA), a component of the gum resin of *Boswellia serrata*, has been recognized as a promising agent for the prevention of intestinal tumorigenesis in a mouse model of inherited carcinogenesis, i. e. APC multiple intestinal neoplasia (min) animals

Aims & Methods: Our aim was to assess whether an enriched nutritional formulation with anti-carcinogenetic properties may prevent inherited intestinal cancer (IC) in animal model.

Eighty male mice were used (40 wild type for diet safety test and 40 adenomatous polyposis coli multiple intestinal neoplasia ApcMin/+). Forty ApcMin/+ mice were divided into two groups: 20 standard and 20 enriched diet. At the100th day, colonoscopy was performed, then animals were sacrificed after 10 days. In each group, four subgroups received intraperitoneal bromodeoxyuridine (BrdU) injection. We evaluated: lesion number/size, histological inflammation/dysplasia/neoplasia, pro-inflammatory cytokine mRNA expression, BrdU/TUNEL.

Results: No mice died during the safety test. Compared to standard, enriched diet reduced solid lesion total number (203 versus 416) and mean number±SD/animal (12.6±5.0 versus 26.0±8.8;p< 0.001). In enriched diet group a reduction in polyp size was observed (p< 0.001). Histological inflammation and pro-inflammatory cytokine expression were similar. Low grade dysplasia (LGD;p< 0.001) and intestinal carcinoma (IC;p< 0.001) areas were decreased in enriched diet. IC was observed in 100% in standard and 85% in enriched formulation assuming animals. Enriched diet showed higher epithelial proliferation/migration and increased apoptosis in normal mucosa and LGD areas (p< 0.001).

Conclusion: Our results are promising for a chemo-preventive synergic effect of enriched formulation in inherited IC.
Disclosure: Nothing to disclose

P0466 MICRORNA 375 REGULATES PROLIFERATION OF COLORECTAL CANCER CELLS BY SUPPRESSING THE MTDH EXPRESSION

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Introduction: MicorRNAs play important roles in the pathogenesis of human diseases by down-regulation of target genes in various cells or tissues. We have previously identified MicoRNA 375 (MIR375) as a colorectal cancer associated microRNA. It is significantly down-regulated in human colorectal cancer tissues. The putative MIR375 target genes were also identified by comparing the mRNA microarray analysis data of MIR375-overexpressing cells with the candidate MIR375 target genes predicted by public bioinformatic tools.
Aims & Methods: The purpose of this study is to determine the correlation between the MIR375 and its novel target gene, metadherin (MTDH), in human colorectal cancer cells and tissues. A luciferase reporter system was used to confirm the effect of MIR375 on MTDH expression. Protein or mRNA expression of the target gene and associated molecules were by western blot or qRT-PCR, respectively. Cell proliferation assays were employed using an EZ-Cytox cell viability assay kit. And flow cytometry was used to compare cell cycle progression.
Results: MTDH is a direct target gene of MIR375. MTDH mRNA and protein expression levels were directly down-regulated by MIR375 mimic transfection. We observed that MIR375 down-regulated the several MTDH-mediated pathways which include PIK3CA, NFκB and BRAF-MAPK-CTNNB1 in colorectal cancer cells. Our results showed that the cell proliferation and angiogenesis in colorectal cancer cells were regulated by MIR375.
Conclusion: Our results indicate that MTDH is a direct target of MIR375 in human colorectal cancer cell lines, and suggest that the down-regulation of MIR375 modulates MTDH signaling pathways in human colorectal cells and tissues. Thus, MIR375 may have a therapeutic value in relation to human colorectal cancer.
Disclosure: Nothing to disclose

P0467 HERV-HX, A NEW HUMAN ENDOGENOUS RETROVIRUS GENE, PROMOTES COLORECTAL CANCER GROWTH AND METASTASIS BY ACTIVATING WNT/β-CATENIN SIGNALING

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Introduction: Human endogenous retroviruses (HERVs) are human DNA sequences that are homologous to exogenous retroviruses. Accumulating evidence has highlighted the close correlation between colorectal cancer (CRC) and HERVs [1]. In a previous study, we identified and designated a new H family HERV (HERV-H) gene, HERV-HX, which is actively expressed in CRC tumor tissues as compared to adjacent normal tissues [2]. However, the functional and clinical significance of HERV-HX remains unexplored.
Aims & Methods: This study aimed to elucidate the biological function, molecular mechanism and clinical significance of HERV-HX in CRC. HERV-HX expression was assessed by TaqMan probe RT-qPCR and in situ hybridization. siRNA specifically targeting HERV-HX and expression vector carrying the ORF of HERV-HX were used for the loss- and gain-of-function assays in different CRC cells. The biological functions of HERV-HX were determined by cell viability assay, colony formation, wound-healing migration and matrigel invasion assays, cell cycle and apoptosis flow cytom-

etry, Ki-67 and TUNEL staining. Effects of HERV-HX on tumorigenicity and metastasis *in vivo* were assessed using subcutaneous xenograft and tail vein injection models respectively. Protein levels were assessed by western blot and immunostaining. Protein localization was investigated by immunofluorescence staining and western blot. Molecular mechanism was investigated by RNA sequencing and pathway luciferase reporter assays.
Results: HERV-HX was specifically upregulated in cell lines of colon cancer but not other cancer types, and was significantly upregulated in CRC tumors as compared to adjacent normal tissues (*P*< 0.0001). HERV-HX expression was not associated with age, gender, lesion location, but was positively associated with TNM staging (rho=0.721, *P*=0.0004). HERV-HX expression was significantly higher in samples with *vs* without lymph node or distant metastasis (*P*< 0.0001), while no significant difference was found between TNM stage I and II or between III and IV cases.
Knockdown of HERV-HX in HT29 and LoVo cells significantly suppressed cell viability and colony formation, induced apoptosis and cell cycle arrest, and inhibited migration/invasion ability. Conversely, overexpression of HERV-HX in SW480 and HCT116 cells produced opposite effects. HERV-HX expression significantly promoted tumorigenicity and also increased metastases to the lung and/or liver *in vivo* (overall metastatic rates: 53% in HERV-HX group *vs* 28% in control group).
In concordance with the growth- and migration-promoting effects of HERV-HX, protein levels of cell cycle markers (p21, p27, cyclin D1 and CDK4), apoptosis markers (cleaved forms of caspase-8, caspase-9, caspase-3 and PARP), the proliferation marker PCNA and epithelial-mesenchymal transition markers (E-cadherin, N-cadherin, β-catenin, Vimentin, Slug and Snail) were significantly altered following knockdown or overexpression of HERV-HX. HERV-HX significantly activated Wnt/β-catenin signaling as indicated by the increased TOP/FOP luciferase activity. Importantly, examination in cells, subcutaneous xenografts and liver/lung metastatic nodules showed that HERV-HX increased the total level and nuclear translocation of β-catenin by inhibiting its phosphorylation.
Conclusion: Upregulation of HERV-HX plays a pivotal role in tumor progression and metastasis of CRC. HERV-HX inhibits phosphorylation-mediated degradation of β-catenin, causes its cellular accumulation and nuclear translocation, and subsequently activates Wnt/β-catenin signaling to promote colorectal tumorigenesis.
References: 1. Mengwen Zhang, Jessie Qiaoyi Liang, Shu Zheng. Expressional activation and functional roles of human endogenous retroviruses in cancers. Rev Med Virol. 2019 Mar;29(2):e2025. doi: 10.1002/rmv.2025. 2. Jessie Qiaoyi Liang, Jiayi Ding, Rongzhen Xu, Zefeng Xu, Shu Zheng. Identification of a novel human endogenous retrovirus and promoter activity of its 5' U3. Biochem Biophys Res Commun. 2009 May;382 (2):470-4. doi: 10.1016/j.bbrc.2009.03.058.
Disclosure: Nothing to disclose

P0468 ABROGATION OF EMILIN1 GC1Q-α4β1 INTEGRIN INTERACTION AFFECTS EXPERIMENTAL COLITIS AND COLON CARCINOGENESIS ENHANCING LYMPHATIC DYSREGULATION AND INFLAMMATORY CASCADE

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Introduction: Colon cancer is one of the principal types where a functional link between inflammation, tumor microenvironment and progression had been noted; colitis-associated cancer is also related to striking changes in the lymphatic vasculature and dysfunction in the intestinal lymphatic network is a well-established feature of human inflammatory bowel disease. The ECM protein EMILIN1 is expressed, among several other tissues, in the normal colonic mucosa; it controls elastogenesis, blood pressure homeostasis and is a key structural element in the maintenance of the integrity of lymphatic vessels. It is an adhesive ligand of α4/α9β1 integrins via its gC1q domain and this interaction down-regulates cell proliferation. The aim of this project is to analyze the possible role of EMILIN1 in inflammatory colon cancer.
Aims & Methods: The impact of intestinal inflammation and carcinogenesis was analysed in *Emilin1^{-/-}* (KO) and E933A EMILIN1 transgenic mice (E933A TG), in which a mutant EMILIN1, unable to be engaged by α4β1,

is deposited. Chronic colitis was induced treating mice with 2% DSS in the drinking water; colon tumours were induced with a single injection of AOM followed by three 1-week exposures to 2% DSS. Colitis and tumour growth were analysed over time by endoscopy; clinical scoring of colitis was performed applying the MEICS and DAI indexes.

Results: KO and E933A-TG presented higher colitis scores and more severe mucosal injury, fibrosis and inflammatory infiltrates than WT. RNAseq analysis confirmed the up-regulation of several inflammatory response genes and the down-regulation of cell-cell adhesion molecules in E933A-TG. KO and E933A-TG mice had also higher tumour incidence, bigger adenomas and less survival. Whole-mount analyses on colon specimens demonstrated that both KO and E933A-TG lymphatic vessels are irregular, dilated and characterized by dysmorphic structures and wide lacunae. This abnormal network architecture leads to enhanced lymphatic dysregulation, decreased lymph flow and impaired inflammatory cell drainage, providing a possible explanation for the reduced inflammatory resolution observed in KO and TG models.

Conclusion: Overall these data demonstrate that EMILIN1 by virtue of its multifaceted functions is centrally located in the context of the development and progression of inflammatory colon cancer. The integrity of EMILIN1 is necessary to control proliferation and to guarantee the regeneration of competent and well functioning lymphatic vasculature .

Disclosure: Nothing to disclose

P0469 STUDIES ON PROTEASE-ACTIVATED RECEPTOR-DEPENDENT REGULATION OF COLON STEM CELLS WITH THE ORGANOID MODEL

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Introduction: Stem cells of the colon epithelium are dysregulated in chronic inflammatory diseases such as ulcerative colitis and colorectal cancer, both pathologies with high incidence in the population. In order to better understand the pathophysiology of those diseases, we used the organoid model to study stem cell functions and demonstrated the critical roles of protease-activated receptors (PAR_1, PAR_2, PAR_3) in stem cell regulation.

Aims & Methods: Colon crypts were isolated from WT or PAR KO male and female mice. Crypts were cultured in 3D conditions as organoids (colonoids) for one week. From day 2 to day 6 of culture, PARs were activated by specific agonist peptides. Number and size of colonoids were measured to analyze survival and proliferation of colon stem cells. Expression of PARs and key signaling molecules were studied by qRT-PCR and immunolabeling.

Results: The PAR activation by specific agonist peptides differently influenced stem cell proliferation. While PAR_1 promoted stem cell proliferation, PAR_2 was found to slow down this process. Interestingly, PAR_2 was highly expressed in colon primitive cells from male mice compared to females. Its brake on cell proliferation was specific of male sex since, in females, stem cell proliferation was increased by both PAR_1 and PAR_2 activation. This sexual dimorphism was linked to the PAR_2-dependent expression of genes implicated in stem cell proliferative pathways. The Glycogen Synthase Kinase 3beta (GSK3beta) plays a critical role in stem cell behavior and has been implicated in colon inflammation and cancer. Using PAR_2 or PAR_3 KO mice, we found its activation under the control of PAR_2 and PAR_3 and critical for male stem cell survival. Finally, better recovery of passaged male colonoids (further improved by PAR_2 activation) and of primitive sorted male cells as colonoids suggested that male stem cells have higher resistance capacities compared to females.

Conclusion: Our results demonstrate that PAR_1, PAR_2 and PAR_3 play specific roles in colon stem cell regulation that could be targeted in anti-inflammatory and anticancer therapies. Work is ongoing to determine the fine impact of PARs on stem cell differentiation and the implication of specific proteases in colon stem cell regulation.

Disclosure: Nothing to disclose

P0470 MIRNAS AS MOLECULAR PREDICTORS OF RESPONSE TO CHEMORADIOTHERAPY IN RECTAL CANCER

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Introduction: Colorectal cancer (CRC) is the main tumour-related cause of death worldwide, being the third most common cancer, with rectal adenocarcinoma accounting for almost one-third of all CRC [1]. Treatment of advanced rectal cancer consists mainly in pre-operative chemoradiotherapy (CRT), a strategy that not always induces tumour response and that decreases the quality of life of patients [2]. In addition, there is no available method to determine whether a patient will benefit from CRT, with all patients receiving the same therapy regardless of its outcomes. Therefore, the possibility to predict disease progression and response of patients to CRT would allow its selective use, thus avoiding toxicity and associated morbidity in non-responders. In this sense, microRNAs (miRNAs) with a role in the pathogenesis of CRC, may function as regulators of tumour response to therapy and are being increasingly evaluated as potential diagnostic, prognostic and predictive biomarkers of response to therapy [3].

Aims & Methods: The aim of this work was to identify miRNAs as potential biomarkers of disease progression and pre-CRT predictors of pathological response in rectal cancer. Using a targeted approach, the expression profile of single miRNAs (miR-16-5p, miR-145-5p, miR-335-5p, miR-135b-5p and miR-21-5p) was analysed in 94 patients with locally advanced rectal cancer. 14 were identified as pathological complete responders (pCR) and 80 as pathological incomplete responders (pIR). Total RNA was isolated from normal (adjacent non-tumour) and tumour rectal samples tissues collected before and after long course CRT by biopsy and protectomy, respectively. The miRNA expression profile was analysed by Real Time-PCR using TaqMan® Advanced miRNA assays. miR-484 was used for normalization.

Results: In pIR patients, miR-21-5p demonstrated higher expression ($p \leq 0.05$) in pre-CRT tumour tissue when compared with pre-CRT normal tissue and the same expression profile was observed in post-CRT samples ($p \leq 0.01$). In addition, a similar expression profile was observed in miR-135b-5p analysis, with higher levels of miR-135b-5p in pre- and post-CRT ($p \leq 0.001$) tumour samples when compared with normal samples. On the contrary, the expression profile of both miR-21-5p and miR-135b-5p showed the opposite tendency in pCR patients, with similar or lower miRNAs levels in pre-CRT tumour samples comparing with normal tissue. This suggests that a lower tumour expression of these miRNAs prior to pharmacological intervention could be indicative of a better response to treatment, which is also in line with the well-described oncogenic role of miR-21 and miR-135. On the other hand, no significant differences were observed in the expression profiles of miR-16-5p, miR-145-5p and miR-335-5p between pIR and pCR patients.

Conclusion: This work highlights that miRNAs are differentially expressed between pre- and post-CRT normal and rectal cancer tumour samples. Among the evaluated miRNAs, miR-21-5p and miR-135b-5p appear to be the most promising predictors of pre-treatment pathological complete response and may provide new insights for consolidating discovery of biomarkers of response to treatment.

References: 1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global Cancer Statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68: 394-424. 2. Li Y, Wang J, Ma X, Li T, Yan Y, Xue C, et al. A review of neoadjuvant chemoradiotherapy for locally advanced rectal cancer. Int J Biol Sci. 2016, 12: 1022-1031. 3. Zhu Y, Peng Q, Lin Y, Zou L, Shen P, Chen F, et al. Identification of biomarker microRNAs for predicting the response of colorectal cancer to neoadjuvant chemoradiotherapy based on microRNA regulatory network. Oncotarget. 2016;8: 2233-2248.

Disclosure: Nothing to disclose

P0471 A GENE PANEL DERIVED FROM GASTRIC CANCER TRANSCRIPTOME ANALYSIS DISCRIMINATES COLONIC POLYPS

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Introduction: There is ongoing debate about factors that drive pathogenesis of different types of colonic polyps. Several studies have reported an enrichment for stomach-specific genes in sessile serrated lesions in the right colon.

Aims & Methods: Aim of the present study was to assess if a gene-panel derived from analysis of upper gastrointestinal cancers can discriminate different phenotypes of colonic polyps.RNA was extracted from 64 colonic samples collected as part of the S:CORT study. This comprised 15 sessile serrated lesions (SSL), 15 tubulo-villous adenomata from the proximal (right) colon (p-TVA), 14 from the distal (left) colon (d-TVA), 10 tubolo-sessile adenomata (TSA), and 5 biopsies each from normal colonic mucosa adjacent to tubolo-villous and to tubolo-serrated adenomata. RNA-Sequencing was performed for transcriptome analysis. Data were logarithmised, and 66 genes have been selected that have been identified in a previous study applying an unsupervised stratification to distinguish phenotypes of oesophago-gastric adenocarcinomas.

Results: Stratification of the colonic samples according to expression of the 66 genes was done by using the mclust algorithm on R. This revealed a distribution into 4 separate groups. The "normal" samples from non-polypoid mucosa clustered in group 3 (100.0%), without any of the polyp samples being represented in this group. SSL clustered in group 4 (86.7%), whereas both p-TVA and d-TVA clustered in groups 1 (64.3%, 46.7%, resp.) and 2 (35.7%, 53.3%, resp). TSA were mainly represented in group 1 (80.0%), together with a subgroup of d-TVA and p-TVA. The phenotype distribution was confirmed in the principle component analysis with the first principle component being dominated by gastric genes (TFF2, MU-C5AC, CTSE, CA2) and the second principle component by intestinal genes (CDX2, PHGR1) as well as genes involved in epithelial cell-cell interaction such as CLDN15 and A1CF. Phenotypic discrimination was further assessed by Fisher's exact test revealing highly significant association of the distribution given by the 66 genes and histopathology results (P< 0.00001).

Conclusion: A gene panel derived form upper GI adenocarcinoma can successfully stratify phenotypes of colonic polyps. This indicates common denominators that are involved in gastrointestinal carcinogenesis, most likely luminal pathogens. SSL, TSA and TVA in the colon can be discriminated by their transcriptome profile. TSA cluster with TVA, not with SSL. There does not seem to be a difference between classic tubulovillous adenomata of proximal and distal location, but but they cluster with a subgroup of tubolosessile adenomata. Prospective validation of the key markers for immuno-histochemistry is ongoing.

Disclosure: Nothing to disclose

P0472 WITHDRAWN

P0473 LINC00152 CONTRIBUTES TO THE PATHOGENESIS OF COLORECTAL CANCER THROUGH PROMOTING CELL PROLIFERATION VIA MULTIPLE MOLECULAR PATHWAYS

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Introduction: Long non-coding RNAs (lncRNAs) contribute to pathomechanism of various cancers including colorectal cancer (CRC). Altered LINC00152 expression in CRC was reported, but its exact localization and detailed role in CRC formation and progression are not well studied.

Aims & Methods: We aimed to evaluate the effects of LINC00152 silencing on whole transcriptome in colon carcinoma cells and to analyze the DNA methylation alterations caused by LINC00152 knockdown. Tissue localization of LINC00152 was investigated by using *in situ* hybridization (ISH). LINC00152 were silenced in SW480 colon carcinoma cells using Stealth siRNAs. Flow cytometric cell cycle analysis was performed using propidium-iodide DNA staining. The effect of LINC00152 silencing to genome-wide gene expression was studied on Human Transcriptome Array 2.0 microarrays. The expression of selected proteins was determined using western blot. DNA methylation alterations after LINC00152 knockdown were evaluated using Reduced Representation Bisulfite Sequencing (RRBS) method.

Results: Using ISH, elevated LINC00152 expression was found in both epithelial and stromal cells of CRC tissue samples. Silencing of LINC00152 significantly suppressed cell growth compared to negative control cells and caused approximately two-fold increase in apoptosis (p< 0.05). Whole transcriptome analysis of LINC00152 silenced cells revealed significant underexpression of genes with oncogenic and/or metastasis promoting function (e.g. STC1, YES1, HES1, KLK6, PORCN) and upregulation of tumor suppressor genes (e.g. DKK1, PERP) (FDR p< 0.05, abs. value of logFC>1). Knockdown of LINC00152 significantly reduced the cyclin D1 expression without attenuation of phospho-S6 protein (p< 0.05). The decreased expression of PORCN and YES1 in LINC00152 silenced cells was also confirmed at protein levels. DNA methylation alterations after LINC00152 silencing could be genome-widely detected by RRBS including hypomethylation in SFRP4 and ALDH1A3 gene promoters.

Conclusion: Our results indicate that LINC00152 lncRNA can contribute to CRC pathogenesis by promoting cell proliferation through upregulation of several oncogenes/metastatic genes in WNT, PI3K/Akt, Notch and TP53 pathways and of cyclin D1 cell cycle progression gene, furthermore, by affecting the promoter methylation status of certain CRC associated genes.

Disclosure: Nothing to disclose

P0474 FAECAL IMMUNOCHEMICAL TESTING IN PATIENTS WITH RECTAL BLEEDING: A WASTE OF TIME?

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Introduction: The faecal immunochemical test (FIT) can be used to rule out bowel cancer. Patients with rectal bleeding (RB) have been recommended not to be tested with FIT due to concerns of a high false positive rate. This study aimed to investigate the positivity rate and diagnostic accuracy for colorectal cancer of FIT in patients with rectal bleeding.

Aims & Methods: Patients referred from primary care in England with symptoms of suspected bowel cancer according to NICE NG12 guidelines were recruited in a prospective, ethics-approved, multicentre, diagnostic test of accuracy study, and were tested with FIT prior to colonoscopy. FIT samples were processed on the HMJACK-arc analyser. Patients were then split into groups, based on the presence or absence of RB symptoms. Faecal haemoglobin (FHb) levels and colonoscopy findings in each group were analysed. Cutoffs of FHb were set at the limit of detection, calibrated at 2ug blood per gram of faeces (ug/g), and the limit of quantification, calibrated at 10ug/g. Statistical analysis was performed on Stata using the Kruskal-Wallis or Chi-Square tests to compare continuous and categorical outcomes.

Results: The results of 5332 patients were analysed, of whom 1730 presented with RB with or without other associated bowel symptoms.
Patients with RB had a higher mean faecal haemoglobin than patients without RB (264.6 (std. dev. 1135) vs 62.8 (std. dev. 493), *p*< 0.01), although the median value in both groups was undetectable FHb (< 2ug/g).
FHb was undetectable (< 2ug/g) in 57% (983/1730) of patients with RB vs 65% (2365/3602) in patients without RB (*p*< 0.01). Faecal haemoglobin was less than 10ug/g in 75% (1289/1730) of patients with RB vs 85% (3065/3602) of patients without RB (*p*< 0.01).
Colorectal cancer was diagnosed in 67 patients without RB, and 65 patients with RB. At a cut-off of 2ug/g, there were 2 missed cancers in patients without RB (3%) vs 2 missed cancers in patients with RB (5%, *p*=0.63). The sensitivity of FIT at a cut-off of 2ug/g for CRC was 95% in patients with RB vs 97% in patients without RB.
At a cut-off of 10 ug/g, there were 9 missed cancers in patients without RB (13%) vs 5 missed cancers in patients with RB (8%, *p*=0.29). The sensitivity

of FIT at a cut-off of 10ug/g for CRC was 92% in patients with RB vs 87% in patients without RB.

Conclusion: FIT can be used to triage patients with RB for investigation. The mean FHb level was significantly higher in patients with RB. However, a substantial number of patients with RB had less than 2 or 10 ug/g of FHb when tested with FIT, with similar sensitivity to patients without RB. This suggests that FIT could be used to rule out cancer in patients with RB and still reduce the negative colonoscopy rate.

Disclosure: Nothing to disclose

P0475 PROTON PUMP INHIBITORS ASSOCIATED WITH FALSE-POSITIVE RESULTS WHEN USING FAECAL IMMUNOCHEMICAL TESTS FOR COLORECTAL CANCER SCREENING

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Introduction: The faecal immunochemical test (FIT) has a specificity of 94% for colorectal cancer (CRC) screening resulting in false positive (FP) results. The use of proton pump inhibitors (PPI) prior to FIT could decrease the accuracy of the test which would lead to a reduction in the efficacy of CRC screening.

Aims & Methods: We included participants with a positive FIT result who underwent total colonoscopy between 2013 and 2014. A FP result was defined as having a positive FIT (≥20 µg haemoglobin per gram of faeces) and follow-up colonoscopy without intermediate/high-risk lesions or cancer. Screening data was anonymously linked to pharmaceutical dispensing during the study period obtained through the public data analysis program for health research and innovation (PADRIS). PPI consumption for each FIT was measured according to whether the individual had collected prescriptions with the ATC code: A02BC for the 3 months prior to the FIT. Logistic regression models, adjusted for sex and age, were carried out to analyse whether PPI consumption increased the risk of FP.

Results: We included 4253 positive FIT (4204 participants) with diagnostic colonoscopy. The proportion of FP was 53.49% (45.8% in men; 54.2% in women). In 1019 (23.96%) FIT, the person had received PPI 3 months prior to testing (21.0% men; 27.8% women). PPI consumption increased the probability of obtaining a FP by 13% (95% CI 9.5-16.3%) from 50.4% to 63.3% (adjusted OR: 1.65; 95% CI: 1.42 to 1.92).

Conclusion: Concurrent use of PPIs at the time of FIT increases the likelihood of a false positive result. The recommendation to avoid their use before colonoscopy could reduce up to 1 out of 8 FP.

Disclosure: Nothing to disclose

P0476 THE NICE FIT STUDY INTERIM RESULTS: PROSPECTIVE, MULTICENTRE, DIAGNOSTIC ACCURACY STUDY OF THE FAECAL IMMUNOCHEMICAL TEST FOR COLORECTAL DISEASE IN 5332 SYMPTOMATIC PATIENTS

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Introduction: The faecal immunochemical test (FIT) detects the amount of blood in stool (faecal haemoglobin or FHb) to the nearest microgram of blood per gram of faeces (µg/g). A recent meta-analysis[1] reported that FIT could be used to rule out colorectal cancer (CRC) if less than 10µg blood was present per gram of faeces. We designed a powered, prospective, diagnostic cohort study to investigate whether this non-invasive, accurate and cheap test could be used rule out serious bowel disease such as CRC, but also high risk adenoma (HRA) and inflammatory bowel disease (IBD) instead of a colonoscopy.

Aims & Methods: Investigate the diagnostic accuracy of the FIT at cut-offs of 2 or 10µg/g for CRC, as well as HRA and IBD.

The study was approved by the UK Health Research Authority to recruit patients prospectively from multiple centers in England. Symptomatic patients meeting NICE referral criteria and awaiting colonoscopy were recruited via telephone and post at over 40 hospitals, and invited to perform a FIT. The HM-JACKarc analyser was used to process all FIT samples. Colonoscopy findings of serious bowel disease ie colorectal cancer (CRC), high risk adenoma (HRA) and inflammatory bowel disease (IBD), were compared to faecal haemoglobin (FHb) levels at cut-offs of 2 or 10 micrograms of blood per gram of faeces (µg/g). 2µg/g has recently been suggested as the limit of detection of faecal haemoglobin[2]. All clinical data underwent a three-level process of quality assurance, including final checks by colorectal surgeons who were all accredited endoscopists. Statistical analysis included Chi-squared test for proportions.

Results: The trial has recruited over 11 000 patients, and quality assured the data of 5332 patients. The prevalence of CRC was 2.5% (132/5332), HRA was 4.3% (230/5332) and IBD was 6.1% (326/5332). At cut-off of 2 or 10µg/g, the sensitivity of FIT for CRC was 96.2% and 89.4% respectively. Significantly more cases of CRC (14 vs 5, *p*=0.03), HRA (107 vs 54, *p*< 0.01) and IBD (181 vs 131, *p*< 0.01)were missed at a cut-off of 10µg/g than 2 µg/g. Less patients would be triaged to colonoscopy at a cut-off of 10µg/g (81.7%) than 2µg/g (62.8%).

Conclusion: The diagnostic accuracy of FIT suggests it could be used to triage symptomatic patients for further investigation. Although a cut-off of 10µg/g permits a greater reduction in referral for colonoscopy, significantly more CRC, HRA and IBD is missed.

References:
1. Westwood M, Corro Ramos I, Lang S, et al. Faecal immunochemical tests to triage patients with lower abdominal symptoms for suspected colorectal cancer referrals in primary care: a systematic review and cost-effectiveness analysis. Southampton (UK): NIHR Journals Library; 2017 May. (Health Technology Assessment, No. 21.33.) Available from: https://www.ncbi.nlm.nih.gov/books/NBK436505/ doi: 10.3310/hta21330
2. Fraser CG, Benton SC. Detection capability of quantitative faecal immunochemical tests for haemoglobin (FIT) and reporting of low faecal haemoglobin concentrations. Clinical Chemistry and Laboratory Medicine (CCLM). 2018 Jul 11.

Disclosure: Nothing to disclose

P0477 DIGITAL CHROMOENDOSCOPY SYSTEMS (I-SCAN AND OPTICAL ENHANCEMENT) FOR COLORECTAL POLYP PREDICTION: THEIR ROLE IN THE NICE CLASSIFICATION

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Introduction: The validity of the narrow-band imaging international colorectal endoscopic (NICE) classification, using other digital chromoendoscopy systems remains unknown.

Aims & Methods: Aim: to validate the NICE classification using digital chromoendoscopy systems (I-scan and Optical Enhancement) for endoscopic colonic polyps prediction.

Methods: consecutive adult patients referred to a tertiary-center for endoscopic polypectomy, or biopsy were prospectively enrolled from April 2017 to May 2018. Lesion size, location and macroscopic features (color, vessels and surface pattern) were recorded. Real-time, endoscopic classification of polyps via NICE classification using digital chromoendoscopy systems was performed. All lesions were photographically recorded and then biopsied or resected for histology analysis (criterion standard). Accuracy, sensitivity, specificity, positive and negative predictive values for each component of the classification and for the overall prediction was calculated. A 30 randomly-selected image set was collected for inter and intra-observer agreement analysis.

Results: A total of 95 patients were enrolled, 52.6% were female. The mean age was 60.30 (±14.04) years. The reasons for colonoscopy were diagnostic (49.5% of cases), surveillance (27.4%), and screening (23.3%). The median Boston bowel preparation scale was 8 (range: 6-9). A total of 139 polyps were found during colonoscopy. 31/139 (22.3%) were located in the left

colon, 27/139 (19.4%) in the right colon, 26/139 (18.7%) in the transverse colon, 25/139 (18.0%) in the sigmoid colon, 19/139 (13.7%) in the rectum, and 11/139 (7.9%) in the cecum. 52/139 of the polyps (37.4%) were ≥10mm, 44/139 (31.7%) were ≤5mm, and 43/139 (30.9%) were 6-9mm. According to the Paris classification: 111/139 (79.9%) were sessile polyps (Is), 19/139 (13.7%) were pedunculated (Ip), 6/139 (4.3%) were subpedunculated, 2/139 (1.4%) were flat elevated lesions of the mucosa, and 1/139 (0.7%) was flat mucosal change. According to the NICE classification, the color was classified as clear (73/139 [52.5%]), intermediate (60/139 [43.2%]), and dark (6/139 [4.3%]); the surface was subdivided into uniform pattern (78/139 [56.1%]), tubular pattern (57/139 [41.0%]), and amorphic pattern (4/139 [2.9%]); vessels were distributed as no vessels (51/139 [36.7%]), regular vessels (69/139 [49.6%]), and irregular vessels (19/139 [13.7%]). NICE types were type 1 (63/139 [45.3%]), type 2 (68/139 [48.9%]), and type 3 (8/139 [5.8%]). Using I-scan and Optical Enhancement, NICE classification reached a sensitivity specificity, positive and negative predictive value of 89%, 70%, 36% and 97%, respectively. Every NICE classification parameter reached an excellent inter and intra-observer agreement (>0.80 κ value) (table 1).

Macroscopic features	Overall accuracy [% (95% CI)]				Interobserver agreement (κ)	Intraobserver agreement (κ)		
	Sensitivity	Specificity	PPV	NPV	M.S.A.	M.S.A.	H.A.E.	J.O.
Color	68 (45 - 86)	96 (78 - 100)	94 (70 - 100)	76 (56 - 89)	0.81	0.93	0.95	0.95
Vessels	55 (32 - 77)	83 (59 - 96)	79 (49 - 95)	62 (41 - 81)	0.92	0.93	0.94	0.94
Surface	86 (65 - 97)	96 (81 - 100)	95 (75 - 100)	90 (73 - 98)	0.85	0.94	0.95	0.94
NICE type	89 (52 - 100)	70 (55 - 83)	36 (17 - 59)	97 (85 - 100)	0.85	0.94	0.89	0.94

[Table 1. Overall accuracy, inter and intraobserver agreement analysis of the NICE classification using digital chromoendoscopy systems.]

Conclusion: Digital chromoendoscopy systems (I-scan and Optical enhancement) are useful also with NICE classification for prediction of polyps histology during colonoscopy.
References: ClinicalTrials.gov Identifier: NCT03155308
Disclosure: Nothing to disclose

P0478 COMPARATIVE STUDY OF GREEK PATIENTS WITH CANCER OF THE LEFT AND RIGHT COLON BASED ON CLINICAL PRESENTATION, COMORBIDITY, HISTOPATHOLOGY AND MOLECULAR BIOMARKERS

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Introduction: The differences in histopathology and molecular biology between right and left colon cancer were first reported in the literature by Bufill in 1990. Since then a large number of studies have confirmed their differences in epidemiology, clinical presentation, comorbidity and biological behavior, which may be related to the difference in prognosis and overall survival between the two groups.
Aims & Methods: Investigating statistically significant differences between Greek patients with right and left colon cancer based on clinical presentation, comorbidity, histopathology and molecular biomarkers. 144 patients diagnosed with colon cancer of any stage who received chemotherapy regimens in a Greek Oncology Hospital were included in the study. Data analysis was performed with the SPSS statistical package.
Results: 144 patients (86 males and 58 females) participated in the study. 100 (69.4%) patients had a primary lesion in the left and 44 (30.6%) in the right colon. The average age of diagnosis was 65.4 years and that of the BMI was 28.3 without statistically significant differences between the two groups. Statistically significant differences resulted from the clinical presentation of the disease, wherein patients with right colon cancer localization were more likely to display anemia (OR=3.09, p=0.008), while patients

with left colon cancer localization were more likely to develop bloody stools (OR=3.37, p=0.003) and feeling of incomplete evacuation (OR=2.78, p=0.05). In the case of comorbidity, patients with right primary lesion were more likely to receive metformin (OR=3.31, p=0.016), while marginal significance (p=0.056) was found in coronary artery disease, where patients with right sided neoplasia suffered from the disease to a greater percentage (20.5% vs. 9% left).Statistically significant differences were also observed in the histological characteristics between the two groups. On one hand the percentage of mucinous differentiation was higher in the right-sided group (15,9% vs 4,0% left-sided group, p=0,035.OR=4,49), while on the other hand the percentage of high grade differentiation was higher in the group of patients with left-sided colon cancer (78% vs 56,1% right-sided group, p=0,010.OR=2,78). Furthermore, the percentage of infiltrated lymph nodes was higher in the group of patients with right colon cancer compared with the left-sided group (N_0 left 33,3% vs 24,3% right , N_{1-3} right 62,2% vs 38,1% left, p=0,039) as it was also the average of removed lymph nodes (right 18,1 vs 14,6 left). The study of three genes (KRAS, NRAS and BRAF) revealed statistically significant difference only regarding the KRAS gene, wherein the neoplasms of the left colon had a higher percentage of wild type KRAS gene (65,2%), in comparison with the right colon cancer group (47,2%) (p=0,062, marginal significance).
Conclusion: The differences in clinical presentation and symptoms of right and left colon cancer were confirmed. The highest rate of metformin and coronary artery disease in patients with right colon neoplasia may reflect correlation with the metabolic syndrome in this group and requires further study. The location of colon cancer seems to play a significant role in the behavior of the disease. Left and right colon cancer present different pathogenic mechanisms, probably related to the differences in histology and molecular pathways between them.
References: 1. Bufill JA. Colorectal cancer: evidence for distinct genetic categories based on proximal or distal tumor location. Ann Intern Med. 1990 Nov 15;113(10):779-88 2. Hansen IO, Jess P. Possible better long-term survival in left versus right-sided colon cancer - a systematic review. Dan Med J 2012;59 3. Katherine Esposito, Paolo Chiodini, Annalisa Capuano. Colorectal cancer association with metabolic syndrome and its components: a systematic review with meta-analysis. Endocrine. December 2013, Volume 44, Issue 3, pp 634-647
Disclosure: Nothing to disclose

P0479 CLINICOPATHOLOGICAL STUDY OF LATERALLY SPREADING TUMORS OF THE COLORECTUM

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Introduction: Laterally spreading tumors (LSTs) of the colorectum are classified into the following four subtypes according to their morphology ; granular homogeneous type (LST-GH), granular nodular mixed type (LST-GM), non-granular flat-elevated type (LST-NGF), and non-granular pseudo-depressed type (LST-NGPD). Clinical features of each subtype of LSTs have not been fully evaluated.
Aims & Methods: The aims of this study was to clarify the clinicopathological features of colorectal LSTs focusing on their subtypes. We reviewed clinical charts and surgical pathology files of 7229 endoscopically resected specimens during January 2007 and December 2018 at our institution. A total of 548 LSTs were detected. We examined the clinical features (mean age, male to female ratio, size, location, Incidence of concomitant carcinoma) according to their subtypes.
Results: Of these 548 lesions, a total of 204 (37.2%) were LST-GH, 61 (11.1%) LST-GM, 246 (44.9%) LST-NGF, and 37 (6.8%) LST-NGPD. Mean age of patients with each subtype was 68.4 years old for LST-GH, 67.2 for LST-GM, 66.9 for LST-NGF, and 66.2 for LST-NGPD. Male to female ratio (M/F) was 1.4 for LST-GH, 1.9 for LST-GM, 1.8 for LST-NGF, and 1.7 for LST-NGPD. Mean size of LST-GH (22.4mm) and LST-GM (26.8mm) were significantly larger than that of LST-NGF (17.0mm) and LST-NGPD (15.6mm). All subtypes were located predominantly in the proximal colon.
Incidences of concomitant carcinomas in LST-GH, LST-GM, LST-NGF, and LST-NGPD were 17.6% (36 out of 204), 37.7% (23 out of 61), 16.7% (41 out of 246), and 51.4% (19 out of 37), respectively. Incidences of concomitant submucosal carcinomas in LST-GH, LST-GM, LST-NGF, and LST-NGPD were 0.5% (1 out of 204), 13.1% (8 out of 61), 2.4% (6 out of 246), and 18.9% (7 out of 37), respectively.

Conclusion: Each subtype of LSTs has distinct clinical features. LST-GM and LST-NGPD have higher malignant potentials than other subtypes. Especially LST-NGPD has the highest risk of invasive carcinoma regardless of its size. Therefore we should carefully detect these lesions and choose appropriate treatment according to the subtypes.
Disclosure: Nothing to disclose

P0480 ELECTRICAL AND VISCOELASTIC PARAMETERS OF ERYTHROCYTES IN COMBINATION WITH THE FATTY ACID PROFILE OF THEIR MEMBRANES AND SERUM AS POTENTIAL BIOMARKERS FOR THE DIAGNOSIS OF COLORECTAL CANCER

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Introduction: The aim of the work was to study the diagnostic efficiency of using the electric and viscoelastic parameters of red blood cells (RBC) in combination with the fatty acid profile (FA) of their membranes and serum (BS) for early diagnosis and evaluation of tumor progression in patients with colorectal cancer (CRC).
Aims & Methods: The CRC patients (62,7±8,6 years old) included 65 patients with early stages (TNM staging I, II) and 64 with late stages (TNM staging III, IV) and different tumor locations. The healthy controls (n=35, 61,7±7,5 years old) were selected by routine clinical examination. Electric, viscoelastic parameters of RBC were studied by dielectrophoresis, RBC membrane and BS FA composition were measured using GC/MS system triple quad Agilent 7000B (USA).
Using the methods of statistical and inductive analysis, a population of logical-mathematical models was formed, from which the best model for each diagnostic task was chosen on the basis of the vector quality characteristic.
Results: In the patients with CRC RBC tended to have much lower findings of the range of deformation, dipole moment, polarizability at 10^6 Hz, capacity of membranes and much higher levels of summarized findings of viscosity, rigidity, indices of destruction, aggregation and conductivity as compared to the ones in healthy subjects under study (p< 0.0001-0.02).
The diagnostic panel containing proportion of deformed cells, the amplitude of RBC deformation at a frequency of 10^6 Hz, the summarized rigidity, electric conductivity - achieved high diagnostic accuracy (0.97) with AUC of 0.95, a sensitivity of 0.97 and a specificity of 0.93 for differentiating early stage patients from healthy controls.
A total of 21 differentially expressed FA in RBC membrane and BS were identified. Each FA class demonstrated specific changing trends in CRC progression (down-regulation in saturated FA, monounsaturated FA and up-regulation in polyunsaturated FA during cancer progression) (p<0.0001-0.001). The combination of the above RBC electrical and viscoelastic parameters and the list of FA, including C18:1;c9, C20:2n-6, C20:3n-6, C20:4n-6, C22:4n-6, C22:5n-3, C22:6n-3 - showed the best predictive power when comparing the early stages CRC patients and late ones (AUC 0.80, diagnostic accuracy 0.77, sensitivity 0.76, specificity 0.78).
Metastasis was associated with significant changes in the electric characteristics of erythrocytes: increase of conductivity (r=0.486, p<0.0001), decrease of electric membrane capacity (r=-0.548, p<0.0001), dipole moment (r=-0.527, p<0.0001) at the background of increase of PUFA, especially C22:5n-3 (r=0.355, p<0.0001) and C22:6n-3 (r= 0.252, p<0.0001).
The significant role of PUFA in carcinogenesis is probably related to the effect of their high concentrations on the immune environment (it can incorporate into the membrane phospholipids to alter their fluidity to inhibit the T-cell proliferation).

Conclusion: Created diagnostic panels, including electric, viscoelastic parameters and fatty acids of RBS membranes and BS, should be considered promising for early diagnosis, detection of progression of CRC.
Disclosure: Nothing to disclose

P0481 CLINICOPATHOLOGICAL STUDY OF SERRATED LESIONS OF THE COLORECTUM

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Introduction: Serrated lesions of the colorectum are the precursors of microsatellite unstable carcinomas. However, their clinical and pathologic features are still unclear and need further exploration.
Aims & Methods: The aims of this study was to clarify the clinicopathological features of colorectal serrated lesions. We reviewed clinical charts and pathology files of 7229 endoscopically resected specimens performed during January 2007 and December 2018 in our hospital. A total of 668 serrated lesions (9.2%) resected were classified into three categories : HP (hyperplastic polyp), SSA/P (sessile serrated adenomas/ polyps), and TSA (traditional serrated adenoma), according to the WHO criteria. We examined the features of these cases and evaluate the morphologic characteristics by using immunochemical staining for Ki-67 and the expression of MUCs (MUC2, MUC5AC and MUC6) in differentiating serrated lesions.
Results: Of these 668 lesions, a total of 348 (52.1%) were HP, 178 (26.6%) SSA/P, and 142 (21.3%) TSA. Male to female ratio (M/F) was 2.28 for HP, 0.94 for SSA/P, and 2.02 for TSA. Mean size of SSA/Ps (12.1mm) and TSAs (13.5mm) were significantly larger than that of HP (8.0mm) (p<0.005, respectively) . SSA/Ps were located predominantly in the proximal colon, whereas HP and TSA were mainly located in the sigmoid colon and rectum. 84% of SSA/Ps were flat in macroscopic appearance. SSA/Ps and HPs were whitish or almost the same as adjacent mucosa in color, whereas TSAs had a tendency to be reddish. Magnified colonoscopy showed Type II open pit pattern as characteristic of SSA/Ps, whereas pinecone-shaped pit pattern as that of TSAs. Incidences of concomitant carcinomas in HP, SSA/P, and TSA were 0% (0 out of 348), 3.4% (6 out of 178), and 3.5% (5 out of 142), respectively. Ki-67 positive cells in HP showed regular, symmetric distribution, and those in SSA/P did irregular asymmetrical pattern, whereas most of those cells in TSA distributed in the so-called ectopic crypts. Expression levels of MUC2, MUC5AC and MUC6 were significantly different between serrated lesions, SSA/Ps and HPs were positive for MUC5AC in comparison with TSAs.
Conclusion: Our studies showed the three types of serrated lesions have their own distinct features and could be helpful to distinguish between them. SSA/P and TSA are premalignant lesions of colorectum and we should detect these lesions and completely remove endoscopically.
Disclosure: Nothing to disclose

P0482 COLONOSCOPIC WITHDRAWAL TIMES AND ADENOMA DETECTION RATE DURING SURVEILLANCE COLONOSCOPY AFTER SURGERY FOR COLORECTAL CANCER

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Introduction: Withdrawal time (WT) and adenoma detection rate (ADR) are widely used quality indicators for colononoscopy. Although current guideline suggests a minimum withdrawal time of 6 minutes during screening colonoscopy, little is known about appropriate withdrawal time during surveillance colonoscopy after colorectal cancer (CRC) surgery.
Aims & Methods: We investigated the association between WT and ADR during surveillance colonoscopy after CRC surgery.
We performed a retrospective analysis of data from 1,341 subjects who underwent 1st surveillance colonoscopy after curative colectomy between January 2013 and April 2018. The colonoscopies were performed by 8 board-certified colonoscopists. We recorded the numbers, sizes, and histologic features of the neoplastic lesions detected during colonoscopy, as well as the duration of insertion and of withdrawal of the colonoscope during the

procedure. Colonoscopists were classified as fast or slow based in their mean WT for colonoscopy without polypectomy. The primary outcome was the ADR for each colonoscopists.

Results: The mean WT during colonoscopy without polypectomy was 8.1 ± 5.6 minutes. Using 8 minutes as cutoff, we classified 5 colonoscopists as fast (mean WT, 6.8 ± 3.2 minutes) and 3 colonoscopists as slow (mean WT, 10.3 ± 4.5 minutes). Each colonoscopist's mean WT correlated with their ADR (r_s=0.874, P=0.005). As compared with colonoscopists with mean withdrawal times of less than 8 minutes, those with mean withdrawal times of 8 minutes or more had higher ADR (49.1% vs. 32.2 %, P< 0.001).

Conclusion: In this study, we found that a minimum of 8 minutes of WT was necessary during surveillance colonoscopy after surgery for CRC. Because patients who underwent CRC surgery possess high risk for metachronous CRC and adenoma, ample amount of time for observation on colorectal mucosa is necessary.

Disclosure: Nothing to disclose

P0483 ADENOMA DETECTION RATE IN COLORECTAL CANCER SCREENING PROGRAMS: MASTER SHOW ME THE WAY TO BECOME A HIGH DETECTOR!

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Introduction: Although the adenoma detection rate (ADR) cut-off for colonoscopies after positive fecal immunochemical tests (FIT) continues to be a debated issue, the ADR is one of the most accepted benchmarks for colonoscopy quality. There is some evidence that the quality of colonscopy screening can be improved by educational interventions.

Aims & Methods: This study aimed to analyze the effect of endoscopist-related characteristics on colonoscopy quality indicators and to evaluate the factors affecting ADR patterns registered in the colorectal (CRC) screening program in the Veneto Region between 2015-2017. The following data about endoscopists in screening programs between 2015-2017 were collected: age, sex, years as physician, specialization, annual colonoscopy volume. During 2010-2014, younger endoscopists (< 40 yr) underwent four meetings with a senior endoscopist (Cristopher Williams), to improve general endoscopic ability and, in particular, the sensibility to detect adenomatous lesions. ADR was calculated for each operator. Data were analyzed with SPSS program.

Results: During the three year period, 191 endoscopists performed a total of 42,706 first colonoscopies after FIT positivity. One hundred forty with at least 20 colonoscopies after FIT positivity/yr, (mean age 48.2yr ± 10.8yr (M±SD), Male 53.9%) were selected. Three hundred eight-two ADRs were collected during the observation period. Overall ADR was 43.7±9.5%. Ninety-six of the endoscopists were specialized in gastroenterology, 35 in general surgery, and 8 in other specialities. ADR was 44.1± 9.7% for the gastroenterologists, 42.7 ±9.6% for the surgeons (p=ns) and 39.5 ±7% for those with other specialities (p=0.033). ADR was significantly higher for the younger endoscopists (30-39yr 47.5%; 40-49yr 44.6%; >50yr 41.4%, with p< 0.001). The ADRs over the three year period were similar (44.2% vs 42.9% vs 43.3%, p= ns). No significant association between ADR and number of screening colonoscopies performed we found. When the ADR in 2017 of 81 endoscopists was analyzed depending on the cumulative number of total colonoscopies/yr, it was found that the those with > 300 colonoscopies/yr had higher ADRs (35.5 ±21.4% vs 43.5±11.5%, p=0.04) in colonoscopies after FIT positivity/yr.

Conclusion: Study findings demonstrated that junior endoscopists and those specialized in gastroenterology were more effective in identifying adenomas during screening colonscopy procedures. High annual colonoscopy volumes and working exclusively as endoscopists but not years of experience or being older were associated with higher ADRs. Educational interventions seemed to be effective in improving sensitivity and performance.

Disclosure: Nothing to disclose

P0484 ENDOSCOPISTS' POLYP DETECTION RATE AS A PREDICTOR OF LONG- TERM POST COLONOSCOPY CANCER AFTER INITIAL NORMAL COLONOSCOPY IN "SYMPTOMATIC/NON-SCREENED SCENARIO"

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Introduction: Polyp detection rate (PDR) is an accepted quality measure of colonoscopy in the average-risk population screening scenario (1).

Aims & Methods: Aim: We aimed to evaluate whether endoscopist's PDR calculated in symptomatic/ non screened situation is associated with long term post colonoscopy cancer (PCC) after initial normal colonoscopy (2).

Methods: A cohort of 16,645 symptomatic patients aged >50 years who underwent first-time colonoscopy in 2003-2010 was analyzed to calculate PDR of each endoscopists [divided into quartiles: Q1 (21.2-26.7), Q2 (27.8-29.6), Q3 (31.4-32.1), Q4 (38.3-42.0)]. Thereafter, 9,497 patients with normal colonoscopy were followed for PCC through National Cancer Registry or death up to Dec 2017. Cox proportional analysis was calculated for PCC and advanced stage disease (stage III,IV).

Results: During a median follow-up time of 7.58 years (interquartile range 6.0-8.3), PCC was documented in 38 patients and advanced cancer in 19 patients. The rate of total PCC and advanced cancer among patients that underwent the procedure by endoscopists with lower quartile (Q_1) vs. other quartiles (Q_{2-3-4}) was 10.0 vs. 4.4 cases/1,000 years and 5.6 vs. 2.0 cases/1,000 years, p=0.012 & 0.023 respectively. After adjusting for multiple covariates the risk of total PCC and advanced stage CRC among subjects that underwent the procedure by endoscopist with lower quartile PDR was HR 1.97 (95%C.I. 1.03-3.78) & 2.47 (1.00-6.14) respectively.

Conclusion: Symptomatic patients who undergo colonoscopy by an endoscopist with lower quartile PDR are at significantly increased risk of total and advanced stage PCC. PDR is a significant predictor of PCC also in the non-average risk population.

References: 1. Kaminski MF, Regula J, Kraszewska E, et al. Quality indicators for colonoscopy and the risk of interval cancer. N Engl J Med. 2010;362:1795-1803. 2. Nakao SK, Fassler S, Sucandy I, Kim S, Zebley DM. Colorectal cancer following negative colonoscopy: is 5-year screening the correct interval to recommend? Surg Endosc. 2013;27:768-773

Disclosure: Nothing to disclose

P0485 SHOULD SESSILE SERRATED POLYPS HAVE SEPARATE SURVEILLANCE

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Introduction: The serrated pathway accounts for up to 30% of colorectal cancer (CRC). Sessile serrated polyps (SSPs) have the highest malignant potential of serrated lesions. SSPs occur sporadically or as part of the serrated polyposis syndrome (SPS). More recently, increased CRC risk has also been associated with an oligo-SPS phenotype and large, ≥10mm lesions.

Aims & Methods: Our aim was to describe and evaluate SSP characteristics in an Irish cohort. Following ethical approval, patients with ≥1 SSP confirmed on histology between 2016-2018 were identified. Patients were stratified into four known risk groups: SPS defined by WHO criteria (SPS), ≥2 SSPs with 1≥10mm (Oligo-SPS), SSP ≥10mm (Large-SSP), and all other SSP's (Low-risk SSP).

Results: 195 SSPs in 145 patients were identified; 4/145 (2.8%) SPS, 10/145 (7%) Oligo-SPS, 25/145 (17%) Large-SSP and 106/145 (73%) Low-risk SSP. Mean SSP size was 6.5mm. The most common SSP location was the ascending colon 54/195 (28%), while a significant proportion were sigmoid lesions 45/195 (23.1%). Overall, SSP subjects had a high synchronous polyp burden; ≥2 SSPs 47/145 (37%), ≥1 advanced adenoma 17/145 (12%), ≥1 non-serrated adenoma 59/145 (41%). This did not differ significantly between

groups; advanced adenomas; SPS 0%, Oligo-SPS 10%, Large-SSP 16%, Low-risk SSP 11% and ≥1 non-serrated adenoma; SPS 25%, Oligo-SPS 40%, large-SSP 44%, low-risk SSP 41%. SPS was recognised by endoscopists in 2/4 (50%) cases.

Conclusion: SSP patients, irrespective of risk, have a high synchronous polyp burden, including advanced adenomas. The sigmoid, excluded by two WHO SPS categories was the location for 1/4 of SSPs. Further studies to evaluate the need for SSP targeted surveillance and to consider broadening the WHO criteria are warranted.

Disclosure: Nothing to disclose

P0486 DECISION MAKING IN THE MANAGEMENT OF ADULTS WITH MALIGNANT COLORECTAL POLYPS: AN EXPLORATION OF THE EXPERIENCES OF PATIENTS AND CLINICIANS

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Introduction: Ten percent of cancers diagnosed within the English Bowel Cancer Screening Programme are polyp cancers. The management of polyp cancers usually involves a choice between surgery and surveillance. This choice is contentious and can be described as 'preference sensitive': a situation where one treatment option does not have superiority in terms of evidence. The best choice therefore depends on how individual patients value the risks and benefits of treatments. Difficulties in decision making for both clinicians and patients can arise because of the unexpected nature of a diagnosis of polyp cancer. This research focuses on the experiences of clinicians and patients of treatment decision making following a diagnosis of colorectal polyp cancer. To date, and to the author's knowledge, there are no previous studies which investigate how patients make the decision between surgery or surveillance, even though each option could have a significant impact on the individual patient's quality of life.

Aims & Methods: This study was carried out across four NHS Trusts within the North East of England. A qualitative approach was taken, using Interpretative Phenomenolagial Analysis (IPA) as the approach to explore the experience and perspectives of both clinicians and patients following an unexpected diagnosis of polyp cancer. In depth semi-structured interviews with ten clinicians who were involved in the care of patients diagnosed with polyp cancer, and five patients who had experience of making a treatment decision were carried out. The focus of the interviews was around the experiences of making the decision between surgery and surveillance. The phenomenological and interpretive nature of IPA allowed the researcher to use her experiences as a nurse consultant within the analysis to identify important themes and issues expressed by the participants.

Results: Analysis of the interview transcripts showed that clinicians and patients were supportive of a shared approach to treatment decision making. Several themes were identified which currently prevent this from taking place. Themes which were common to both groups include: complexity of the risk information; lack of patient information resources; system (patient pathway) factors and time. Additional clinician related themes included lack of clinical data to support discussion, and influences from the multi-disciplinary team. Patient related themes included the influence of family and significant others. Many of the themes were directly related to the unexpected nature of the diagnosis of polyp cancer.

Conclusion: This research study has evidenced several factors which are preventing patients being fully involved in important treatment decisions following a diagnosis of polyp cancer. Recommendations for improvements in practice resulting from this study include: improving awareness of preference sensitive decisions amongst the population; improvements in patient pathways and improved access to information and resources relating to polyp cancer management for patients.

Disclosure: Nothing to disclose

P0487 COMPARISON OF LONG-TERM OUTCOME OF THE COLONIC STENT VERSUS TRANSANAL DRAINAGE TUBE AND EMERGENCY SURGERY FOR LEFT-SIDED OBSTRUCTIVE COLORECTAL CANCER: A RETROSPECTIVE MULTI-CENTER OBSERVATIONAL STUDY

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Introduction: As colonic stent has been covered by Japanese medical insurance, emergency operation and colonic stent have become a mainstream of treatment for the colorectal cancer obstruction instead of transanal decompression tube. But "Bridge to Surgery" by colonic stent is not recommended in the European guidelines 2014.

Aims & Methods: We evaluated retrospectively the treatment outcomes and long-term outcome of patients with obstructive colorectal cancer in Japan. This is a retrospective multi-center observational study under the Japan Colonic Stent Safe Procedure Research Group. The subjects were patients with histologically proven stage II/III left-sided colon or upper rectal cancer with obstruction, who underwent subsequent surgery with curative resection between 2010 and 2014. The patient age ranged from 20 to 80 years. The definition of the obstruction was defined as the necessary of continual decompression or the difficulty of oral intake. There were 302 patients from 27 institutions. Patients were divided into three groups; group E (emergency surgery, n=103), group S (stent placement, n=114), and group T (transanal decompression tube placement, n=85).

Results: There were no significant differences in age, gender, site of primary tumor between the E group and the S group. The ratio of rectal cancer was significantly higher in the group T than the group E, and the ratio of Stage IIIb was significantly higher in the group S and in the group T than the group E. The 3-year Recurrence Free Survival (RFS) rate was 64.8 % in S group, 68.9 % in E group, 53.0 % in T group, respectively. There was no difference between S group and E group, and T group was significantly lower than E group (p=0.0170). Subgroup analysis showed that the 3-year RFS of patients with colon cancer did not differ among the three groups, while the 3-year RFS in patients with upper rectal cancer was lowest in the in the T-group (P< 0.05). Technical success rate was not different between group S: 99.1% and group T: 94.1%, but clinical success rate was higher in group S: 98.2% compared with group T: 85.9%. Complications of perforation and migration tended to be high in group T: 7.1% compared with group S: 1.8%. Complications after curative surgery are lower in S group and T group than in Group E. Temporary or permanent stoma rate was significantly lower in group S than in group E.

Conclusion: There was no difference in 3-year relapse-free survival rate between emergency surgery and colon stent, and the transanal ileus tube was poor. This is possibly due to tumor locations and stages, as well as complications related procedure such as perforation and migration. Safe colonic stenting has good treatment outcomes and might have not poor prognosis compared with other procedure for the patients of obstructive colorectal cancer.

Disclosure: Nothing to disclose

P0488 INITIAL TREATMENT OF LEFT SIDED MALIGNANT COLONIC OBSTRUCTION WITH SELF-EXPANDING METAL STENTS IN ELDERLY PATIENTS. A COMMUNITY HOSPITAL EXPERIENCE

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Introduction: The European Society of Gastrointestinal Endoscopy (ESGE) guideline1 suggests that, if available, self-expandable metal stent (SEMS) insertion should be considered in elderly (age > 70 years) or frail patients with malignant colorectal obtruction (MCRO). After initial obstruction relief SEMS can serve either as a definitive palliation or as a "bridge to elective surgery" (BTS). We aimed to evaluate the outcomes of this procedure in a Community Hospital.

Aims & Methods: Retrospective analysis. MCRO was diagnosed using a combination of clinical symptoms, radiographic exams and colonoscopy. SEMS insertion was attempted from eight cm above the anal verge to the splenic flexure. Two methods were employed. For tumors located between eight to 20 cm, an ultrathin gastroscope with an outer diameter of 6 mm was employed to pass the stricture. A metal Savary guidewire (GW) was placed beyond the stenosis through the working channel. The ultrathin gastroscope was withdrawn leaving the GW in place. Afterwards an Ultraflex Precision stent (Boston Scientific, Natick, Massachusetts) was inserted over the wire (OTW) and deployed monitored with the ultrathin gastroscope placed side by side). No fluoroscopy was employed. For tumors beyond 20 cm, an endoscope with therapeutic channel was used to reach the stricture, which was subsequently negotiated, under fluoroscopic control, with a 0.035 in hydrophilic tip GW, loaded into an ERCP catheter. Once the GW traversed the stricture, a Wallflex colonic stent (Boston Scientific) was inserted through the scope (TTS) and deployed both under fluoroscopic and endoscopic guidance. All procedures were performed by an experienced endoscopist.

Results: In the last five years stenting was attempted in 31 patients (18 M and 13 F, mean age 81.46 years [SD 6.15] range 72-91). There were 20 OTW and 11 TTS procedures respectively. Tumor location was: rectum five cases, recto-sigmoid junction four, sigmoid colon 14, descending colon seven and splenic flexure in one case. Technical success was 29/31 (93.5%). There were two failures for inability to traverse the stricture (one in each group, OTW and TTS). MCRO symptoms did not improve in the tumor located in the splenic flexure. Therefore, clinical success was 28/31 (90 %). One patient died two days after the procedure for a not technique-related cause. Out of the 27 remaining patients SEMS served as a BTS in 10 (37%) and 17 (63%) had the stent as a definitive palliation. Two patients presented mild tenesmus, and one had stent migration.

Conclusion: Colorectal stenting using either the OTW or TTS technique appears to be safe and effective in this elderly population for the initial treatment of MCRO.

References: 1van Hooft JE et al. Self-expandable metal stents for obstructing colonic and extracolonic cancer: ESGE Clinical Guideline. Endoscopy 2014: 46:990

Disclosure: Nothing to disclose

P0489 WITHDRAWN

P0490 WITHDRAWN

P0491 CHEMOPREVENTION AGAINST COLON CANCER BY DIETARY INTAKE OF SULFORAPHANE

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Introduction: Sulforaphane (SFN), a phytochemical compound, which belongs to isothiocyanates family found in abundance in broccoli sprouts, potently induces a variety of antioxidant enzymes via NF-E2-related factor 2-Kelch-like ECH-associated protein 1-mediated pathway, thereby protects cells from injury induced by various kinds of oxidative stresses. We have previously shown that SFN protects gastric mucosa from oxidative injury induced by *H. pylori* infection. SFN also down-regulates histone deacetylase (HDAC) activity, thereby induces apoptosis and inhibits proliferation of tumor cells in variety of tissues. On the other hand, colon cancer has been increasing in Japan. Since numerous epidemiological studies have shown that colon cancer is inversely associated with intake of anti-oxidant vegetables, we examined if daily intake of SFN prevents colon tumorigenesis in mice, and in human subjects.

Aims & Methods:

1. Effects of SFN on Colonic tumorigenesis in Mice Treated with Chemical Carcinogen: Effects of SFN on colonic tumorigenesis were examined in the ICR male mice, pretreated with a chemical carcinogen, azoxymethane (AOM) (15 mg/kg). The mice treated with AOM for 3 or 6 times were fed for 8 or 24 weeks with or without sulforaphane glucosinolates (SGS: 2,200 ppm/kg/day), which is a precursor of SFN. Effects of SGS treatment on formation of the microscopic aberrant crypt foci (ACF), and the macroscopic tumors in colonic mucosa were evaluated.

2. Effects of SFN on formation of Colonic ACF in patients with colonic adenoma: Effects of intake of raw broccoli sprouts (BS), 50 g/day, which contains 220 mg SGS every other day, for 6 months on changes in the number of ACF in rectal mucosa was examined by colonoscopy in patients with colonic adenoma. This study was conducted by members of Tsukuba Cancer Clinical Trial Group.

3. Effects of SFN on intestinal microbiota in human subjects: Effects of dietary intake of raw BS, 20 g/day, which contains 88 mg SGS every other day, for 2 weeks on intestinal microbiota in healthy volunteers was assessed by measuring composition of stool bacteria, using a method of terminal restriction fragment length polymorphism flora analysis. In human studies, alfalfa sprouts, which contains no SFN was used as a placebo control. The human studies 1 and 2 were approved by the ethical committee of each hospital, and were registered with the University Hospital Medical Information Network in Japan (Study 1: UMIN-000012022; Study2: UMIN-000032565).

Results:

1. Daily administration of SGS suppressed formation of microscopic ACF and macroscopic colonic tumors in the AOM-pretreated mice in vivo.

2. Intake of BS for 6 months tended to decrease the number of colonic ACF in patients with colonic adenoma.

3. Intake of BS for 2 weeks increased percentages of *Bifidobacterium* and *Clostridium XVIa*, which has been shown to enhance protection of colonic mucosa by increasing butyrate production in colonic lumen.

Conclusion:

1. Daily intake of SFN affords chemoprotection against colonic tumors in the mice treated with a chemical carcinogen.

2. The present study further suggests that, in addition to previously reported mechanisms, changes in the intestinal microbiota by SFN intake may also play a role in chemoprevention against colon cancer.

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P0492 WITHDRAWN

P0493 ROLE OF LOW GRADE DYSPLASIA SMALL POLYPS DURING SCREENING COLONOSCOPIES SURVAILLANCE: A PROSPECTIVE COHORT STUDY

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Introduction: The role diminutive polyps and small polyps play in the development of advanced neoplasia (AN) or cancer during follow-up (FU) continues to be debated. Recent studies have shown that the risk of AN development during FU is higher in patients with > 5 small polyps but similar in patients with 1-2 or 3-4 small polyps[2,3].

Aims & Methods: the current study aimed to evaluate if current European FU guidelines[1] at first screening colonoscopy according to the number of low-grade dysplasia tubular adenoma < 1 cm ("micropolyps", MP) are too strict. A longitudinal cohort study was carried out on a representative sample (50%) of patients who underwent a screening colonoscopy (clean colon) in 2010 showing at least 1 polyp. Patients with AN or cancers were excluded. Polyps > 1 cm or villous or high grade dysplasia/carcinoma in situ were considered AN. These patients made a FU colonscopy according to UE screening CCR guidelines. Patients were split up according to European guidelines in Low risk (1-2 MP), Intermediate risk (3-4 MP) and High risk (>5 MP). Data were analyzed by SPSS program.

Results: Of 640 patients included in the sample 172 (27%) were included in the surveillance program (mean age 62,2± 5,7 yr, 50-70), 120 male (69,8%). During first colonoscopy (2010) 370 MP were detected (M±SD 2,1±1,5, range 1-13 polyps for each patient). During FU (median 5.5 years), 315 colonoscopies were performed (mean 1.8; range 1-5) and an AN was detected in 23 patients (13.4%): 20/23 tubulovillous microadenoma, 1/23 high grade dysplasia, 2/23 tubular adenoma > 1 cm. The detection of AN among patients in treatment with ASA was non significantly lower than the others. AN detection was lower among Low risk patients (13/108; 10.7%) as compared to Intermediate risk (7/33; 17.5%) and High risk (3/8; 27.3%) (P=ns). According to Kaplan-Meier analysis, the cumulative risk of AN among High risk was significantly increased (p=0.035) . No interval cancers were found during the follow-up.

Conclusion: These findings suggest that EU guidelines for surveillance colonoscopies for > 3 small LGD polyps are excessively strict. We propose extending the time for a repeat colonscopy FU for these patients to 5 yrs

References: 1Segnan N. et al. European Guidelines for Quality Assurance in Colorectal Cancer Screening and Diagnosis - First Edition 2011 2Chang MM et al. Digest Liv Dis 2018; 50: 847-852 3Jung YK et al. Am J Gastroenterol 2018: 113(12):1855-61.

Disclosure: Nothing to disclose

P0494 PERFORMANCE OF PROPOSED ALGORITHMS FOR ESTABLISHING RISK OF ADVERSE OUTCOME IN T1 COLORECTAL CARCINOMA

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Introduction: Recently, two simplified prediction models have been published to determine which patients should undergo adjuvant surgery after endoscopic resection of T1 colorectal cancer (CRC). In the Scottish screen-detected T1 CRC based algorithm (Scottish model), the model identified low-risk cases based on completeness of resection (resection margin >0.1 mm) and absence of lymphovascular invasion (LAI).[1] The model of the French group identified low-risk cases based on a resection margin of ≥1 mm (French model).[2] Both models showed promising results but were never externally validated.

Aims & Methods: In this study, we investigated two proposed algorithms and the Dutch guideline for prediction of adverse outcome in T1 CRC after endoscopic resection. Adverse outcome was defined as lymph node metastasis (LNM) at baseline or any recurrence at follow-up. Cases were derived from a multicenter retrospective observational cohort of patients with an endoscopic resection of a T1 CRC diagnosed from 2014-2017 in 8 hospitals in the Netherlands. Recorded features included: screen-detection, polyp morphology and histological parameters (LAI, differentiation grade, and resection margins). Risk classification by the Dutch guideline algorithm (Dutch model) included absence of LAI, good/moderate differentiation and a resection margin of >1 mm as low-risk factors. The endpoints of the study were the percentage of low-risk cases identified, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy for each model.

Results: In 754 endoscopically treated T1 CRCs (median follow-up 20 months, IQR 13-28), 250 patients (33.1%) had secondary surgery. A total of 55 (7.3%) patients had an adverse outcome. LNM was present in 40 (5.3%) and recurrence in 17 (2.3%) patients (2 patients with LNM also developed recurrence). The Dutch, Scottish and French models identified 256 (35%), 394 (68%), and 347 (70%) patients as low-risk respectively. Sensitivity, specificity and accuracy were 92.5%, 36.6%, and 40.6% for the Dutch model, 77.1%, 71.1%, and 71.5% for the Scottish model and 67.7%, 72.4%, and 72.1% for the French model (see table 1 for PPV, NPV and corresponding 95%CIs). This corresponded with 4 (0.5%), 8 (1.4%), and 11 (2.2%) missed cases with an adverse outcome in the total cohort for the Dutch, Scottish and French model respectively. Within the predicted high-risk groups according to the Dutch, Scottish and French model, 49 (10%), 27 (15%), and 23(15%) patients truly had an adverse outcome respectively. The models did not perform differently when stratified for polyp morphology or screen-detection.

Conclusion: For endoscopically treated T1 CRCs the analyzed models could adequately identify cases at low risk for adverse outcome in a large cohort (screen- and non-screen detected). These results show that a stringent model, such as the Dutch model, has the highest sensitivity, but leads to 59% of patients being referred for surgery without any benefit. Less stringent models such as the Scottish and French models may result in an absolute reduction of unnecessary surgery referrals of up to 33%, but at the cost of an increase in missed adverse outcomes. Considering these results there is room for improvement of the current Dutch model, provided that a cautious approach is taken.

	Dutch model	Scottish model	French model
Sensitivity, (95% CI)	92.5% (81.8%-97.9%)	77.1% (59.9%-89.6%)	67.7% (49.5%-82.6%)
Specificity, (95% CI)	36.6% (33.0%-40.3%)	71.1% (67.1%-74.9%)	72.4% (68.1%-76.4%)
Positive predictive value,(95% CI)	10.1% (9.25%-11.0%)	14.7% (12.1%-17.7%)	15.2% (12.0%-19.1%)
Negative predictive value,(95% CI)	98.4 % (96.1%-99.4%)	98.0% (96.3%-98.9%)	96.8% (94.9%-98.0%)
Accuracy, (95% CI)	40.6% (37.0%-44.2%)	71.5% (67.6%-75.1%)	72.1% (67.9%-76.0%)

[Performance of proposed risk models for adverse outcome in T1 CRC]

References: 1. Richards CH, Ventham NT, Mansouri D, Wilson M, Ramsay G, Mackay CD, et al. An evidence-based treatment algorithm for colorectal polyp cancers: results from the Scottish Screen-detected Polyp Cancer Study (SSPoCS). Gut. 2018;67(2):299-306.
2. Lopez A, Bouvier AM, Jooste V, Cottet V, Romain G, Faivre J, et al. Outcomes following polypectomy for malignant colorectal polyps are similar to those following surgery in the general population. Gut. 2019;68(1):111-7.
Disclosure: Nothing to disclose

P0495 ABSENCE OF NEO1 PREDICTS A POOR PROGNOSIS AND PROMOTES TUMOR PROGRESSION IN COLORECTAL CANCER

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Introduction: Colorectal cancer (CRC) is one of the most common malignancies worldwide, and its morbidity is increasing sharply in the young population. CRC progression and prognosis are associated with oncogene activation and tumor suppressor gene inactivation. Recently, many bioinformatics methods provided the platform to screen biomarkers with prognostic and treatment implications of CRC. As a homologue of the Deleted in Colorectal Cancer (DCC) gene, NEO1 has been reported to be downregulated in CRC and other several cancer types, but the specific role of NEO1 in CRC needs further exploration. The present study aimed to validate NEO1 expression in CRC and explore the role and potential mechanism of NEO1.
Aims & Methods: Firstly, several bioinformatics methods were utilized to examine NEO1 expression in CRC. Quantitative real-time PCR was further performed to validate NEO1 expression in CRC tissues. Next, ROC curve analysis and Survival analysis were used to test the relationship between NEO1 and prognosis of CRC. Subsequently, the effects of NEO1 were evaluated through colony formation, cell proliferation, migration and invasion assays by transfection NEO1 plasmids or siRNAs. Finally, we took advantage of Gene Ontology (GO) analysis and Gene Set Enrichment Analysis (GSEA) to explore potential function and mechanism of NEO1 in CRC.
Results: In our study, results showed that NEO1 was downregulated in online CRC datasets, GSE41258 dataset and CRC tissues. Its low expression was associated with shortened survival of CRC patients. Moreover, overexpression of NEO1 promoted CRC cell proliferation, migration and invasion while silencing NEO1 inhibited CRC cell proliferation, migration and invasion. Finally, GO analysis revealed that NEO1 was associated with iron transport and response to wounding. GSEA indicated that NEO1 lower expressed samples were enriched in DNA repair.
Conclusion: In conclusion, a tumor suppressor gene NEO1 was identified and demonstrated to be associated with the progression and prognosis of CRC, which might be a potential therapeutic target and prognostic biomarker for CRC patients.
Disclosure: Nothing to disclose

P0496 ENDOSCOPIC INTERMUSCULAR DISSECTION (EID) OF THE M. PROPRIA FOR DEEP SUBMUCOSAL INVASIVE CANCER IN THE RECTUM

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Introduction: Endoscopic submucosal dissection (ESD) offers a minimally invasive *en-bloc* resection technique for rectal lesions with superficial submucosal invasion (T1 CRCs). However, as ESD dissects through the submucosa, it is often impossible to obtain a radical deep resection margin when deeper invasion in the submucosa (Sm2-3) is present. There is accumulating evidence that deep submucosal invasion is not an independent predictor of lymph node metastasis. Therefore, there is need for endoscopic techniques for resection of deep submucosal invasive T1 CRCs. Instead of dissecting through the submucosa, dissection between the circular and the longitudinal layers of the m. propria (intermuscular dissection), could provide the necessary radical deep margin, but without compromising the mesorectal fat plane allowing future completion surgery.
Aims & Methods: In this prospective cohort, 15 rectal tumors with optical features of deeper invasion in the submucosa were treated with an intermuscular dissection (EID). Brief description of the technique: Standard submucosal dissection was performed until non-lifting developed. The intermuscular space was then lifted, followed by careful selective circumferential myotomy of the circular muscle layer, until the longitudinal muscle fibres were visualized. Then the intermuscular space was dissected. The EID area was not routinely clipped. Prophylactic antibiotics were administered intravenously. Patient-, polyp, procedural, and histological characteristics were recorded. Primary endpoints were feasibility of performing EID, ability to obtain an R0 resection, and complication rate. Technical success was defined as achieving an *en bloc* resection. R0 resection was defined as free deep and lateral resection margins confirmed by histology.
Results: Between December 2018 and April 2019, 15 patients (73% male, mean age 67 yrs, SD ± 11 yrs) with a lesion with suspicion of deeper submucosal invasion in the rectum were treated with EID (mean size 28 mm (range 16 to 50 mm)). The Paris classification was 0-Is in 66%, and 0-IIa in 33%. Surface morphology was non-granular in 80%, and a depression was present in 79%. Optical diagnosis with NBI showed a Hiroshima C1 pattern in 1 (7%), C2 in 2 (13%) and C3 in 12 (80%) cases. Technical success was achieved in 13/15 (87%) of cases. In the 2 failed cases, it was impossible to discriminate and lift the intermuscular space. An R0 resection was achieved in 11/13 (85%) technically successful cases. In 2 cases, a small area of fat was visualized which was closed with 2 hemoclips.Two cases had a positive deep resection margin. All these lesions were carcinomas microscopically. The depth of submucosal invasion was Sm1 in 1 (7%), Sm2 in 3 (23%), Sm3 in 8 (61%), and T2 in 1 (7%) cases. Lymphovascular invasion was observed in 7/13 (54%) cases, high-grade (Bd2-3) tumor budding in 4/12 (25%), and poor differentiation in 1/13 (7). One patient developed fever postoperatively without need for intervention. No other complications were observed. In total 6/13 (46%) cases had no histological risk factor other than deep invasion. A wait and see follow-up strategy was applied in 7/13 (54%) technically successful cases. No residual carcinoma was detected at the scar in the surgical specimen, and lymph node metastasis was detected in 1 case.
Conclusion: Endoscopic intermuscular dissection (EID) seems a promising and safe new technique to remove deep submucosal invasive T1 carcinomas in the rectum, with a technical success rate of 87% and an R0-resection rate of 85%.
Disclosure: Consultant for Boston Scientific

P0497 LYMPHOVASCULAR INFILTRATION IS A HIGH RISK FACTOR FOR LYMPH NODE METASTASIS INDEPENDENT OF DEPTH OF INVASION IN T1 COLORECTAL CANCERS

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Introduction: Depth of submucosal invasion is commonly used to predict risk for lymph node metastasis in T1 colorectal cancers although published data are conflicting on the risk of metastasis in relation to level of submucosal growth.
Aims & Methods: The aim of this study was to identify risk factors for lymph node metastasis in T1 colorectal cancers. Data on all patients with T1 colorectal cancer undergoing surgical resection between 2009-2017 were collected from the Swedish Colorectal Cancer Registry. Potential risk factors for lymph node metastasis, including age, gender, tumour location, submucosal invasion (Sm1-3), grade of differentiation, lymphovascular invasion, perineural invasion, tumour deposits and mucinous subtype were recorded. Patients lacking one of these factors were not included.
Results: 991 patients (51% male) were included with median age of 72 years. 110 patients (11%) had lymph node metastasis in the surgical specimens. The overall incidence of lymph node metastasis was 8% (26/314) in Sm1, 12% (28/231) in Sm2 and 13% (56/446) in Sm3. In the absence of lymphovascular infiltration, the rate of lymph node metastasis was 6% in Sm1, 9% in Sm2 and 13% in Sm3.
Notably, the incidence of lymph node metastasis markedly increased to 40% (37/92) in cases with lymphovascular infiltration regardless of Sm classification. Presence of tumor deposits (14 cases) and perineural invasion (15 cases) also increased the rate of metastasis but the numbers of these cases were too few for solid conclusions. Grade of differentiation and mucinous subtype had only a minor impact on the incidence of lymph node metastasis (16%).
Conclusion: Thisis the largest study in the literature examining risk factors for lymph node metastasis in T1 colorectal cancers. Our results show that depth of submucosal invasion has limited influence and that lymphovascular infiltration is the most important risk predictor for lymph node metastasis in T1 colorectal cancers.
Disclosure: Nothing to disclose

P0498 PERINEAL FLAP RECONSTRUCTION FOLLOWING PELVIC EXENTERATION

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Introduction: Perineal wound complications following pelvic exenteration (PE) are a significant cause of morbidity. We assessed our long-term experience of using perineal flap reconstruction for patients undergoing PE at a tertiary referral unit.
Aims & Methods: Retrospective review of all PE procedures from 2009-2018 was performed. Demographics, neoadjuvant/adjuvant or historical chemoradiotherapy, perineal wound closure, flap type, inpatient stay and post-operative complications were recorded.
Results: 209 PEs were performed, 120 (57%) patients had reconstruction with a perineal flap. 87% of these were for locally advanced or recurrent rectal cancer. 88% had prior pelvic radiotherapy. 75% of defects were closed using an inferior (IGAP) or superior (SGAP) gluteal artery perforator flap. Other flaps used were gracillis, vertical rectus abdominis and anterolateral thigh. 58% suffered wound complications, 14% were classified as a major complication (return to theatre within 90 days or readmission with a wound complication). Superficial dehiscence requiring vacuum dressing was the commonest complication (34%). Perineal wound complications increased median length of stay from 22 to 34 days (p= 0.001). No significant association between BMI, neoadjuvant treatment, complexity of resection, post-operative nutrition and wound complications was observed. IGAP flap was associated with fewest complications OR 0.40 (0.18-0.87).

Conclusion: Perineal wound complications cause significant morbidity increasing inpatient stay, IGAP flaps have fewer post-operative complications in our series. Strategies to optimise perineal wound care are needed.
Disclosure: Nothing to disclose

P0499 TAILORING LYNCH SYNDROME SURVEILLANCE

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Introduction: Lynch syndrome (LS) is associated with increased risk of colorectal cancer (CRC) as well as extracolonic cancer. Identification and follow-up of individuals with LS is extremely important because they can benefit from surveillance programmes by reducing cancer-risk. There is an increased awareness that cancer risk varies with specific mismatch repair mutation. However, gene-specific surveillance as well as family-specific surveillance have not been systematically studied.
Aims & Methods: Our aim was to assess the surveillance programme and tailoring strategies in a terciary centre. We conducted a retrospective cohort of all patients (n=241) under surveillance programme in our centre since their admission or treatment of the index cancer (median time of 4 years). The main outcomes were cancer-related death and risk for new lesions.
Results: Forty-eight percent had MSH2 mutation, 32% MLH1, 15% MSH6 and 5% PMS2. 95% had family history of CRC, 37% of endometrial cancer, 32% of gastric cancer and 12% of urinary tract cancer. From the 68 (28%) patients with CRC at admission, 4% developed metachronous cancer and 3% died of CRC. Left-colectomy was related to higher risk of metachronous lesions than right-colectomy (RR=12, p< 0,006). From the 173 patients without CRC on admission, 26% developed low-risk lesions, 23% high-risk lesions and 5% CRC. From the 237 patients without gastric cancer on admission, 3% developed dysplasia or adenocarcinoma. From the 108 patients without endometrial cancer on admission, 7% developed endometrial cancer and 53% underwent prophylactic hysterectomy (10% with atypia and 5% with cancer on the surgical specimen). The risk of endometrial cancer was higher when family history was present (RR=2,38 p< 0,007). From the 237 patients without urinary tract cancer on admission, 7 develop this cancer (4 were asymptomatic and diagnosed by imaging). The risk of urinary tract cancer was higher with MSH2 mutation (RR=8, p< 0,001) or when family history was present (RR=11, p< 0,004). 3% of patients on follow-up died of extracolonic cancer (median time of 7 years).
Conclusion: This cohort demonstrates the effectiveness of SL surveillance programme and suggests the possibility of tailoring strategies by gene and family history.
Disclosure: Nothing to disclose

P0500 PREVALENCE OF OPIOID THERAPY IN PATIENTS WITH FUNCTIONAL GASTROINTESTINAL DISORDERS REVIEWED AT A TERTIARY CENTRE

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Introduction: The appropriateness of chronic opioid use in patients with non-cancer pain is increasingly challenged due to limited evidence of its efficacy and the risk of problematic use and dependence. The side effects of opioids on gut function suggest this therapy should be particularly avoided in patients with functional gastrointestinal (GI) disorders. Data on the prevalence of opioid use in patients with functional GI disorders is unknown. We aimed to evaluate the prevalence of opioid use in functional GI patients referred to a tertiary Neurogastroenterology clinic and to determine the risk factors for their initiation.
Aims & Methods: 100 consecutive outpatients (85 females, 37±15 years) with functional GI disorders referred for a specialist opinion at our tertiary referral centre were retrospectively reviewed. Two independent research-

ers (AM and FL) carried out a detailed chart evaluation of the presence and type of comorbidities and concomitant pharmacotherapy. Patients were also specifically asked about opioid use, the duration of therapy and the clinical indication for starting the opioids.

Results: Twenty-one patients (20F, 38±12 years) were taking chronic opioid therapy. The main reason for opioid initiation was chronic musculoskeletal pain (12 patients, 57%), chronic abdominal pain (5 patients, 24%) and chronic pelvic pain (1, 5%). The mean duration of the opioid treatment was 2.7±1 years. The risk factors associated with opioids use are depicted in table 1. In terms of management, patients under opioid were offered naloxegol (20%), psychology-based interventions (29%), and referral to pain specialists to rationalize opioid use (38%). The majority of the patients in the opioid group (80%) were referred for tertiary opinion from other areas of the UK, as compared to the 60% of patients without chronic opioid use.

Conclusion: Female patients with chronic functional GI disorders with associated extra-intestinal functional pain syndromes and psychological comorbidity are prescribed opioid therapy more frequently. These patients are at increased risk of developing eating difficulties requiring advanced nutritional support, which is known to be more complicated in opioid users. Access to multidisciplinary coordinated therapy including pain management and psychological therapy is required early in these patients to avoid these adverse outcomes.

Disclosure: Nothing to disclose

P0501 CLUSTER ANALYSIS OF CHRONIC SYMPTOM PROFILES CHARACTERIZES SUBGROUPS OF FUNCTIONAL GASTROINTESTINAL DISORDERS THAT DIFFER IN THEIR SENSORY RESPONSE TO SUGAR BREATH TESTING

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Introduction: Patients with gastrointestinal (GI) symptoms but devoid of recognizable pathology are classified into various functional gastrointestinal disorders (FGID) according to their GI symptoms. Sugar breath tests are used in patients with FGID to elucidate possible mechanisms, such as malabsorption and hypersensitivity. Due to the heterogenous nature of FGIDs, underlying mechanisms and the reactions during breath tests are likely to be divergent.

Furthermore, the presence of prominent extra-GI symptoms may indicate a different pathogenesis than when GI symptoms related to intestinal fermentation preponderate.

Aims & Methods: The aim of this large study was to examine the symptom and gas responses during sugar breath tests in patients with FGID grouped according to their long-term GI and extra-GI symptoms by cluster analysis. Successive male and female patients over 18 years of age referred to our GI practice in the past 10 years for investigation of FGID and without evidence of organic disease were included in this study. Patients completed a standardized questionnaire rating their long-term GI and extra-GI symptoms. These data were subjected to latent class analysis to identify unobserved clustering in the patient population. Patients also performed standardised fructose and lactose breath tests (35g and 50g, respectively), and GI and extra-GI symptoms as well as H_2 and CH_4 breath concentrations were documented hourly for 5h during the breath test. The areas-under-the-curve (AUC) of aggregate GI and central nervous system (CNS) symptoms and of the breath gas concentrations were compared between the patient clusters.

Results: In total 2083 FGID patients (mean age 39.7 years, 70% females) were enrolled in the study and subjected to cluster analysis. The optimal number of clusters defined was 6, with good face validity. GI fermentation-type symptoms were present across all 6 clusters and exclusively characterized Cluster 1 (35% of patients). The further clusters were distinguished by additional reflux-like (cluster 2: 19%), allergy-like (cluster 3: 6%), central nervous system (cluster 4: 17%), musculoskeletal (cluster 5: 10%), and generalized extra-GI (cluster 6: 14%) symptoms. Complete fructose and lactose breath tests were available in 1422 patients. The areas-under-the-curve (AUCs) of hydrogen and methane breath concentrations were not significantly different across all the 6 clusters following fructose and lactose (all p>0.05).

However, the AUCs of both GI and CNS aggregate symptoms scores differed significantly across the 6 clusters during fructose and lactose breath tests (all p< 0.001). Maximum aggregate symptom scores were consistently greater in the clusters with most extra-GI symptoms.

Conclusion: The chronic symptom clusters of patients with FGID, distinguished mainly by extra-GI symptoms, did not differ in their breath gas concentrations following fructose or lactose ingestion. The distinct symptom patterns are consequently not explained by differences in the gaseous markers of malabsorption. The clusters were, however, distinguished by differences in the GI and CNS symptoms provoked following both sugars. Clearly, patients with a greater number of chronic extra-GI symptoms also show significantly more GI and CNS symptoms after fructose or lactose ingestion than those with mainly chronic GI symptoms. These results suggest malabsorption does not explain the different phenotypical presentations of FGID. We hypothesize that hypersensitivity to the sugars or their metabolites underlies the differing symptoms, especially the multiorgan, extra-GI symptoms, in FGID.

Disclosure: Nothing to disclose

P0502 SYMPTOMS ASSOCIATED WITH MAST CELL ACTIVATION SYNDROME ARE COMMON IN PATIENTS WITH FUNCTIONAL GASTROINTESTINAL DISORDERS

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Introduction: Patients with functional gastrointestinal disorders (FGID) often have a wide range of gastrointestinal (GI) and extra-GI symptoms. Extra-GI symptoms are not included in the diagnostic criteria for FGID and are often attributed to separate functional or somatization syndromes. The mast cell activation syndrome (MCAS) encompasses a variety of disorders with either increased numbers or activation of mast cells leading to a wide range of both GI and extra-GI symptoms. Idiopathic MCAS is currently defined by typical symptoms and the response to medications targeting mast cell activation, as there are no specific biochemical markers. The apparent overlap in symptoms associated with MCAS and FGID, the increases in mast cell numbers and/or activation in FGID, and the abnormalities in histamine pathways shown in irritable bowel syndrome (IBS) suggest a potential functional association.

Aims & Methods: The aim of this large single-centre study was to investigate the overlap in GI and extra-GI symptoms most frequently associated with MCAS with the symptoms seen in patients with FGID.

Successive male and female patients over 18 years of age referred to our GI practice for investigation of FGID and without evidence of organic disease were included. Patients completed a standardized, extensive GI and extra-GI symptom questionnaire and FGID was classified as IBS and functional dyspepsia (FD) according to the Rome III criteria. The prevalence of at least 7 of the symptoms most commonly used to define MCAS (abdominal pain, bloating, diarrhoea, nausea, gastro-oesophageal reflux, excessive tiredness, problems concentrating, headache, anxiety/depression states, skin rash, urticaria/pruritus, chronic sinusitis/rhinitis, irregular heartbeat, joint pain, myalgias) was determined for the overall patient cohort and for the Rome III subgroups.

Results: We included 2083 patients with FGID in the study (mean age 39.7 years, 70% females). IBS was diagnosed in 672 (32%), FD in 1839 (88%) and overlapping IBS and FD in 625 (30%) of patients. More than 7 of the defining symptoms of MCAS were reported in 748 (36%) of all 2083 patients, and in 281 (42%) of IBS patients, in 702 (38%) of FD patients and in 266 (43%) of patients with overlapping IBS and FD. Of the 748 patients with more than 7 symptoms of MCAS, 281 (38%) had IBS, 702 (94%) had FD and 266 (36%) had overlapping IBS and FD.

Conclusion: Symptoms associated with mast cell activation syndrome are common in patients with functional gastrointestinal disorders. Conversely, functional gastrointestinal disorders are common in patients with symptoms of MCAS. Mast cells and associated biogenic amines, such as histamine and serotonin, have been shown to be involved in the pathogenesis of both syndromes. The significance of the relationship between MCAS and FGID needs to be investigated further, as a better understanding of this overlap may open new treatment possibilities in FGID.

Disclosure: Nothing to disclose

P0503 HISTOMORPHOLOGICAL AND MOLECULAR CHARACTERIZATION OF PARKINSON'S DISEASE PATIENTS WITH CHRONIC CONSTIPATION: A PILOT STUDY

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Introduction: Parkinson's disease (PD) patients can report gastrointestinal symptoms even years before the onset of neurological symptoms. It has been suggested that the digestive pathways could be used by a pathogen to access the target neuronal populations inducing PD.

Aims & Methods: The aim of this pilot study was to evaluate constipated PD patients for: 1) possible changes of inflammatory markers in blood and stool; 2) alterations of colonic mucosal factors involved in the maintenance of the intestinal barrier; 3) possible correlations of these parameters with the severity of motor and non-motor symptoms and impairment of quality of life.

Ten constipated PD patients and 10 constipated, sex and age matched, patients (Rome IV) were enrolled. All patients were requested to fill gastroenterological (Bristol Stool Chart, PAC-SYM, PAC-QoL, ODS score) and neurological (UPDSRS, PDQ-39, MMT, HAMD-17, SCOPA-AUT, NMSS) questionnaires. Blood (CBC, TSH, CRP, TNF, IL-1β, LBP) and stool (Hp antigen, fecal calprotectin, IL-1β, TNF) tests were carried out. All subjects underwent a colonoscopy with biopsies (sigma and descending colon). Colonic samples were processed for morphological evaluations (haematoxylin/eosin, sirius red/fast green, toluidine blue, confocal immunofluorescence) to evaluate respectively: eosinophilic density (inflammatory index) and collagen deposition (marker of remodelling due to chronic inflammation) in the lamina propria; acid mucin (changes in mucus producing cells) and claudin-1 (component of tight junctions) in intestinal epithelial barrier.

Results: The onset of constipation anticipated that of PD onset in 7/10 patients. Faecal IL-1β levels were higher in PD patients as compared to controls (18.2±9.7 pg/g vs 9.3±3.7 pg/g; p< 0.05). Faecal TNF and serum LBP levels were higher in PD, without reaching statistical significance (66.2±47.5 vs 56.3±34.6 pg/g and 33.6±14.8 vs 23.9±5.6 ng/ml, respectively). Eosinophilic density was higher in controls than PD patients (56±16 vs 13±4 / mm²; p< 0.05). Collagen levels and acid mucin were higher in PD patients (18.6±2.5 vs 13.1±1.3 PPP; p< 0.05, and 14.7±1.6 vs 10.3±1.5 PPP; p< 0.05). Claudin-1 expression decreased along the epithelial surfaces in PD patients. A lack of correlation was found between these findings and the severity of digestive and neurological symptoms.

Conclusion: PD constipated patients display higher levels of intestinal inflammation and tissue remodeling, as well as a higher degree of enteric barrier impairment than constipated patients without PD. These findings confirm an intestinal involvement in PD, and open the way for future pathophysiological studies.

Disclosure: Nothing to disclose

P0504 ALLERGIES AND EXTRA-DIGESTIVE MANIFESTATIONS IN FUNCTIONAL GASTROINTESTINAL DISORDERS

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Introduction: Extra-digestive manifestations are frequently reported by patients with functional gastrointestinal disorders (FGIDs). Gut neuroinflammation and gut-brain axis are putative shared mechanisms. Gut barrier damages associated with mast cells and/or eosinophils infiltration are common features of FGIDs, suggestive of a possible pathogenetic role of allergic reactions. An association between allergies and extra-digestive disorders in FGIDs has never been elucidated.

Aims & Methods: Aim. To evaluate prevalence of food and non-food allergies in Fgid patients with and without extra-digestive manifestations.

Materials and Methods. In a single center setting, we prospectively investigated clinical features and allergies in outpatients referred for digestive symptoms. Each patient answered validated questionnaires on digestive and extra-digestive symptoms and underwent both serum and cutaneous allergological tests: IgE and skin prick testing to food and inhalant allergens; patch testing (SIDAPA 40 aptens). FGIDs were diagnosed according the Rome III criteria. Extra-digestive syndromes included general (tiredness, foggy mind, joint or muscle pain), neurologic (restless leg syndrome, migraine/headaches, dizziness, epilepsy, sensory symptoms), psychological (anxiety/panic disorders, depression, sleeping disorders, eating disorders), rheumatologic and immunologic (psoriasis, Raynaud's, fibromyalgia, Sjogren, multiple sclerosis), urogenital (cystitis, vaginitis, prostatitis, vestibulitis, dyspareunia, dysmenorrhea, infertility), cutaneous (acne, alopecia) and other manifestations (tachyarrhythmias, presyncope, discopathies, endometriosis, multiple chemical sensitivity). The study was approved by the S. Orsola University Hospital Ethic Committee.

Results: Between 2011 and 2014, 80 patients with organic diseases (F=51.3%, age 48.7±16.7 yrs, m±SD) and 970 FGID patients were enrolled (F=75.1%; 42.8±14.6 yrs). 827 FGID patients (85.3%; F=78.1%; 43.2±14.5 yrs) complained of ≥1 extra-digestive disorders (ExtraD-FGIDs) vs 53 organic patients (71.6%; F=78.1%; 49.2±17.1 yrs; p=0.004). 718 FGID patients (74.0%; F=76.7% 41.8±14.3 yrs) vs 42 patients with organic diseases (52.5%; F=52.4%; 43.7±14.9 yrs; p=0.001) had ≥1 positive allergic tests. 622 patients (75.2%) with and 96 (67.1%) without extraD-FGIDs had ≥1 positive allergic tests (p=0.049). The difference was driven by a higher prevalence of chemical allergies (40.1% vs 28.5%; p=0.014), while no significant difference was found for food or inhalant allergies. Specifically, a significant higher frequency of chemical allergies was detected in patients with than in those without urogenital (47.2 % vs 33.2%, p=0.001), cutaneous (58.1% vs 37.7%, p=0.025), neurological (43.9% vs 36.1%, p=0.019), and psychological manifestations (41.4% vs 33.6%, p=0.013).

Conclusion: Extra-digestive disorders are frequent in allergic patients with FGIDs. Non-food and specifically chemical allergies are significantly associated to urogenital, cutaneous, neurological and psychological disorders in patients with FGIDs.

Disclosure: Nothing to disclose

P0505 ARE DIGESTIVE SYMPTOMS FREQUENT IN PATIENTS WITH CHRONIC ADRENAL INSUFFICIENCY?

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Introduction: Acute adrenal insufficiency is frequently associated with digestive symptoms such as vomiting, diarrhea and abdominal pain. However their prevalence in patients having a chronic adrenal insufficiency (CAI) is unknown. The hypothalamic-pituitary-adrenal axis plays also a role in the pathophysiology of irritable bowel syndrome (IBS).

Aims & Methods: The aim of this study was to characterize and to quantify digestive symptoms in CAI patients using Rome IV questionnaire.

An online questionnaire was published on the website of a CAI patients association from June to October 2017. Information about demographics, adrenal insufficiency (age at diagnosis, etiology, type of medication) and quality of life was collected. Patients also answered to a French version of the Rome IV questionnaire and the Bristol scale.

Results: We analyzed responses from 165 patients (Addison's disease (AD) (n=74), congenital adrenal hyperplasia (CAH) (n=56), impairment of the hypothalamic-pituitary-adrenal axis (IHA) (n=35). Abdominal pain at least once a week during the 3 last months was reported by 38%, 31% and 54% of patients with AD, CAH and IHA respectively. Symptoms were consistent with the IBS criteria in 24%, 31% and 31% of patients with AD, CAH and IHA respectively.

Patients described their quality of life as bad in 34%, 21% and 54% of patients with AD, CAH and IHA respectively.

Conclusion: Our study is the first to our knowledge to consider digestive symptoms in CAI beside acute adrenal insufficiency. Digestive symptoms are frequent and invalidating in CAI patients and are close to those of IBS patients in 50% of CAI patients.

Disclosure: Nothing to disclose

P0506 ELEVATED EXPRESSION OF UROKINASE-TYPE PLASMINOGEN ACTIVATOR MARKS STRESS-INDUCED VISCERAL HYPERSENSITIVITY IN RATS

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Introduction: Visceral hypersensitivity, i.e. the increased response towards colonic stimuli, contributes to abdominal pain complaints observed in irritable bowel syndrome (IBS). In this study, we aimed to identify targets for stress-induced visceral hypersensitivity. To this end, we analyzed the transcriptome through RNA sequencing (RNAseq) of descending colon samples obtained from our rat model after which we confirmed our findings in a separate cohort of rats, as well as in patient biopsies.

Aims & Methods: In this study, we aimed to identify genes involved in the development of post-stress visceral hypersensitivity in rats. In the discovery cohort, adult maternally-separated (MS) rats and non-handled (NH) rats were exposed to acute water avoidance (WA)-stress for one hour or left undisturbed (4 groups, n=3). Rats were sacrificed 4 hours after WA after which RNA was isolated for subsequent sequencing at GenomeScan (Leiden, The Netherlands; NextSeq 500, 10M reads). Statistical significance of differentially expressed genes was defined as genes with a Benjamini-Hochberg adjusted p-value of less than 0.05.

Subsequent validation of the gene of interest was done using quantitative real-time polymerase chain reaction (qRT-PCR) on distal colon samples obtained from an independent rat cohort. In this experiment, NH and MS animals were sacrificed 21 days after WA (n=8-9)[1].

Qualitative PCR analyses of the same gene of interest was performed in human biopsies obtained from colon descendens of normosensitive healthy volunteers and hypersensitive IBS patients (n=10 per group)[2]. Additionally, immunohistochemical staining on paraffin-embedded tissues was performed to investigate whether possible changes in gene expression manifested at protein level; uPA positive cells were counted manually and quantified as positive cells per mm².

Results: RNAseq analysis of the four groups did not reveal differentially expressed genes. However, comparing MS without WA vs. MS after WA, revealed 1 differentially expressed gene: Plau (effect size =1.256 log2 fold change; p_{adj}=0.0011), which encodes for the protein urokinase-type Plasminogen Activator (uPA). qPCR analysis on the independent rat cohort confirmed an increased expression of Plau in colonic tissue after maternal separation plus WA (NH after WA vs. MS after WA; Mann-Whitney test; p< 0.005). Further investigation of the ortholog PLAU in human colon descendens revealed no statistically significant differential expression (Mann-Whitney test; p=0.0575). Nonetheless, subsequent immunohistochemistry revealed a non-significant increase in the number of uPA-positive cells in hypersensitive IBS colon (t-test; p=0.49).

Conclusion: In this exploratory analysis we observed elevated expression of Plau associated with stress-induced visceral hypersensitivity in rat. Enhanced expression of this gene transcript was confirmed in an independent rat cohort that underwent MS and WA stress. However, we could not confirm these findings in hypersensitive IBS patients on neither mRNA nor protein expression. Based on literature, uPA may activate protease activated receptor-1 (PAR-1)[3]. PAR-1 antagonism was found to successfully reduce activity of sensory neurons in vitro upon exposure to supernatants of colonic IBS biopsies[4, 5]. To address the translational relevance of these findings, additional research should be performed on uPA protein levels and activity in human colon.

References: 1. Botschuijver, S., et al., Intestinal Fungal Dysbiosis Is Associated With Visceral Hypersensitivity in Patients With Irritable Bowel Syndrome and Rats. Gastroenterology, 2017. 153(4): p. 1026-1039. 2. Braak, B., et al., Mucosal immune cell numbers and visceral sensitivity in patients with irritable bowel syndrome: is there any relationship? Am J Gastroenterol, 2012. 107(5): p. 715-26. 3. Kanno, Y., et al., uPA Attenuated LPS-induced Inflammatory Osteoclastogenesis through the Plasmin/PAR-1/Ca(2+)/CaMKK/AMPK Axis. Int J Biol Sci, 2016. 12(1): p. 63-71. 4. Desormeaux, C., et al., Protease-activated receptor 1 is implicated in irritable bowel syndrome mediators-induced signaling to thoracic human sensory neurons. Pain, 2018. 159(7): p. 1257-1267. 5. Buhner, S., et al., Protease signaling

through protease activated receptor 1 mediate nerve activation by mucosal supernatants from irritable bowel syndrome but not from ulcerative colitis patients. PLoS One, 2018. 13(3): p. e0193943.
Disclosure: AFY Li Yim is an employee at GSK.

P0507 PATIENTS WITH IRRITABLE BOWEL SYNDROME HAVE LOW ENZYMES ACTIVITY OF THE MEMBRANE DIGESTION IN THE SMALL INTESTINE

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Introduction: The decrease in enzymes activity of the membrane digestion (EAMD) in the small intestine providing digestion of carbohydrates can cause clinical symptoms of irritable bowel syndrome (IBS).

Aims & Methods: To estimate EAMD, namely glucoamylase (GA), maltase (M), sucrose (S) and lactase (L), in patients with IBS and the effect of their activity in long-term therapy with rebamipide. 102 patients with IBS, aged from 18 to 50 (41 men and 61 women) were examined. According to Rome IV criteria (2016), 68 patients had IBS with predominance of diarrhea, 20 patients had IBS with predominant constipation and 14 patients showed mixed type of IBS. In all patients there was a more or less pronounced association of intestinal symptoms when consuming product containing milk (48.6%), potato starch (47.3%) and sugar (27.0%). The activity of GA, M, S and L were determined by Dahlquist-Trinder method in duodenal biopsies obtained during esophagogastroduodenoscopy. The control group consisted of 20 healthy people aged 23-47. They showed following enzyme activity: L - 42 ±13 ng glucose/mg tissue x min, GA − 509 ±176, M − 1735 ±446, S - 136 ±35 ng glucose/mg tissue x min. These figures were taken as the norm.

Results: 10,8% of the study group showed normal EAMD (11 out of 102 patients), 32.3% had decreased activity of all studied enzymes and 58.8% had selective reduction of EAMD. Thirteen patients with reduced EAMD were recommended the FODMAP diet and ingest rebamipide 3 times a day x 200 mg for 3 months. Before the treatment the activity of GA of these patients averaged 83 ±78, M-417 ±221, S − 32 ±17, L-11 ±17 ng glucose/mg tissue x min. After the treatment 11 patients reported a decreased or no flatulence, abdominal pain, stool disorder; 2 people reported no change. The activity of GA increased to an average of 149 ±82 (by 78%, p = 0.016), M to 864 ±472 (by 131%, p = 0.0019), S - 63 ±35 (by 95%, p = 0.0041) and L − 10 ±8 ng glucose/mg tissue x min.(the activity did not change significantly).

Conclusion: In 89.2% of patients with IBS, there was a decrease of EAMD responsible hydrolysis of carbohydrates. The 3-month treatment with rebamipide helped reduce clinical symptoms and increase EAMD.
Disclosure: Nothing to disclose

P0508 EFFICACY AND SAFETY OF *SACCHAROMYCES BOULARDII* CNCM I -745 IN THE TREATMENT OF SMALL INTESTINAL BACTERIAL OVERGROWTH IN PATIENTS SUFFERING IRRITABLE BOWEL SYNDROME WITH DIARRHEA

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Introduction: Irritable bowel syndrome (IBS) is a very common chronic gastrointestinal condition with abdominal pain, altered bowel habits and stool consistency. IBS-D is a sub-type with predominant diarrhea. Altered intestinal microbiota and the presence of small intestinal bacterial overgrowth (SIBO) have been documented in IBS. *Saccharomyces boulardii* CNCM I-745 (*S boulardii*) is a probiotic yeast with proven efficacy in antibiotic-associated diarrhea and acute gastroenteritis. However, there is scarce evidence regarding the impact of *S boulardii* on IBS-D patients.

Aims & Methods: Aim: To assess the efficacy and safety of *S boulardii* on SIBO-positive IBS-D patients.

Materials and methods: It was a randomized open label phase IV study on adult patients from two referral centers in Buenos Aires, Argentina with a diagnosis of IBS-D (Rome III criteria), with no systemic or severe diges-

tive signs nor intake of drugs known to alter microbiota. Patients were randomized to receive either *S boulardii* 250 mg *b.i.d.* plus dietary advice (Sb group) OR dietary advice only (Control group) for 15 days. SIBO was assessed by lactulose hydrogen breath test (LHBT). LHBT was done at inclusion (D0) and end of study (D15). Other criteria included IBS Symptom Severity Scale IBS-SSS (values 0 to 500), Bristol Stool Scale, Quality of Life (measured with the IBS-QoL questionnaire) and safety.

Results: Fifty-four patients were included and treated, 6 were prematurely discontinued from the study and 48 (27 Sb, 21 Control) were included in the efficacy analysis. Mean age was 44-years old, BMI 25. At D15 the mean change from baseline of LHBT area under the curve (AUC) was greater in the Sb group (Table 1 part A). More patients in the Sb group had decreased LHBT AUC : 74% vs 57% (p=0.217). A post-hoc ANCOVA adjusted on baseline AUC level showed that the inter-group difference of approximately 1800 ppm was statistically significant (Table 1 part B & Fig2) and also that AUC at D0 had a strong impact on change under treatment. IBS-SSS decreased from 306 and 300 in the Sb and Control groups respectively to 180 and 203 at D15.

A trend to a higher proportion of patients with normal stool consistency was observed in Sb group (70.4% vs 47.6%, p=0.07). In each group, 5 patients reported at least an adverse event (AE). One AE was serious (papillophlebitis, Control) and another one (sinusitis, Sb) led to study discontinuation, both unrelated to the treatment.

Conclusion: This pilot study suggests that Sb in addition to dietary advice seems to positively affect SIBO in patients with IBS-D, although the difference between groups was statistically significant only in a post-hoc parametric analysis, without any safety issue. A confirmatory study is needed.

Disclosure: Dr. Luis Bustos Fernandez is member of the Latin American Board of Biocodex

P0509 IMPACT OF SACCHAROMYCES BOULARDII CNCM I-745 ON MICROBIOTA & MYCOBIOTA FOR THE TREATMENT OF BACTERIAL OVERGROWTH IN IBS-D PATIENTS

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Introduction: Intestinal microbiota dysbiosis is thought to be associated with diarrhea-predominant Irritable Bowel Syndrome (IBS-D); therapeutic alternatives that could modify microbiota (e.g. diet, antibiotics and probiotics) have been proposed for the treatment of IBS-D. Probiotics such as *S. boulardii CNCM I-745* (Sb) may be efficacious in IBS associated to dysbiosis or bacterial overgrowth.

Aims & Methods: To compare the efficacy and safety of Sb plus dietary advice versus dietary advice only on small intestinal bacterial overgrowth (SIBO) in IBS-D patients and to describe their impact on intestinal microbiota composition and clinical improvement.

Adult patients from 2 referral centers in Buenos Aires with IBS-D (Rome III criteria) and SIBO were randomized (1:1) to receive either Sb plus dietary advice (Sb group) or dietary advice only (Control group) for 15 days. At the beginning and at the end of treatment, patients were asked to collect a fecal sample and underwent a lactulose breath test. Severity of symptoms was assessed with the IBS-SSS score and stool consistency was evaluated with the Bristol Stool Scale. Bacterial and fungal composition of fecal samples were analyzed based on 16S rDNA and ITS2 sequencing respectively. Additional qPCR analysis was performed to quantify the abundance of *F. prausnitzii, M. smithii, B. thetaiotomicron* and *P. aeruginosa.*

Results: Fifty-four patients were included and 48 (27 Sb, 21 control) were evaluated for efficacy. Sb treatment led to a significant decrease of hydrogen excretion (difference between groups: -1800, IC95[-3595 ; -53], p=0.04). Microbiological analyses showed an adequate alpha and beta diversity, which enforced the good quality of samples.

With regards to bacterial composition, c_Coriobacteriia (-67%), c_Deltaproteobacteria (-77.6%) and g_Hungatella (-74.9%) were decreased. Interestingly, *F. prausnitzii* was more abundant in patients with marked clinical improvement with Sb: stool consistency normalization (+120%), negative SIBO with improved IBS-related symptoms (+400%), such as reduction of abdominal pain (+76.5%).

Mycobiota analyses showed significant modifications in Saccharomyces and phylogenic related lineage (g_Saccharomyces (+27%), g_Debaryomyces (-88%)) and g_Filobasidium (>1000%) and upper related taxa. In addition g_Penicilium and upper related lineage were 100 times more abundant in SIBO negative samples after Sb treatment. Five patients in each group reported at least one adverse event (AE). One patient reported 1 serious AE (papillophlebitis) unrelated to the treatment.

Conclusion: Sb CNCM I-745 reduced the bacterial overgrowth and improved digestive symptoms in IBS-D patients. These effects were associated with intestinal microbiota modifications. The increased abundance of *F. prausnitzii* observed in *S. boulardii* patients with symptom resolution merits further research.

Disclosure: Dr. Luis Bustos Fernandez is member of the Latin America Board of Biocodex

P0510 HOW ADDİNG PROBİOTİCS TO FODMAP DİET EFFECTS SYMPTOMS OF IRRİTABLE BOWEL SYNDROME: RANDOMİZED DOUBLE BLİND PLACEBO-CONTROLLED STUDY

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Introduction: In the treatment of Irritable Bowel Syndrome (IBS), physician-patient relationship, diet and lifestyle changes should be considered in addition to medical treatment. Recent studies have shown that FODMAP (fermentable oligo- di- monosaccharides and polyols) restricted diet and probiotics may affect IBS symptoms.

Aims & Methods: The aim of this study was to evaluate the combined effect of FODMAP-restricted diet and probiotic supplementary food products on IBS symptoms. In this study, out of all patients diagnosed with IBS according to Rome IV criteria, 51 of them are randomly placed in FODMAP + probiotics group and the other 51 are randomly placed in FODMAP + placebo group. Before starting the study, all patients are asked to fill in questionnaires for Visual Pain Score, Bristol Stool Chart and IBSSS. Patients forwarded to a dietician to receive nutrition advice on low FODMAP diet. Low FODMAP diet applied as 9 gr/day. Patients, who are in low FODMAP diet + probiotics group, received food supplement containing 2 grams of probiotics once a day while the other group were receiving a placebo once a day in addition to their diet. Patients are assessed and scored via same tools in 1 month. A data analysis was made using abovementioned scales and scores about patients in FODMAP + probiotics group and FODMAP + placebo group before and after this program.

Results: In both groups, placebo and probiotic fractures were significantly improved in VAS and IBSS scores. The change in VAS score was 2.56 (p=0.002) in the probiotic group and 2.77 (p=0.019) in the placebo group. When the IBS score was evaluated, the score of 307.46 in the probiotic group was 176.64; in the placebo group, it decreased from 310.26 to 183.87.

Conclusion: A low FODMAP diet is a treatment option that has a positive effect on IBS symptoms. In our study, the low FODMAP diet showed significant efficacy in correcting symptoms, but no additional contribution of probiotic was found.

Disclosure: Nothing to disclose

P0511 LOW FODMAP DIET IN THE LONG TERM: EFFICACY, ACCEPTABILITY AND INDIVIDUAL PERCEPTION OF TRIGGER FOODS: A PILOT STUDY

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Introduction: The low-FODMAP diet (LFD) in IBS patients is efficacious in the short term, however, its acceptability and long-term effects still need to be clarified. Moreover, it is not clear if what patients report during the clinical history about the "trigger" FODMAP foods is reliable.

Aims & Methods: The aim of this ongoing study was to evaluate: 1) the efficacy and acceptability of a long-term FODMAP diet; 2) the patients' reli-

ability in detecting the real FODMAP foods able to provoke their symptoms. Sixty-three IBS patients (Rome IV), consecutively recruited, started (T0) a LFD for 8 weeks (T1), and then followed a 8-12 week reintroduction period (T2). After that a personalized adapted LFD (aLFD) was issued to each patient. To assess long-term effects, patients were evaluated again at least 6 months after T2 (T3). The following scales were used: IBS-SSS for assessing the severity of IBS symptoms, Likert scales to evaluate the degree of symptom relief and the degree of satisfaction with the diet, and the FODMAP Adherence Report Scale (FARS) to evaluate dietary adherence. Patients' opinions about FODMAP trigger foods at T0 were compared with data obtained at the end of the reintroduction period. Dietary acceptability and food-related quality of life were evaluated using a 20-item questionnaire adapted from the nutrition-related QOL questionnaire.

Results: At T3 (11.2±4.2 months) IBS-SSS improved compared to T0 (218.9±105.8 vs 324.1±90.2; p< 0.002). Patients' satisfaction with aLFD was 7.5±2.4 on a 10-point Likert scale and degree of relief was 1.8±1.3 on a 7-point Likert scale). Regarding dietary acceptability patients reported that they needed more time for cooking (P< 0.0001), it had higher costs (p< =0.00001) and they had problems eating out (P< 0.0001) during the LFD, but not during the aLFD. Adherence to the LFD was constantly high (T1: 24.2 ± 0.9; T2: 24.2 ± 0.8; T3:24.0 ± 1.5 ns). Regarding patients' perception of trigger foods, a moderate concordance was found only for lactose (k: 0.54), a fair one for fructans, fructose and galactans (k: 0.38, 0.27 and 0.28, respectively) and a poor one for polyols (k: 0.12).

Conclusion: IBS patients are satisfied with LFD because it improves symptoms. A LFD is well accepted and effective also in the long term. The patients' perception regarding "trigger" foods reported during their clinical history is not reliable.

Disclosure: Nothing to disclose

P0512 FECAL TRANSPLANTATION ADMINISTERED VIA COLONOSCOPY IN IRRITABILE BOWEL SYNDROME: RESULTS OF A RANDOMIZED PLACEBO-CONTROLLED STUDY

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Introduction: Irritable bowel syndrome (IBS) is a common functional gut disorder with unknown etiology. Aberrant microbiota composition has been associated with IBS and is considered to play a role in the symptom development. Fecal microbiota transplantation (FMT) has been shown to be highly successful in treating patients with recurrent Clostridium difficile infection. We performed a randomized, double blind, placebo-controlled trial to evaluate the effect of a single FMT administered in colonoscopy on the symptom relief of IBS patients.

Aims & Methods: We recruited 56 adult IBS patients with any level of symptom severity and including all the IBS subtypes. The participants were randomized 1:1 to receive either frozen and thawed FMT from a tested general donor or a placebo made from patients own fresh stool. The participants were asked to fill questionnaires at baseline and at 4, 8, 12, 26 and 52 weeks after the FMT. Changes in symptom severity were recorded with IBS Symptom Severity Score (IBS-SSS) scored 0-500. Additionally, quality of life was recorded with questionnaires IBS-QoL and 15-D, anxiety with Beck Anxiety Inventory (BAI) and depression with Beck Depression Inventory (BDI).

Results: The primary endpoint of the study was a sustained reduction of IBS symptoms defined by a drop of IBS-SSS score of 50 points. This was achieved only at 12 weeks after the FMT in the treated group when compared to the baseline (unpaired t-test p=0.03, 95%, CI 3.79 to 126.71). There was no statistical difference between the placebo and treated group at any time point. There were no other significant changes in the mental health status or quality of life measures between the treatment or placebo group or compared to the baseline.

Conclusion: In this randomized placebo-controlled trial we did not find significant differences between FMT and placebo. The IBS symptom severity of the treatment group decreased significantly 12 weeks after FMT as compared to the baseline, but the change was transient. Adverse events

were mild and indifferent between the two groups. The transient relief of IBS symptoms in the FMT treatment group indicate that microbiota is a potential therapeutic target in IBS. Larger placebo-controlled studies are needed with more homogenous study population and with different treatment protocols. Currently, FMT cannot be recommended in treatment of IBS outside of study protocols.

Disclosure: Nothing to disclose

P0513 COMPLIANCE TO PROBIOTIC THERAPY IN IRRITABLE BOWEL SYNDROME IN CLINICAL PRACTICE: A REAL-LIFE STUDY

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Introduction: Probiotics have been evaluated in multiple clinical trials on irritable bowel syndrome (IBS) showing efficacy on different IBS-related symptoms. Among them, the multistrain probiotic VSL#3 (manufactured by Nutrilinea Srl and distributed by Ferring SPA) has been the object in clinical trials evaluating its administration for 4 to 8 weeks. However, whereas in clinical trials patients are closely monitored for compliance, in real-life setting long term compliance could be low. Furthermore, in many countries probiotics are fully paid by patients and the cost of therapy could further limit the compliance to probiotic therapy.

Aims & Methods: This is a single-center, observational, prospective study to evaluate the compliance to prescription of probiotic therapy in real life and to identify factors able to influence adherence to therapy. Patients diagnosed with IBS according to Rome IV criteria and receiving a clinical prescription of VSL#3 for their IBS symptoms were evaluated for eligibility. Patients providing informed consent received a diary at the start of therapy to evaluate safety and effect of treatment for two months. After two months a final visit (at clinic or by telephone) was made to assess compliance and eventual reasons for discontinuation.

Results: Fifty patients (mean age 41± SD 14.4 years, 26% males) have been enrolled and 49 completed the planned follow up. IBS subtypes are distributed as following: 44% diarrhea, 42% constipation and mixed in the remaining cases. Eighty-six percent of patients received a 4-week prescription of one sachet per day. Sixty percent of patients resulted adherent in the FAS population. Among the 20 patients with reduced compliance, 5 assumed less than 50%, 12 assumed 50% and 2 assumed more than 50 but less than 80% of prescribed doses. Principal reasons of not adherence among the 20 patients are the price of the product (40%), mild adverse events (AEs) (30%) and poor appreciation of flavour (15%). Furthermore, one patient (5%) forgot to take the treatment, one (5%) stopped the treatment for inefficacy and, for the patient who was lost at follow up (5%), the reason was not available. About AEs, 20% of patients experienced at least one (only one patient two AEs). All AEs were mild and they were: bloating (6/10 patients), constipation (2/10 patients) and flatulence (3/10 patients). The AEs were considered related to treatment in 9/10 cases and they were a reason for discontinuation in 6/10 cases. All AEs completely resolved without sequelae. No serious adverse events have been reported. Sixty-two percent of patients who assumed the therapy reported overall satisfactory benefit on their IBS symptoms with the prescribed therapy.

Conclusion: According to our results, despite a good safety profile, 60% of patients assumed all the prescribed probiotic therapy in real life setting with reported overall satisfactory benefit. The main reasons for lack of compliance were price of the product, mild AEs (mainly bloating) and low palatability.

Disclosure: L.L. consultant for Actial Farmaceutica. Lecturer for Janssen. M.N. nothing to disclose F.S. lecturer for Sanofi, Cadigroup and MSD E.G. nothing to disclose A.G. Speaker's bureau for MSD, Abbvie, Gilead, Alfasigma, Biocure, Actial Farmaceutica, Sanofi, Takeda, Dicofarm

P0514 TREATMENT OF PERIANAL FISTULA IN PROCTOLOGY CONSULTATION: ASSESSMENT OF EFFICACY AND SAFETY

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Introduction: Perianal fistula significantly decrease quality of life and are traditionally treated by fistulotomy or fistulectomy. Efficacy and safety of fistula seton placement followed by superficial fistulotomy have been discussed in the past years.
Aims & Methods: The aim of our study is to evaluate the efficacy and safety of this procedure on the treatment of perianal fistula.
This is a retrospective observational study of patients with cryptogenic perianal fistula aged 18 to 90 years old, who were followed in a central hospital proctology consultation between January 2006 and December 2017. Clinical records of patients informatically coded as having anal fistula were analysed. Parks Classification was used to characterize anal fistula. We identified 263 patients, of whom 167 were excluded: 111 for incomplete information, 19 for submucosal fistula, 16 for coding error, 7 for complex fistula, 7 for HIV infection, 4 for inflammatory bowel disease, 2 for still having seton in situ at the time of data collection and 1 for age over 90.
Fistula were characterised by proctologic examination and imaging (anorectal ultrasound and/or MRI). The treatment consisted of defining fistula anatomy by passing a probe through the fistula tract (cannulation). This was followed by seton placement which remained in situ for a variable time until fistula tract was exteriorized. Superficial fistulotomy was then performed with an electric cautery, under local anesthesia.
Results: Ninety six patients with perianal fistula were included (66.67% males, mean age 56±15 [23-86] years old). Nineteen (19.89%) patients had previous history of anal fistula and 14 (14.58%) previous anorectal surgery. Of the 96 patients, fistula cannulation was not possible in 2 (2.08%), for a partially closed fistula tract. Of the 94 patients submitted to fistula cannulation, fistulotomy was possible in 74 (78.72%). Among the others, fistulotomy was not possible due to: loss of follow up - 16 patients (17.02%), loss of seton - 3 patients (3.19%) and therapeutic failure due to nonprogression of seton - 1 patient (1, 06%) - (ITT 80.2%, PP 98.7%).
We evaluated 74 patients submitted to cannulation and fistulotomy for perianal fistula treatment. The mean follow-up time was 59±45 [6,144] months. Of these patients, 47 (63.51%) had intersphincteric fistula (time with seton 15±31 weeks), 26 (35.14%) transsphincteric fistula (time with seton 32±47 weeks), 1 (1.35%) suprasphincteric fistula (time with seton 11 weeks).
Adverse events were reported in 4 (5.4%) patients: 2 (2.7%) had transient pain after the procedure and 2 (2.7%) reported incontinence.
Two patients (2.7%) had recurrence after fistulotomy, in less than 8 weeks.
Conclusion: Placement of seton followed by fistulotomy is a safe and effective method for perianal fistula treatment.
Disclosure: Nothing to disclose

P0515 "ANAL TAPE" A GENUINE EXTERNAL DEVICE FOR FECAL INCONTINENCE

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Introduction: Fecal incontinence (FI) is a common underreported, debilitating condition with devastating negative impact in quality of life. Its prevalence ranges from 7-18%. Management includes: Conservative / behavioral treatment, anal or vaginal plugs, and invasive methods. We developed an "anal tape" with an adjusting applicator to adapt the device to the skin surrounding the anus. We used an available elastic band with a special adhesive that is approved for use in the skin.
Aims & Methods: The aim of this study was to determine the safety and efficacy of the "anal tape" device in patients with fecal incontinence. This is a four week prospective, self-controlled open label study of patients

with mild to moderate FI. The primary outcome was improvement in any of the 4 domains in the "Fecal Incontinence quality of life scale (FIQOLS)" using a 5 point Likert scale (higher score meaning better quality of life) . Secondary outcomes included improvement in severity and frequency of FI events according to the Wexner score and stool diaries, and safety. The first two weeks, served as the control period since no treatment was provided. During the third and fourth week, the tape was applied and served as the study period. Questionnaires were completed on days 0, 14 and 28 of the study. At day 28 patients were asked to rate their general satisfaction and willingness to use the anal tape in the future using a visual analog scale.
Results: Twenty patients were included, all females. The median age was 64 (Range 27-82). Four patients developed FI after an obstetric anal sphincter injury (OASIS) and one had FI secondary to peripheral neuropathy; In 15 the FI was considered idiopathic, but seven of them had a remote history of OASIS. Significant improvement was observed in all domains of the FIQOLS from baseline to day 28 (Lifestyle: 2.8(0.69) to 3.3(0.68) p< 0.001; Coping/Behaviour 1.9(0.64) to 2.5(0.73) p=0.0002; Depression/Self-Perception 3.1(0.75) to 3.5 (0.74) p=0.006); Embarrassment 2.13(0.67) to 2.65 (0.76) p=0.002) but not between baseline and day 14 (Lifestyle: 2.8(0.7) to 2.9 (0.7) p=0.6; Coping/Behaivoir 1.9(0.64) to 2.1(0.0.67) p=0.06; Depression/Self-Perception 3.1(0.75) to 3.2 (0.71) p=0.09; Embarrassment 2.13(0.67) to 2.26 (0.89) p=0.4). Quality of life Improved significantly between day 14 and day 28 in all domains except Depression/Self-Perception (p=0.08, in all other comparisons p value was < 0.04). The mean Wexner score in days 0, 14 and 28 was 12.5(3.6), 11.9(3.5) and 10.3(4.8) (day0 vs. day14 p=0.13, day0 vs day28 p=0.054, day14 vs. day 28 p=0.18). Fifteen complete stool diaries were available for analysis.
Absolute number of FI events between the control period and the treatment period decreased by a mean of 52.3% in 11/15 patients, 2 patients reported no change and 2 patients had a small (non-statistically significant) increased in the number of FI events. Fife patients (25% intention to treat) had 50% or more improvement in FI events. Out of 17 patients that completed the VAS scales, the median overall satisfaction with the device was 80 (IQR 30-85) mm and the willingness to use the anal tape in the future was 90 (IQR50-90) mm. Other than mild difficulty to remove the anal tape, no adverse events were reported.
Conclusion: The use of the anal tape was safe and effective. The primary outcome of significant improvement in quality of life was achived
Disclosure: Nothing to disclose

P0516 CONSERVATIVE MANAGEMENT OF CHRONIC ANAL FISSURE: IS THE BOTOX A GOOD RESCUE THERAPY?

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Introduction: Chronic anal fissure (CAF) is one of the commonest proctological diseases that presents with severe perianal pain and bleeding. Because of the disability associated with anal surgery, medical alternatives have been sought. Most recently, pharmacologic methods that relax the anal smooth muscle have been used to obtain fissure healing.
Aims & Methods:
Aim: To investigate the effectiveness and the factors associated to CAF healing with conservative management.
Methods: Retrospective study. Included consecutive patients referred for CAF to coloproctology consultation between March 2015 and June 2018. All the patients had a minimum follow up of 3 months.
Results: Included 75 patients, 55 (73.3%) female with mean age of 47.0±16.1 years. Nine patients (12.0%) had previous history of anal surgery and 6 (8%) suffered from IBD. The CAF was anterior in 19 patients (25.3%), posterior in 49 (65.3%) and 7 patients presented anterior and posterior CAF. All the patients were appropriately started on conservative dietary therapy and laxatives. Associated with this therapy all the patients performed topical medications (1 or 2 cycles): nitroglycerin in 85.6% of the patients and in 68% diltiazem. 43 patients (55.1%) were submitted sequentially to the 2 topical treatments. CAF healing was achieved with topical treatment in 33 (44%) patients.

The remaining patients who did not achieved CAF healing with topical therapy (56%) underwent botulinum toxin injection (Botox®). Fissure healing was observed in 54.7% (n=23) and partial healing in 3 patients (7.1%) with Botox®.

Two patients were re-injected with Botox®, one achieving complete fissure healing. Sixteen (21.3%) were referred to anal surgery. Nevertheless, we observed that patients with higher age more frequently had fissure healing with medical therapy (49.4vs40.7 years; p=0.034).

Conclusion: We observed that more than three quarters of the patients presented fissure healing with conservative management (topical+botox injection). Older patients may respond better to conservative management. This highlights the benefit of early conservative and medical management of CAF, before attempting anal surgery.

Disclosure: Nothing to disclose

P0517 EVOLUTION IN THE MANAGEMENT OF PRESACRAL TUMOURS

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Introduction: Presacral tumours represent a small group of pathologies encountered by colorectal surgeons where specialist input is likely to be required. They represent a disparate number of pathological phenomena which are classified together through a shared anatomical association. These rare tumours can be either benign or malignant and arise de novo or from embryological remnants in the pelvis. With the increased use of radiological investigations there has been an increase in the identification of these lesions many of which are incidental. Understanding how the management of such tumours has evolved would be informative to the colorectal community.

Aims & Methods: Retrospective database assessment of presacral tumours treated in a tertiary referral hospital from 1980s-2019. Patient demographics and related radiological and clinico-pathological data were assessed in relation to short and long term outcomes. From 2008, presacral tumours have been assess through a formal MDT process.

Results: 132 presacral tumours were identified: 72% Female: 98 congenital benign; 10 congenital malignant; 8 benign neurogenic; 4 malignant neurogenic; 2 malignant osseous; 6 miscellaneous malignant; 4 miscellaneous benign. 102 [77%] underwent surgical excision; 30 [23%] deferred surgery or in surveillance. The total number cases seen has increased each decade from 13 in 1980s, 19 in 1990s, 23 in 2000s to 77 patients in 2010s. Surgical intervention occurred in nearly all early cases with 90% of patients in 2000s undergoing resection. There has been a shift towards surveillance in the 2010s with 64% operated and 36% in surveillance. Stoma formation was required in 10%. Increasing proportions of patients were asymptomatic and noted incidentally on imaging.

Conclusion: Presacral tumours are increasingly noted incidentally on imaging and significant proportions may be managed with radiological surveillance. A formal specialist MDT process is required and referral to a specialist centre is recommended.

Disclosure: Nothing to disclose

P0518 HOW TO ESTABLISH A DEDICATED LOW ANTERIOR RESECTION SYNDROME (LARS) CLINIC

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Introduction: Sphincter saving resection with TME with/without preoperative radiotherapy are considered standard treatment for rectal cancer. This can result in bowel dysfunction of variable severity in these patients, including faecal urgency and frequency, incontinence, and difficult or incomplete evacuation. An internationally validated patient-reported outcome measure, Low Anterior Resection Syndrome (LARS) score, enables these symptoms to be measured. The Pre-Operative LARS score (POLARS) is a validated online tool developed by the Pelican Group, Basingstoke, which may be used to predict bowel dysfunction severity prior to anterior resection to help patients understand their risk of bowel dysfunction and also to highlight those patients who may require additional postoperative support.

Aims & Methods: We aimed to assess the risk factors for and the predicted incidence of LARS in our anterior resection patient population to validate the need for a LARS clinic in our Lower GI physiology department.

All patients who had undergone curative surgery for rectal cancer in our district general hospital Jan 2016 - Dec 2018 were included in the study. Only those who had undergone restorative anterior resection were included- the rest, including non-resection procedures (TEMS/ EMR etc) or AP resections with permanent colostomy, were excluded. Demographics, tumour height from the anal verge, preoperative treatment and details of the surgery were documented and the POLARS for each patient was calculated.

Results: There were 53 male and 31 female patients in the study; the age ranged from 36 to 98 years, with 80.92% in the 51-80 year age group, 58.33% in the 61-80 year group. The incidence of Major LARS was predicted as 8.33%, minor LARS was 78.57% and no LARS was only 13.1%. Interestingly, the mean age in the Major LARS group was 53 as compared to 77 years in the no LARS group. The mean distance of the tumour from the anal verge was 10.14 cm in the Major LARS group as compared to 22.82 cm in the no LARS group. No patient in the no LARS group had preoperative radiotherapy as compared to 71.43 % in the major LARS group. There was only 1 female in the no LARS group whereas in the major LARS group 71.43 % patients were female.

Conclusion: Bowel dysfunction is well known following sphincter-preserving resection. We used the POLARS to help target the patients needing intensive support post treatment to prevent QOL issues. We found the risk of major LARS strongly correlated with female sex and younger age group patients as well as a shorter distance of the tumour from the anal verge; it was significantly higher in the group that had neoadjuvant therapy. We found our predicted incidence of minor/major LARS was 86.9% of our anterior resection population on POLARS. Therefore, we set up a LARS clinic in the lower GI physiology department, specifically for these patients following oncologic/surgical treatment of pelvic cancer- we have already received excellent feedback from the patients.

Disclosure: Nothing to disclose

P0519 FECAL INCONTINENCE EVALUATION AND ITS CONSEQUENCES ON QUALITY OF LIFE - STUDY IN A SECONDARY ATTENTION CLINIC

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Introduction: Anal incontinence (AI) is a involuntary loss of stool or gas and affects the individual quality of life in regards to physical, psychological and social spheres. It is known that quality of life is usually under the influence of the grade of anal incontinence, but social facts can also affect the real quality of life, for exemple, older patients may be less disturbed by the symptoms.

Aims & Methods: To evaluate the relation between the prevalence of anal incontinence and its grades of gravity in a population from a secondary care clinic and the real impact of symptoms in quality of life of those individuals, using quantitative and qualitative scores (of symptoms and of quality of life).

This is a transversal analytic stud with the application of questionnaires in patients from secondary care clinic. A personal and medical health survey were applied as well as two questionnaires, already validated in medical literature (Jorge-Wexner Anal Incontinence Scale and Fecal Incontinence Quality of Life - FIQL) were also applied in patients with FI symptoms (FI solid, liquid and gas; soiling, non-sensitive loss, urgency evacuation. FIQL scale already underwent both translation and cultural adaptation processes and consists of four different domains: lifestyle, behavior, depression and embarrassment. Jorge-Wexner scale is the most utilized to evaluate grades of AI. The patients were divided in 2 groups: mild AI (score 1-9) and moderate/serious AI (score 10-20) and according to age 18-59 and older than 60.

Results: The reproducibility was tested through application of 1200 personal and medical questionnaires, being the population predominantly female (64.1%), with median age: 54 (iq 40-65). 162 patients (16%) presented AI symptoms. Among these patients, 153 that answered Jorge-

Wexner scale, 116 (75.8%) demonstrated mild AI. 9 patients did not have symptoms that were nominated in the scale (soiling, non-sensitive loss and urgency evacuation). The media of aspects assessed at FIQL scale was, respectively, in mild and moderate/serious AI: lifestyle 3.36 (sd 0.95) vs 2.4 (sd 1.04), behavior 3.35 (sd 0.89) vs 2.09 (sd 0.88), depression 3.64 (sd 0.82) vs 2.38 (1.0) and embarrassment 3.25 (sd 0.94) vs 2.15 (0.96); all comparisons were statistically significant (p< 0.05). Moreover, the patients were divided in two range of ages: patients from 18 until 59 years old and more than 60 years old. Comparing FIQL scale between those groups, there was no statistical diference regarding all aspects of the questionnaire: (lifestyle p=0.74); behavior p=0.61; depression p=0.99 and embarrassment p=0.39).

Conclusion: In the studied population, there was a direct association between the severity of AI, as stated by Jorge-Wexner scale and the quality of life, according to the classification of mild AI and moderate/serious AI. On the other side, there is no correlation between worse quality of life in patients younger than 60 years of age, despite the gravity of AI.

Disclosure: Nothing to disclose

P0520 ASSESSING THE RISK FOR GASTROESOPHAGEAL REFLUX DISEASE AND ITS COMPLICATIONS IN PATIENTS WITH CONSTIPATION

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Introduction: Constipation is a common gastrointestinal disorder which can result in infrequent hard stools that are difficult and/or painful to pass. Constipation is also frequently associated with straining which is known to promote gastroesophageal reflux disease (GERD). Data on the presence of GERD in patients reporting constipation is limited. The aim of this study was to investigate if constipation increases the risk for GERD and its main complications including Barrett's esophagus (BE), esophageal stricture (ES) as well as esophageal cancer (EC) using a large patient database.

Aims & Methods: Using data from the National Inpatient Sample (NIS) database between 2004 and 2014, we identified patients who were diagnosed with constipation using appropriate ICD 9 coding. The control group were patients who did not have a diagnosis of constipation. Demographic information, tobacco use, hernia presence and GERD diagnosis along with its complications (esophageal stricture, Barrett's esophagus as well as esophageal cancer), by ICD 9 coding, was then compared between the 2 groups to determine if any association existed using univariate and multivariate logistic regression.

Results: The total population studied in the NIS database comprised of 53,237,367 patients, of which 1,751,039 (3.2%) were diagnosed with constipation. Constipated patients were older (61 years old vs 49), more likely to be female (59.8% vs 57.8%) and African American (15.7% vs 14.6%) compared to the control group (P < 0.01 for all). Furthermore, patients with constipation were more obese (10.3% vs 9%), had increased tobacco use (11.8% vs 11%) and diaphragmatic hernias present (3% vs 1.6%) compared to those without constipation (P< 0.01 for all). Of note, constipated patients had less alcohol abuse (3.1% vs 3.8%) and bariatric surgery (0.1% vs 0.4%) compared to the control group (P< 0.01 for both). History of paraesophageal surgical repair was similar in both groups (0.1%). Using multivariate logistic regression, constipated patients had statistically significant higher rates of GERD (OR 1.57, 95% CI 1.56-1.58), BE (OR 1.24, 95% CI 1.21-1.27), ES (OR 1.21, 95% CI 1.18-1.24) and EC (OR 1.68, 95% CI 1.61-1.74) (P < 0.001 for all) compared to patients without constipation.

Conclusion: Constipation is associated with a significant increase in risk for GERD and complications of GERD. The most significant association is for esophageal cancer. Screening for and treating GERD along with its complications, if present, is essential for the optimal management of patients with constipation.

Disclosure: Nothing to disclose

P0521 RECENT TRENDS IN GASTROENTEROLOGY AND ENDOSCOPY RELATED MEDICAL PROFESSIONAL LIABILITY CLAIMS IN THE UNITED STATES OF AMERICA

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Introduction: In the recent years medical malpractice claims have contributed significantly to the rising cost of medical practice in all specialties in the United States by increasing the malpractice insurance premiums and costs associated with the practice of defensive medicine. Being a procedure oriented specialty, the trends in gastroenterology diagnoses and endoscopy related malpractice claims need to be studied to educate the gastroenterologists and allied health care professionals towards risk management and cost containment in this field.

Aims & Methods: Retrospective analysis of Medical professional liability (MPL) claims data for the years 2006-2015 obtained from the MPL association [formerly the Physician Insurers Association of America (PIAA) Data Sharing Project (DSP)] was done. Among the gastroenterology claims the presenting medical condition, operative procedure, outcomes of the claims and the costs associated with the closed claims were compared between 2006-2010 and 2011-2015 time periods to analyze the trend over the years.

Results: From 2006-2015, there were 90,743 MPL closed claims and 24,106 paid claims in all medical and surgical specialties. Out of all the claims, 2.07 %(1879) of closed claims and 1.5% (367) of all paid claims were against gastroenterologists. In the claims against gastroenterologists, 71.0% of were dropped, withdrawn, or dismissed. Out of the claims that went to trial, 88.4% of claims that received a verdict were favorable toward the gastroenterologists. Within the GI, MPL claims involving diagnostic procedures of large intestine were the most common accounting for 26% of all closed claims leading to a payment of $18,392,668 in total and $301,519 as average indemnity. Average indemnity was highest for diagnostic procedures of gallbladder and biliary tract including ERCP procedures ($484,364).This was followed by procedures involving small intestine ($336,078), large intestine ($301,519) and esophagus ($267,577). In the time frame 2006-2015, the average indemnity increased by 8.2% from $341,563 in 2006-2010 to $369,508 in 2011-2015. Amount spent on legal defense also increased by 8.7% ($44,625 vs. $48,506) in gastroenterology related claims for the respective time periods.

Conclusion: Gastroenterology specialty has an increasing trend in spending on average indemnity and defense. Diagnostic procedures of the biliary tract including ERCP have the highest average indemnity among the endoscopic procedures. Adequate endoscopic training, meticulous focus on procedural indication and well informed consent might help to reduce the costs associated with claims. Further studies are needed to investigate the variables associated with this trend in gastroenterology.

References: PIAA MPL specialty specific series -Gastroenterology 2006-2015

Disclosure: Nothing to disclose

P0522 COLORECTAL BRADYARRHYTHMIA SYNDROME AS PREDICTOR OF CONSTIPATION AND COLORECTAL CANCER

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Introduction: Constipation increases the risk of colorectal cancer [1-4]. Low frequency of defecation increases the risk of cardiovascular mortal-

ity by 21-39% [5]. Constipation increases the risk of obesity [6]. However, the most initial risk factors for constipation and colorectal cancer remain poorly understood.

Aims & Methods: Aim of this study was the description of the Colorectal Bradyarrhythmia Syndrome (CBS) as an early risk factor of constipation and colorectal cancer.

Using the method of "Chronoenterography" - weekly monitoring of enteral circadian rhythm [7, 8] surveyed 3 groups of volunteers. The first group was 356 medical students (20-22 years, 71% of women). The second - was 100 gastroenterologists (30-64 years, 41% of women). The third - 2501 doctors (24-75 years, 66% of women). 4 rhythms of defecation were revealed: normal (daily) - regular colorectal rhythm (RCR) - 7 times a week, CBS-I - 5-6 times/wk., CBS-II - 3-4 times/wk., CBS-III - 1-2 times/wk., (constipation). The presence of physiologically optimal morning (06:00-12:00) acrophase of the circadian rhythm of defecation was determined. 3 levels of quality of life (QOL) were estimated: high - 80-100% of optimal; medium - 60-80%; low - 40-60%. The level of mood and laxative were revealed.

Results: RCR was detected in 53% of medical students, CBS - in 47%. Morning phase of defecation was almost 3 times more common for students with RCR than with CBS. CSC-I, CSC-II and CSC-III were detected in 33%, 11% and 3% of students, respectively. The high level of QOL in students with RCR was (in 36%) 1.5 times more often than with CBS (in 24%). The low level of QOL in students with CBS was (21%) 1.7 times more often than in students with RCR (12%).

Low mood level was found in 34% with CBS-I, but in 55% of students with CBS-III.

Laxatives took 13%, 30% and 64% of students with CBS-I, CBS-II and CBS-III, respectively.

RCR was detected in 57% of gastroenterologists, and CBS - in 43%. Morning phase of bowel habits was almost 7 times more likely for gastroenterologist with RCR than for persons with CBS. High QOL level was found for 63% gastroenterologist with RCR but only for 49% with CBS.

Regular colorectal rhythm was detected in 56% of doctors, and CBS - in 44%. Morning phase of defecation was 4 times more common for doctors with RCR than with CBS. CBS -I, CBS -II, CBS -III (constipation) was detected in 27%, 13% and 4% of doctors respectively. Doctors with RCR had predominantly the high level of QOL (80-100% of optimum), but doctors with CBS - had predominantly average level of QOL (60-80% of the optimum). CBS was associated with a significant decrease in the level of mood in 30-55% of medical students. CBS is characterized by a progressive increasing in using laxatives (from 13% in CBS-I to 64% in CBS-III).

Conclusion: CBS occurs in all age groups, starting from the age of 20. CBS-I was 7-10 times more common than CBS-III (constipation). CBS-I is the earliest predictor of constipation. The QOL of persons with CBS was lower than of persons with RCR. CBS is manifested by 3 main features: slowing the rhythm of defecation, the absence of the morning phase of defecation and the decreasing QOL level. Screening of the CBS is necessary for the earliest (at 20 years) detection of this syndrome as a functional predictor of constipation. CBS can be used for the functional primary prevention of colorectal cancer and to identify new risk groups for endoscopic screening of this type of cancer.

References: 1. Talley N.J., Lasch K.L, Baum C.L. A gap in our understanding: chronic constipation and its comorbid conditions.Clin Gastroenterol Hepatol. 2009 Jan; 7(1):9-19. 2. Tashiro N, Budhathoki S, Ohnaka K. Constipation and Colorectal Cancer Risk: The Fukuoka Colorectal Cancer Study. Asian Pac. J. of Cancer Prevention, Vol 12, 2011, 2025-2030. 3. Guerin A, Mody R, Fok B et al. Risk of developing colorectal cancer and benign colorectal neoplasm in patients with chronic constipation. Alim. Pharm. Ther. 2014 Jul; 40(1):83-92. 4. Shemerovskii KA. Constipation - a risk factor for colorectal cancer. Klin Med 2005, 83(12): 60-64. 5. Honkura K., Tomata Y., Sugiyama K. et al. Defecation frequency and cardiovascular disease mortality in Japan: The Ohsaki cohort study // Atherosclerosis. 2016. N246. P. 251-256. 6. Shemerovskii K.A, Ovsiannikov V. I, Mitreikin V. F. Irregular Bowel Habit Increases Risk of Obesity. UEG Journal, 2015, 3 (5S), A504, P1223. 7. Shemerovskii K. A. Chronoenterography: monitoring of circadian rhythm of intestinal evacuatory function. Bull Exp Biol Med. 2002 May; 133(5):503-5. 8. Shemerovskii K. A., V. I. Ovsiannikov, V. F. Mitreikin. Screening of Irregular Bowel Movement Frequency. 20th UEG Week 2012, Amsterdam, The Netherlands, 20-24 October 2012, Gut 2012; 61 (Suppl 3), A305-306, P0957.

Disclosure: Nothing to disclose

P0523 HEALTH CARE UTILISATION AND COSTS IN IRRITABLE BOWEL SYNDROME COMPARED WITH ACTIVE AND INACTIVE INFLAMMATORY BOWEL DISEASE IN A HOSPITAL OUTPATIENT SETTING

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Introduction: Drivers of health care utilization in the irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD) are unclear but symptoms and psychological distress may be important.

Aims & Methods: This study aimed to explore the links between health care utilisation, type of bowel symptoms and severity of bowel symptoms in patients with IBS and IBD referred by GPs to a tertiary hospital. We randomly selected 282 patients without evidence for structural causes for GI symptoms who had an outpatient appointment between 15 and 18 months ago. Symptoms were assessed with the validated SAGIS-instrument and patients categorised based upon the symptom pattern as (IBS-M (IBS with diarrhea and constipation symptoms), IBS-C (constipation) and IBS-D (diarrhea), and non-IBS symptoms. In addition, we selected 149 patients with IBD. Electronic medical records were reviewed and episodes of care, hospital admissions, gastroenterology and other specialists outpatient department (OPD) consultations, diagnostic procedures (MRI, CT, ultrasound) and the number of therapeutic day procedures for a period of 12 month before and 12 month after the index consultation determined. Costs for outpatients' consultations and other procedures were quantitated based upon published data costs for the respective jurisdiction. Group differences were analysed using one-way analysis of variance and correlations were measured using Pearson correlation coefficients.

Results: Out of 282 patients, 61 reported a mix of IBS diarrhea and constipation (21.6% 95%CI 17.2-26.8), 106 (37.5% 95%CI 32.1-43.4) IBS diarrhea, 17 (6.0%, 95% CI 3.8-9.4) IBS constipation only and 98 (34.8% 95%CI 29.4-40.5) with other non-IBS symptoms. In total 149 patients had IBD but 83 IBD patients did not report clinically relevant GI symptoms (total SAGIS score < 10). As shown in Table 1 patients with active IBD had higher health care utilisation, in particular gastroenterology outpatient consultations and imaging compared with patients with IBD in remission but were *not* different to those with IBS.

Patient Group	Hospital admissions	OPD GI	OPD other	MRI	CT	Ultra-sound	Procedures
IBD-remission (n=83)	1.16 (1.87)	4.35 (1.80)*	2.28 (4.32)	0.49 (0.83)*	0.63 (0.91)	0.32 (0.63)	1.80 (2.78)
IBD-active (n=66)	1.88 (2.61)	5.30 (2.92)	2.09 (4.55)	1.27 (2.01)	0.80 (1.43)	0.50 (0.93)	2.24 (1.61)
IBS-M (n=61)	2.48 (4.40)	4.15 (2.48)	4.41 (7.76)	1.38 (2.49)	0.82 (1.71)	0.39 (0.86)	2.12 (1.53)
IBS-D (n=106)	1.68 (3.32)	4.10 (2.46)	3.51 (5.41)	0.70 (1.07)	0.64 (0.92)	0.41 (0.76)	2.03 (3.09)
IBS-C (n=17)	1.23 (1.75)	3.65 (2.85)	4.82 (6.44)	0.29 (0.49)	0.71 (0.95)	0.43 (0.53)	2.43 (1.40)
Other (n=98)	0.84 (1.68)	4.03 (3.47)	2.42 (5.79)	0.71 (1.17)	0.71 (1.02)	0.38 (0.79)	1.76 (1.51)

*IBD remission versus active P< 0.05

[Table 1. Total health care utilisation among patient groups, all cell entries are mean (SD)]

Gastroenterology outpatient costs were significantly higher in patients with active IBD ($2,121) compared with IBD in remission ($1,739) (P=0.02) and similar to patients with IBS-M ($1659), IBS-D ($1,642), IBS-C ($1,459) and IBS-other ($1,612). Compared with non- IBS patients with symptoms, patients with IBS-D (P=0.03), IBS-C (P=0.03) and IBS-M (P=0.02) had higher other OPD costs. Other procedure costs were similar in patients with IBS and active IBD but higher than in non-IBS patients.

SAGIS intensity scores were correlated with the number of hospital admissions r=0.23, P< 0.001, length of stay r=0.12, P=0.01, other outpatient consultations r=0.18, P< 0.001, CT scans r=0.115, P=0.02, other OPD costs r=0.18, P< 0.001, anxiety r=0.31, P< 0.001 and depression r=0.28, P< 0.001.
Conclusion: Health care utilisation in patients with IBS is not different to patients with active inflammatory bowel disease and exceeds health care utilisation of patients with inactive inflammatory bowel disease. The intensity of gastrointestinal symptoms is significantly associated with health care utilisation and health care costs.
Disclosure: This study was sponsored by Allergan Pty Ltd.

P0524 THE ROLE OF AN 'ADVANCED ENDOSCOPY MULTIDISCIPLINARY TEAM MEETING' FOR OPTIMAL MANAGEMENT OF PATIENTS REFERRED FOR COMPLEX ENDOSCOPIC PROCEDURES: ONE YEAR EXPERIENCE FROM A TERTIARY REFERRAL CENTRE

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Introduction: Optimisation of patient care though multidisciplinary team (MDT) meetings is now established as the standard of care in cancer pathways. Cases presented at MDTs are discussed by a panel of multidisciplinary experts in order to provide optimal management, tailored to the needs of individual patients, also considering co-morbidities and available expertise. Within the subspecialty of endoscopy, management of pathological findings may vary significantly and could be approached through an array of different techniques/procedures. Similar to cancer pathways, an advanced endoscopy MDT platform, may help to achieve consensus on decision-making and management of complex cases, clinical outcomes and patient satisfaction.
Aims & Methods: Over the last year, in our tertiary referral institution, we developed and adopted an 'advanced endoscopy MDT' to evaluate and manage complex cases referred to us for advanced endoscopic intervention. An hourly bi-weekly meeting was established with the presence of at least two expert interventional endoscopists, a radiologist, a histopathologist, a dedicated gastrointestinal (GI) surgeon and a nurse endoscopist. Depending on the cases discussed, additional experts were also in attendance (e.g. hepato-pancreatico-biliary surgeons and neuroendocrine tumor specialists). Patients from our institution and other centres referred with lesions of the upper, lower and mid GI tract were presented and thoroughly discussed. Endoscopic images, radiological scans and histopathology reports were assessed in order to decide treatment options and surveillance intervals. We retrospectively reviewed all patients that were presented at our MDT over the last 12 months. Demographic, clinical, endoscopic findings and outcome data were analysed.
Results: Over 12 months, 25 meetings were conducted; 312 cases were discussed for a total of 217 patients. Fifty-two patients (24%) were tertiary referrals from other centres. The main reasons for MDT referral were for consideration of double-balloon enteroscopy (DBE) (56 patients; 26%) and for appropriate endoscopic or surgical management of mucosal/submucosal GI lesions. Through MDT discussion, 15 patients (7%) were referred for surgical management; 30 patients were treated with endoscopic submucosal dissection (ESD) and 41 patients with endoscopic mucosal resection (EMR) (14% and 19% respectively). One ESD procedure was abandoned due to high suspicion of deep invasion and was referred for surgery. From the remaining 29 cases, R0 margins were reported for 28/29 patients. Five patients referred for DBE did not require endoscopic input and 17 cases were reviewed twice as additional radiological investigations or small bowel capsule endoscopy were deemed necessary.
All patients were informed about the MDT's outcome and 16 (7%) were offered an additional clinic appointment to discuss management options; all patients were reviewed in clinic after any endoscopic intervention. No ma-

jor adverse event including perforation, severe delayed GI bleed or sepsis occurred after any endoscopic procedure discussed at the MDT.
Conclusion: Based on our preliminary one-year experience of an 'Advanced Endoscopy MDT' is a useful platform for the safe, effective and efficient management of complex advanced endoscopic procedures. In our experience, it also appears to improve the quality of the service, clinical outcomes and facilitates optimal management. Studies are warranted to further assess the role of the MDT in endoscopy and patient satisfaction aspects.
Disclosure: Dr Despott and Dr Murino receive research/ education support from Aquilant Medical, Fujifilm, Olympus and Pentax Medical. All other authors disclosed no financial relationships relevant to this publication.

P0525 OVERDIAGNOSIS IN COLORECTAL CANCER SCREENING WITH FECAL OCCULT BLOOD TESTING

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Introduction: Overdiagnosis is the diagnosis of a disease that would not have developed to cause symptoms or death in the patient's lifetime. While largely disregarded 10 years ago, overdiagnosis is now increasingly recognized as a major harm of cancer screening.
Aims & Methods: We used data from a randomized trial comparing screening with guaiac-based fecal occult blood testing (FOBT) every other year with no screening in Nottingham, UK, and estimated colorectal cancer overdiagnosis in FOBT screening [1,2]. 152,850 individuals aged 45-74 were randomized to screening (three to six screening rounds), or no screening. Attendance to at least one screening round was 59.9%, and 38.2% attended all screening rounds. Since screening might prevent cancer also through adenoma removal, estimation of overdiagnosis requires knowledge about the natural history of adenomas to colorectal cancer - which cannot be observed. We used the following microsimulation models to inform the natural growth of adenomas to colorectal cancer: 1. the Microsimulation Screening Analysis, MISCAN; 2. the Colorectal Cancer Simulated Population model for Incidence and Natural history, CRC-SPIN; 3. the Simulation Model of Colorectal Cancer, SimCRC; and 4. a model derived by the German Cancer Research Center.
We calculated annual transition rates for the progression from adenoma to cancer using the published median dwell time in the different models. For model 4, annual transition rates from non-advanced adenoma to advanced adenoma differed depending on age and sex, and we used the lowest (German, low) and the highest (German, high) reported rate in two independent analyses.
We estimated overdiagnosed cancers as the difference between the number of cancers expected in the screening group (i.e. the total of observed cancers and cancers prevented by adenoma removal) and the number of cancers observed in the control group. The amount of overdiagnosis (percentage) is presented as the number of overdiagnosed cancers divided by cancers observed in the control group.
Results: The observed colorectal cancer incidence was 3.0% in the screening group and 3.1% in the control group after a median of 19.5 years of follow-up (hazard ratio 0.97; 95%CI 0.91-1.03). In the screening and control group, respectively, 2,139 (2.8%) and 1,484 (2.0%) individuals had at least one adenoma resected. The number of cancers prevented due to adenoma removal ranged from 45 to 296 in the screening group and from 37 to 179 in the control group. The expected number of cancers in the screening group was between 2,324 and 2,575, which is 30 fewer to 221 more cancers than observed in the control group. Overall, the amount of overdiagnosed cancers is between -1.3% to 9.4%.

Conclusion: This is the first study to report overdiagnosis in colorectal cancer screening with FOBT. Our results indicate that the amount of overdiagnosis of colorectal cancer in FOBT screening is less than 10%, but the estimates are highly dependent on adenoma transition rates.

References: [1] Scholefield JH, Moss SM, Mangham CM, Whynes DK, Hardcastle JD. Nottingham trial of faecal occult blood testing for colorectal cancer: a 20-year follow-up. Gut. 2012;61(7):1036-40. [2] Hardcastle JD, Chamberlain JO, Robinson MH, Moss SM, Amar SS, Balfour TW, et al. Randomised controlled trial of faecal-occult-blood screening for colorectal cancer. Lancet (London, England). 1996;348(9040):1472-7

Disclosure: Nothing to disclose

Paediatric: Lower GI I

10:30-17:00 / Poster Exhibition - Hall 7

P0526 TRENDS IN HEALTHCARE RESOURCE UTILIZATION AND MEDICATION USE OF PEDIATRIC CROHN'S DISEASE PATIENTS IN THE UNITED STATES, 2007-2017

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Introduction: This study aimed to analyze the healthcare resource utilization (HCRU) and medication use of pediatric Crohn's Disease (CD) patients in the United States (US) insured population from 2007 to 2017.
Aims & Methods: Trends in HCRU (emergency department (ED) visits, inpatient visits, any outpatient visits, and bowel surgery) and medication use were calculated for the 11-year period covering January 1, 2007 to December 31, 2017. Pediatric (0-17 years) patients with ≥1 CD diagnosis code (ICD-9: 555.x; ICD-10:K50.x) within the calendar year were included in this retrospective analysis of medical and pharmacy claims data from the IBM Marketscan Commercial, Medicaid, and Medicare-Supplemental Claims database. Patients with an Ulcerative Colitis diagnosis were excluded from this study.
Results: The rate of biologic use among pediatric CD patients increased from 15.6% in 2007 to 52.9% in 2017. During this time, rates of corticosteroids (35.8% to 29.6%), immunomodulators (37.9% to 18.5%), opioids (26.0% to 25.0%), and 5-ASAs (49.9% to 24.8%) decreased. Rates of bowel surgery remained stable in the pediatric CD population between 2007 and 2017. However, gastroenterologist visits and ED visits increased, while inpatient visits decreased (Table 1). The mean number of outpatient visits increased from 16.64 in 2007 to 21.63 in 2017.

	2007 N=2,506	2012 N=5,737	2017 N=4,507
Surgery; n (%)	63 (2.5%)	218 (3.8%)	134 (3.0%)
Gastroenterologist Visit; n (%)	1,309 (52.2%)	2,572 (44.8%)	2,709 (60.1%)
Emergency Department Visit; n (%)	791 (31.6%)	2,083 (36.3%)	1,762 (39.1%)
Inpatient Hospital Visit; n (%)	479 (19.1%)	1,092 (19.0%)	688 (15.3%)
Outpatient Visit; n (%)	2,503 (99.9%)	5,733 (99.9%)	4,506 (100.0%)
Number of Outpatient Visits; mean (SD)	16.64 (19.32)	19.06 (23.35)	21.63 (29.73)

[Table 1. Healthcare Resource Utilization among Pediatric Crohn's Disease Patients]

Conclusion: This study provides real-world evidence on the medication use and HCRU of pediatric patients with CD in the US. From 2007-2017, there was an increase in HCRU and over half of pediatric CD patients were prescribed a biologic. Real-word data are needed to capture changes in HCRU patterns due to the evolving CD treatment landscape.
Disclosure: Nothing to disclose

P0527 TRENDS IN MEDICATION USE AND HEALTHCARE RESOURCE UTILIZATION OF PEDIATRIC ULCERATIVE COLITIS PATIENTS IN THE UNITED STATES, 2007-2017

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Introduction: This study aimed to analyze the healthcare resource utilization (HCRU) and medication use of pediatric Ulcerative Colitis (UC) patients in the United States (US) insured population from 2007 to 2017.
Aims & Methods: Trends in HCRU (emergency department (ED) visits, inpatient visits, any outpatient visits, and bowel surgery) and medication use were calculated for the 11-year period covering January 1, 2007 to December 31, 2017. Pediatric (0-17 years) patients with ≥1 UC diagnostic code (ICD-9: 556.x; ICD-10:K51.x) within the calendar year were included in this retrospective analysis of medical and pharmacy claims data from the IBM Marketscan Commercial, Medicaid, and Medicare-Supplemental Claims database. Patients with a Crohn's Disease diagnosis were excluded from this study.
Results: The rate of biologic use among pediatric UC patients increased from 3.2% in 2007 to 22.4% in 2017. Corticosteroids use increased from 28.6% to 34.8%, while rates of immunomodulators (20.6% to 15.6%), opioids (24.8% to 22.5%), and 5-ASAs (62.7% to 60.0%) decreased. Rates of bowel surgery remained stable in the pediatric UC population between 2007 and 2017. However, gastroenterologist visits and ED visits increased, while inpatient visits decreased (Table 1). The mean number of outpatient visits increased from 15.92 in 2007 to 20.89 in 2017.

	2007 N=1,327	2012 N=2,767	2017 N=2,296
Surgery; n (%)	24 (1.8%)	55 (2.0%)	43 (1.9%)
Gastroenterologist Visit; n (%)	655 (49.4%)	1,304 (47.1%)	1,357 (59.1%)
Emergency Department Visit; n (%)	422 (31.8%)	904 (32.7%)	905 (39.4%)
Inpatient Hospital Visit; n (%)	257 (19.4%)	488 (17.6%)	414 (18.0%)
Outpatient Visit; n (%)	1,327 (100%)	2,765 (99.9%)	2,295 (100%)
Number of Outpatient Visits; mean (SD)	15.92 (25.62)	17.80 (24.99)	20.89 (31.27)

[Table 1. Healthcare Resource Utilization among Pediatric Ulcerative Colitis Patients]

Conclusion: This study provides real-world evidence on the medication use and HCRU of pediatric patients with UC in the US. From 2007-2017, there was an overall increase in the use of biologics and corticosteroids, as well as HCRU. Real-word data are needed to capture changes in HCRU patterns and cost due to the evolving UC treatment landscape.
Disclosure: Nothing to disclose

P0528 IMMUNIZATION STATUS OF BULGARIAN PAEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Paediatric inflammatory bowel diseases (PIBD), comprising Crohn's disease (CD), ulcerative colitis (UC) and inflammatory bowel disease unclassified (IBDU) are immune-mediated disorders characterized by dysregulated immune responses leading to tissue damaging inflam-

mation. The treatment regimens for patients with IBD often involve immunosuppressive therapy and increase susceptibility to infections, many of which can be prevented by vaccinations. The aim of our study was to analyze the immunization status of children diagnosed with IBD and identify factors affecting the immunization coverage.

Aims & Methods: We retrospectively reviewed the medical records of paediatric IBD patients treated in the Department of Gastroenterology and Hepatology at the University Paediatric Hospital "Prof. Ivan Mitev", Sofia and the Department of Paediatrics at the University Hospital "Saint George", Plovdiv for the period September 2013-September 2018. The immunization status of the enrolled patients was assessed as per the national immunization programme.

Results: A total of 90 children (39 girls and 51 boys) were included in the final analysis. The median age of the study participants was 15 years (range 2-17 years), 52.2% (47/90) were with UC, 45.5% (41/90) with CD and 2.3% (2/90) with IBDU.

The overall immunization coverage with traditional vaccines (hepatitis B, tuberculosis, poliomyelitis, diphtheria, tetanus and pertussis, 1st dose measles, mumps and rubella) was very good. 28.8% (26/90) of the study participants had incomplete immunization course against measles, mumps and rubella. 95.5% (86/90) of them were non-immunized against *Haemophilus influenzae type b* disease and pneumococcal disease (Both vaccines were included in the Bulgarian childhood immunization schedule in 2010 and the vaccination rates are still low).

Despite having a full course of hepatitis B vaccination in the infancy, 25.5% (23/90) of our patients had undetectable antibodies against hepatitis B. Only three girls had a human papillomavirus (HPV) vaccination. Child's age was the main factor affecting the immunization coverage.

Conclusion: The assessment of the immunization status at IBD diagnosis is a critical step in the treatment planning process. It is important to administer all necessary vaccinations as soon as possible before the initiation of an immunosuppressive therapy.

Disclosure: Nothing to disclose

P0529 QUANTIFIED TERMINAL ILEAL MOTILITY DURING MR ENTEROGRAPHY AS A BIOMARKER OF CROHN'S DISEASE ACTIVITY A PEDIATRIC POPULATION: A RETROSPECTIVE STUDY

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Introduction: A relationship between small bowel motility and inflammatory activity in Crohn's Disease is now well described in adults against endoscopic and histopathological measures of activity. This retrospective study explores this relationship between terminal ileal (TI) motility in children against an endoscopic endpoint.

Aims & Methods: A review of Great Ormond Street Hospital paediatric imaging database was performed to identify subjects with good quality MRE studies and an endoscopic review ±3 months to determine an endoscopic score for disease activity (SES-CD score). 38 subjects were identified (median age 11, range 5 to 18) with dynamic 'cine' imaging through the terminal ileum.

The dynamic imaging was processed, blind to any clinical data, with a previously validated motility assessment algorithm (GIQuant®, Motilent, London, UK). A consultant radiologist delineated the TI on each subject within 5 cm of the ileocecal valve and the motility score derived.

The TI was used as a reproducible reference to enable comparison between subjects. The TI motility score was correlated against the SES-CD and the population split into 'active' and in-active groups based on SES-CD <2 = remission

Results: The median TI motility was 0.2 (range 0.05 to 0.6) and the median SES-CD score was 9.5 (range 0 to 32). The correlation between the two measures was R = -0.45, P = 0.005. The median SES-CD active motility was 0.17 (range 0.05 - 0.47) and inactive was 0.37 (range 0.2 - 0.6) and mean difference was 0.16, P = 0.006.

Conclusion: Increased endoscopic activity correlated negatively with TI motility, consistent with observations in adults. The motility score was quick to calculate and represents a potential novel biomarker of disease activity in the paediatric population that now needs prospective validation.
Disclosure: Nothing to disclose

P0530 WITHDRAWN

P0531 WITHDRAWN

Oesophageal, Gastric and Duodenal Disorders I
10:30-17:00 / Poster Exhibition - Hall 7

P0532 AUTOPHAGY IS INCREASED AND ASSOCIATED WITH POOR PROGNOSIS IN ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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Introduction: The cellular and molecular carcinogenesis of the esophageal squamous cell carcinoma (ESCC) involves alterations in cell growth, death and metabolism. Advances in basic tumor biology and prognosis biomarkers may contribute to the clinical management and the development of new therapeutic strategies to these tumors. Autophagy is a self-catabolic physiological mechanism involved in the degradation of aged or malfunctional organelles and proteins. Molecularly, autophagy is mediated by the Atg family of proteins, which mediates the formation of a double-membrane structure called autophagosome. Key markers in this process are Beclin-1(Atg6), which forms a protein complex to initiate the formation of autophagosome, and MAP1LC3(Atg8), that mediates the closure of autophagosome.[9,10] Autophagosome englobes cellular components marked to degradation by adaptor proteins such as Sequestosome 1 (SQSTM1 or p62). The autophagosome fuses with lysosomes to form the autolysosome where cell components are degraded. The products of degradation are then released through lysosomal permeases back to the cytoplasmic environment. The role of autophagy depends on the step of carcinogenesis and the tumour type. In different cancers, its promotion and progression involves the reactivation of autophagy, allowing the tumor cells to adapt to the metabolic stress associated with tumor growth. Disturbs in autophagy have been associated with carcinogenesis.

Aims & Methods: We compared the levels of three autophagy markers, SQSTM1, MAP1LC3B and BECN1 in ESCC and non-neoplastic biopsy samples. Then we evaluated the influence of autophagy gene expression in the survival and staging of ESCC in TCGA database. We also used a Nuclear Morphometric Analysis (NMA) to correlated nuclear morphometry with autophagy.

Results: The three markers were significantly increased in ESCC samples in comparison to control. We proposed an Autophagic Index (AutoIndex), by adding the individual levels of the three proteins and found this a stronger indication of the autophagic status. AutoIndex displayed an even higher difference, between ESCC and control, than single autophagy markers. ESCC samples showed a reduction in nuclear area, which correlated negatively with the increase of autophagy. Using the TCGA database we discovered that high levels of MAP1LC3 A/B, SQSTM1, Atg4A and Atg12 expression were associated with a poor prognosis and advanced staging, suggesting that autophagy contributes to ESCC aggressiveness.

Conclusion: We found that an increase of autophagy may be involved in the progression of normal esophageal epithelia to ESCC. The combination of autophagy markers (AutoIndex), instead of its single values, has a great potential to be used as a prognostic tool in the strategy to diagnose and treat the ESCC.

Disclosure: Nothing to disclose

P0533 WITHDRAWN

P0534 WITHDRAWN

P0535 WHOLE GENOME SEQUENCING ANALYSIS OF GASTROPARESIS IDENTIFIES NOVEL RISK LOCI

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Introduction: Gastroparesis is a disorder characterized by delayed gastric emptying of solid food in the absence of a mechanical obstruction of the stomach, resulting in the cardinal symptoms of early satiety, postprandial fullness, nausea, vomiting, belching and bloating. To ascertain the genetic risk factors for gastroparesis we conducted the first to date whole genome sequencing (WGS) study of gastroparesis cohort.
Aims & Methods: We investigated the frequency and effect of rare loss-of-function (LOF) variants in patients with idiopathic and diabetic gastroparesis enrolled in a clinical study, VLY686-2301. The dataset consisted of 119 WGS samples.
Results: Among rare LOF variants, we report an increased frequency of a frameshift mutation within Motilin Receptor (MLNR) gene, variant rs562138828. Motilin is a 22 amino acid peptide hormone expressed throughout the gastrointestinal (GI) tract. The protein encoded by this gene is a motilin receptor which is a member of the G-protein coupled receptor 1 family. We have shown an increased frequency of a frameshift mutation with MAF 0.01 as compared 0.0009 AF in GNOMAD (p-value = 0.01) with Odds Ratio of 21.9. We detect 4/119 gastroparesis patients carry the variant of interest that results in p.Leu202ArgfsTer105.
Noteworthy is the fact that the 4 cases were equally split among idiopathic and diabetic, so this possible GP risk factor appears to be agnostic as to condition. The finding may be of direct relevance to treatment as individuals with the identified mutation may respond differently to gastroparesis treatments especially those targeting MLNR.
Among other rare LOF, we identified a case of CHD7 discussed in literature in gastro-related context and a case of CFTR duodenal stenosis pathogenic variant. The CFTR variant has been seen in pancreatitis and is likely causative of Cystic Fibrosis Gut which is characterized by increased mucous viscosity and development of intestinal inflammation, dysbiosis and dysmotility.
Conclusion: Whole genome sequencing of gastroparesis patient samples showed enrichment for rare variants in the MTLR in cases compared with controls. The identified LOF variants within the region can serve as risk factor for disease as well as inform treatments, especially given the knowledge of different response to treatment.
Disclosure: Nothing to disclose

P0536 THE EXPRESSION AND BIOLOGICAL FUNCTION OF DERMATOPONTIN IN COLORECTAL CANCER

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Introduction: Colorectal cancer (CRC) is a complex disease caused by the interaction of environmental and genetic factors. due to the insidious symptoms of colorectal cancer, about 50% of patients with colorectal cancer have reached the advanced stage at the time of diagnosis, hence, missed the optimal time for surgical treatment and had a poor prognosis. Therefore, we need to explore new biomarkers for colorectal cancer and find a convenient and effective screening method to achieve the purpose of early diagnosis and treatment. Tumor microenvironment has become one of the hotspots of research.
More and more studies have confirmed that the development of tumor is closely related to the extracellular matrix (ECM). some researches have shown that DPT is involved in the occurrence and development of many types of tumors, but there are no studies on the expression and regulatory mechanism of DPT in colorectal cancer.

Aims & Methods: In this study, we aimed to investigate the expression of DPT in colorectal cancer and its effect on the growth, proliferation, migration and invasion of human colorectal cancer cell lines. 126 pairs of colorectal cancer tissues and corresponding adjacent normal tissues were selected from the west China hospital of Sichuan university. The expression level of DPT gene in tissue samples was detected by real-time quantitative PCR, and the correlation between the expression level of DPT and the clinical pathological characteristics and prognosis of patients was further analyzed. In addition, colorectal cancer cell lines with stable overexpression of DPT gene was constructed and verified by real-time fluorescence quantitative PCR. After that, cck-8 and Transwell cell migration and invasion experiments were used to detect the influence of overexpression of DPT gene on the growth, proliferation, migration and invasion ability of human colorectal cancer cells.
Results: qRT-PCR showed that the expression of DPT mRNA in colorectal cancer tissues was significantly lower than that in adjacent normal tissues. Patients with low DPT expression level were more likely to have low grade differentiation (P=0.040), poor TNM stage (P=0.004) and lymph node metastasis (P=0.025) than those patients with high DPT expression level. Kaplan-meier survival analysis found that the cumulative survival rate of colorectal cancer patients with higher DPT expression level was significantly better than those with lower DPT expression level (P=0.0224). Further Cox multivariate analysis showed that the expression level of DPT was an independent risk factor for the prognosis of patients with colorectal cancer (P=0.035).By comparing the expression levels of DPT mRNA in such human colorectal cancer cell lines: RKO, HCT15, HCT116 and LS174T, we selected HCT15 and HCT116 to construct DPT overexpression and blank control cell lines.CCK-8 assay showed that overexpression DPT could significantly inhibit the proliferation of HCT15 and HCT116 cells. Further transwell migration and invasion assay showed that overexpression DPT could significantly inhibited the migration and invasion ability of HCT15 and HCT116 cells.
Conclusion: The abnormal expression of DPT is related to the occurrence of colorectal cancer. DPT can be used as a potential molecular biomarker to predict the prognosis of colorectal cancer patients.
Disclosure: Nothing to disclose

P0537 EVOLUTION OF GASTRIC HISTOPATHOLOGIC LESIONS IN AUTOIMMUNE ATROPHIC GASTRITIS

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Introduction: Autoimmune atrophic gastritis (AAG) is an organ-specific disease characterised by a wide clinical spectrum. AAG affects individuals of any age, causing atrophy of the corpus-fundus mucosa of the stomach, with vitamin B12 and iron malabsorption. The aim of this study was to investigate AAG-related histopathological lesions and their evolution during a prolonged follow-up.
Aims & Methods: Between January 2007 and July 2018 we enrolled and followed-up all patients diagnosed with AAG at our Gastroenterology outpatient clinic. For each patient we collected and analysed data from gastric biopsy specimens and AAG-specific laboratory investigations (anti-parietal cell antibody, gastrin, and serum chromogranin A level).
Results: 1059 gastric biopsy samples from 307 patients with AAG (mean age 59±15 years, F:M 2,3:1 ratio) were analysed. Typical histopathological features were present in 282/307 patients. Of these, 15% were classified as early stage, 19% as florid stage, and 67% as end stage. Only 4% had a complicated disease at diagnosis (8 patients presented dysplasia and 4 NETs). Intestinal and pseudopyloric metaplasia are increasingly evident in end stages (in early stage 20/41 have intestinal metaplasia and 14/20 have pseudopyloric metaplasia, whereas in end stage 138/175 have intestinal and 150/175 pseudopyloric metaplasia); enterochromaffin-like cells hyper-

plasia is more commonly linear in early stage (21/41) and micronodular in end stage (141/175). A progressive increase in gastrin level through stages (326±435 vs 832±761; p< 0.05) was noticed, whereas chromogranin A level is similar in all stages (196±249 vs 178±180; p=ns). Anti-parietal cell antibodies were detected in 80% of patients. Data indicated that 34% of early stage disease evolves unfavourably within 5 years. Dysplasia showed a prevalence of 8% in 5 years and 11% in 10 years, whilst NET G1 5% and 7% in 5 and 10 years, respectively. Among patients with no histopathological features of AAG, 17/25 demonstrated autoantibodies against parietal cells and have been defined as potential AAG. At 24 months follow-up, 50% developed overt AAG, of which 2 patients lately evolved in end stage and 1 progressed in NET after 11 years.

Conclusion: We herein showed that in AAG natural history, histological lesions progress from early to end stage within 10 years in most patients. Irrespective of the stage, patients must undergo a surveillance endoscopic program. The presence of antibodies directed against parietal cells could be an indicator of pre-atrophic autoimmune gastritis.

Disclosure: Nothing to disclose

P0538 DO WE STILL NEED OF BIOPSY FOR DIAGNOSIS OF GASTROINTESTINAL MALIGNANCY? UTILITY OF CRUSH CYTOLOGY IN FAST DIAGNOSIS OF GI MALIGNANCY

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Introduction:
· Gastrointestinal malignancies are commonly encountered in medical practice, and endoscopic examination and biopsy are extremely important first diagnostic modalities.
· Crush cytology of gastrointestinal malignancy is a simple, cheap, and readily available technique that increases diagnostic yield and expedites diagnostic workup of such cases.
· Compared with biopsy, crush preparations require a minute amount of tissues and provide rapid diagnosis.Hence, the study was designed to access the diagnostic performance of crush cytology.

Aims & Methods: To see the efficacy of crush cytology (smears prepared from biopsy material) in obtaining rapid diagnosis of GI cancers
Method:
· All cases of gastrointestinal malignancy of the esophagus, stomach, and colo-rectum, which underwent endoscopic examination from August 2018 to March 2019, in SIDS Hospital and Research Centre, Gujarat, India, were included in the study.
· The diagnosis on crush cytology stained with H-E stain andhistopathological diagnosis based on paraffin-embedded H&E sections was compared. Diagnostic accuracy, sensitivity,

Results:
· A total of 197 cases of gastrointestinal malignancy were evaluated with endoscopy and crush cytology during this period.
· There were 187 cases of histologically confirmed carcinomas
· Rest 10 cases of polyps (n = 7), ulcers (n = 2) and stenosis (n = 1).
· Crush smear cytology positively diagnosed 161 cases of carcinomas
· Male/female ratio - 2.6:1 and
· Mean age - 60.3 years.
· Incidence of carcinomas was highest in the seventh decade of life, with 36.6% cases.
· The most common site of carcinoma was Colorectal (57.8%) followed by esophagus (24.1%), stomach (13.9%), and ampulla of vater with 4.3% cases each.
· The most common histological types of gastric and colorectal malignancy were well-differentiated adenocarcinoma (83.8% & 69.2%) and poorly-differentiated adenocarcinoma (2.7% & 30.8%), respectively.
· Squamous cell carcinoma (52.9%) was the most common malignancy of the esophagus. Crush smears were unable to provide definite diagnosis in 26 cases because of the morphological characteristics- well-differentiation (61.5%), low cellularity (23.1%) and carcinoma in-situ (15.4%).
· The sensitivity of crush cytology was 79.5%, with a specificity of 100%, positive predictive value 90.3%, and negative predictive value of 19.8%.
· The diagnostic accuracy of crush cytology was 82.5%.

Conclusion: · Crush cytology is a cost-effective diagnostic tool with high diagnostic accuracy, specificity, and sensitivity, and it provides early diagnosis, which is helpful in planning further management of gastrointestinal carcinoma cases.

Disclosure: Nothing to disclose

P0539 CD24 FOR EARLY DETECTION AND SURVEILLANCE OF CANCER USING A UNIVERSAL SIMPLE BLOOD TEST

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Introduction: In 2018, the global cancer burden has risen to 18.1 million new cases with 9.6 million deaths. The ultimate cancer therapy is prevention or at least early detection. There are many attempts to develop a blood test for early detection, but none is in clinical use. CD24, a mucin-like cell surface protein, is overexpressed in numerous human cancers. We have shown that a simple non-invasive blood test evaluating CD24 levels had good sensitivity and specificity for detecting colorectal adenomas and cancer in patients undergoing screening colonoscopy at an urban medical center.

Aims & Methods: To develop a universal improved simple blood test that could reliably identify individuals with common cancer types through assessment of the levels of CD24 on PBLs.
Blood samples were obtained from consecutive patients and healthy volunteers. 1×10^6 leukocytes were stained using anti-CD11b-PerCp-Cy5.5 and anti-CD24-FITC and analyzed by flow cytometry. Percentage of positive cells was determined by subtracting the percentage of CD24 and CD11b-positive cells (dual stain) from CD24-positive cells (single stain). Healthy subjects underwent a thorough evaluation at the ICPC. All cancers were verified histologically.

Results: The suggested screening assay distinguished normal from patient subjects especially with breast, pancreas, lung and colorectal cancers as well as early stage of adenoma (table 1). Interestingly, the levels of CD24 drop back to near normal level following successful surgery/chemotherapy. Furthermore, CD24 score, in normal individuals with family history of cancer, was higher than those without family history (11.7±7.1 and 19.3±8.9%, respectively).

	Healthy	Healthy with F.H	Healthy without F.H	All cancers	Bladder	Pancreas	CRC	Colon Adenoma	Stomach
CD24 score	17 ±8	20 ±8	14 ±7	38.3±11	39 ±13	35 ± 8	39 ± 7	33 ± 11	40 ± 8.5
Sensitivity				94%	100%	89%	100%	87%	100%
Specificity	84%	74%	95%						
NPV Vs.H F.H No F.H				94% 93% 96%	100%	98% 98% 99%	100%	98% 96% 97%	100%

[Table 1]

Conclusion:
1. CD24 expression in PBLs may serve as a universal blood test for the early detection of numerous cancers.
2. The first ever blood test to detect adenomas.
3. CD24 may serve as a novel predictive marker in cancer therapy.
4. The test can identify family members that are at an increased risk for cancer.
5. Obviously, the test has to be validated in a prospective multi-center study.

Disclosure: Nothing to disclose

P0540 MOUSE ORGANOID CULTURES ARE THE NOVEL MODEL TO STUDY THE ESOPHAGEAL ION TRANSPORT MECHANISMS

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Introduction: Esophageal epithelial cells (EECs) protect the lower layers during esophageal reflux. One of the major components of the epithelial defensive mechanisms is the ion transport processes, however their role under pyhisiological and pathophysiological conditions is not completely clear. One of the reason for this is the lack of good experimental models on which the functional changes of EECs can be investigated. Therefore, our aim in this study was to generate esophageal organoid cultures (EOC) from epithelial tissue of mice and to characterize the presence of ion transporters on these EOCs.
Aims & Methods: EECs were isolated from three different mice strains (CD1, C75/Bl6 and FVB/N). The esophagus was removed and digested with dispase (2 U/ml) for 30 min. After the digestion the epithelia was peeled from the submucosa and incubated with trypsin in order to obtain individual cells. Cells were then suspended in Matrigel for 10-14 days and media was changed in every second days. Changes in intracellular pH (pH$_i$) was measured using microfluorometry and the pH-sensitive dye, BCECF-AM. For determining the resting pH$_i$, the high K$^+$/nigericin technique was used.
Results: EOCs were succesfully generated from all three mouse strains. In each cases, organoids have a three-dimensional, approximately spheroidal structure, growing in the extracellular matrix. Their maximum size was about 200 μm at the end of the second week, although differences in morphology and size have been observed between the mice strains. Using EOCs, generated from CD1 mice, we have determined the resting pH$_i$ and the buffering capacity of the cells. Microfluorometric measurement showed the presence of functionally active Na$^+$/H$^+$ exchanger (NHE) and Cl$^-$/HCO$_3^-$ (CBE) transporters on the EOCs.
Conclusion: We have successfully set up the culturing of mice esophageal organoids and our preliminary results showed that EOCs express both alkalizing (NHE) and acidifying (CBE) transporters. We strongly belive that EOCs are a suitable, *in vitro* experimental model to study esophageal epithelial function and can also be used to investigate the pathomechanism of reflux-induced esophageal diseases. This study was supported by the National Research, Development and Innovation Office (FK123982) and the National Research, Development and Innovation Office, by the Ministry of Human Capacities (EFOP 3.6.2-16-2017-00006).
Disclosure: Nothing to disclose

P0541 ROLE OF LEUKAEMIA INHIBITORY FACTOR (LIF) ON THE TUMORIGENIC PROPERTIES OF CANCER STEM CELLS IN GASTRIC ADENOCARCINOMA

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Introduction: Cancer stem cells (CSCs), a small cell subpopulation having intrinsic chemo resistance mechanisms and expressing CD44 cell surface glycoprotein, have been characterised in gastric adenocarcinoma. The link between the Hippo/YAP/TEAD pathway, key regulator of organ size and tissue homeostasis, and CSC properties has recently been suggested in gastric adenocarcinoma. Recent studies have defined Leukaemia Inhibitory Factor Receptor (LIFR) and its ligand Leukaemia inhibitory Factor (LIF) as being upstream regulators of the Hippo pathway and LIF/LIFR signalling as having an anti-metastatic role in breast cancer cells.
Aims & Methods: Consequently, this study aimed to determine the effect of LIF supplementation on the YAP/TEAD pathway and its impact on CSC phenotype and properties in gastric adenocarcinoma. AGS and MKN45 gastric cancer cell lines as well as patients' derived gastric adenocarcinoma cells were used. The expression of Hippo/YAP/TEAD pathway related genes and

of CSC markers was assessed by RTqPCR, western blot and immunofluorescence analysis. YAP/TEAD transcriptional activity was evaluated by TEAD-luciferase reporter assay and proliferation assays as well as tumorsphere assays were carried out *in vitro* to evaluate CSC functional properties.
Results: Results demonstrate that LIF supplementation represses the YAP/TEAD pathway through a decreased YAP translocation to the nucleus and decreased expression of YAP/TEAD target genes. In addition, LIF decreases proliferation, tumorsphere initiation capacity and expression of gastric CSC markers in gastric adenocarcinoma cells.
Conclusion: Our results indicate that LIF represses the YAP/TEAD pathway and presents anti-tumorigenic effects on gastric adenocarcinoma cells. Whether the effect of LIF on CSC properties passes through the YAP/TEAD pathway repression needs to be further investigated. This could *in fine* lead to the development of targeted strategies against CSCs to help decrease the number of relapse cases and bad prognosis in gastric cancer.
Disclosure: Nothing to disclose

P0542 WITHDRAWN

P0543 ELAFIN IS A MULTIFACETED PROTEIN PROTECTING GUT EPITHELIAL BARRIER FROM INFLAMMATION

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Introduction: In the gastrointestinal tract, proteolytic activity is tightly regulated to prevent inappropriate and potentially harmful proteolysis. In IBD this regulation is broken and our recent work has demonstrated that elastolytic activity is significantly increased in colonic epithelium from IBD patients. We have shown that (i) the expression of the only elastase released by epithelial cells ELA2 is up-regulated; and (ii) the selective elastase inhibitor ELAFIN is severely down regulated in colonic epithelium from IBD patients. We showed that oral treatments with ELAFIN-expressing *L. Lactis bacteria* restored proteolytic balance in the inflamed gut and was protective against acute and chronic colitis.
ELAFIN is a low-molecular weight molecule (10-kDa), which specifically inhibits elastases. At N-terminal terminus, a cationic helix showed antimicrobial activities and could interact with phospholipids. Moreover ELAFIN is also able to inhibit NFkB and AP-1 activation but this domain is not localized on protein. Therefore, several mechanisms of action are thus possible to explain ELAFIN's protective property, either from the extracellular or the intracellular compartment.
Aims & Methods: If ELAFIN-recombinant *L. lactis* has to be considered as a possible treatment for IBD in human, there is an absolute need to define the mechanisms by which ELAFIN delivery protects against intestinal inflammation.
Because ELAFIN has demonstrated several biological properties, we generated and expressed in LAB ELAFIN's mutants allowing investigation the biological properties of ELAFIN individually. To decipher the mechanisms by which ELAFIN is protective against intestinal inflammatory insult, different forms of ELAFIN-recombinant LAB were co-culture with thapsigargin (10mg/ml) and ELAFIN (10^7 CFU/well). After 6H, cells were additionally exposed to gentamicin (100 mg/ml) to limit bacterial development. The barrier function was measured using FITC-dextran passage through the epithelial layer. The elastolytic activity and CXCL8 release were quantified from the culture media. Expression of inflammatory mediators was quantified by qPCR.
Results: Addition of thapsigargin for 24H on Caco2 cells induced ER-stress and disruption of elastolytic balance. ELAFIN expression was decreased with up-regulation of ELA2, leading to increase of elastolytic activity in medium, disclosed in IBD patients. Concomitantly, barrier function was reduced, and expression of *CXCL8, CXCL10 and hBD2* was increased. Co-culture with ELAFIN expressing-LAB normalized all these parameters confirming anti-inflammatory properties of ELAFIN.

Neutralization of a-helix (mutant K44D/K50G) did not modify ELAFIN's properties. However, disruption of protease inhibitory function (mutant A62G/M63G) was not able to modify permeability and inflammatory phenotype induced by exposure of intestinal epithelial cells to thapsigagin, showing that anti-inflammatory activity of ELAFIN was based on the control of elastase activity released by epithelial cells.

Surprisingly, ELAFIN immunostaining revealed the exogenous protein in the epithelial cells, in the nucleus. The ELAFIN's transport was dependent to its elastase inhibitory function. We showed that epithelial cells expressed LRP1 (LDL-related receptor 1) which is known to internalize complexes of proteases and proteases inhibitors.

Conclusion: This suggests that ELAFIN could act as anti-inflammatory molecule based on multifactorial mechanisms from outside to inside the epithelial cells.

Disclosure: Nothing to disclose

P0544 PROPHYLACTIC TRANSCATHETER ANGIOGRAPHIC EMBOLIZATION REDUCES THE RISK OF REBLEEDING IN PATIENTS WITH FORREST IIA ULCER: A RETROSPECTIVE STUDY

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Introduction: About 20% of Forrest IIa ulcers rebleed even after endoscopic hemostasis. Prophylactic transcatheter angiographic embolization (p-TAE) might be a feasible way to reduce rebleeding, but its efficacy is controversial.

Aims & Methods: This study aimed to evaluate the clinical efficacy of p-TAE to prevent rebleeding and to assess the risk factors for rebleeding in the patients with Forrest IIa ulcers after endoscopic hemostasis. The patients with Forrest IIa ulcer underwent endoscopic hemostasis in West China Hospital during May 2009 and May 2018 were retrospectively reviewed. The patients were assigned to endoscopy (E) group and endoscopy plus p-TAE (E+p-TAE) group according to whether they received p-TAE after endoscopic hemostasis. Demography, data of laboratory tests, medication intake history, amount of fluid and red cell suspension infusion, time duration between admission and initial endoscopic hemostasis, morphological characteristics of ulcers and non-bleeding visible vessels, Glasgow-Blatchford score, modalities and sessions of endoscopy hemostasis, rebleeding rate after endoscopic hemostasis, rate of salvage hemostasis and intensive care unit transfer, hospital stay and mortality were collected for comparison of baseline characteristics, clinical efficacy and risk analysis of rebleeding.

Results: Most of the baseline data in the two groups except for the protruded blood vessel and fluid infusion pre-procedure were comparable. The rebleeding occurrence of E+p-TAE group (n = 27) were significantly lower than that of E group (n = 86), 3.7% *vs* 25.6%, P =.014. Survival analysis also showed lower rebleeding risk of E+p-TAE group, P = .016. Protruded vessel in Forrest IIa ulcer (OR: 5.316, 95% CI: 1.538 - 18.374, P = .008) and no p-TAE intervention (OR: 20.932, 95% CI: 2.067 - 211.984, P = .010) were identified as independent risk factors for rebleeding of Forrest IIa ulcers. The rebleeding occurrence of protruded vessel within the first week after initial endoscopic hemostasis was significantly decreased by E+p-TAE intervention (E *vs* E+p-TAE, 18.6% *vs* 0%, P = .011).

Conclusion: No p-TAE after endoscopic hemostasis and protruded visible vessels were the independent risk factors for rebleeding of the patients with Forrest IIa ulcer. p-TAE following endoscopic hemostasis may effectively prevent rebleeding for those patients partly through compensation for the inadequate endoscopic hemostasis due to the technical heterogeneity of endoscopists.

Disclosure: Nothing to disclose

P0545 A PROSPECTIVE STUDY OF HEMOSTASIS RADIOTHERAPY FOR INOPERABLE GASTRIC CANCER

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Introduction: The first choice of treatment of gastric cancer is surgery, and adjuvant chemotherapy is performed in advanced stage. External beam radiotherapy (RT) alone is an effective and well tolerated modality in the local palliation of gastric cancer, with palliation lasting the majority of patients' lives. Endoscopic hemostasis techniques for gastric cancer, the rebleeding hemostatic response rate is high. Treatment for the inoperable progressive stomach cancer includes hemostasis RT. Effectiveness of RT is well known. Tey et al. reported the review of palliative RT for gastric cancer of 7 researches. However, their analyses were all retrospective study, there were no prospective study of hemostasis RT in our best knowledge. From those results, we conducted prospective study.

Aims & Methods: A total of 28 patients with gastric cancer with bleeding was enrolled. The initial dose was 20 Gy / 5 fractions for all stomach. The salvage dose was 15 Gy / 5 fractions for partial stomach. When hemoglobin level stabilized by blood test within 2 weeks after irradiation, we judged a hemostatic effect was achieved. When re-bleeding was found, the patients selected whether to take re-irradiation or not.

Results: The response ratio of initial RT was 85% (22 / 26 patients). Six patients underwent re-irradiation, and all of them responded (100%). The median OS of all patients was 52 days. The median OS of non re-irradiation (one-time) group and re-irradiation group were 54 days and 36 days without statistically significant. The adverse events were not occurred 3 or more in all patients.

Conclusion: The salvage RT followed by initial RT is effective to reduce adverse event. The OS was same between one-time irradiation and re-irradiation group. No grade 3 or more AEs was occurred. This RT is completed only 5 days and re-irradiation option is favorable to the patients. The range of effective hemostatic time was wide and no predictive factors was found in our prospective study. It might be necessary to determinate ideal dose and fraction number of initial irradiation, preferably less than 20 Gy.

References: Tey J, Soon YY, Koh WY, et al. Palliative radiotherapy for gastric cancer: a systematic review and meta-analysis. Oncotarget. 2017;8:25797-25805

Disclosure: Nothing to disclose

P0546 OVER-THE-SCOPE CLIP AS FIRST-LINE THERAPY IN THE MANAGEMENT OF HIGH-RISK BLEEDING PEPTIC ULCERS: A CASE-MATCH CONTROL STUDY

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Introduction: Nonvariceal upper gastrointestinal (GI) bleeding have an associated morbidity and mortality. Through-the-scope (TTS) hemostatic clips limitations are difficult of clip application during active bleeding, use in ulcers with a fibrotic base, or difficult-to-access because anatomic locations or large size. The over-the-scope clip (OTSC) is an atraumatic, large-size clipping device, with a high-pressure closure for larger a deeper ulcers.

Aims & Methods: Aim: to evaluate the efficacy and safety of OTSC as first-line therapy in patients with high-risk (HR) bleeding ulcers compared to combined therapy (TTS clip and adrenaline injection).

Methods: A retrospective analysis of a prospectively collected data in consecutive patients who presented with HR ulcer GI-bleeding between May-2014 and September 2018. High risk upper GI bleeding were considered as those ulcers located in a major arterial territory, if the lesion had an endoscopically visible large-caliber artery (>2 mm), if there was a fibrotic ulcer with high-risk endoscopic stigmata (Forrest classification types I and II). The primary endpoint was the incidence of rebleeding or perforation with-

in 30 days of index endoscopy. Patients were excluded if they had bleeding caused by varices, received OTSC for fistula or tissue defect closure or if the bleeding did not meet the criteria for HR ulcer bleeding. Baseline characteristics were confirmed through the corresponding hypothesis test. Analysis was performed on R v3.4.3.

Results: 95 patients were included, 46 received an OTSC as primary therapy for HR bleeding ulcers and 49 matched cases received TTS hemostatic clips in combination with epinephrine injection (combined therapy). The mean age was 60.9 ± 19.1, 32.6% female. Most lesions were gastric ulcers (71.6%). The median number of OTSC used was 1 (1 - 3), whereas for combined therapy was 2 (1 - 8) TTS clips. Table 1 summarizes baseline characteristics.

Six cases of rebleeding (6.3%) were observed: two in the OTSC group and four in the combined therapy group (p=0.444). Two cases of the OTSC group (4.3%) had rebleeding after 48 hours of the procedure; meanwhile, one case of rebleeding was observed in the combined therapy group at the same period and was treated with APC (p=0.520). Three cases in the combined therapy group had rebleeding in less than 48 hours after the procedure (p=0.088), two treated with an OTSC and one with APC. The median procedure time was 11 (10-15) mins for OTSC and 20 (15-40) for combined therapy (p< .001) (table 1).

	OTSC (n=46)	Combined therapy (n=49)	p-value	
Age, mean ± SD	60.9 ± 19.1	62 ± 17.4	59.8 ± 20.6	<0.001
Female, n (%)	31/95 (32.6%)	16/46 (34.8%)	15/49 (30.6%)	0.664
No anticoagulation therapy, n (%)	72/95 (75.7%)	34/46 (73.9%)	36/49 (76.5%)	0.140
NSAID therapy, n (%)	6/95 (6.3%)	3/46 (6.5%)	3/49 (6.1%)	0.886
Previous transfusion, n (%)	15/95 (15.8%)	9/46 (19.5%)	6/49 (12.2%)	0.294
Lesion detected, gastric ulcer/duodenal ulcer	68/27	32/14	36/13	0.583
Forrest classification of Upper GI Bleeding, IA-B / IIA-C	15/80	11/35	4/45	0.009

[Table 1. Baseline characteristics of included patients.]

Conclusion: The OTSC as first line single therapy is as safety and effective as combined therapy for the management of HR bleeding peptic ulcers; improving the procedure time statistically significant. The OTSC could become in the future as a first line-therapy for HR bleeding peptic ulcers.

Disclosure: Nothing to disclose

P0547 THE INCIDENCE OF MAJOR BLEEDING EVENT AND PERFORATION AFTER ENDOSCOPIC BALLOON DILATION: A RETROSPECTIVE MULTICENTER STUDY

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Introduction: Endoscopic balloon dilation (EBD) has been established as an effective treatment for gastrointestinal stricture. However, bleeding and perforation are main complications associated with EBD, and EBD is classified as a high-risk endoscopic procedure in the guidelines concerning the endoscopy in patients on antithrombotics from *European Society of Gastrointestinal Endoscopy*. Although the incidence of these complications has been previously reported based on small studies, there are still few data to judge EBD as a high-risk procedure.

Aims & Methods: The aim of this study was to investigate the incidence of bleeding and perforation after EBD and evaluate whether antithrombotic agents increases bleeding events through a large-scale study. This study

was a retrospective multicenter study conducted in six hospitals across Japan. From April 2010 to March 2015, the patients who underwent EBD for upper gastrointestinal stricture were enrolled. Medical records and endoscopic findings were reviewed, and the primary endpoints were the incidence of major bleeding event and perforation after EBD.

Results: 878 patients with upper gastrointestinal stricture were analyzed. The causes of stricture were as follows: surgery 417, endoscopic resection 280, chemo-radiotherapy 130, tumor 18, and benign disease 33. A total of 4884 procedures of EBD were performed in 878 patients and the mean number of EBD session per patient was 5.6 times. The incidence of major bleeding events which required urgent endoscopic hemostasis and hospitalization was 0.18% per total EBD session (9/4884). Endoscopic hemostasis was successfully achieved in all the bleeding events and 3 patients required blood transfusion. 670 EBD sessions were performed under antithrombotic therapy. The major bleeding rate in the antithrombotic-users was higher than that in the non-users (0.75% vs 0.09%, *P*=0.004). On the other hand, there was no significant difference between the continued-use group and the cessation group (1.01% vs 0.71%, *P*=0.657, respectively). The incidence of perforation was 0.43% (21/4884). As for the management of perforation, 17 patients could recover by conservative treatment including endoscopic closure, and 4 patients received urgent surgery.

Conclusion: This retrospective study with a large sample size demonstrated that EBD could safely be performed even under continued use of antithrombotic agents.

Disclosure: Nothing to disclose

P0548 PRONOSTIC FACTORS ASSOCIATED WITH UPPER GASTROINTESTINAL BLEEDING IN A FRENCH MULTICENTRE STUDY: THE SANGHRIA PROJECT

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Introduction: During the past decade, potential risk and prognostic factors for upper gastrointestinal bleeding (UGIB) have been evolved in developed countries in particular with an increased use of direct oral anticoagulants in thromboembolic diseases and a better management of UGIB by gastroenterologists with the use of new effective endoscopic haemostatic devices. As few studies investigated prognostic factors associated with UGIB in this context, we conducted such a study to better understand the role of new determinants of UGIB on its outcomes.

Aims & Methods: From November 2017 to October 2018, we carried out a prospective study in 46 public hospitals. We enrolled patients with symptoms of UGIB and subsequently confirmed UGIB by endoscopy (those who were admitted to the emergency medicine departments (EDs) with UGIB symptoms and those who were hospitalised for other reasons than UGIB). They were followed up at least for six weeks. Patients' characteristics, endoscopic and follow-up data were collected and analysed. Univariable and

multivariable analyses using logistic regression models were performed to identify predictors of rebleeding and those of in-hospital and six-week mortality.

Results: Of the 2498 enrolled patients, 74.6% were diagnosed with UGIB after admission to EDs and 25.4% during hospitalisation. Median age of patients was 68.5 years +/- 16.3, 67.1% were men and 20.9% had a cirrhosis. Median Charlson score was 2 (IQR: 1-4), median Blatchford score was 11 (IQR: 7-13), and median Rockall score was 5 (IQR: 3-6). Among included patients, 19% had an oral anticoagulant medication: 43.8% of them with direct oral anticoagulants. Endoscopy was performed within 24 hours in 84.2% of patients and with general anaesthesia in 31%. An endoscopic assistant was present in most cases (91.5%).

Main causes of bleeding were: 1) peptic ulcers and gastroduodenal erosions (44.9%), 2) lesions related to portal hypertension (18.8%) and 3) oesophagitis (11.5%). Active bleeding was observed in 24.5% of patients, mainly associated with peptic ulcers and portal hypertensive lesions, and was endoscopically treated in 86.7% and 79.6% of the cases, respectively. During hospitalisation, 10.5% of patients experienced rebleeding and 8.6% of them died. In-hospital mortality rate was lower among patients from EDs than those who were hospitalised (5.8% vs 16.8%, p< 0.0001). Predictors associated with rebleeding were in-hospital bleeding (OR=1.36; 95%CI: 1.03-1.79), Blatchford score>11 (OR=1.45; 95%CI: 1.08-1.94) and active bleeding (OR=1.94; 95%CI: 1.48-2.55).

The six-week mortality rate was 12.0%. It was significantly lower in the EDs group than in the in-hospital group (9.1% vs 22.2%; p< 0.0001). Predictors associated with six week mortality were initial transfusion (OR=1.53; 95%CI: 1.04-2.27), Charlson score>4 (OR=1.80; 95%CI: 1.31-2.48), Rockall score>5 (OR=1.97; 95%CI: 1.39-2.80), in-hospital bleeding (OR=2.44; 95%CI: 1.75-3.40), and rebleeding (OR=2.59; 95%CI: 1.85-3.64).

Conclusion: This study showed an improved management of UGIB compared to previous studies. Despite this improvement, mortality rate remained high at six-week follow-up in particular for patients who experienced UGIB while they were hospitalised for other reasons than UGIB. This can be explained by the severity of underlying disease for which patients were initially hospitalised. Strong predictors of mortality were in-hospital bleeding and rebleeding without major role of the anticoagulation therapy. This study confirmed that previously known predictors were still valid in the recent advancement in the management of UGIB patients.

Disclosure: Nothing to disclose

P0549 CONTINUED USE OF ANTI-PLATELETS DURING ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) DOES NOT DECREASE CARDIAC ISCHEMIC EVENTS, BUT INCREASES GASTROINTESTINAL BLEEDING EVENTS

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Introduction: Anti-platelets drugs are one of the most important drugs in this aging society, widely utilizing for cardiovascular and cerebrovascular diseases. Over the past decades, it has been common to discontinue antiplatelet drugs prior to gastrointestinal endoscopy, with emphasis on the prevention of bleeding. In recent years, non-interruption of anti-platelets peri-operatively is recommended in guidelines for endoscopic submucosal dissection (ESD) as a treatment for early gastric cancer (EGC). Although there have been several reports(1,2), the art of balancing between ischemia and bleeding during ESD remains unclear.

Aims & Methods: In this study, we investigated the association between the aggressive continuation of anti-platelets in recent years and both cardiac ischemic and bleeding events after ESD in the real world clinical settings. We conducted a retrospective cohort study comprising 1383 consecutive patients, who were hospitalized for ESD at the Department of Gastroenterology in our hospital between January 2007 and July 2018. Among them, patients regularly taking anti-platelet drugs before hospitalizations (n = 255) were extracted and divided into two groups: anti-platelets discontinued group (n = 164) and continued group (n = 91). Primary outcomes were 30-days cardiac ischemic and gastrointestinal bleeding events. We defined 3rd look endoscopy and blood transfusion as the bleeding events, and urgent electrocardiogram (ECG) and coronary angiography (CAG) as the ischemic events, respectively. We performed bivariate analysis, multivariate

analyses, and propensity score matching for 19 baseline characteristics, which are known as ischemic or bleeding risks reported before.

Results: ESDs are increasingly being performed without interrupting antiplatelet drugs in our hospital; 13% in 2007, 64% in 2017. Bleeding event rate (3rd look endoscopy and blood transfusion) was significantly higher in the continued group than in the discontinued group (38.5% v.s 23.8% p = 0.015 and 12.1% v.s 2.4% p = 0.004).

However, there are no significant differences about ischemic event rate (urgent ECG and CAG) between two groups. Patients in the anti-platelets continued group were observed to have older age, higher prevalence of hypertension, dyslipidemia, diabetes, ischemic heart disease, heart failure, and cerebral infarction, lower serum albumin revel, and lower hemoglobin revel.

Comparison of propensity score matched groups (n=91, each) also revealed that continuation of anti-platelets during ESD was associated with higher bleeding risk (38.5% v.s. 24.2% p = 0.055 and 12.1% v.s. 3.3% p = 0.048), but it was not associated with lower ischemic events.

	anti-platelets discontinued group (n=91)	anti-platelets continued group (n=91)	p-value
3rd look(%)	22(24.2%)	35(38.5%)	0.055
blood transfusion(%)	3(3.3%)	11(12.1%)	0.048
urgent ECG(%)	6(6.6%)	7(7%)	NS
urgent CAG(%)	1(1.1%)	0(0%)	NS

[Bleeding and ischemic events: comparison of propensity score matched groups]

Conclusion: This study reveals that continued use of anti-platelets during ESD does not decrease cardiac ischemic events, but may increases gastrointestinal bleeding events. Gastroenterologists and cardiologists need to discuss more carefully in judging the continuity of antiplatelet drugs in the ESD perioperative period, and continued use of anti-platelets may have to be limited to the patients with higher risk of ischemia in the future.

References: (1)Turk J Gastroenterol. 2017 Sep;28(5):329-336. (2)Ann Gastroenterol. 2018 May-Jun;31(3):344-349.

Disclosure: Nothing to disclose

P0550 EFFICACY OF GLASGOW BLATCHFORD SCORE TO PREDICT THE DIFFICULTY OF ENDOSCOPIC HEMOSTASIS FOR ACTIVE DUODENAL ULCER HEMORRHAGE

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Introduction: Endoscopic procedure is performed for active duodenal ulcer hemorrhage. But if endoscopic hemostasis fails, transarterial embolization (TAE) or operation is considered. The risk factors for difficulty of endoscopic hemostasis are poorly documented, whereas Glasgow Blatchford Score (GBS) has been attracting attention for predicting intervention for upper gastrointestinal hemorrhage and some studies have described the usefulness.

Aims & Methods: We performed a retrospective analysis involving patients with hemorrhage of benign duodenal ulcer who had been admitted to our hospital and had endoscopic therapy from April 2005 to December 2017. We compared each GBS in the groups in which only endoscopic procedure were performed (endoscopy group) and interventional radiology was additionally performed (TAE group), having made statistical analysis for items of GBS.

Results: A total of 154 patients were included in this study. 141 patients (91.6%) of them were success in only endoscopic procedure, 12 patients (7.8%) were underwent TAE additionally, and 1 patient (0.6%) was underwent operation. The mean GBS (±*SD*) in endoscopy group was 11.1±3.6, and the mean GBS in TAE group was 13.8±2.1. The GBS in TAE group was statistically higher than in endoscopic group (*p*=0.0087), and the area under the receiver operating characteristic curve (AUROC) was 0.74 (95% confidence interval 0.63 to 0.86). A threshold GBS of 12 or more was best at predicting TAE, with sensitivity of 54.0%, specificity of 91.7%. Making an analysis of each item of GBS, haemoglobin was statistically lower (*p*=0.0076) in TAE

group. The other items (blood urea, systolic blood pressure, pulse, melaena, syncope, hepatic disease, and cardiac failure) were no significant difference between two groups.

Conclusion: The GBS is useful to predict need for TAE for active duodenal ulcer hemorrhage. This study may suggest that GBS≥12 is high risk of endoscopic hemostasis fails and TAE performed.

Disclosure: Nothing to disclose

P0551 RISKS OF HOSPITALIZATION FOR UPPER GASTROINTESTINAL BLEEDING IN SELECTIVE SEROTONIN REUPTAKE INHIBITORS USERS AFTER *HELICOBACTER PYLORI* ERADICATION: A TERRITORY-WIDE COHORT STUDY

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Introduction: Selective serotonin reuptake inhibitors (SSRIs) are currently recommended as the first line treatment for depression. Though many studies have evaluated the risk of upper gastrointestinal bleeding (UGIB) associated with SSRI use, the potential confounding effects of *H. pylori* (HP) and other medications have not been addressed.

Aims & Methods: This was a propensity score matched cohort study to determine the risk of UGIB in HP infected patients who used SSRI after HP eradication therapy. HP-infected patients who had received a course of clarithromycin-containing triple therapy between 2003 and 2012 were identified from the territory-wide electronic health database. We excluded patients who failed HP eradication therapy and those who had used SSRI before the study start date. The follow-up period commenced from 60 days after the HP therapy until the occurrence of UGIB, death or the end of the study. The primary outcome was hospitalization for UGIB. To address for potential immortal time bias, time-dependent Cox regression model was used to compute the hazards ratios (HR) and 95% confidence intervals (CI) of UGIB risk, in which follow-up time was split into 1-month intervals. Covariates included baseline characteristics, medical conditions and concurrent medications. As SSRIs and other medication uses could change over time, drug usage was defined as at least one day use in each interval. To adjust for the baseline difference between SSRI users and non-users, propensity score (PS) matching analysis with a ratio of 1:2 was performed, in which concurrent medications uses in the first 1-month interval were used to calculate the propensity scores. Multivariate time-dependent Cox regression model was performed as sensitivity analysis.

Results: 61,264 patients who had received HP eradication therapy were analyzed, including 3,358 SSRI users and 57,906 non-users. The median follow-up duration was 7.7 (interquartile range, 5.3-10.4) years. The overall crude incidence rate of hospitalization for UGIB was 3.98 (95% CI 3.80-4.16) per 1000 person-year. In the time-dependent Cox model with 1:2 PS matching, SSRI was associated with higher risk of hospitalization for UGIB than non-users (HR1.95, 95% CI 1.41-2.70). This result was consistent in multivariate analysis (HR 1.81, 95% CI 1.34-2.45). After stratifying by age, the increased risk of SSRI was only significant among older patients (> 50 years old). Apart from SSRIs, other independent risk factors of UGIB includes older age, male sex, history of UGIB or ulcer, presence of comorbid illnesses (hypertension, diabetes, cirrhosis and renal disease) and concomitant use of aspirin, other antiplatelet drugs, non-steroidal anti-inflammatory drugs (NSAIDs), anticoagulants and corticosteroids (Table). In contrast, gastroprotective agents was associated with lower risk of UGIB (HR 0.54, 95% CI 0.47-0.63).

Variables	HR (95% CI)
Age	1.06 (1.05-1.06)
Male sex	1.31 (1.19-1.44)
History of UGIB or ulcer	3.21 (2.91-3.55)
Gastroprotective agents	0.54 (0.47-0.63)
Aspirin	1.95 (1.67-2.28)
Other antiplatelets	2.04 (1.63-2.54)
NSAIDs	1.80 (1.46-2.22)
Anticoagulants	2.36 (1.76-3.16)

[Hazard ratios for UGIB]

Conclusion: SSRI users have a higher risk of hospitalization for non-variceal UGIB than non-users even after treatment for *Helicobacter pylori*, particularly among older patients, those with history of UGIB, comorbid illnesses and concurrent use of other medications that increased the bleeding risk.

Disclosure: Nothing to disclose

P0552 HEMORRHAGIC COMPLICATIONS IN PATIENT RECEIVING ANTI-PLATELET AND/OR ANTICOAGULANT WITH OR WITHOUT PROTON-PUMP INHIBITORS

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Introduction: Antiplatelet and anticoagulant are widely used in various indications. Bleeding complications usually raise physicians' concern; especially gastrointestinal bleeding (GIB). Proton-pump inhibitors (PPI) have been co-prescribed with the aforementioned drugs. However, there were evidence indicated that PPI might increase the risk of bleeding complications when they were co-administered with clopidogrel or warfarin, as it synergist metabolisms of these drugs.

Aims & Methods: To study bleeding events in patient receiving antiplatelet and/or anticoagulant, both GIB and extra-gastrointestinal bleeding (EGIB) compared between PPI status (with/without PPI).

Methods: This is a nested case-control study. We recruited subjected who developed bleeding as defined by new onset of anemia or any visible bleeding after taking antiplatelet/anticoagulant. Data were retrospectively collected from medical records of Siriraj Hospital from January 2013 to July 2014. Demographic data, co-morbidities, bleeding outcomes were recorded. Events of both GIB and EGIB between 2 groups (with/without PPI) were compared. Descriptive data were presented in mean±SD and comparative data were analyzed using chi-square. Multivariate analysis was also conducted when appropriate.

Results: 1146 cases (mean age 71.89 ± 13.3 years) met the inclusion criteria. PPI was prescribed in only 495 cases. Most of the patients (99.7%) had multiple comorbid diseases. Hypertension (83.7%), Diabetic Mellitus (51.6%) and Chronic Kidney Disease (42.84%) were the 3 most common. 392 patients were receiving anticoagulant. Minor bleeding (the patient who developed new onset of anemia but no visualized bleeding) were found in 681 cases (59.42%) while major bleeding (anemia with visualized bleeding) 465 cases (40.6%). In major bleeders, 553 cases (48.25%) had UGIB, 202 cases (17.6%) had LGIB and 100 cases (8.72%) developed EGIB (56 patients had internal organ bleeding, 24 patients had skin and soft tissue bleeding and 20 patients had intracranial hemorrhage). In patients with GIB, PPI group had less UGIB [43.23% vs 52.38% OR = 0.692 (95%CI 0.547-0.876) P= 0.002 in antiplatelet and/or anticoagulant takers, and 44.17% vs 57.97% OR= 0.573 (95%CI 0.422-0.788) P < 0.001 in aspirin monotherapy taker]. However, there were no differences of overall bleeding between PPI/non-PPI group. Amongst EGIB; sites of bleeding between PPI/non-PPI groups were comparable. Patients who took warfarin containing regimen had a greater proportion of bleeding compared to aspirin monotherapy group; 34 patients (70.83%) with warfarin containing regimen tended to have more bleeding than 6 patients (12.5%) with aspirin alone in PPI group. These findings were similar to non-PPI group. Interestingly, aspirin combined with warfarin had more EGI bleeding in PPI group compared to non-PPI group, 31.25% vs 11.53%; OR 3.484 (95%CI 1.233-9.929), P = 0.019. The medians of overall INR level were 3.13 (1.33-4.40) and 3.07(1.88-4.40) in EGIB and GIB respectively with P = 0.309.

Conclusion: As in general knowledge, our study demonstrated that PPI helped in alleviating UGIB in patients who took aspirin monotherapy regardless of PPI status. Interestingly, EGIB was high in our study, most of the cases were contributed from warfarin containing regimen although all group were in therapeutic level. Warfarin combine with aspirin significantly increased EGIB in PPI group in particular, this interaction need to be explored.

Disclosure: Nothing to disclose

P0553 OPTIMAL ENDOSCOPY TIMING IN PATIENTS WITH ACUTE VARICEAL BLEEDING: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Although current guidelines recommend performing endoscopy within 12 hours for acute variceal bleeding (AVB), the optimal timing of endoscopy for AVB remains controversial.

Aims & Methods: To perform a systematic review and meta-analysis of all eligible studies to assess the effect of endoscopy timing on mortality and re-bleeding in AVB.

PubMed, Cochran Library, and EMBASE through January 2019 were searched for relevant publications. Overall mortality rate, re-bleeding rate, and other clinical outcomes (successful hemostasis, need for salvage therapy, length of hospital stay, and number of blood transfusions) were determined. Methodological quality of included publications was evaluated using the Risk of Bias Assessment tool for Non-randomized Studies. Mantel-Haenszel random effect model of RevMan software (Cochrane) was used to analyze binary endpoints and inverse variance method was used to analyze continuous outcomes.

Results: This meta-analysis included five studies with 854 and 453 participants undergoing urgent endoscopy (≤ 12 hours) and non-urgent endoscopy (> 12 hours), respectively. There was no significant difference in overall mortality rate between urgent and non-urgent groups (OR: 0.72, 95% CI: 0.36 - 1.45, $P = 0.36$). Re-bleeding rate was similar between urgent and non-urgent groups (OR: 1.21, 95% CI: 0.76 - 1.93, $P = 0.41$). Other outcomes were also similar between the two groups.

Conclusion: This study demonstrated that endoscopy timing did not affect mortality or re-bleeding rate of patients with AVB. Therefore, an appropriate timing of endoscopy would be more important than an urgent endoscopy depending on each patient's condition.

Disclosure: Nothing to disclose

P0554 STUDY OF RECENT MYOCARDIAL ISCHEMIA IN PATIENTS PRESENTED WITH UPPER GASTROINTESTINAL BLEEDING WITH AND WITHOUT PORTAL HYPERTENSION

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Introduction: Upper gastrointestinal bleeding(UGIB) and acute myocardial injury(AMI) are potentially life-threatening conditions that must be managed urgently (1). UGIB can be complicated by hypovolemia, hypotension, and diminished oxygen-carrying capacity, which cause myocardial ischemia and necrosis (2). liver cirrhosis is known to cause bleeding tendency, but sometimes may cause ischemic manifestations. Both UGIB and liver cirrhosis have a higher mortality when developing AMI than either of them alone (1).

Aims & Methods: To assess the relationship between UGIB in both portal hypertensive cirrhotic and non-cirrhotic groups and the development of AMI. A single-center prospective study done on 263 patients presented with UGIB, divided in to 4 groups; GI (no=118) cirrhotic patients with UGIB, GII: non-cirrhotic patients with UGIB (n=85), GIII: cirrhotic patients (30) with no history of UGIB and GIV: the healthy control group (30).

Results: Age is higher in GI than GII(P=0.0001). Smoking, diabetes, history of previous MI and ICU admission were common associations in patients with UGIB and MI. Cardiac troponin I (cTn-I) level was not statistically significant different between the groups (p=0.16), but cTn-I was positive for MI in 18/118 (15.3%) in GI and in 20/85 (23.5%)in GII (P=0.001). ECG ischemic signs were statistically significant different (P=0.01). OVs and PU were the most common causes of bleeding in GI&II (63.6%&90.6%), respectively (p=0.0001). Mortality rate was 11/118(9.3%)in GI and 4/85 (4.7%) in GII (P=0.0001). Length of hospital stay (LOS) was higher in GI than GII>5days

(83.1% vs 31.8%). There was a positive correlation between Glasgow Blatchford score (GBS) and cTn-I elevation (R+0.19, P=0.003). There was a high statistical significant difference between GI &II regarding GBS at cut off level (15 days)(p= 0.0001). In cTn-I positive cases, ROC curve for Troponin elevation was AUC 0.97,sensitivity and specificity were 97.4 & 100%, respectively. Odds ratio of smoking, viral hepatitis and LOS in cTn-I positive patients were 12.61, 14.49 & 2.76 times troponin negative patients, respectively (P=0.0001).

Conclusion: UGIB in cirrhotic patients may predispose to AMI especially in older ages, men, comorbid diseases than non-cirrhotic. Patients with cirrhosis when developing UGIB have increased LOS, more complications and higher mortality than non-cirrhotics. Also, bleeding severity is positively correlated with developing AMI in all groups. cTn-I level is not different statistically between the groups.

References: 1.Lingjie, H., Jianwei, Z.,1 and Shutian, Z., Risk factors of in-hospital mortality among patients with upper gastrointestinal bleeding and acute myocardial infarction. Saudi J Gastroenterol. 2018; 24(3): 177-182. 2.Chia-Jung, W., Hung-Jung, L., Shih-Feng, W., et al., Acute Myocardial Infarction Risk in Patients with Coronary Artery Disease Doubled after Upper Gastrointestinal Tract Bleeding: A Nationwide Nested Case-Control Study. PLoS One. 2015; 10(11): e0142000.

Disclosure: Nothing to disclose

P0555 PATIENTS PRESENTING WITH AN ACUTE UPPER GI BLEED CAN BE SAFELY DISCHARGED TO RETURN FOR OUTPATIENT ENDOSCOPY WHEN THEIR GLASGOW-BLATCHFORD SCORE IS ≤2

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Introduction: Upper Gastrointestinal (GI) Bleeding is one of the most common presentations to hospitals worldwide with an estimated incidence of between 40-150/100,000 annually.[1] In the UK this translates to approximately 1 presentation every 6 minutes and results in a significant financial burden for the National Health Service (NHS).[2,3]

Current guidelines in the UK and Europe suggest the use of the Glasgow Blatchford Score (GBS) to predict high and low risk patients.[1,4,5]The outpatient management of patients who score as low risk is widely accepted as a way of reducing pressure on inpatient services and potentially offsetting some of the aforementioned financial burden. In the UK, the guidelines suggest this strategy only for those who score 0, in Europe this is extended to 0-1.[1,4]Recently, a number of research papers have hypothesised that this could safely be extended further.[3,6]

At St Helens and Knowsley NHS Trust, UK, the score threshold has already been extended to those with a GBS of 2 or less with the introduction of an Ambulatory GI Bleed Pathway in 2016. The aim of this audit was to evaluate the safety of this pathway, which may subsequently influence future guidelines by revealing ambulatory care is safe for those with a higher GBS.

Aims & Methods: Data was collected retrospectively from May 2016-December 2018. Scanned medical notes were accessed and data collected under a number of headings: basic demographics, documented GBS, presenting date, date of endoscopy and findings at endoscopy. The 3 main end-points assessed were:

1. The need for endoscopic intervention.
2. Re-bleed rates within 30 days.
3. Thirty day mortality rate.

Results: A total of 224 patients were referred via the ambulatory GI bleed pathway with the majority presenting with fresh haematemesis, 'coffee-ground' vomit or malaena. Patients were excluded from analysis for a number of reasons including those who were inappropriately referred. Of the remaining 196 patients, 54.59% (107) were male and 45.41% (89) were female. The average age of presentation was 39 years of age (range 18-79). The mean GBS was 0.57 (mode 0).

The average number of days from presentation to endoscopy was 2.35 (range 0-19). We found 24 patients did not attend their appointment. 3 did not tolerate the procedure. 57 patients had an entirely normal endoscopy. Of the remaining 112, a number of diagnoses were seen at endoscopy. Of most significance, only 3 patients required endoscopic therapy, GBS scores for these patients were 0, 0 and 2. Just 2 suffered a re-bleed (GBS 0 and 0) within 30 days and 30-day mortality was 0%.

Conclusion: Although more than half of patients had a diagnosis at endoscopy (57.14%), only a very small number of patients required intervention (1.5%), even fewer (1%) suffered a re-bleed and no patients died within 30 days of being referred onto the ambulatory GI bleed pathway. Therefore, we conclude that ambulating patients presenting with Acute Upper GI Bleed who have a GBS of 2 or less is safe and that following more robust, multi-centre studies, perhaps this could be adopted into future guidance.

References: 1. Gralnek IM, Dumonceau JM, Kuipers EJ et al. Diagnosis and management of nonvariceal upper gastrointestinal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy 2015; 47: a1-a46 2. Siau, K., Chapman, W., Sharma, N., Tripathi, D., Iqbal, T. and Bhala, N. (2018). Management of acute upper gastrointestinal bleeding: an update for the general physician. Journal of the Royal College of Physicians of Edinburgh, 47(3), pp.218-230. 3. Chatten, K., Purssell, H., Banerjee, A., Soteriadou, S. and Ang, Y. (2018). Glasgow Blatchford Score and risk stratifications in acute upper gastrointestinal bleed: can we extend this to 2 for urgent outpatient management?. Clinical Medicine, 18(2), pp.118-122. 4. National Institute for Health and Care Excellence. Acute upper gastrointestinal bleeding in over 16s - management. Clinical Guideline CG141. London: NICE, 2012. 5. Scottish Intercollegiate Guidelines Network. Management of acute upper and lower gastrointestinal bleeding. SIGN Clinical Guideline 105. Edinburgh: SIGN, 2008. 6. Stanley, A., Laine, L., Dalton, H., Ngu, J., Schultz, M., Abazi, R., Zakko, L., Thornton, S., Wilkinson, K., Khor, C., Murray, I. and Laursen, S. (2017). Comparison of risk scoring systems for patients presenting with upper gastrointestinal bleeding: international multicentre prospective study. BMJ, 2017 Jan 4;356:i6432. doi: 10.1136/bmj. i6432

Disclosure: Nothing to disclose

P0556 ENDOSCOPIC TREATMENT ON GASTROESOPHAGEAL VARIX AFTER OXALIPLATIN-BASED CHEMOTHERAPY

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Introduction: Oxaliplatin has been used as the first choice for colorectal cancer, which might induce sinusoidal endothelial injury and portal hypertension. However, gastroesophageal varix formation after oxaliplatin-based chemotherapy may sometimes be overlooked when these patients presented with melena or hematemesis.

Aims & Methods: The aim of this study was to investigate the characteristics of oxaliplatin-induced portal hypertension and the efficacy of endoscopic prophylaxis of re-bleeding. Between 2010 and 2017, patients with gastroesophageal varix after oxaliplatin-based chemotherapy were included. We excluded patients with hepatitis, alcoholic, and other known etiology of cirrhosis. In the same time period, cirrhotic patients with hepatitis B related variceal bleeding and received first endoscopic treatment for prophylaxis of rebleeding were included as controls.

Results: A total of 31 patients with colorectal cancer and portal hypertension were identified, with an average of 6 cycles of oxaliplatin-based chemotherapy. Among them, 28 (90.32%) patients had an episode of variceal bleeding. The mean period retrospect to the start time of chemotherapy and the diagnosis of gastroesophageal varix was 61.9 ± 6.63 months. Liver biopsy confirmed no evidence of liver fibrosis while the obstruction of hepatic vessels. Two of them had liver arterio-portal fistula and eight patients had portal-systemic shunt. Endoscopic ligation and cyanoacrylate injection were performed in 22 patients with a history of variceal bleeding episode. The other 6 six patients had endoscopy evaluation for unsuitable for endoscopic treatment. Four patients received drugs (Carvedilol) and two received interventional procedures (transjugular intrahepatic portosystemic shunt (TIPS) and partial splenic embolization (PSE)). The comparison between oxaliplatin-based portal hypertension patients and cirrhotic patients with hepatitis B were showed in Table 1. Prothrombin time (PT), INR, alanine transaminase (ALT) and aspartate aminotransferase (AST) and MELD scores were much lower in chemotherapy patients (p< 0.001). Kaplan-Meier analysis revealed that the 3-year re-bleeding rate for patients received oxaliplatin-based chemotherapy was higher than cirrhotic patients with hepatitis B (p=0.0018). Multivariate cox regression analysis included age, MELD score, portal vein thrombosis, PT, AST, AST and platelet count indicated that oxaliplatin-based chemotherapy were the independent factors for re-bleeding (95% CI 1.228-6.282, p=0.014).

	oxalipaltin-induced portal hypertension	cirrhosis with hepatitis B	p value
age at first diagnosis of varix	61.82±1.96	50.45±1.00	<0.001
sex(male)	10(45.5%)	84(75%)	p=0.007
hemoglobin (Hb)	88.24±5.25	89.98±2.13	0.748
platelets	81.48±9.6	62.80±2.62	0.077
prothrombin time	13.28±0.20	14.35±0.14	<0.001
INR	1.15±0.016	1.25±0.012	<0.001
ALT	17.22±1.29	34.00±3.30	<0.001
AST	23.84±1.86	40.03±3.07	<0.001
total bilirubin	14.31±1.68	16.08±0.77	0.361
albumin	36.21±0.93	34.08±0.51	0.088
creatinine	67.39±3.92	72.70±2.09	0.241
Child Pugh score	6.55±0.23	6.38±0.11	0.543
MELD score	7.95±0.27	9.10±0.032	<0.001
portal vein thrombosis (%)	5(22.7%)	25(22.3%)	0.580

[Baseline clinical and biochemical characteristics]

Conclusion: Oxaliplatin-induced portal hypertension may lead to portal hypertension with mild liver injury. Endoscopic treatment can be used for preventing variceal bleeding, however, the rebleeding rate was much higher than other cirrhotic portal hypertension.

Disclosure: Nothing to disclose

P0557 IMPLEMENTATION OF THE UK ACUTE UPPER GI BLEEDING BUNDLE RESULTS IN SIGNIFICANT IMPROVEMENTS IN QUALITY STANDARDS

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Introduction: The 2015 UK National Confidential Enquiry into Patient Outcome and Death (NCEPOD) report 'Time to Get Control' highlighted the need to improve the quality of care of patients with acute upper GI bleeding (AUGIB)[1]. The British Society of Gastroenterology Endoscopy Quality Improvement Project created an evidence based care bundle for AUGIB targeting ward based management of patients within the first 24 hours (The UK AUGIB bundle). The impact of implementation of the UK AUGIB bundle has not been assessed in clinical practice.

Aims & Methods: An audit of the impact of the UK AUGIB bundle was undertaken in 15 Scottish hospitals. Data were collected relating to demographics and management of patients with AUGIB within the first 24 hours of presentation, for a six-week period pre- and post-implementation of the UK AUGIB bundle. A period of bundle promotion was undertaken in all centres between data collection cycles. Outcomes measures included documentation of bundle implementation, risk scores and transfusion strategy. Caldicott approval was obtained in each site.

Results: A total of 459 patients were included in the pre-bundle audit period, and 434 patients in the post-bundle audit period. Following implementation, the AUGIB bundle was utilised in 41.2% of patients. The table demonstrates patient demographics and the impact of bundle implementation, highlighting improvements in recording of the Glasgow-Blatchford score and a re-bleeding plan, and improvements in transfusion strategies.

Variable	Pre-bundle period	Post-bundle period	p-value	Bundle not used	Bundle used	p value
DEMOGRAPHIC VARIABLES						
Number of patients	459 (51.4%)	434 (48.6%)	N/A	205 (53.4%)	179 (46.6%)	N/A
Age (years)	64.7 (63.0-66.4)	64.4 (62.7-66.0)	0.772	65.8 (63.4-68.1)	62.2 (59.5-64.8)	0.043
Male/ Female	264 (57.8%)/ 193 (42.2%)	266 (61.4%)/ 167 (38.6%)	0.530	123 (60.0%)/ 82 (40.0%)	113 (63.1%)/ 66 (36.9%)	0.395
Glasgow Blatchford score	6.3 (0-19)	7.4 (0 - 20)	0.011	7.0 (0 - 18)	8.0 (0 - 20)	0.141
Varices	27 (7.3%)	51 (13.3%)	0.007	24 (13%)	24 (14%)	0.733
BUNDLE VARIABLES						
Glasgow Blatchford Score recorded	163 (38.4%)	225 (57.3%)	<0.001	86 (42.2%)	122 (74.0%)	<0.001
Target haemoglobin stated	53 (35.3%)	78 (44.8%)	0.083	34 (36.6%)	35 (53.0%)	0.039
Transfusion threshold appropriate	58 (13.3%)	83 (19.6%)	0.012	40 (19.6%)	36 (20.2%)	0.880
Rebleeding plan documented	121 (33.2%)	196 (50.7%)	<0.001	83 (44.9%)	95 (56.55%)	0.028

[Patient demographic and bundle variables.]

No significant differences were observed in use of PPI in high risk bleeders, use of terlipressin/antibiotics in variceal haemorrhage or resumption plan for antithrombotics, with high pre-bundle performance in these domains.

Conclusion: Implementation of the UK AUGIB bundle in Scottish hospitals resulted in significant improvements in quality standards including documentation of risk scoring, target haemoglobin, transfusion thresholds and re-bleed plan.

References: 1. Gastrointestinal haemorrhage: Time to Get Control? National Confidential Enquiry into Patient Outcome and Death. July 2015. Accessed April 2019 http://www.ncepod.org.uk/2-15gih.html

Disclosure: Nothing to disclose

P0558 MULTIPROFESSSIONAL IN SITU SIMULATION IS AN EFFECTIVE METHOD OF IDENTIFYING LATENT PATIENT SAFETY THREATS IN GASTROINTESTINAL EMERGENCIES

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Introduction: Identifying errors in the ward environment, healthcare organisation or interaction between multiprofessional team members is crucial. Such identification may prevent serious mistakes that can occur in high pressure gastroenterology emergencies. Unannounced multiprofessional in situ simulation can be an effective means of identifying latent patient safety threats before they occur. We set up a standardised in situ simulation programme centred around speciality specific emergency scenarios; not only to improve skills, team working and communication but also to identify and address latent errors. The in situ faculty consisted of a consultant gastroenterologist; skills tutor; education fellow and director of medical education.

Aims & Methods: We identified key learning objectives for several different emergency scenarios including: massive upper gastrointestinal haemorrhage; septic shock; post-procedure complications and cardiac arrest. Using a wireless high fidelity simulation manikin we ran 18 unannounced sessions between February 2017 and April 2019. There was a minimum of three faculty in attendance in each of the sessions and an overall total of 79 participants representing the spectrum of different professions including: doctors; nurses; health care assistants and students from nursing,

medical, and physician associate backgrounds. Following completion of the scenario a structured debrief was conducted. Latent errors affecting patient safety at an individual, team or organisational level were identified and discussed. Following the scenarios, actions were put in place designed to address the identified errors in a timely fashion.

Results: During the 18 unannounced sessions between February 2017 and April 2019 we identified the following latent errors:
· unavailability of Sengstaken-Blakemore tubes, Bair Huggers, electrocardiogram machines and a step for CPR on the ward
· lack of awareness as to how to activate the major haemorrhage protocol
· not checking allergy status before administering antibiotics
· junior doctors without working pagers
· deficiencies in resuscitation skills amongst non-training grade doctors
· members of the multiprofessional team forgetting each others' names and parts of the ALS algorithm
· not knowing where the oral glucose gel is kept on the ward
Since the identification of these errors, corrective measures have included: laminated ALS algorithms attached to the resuscitation trolleys and dedicated major haemorrhage protocol training at junior doctor induction. Equipment availability has been addressed by ward management. Dedicated training days for the non-training grade doctors has also been undertaken.

Conclusion: In situ simulation is highly effective in identifying latent errors that could have potentially deleterious consequences on patient safety. This allows corrective measures to be undertaken in advance of real-life emergencies.

Disclosure: Nothing to disclose

P0559 AN ENDOSCOPIC MAPPING DEVICE FOR GASTROINTESTINAL SLOW WAVE PROPAGATION PATTERNS

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Introduction: Gastric slow waves regulate peristalsis, and gastric dysrhythmias have been implicated in functional motility disorders. To accurately define slow wave patterns, it is currently necessary to collect recordings during open surgery, which is invasive and limit their application. We therefore developed a novel gastric slow wave mapping device for use during endoscopic procedures. We aimed to assess feasibility of the new device for acquisition of gastrointestinal slow wave.

Aims & Methods: The device consists of a spreading catheter constructed of a flexible core coated with Pebax. Acquisition of gastric electrical signals was performed on healthy fasted weaner pigs under general anesthesia. Once deployed with endoscopic guidewire, catheter arrays is revealed with 12 electrode at 5mm intervals. A multi-channel recorder (Acknowledge 4.4, MP150; Biopac Systems, Santa Barbara, CA) was used to record gastric myoelectrical activity throughout the study. We compared gastric electrical signals from gastric mucosal according to various lesions.

Results: Gastric slow wave activity was successfully recorded simultaneously via both the novel endoscopic probe and the serosal measurement. Recordings from the device and a reference array in pigs were identical in frequency, and activation patterns and velocities were consistent. Device and reference amplitudes were comparable.

Conclusion: In conclusion, the novel endoscopic device achieves high-quality mucosal slow wave recordings. It might be applied for endoscopic diagnostic studies to document slow wave patterns in patients with gastric motility disorders.

Disclosure: Nothing to disclose

P0560 ELECTROPHYSIOLOGICAL AND PERMEABILITY PROPERTIES OF ESOPHAGEAL EPITHELIUM IN PATIENTS WITH ACHALASIA BEFORE AND AFTER BALOON DILATATION

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Introduction: Achalasia is a rare disorder with an incidence of approximately 1.6 cases per 100,000. The etiology of the disease especially changes at the epithelial permeability is not known.
Aims & Methods: The aim of this study was to investigate the electrophysiological and permeability characteristics of esophageal epithelium in patients with a diagnosis of achalasia before and after baloon dilatation compared with healthy controls and gastroesophageal reflux phenotypes. 27 patients (F: 17, M: 10, mean age 46 ± 15) diagnosed with upper gastrointestinal endoscopy with distal esophageal biopsies, timed barium swallow radiology, high resolution esophageal manometry (HRM) (according to Chicago 3.0v; 4 Type 1; 20 Type 2; 3 Type 3). 23 healthy volunteers and 60 erosive gastroesophageal reflux patients (ERD A / B: 48, ERD C / D: 12) were also included. Upper gastrointestinal endoscopy, HRM, 24h pH-MII studies were performed in both healthy volunteers and ERD patients. Esophageal electrophysiology and permeability measurements were performed before the treatment of 27 achalasia patients. 14 patients were also evaluated 2-3 months after the balloon dilatation. 3-4 esophageal biopsies were put into the mini-Ussing chambers to measure the transepithelial resistance (TEER), potential difference and tissue permeability via fluorescein diffusion within 2 hours.
Results: TEER and permeability of esophageal epithelium of Achalasia patients were not significantly different compared to the healthy volunteer group. However, when compared to the ERD group, the tissue resistance of achalasia patients were significantly higher and the permeability of the esophageal epithelium was significantly lower. Both tissue resistance and permeability of the esophageal epithelium after treatment were significantly higher, epithelial permeability was significantly lower in Achalasia patients compared to healthy volunteer and ERD groups. When pre- and post-treatment were compared, an increase in tissue resistance and decrease in epithelial permeability were determined after treatment, but no significant difference was found (Table).

	TEER (ohm) (mean±sd)	Permeability (pmol) (mean±sd)
Healthy volunteer	166,8 ± 47,2 §§§	36,9±13,8 §§
Achalasia (pre-treatment)	188,3± 55.7	33,6±15
Achalasia (post- treatment)	216± 80	22,2±9,1
ERD A/B	133,2 ± 34,4 * §§	49,6±28,4 ** §
ERD C/D	112,1 ± 38,6* §	60,1±40,5*** §§§

*p<0,001 vs Achalasia (pre- treatment), ** p<0,005 vs Achalasia (pre- treatment), *** p<0,05 vs Achalasia (pre- treatment), §p<0,001 vs Achalasia (post- treatment), §§p<0,005 vs Achalasia (post- treatment), §§§p<0,05 vs Achalasia (post- treatment)

[TEER and Permeability Results]

Conclusion: Patients with achalasia have less gastric reflux however the mechanical trauma and long-term stasis of food inside the esophagus might have a noxious effect on the epithelium. Different than the expectations, pre-treatment findings of esophageal epithelial resistance and tissue permeability were similar with HC. GERD is not uncommon in Achalasia patients following treatments. In spite of that, no significant change was determined when the patients' esophageal epithelial resistance and permeability were compared before and after treatment with balloon dilatation. Based on these results, we assume that, an adaptive cytoprotective mechanism might develop in the esophageal epithelium of achalasia patients.
Disclosure: Nothing to disclose

P0561 PROTON PUMP INHIBITORS REDUCE DUODENAL HYPERPERMEABILITY, DUODENAL EOSINOPHILIA AND SYMPTOMS IN FUNCTIONAL DYSPEPSIA PATIENTS BY ACID-INDEPENDENT MECHANISMS

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Introduction: The role of acid suppression with proton pump inhibitors (PPI) in relation to duodenal alterations and symptoms in functional dyspepsia (FD) patients is unknown. We studied duodenal permeability, eosinophil infiltration and symptoms in healthy volunteers (HV) and FD patients before and during PPI treatment.
Aims & Methods: Duodenal biopsies and blood samples were collected in healthy volunteers (HV) and FD patients before and after treatment with pantoprazole 40mg OD for 4 weeks. Transepithelial electrical resistance (TEER) and paracellular passage of a fluorescein-labeled dextran (4kDa) were measured in Ussing chambers and eosinophils counted on H&E-stained sections per high-power field (HPF; 0.24mm²). After each endoscopy, a naso-duodenal tube was positioned in the second part of the duodenum with aspiration of fasting and fed (Fortimel, 300kCal) fluids with measurement of pH. Plasma high-sensitivity C-reactive protein (hs-CRP), the Patient Assessment of Gastrointestinal Disorders Symptom Severity Index (PAGI-SYM) and Perceived Stress Scale (PSS) were measured at both visits. Non-parametric and correlation analyses were performed within- and between-groups.
Results: In total, 24 HV (15 female, median (IQR) age 26 (24-32) years) and 15 FD (13 female, 27.5 (22-34) years) were included. TEER was similar within- and between-groups. Dextran passage was higher in FD vs. HV off-PPI (p< 0.01) and significantly decreased in FD patients on-PPI. Duodenal eosinophil counts were higher in FD vs. HV both off- (p< 0.0001) and on-PPI (p=0.03) despite a significant reduction in eosinophilia in FD patients on-PPI. Duodenal fasting (p=0.02) and fed pH (p=0.03) were higher in FD vs. HV off-PPI with a trend for higher fed pH (p=0.08) in FD vs. HV on-PPI and an increase in both HV and FD on-PPI. Plasma hs-CRP was higher in FD vs. HV off-PPI (p=0.06) with a trend for decreased hs-CRP in FD on-PPI. PAGI-SYM decreased in FD on-PPI and was higher in FD vs. HV off- and on-PPI (both p< 0.0001). PSS was similar in FD on-PPI with higher scores in FD vs. HV both off- (p=0.04) and on-PPI (p< 0.01). Correlations were found between hs-CRP and passage (r=0.65, p=0.01) in FD off-PPI. Fed pH correlated positively with passage (r=0.58, p=0.03) in FD on-PPI. PAGI-SYM correlated with duodenal eosinophil counts (r=0.57, p=0.02) in FD off-PPI but not on-PPI. No correlations were found for HV.

	HV (n= 24)			FD (n= 15)		
Variable	Off-PPI	On-PPI	p-value	Off-PPI	On-PPI	p-value
TEER (Ω*cm2)	25.3 (19.7-31.5)	23.1 (19.8-26.4)	0.56	22.1 (19.2-27)	26.6 (20.7-28.5)	0.27
Paracellular passage (pmol)	19 (10.1-23.2)	22.7 (12.9-33.1)	0.07	25.6 (20.2-31)	15.5 (11.4 -29.3)	0.02
Eosinophils (per HPF)	3 (2-4)	1 (3-4)	0.72	12 (9-18)	4 (3-6)	<0.001
Fasting pH	5.9 (3.9-6.7)	7.2 (6.7-7.3)	<0.001	7 (5-7.4)	7.2 (6.6-7.5)	0.02
Fed pH	6.3 (5.2-6.5)	6.6 (6.4-6.8)	<0.01	6.4 (6-6.9)	6.8 (6.7-7.0)	0.03
hs-CRP (mg/L)	0.9 (0.3-1.5)	0.7 (0.2-1.6)	0.57	2 (0.6-5.5)	0.9 (0.2-1.6)	0.06
PAGI-SYM	0 (0-0.3)	0 (0-0.4)	0.75	2.8 (2-3)	1.5 (1-2.3)	<0.01
PSS	5 (2.5-9.5)	5 (1-6)	0.12	13.5 (8.8-18.3)	12.5 (1.8-18)	0.40

[Table 1]

Conclusion: In FD, elevated duodenal permeability, eosinophilia and symptoms but not stress are reduced by PPI and may be associated with systemic inflammation, which is associated with increased paracellular

passage in FD off-PPI. Increased duodenal pH on-PPI is associated with increased passage and hence is unlikely to explain the restored permeability in FD patients observed during PPI, suggesting the involvement of other factors such as duodenal eosinophils, which may drive dyspeptic symptoms.
Disclosure: Nothing to disclose

P0562 CARBON MONOXIDE (CO) RELEASED FROM ITS PHARMACOLOGICAL DONOR PREVENTS ESOPHAGEAL MUCOSA AGAINST EXPERIMENTAL REFLUX ESOPHAGITIS. POSSIBLE INVOLVEMENT OF ANNEXIN 1, PROSTAGLANDIN E2, ENDOGENOUS HYDROGEN SULFIDE PRODUCING ENZYMES AND SELECTED VASOACTIVE MECHANISMS

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Introduction: Carbon monoxide (CO), similarly to hydrogen sulfide (H_2S) is a gaseous mediator. CO is produced from heme via activity of heme oxygenase-1 (HO-1) and HO-2. CO and H_2S exert anti-inflammatory and anti-oxidant effects. However, possible preventive effect of CO released from its pharmacological donor, tricarbonyldichlororuthenium (II) dimer (CORM-2) against acute reflux esophagitis (RE)-induced esophageal damage has not been explained.
Aims & Methods: The RE was induced in Wistar rats within 4 h by ligating pylorus and transitional region between the forestomach and glandular portion. Before induction of RE animals were pretreated with CORM-2 (0.5 - 10 mg/kg i.g.), HO-1 inducing hemin (5 mg/kg i.g.) or HO-1 inhibiting zinc protoporphyrin IX (ZnPP, 10 mg/kg i.p.). CORM-2 was applied alone or in combination with indomethacin (5 mg/kg i.g.) to inhibit PG biosynthesis, L-NNA (15 mg/kg i.g.) to inhibit NO-synthase activity, capsazepine (5 mg/kg i.g.) to block TRPV1 activity or capsaicin (125 mg/kg s.c.) to suppress the activity of sensory nerves. $RuCl_3$ (2.5 mg/kg i.g.) which is not a CO releaser, was administered as a negative control for CORM-2. The esophageal blood flow (EBF) was determined by laser flowmetry, esophageal lesions index (LI) and mucus production was assessed by macro- and microscopically by planimetry and histology (H&E, alcian blue/PAS staining), the mucosal expression of mRNA and/or protein for HO-1, HO-2, Annexin-1, Nrf-2, hypoxia inducible factor 1α (HIF-1α), IL-1β and TNF-α, COX-1 and COX-2, TRPV1 and endogenous H_2S producing enzymes CTH, CBS and MPST were analyzed by real-time PCR, Western blot and/or immunohistochemistry. 8-hydroxyguanosine (8-OHG) as DNA oxidation marker and PGE_2 concentration in esophageal mucosa were determined by ELISA.
Results: CORM-2 reduced LI, maintained mucus production and increased EBF with selected ED50 dose being 2.5 mg/kg i.g.Similar effects were observed for hemin but not for RuCl3 or ZnPP. Capsazepine and capsaicin denervation but not L-NNA or indomethacin reduced esophagoprotective effects of CORM-2. CO donor increased HO-1/Nrf-2 or TRPV1 but did not affected CTH, CBS or MPST expression. CORM-2 downregulated COX-2, TNF-α, IL-1β and iNOS esophageal expression, decreased 8-OHG concentration and maintained Annexin-1 and HIF-1α expression and PGE2 concentration increased by RE.
Conclusion: We conclude that CO released from CORM-2 prevents esophageal mucosa against the damage induced by RE via its hyperemic, anti-inflammatory and anti-oxidative properties. These effects involved in CORM-2-mediated esophagoprotection are partly mediated by the ability of CO to maintain protective PGE_2 level and by the activity of Nrf2, Annexin-1 and HIF-1α but the possible role of H_2S biosynthesis enzymes remains unclear. [Funding source: National Science Centre, Poland (UMO-2016/23/D/NZ4/01913)].
Disclosure: Nothing to disclose

P0563 ENDOGENOUS GLUCAGON-LIKE PEPTIDE 2 PLAYS AN IMPORTANT PHYSIOLOGICAL ROLE IN THE ADAPTIVE RESPONSE AFTER SMALL INTESTINAL INJURY

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Introduction: Acute small intestinal injury such as chemotherapy-induced gastrointestinal mucositis often leads to extensive loss of mucosa, which can lead to malabsorption, abdominal pain and increased infection risks[1,2]. Intestinal adaptation is an important response and a natural compensatory mechanism to the acute injury and is critical for recovery. Glucagon-like peptide 2 (GLP-2) is secreted from enteroendocrine L-cells in response to food intake. GLP-2 has been demonstrated to enhance mucosal repair following intestinal damage[4], however, whether the endogenous secretion of GLP-2 is physiologically essential for mucosal repair and protection remains unresolved.
Aims & Methods: This study aims to investigate whether deficiency of GLP-2 receptor (GLP-2R) activity increases intestinal susceptibility and reduces the adaptive response to injury, using a model of chemotherapy-induced mucositis.
Female GLP-2R knock out (KO) mice and their wild type (WT) littermates received an intraperitoneal injection of chemotherapy (5-fluorouracil 400 mg/kg) inducing acute mucositis followed by regeneration. Additionally, GLP-2R KO and WT control received a saline injection. Bodyweight was monitored daily and recorded.
Mice were sacrificed 3 or 6 days after induction of injury; the small intestines were harvested, cleaned and the weight was recorded. Tissue from duodenum, jejunum, and ileum was analysed for myeloperoxidase (MPO) activity.
Results: The body weight of GLP-2R KO mice and their WT littermates showed the same decrease in the acute phase of injury and the same increase in the adaptive phase. No difference in small intestinal weight between the KO and WT was found in the acute phase of injury. Six days after injury GLP-2R KO mice showed a significant decrease in small intestinal weight compared to the WT mice (P< 0.0001).
Only WT mice were able to show the additional adaptive regrowth normally seen after chemotherapy-induced injury in mice; with a small intestinal weight significantly higher than healthy WT controls (P< 0.0001). In the acute state of injury, a significant increase in the inflammatory marker MPO was detected for the GLP-2R KO mice compared to their WT littermates in the middle part of the small intestines (P< 0.05).
Whereas no significant difference was found in the proximal and distal part of the small intestine. During the adaptive phase of injury, the MPO activity was back to baseline for both the GLP-2R KO and WT mice compared to the healthy controls.
Conclusion: This study shows that in the acute phase of injury GLP-2R activation might be less in important for intestinal protection. However GLP-2R activation seems to play an important physiological role in the adaptive response after intestinal injury.
References: 1 Elting, L. S. et al. The burdens of cancer therapy: clinical and economic outcomes of chemotherapy-induced mucositis. 98 (7), 1531-1539, (2003). 2 Kissow, H. J. C. o. i. s. & care, p. Glucagon-like peptides 1 and 2: intestinal hormones implicated in the pathophysiology of mucositis. 9 (2), 196-202, (2015). 3 Yusta, B. et al. GLP-1R Agonists Modulate Enteric Immune Responses Through the Intestinal Intraepithelial Lymphocyte GLP-1R. Diabetes. 64 (7), 2537-2549, (2015). 4 Hytting-Andreasen, R. et al. Endogenous glucagon-like peptide-1 and 2 are essential for regeneration after acute intestinal injury in mice. 13 (6), e0198046, (2018).
Disclosure: Nothing to disclose

P0564 WITHDRAWN

P0565 COMPREHENSIVE ANALYSIS OF GERD AFTER PER-ORAL ENDOSCOPIC MYOTOMY: A LARGE SINGLE CENTRE STUDY

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Introduction: Per-oral endoscopic myotomy (POEM) has established its place in the management of achalasia. Gastroesophageal reflux is an important concern after POEM. However, there is limited data on the risk factors for GER after POEM.
Aims & Methods: In this study, we aim to analyse the variables affecting the occurrence of GER after POEM.
All patients who underwent POEM (December 2017 to January 2018) at a single tertiary centre were offered GER evaluation using 24-hour pH impedance, esophagogastroduodenoscopy (EGD) and symptoms. Multivariate analysis was performed to identify the variables affecting the incidence of GER after POEM.
Results: A total of 260 patients with achalasia underwent POEM during the study period. 167 (64.2%) patients (mean age 41±14.42 years, 47.6% females, mean body mass index 22.2±3.89 kg/m²) underwent comprehensive evaluation of GER. Majority (70.6%) of the patients were treatment naïve. High De-Meester score (>14.7) and reflux esophagitis was identified in 47.9% and 41.9% of patients, respectively. Symptomatic GER was found in 29.3% patients. On univariate analysis only sigmoid oesophagus was found to be associated with GER (OR 0.20; CI 0.04-0.99; p=0.04). On multivariable analysis type of achalasia, technique of POEM (anterior vs posterior), objective variables including pre or post POEM esophageal manometry and patient characteristics (age, sex, BMI, type of achalasia) were no associated with GER.

	Odds Ratio	95% Confidence interval	p value	Adjusted odds ratio	95% confidence interval	p value
Age (years) Male Gender Female Gender	1.31 1.00 0.63	0.71-2.40 Reference 0.34-1.17	0.39 0.15	0.74 1.00 0.67	0.35-1.55 Reference 0.42-1.49	0.43 0.72
Body mass Index (kg/m<2>	1.31	0.71-2.42	0.38	0.67	0.32-1.41	0.29
Previous therapy (yes/no)	1.09	0.56-2.14	0.78	1.21	0.53-2.76	0.64
Sigmoid oesophagus	0.20	0.04-0.99	0.04	6.35	0.55-72.98	0.14
Length of Myotomy (cm) Esophageal Gastric	1.31 2.32	0.71-2.46 0.68-8.18	0.38 0.17	1.12 1.67	0.51-2.44 0.52-5.37	0.77 0.39
Orientation of myotomy Anterior Posterior	0.89	0.47-1.66	0.71	1.14	0.51-2.44	0.74
Post POEM Eckardt score	1.21	0.65-2.22	0.38	1.35	0.64-2.86	0.426
Post POEM manometry IRP LES pressure	1.07	0.57-2.01	0.82	0.79 1.37	0.35-1.80 0.60-3.12	0.59 0.44
Type of Achalasia Type I nad III				0.66	0.32-1.42	0.31

[Logistic regression analysis of factors associated with gastroesophageal reflux after POEM]

Conclusion: The incidence of post POEM GER is high and should be identified early to prevent complications. There are no procedural or patient related variables which appear to affect the incidence of GER.
Disclosure: Nothing to disclose

P0566 DOES ETIOLOGY, PRIOR THERAPIES AND OPERATIVE TIME AFFECT OUTCOME OF G-POEM IN REFRACTORY GASTROPARESIS - A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Gastric per-oral endoscopic myotomy (G-POEM) was first introduced in 2013 for the management of refractory gastroparesis. Most of the studies included small sample size with short term follow up. Literature on the efficacy of G-POEM when considering the etiology of gastroparesis, prior therapies and total operative time is limited.
Aims & Methods: We performed a systematic review and meta-analysis to evaluate the clinical efficacy of G-POEM in patients with refractory gastroparesis. We also evaluated if variation in total operative time, prior therapies (botulinum toxin, gastric electrical stimulation) and etiology affected clinical success. We conducted a search of several databases to locate items pertaining to peroral endoscopic pyloromyotomy or gastric peroral endoscopic myotomy (G-POEM) in patients with refractory gastroparesis (Jan 2013 to Feb 2019). Random-effects model was used. Heterogeneity between study-specific estimates was calculated using Cochran Q test and I² statistics. Publication bias was ascertained by funnel plot and Egger test. The outcome assessed was the pooled rate of clinical success with G-POEM as determined by total Gastroparesis Cardinal Symptom Index (t-GCSI) ≤2 at follow up and improvement in the 4-hr Gastric Emptying Study (GES). Sub-group analysis was performed based on the total operative time. Meta-regression analysis was used to evaluate the effect of prior treatments on clinical success.
Results: Our initial search yielded 67 results. After excluding duplicates and non-english literature, 62 full length articles were screened and 16 studies with 442 patients were included in the final analysis. Follow up t-GCSI and 4-hr GES data was available for 373 and 258 patients respectively. The pooled rate of clinical success based on t-GCSI was 75.9% (95% CI 69.7-81.2, I²=37.8) and based on improvement in 4-hr GES was 84% (95% CI 71.9-91.5, I²=66.2). Sub-group analysis was done to evaluate the clinical success of G-POEM as influenced by the total procedure time. Based on t-GCSI scores, for a procedure time of < 50 min (8 studies, 214 patients) the pooled rate of clinical success was 74.6% (95% CI 65.6-81.8, I²=3.3) whereas for >50 min (8 studies, 159 patients) it was 78.4% (95% CI 68.4-85.9, I²=57.9). There was no statistical difference between the two (p=0.53). Similarly, based on 4-hr GES for a procedure time of < 50 min (6 studies, 126 patients) the pooled rate of clinical success was 76.5% (95% CI 56.2-89.2, I²=73.5) whereas for >50 min (8 studies, 132 patients) it was 88.7% (95% CI 75-95.4, I²=36.4). There was no statistical difference (p=0.20) between the two. The pooled rate of total adverse events was 13.4% (95% CI 6.8-24.8, I²=63.7) and follow up time ranged from 2 months (shortest) to 18 months (longest). Length of hospital stay ranged from 1 to 6 days. On meta-regression analysis, prior treatment with botulinum toxin injection (2-sided p-value =0.03) and gastric electrical stimulation (2-side p-value=0.03) seemed to significantly influence 4-hr GES success rate. Etiology (diabetes, idiopathic, post-surgical) and/ or prior treatments did not affect the outcome of G-POEM based on t-GCSI score.
Conclusion: G-POEM is an effective and safe treatment modality for refractory gastroparesis. Our study shows that there is no difference in the successful outcomes based on the etiology of gastroparesis or total operative time. However, prior treatment with botulinum toxin and gastric electrical stimulation had a statistically significant influence on the success rate based on 4-hr gastric emptying.
Disclosure: Nothing to disclose

P0567 PREDICTORS OF REFLUX ESOPHAGITIS AFTER PER-ORAL ENDOSCOPIC MYOTOMY (POEM)

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Introduction: Per-oral endoscopic myotomy (POEM) is known as an effective therapeutic option for patients with achalasia and also for spastic esophageal disorders including Jackhammer esophagus and defuse esophageal spasm. Gastroesophageal reflux disease (GERD) is common in patients who undergo POEM, with a reported prevalence of up to 40%, due to the lack of fundoplication. Subset of such patients clinically require an additional laparoscopic fundoplication due to a poor response to acid neutralization therapy. However, potential risks of GERD after POEM remains unstudied.

Aims & Methods: The aim of this study is to propose predictors of post-POEM GERD. All patients who were diagnosed with achalasia and spastic esophageal disorders at our tertiary referral esophageal center are entered into a prospectively maintained institutional database. After Institutional Review Board approval, we queried this database to identify patients who underwent POEM procedure between January 2016 and March 2019 (n=42). Of these, patients with a history of prior endoscopic/laparoscopic myotomy (n=8) or whose post-operative upper endoscopic evaluation were unavailable (n=8) were excluded. Endoscopic surveillance was conducted at 3 months, 1 year, and then yearly after POEM procedure. The patients were divided into two groups based on post-POEM endoscopic findings using the Los Angeles classification, ie, non-GERD group (grade N or M) and GERD group (grade A or more). Pre-operative evaluations based on timed barium esophagogram (TBE), high-resolution esophageal manometry (HRM), and Eckardt score were compared between the groups.

Results: Twenty-six patients met the study criteria. Their median age was 47 years, 16 patients were men, and the median BMI was 21.4 kg/m². The median follow up period was 13 months. Eleven of 26 patients (42%) had an evidence of GERD based on post-POEM endoscopy. Age, sex, and BMI were comparable between the patients with and without GERD. Duration of disease was longer in patients with post-POEM GERD than those without GERD, although it did not reach statistical significance (120 vs. 36 months, p=0.069). Pre-operative Eckardt score was similar between the groups. According to Japan Esophageal Society classification of esophagogram in patients diagnosed with achalasia, there were no differences in morphology type (straight esophageal type: sigmoid type: advanced sigmoid type, 11:3:0 in non-GERD group and 8:2:1 in GERD group; p=0.793) and maximal esophageal transverse diameter (41.0 mm in non-GERD group vs. 44.0 mm in GERD group, p=0.536) between the groups. Manometric diagnosis based on Chicago classification v3.0 was similar between the patients in non-GERD group and those in GERD group (achalasia type I: type II: type III: Jackhammer esophagus, 3:8:3:1 in non-GERD vs. 4:5:2:0 in GERD, p=0.922). No patient had a manometric hiatal hernia. The resting lower esophageal sphincter (LES) pressure and intraabdominal LES length were similar among the groups; however, the patients in the GERD group had significantly shorter overall LES length (OL) than those in the non-GERD group (2.9 vs. 3.5 cm, p=0.003). ROC curve analysis for OL revealed the cut-off value of 3.0 cm (AUC 0.885 [95%CI: 0.722-1.000], p=0.006) with the sensitivity of 100% and specificity of 71%. Prevalence of GERD was 100% in patients with OL < 3 cm and 13% in patients with OL ≥3 cm (p=0.001).

Conclusion: Longer duration of disease may be a risk factor of esophagitis after POEM. Longer OL (≥3 cm) appears to prevent reflux esophagitis after POEM. Further study is warranted.

Disclosure: Nothing to disclose

P0568 EFFECT OF CLEARANCE RATE OF THE ESOPHAGUS FOR SYMPTOMS AND SURGICAL RESULTS IN PATIENTS WITH ESOPHAGEAL ACHALASIA

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Introduction: Esophageal achalasia is one of the primary esophageal motility disorders, and dysphagia and vomiting due to difficult passage at the lower part of the esophagus are main symptoms in patients with esophageal achalasia. Timed barium esophagogram (TBE) is a useful method to evaluate the clearance at the lower part of the esophagus in patients with esophageal achalasia, which we usually performed before and after surgery. Meanwhile, laparoscopic Heller-Dor operation (LHD) is a gold standard treatment of esophageal achalasia and is prevalent all over the world.

Aims & Methods: The aim of this study is to analyze the effect of clearance rate of the lower part of the esophagus for symptoms and surgical results in patients with esophageal achalasia. Between May 2002 and March 2019, 588 patients who underwent LHD at our institution were extracted from the database. Out of these, 433 patients met our inclusion criteria; such as the patients who underwent LHD as an initial operation with complete evaluation of preoperative esophageal clearance by TBE. These patients were divided into three groups based on the clearance rate of the lower part of the esophagus (Group A: clearance rate <10%, Group B: 10%≤clearance rate <50%, and Group C: 50%≤clearance rate). Patients' background, pre- and post-operative symptom scores, surgical results and post-operative course were compared. Before and after surgery, a standardized questionnaire was used to assess the degree of frequency and severity of symptoms (dysphagia, vomiting, chest pain and heartburn). For each symptom, frequency and severity were separately assessed on a five-point scale (range: 0-4), and a symptom score was calculated by multiplying these points (range: 0-16). Moreover, satisfaction with operation was evaluated using the standardized questionnaire. Statistical analysis was performed by using Krasukal-Wallis test or chi-square test, and p-value less than 0.05 was defined as statistically different.

Results: Their mean age was 44.6 years and 217 of them were male (50.1%). One hundred and eighty-six patients (43.0%) were in Group A, 163 (37.6%) in Group B, and 84 (19.4%) in Group C. The maximum width of the esophagus in Group C was smaller than that in other groups (p=0.0181). As to the pre-operative symptom score, dysphagia was significantly lower in Group C (p=0.0442), whereas chest pain was significantly higher in Group C (p=0.0489). Surgical outcomes including the incidence of mucosal injury were not different among three groups. Moreover, the patient satisfaction with LHD was excellent regardless of preoperative esophageal clearance.

Conclusion: Pre-operative clearance rate of the lower part of the esophagus correlated with pre-operative dysphagia and chest pain, but did not affect the surgical outcomes of LHD, post-operative course or post-operative symptoms in patients with esophageal achalasia.

Disclosure: Nothing to disclose

P0569 LONG TERM RESULTS OF PERORAL ENDOSCOPIC MYOTOMY: A SINGLE CENTER EXPERIENCE WITH MORE THAN 300 PROCEDURES

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Introduction: Peroral endoscopic myotomy (POEM) is nowadays considered as a standard method for treatment of esophageal achalasia, however, the

high risk of post-POEM reflux tempers the POEM enthusiasm. The aim of our case series was to assess the long-term clinical outcome of POEM and a thorough analysis of post-POEM reflux.

Aims & Methods: A retrospective analysis of prospectively collected data of consecutive patients undergoing POEM at our tertiary center (December 2012- March 2019). All patients were scheduled for follow up at 3and 12 months after the procedure and every year thereafter. Upper GI endoscopy, high-resolution manometry (HRM) and 24-hour pH monitoring were performed 3 months after POEM; endoscopy was then repeated between 24-36 months. Main outcomes were treatment success defined as Eckardt score < 3, recurrence rate and parameters of post-POEM gastroesophageal reflux evaluated by 24h pH monitoring, presence of reflux esophagitis, reflux symptoms and use of proton pump inhibitors (PPIs).

Results: A total of 292 patients with achalasia underwent 306 POEM procedures. Follow- up visits at 3, 12, 24, 36 and 48 months were completed in 250, 179, 131, 69 and 28 patients. At 3, 12, 24, 36 and 48M, treatment success was achieved in 98% (CI 96-100), 95% (92-98), 90% (85-95), 82% (73- 91) and 79% (67-91) of patients. A total of 25 patients experienced treatment failure (n=6) or recurrence (n=19). At 3 months, reflux esophagitis was observed in 107/251 (42.6%, LA C/D in 12 patients). Abnormal acid exposure was detected in 93/215 (44.3%) patients. At 24-36 months, endoscopy was performed in 84 patients and reflux esophagitis was present in 27 patients (32.1%). PPIs were administered to 37.2% and 42.7% of patients at 3 and 24 months, respectively.

Conclusion: POEM is a highly effective endoscopic treatment for achalasia with still favorable treatment success of almost 80% at 4 years after the procedure. Higher rate of post-POEM reflux esophagitis seems to decrease over time.

Disclosure: Nothing to disclose

P0570 FUNCTIONAL VERSUS STRUCTURAL ESOPHAGEAL JUNCTION OUTFLOW OBSTRUCTION: ARE REALLY TWO DISTINCT MANOMETRIC CONDITIONS?

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Introduction: Esophageal junction outflow obstruction (EGJOO) is a new diagnosis recently introduced in Chicago Classification V3.0. It is a pathological entity of unclear clinical significance and represents a heterogeneous range of conditions. It may be classified as structural (SO) when there is a mechanical cause for the obstruction such as the presence of hiatal hernia, esophageal rings and post-surgery or as functional (FO) when a potential obstructive cause is not identified.

Aims & Methods: Aim: to evaluate the prevalence of EGJOO and to compare the clinical, manometric and phmonitoring characteristics of the patients according to the cause: SO versus FO.

Methods: Retrospective and single center study. All patients presented a High Resolution Manometry (HRM) with 36 channels of solid state. All the HRM between 01/2012 and 01/2019 were reviewed and were included patients with EGJOO diagnosis and then classified in SO and FO.

Results: From 2357 HRM reviewed, 79 (3.4%) patients met criteria of EGJOO according to Chicago Classification v3.0, 57.0% females with mean age of 59.8 (±13.8) years. Of them, 42 (53.2%) patients presented simultaneous esophageal pH monitoring.

Forty patients (50.6%) were categorized as SO and 39 (49.4%) as FO.

Fourteen patients presented previous history of Nissen fundoplication, 3 presented bariatric surgery, 3 distal esophageal ring and 26 hiatal hernia.

Patients with SO presented more frequently typical symptoms (52.5%vs 20.5%; p=0.003) and atypical symptoms (22.5%vs5.1%; p=0.026) of GERD when compared to FO.

Patients with FO presented higher intrabolus pressure (18.4 vs 15.5; p=0.039) when compared to SO and in multiple swallowing, FO presented higher distal contractile integral (DCI) (2818.3 vs 1670.9; p=0.003) comparing to SO.

No other differences were observed between the groups regarding other HRM parameters and pH monitoring.

Conclusion: The frequency of EGJOO in our population was low and it represents a heterogeneous group of patients. The differences between SO and FO are scarce, however we found higher intrabolus pressure and DCI on multiple swallows in patients with FO.

Disclosure: Nothing to disclose

P0571 WITHDRAWN

P0572 CLARIFICATION OF ACHALASIA PATIENTS' SYMPTOMS AND THE RELATIONSHIP BETWEEN MANOMETRIC SUBTYPE AND SYMPTOM DETAILS

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Introduction: Some patients feel dysphagia as a stuck sensation in their throat, while the real obstruction site is in their lower oesophagus. Chest pain is also often reported by achalasia patients, but the mechanism of chest pain is still unknown. High-resolution manometry (HRM) enable us to categorize achalasia into three distinct subtypes by the status of the oesophageal body (Chicago classification :CC).

Aims & Methods: The aim of this study was to clarify the symptoms of oesophageal achalasia patients using HRM. Seventy one newly diagnosed achalasia patients were enrolled. Symptoms, HRM and radiographic findings were retrospectively reviewed. A structured self-reported questionnaire focused on dysphagia and chest pain were obtained from all the patients. The questionnaire consists of the main site of symptom (dysphagia and chest pain), timing, duration, food or behavior that cause symptoms, accompanying symptoms, and the preferable way to relieve symptoms. HRM was performed with ManoScan and assessed by CC v3.0. Oesophagograms were taken with 100ml of barium. Characteristics of the symptoms and the differences in symptom details among the manometric subtypes were investigated.

Results: Of total 71 patients, 69 patients(97%) reported dysphagia and 39patienpatiens(54%) reported chest pain. According to HRM findings, patients were classified into types I/II/III 25/37/9 patients (35/52/12%) by CC. The pressurization of oesophageal body after swallows was different among the subtypes (I/II/III 13.4/27.7/70.3mmHg, p< 0.05). Oesophagogram also showed the difference in the diameter of the oesophagus (I/II/III 5.4/4.8/3.1cm, P< 0.05). Regarding dysphagia, Type II patients mostly felt dysphagia in the throat (54%), while type I and III patients mostly felt it in the epigastrium (52%, 55%). Type II patients often had dysphagia immediately after swallowing (41%), but that was only the case in 8.7% of type I and 33% of type III patients (p< 0.05). Drinking water was preferred to relieve dysphagia in type I and II patients (78% and 70%), but less so in type III (33%). About chest pain, patients with chest pain had higher pressurization in the oesophageal body than patients without pain (34.8 vs. 21.5mmHg, p< 0.05). Type I patients rarely felt pain in the interdigestive period (14%), but more often while sleeping (43%) and in early morning (43%). Type III patients reported more pain in the interdigestive period (67%), but none while sleeping. The most reported answer for the duration was 5-10minutes for type I (36%), within 1 minute for type II (26%), and 1-5minutes for type III (67%). Type III patients reported more often than type I and II patients that solid food caused pain (I/II/III 0/10/33%, p=0.09).

Conclusion: Detailed symptoms of achalasia, such as its site and timing, varied by subtypes. The status of the oesophageal body might induce those differences in symptoms.

Disclosure: Nothing to disclose

P0573 COMPARISON OF PERORAL ENDOSCOPIC MYOTOMY BETWEEN DE-NOVO ACHALASIA AND PRIOR TREATMENT FAILURE ACHALASIA

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Introduction: Peroral endoscopic myotomy (POEM) has been recognized as an effective treatment for patients with achalasia (1). Prior treatment may affect the outcome of subsequent treatment (2). We aimed to compare the safety and efficacy of POEM in treatment-naive patients (TN) vs. those with prior treatment failure (PTF).

Aims & Methods: We retrospectively analyzed the data of achalasia patients who underwent POEM from November 2011 to January 2018. A comparative analysis was performed between TN and PTF cases. Technical and clinical success, adverse events, operative time for POEM, hospital stay and length of myotomy were compared between the two groups.

Results: Overall, 209 patients with achalasia underwent POEM during the studied period, including 113 patients (54%) in the TN group and 96 patients (45%) in the PTF group. The baseline characteristics of the TN and PTF groups were not significantly different except for duration of disease. The PTF group had longer disease duration than the TN group. (7.92 ± 9.28 vs 4.45 ± 5.67 years respectively p=0.005). Both groups were technically successful. All of the POEM cases' procedures were completed successfully. Operative time was longer in the PTF group than that in the de novo group, but the difference was not statistically significant. The occurrence rates of gas-related events and severe complications were similar in both groups. The operation time, hospital stay, length of myotomy were not significantly different between the two groups.

Changes in the Eckardt score before and after POEM (5.11 ± 0.23 vs. 4.99 ± 0.253; P=0.042 vs. P=0.001) were comparable in the TN and PTF cases. IRP and LES pressure decreased after POEM. The decreases in the IRP and LES pressure values were significantly different between TN group and the PTF group (Table 1). After 6 months, more patient suffered from reflux symptoms in the PTF group but DeMeester score and endoscopic evaluation were not significantly different between the two groups.

	Treatment naive group(n=113)	PTF group (n=96)	P-value
Technical success, n (%)	113 (100%)	96 (100%)	not applicable
Length of myotomy, cm (Esophagus)	7.22 ± 2.27	7.11 ± 1.97	0.630
Length of myotomy, cm (Stomach)	1.81 ± 0.59	1.82 ± 0.54	0.979
Operation time, minute	74.08 ± 31.93	76.52 ± 32.27	0.539
Duration of nill per oss, day	5.23 ± 1.51	5.28 ± 1.46	0.884
Hospital stay, day	7.23 ± 1.51	7.28 ± 1.46	0.884
Adverse event, n (%)	52 (46.0)	66 (68.7)	0.214
Clinical success (Eckardt score ≤3)	107 (94.6%)	91 (94.7%)	0.978
Difference of Lower esophageal sphincter pressure	22.88 ± 18.17	8.83 ± 18.10	0.001
Difference of Integrated Relaxation Pressure	18.02 ± 21.92	7.32 ± 14.21	0.004
Reflux symptoms after 6 months (Yes : No), n	41 : 71	47 : 46	0.045

[Table 1]

Conclusion: Our results were comparable to other studies that compared TN and PTF in terms of the mean values of adverse effects, operation time and technical and clinical success of POEM (3,4). POEM is safe and equally effective for de-novo patients and for those in whom prior treatment failed. POEM should be considered as the treatment of choice in patients with history of failed prior treatment.

References: [1] Inoue H, Minami H, Kobayashi Y, Sato Y, Kaga M, Suzuki M, et al. Peroral endoscopic myotomy (POEM) for esophageal achalasia. Endoscopy 2010;42:265-71. [2] Wu QN, Xu XY, Zhang XC, Xu MD, Zhang YQ, Chen WF, et al. Submucosal fibrosis in achalasia patients is a rare cause of aborted peroral endoscopic myotomy procedures. Endoscopy 2017;49:736-44. [3] Nabi Z, Ramchandani M, Chavan R, Tandan M, Kalapala R, Darisetty

S, et al. Peroral endoscopic myotomy in treatment-naive achalasia patients versus prior treatment failure cases. Endoscopy 2018;50:358-70. [4] Louie BE, Schneider AM, Schembre DB, Aye RW. Impact of prior interventions on outcomes during per oral endoscopic myotomy. Surgical endoscopy 2017;31:1841-8.
Disclosure: Nothing to disclose

P0574 ENDOSCOPIC CLIPS VERSUS ENDOSCOPIC SUTURE FOR MUCOSAL CLOSURE AFTER PER-ORAL ENDOSCOPIC PYLOROMYOTOMY (G-POEM)

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Introduction: G-POEM is an emerging method for treatment of severe gastroparesis (GP). Safe and reliable mucosal closure is necessary to avoid major adverse events.

Aims & Methods: The aim of this prospective (ongoing) study was to compare the effectivity of two closure methods: endoscopic clips (Resolution™® or Instinct™®) and endoscopic suturing (ES, Apollo OverStitch™®) in patients undergoing G-POEM for refractory GP.

A single center, prospective study (NCT:03679104). All patients, who underwent G-POEM in our centre and agreed to participate were enrolled. The closure method was assigned at the discretion of an endoscopist (one endoscopist performed all procedures) prior to the procedure. The main outcome was the proportion of subjects with successful closure. Unsuccessful closure was defined as a need for a rescue method, or a need for an additional intervention (e.g. in case of leak). Secondary outcomes were easiness of closure [measured by means of a questionnaire on a VAS (visual analogue scale, 0=impossible, 10=very easy, scored by endoscopist as well as an endoscopy nurse)] and closure time.

Results: A total of 15 patients [M:F/7:8; mean age 50.5 (29-74)] have been included so far; 8 patients received ES closure and 7 patients received a closure with endoclips [mean 6, range (5-19)]. All patients with ES had successful closure but 2 pts (29%) with clips needed a rescue method (n=1, KING closure with an endoloop) and an additional clipping because of leak on POD1 (n=1). The remaining patients (n=5, 71%) had a successful closure with clips. Closure with clips tended to be quicker [mean closure time and range 10.4 (8-13) vs 14.8 (9-20) min, p=0.189]. Endoscopist assessed closure with ES easier compared to clips [mean VAS, SD: 7.6 ±1.3 (ES) vs. 5.4 ±1.7 (clips) p=0.02], nurses assessed easines of both closure methods as comparable (VAS 6.6 ±2.6 (ES) vs 7 ±1.2 (clips) p= 0.536].

Conclusion: Endoscopic suturing system may be more reliable than clipping for mucosal closure in patients undergoing G-POEM, even though is technically more demanding. Besides clips, centers performing G-POEM should have an alternative (rescue) closure method. (Supported from Czech Ministry of Health 17-28797A). Clin Trial: NCT03679104

Disclosure: Nothing to disclose

P0575 PERORAL ENDOSCOPIC MYOTOMY (POEM): A COMPARATIVE STUDY BETWEEN CHAGASIC AND IDIOPATHIC ACHALASIA

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Introduction: Achalasia is a benign esophageal motor disorder that results from a progressive degeneration of ganglion cells in the myenteric plexus of the esophageal wall. It leads to failure of relaxation of the lower esophageal sphincter associated to the loss of the peristalsis in the distal esophagus. The etiology of the primary or idiopathic achalasia is unknown. In Chagas disease, the esophageal infection with the protozoan parasite Try-

panosoma cruzimay result in the loss of the intramural ganglion cells. The peroral endoscopic myotomy (POEM) is an effective and safe treatment for achalasia. However, there is no study comparing outcomes of POEM according to the etiology of the achalasia.

Aims & Methods: We evaluated our prospectively collected database of POEM procedures performed at a single institution from November 2016 to August 2017. Demographic data, clinical success, Eckardt score, lower esophageal sphincter (LES) pressure, body mass index (BMI), erosive esophagitis, adverse events, pneumoperitoneum requiring needle decompression, operative time, and length of hospital stay were assessed. Clinical success was defined as an Eckardt score ≤ 3 at 1 year. Student T-test and Logistic regression analyses were performed.

Results: Fifty-one patients (52,9% F, mean age 50 ± 13.8) underwent POEM as a treatment for achalasia in this period, 20 patients with chagasic and 31 with idiopathic etiology. All procedures were posterior full-thickness POEMs. The overall clinical success rate was 92.2%. There was no statistical difference between groups regarding clinical success (90% in the chagasic group vs 93.6% in the idiopathic group, p= 0.640). Both groups presented significant reduction in Eckardt score compared to baseline (1.00 vs 7.50 in the chagasic group, p< 0.001; and 0.00 vs 8.00 in the idiopathic group, p< 0.001), LES pressure (10.32 vs 21.76 in the chagasic group, p< 0.001; 10.70 vs 25.21 in the idiopathic group, p< 0.001), and increase in BMI (27.11 vs 25.41 in the chagasic group, p< 0.001; 25.99 vs 22.17 in the idiopathic group, p< 0.001) at 1 year follow-up. There was no statistical difference between groups regarding Eckardt score (p= 0.439), LES pressure (p= 0.507), and BMI (p= 0.254) at 12 months. There were no significant differences between groups concerning the rates of erosive esophagitis (35% vs 44%, p= 0.432), adverse events (30% vs 12%, p= 0.311), pneumoperitoneum requiring needle decompression (35% vs 35%, p= 0.81), operative time (101.3 min vs 99.1 min, p= 0.840), and length of hospital stay (3.75 days vs 3.58 days, p= 0.622).

Conclusion: POEM is an effective and safe treatment in patients with achalasia. There is no difference in outcomes comparing chagasic and idiopathic achalasia.

Disclosure: Nothing to disclose

P0576 ESOPHAGEAL MOTILITY DISORDERS IN EOSINOPHILIC ESOPHAGITIS

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Introduction: Eosinophilic Esophagitis (EoE) is a chronic immune/antigen-mediated disorder, characterized by symptoms of esophageal dysfunction and esophageal eosinophilic-infiltration. EoE has been often associated with esophageal motility abnormalities, ranging from hypo- to hyper- contractile motility disorders.

Aims & Methods: The aim of this study is to evaluate the incidence and clinical characteristics of esophageal motility disorders in EoE.
97 consecutive patients (mean age 39, range 18-75yo, 20 F) with a diagnosis of EoE assessed in our unit between 2012 to 2018, were included. The diagnosis was posed according to international criteria. Among 97 patients, in 47 (48%) high resolution manometry (HRM) was not performed, so they were excluded from the study. Patients undergone HRM, were studied using the standardised international protocol and manometric diagnoses were made according to Chicago Classification 3.0. For the statistical analysis Fisher exact test was used.

Results: Among 50 patients included (mean age 41, range 20-75 yo, 42M), 26 (52%) showed normal manometric pattern. Between EoE patients with pathological pattern, 16 (67%) had hypocontractile disorders, and 8 (33%) had hypercontractile abnormalities. In particular, EoE patients with hypocontractile patterns had frequent failed peristalses (N=4), ineffective esophageal motility (N=6), fragmented peristalsis (N=4), absent peristalsis (N=2). Among EoE patients with hypercontractile patterns, we found achalasia type III (N=2), achalasia type II (N=2), achalasia type I (N=1), EGJ outflow obstruction (N=1), Jackhammer esophagus (N=1), and 1 distal esophageal spasm (N=1).

We then analysed both patients with normal and pathological manometric pattern in terms of age, sex and response to PPI.
Patients with normal motility n=26 (52%) showed:
Age (mean and median) 43,4yo; 40,5yo
Age at diagnosis (mean and median) 36,1yo; 33yo
Sex 22M (84,6%)
PPI response (9 of 17) 52,9%
Patients with motility disorders n=24 (48%) showed:
Age (mean and median) 37,9yo; 33,7yo
Age at diagnosis (mean and median) 29,2yo; 25yo
Sex 20M (83,3%)
PPI response (7 of 18) 38,9%
Among the group with abnormal motility, the same characterization was done.
Patients with hypercontractile disorders n=8 (33%)
Age (mean and median) 41,9yo;36,2yo
Age at diagnosis (mean and median) 27,2yo; 29,5yo
Sex 6M (75%)
PPI response (2 of 9) 22%
Patients with hypocontractile disorders n=16 (67%)
Age (mean and median) 36yo; 32yo
Age at diagnosis (mean and median) 30,4yo; 24yo
Sex 14M (87.5%)
PPI response (5 of 9) 55%
There was no difference in terms of prevalence of motility abnormalities (p=0.49) nor a predominance of hypo/hyper contractile pattern (p=0.14), between PPI responsive/non-responsive patients. Similarly, no difference in terms of motility abnormalities (p=1), nor a predominance of hypo/hyper contractile (p= 0.60) were found between females and males. Considering the mean age of the group (39yo), there was a different prevalence of motility abnormalities between younger and older patients, with greater frequency of pathological pattern in young patients (p= 0.045). However, there was no difference in terms of frequency of hypo- or hypercontractile disorders between young and old EoE patients (p= 0.49).

Conclusion: This series shows that esophageal motility abnormalities are present in about half of EoE patients, especially in young subjects who showed a higher prevalence of hypocontractile disorders. A correlation with patient's gender or response to PPI therapy was not observed.

References: Nurko S, Rosen R. Esophageal dysmotility in patients who have eosinophilic esophagitis. Gastrointest Endosc Clin N Am. 2008;18(1):73-ix. Lucendo AJ, Molina-Infante J, Arias Á, et al. Guidelines on eosinophilic esophagitis: evidence-based statements and recommendations for diagnosis and management in children and adults. United European Gastroenterol J. 2017;5(3):335-358.

Disclosure: Nothing to disclose

P0577 A PROSPECTIVE MULTICENTER STUDY ON THE PREVALENCE OF EOSINOPHILIC OESOPHAGITIS IN THE RUSSIAN FEDERATION AMONG ADULTS UNDERGOING UPPER ENDOSCOPY

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Introduction: Eosinophilic oesophagitis (EoE) is a common cause of oesophageal disease in Europe and the USA. Limited data have been reported on its epidemiology in the Russian Federation. The aim of this study was to evaluate the prevalence of EoE in the Russian Federation among adult patients undergoing esophagogastroduodenoscopy (EGDS) due to upper gastrointestinal (UGI) symptoms.

Aims & Methods: This study was conducted in 11 endoscopy departments in the Russian Federation (4 in Moscow, 1 in Yaroslavl, 1 in Ivanovo, 1 in Kazan, 2 in Saint Petersburg, 1 in Ekaterinburg, 1 in Kemerovo) between October 2017 and March 2018. We enrolled 49240 patients aged 18 to 80 years old who underwent an EGDS due to UGI symptoms (heartburn, dysphagia, food impaction, acid regurgitation, chest pain, epigastric pain, nausea, vomiting). Patients with endoscopic findings of EoE (oedema, rings, exudates, furrows, and strictures) were underwent oesophageal biopsy (at least 6 biopsies were obtained from the proximal and distal oesophagus to quantify the maximum eosinophil count per high-power field (eos/hpf; hpf=0.24 mm). Patients were diagnosed with EoE if the number of eosinophils was ≥15.

Results: EGDS revealed endoscopic features of EoE in 137 patients. Oesophageal biopsy confirmed eosinophilic oesophagitis in 62 cases. EoE patients had a mean age of 38.2 years (rank 20-67) years, 83.3% of patients were under 45 years of age, 79.1% patients were male. Individuals with EoE suffered predominantly from dysphagia (62.5%), heartburn (54.1%), food impaction (37.5%), and nausea (29.1%). 79.1% of EoE patients had a past history of gastroesophageal reflux disease, 25% suffered from allergic rhinitis, 33.3% had atopic dermatitis, 8.3% -asthma. 1 patient had a family history of EoE (his sibling and mother also suffered from dysphagia due to EoE).

Conclusion: The prevalence of EoE among adult patients undergoing upper endoscopy in the Russian Federation is 1 case for 794 UGI endoscopies (0.13%). The characteristic findings of EoE patients included male gender, age under 45 years and history of atopic diseases.

Disclosure: Nothing to disclose

P0578 A DECREASED ABUNDANCE OF *CLOSTRIDIA* CHARACTERIZES THE GUT MICROBIOTA IN EOSINOPHILIC ESOPHAGITIS

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Introduction: Eosinophilic esophagitis (EoE) is an allergic disorder characterized by a Th2 mediated immune response, esophageal dysfunction and esophageal eosinophilic infiltration. While several genetic, and environmental factors have been implicated in EoE, recent evidence supports a role for the gut microbiome. Abnormalities in the gut microbiome are associated with suppressed Th2 response and predisposition to atopic disease such as asthma and eczema.

Aims & Methods: In this study we evaluated the gut microbiome represented in the stool from patients with EoE matched to healthy controls. All human studies were approved by the institutional IRB. Stool bacterial DNA was extracted using MoBio fecal DNA extraction kit, followed by 16S rRNA amplification using primers flanking the V4 hypervariable region (515F, 806R) and sequenced on Illumina MiSeq. Paired sequence reads were processed via the *hybrid-denovo* bioinformatics pipeline. A linear regression model (t-test) was used for testing the association with alpha-diversity after rarefaction to 20,000 reads/sample. Taxa-level association analyses were performed at multiple taxonomic levels. Permutation-based false discovery rate (FDR) control was used to correct for multiple testing on each taxonomic level, and FDR-adjusted p-values or q-values ≤ 0.1 were considered significant. All statistical analyses were performed in R 3.4.2.

Results: Patients with EoE had a median age of 48 (34-64), body mass index (BMI) was 29.51 (22.40-36.49), 4 were male and all were Caucasian. Only one patient had asthma and one had atopic dermatitis. Six patients were on a regular diet. No patients were on PPIs. The healthy control patients had a median age 51 (33-61), BMI 24.75 (19.73-41.39), 3 were male and all were Caucasian.

We compared the 16S rRNA-based microbial community composition in stool samples from the patients with EoE (n=12) and healthy control subjects (n=12). At the phylum level, we observed a marked decrease in Firmicutes and increase in Bacteroidetes in patients with EoE. The gut microbial communities from patients with EoE were characterized by a lower alpha diversity (species richness, p = 0.09; Shannon index, *p* = 0.01; linear regression). The beta-diversity was also significantly different between patients with EoE and healthy controls (p = 0.03, PERMANOVA based on weighted UniFrac; p = 0.04, omnibus test combining multiple beta diversity measures). There were significant differences in relative abundance at

multiple taxonomic levels when comparing the two communities, which included significant decreases in *Clostridia* and *Clostridiales* in patients with EoE (*q* ≤ 0.1, permutation test with t-statistic).

Conclusion: This finding is particularly important as previous studies show that members of *Clostridia* group are protective against the development of food allergies in a rodent model. *Clostridia*-containing microbiota is also associated with the expansion of intestinal regulatory T cells, and induction of IL-22 production by RORγt+ ILCs promoting an immune environment conducive for tolerance to dietary antigens. While our study is limited by the small sample size, the strengths of the study are a lack of confounders that have been associated with altered stool microbiome such as proton pump inhibitors, and other atopic illnesses in most patients. Our findings suggest defined microbial consortia containing *Clostridia* may be a potential therapeutic option in EoE.

Disclosure: Advisory board uBiome and ad hoc Salix.

P0579 OUTCOMES OF A SAME SESSION OESOPHAGEAL DILATION AFTER REMOVAL OF IMPACTED FOOD BOLUS: RESULTS OF A RANDOMIZED CONTROLLED STUDY

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Introduction: Majority of food bolus obstruction (FBO) is caused by a benign esophageal stricture for which endoscopic dilation is an effective treatment. However, it is unknown whether same-session endoscopic dilation (SSED) after removal of food bolus (FB) is clinically safe.

Aims & Methods: : To evaluate the safety of performing SSED immediately after FB removal. **Methods**: A randomized controlled study was conducted between 2017-2019 on patients who had FBO due to oesophageal stricture were randomized into 2 groups: (i) SSED group - who had SSED using wire-guided Savary Gillard dilators vs (ii) non SSED group - deferred dilation to another date. Primary outcome measures were technical success, procedural-related complication(s) and mortality.

Results: 456 patients had endoscopic removal of food bolus, of which 236 were excluded due to absence of an oesophageal stenosis (n=93), concurrent anticoagulation or antiplatelet (n=136), dilators were not available (n=7). 220 patients were randomized to group SSED (n=110) and non SSED group (n=110). Technical success of dilation and immediate clinical response were achieved in all patients. The median maximal dilation diameter was 14mm (range 11-18mm). Apart from chest pain occurred in 9 (8%) patients immediately after dilation that resolved with simple analgesia, there was no perforation, major bleeding requiring blood transfusion or death. Recurrent of FBO occurred in 41 (18.6%) at a mean time of 31 ± 19 days, and was significantly higher in the non-SSED than SSED group (39 vs. 2; P < 0.01).

Conclusion: Same-session esophageal stricture dilation after FB removal is safe and significantly reduced the risk of recurrence, preventing repeat admission. Thus, our data support the use of routine use of SSED for patients who present with FBO.

References: 1. Longstreth G. F., Longstreth K. J., Yao J. F. Esophageal food impaction: epidemiology and therapy. A retrospective, observational study. Gastrointestinal Endoscopy. 2001;53(2):193-198. 2. Mahesh VN, Holloway RH, Nguyen NQ. Changing epidemiology of food bolus impaction: is eosinophilic esophagitis to blame? J Gastroenterol Hepatol 2013 Jun;28(6):963-6. 3. Vicari J. J., Johanson J. F., Frakes J. T. Outcomes of acute esophageal food impaction: success of the push technique. Gastrointestinal Endoscopy. 2001;53(2):178-181. 4. Smith MT, Wong RKH. Esophageal foreign bodies: Types and techniques for removal. Curr Treat Options Gastroenterol. 2006;9:75-84. 5. ASGE Standards of Practice Committee. Ikenberry SO, Jue TL, et al. Management of ingested foreign bodies and food impactions. Gastrointest Endosc. 2011;73:1085-1091.

Disclosure: Nothing to disclose

P0580 A NOVEL BUDESONIDE ORODISPERSIBLE TABLET WITH A SPECIAL ESOPHAGEAL-TARGETING CAN INDUCE COMPLETE CLINICAL, ENDOSCOPIC AND HISTOLOGIC REMISSION IN ACTIVE EOSINOPHILIC ESOPHAGITIS: RESULTS FROM A *POST-HOC* ANALYSIS OF THE RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED EOS-1 TRIAL

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Introduction: A 6-week treatment with a novel budesonide orodispersible tablet twice daily (BOT 1mg BID), with a unique mode of delivery and esophageal targeting, was highly effective and safe in the EOS-1 study for induction of clinico-histological remission in adult patients with active eosinophilic esophagitis (EoE) according to standard criteria (1). Here we present in a *post-hoc* analysis the efficacy of BOT 1mg BID using new, most stringent criteria, e.g., as previously suggested by Greuter et al. (2).

Aims & Methods: To assess the efficacy of BOT 1mg BID using most stringent endpoints for the induction of complete normalization of esophageal biopsies, absence of endoscopic abnormalities and absence of clinical symptoms in adult patients with active EoE.

Adults with active EoE (n=88) randomly received 6-weeks double-blind treatment with either BOT 1mg BID (n=59) or placebo BID (n=29).

A priori **defined endpoints were: Clinico-histological remission:** < 16 eos/mm² hpf AND ≤2 points on daily numerical rating scales (0-10 points) each for dysphagia and odynophagia on each of the last 7 days

Histological remission: peak < 16 eos/mm² hpf

Clinical remission: ≤2 points on numerical rating scales (0-10 points) each for dysphagia and odynophagia on each of the last 7 days.

Post-hoc **stringently defined endpoints were:**

Deep clinical remission (2): '0' points on daily numerical rating scales (0-10 points) each for dysphagia and odynophagia on each of the last 7 days.

Deep endoscopic remission (2): modified EREFS subscores: fixed rings = 'Grade 0: none' or 'Grade 1: mild', exudates = 'Grade 0: none', furrows = 'Grade 0: absent', and edema = 'Grade 0: absent'.

Histological remission (2): peak < 15 eos/hpf

Deep histological remission: '0' eos/mm² hpf in all biopsies.

Deep disease remission (2): Being in deep clinical AND deep endoscopic AND histologic remission.

Results: BOT 1mg BID was highly statistically superior to placebo in achieving all stringently defined clinical, endoscopic, and histological endpoints (see Table).

	Number (%) of patients at week 6 (LOCF)		
	BOT 1mg BID (n=59)	Placebo BID (n=29)	p-value (2-sided)
A priori defined endpoints: Clinico-histological remission	34 (58%)	0 (0%)	< .0001
Histological remission	55 (93%)	0 (0%)	< .0001
Clinical remission	35 (59%)		< .0001
Post-hoc defined most stringent endpoints: Deep clinical remission (2)	15 (25%)	0 (0%)	= .0018
Deep endoscopic remission (2)	34 (58%)	0 (0%)	< .0001
Histological remission (2)	56 (95%)	0 (0%)	< .0001
Deep histological remission	53 (90%)	0 (0%)	< .0001
Deep disease remission (2)	12 (20%)	0 (0%)	= .0072

[Table: Standard & stringent efficacy endpoints]

Conclusion: A 6-week treatment with BOT 1mg BID was highly effective for inducing deep histological, endoscopic and clinical remission as well as deep disease remission in adult EoE patients according to most stringent criteria.

References: (1) Lucendo AJ, et al. Gastroenterology 2019, DOI:https://doi.org/10.1053/j. gastro.2019.03.025 (2) Greuter T, et al. Am J Gastroenterol. 2017;112:1527-35.

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P0581 DIAGNOSTIC DELAY AND APPROPRIATENESS IN MANAGEMENT OF EOSINOPHILIC OESOPHAGITIS ALONG TIME IN THE EOE CONNECT REGISTRY: THE EFFECT OF CLINICAL GUIDELINES TO IMPROVE CLINICAL PRACTICE

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Introduction: Eosinophilic oesophagitis (EoE) is a chronic inflammatory disease characterised by a dense eosinophilic infiltration of the oesophagus and symptoms of oesophageal dysfunction. EoE is recognized as a particular form of non-IgE-mediated food allergy commonly associated with other IgE-mediated atopies. The novelty of the disease has contributed to a considerable diagnostic delay in many cases and to variable management of patients in clinical practice, who frequently underwent serum and skin allergy testing to find triggering antigens. Recent evidence discourages this practice due to its low yield.

Aims & Methods: To investigate delay in EoE diagnosis, number of previous useless endoscopies performed in these patients and unneeded allergy testing (laboratory, skin prick and atopy patch testing) once a EoE diagnosis is established, we searched within the *EoE CONNECT* database, a prospectively-maintained registry that resulted from the UEG Link Award program.

Patients' data was extracted on 25th March 2019. For statistical comparisons, all variables were assessed depending on the date in which the different EoE clinical guidelines were published (2007, 2011, 2013 & 2017). Statistical analyses (Mann-Whitney test and Kruskal-Wallis test followed by Dunn post-hoc test) were performed using GraphPad software.

Results: Data from 608 EoE patients recruited at 9 hospitals in Spain and 1 more in Italy were retrieved from the *EoE CONNECT* registry. From those, dates for both symptoms onset and definitive EoE diagnosis were available for 434 patients. The diagnostic delay resulted in a mean ± standard deviation (SD) of 1778 ± 2411 days (approximately 4 years and 10 months). A significant decrease in diagnostic delay along time was noted, when patients were classified in five groups according to the publication dates of the different EoE guidelines (p< 0.001). Thus, for patients diagnosed up to 2007 the diagnostic delay was 4661 ± 3123 days, while it was only 164 ± 142 days for patients diagnosed after the release of 2017 guidelines. Group comparisons displayed significant differences between most of the periods analysed.

Twenty-eight patients had information on dates of upper endoscopies performed prior to EoE diagnosis. Overall, 37 exams were performed before the one that provided an EoE diagnosis. The number of superfluous endoscopies were higher for patients diagnosed up to 2011 (n=13; 1.6 ± 1.0) compared to those diagnosed after 2011 (n=15, 1.1 ± 0.3) (p< 0.05).

An assessment of allergy tests performed after a diagnosis of EoE as a part of the diagnostic or therapeutic management was performed in 173 patients who had at least one laboratory, skin prick or atopy patch test after the date of diagnosis. The overall number of allergy tests was 348, with a mean ± SD of 2.0 ± 1.2 per patient. Three groups of patients were considered for statistical analysis: diagnosis in 2011 or before (n=50, 2.8 ± 1.5), 2012-2013 (n=35, 1.8 ± 1.1), and after 2014 (n=88, 1.6 ± 0.7). Significant reductions in the performance of allergy tests were noted among periods (p< 0.001) and for two group comparisons, when diagnosis ≤2011 vs 2012-2013 and diagnosis ≤2011 vs ≥2014 were compared (both p< 0.001).

Conclusion: Our data demonstrate an increased awareness on EoE over time, with significant reductions in diagnostic delay and number of superfluous endoscopic exams as new clinical practice guidelines were released. The performance of allergy testing for the diagnostic and therapeutic management of EoE reduced significantly. A significant effect towards a proper management of EoE was found for the 2011 guidelines.

Disclosure: Nothing to disclose

P0582 ACHALASIA IS A COMMON FINDING IN PATIENTS WITH EOE UNDERGOING HIGH-RESOLUTION MANOMETRY

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Introduction: Eosinophilic Esophagitis (EoE) is a chronic immune/antigen-mediated disorder, characterized by symptoms of esophageal dysfunction (dysphagia and/or food impaction) and, histologically, by eosinophilic-infiltration. EoE has been associated with various esophageal motility disorders, ranging from hypo- to hyper- contractile motility abnormalities, and more recently achalasia.

Aims & Methods: The aim of this study was to assess the incidence of achalasia in patients with EoE, and to evaluate the disease course of EoE after achalasia treatment.

97 consecutive patients (mean age 39, range 18-75 yo, 20 F), with a diagnosis of EoE assessed in our Unit between 2012 to 2018, were included. The diagnosis was posed according to international criteria (presence of typical symptoms of esophageal dysfunction; at least 15 eosinophils per high-power field at mid/proximal oesophagus), excluding other causes of eosinophilia. Among 97 patients, in 47 (48%) conventional manometry (CM) or high resolution manometry (HRM) were not performed and were excluded from the study. Patients who accepted to undergo HRM, were studied by suing the standardised international protocol and manometric diagnoses were carried out according to Chicago Classification 3.0.

Results: Among the 50 EoE patients (mean age 41, range 20-75 yo, 8 F), 26 (52%) showed normal manometric pattern. Between patients with abnormal manometric pattern, 16 (67%) had hypocontractile disorders, 8 (33%) hypercontractile abnormalities and 5 (21%) had a diagnosis of achalasia. Among them 1 type I achalasia, 2 type II achalasia and 3 type III achalasia were present. 3 was male; 3 received EoE diagnosis in adolescent age, 2 after fifties, with a significant diagnostic delay. 3 had history of allergic disease. The main symptom was dysphagia (4patients), but also globus, odynophagia and regurgitation were present in some of them. 3 of them showed EREFS score=3, 1 showed value of 4 and 1 value of 5. At the esophagogram 4 of them had narrowed EGJ and 2 of them with dilation of the esophagus, 1 showed delayed esophageal empting. From a therapeutic point of view, only 2 patients responded to PPI. There was a response to topic steroid therapy in 2 cases, no response in 2 cases, no administration in 1. Considering therapy of achalasia, in 2 cases no treatment was required, in 1 case endoscopic dilation was performed, in 1 case surgery was accomplished and in 1 case endoscopic and then surgical therapy was necessary. Basing on this data, patients was characterized as follows: 2 PPI-responder, 1 refractory EoE, 2 steroid responder EoE

Conclusion: This retrospective study of consecutive patients showed that achalasia, is not uncommon in patients with EoE, affecting about 10% of patients of this cohort. No specific subtype of achalasia is associated with EoE. The high frequency of this association seems to hypothesize a causal link between these two pathologies, whereas all this variability in mano-metric pattern, epidemiological characteristic and response to therapy, suggests that the relationship is not univocal and that there may be different mechanisms that act independently to determine such association.

References: Spechler SJ, Konda V, Souza R. Can Eosinophilic Esophagitis Cause Achalasia and Other Esophageal Motility Disorders? Am J Gastroenterol. 2018 Nov;113(11):1594-1599

Disclosure: Nothing to disclose

P0583 EOSINOPHILIC ESOPHAGITIS QUALITY OF LIFE QUESTIONNAIRE WELL CORRELATES WITH DISEASE ACTIVITY AND RESPONSE TO THERAPY IN ACTIVE EOSINOPHILIC ESOPHAGITIS PATIENTS

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Introduction: Eosinophilic Esophagitis (EoE) is a chronic disease characterized by significant impairing of quality of life (QoL). The EoE-QoL-A (EQA) is a 5-scale, 30-item, self-reported, validated questionnaire for the assessment of QoL in these patients. Data on the usefulness of this questionnaire in clinical practice are lacking.

Aims & Methods: The aim of the study is to apply the EQA in a consecutive population of EoE Italian patients, in order to evaluate whether the EQA changes on the basis of histological disease activity and therapeutic response to drug administration.

Thirty patients (7 Female, mean age 33-yo, range 18-75-yo) with a definite diagnosis of EoE, referred to our Unit, were included. The diagnosis was done according to the latest international criteria. Patients were enrolled at outpatient level, at first admission or follow-up, between January 2018 to February 2019. Patients, were evaluated clinically and histologically before (baseline) and after medical therapy (proton pump inhibitors or topical steroid for 8weeks). At both time points, EoE patients completed the EQA. Histological activity was described as dichotomous parameter: 0 for less than 15eos/hpf and 1 for more than 15 eos/hpf. Pearson correlation coefficient and paired t test were used for the analysis.

Results: At baseline, all patients were histologically active, with a mean value of EQA of 45.07±SD32.69. After 8 weeks of medical treatment, EQA mean value was 37.63±SD28.37. A strong significant decrease of EQA score was therefore observed (p=0.021). After 8 weeks of medical treatment, 21 patients (70%) achieved histological response. However, no difference in terms of EQA values between histological responders and non-responders, was shown (p=0.296). Moreover, no significant EQA changes occurred in non-responder patients, before and after treatment (p=0.878). In contrast, EQA significantly improved in histologically responder patients, before and after treatment (p=0.0113).

Conclusion: EQA is a valid, reliable disease-specific tool for the measurement of QoL in adult EoE Italian population. It can facilitate the assessment of therapeutic response and histological remission. Our data confirmed that therapy significantly improves QoL in EoE, mainly when histological remission is achieved. Developing multiple national-language versions of EQA is an important step in the standardization of research protocols and ambulatory management of this disease.

References: Taft TH, Kern E, Kwiatek MA, Hirano I, Gonsalves N, Keefer L. The adult eosinophilic oesophagitis quality of life questionnaire: a new measure of health-related quality of life. Aliment Pharmacol Ther. 2011 Oct;34(7):790-8. Lucendo AJ, Sánchez-Cazalilla M, Molina-Infante J, Pérez-Martínez I, Tenías JM, Barrio J, Nantes Ó, Ciriza-de-los-Ríos C, Perelló A, Arias Á. Transcultural adaptation and validation of the "Adult Eosinophilic Esophagitis Quality of Life Questionnaire" into Spanish. Rev Esp Enferm Dig. 2014 Jun;106(6):386-94.

Disclosure: Nothing to disclose

P0584 USEFULNESS OF REAL-TIME MEASURE OF GASTRIC PH AND STANDARD CLINICAL PARAMETERS TO PREDICT PERSISTENT ACID REFLUX IN A PATIENT TREATED WITH PROTON-PUMP INHIBITORS FOR GASTROESOPHAGEAL REFLUX DISEASE

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Introduction: Gastroesophageal reflux disease (GERD) is the second commonest GI outpatient diagnosis in the US and has a prevalence reaching up to 30% in many western countries. Proton-pump inhibitors (PPIs) are the mainstay of GERD treatment, however, up to one-third of patients have a poor symptomatic response. PH-impedance is the gold standard to assess whether this is due to persistent acid reflux, however, this test is inconvenient for patients and requires two hospital visits with significant indirect costs. PPIs suppress the acid production in the stomach, hence, gastric acidity might provide important information on pharmacological response to PPIs. EndoFaster is a novel endoscopic adjunct device that uses the gastric juice suctioned during endoscopy to provide a real-time measure of the gastric pH.

Aims & Methods: We aimed to assess whether clinical parameters, including real-time gastric pH measure with EndoFaster device, could be useful in predicting persistent acid reflux during PPI therapy and stratify patients for further testing. We prospectively recruited patients with GERD on PPIs that underwent gastroscopy as either initial investigation or surveillance for Barrett's esophagus. All patients filled out a dedicated symptom questionnaire (RDQ) and received their clinically indicated endoscopy with gastric pH analysis by EndoFaster, immediately followed by ambulatory 24-hour pH-impedance. We used a modified cut-off of 1.3% for pathological esophageal acid exposure time (AET). Multiple linear regression models were used to analyze the correlation between AET and predictive variables. The accuracy of gastric pH in predicting persistent acid reflux was calculated.

Results: We recruited 122 patients, of which 91 (74.6%) were included in the final analysis [46 male (50.5%), median age 53 years (IQR: 41-65)]. Forty-one patients (45.1%) had persistent acid reflux (AET≥1.3%) and were classified as PPI non-responders, and 50 had AET < 1.3% (PPI responders). Median AETs were 2.4 (IQR 1.2-4.9) and 0.1 (IQR 0.0-0.2), respectively (P<.001).

There was no difference in age, gender, BMI, PPI-regimen, presence of hiatus hernia and BE, and severity of symptoms between groups. Gastric pH was significantly lower in non-responders as compared to responders [6.2 (±1.6) vs. 5.3 (±2.2), P=.037)] with a mean difference in pH of 0.9 (95%CI 0.06 - 1.73).

Single-point gastric pH significantly correlated with AET (P=.042; R^2=11.0%). A pH cut-off of 5.05 had the best diagnostic accuracy in predicting persistent acid reflux on PPIs with a sensitivity and specificity of 39.5% and 85.4%, respectively.

Conclusion: Symptoms and clinical characteristics are not useful to predict persistent acid reflux in GERD patients on PPIs. One-point gastric pH is significantly lower in PPI non-responders as compared to responders, and correlates with 24-hour esophageal AET. Endofaster, in association with systematic symptoms assessment, could be used to triage patients for pH-impedance test and should be evaluated in larger trials.

Disclosure: Nothing to disclose

P0585 WITHDRAWN

P0586 WITHDRAWN

P0587 GASTROESOPHAGEAL REFLUX DISEASE AND PAROXYSMAL NON-VALVULAR ATRIAL FIBRILLATION - A CASE-CONTROL STUDY

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Introduction: There is still a controversy regarding the relationship between gastroesophageal reflux disease (GERD) and paroxysmal non-valvular atrial fibrillation (AF). Having the same predisposing factors as well as the adjacent anatomical positioning and nerve innervations between esophagus and atria can explain this relationship. The aim of this study was to evaluate the association between GERD and AF.

Aims & Methods: A prospective case-control study was conducted at a tertiary care centre from North-East of Romania over a period of 13 months (July 1, 2014 - July 31 2015). We included 135 patients divided in four groups: patients with GERD and paroxysmal non-valvular AF (GERD+AF group), patients with GERD and sinus rhythm (GERD+non-AF group), patients with AF and non-GERD (AF+non-GERD group) and patients without GERD and AF (non-GERD+non-AF group). All patients underwent upper endoscopy, echocardiography, 24-hour electrocardiographic Holter monitoring and lab tests.

Results: The 135 patients were divided as follow: 36 GERD+AF patients, 25 GERD+non-AF patients, 39 AF+non-GERD patients and 35 non-GERD+non-AF patients. All groups were homogenous regarding sex distribution and age. Esophagitis increased the relative risk of the association of AF and GERD by 2.5 times (p< 0.005). Heart rate variability in terms of time-domain parameter (SDNN) was lower in GERD+AF group patients than the other three groups (69.60 vs 109.33 vs 123.56 vs 12.1, p< 0.005). Regarding cardiac ultrasound parameters, median value of left atrial area in the group with GERD and AF patients was statistically higher comparatively with GERD+non-AF group (25.79±5.13 cm² vs 23.88±5.10 cm², p< 0.005). Hypertriglyceridemia was statistically significantly higher in GERD+AF group than in the other groups (p=0.005).

Conclusion: These results suggest the association of GERD and AF, which is sustained by both the theory of inflammation and of the autonomic nervous system imbalance.

Disclosure: Nothing to disclose

P0588 THE ROLE OF ESOPHAGEAL HIGH-RESOLUTION MANOMETRY IN APPROACH OF GASTROESOPHAGEAL REFLUX DISEASE

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Introduction: Recent studies have demonstrated the important role of high-resolution manometry (HRM) in assessment of patients with gastroesophageal reflux disease (GERD) and it is now formally recommended by The Lyon Consensus.

Aims & Methods: We intended to relate the findings in HRM with those of 24h pHmetry in patients with GERD.

Retrospective study, with inclusion of patients who were referred to perform 24h pHmetry and submitted to HRM, in a tertiary referral center, between March 2018 and July 2019. Chicago Classification v3.0 and The Lyon Consensus were used for the interpretation of data from the procedures.

Results: A total of 49 patients were included, 53% females, with a mean age of 50±14 years.

In pHmetry assessment, 38% of patients had findings compatible with GERD and 9% with reflux hypersensivity. Among the referenced patients, 71% presented changes in HRM: 38% esophagogastric junction obstruction (EGJ), 15% hypotonicity of the LES and 5% ineffective esophageal motility (IEM). The presence of IEM was associated with an abnormal pHmetry (p=0.040) as well as with the positive symptom association probability (SAP). The median acid exposure times (AET) was 0.7% (IQR 0.2-5.5%)

and the median DeMeester score (DmS) was 3.8 (IQR 1.2-10). HRM was performed after a median time of 5 years (IQR 2-8) after the symptoms' onset. The most prevalent symptom was the heartburn (67%) but regurgitation and chronic cough were those more often associated with reflux in the pHmetry (p=0.002 and p=0.014, respectively). In 75% of cases there was a previous therapeutic trial with proton pump inhibitor, mostly without clinical improvement (57%); this fact was related with a LES hypotonicity in HRM (p=0.018). In 71% of patients, the HRM's findings had an impact in the subsequent patients' therapeutical strategy.

Conclusion: The routine performance of a manometric study in patients submitted to a pHmetry allows the identification of motor findings in approximately three-quarters of patients, facilitating the subsequent therapeutic approach.

Disclosure: Nothing to disclose

P0589 CLINICAL APPLICATION OF THE GASTROESOPHAGEAL REFLUX DISEASE QUESTIONNAIRE IN PATIENTS WITH SUSPECTED LARYNGOPHARYNGEAL REFLUX SYMPTOMS

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Introduction: Gastroesophageal reflux disease(GERD) is one of the most common esophageal diseases in Gastroenterology. Laryngopharyngeal reflux(LPR) is different clinical symptoms that occur simultaneously with GERD.

Aims & Methods: To evaluate the usefulness of Gastroesophageal Reflux Disease Questionnaire (GerdQ) in patients with suspected laryngopharyngeal reflux (LPR) symptoms (globus, cough, hoarseness and throat pain)
A total of 111 patients with suspected LPR symptoms were incorporated from either
otorhinolaryngology or gastroenterology clinic. Patient's laryngoscopic findings were graded by reflux finding score (RFS, n = 98), and RFS ≥ 7 was considered as positive LPR. Patient's LPR symptoms were evaluated using reflux symptom index (RSI). Erosive esophagitis by endoscopy (n = 111) or abnormal results on 24-hr multichannel intraluminal impedance-pH (MII-pH) testing (n = 111) were used as diagnostic references for gastroesophageal reflux disease (GERD). Esophageal motor function
was evaluated using high resolution esophageal manometry (HREM, n = 111); distal contractile integral (DCI) < 450mmHg•cm•s or fragmented peristalsis (defect > 5cm) or absent peristalsis was considered as esophageal hypomotility.

Results: Ninety-one of 98 (92.9 %) subjects were diagnosed as LPR but only 17 of 111 (15.3 %) had GERD. For GerdQ, the cutoff value of 9 showed the highest area under curve (AUC) by receiver operating curve (ROC) analysis (AUC = 0.616); the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were 52.9 %, 70.2 %, 24.3 % and 89.2 %, respectively. For RSI, the cutoff value of 13 showed the highest diagnostic yield (AUC = 0.654); the sensitivity, specificity, PPV and NPV were 75.3 %, 40.0 %, 95.9 % and 8.0 %, respectively. In patients with GERD (n = 17), both distal and proximal baseline impedance levels (3 cm and 15 cm above esophagogastric junction, respectively) were decreased (p < 0.05) and proximal extent of reflux were increased (p < 0.001). However, there was no difference in esophageal body motor function between patients with or without GERD (p >0.05).

Conclusion: GERD is infrequent among patients with suspected LPR symptoms. In this population, the sensitivity of GerdQ is low thus GerdQ has a limited role in GERD diagnosis.

Disclosure: Nothing to disclose

P0590 MNBI IS A BETTER MARKER OF OESOPHAGEAL DISEASE SEVERITY COMPARED TO USING TOTAL ACID REFLUX

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Introduction: The Lyon Consensus 2018 describes mean nocturnal baseline impedance (MNBI) as a possible measure of oesophageal mucosa permeability, with lower values associated with damage; however MNBI has not yet entered routine clinical practice. This study aims to determine the relationship of MNBI across three common presentations of reflux; Barrett's oesophagus, NERD and functional heartburn (FH).

Aims & Methods: Standard pH-Impedance measurements as well as symptom index (SI) were acquired for all patients. The impedance channel at 3cm was used to calculate MNBI by averaging 3 nocturnal 10 minute intervals 1hr apart. Consecutive tracings between 2014 and 2016 for 3 reflux subgroups were analysed; 22 Barrett's Oesophagus (13 on proton pump inhibitors; PPI), 26 NERD and 26 FH. Results are presented as median (IQR; interquartile ratio). Comparisons were made using Kruskall-Wallace test and Mann-Whitney U test as appropriate. Correlations were performed using Spearman's correlation coefficient.

Results: There was no significant difference in total reflux (TR) between patients with Barrett's (median TR 11.2%(2.5%,18.7%) and NERD (8.1%(5.5%,12.9%) (p=0.497). The difference with FH (TR 22%(12%,34%) is defined by the entry criteria (p< 0.0001). SI was significantly lower in Barrett's (SI 4%(0%,25.6%) than NERD (30%(0%,45.2%) (p=0.48), but not FH (0%(0%,7.9%) (p=0.129).

There was no statistically significant difference in MNBI between Barrett's while on or off PPIs (p=0.556). There was also no difference in MNBI between 9 patients with persistent Barrett's who had attempts at ablation therapy compared to the 13 who had not (p=0.96). Using the Kruskall-Wallace test, there was a significant difference observed in MNBI between all 3 categories of reflux (p< 0.0001). Specifically, there was a difference in patients with Barrett's (median MNBI 429.5Ω(293Ω,950Ω) compared to NERD (1160Ω(964.5Ω,2764Ω) (p=0.003) and FH (3355Ω(2866.5Ω,3809.25Ω) (p< 0.0001). There was also a significant difference in patients with NERD compared to FH (p< 0.0001).

There was a moderately inverse correlation between Barrett's segment length (median 6cm(3cm,10cm) and MNBI (r = -0.436; p=0.038).

Conclusion: In keeping with the published literature, this study shows that severity of reflux disease, as measured by ambulatory pH-impedance monitoring, was not dissimilar between Barrett's oesophagus and NERD, while symptom burden was greater in NERD. On the other hand, MNBI can differentiate between the disease states despite the reduced symptom burden. Also, it correlates with the degree of mucosal damage associated with Barrett's regardless of PPI use or previous therapy. MNBI may be a better marker of reflux disease severity than standard pH measurements.

Disclosure: Nothing to disclose

P0591 A RE-ASSESSMENT OF UPPER ABDOMINAL SYMPTOMS BASED ON 24-HOUR PH TESTING

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Introduction: Differentiating functional dyspepsia (FD) from gastroesophageal reflux disease (GERD) by symptoms continues to remain a challenge. It has been thought that symptoms including upper abdominal pain, nausea, bloating correlates more with a diagnosis of functional dyspepsia whereas burning chest pain after eating and worse with lying down is thought to be more related to GERD. We analyzed the relationship of symptoms to 24 pH measurements to help better differentiate between FD and GERD based on symptoms.

Aims & Methods: We performed a prospective study at one center involving 124 patients who have been experiencing various types of upper GI symptoms from 2015-2018. A survey was given to each patient to record

whether they had what was thought to be symptoms of GERD (burning, upward abdominal pain, ascending chest pain, awakened by symptoms) vs. symptoms of FD (intermittent, non-radiating upper abdominal pain, nausea, vomiting, bloating). Each patient then had a Bravo 24-hour pH study and De Meester scores were recorded to serve as the gold standard. Univariate analyses, including chi square and Fisher exact test, and multivariate logistic regression was done.

Results: There was a total of 124 patients, 80 women and 44 men, with a mean age of 52.97 years were recruited. There were 113 Caucasians, 7 Hispanics, 3 Asian Americans, and 1 African American. Mean BMI was 30.73. Mean De Meester score was 31.71. Most symptoms were found to be not clinically significant for evaluation of GERD vs. FD, apart from radiating upward pain as a negative predictor of true GERD (p=0.006) and intermittent nature of pain as a positive predictor of true GERD (p=0.001). From here, an equation was formulated incorporating this data: (Ascending pain * -1.51) + (Intermittent pain * 1.89) and a ROC curve was developed (graph 1) with ROC area of 0.76 with sensitivities and specificities listed in table 1.

Cutpoints on ROC curve	Sensitivity (%)	Specificity (%)	Correctly Classified (%)	Positive Likelihood Ratio	Negative Likelihood Ratio
≥-1.51	100	0	18.26	1	
≥0	85.71	32.98	42.61	1.2789	0.4322
≥.38	76.19	61.7	64.35	1.9894	0.3859
≥1.89	57.14	91.49	85.22	6.7143	0.4684
>1.89	0	100	81.74		1

[Table 1: Sensitivities and specificities of GERDYS equation]

Conclusion: This study revealed that most "classic" symptoms of GERD and FD cannot truly differentiate between the two. Using our GERDYS equation as above can help support one diagnosis vs. the other with the understanding that overlap of these conditions occurs. This also demonstrates the necessity of performing pH studies on any patient presenting with symptoms that could be concerning for either or concurrent disease processes. The importance of differentiating the two lies in the differing treatment of each disorder. Ultimately, this study acts as a stepping stone in better differentiating GERD from FD and in the future will help promote a decrease in the inappropriate use of proton pump inhibitors in the community and improve patient care as well as reduce costs.

Disclosure: Nothing to disclose

P0592 NOVEL MII-PH PARAMETERS ARE ABLE TO DISTINGUISH PATIENTS WITH GERD AMONG SUBJECT WITH EXTRA-ESOPHAGEAL SYMPTOMS PRESENTATION

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Introduction: The novel metrics from pH-impedance monitoring, postreflux swallow-induced peristaltic wave (PSPW) index and the mean nocturnal baseline impedance (MNBI) appear particularly useful for the diagnosis of gastroesophageal reflux disease (GERD). The threshold values for PSPW index and MNBI are 61% and 2292 Ω respectively.

Aims & Methods: We aimed to evaluate the power of PSPW index and MNBI to predict PPI response in patients with extra-esophageal syndrome. We enrolled 44 consecutive patients (M/F 19/25, mean age 48.8±14.3 yrs, BMI 24.7±5.6). The predominant symptoms were hoarseness (76.1%), globus (73.9%) chronic cough (63%), sore throat (60.9%), throat discomfort (43.3%) and heartburn (38.6%). They underwent EGD according to Los Angeles classification. Off-medication pH-impedance was performed.

Results: According with the pH-impedance results GERD was confirmed in 17 out of 44 pts (group GERD) and 27 subjects resulted negative for reflux (group No-GERD). Upper endoscopy showed erosive esophagitis in 7 out 44 pts (15.9%). Acid refluxes were significantly higher in group

GERD (26.8±19) than in group No-GERD (10.4±8.3) (p=0.0003). Weakly acid refluxes didn't differ between the two group (group GERD 14.4±12.8 vs. group No-GERD 9.6±6, p=0.099). PSPW index and MNBI had shown a significantly lower value in group GERD (MNBI 1660.6±489 Ω; PSPW index 36±16.8%) than in group No-GERD (3222±671.2 Ω; PSPW index 73.4±11.8%) (p < 0.0001).

PPI response was higher in group GERD than in group No-GERD for both heartburn (10/17 group GERD vs 1/27 group No-GERD) and extra-esophageal symptoms (11/17 group GERD vs 1/27 group No-GERD) (p< 0.0001). Patients with a positive response to PPI, regardless of group which they belonged, had lower MNBI and PSPW index values (MNBI p=0.003; PSPW index p=0.003).

Conclusion: The evaluation of PSPW index and MNBI showed statistically significant differences between GERD and No-GERD patients and between PPI responders and PPI non-responders. MNBI and PSPW index are the best parameters to identify patients with GERD and the response to PPI therapy, underlying the importance of evaluation in clinical setting of patients with GERD.

Disclosure: Nothing to disclose

P0593 VIRTUAL BIOPSY BY IMPEDANCESPECTROSCOPY IN BARRETT'S ADENOCARCINOMA

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Introduction: Early detection of adenocarcinoma in the esophagus is essential for curative treatment. Targeted and random biopsies are the standard in diagnostic gastroscopy. This approach is time consuming and results are depending on endoscopists experience.

Aims & Methods: The aim of the study was to investigate the diagnostic value of impedancespectroscopy in Barrett's esophagus. We developed a pencil probe with eight golden electrodes for impedance measurement from 100 Hz to 1MHz. Immediately after endoscopic resection of esophageal neoplasia in Barrett's esophagus, the specimen was pinned on cork. Subsequently the tissue was measured in 10 different electrode combinations and after that ink- marked for further pathological assessment.

Results: From February 2017 to February 2018, 47 patients (45♂ ,2♀) with 87 measurements were included. The mean age of patients was 66y (min 48y to max 91y). Measurement from 58khz to 119kHz showed significant (p< 0.005) difference in impedance to distinguish between Barrett's mucosa and high-grade intraepithelial neoplasia / adenocarcinoma. A cut-off value of > 291 Ω (at a frequency of 58kHz) showed a sensitivity of 81% by ROC-analysis. However, the specificity remains low at 41%.

Conclusion: Impedancespectroscopy has the potential as a screening tool for Barrett's neoplasia. Further development for an in-vivo model are necessary to proof this novel diagnostic tool.

Disclosure: Nothing to disclose

P0594 ANALYSIS OF SELECTED BILE ACIDS IN SALIVA BY HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY-MASS SPECTROMETRY AS A POTENTIAL NEW NON-INVASIVE DIAGNOSTIC METHOD FOR BARRETT'S ESOPHAGUS

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Introduction: Barrett's esophagus (BE) is defined as the replacement of squamous epithelium in the distal esophagus with metaplastic intestinal columnar epithelium and develops because of chronic inflammation resulting from gastroesophageal reflux disease. BE is associated with an increased risk of developing esophageal adenocarcinoma (EAC). Experimental, clinical and immunohistochemical studies show that one of the

factors in the pathogenesis of esophageal injury, BE and EAC is duodenal reflux and the associated synergistic damage to the esophagus by bile acid (BA) and gastric acid reflux. Oxidative stress secondary to bile acids (BAs) exposure has been associated with metaplastic degeneration of normal esophageal mucosa into BE cells and eventually EAC.

At the current time, a diagnosis of Barrett's esophagus can only be made using endoscopy and detecting a change in the lining of the esophagus. The definitive diagnosis of Barrett's esophagus requires biopsy confirmation of the change in the lining of the esophagus.

The Prague classification system is universally accepted standardized endoscopic grading system for BE and uses the "C" value as the "circumferential extent" and the "M" value as "maximal extent" of BE above the gastroesophageal junction in centimeters for endoscopic standardization of BE lengths.

Aims & Methods: We studied the content of selected BAs in saliva samples in a cohort of 15 patients with endoscopically and histologically proven BE (Prague Classification C: 1-10, M: 2-13) and a control group consisting of 10 subjects without known medical history or treatment for GERD or BE at least in the last 5 years. Concentration of major salivary BAs (glycocholic acid, glycodeoxycholic acid, and glycochenodeoxycholic acid) in saliva were analyzed using high-performance liquid chromatography-mass spectrometry (HPLC-MS) detection.

Saliva samples were collected from healthy individuals and patients with BE during the day, but all subjects were asked not to eat, drink nor brush their teeth at least 3 hours before sampling. Afterwards were samples stored at -80 °C.

Before the measurement saliva samples were let to thaw at room temperature. After that 900 µl of MeOH was added to 300 µl of saliva sample for protein precipitation. This mixture was vortexed, sonicated and centrifugated and 1 mL of the supernatant was transferred to a new vial. Supernatant was dried under stream of nitrogen. Dried sample was re-dissolved in 300 µl of 80% MeOH, vortexed, sonicated and the supernatant was analyzed by HPLC-MS. The analysis was completed under 4 minutes.

Results: We compared the concentrations of selected BAs in both groups of patients, and we found significantly increased concentrations of glycochenodeoxycholic acid (p < 0.01) in the group of patients with BE. Significantly better statistical differentiation of samples was observed by using principal component analysis, especially in patients with high C and M values of BE length by Prague classification.

Conclusion: Analysis of selected bile acids in saliva by HPLC-MS appears to be a potential new non-invasive diagnostic method for detection of Barrett's esophagus and for estimation of its severity. HPLC-MS is a highly sensitive method to measure low amounts of bile acids in human saliva. The analysis is fast, but the sample preparation is more complicated. Further refinement of this new diagnostic method is needed.

P0595 BARRETT'S ESOPHAGUS AND COMPLICATIONS PREVALENCE: TWENTY YEARS OBSERVATIONAL RETROSPECTIVE STUDY IN A GENERAL POPULATION

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Introduction: Barrett's esophagus (BE) is defined as the presence of columnar metaplasia in the lining of the distal esophagus instead of squamous epithelium. This condition represents a factor that predispose to esophageal adenocarcinoma,neoplasia significantly incremented in the last decade. BE, a know precursor,has a high prevalence but only few patients with this condition progress to malignancy. Surveillance and screening programs are controversial and lack proven efficacy.

Aims & Methods: The aim of this retrospective analysis was to establish the prevalence of BE and related complications (dysplasia and adenocarcinoma appearance) by reviews the database of consecutives patients presenting in our Endoscopy Unit from January 1997 to March 2019 for upper endoscopy.

We retrospectively assessed 148.000 the endoscopic reports of 63.994 outpatients seen in our Endoscopy Unit from January 1997 to March 2019, evaluating the prevalence of BE and analyzed the demographic (sex,age) and endoscopic findings (BE extension).Collaterally we evaluate in BE

population the presence of hiatal hernia and Hp infection. In 1428 cases the endoscopist described the presence at the distal esophagus of columnar epithelium (suspected BE) and in this group the pathologist confirmed in 690 the presence of BE (defined histologically as replacement of the normal squamous epitelium of the distal esophagus by columnar epitelium containig intestinal metaplasma). The presence of short Barrett (< 1cm) it was not considered in the analysis,because the risk of progression to high grade dysplasia or esophageal adenocarcinoma seem very low in this subset of patients.

Results: The Database analysis shows that the prevalence of Barrett's esophagus in our endoscopic population in the last twenty years was 1,07% .The mean age of patients with Barrett's esophagus at the diagnosis was 57 year (range 17-96 yr) and the male sex was prevalent (435 vs 256). The extension of columnar epithelium,measured in accord to Prague Classification (M Prague score) (Pearson's correlation coefficient for the relationship r=-0,0007) and the presence of hiatal hernia (r=0,013) weren't independently associated with Barrett's esophagus. The prevalence of Hp infection in patients with BE was 14,2%.

In all cases with progression to malignancy, the extension of metaplastic epithelium was >3 cm (long BE).

Conclusion: In our population the overall prevalence of BE was 1,07 % with predominance of male sex,middle age and gastroesophageal reflux symptoms as suggested by the high prevalence of hiatal hernia. Our data confirmed also that the appearance of dysplasia or adenocarcinoma is related to BE extension,regarding only the cases of long Barrett. This suggest that in the next years the surveillance programs,also in terms of cost-effectiveness,will be to differentiate and ask in this direction.

Disclosure: Nothing to disclose

P0596 EXPRESSION PROFILE IN BARRETT'S ESOPHAGUS (BE) OBSERVED IN HUMANS, SURGICAL ANIMAL AND IN VITRO MODEL INVOLVING HUMAN-DERIVED ESOPHAGEAL CELL LINES. MOLECULAR MARKERS SELECTION CHARACTERISTIC FOR CLINICAL BE AND REFLECTED IN EXPERIMENTAL MODELS FOR FURTHER TRANSLATIONAL PHARMACOLOGICAL STUDIES

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Introduction: Barrett's esophagus (BE) is a premalignant condition of esophageal epithelium caused by gastroesophageal reflux disease (GERD). Thus, several in vivo animal and in vitro models of GERD and BE were developed. However, clinical relevance of each of them implemented separately was considered to be questionable.

Aims & Methods: Therefore, we aimed to select appropriate translational molecular expression markers comparing particular genes expression profile observed in clinical biopsies derived from BE patients, animal surgical model and in vitro model of GERD involving human derived esophageal cell lines, optimizing this in vitro model to reflect as much as possible these molecular alterations observed clinically.

Gene Expression Omnibus 2R (GEO2R) tool and GSE34619, GSE1420, GSE13083 database were used to select up/downregulated genes in human BE: KRT1, KRT4, KRT5, KRT7, KRT8, KRT14, KRT15, KRT18, KRT19, KRT20, MUC2, MUC5ac, MUC6, MUC3, TFF1, TFF2, TFF3, VILL1. 2. Male Wistar rats underwent microsurgical procedure to generate duodenoesophageal anastomosis leading to the development of metaplasia after 12 weeks in 70% of animals.

Esophageal biopsies were collected to assess mRNA expression for abovementioned genes using TaqMan probes and real-time PCR only in samples with confirmed microscopically metaplasia development. We also determined whether Barrett's esophagus (BE) - specific mRNAs are regulated in squamous esophageal epithelial (HET-1A) and esophageal keratinocytes (EPC2-hTERT) human cell lines after exposure to hydrochloric acid and bile mixture (BA). EPC2-hTERT and HET-1A cells were exposed for 30 minutes to the medium adjusted to a pH of 7.0 or 5.0 using HCl together with BA or separately mixture at increasing concentrations

(0-600 μM). Concentration range was determined by cell viability MTT assay (50% inhibitory concentration (IC50) = 1250 μM for pH 7.0; IC50 = 65 μM for pH 5.0). The BA mixture consisted of 25% deoxycholic acid, 45% glycocholic acid and 30% taurochenodeoxycholic acid. The treatment was implemented one time or repeated daily during one week. After the treatment period, the cells were harvested and RNA was isolated and mRNA expression for abovementioned genes was determined by real-time PCR using TaqMan probes.

Results: Changes in mRNA level were observed only for KRT genes in EPC2-hTERT cell line (up regulation of KRT7, KTR18 and KRT19; down-regulation of KRT4, KRT5, KRT14 and KRT15) in acidic medium with the BA concentrations close to IC50. In HET-1A cell line BA treatment slightly up-regulated MUC2, KRT8, KRT19 and down-regulated KRT15. Alterations in gene expressions in both investigated cell lines are consistent with gene expression profiles in human BE.

We conclude that in contrast with single treatment, one-week treatment with BA and HCl mixture in concentrations close to IC50 is able to induce BE specific factors in EPC2-hTERT cell line. In animal model of BE, KRT-4, KRT-8, KRT-15, KRT-18, KRT-20, MUC-2, MUC-6, MUC-13, TFF-2, VILL-1 mRNA expressions were modulated in the manner observed in human BE.

Conclusion: We conclude that one week of daily treatment of EPC-2 or HET-1A cells with 100 uM of BA in pH= 5.0 reflects the most efficiently molecular profile of human BE. Moreover, we conclude that animal model of GERD (12 weeks) modulates expression profile reflecting in about 80% these alterations observed in human BE. We assume that combination of these two experimental BE models is relevant to be implemented in further pharmacological studies testing possible novel therapeutic targets of this disorder.

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P0597 ALCOHOL AND SMOKING INFLUENCE IONTRANSPORTER MECHANISMS OF GUINEA PIG ESOPHAGEAL EPITHELIAL CELLS, CP-D DYSPLASTIC BARRETT'S CELL LINE AND OE-33 ADENOCARCINOMA CELL LINE

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Introduction: Several clinical studies indicate that alcohol and smoking predispose the consumers to esophageal inflammatory and malignant diseases, but the cellular mechanism is not completely clear. Iontransporters play an important protective role in the esophageal epithelial cells (EECs), however the effect of ethanol (EtOH) and smoking on them is not known. Our aim in this study was to examine the effect of EtOH and smoking on the esophageal epithelial iontransport mechanisms.

Aims & Methods: EECs were isolated from guinea pig after an enzymatic digestion. Changes in pH_i were measured using a fluorescent dye, BCECF-AM. For the determination of the starting pH the high-K^+/nigericin method was used. Total buffering capacity of EECs was measured by the NH_4 pulse technique. The effect of EtOH (0.1, 1 and 10% vol) and cigarette smoke extract (CSE) (1, 10, 100 μg/ml) on Na^+/H^+ exchanger (NHE) activity was estimated by the NH_4Cl pulse technique. CP-D and OE-33 cells were treated with various concentrations of EtOH and CSE for 6 and 24 hours. Total mRNA was isolated and transcripted to cDNA. mRNA expression of NHE1 was detected using qPCR.

Results: We have improved an EEC isolation technique which allows the functional characterization of these cells. The resting pH of the EEC preparation was 7.59±0.011. EtOH dose-dependently decreased the pH_i of both guinea pig EECs and OE33 cells and also the activity of NHE. 1-hour incubation with CSE increased the NHE activity in EECs, but decreased it in CP-D cells. 6-hour incubation of OE33 cells with CSE and EtOH increased, whereas 24-hour incubation with these agents decreased the mRNA expression of NHE. Interestingly, combination of EtOH and CSE induced the most robust effect in the expression of NHE. In CP-D cells, alteration of NHE1 expression was not significant.

Conclusion: We optimized an EEC isolation technique by which the ion-transporter activity of EECs can be investigated. Our results have shown that alcohol induces acidosis and significantly impairs NHE function thus decreases the defensive mechanisms. As a result of CSE incubation, NHE

activity rises, which can be a compensatory reaction for this toxic agent. In order to estimate the importance of these results in the pathology of inflammatory esophageal diseases further investigations are needed.

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P0598 L-TRYPTOPHAN, AN ESSENTIAL AMINO ACID AND PRECURSOR OF MELATONIN, ATTENUATES THE ESOPHAGEAL DAMAGE IN EXPERIMENTAL RAT MODEL OF BARRETT'S ESOPHAGUS. ROLE OF PINEAL GLAND AND ESOPHAGEAL BLOOD FLOW

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Introduction: Barrett's esophagus may develop after an irritation in the lining of the esophagus caused by chronic gastrointestinal reflux into the esophagus. The long exposure to mixed reflux of the gastroduodenal contents can predispose to chronic esophagitis and premalignant Barrett's esophagus. Histamine H_2-receptor antagonists and proton pump inhibitors (PPI) are effective against esophageal reflux but efficacy of L-tryptophan, an essential amino acid considered as melatonin precursor from pineal gland in experimental rat model of Barrett's esophagus has not been fully clarified.

Aims & Methods: We determined whether the treatment with L-tryptophan which is considered as the precursor of melatonin, can reduce the mucosal damage induced by chronic reflux esophagitis progressing into Barrett's esophagus in rat model which resembles human Barrett's esophagus. Eighty rats prepared with esophagogastroduodenal anastomosis (EGDA) with or without pinealectomy (removal of pineal gland) resulting in chronic esophagitis were randomly divided into 4 groups treated i.g. daily either with: 1) vehicle 2) L-tryptophan (200 mg/kg-d i.g.) or melatonin (20 mg/kg-d i.g.) applied alone or combined with luzindole, the antagonist of Mel1 receptor, 3) PPI pantoprazole (10 mg/kg-d) or H_2-receptor antagonist, ranitidine (30 mg/kg-d). At 4 months, the macroscopic and microscopic lesion score, the esophageal blood flow (EBF) was determined by H_2-gas clearance method, and plasma levels (ELISA) of TNF-α and IL-1β and , and mucosal expression of COX-2, EGF and EGFR mRNA was evaluated by RT-PCR.

Results: Macroscopic and microscopic chronic esophagitis was developed in all EGDA animals followed by a decrease in the EBF and the significant rise in the plasma TNF-α and IL-1β levels. Extensive esophageal ulcerations with development of columnar epithelium and formation of mucus glands in squamous epithelium, intestinal metaplasia distant to anastomosis were observed. Pinealectomy, which blunted the plasma melatonin levels, aggravated the damage score and significantly decreased EBF compared with vehicle-control animals. Treatment with L-tryptophan or melatonin significantly reduced the LI by 45% and 39%, respectively, while causing a significant rise in the EBF.

These beneficial effects of melatonin and L-tryptophan were significantly abrogated by co-treatment with luzindole. The expression of COX-2, EGF and EGFR mRNAs were absent in the esophageal mucosa of sham-control animals but strongly upregulated in metaplastic Barrett's epithelium and this effect was significantly decreased by treatment with L-tryptophan, melatonin, or standard antisecretory agents pantoprazole or ranitidine. Concurrent treatment with the COX-2 inhibitor celecoxib significantly reduced the L-tryptophan and melatonin-induced damage to esophageal mucosa in EGDA rats.

Conclusion: The development of chronic reflux esophagitis in experimental rat model of esophageal injury resembling Barrett's esophagus in humans is associated with severe morphology changes, an impairment of EBF due to excessive release of TNF-α, IL-1β and PGE_2 overexpression of COX-2, EGF and its receptor, 2) treatment with L-tryptophan or melatonin acting on Mel2 receptors exert beneficial effect in Barrett's esophagus *via* the suppression of the release of TNF-α and IL-1β and attenuation of mRNA ex-

pression of COX-2, EGF, and its receptor in esophageal mucosa, and 3) acid suppressive drugs such as pantoprazole, could be useful as the therapeutic option in the treatment of Barrett's esophagus.
Disclosure: Nothing to disclose

P0599 MUCOSAL SIGNATURE OF ESOPHAGEAL MICROBIOTA IN PATIENTS WITH BARRETT'S ESOPHAGUS AND ESOPHAGEAL ADENOCARCINOMA

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Introduction: Improved diagnostic tools to dissect the risk factors that drive the transition from normal epithelium to Barrett's Esophagus (BE) and Esophageal Adenocarcinoma (EAC) represent a clear need for new therapeutic alternatives. Gut microbiota exerts a crucial role in health, as well as in several gastrointestinal diseases and in various types of cancers.
Aims & Methods: The aim of our study was to characterize esophageal microbiota composition and the microbiota-related functional predictions in patients with BE and EAC. A total of 26 patients was enrolled on the base of specific including and excluding criteria: 10 without any endoscopic sign of pathological mucosa at the gastroscopy, as control group (1:1 ratio according to PPI use); 10 with a new diagnosis of BE (1:1 ratio according to PPI use); and 6 with a new diagnosis of distal esophageal/esophagogastric junction cancer, confirmed histologically. Genomic DNA was extracted from distal esophagus biopsies obtained during gastroscopy and V3-V4 regions of the 16S rRNA gene were sequenced by MiSeq Illumina platform. In patients with BE, biopsies were obtained from both the esophageal metaplastic lesion (BEM) and the normal esophageal mucosa (BEU).
Results: BE and EAC patients showed a higher level of biodiversity. BEU samples showed significant higher values of α-diversity when compared with control patients, while BEM shared similar values with EAC, being lower than BEU and higher than control patients. A substantial divergence on the first axis was registered for unweighted Unifrac with control patients significantly separated from BEU and EAC. A lower level of Firmicutes and a significantly higher percentage of Bacteroidetes in BEU and EAC compared with control subjects was assessed. BEU and BEM exhibited a significantly higher presence of Fusobacteria compared with controls. Streptococcus relative abundance showed a progressive significant reduction in the disease spectrum from controls to EAC. Veillonella exhibited a gradual abundance increase in this spectrum. Porphyromonas and Prevotella resulted consistently higher in BEU, and in both BEU and EAC, respectively, compared with controls. Actinobacillus was significantly higher in both BEU and BEM compared with controls and EAC. Fusobacterium and Leptotrichia levels were consistently increased in BEU and in both BEU and BEM, respectively, when compared with controls. Patients with EAC showed significantly upregulated microbial genes related to energy metabolism, metabolism of cofactors and vitamins, cellular processes and signaling, while immunologic system disease and apoptosis pathways were consistently down-regulated compared with controls. Microbiota associated to BEM was characterized by a high potential for replication and repair, genetic information processing, metabolism of cofactors and vitamins, energy metabolism, amino acids, nucleotides, lipids and gly-

can metabolisms compared with controls. When compared EAC and BEM samples, EAC-associated microbiota showed a significantly increased aminoacid and energy metabolism with a decreased apoptosis pathway compared with BEM group.
Conclusion: Overall, these data describe a specific microbial signature for both BE and EAC with a consequent functional impact on esophageal mucosa metabolism and open new horizons towards the identification of potential risk factors and innovative diagnostic/therapeutic tools.
Disclosure: Nothing to disclose

P0600 QUANTIFICATION OF MICROVASCULAR CHANGE FOR DIAGNOSING EARLY DIGESTIVE SQUAMOUS CELL CARCINOMA BY OPTICAL COHERENCE TOMOGRAPHY

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Introduction: Early diagnosis of squamous cell carcinoma (SCC) in digestive tract including oral, pharynx to esophagus is difficult under current imaging tool. Microvascular change, like intrapapillary capillary loop (IPCL) observed by magnifying endoscope with narrow band imaging (NBI), is the most important key to differentiate benign and early malignant lesion of these area. However, the operation of the scope is sometimes difficult and limited by anatomy, especially in oral cavity. The judgment of IPCL morphology is also subjective and needs learning curve. Optical coherence tomography (OCT) is a new optical imaging system with characteristics of non-contrast, non-contact, high resolution and 3D imaging. In our published study, the morphology of IPCL presented by the OCT angiography is similar to endoscopic imaging and can be a diagnostic marker for early SCC. In addition to the IPCL, OCT angiography can further image deeper submucosal vessels and quantify these microvascular changes. The aim of this pilot study is to quantify the microvacular change to diagnose the early SCC in mice model.
Aims & Methods: 12 weeks 4NQO induction was done to produce tongue SCC in mice model. The OCT imaging was performed every month after induction to observe different stage of carcinogenesis, including hyperplasia, dysplasia, carcinoma in situ to early SCC. The mice was sacrificed after OCT imaging and the induced lesion was sent for histology. The histological results were classified into three stages: normal (control mice), hyperplasia to low-grade dysplasia and high-grade dysplasia to early SCC. Three microvascular parameters of OCT angiography including density, diameter and tortuosity were analyzed and were compared between different stages
Results: Total seventeen lesions were analyzed. Among them, three lesions were normal, nine lesions were hyperplasia to low-grade dysplasia and five lesions were high-grade dysplasia to early SCC. It is easy to identify the tumor area on en-face microvascular mapping because change of microvascular pattern. After quantification, significant increased microvascular density (p< 0.05) and diameter (p< 0.01) is seen in high-grade dysplasia to early SCC than other stages. But the change of tortuosity is not significant between high grade-dysplasia to early SCC than hyperplasia to low-grade dysplasia.
Conclusion: Like morphology of IPCL, the change of microvascular density, diameter and tortuosity can be a marker to diagnose early SCC. This is a first study to mapping this microvascular change en-face and quantify it in diagnosing SCC. These "quantified and objective markers" may be an automatic tool for diagnosing SCC in the future.
Disclosure: Nothing to disclose

P0601 ESD FOR ESOPHAGEAL SQUAMOUS CELL CARCINOMA: A EUROPEAN TERTIARY CENTER PROSPECTIVELY COLLECTED EXPERIENCE

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Introduction: Endoscopic submucosal dissection (ESD) is a widely recognised treatment for superficial esophageal squamous cell carcinoma (SCC). However, reports from European centres on this endoscopic technique remain scarce and most of the available data still originates from Japanese series.

Aims & Methods: The aim of our study is to present the results and evaluate the efficacy and safety of ESD treatment for superficial oesophageal SCC in one European academic tertiary center.

We performed a single-center systematic prospectively collected registry, including all the patients with superficial oesophageal SCC treated by ESD from mars 2016 to november 2018. Our main outcomes were: R0 resection (defined as vertical and lateral margins clear from carcinoma or dysplasia), curative resection (an en-bloc R0 resection with histology no more advanced than pT1a m2 SCC, with no lymphovascular invasion and no poor differentiation, as defined by the European Society of Gastrointestinal Endoscopy), procedure-associated complications and locally or distant recurrence rate.

Results: We included twenty ESD independent procedures performed on nineteen patients (mean age 65 [41-83] year old, 55% men). Most of the lesions were located in the medium and distal esophagus (45%, respectively), with only 2 lesions (10%) located in the proximal region. The mean lesion size was 39 [15-100] mm and the mean procedure duration was 115 [30-180] min. 65% occupied more than 50% of esophageal circumference. En-bloc resection was achieved in 20 cases (100%) and R0 resection in 18 cases (90%), with 2 patients presenting focal positive horizontal margins. A 6 months follow-up available in both cases showed no endoscopic or pathologic signs of SCC suggesting a coagulation artefact on the specimen. Curative resection was accomplished in 9 cases (45%). The resection was non curative in 11 cases for the following reasons: 3 en-bloc R0 G1 pT1a m3 SCC, 6 deep submucosal (sm2) SCC with free vertical margins, and 2 due to positive lymphovascular infiltration.

One patient benefited from complementary radio-chemotherapy and one was submitted to complementary oesophagectomy (pT0N0). Other patients were followed endoscopically knowing their age or comorbidities, after multidisciplinary discussion.

The endoscopic follow-up (median 15 [1-29] months) was available for 13 of the 17 patients without adjuvant oncological therapy and disclosed that 12 (92.3%) patients had no signs of recurrence.

The only case with lymphatic recurrence appeared in a patient with non curative ESD and past history of lymph node metastatic pharyngeal SCC.

In 80% of the cases, there were no complications needing any intervention.

Despite steroid administration in 65% of cases for secondary strictures prevention (locally injected triamcinolone for >50% circumference resection or oral steroid for circumferential resections), 3 patients developed symptomatic strictures requiring endoscopic treatment.

One patient presented delayed post-ESD local hemorrhage, treated successfully by endoscopic hemostasis.

Conclusion: Our preliminary data confirm the safety and technical quality of esophageal ESD for SCC in a tertiary European center. The complexity to predict the oncological stage opens the room for staging ESD with the major limit being the risk of secondary stricture. Further work must be done by multicentric studies to better stratify the place of adjuvant oncologic treatment.

Disclosure: Nothing to disclose

P0602 MULTIPLE PRIMARY TUMORS IN PATIENTS WITH ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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Introduction: Patients with primary esophageal squamous cell carcinoma (P-ESCC) may develop multiple primary tumors (MPTs) in the upper aero digestive tract (UADT).[1] The MPT prevalence in these patients is reported to be high, up to 21.9%.[1-3] Most studies, however, are performed in Asia, where the ESCC prevalence is higher than in Western countries.[4]

Aims & Methods: The aim of this study was to evaluate the prevalence of MPTs in the UADT in patients with P-ESCC in a Western population. We performed a nationwide, retrospective cohort study in collaboration with the Netherlands Comprehensive Cancer Registry (IKNL). All adult patients, diagnosed between 2000 and 2016 with ESCC as index tumor were included in this study.

Follow-up data were available until January 2018. No screening programs for MPTs were in place within this timeframe. Our primary endpoint was the prevalence of MPTs in the UADT in patients with P-ESCC. Secondary endpoints were; (1) MPT localization, (2) MPT histology, (3) the proportion of patients with synchronous (within 6 months before and after diagnosis of P-ESCC) or metachronous (> 6 months after diagnosis of P-ESCC) MPTs, and (4) risk factors associated with MPT development. We performed univariate and multivariate analysis to analyze these risk factors.

Results: A total of 9,058 patients were diagnosed with P-ESCC between 2000 and 2016 (male: 57.3%). The median age was 67 years (IQR 60-75). Initial ESCC tumor stage was high (stage III/IV) in the majority of patients (59.9%). Most patients were treated with radiotherapy (n=2,163; 23.9%) or chemoradiotherapy (n=1,812; 20.0%). In 850 (9.4%) patients, ESCC was treated by primary surgery or endoscopic resection, and 1,288 (14.2%) patients received neoadjuvant therapy before surgery.

A total of 545 MPTs were registered in 476 (5.3%) patients. Most MPTs were located in the head and neck region (47.9%), followed by the lungs (40.8%) and stomach (6.6%). Squamous cell carcinoma (61.8%) was the most common histology, followed by adenocarcinoma (14.5%). Of all MPTs, 329 (60.4%) were diagnosed synchronously and 216 (39.6%) metachronously.

Of all patients who were alive 6 months after P-ESCC diagnosis (n=5,938), 191 patients (3.2%) developed a metachronous MPT. The median time between diagnosis of P-ESCC and the metachronous MPT was 3.0 years (IQR 1.8-5.9). Of patients with metachronous MPT, MPT stage was high (stage III/IV) in 57.4%. These patients had a significantly worse 2-year survival than low stage MPT (stage I/II) (15.1% vs. 51.9%, p <0.01).

The following factors were significantly correlated with MPT development: male sex (OR: 1.519; p <0.01), age ≤ 70 years (OR: 2.129; p <0.01), and lower tumor stage (stage I/II vs. III/IV) (OR: 2.053; p<0.01).There was no significant difference in P-ESCC tumor stage between patients with synchronous and metachronous MPTs.

Conclusion: Based on this nation-wide registry study a minimum of one out of twenty patients with P-ESCC develops an MPT. The majority of the registered MPTs were detected synchronously, screening from diagnosis of P-ESCC should therefore be recommended. Since patients with metachronous MPTs had more often high-stage MPTs and a worse survival compared to low-stage metachronous MPTs, we should screen for metachronous MPTs to detect MPTs at an earlier, and lower tumor stage.

References: 1. Lee, G.D., et al., Esophageal Cancer Associated with Multiple Primary Cancers: Surgical Approaches and Long-term Survival. Ann Surg Oncol, 2013. 20(13): p. 4260-6. 2. Noguchi, T., et al., Necessity of screening for multiple primary cancers in patients with esophageal cancer. Ann Thorac Cardiovasc Surg, 2002. 8(6): p. 336-42. 3. Kumagai, Y., et al., Multiple primary cancers associated with esophageal carcinoma. Surg Today, 2001. 31(10): p. 872-6. 4. Arnold, M., et al., Global incidence of oesophageal cancer by histological subtype in 2012. Gut, 2015. 64(3): p. 381-7.

Disclosure: Nothing to disclose

P0603 THE ACCURACY OF THE PREOPERATIVE DIAGNOSIS OF LYMPH NODE METASTASIS USING COMPUTED TOMOGRAPHY FOR T1B ESOPHAGEAL CANCER PATIENTS RECEIVING ESOPHAGECTOMY AFTER ENDOSCOPIC TREATMENT

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Introduction: The standard treatment for T1b esophageal squamous cell carcinoma (tumor invasion to submucosa) is esophagectomy with lymphadenectomy in Japan. However, some cases are given endoscopic treatment as the initial therapy. Based on the histopathological findings, the patients in whom the tumor has invaded to the submucosa are then recommended to undergo additional therapy. The accurate clinical evaluation of the lymph nodes is therefore crucial for selecting the optimum treatment strategy for individual esophageal cancer patients.

Aims & Methods: To investigate the accuracy of the preoperative diagnosis of lymph node metastasis for T1b esophageal cancer patients given esophagectomy after endoscopic treatment.Between January 2002 and December 2016, 139 cases of T1b esophageal cancer were treated with endoscopic treatment as the initial treatment. Thirty-six patients (25.9%) received esophagectomy with lymphadenectomy. The concordance between the clinical and pathological nodes was then evaluated. The preoperative diagnosis was based on computed tomography (CT) findings.

Results: The patient background characteristics were as follows: male/female, 30/6; median age, 64 years old (range 41-78); primary tumor site at cervical/upper/middle/lower/Barrett's esophagus, 2/5/15/10/4; cN0/cN1, 32/4. Lymph node metastasis was observed in 13 patients and 19 lymph nodes (36.1%). The number of lymph node metastases was one in eight cases, two in one case, three in three cases and five in one case. The lymph node-positive sites were cervical/thoracic/abdominal in 11/5/3 cases. Lymph node metastasis was most frequently observed in the right para-thoracic area. The sensitivity and specificity of clinical nodes for a diagnosis of pathological nodes were 30.8% and 100%, respectively, and the positive and negative predictive values were 100% and 71.9%, respectively. In 12 (63.1%) of the 19 sites, the size of the lymph nodes with metastasis was estimated to be < 3 mm on CT.

Conclusion: The diagnosis of clinical nodes has low sensitivity and a low negative predictive value for the prediction of the pathological node category in the preoperative diagnosis of lymph node metastasis for patients with T1b esophageal cancer treated endoscopically. We therefore need to carefully consider indications of endoscopic treatment for T1b esophageal cancer. Clinical staging techniques should be improved.

Disclosure: Nothing to disclose

P0604 THE EFFICACY OF PHOTODYNAMIC THERAPY WITH A NEW PHOTOSENSITIZER (TALAPORFIN SODIUM) AS A SALVAGE TREATMENT FOR ESOPHAGEAL CANCER WITH A FOCUS ON THE EFFECT OF VASCULAR SHUTDOWN

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Introduction: Esophageal cancer is one of the most common cancers worldwide. Chemoradiotherapy (CRT) is one of the curative treatments for esophageal cancer in patients with unresectable tumors or those who refuse surgery. However, local failure after CRT is a problem. An alternate treatment in such patients is photodynamic therapy (PDT).

PDT consists of the intravenous administration of a photosensitizer, followed by activation with a specific wavelength light. Activation of the photosensitizer causes the conversion of molecular oxygen into various reactive oxygen species that directly induce the death of the tumor cells or shut down the tumor-associated vasculature. However, the mechanism of the vascular shut down is not clear.

Talaporfin sodium, a second-generation photosensitizer, is rapidly cleared from the skin and requires a shorter sun-shade period. Furthermore, the depth of effect is expected to extend to deeper layers.

In this study, we evaluated the efficacy of PDT with Talaporfin for esophageal cancer focusing on the vascular shutdown effect.

Aims & Methods: Patients with histologically proven local failure limited within the muscularis propria after radiotherapy (RT) of 50 Gy or more for esophageal cancer were eligible.

The PDT procedure commenced with intravenous administration of a 40 mg/m²-dose of talaporfin sodium, followed by laser irradiation at a 664-nm wavelength 4 to 6 hours after administration.

The local efficacy was classified based on endoscopic evaluation as local complete response (L-CR). The L-CR rate per patients was the primary endpoint of this study. The secondary endpoints were confirmed local progression-free survival (L-PFS), and overall survival (OS).

Xenograft tumor mouse models were established with colon cancer cell lines (HCT116). After talaporfin intravenous injection, tumors were illuminated with the diode laser system (664nm). Tumor blood flow was measured by a laser speckle blood flow analyzing system; OMEGA ZONE2. Temporal changes of the flow were compared with the positive control; Combretastatin A-4 phosphate (CA4P).

Results: Sixteen patients with a total of 19 lesions received additional laser irradiation. The median total laser exposure dose was 298 (range: 100-800) J. Thirteen patients with a total of 16 lesions achieved L-CR after PDT (L-CR rate: 84.2%). The L-CR rate of T1 failure lesions was 92.8% (13/14), whereas the L-CR rate of T2 failure lesions was 60.0% (3/5).

PDT with Talaporfin decreased the blood flow in tumors but not in the neighboring healthy tissue.

Conclusion: The possibility of esophageal perforation after PDT should be considered for longer than 1 month post-therapy. PDT with Talaporfin decreased the tumor blood flow significantly in vivo. The vascular shutdown effect of PDT with Talaporfin was suggested as an important part of its antitumor effects. PDT using talaporfin sodium and a diode laser is a curative salvage treatment for local failure after CRT for patients with esophageal cancer.

Disclosure: Nothing to disclose

P0605 RISK FACTORS FOR STRICTURE AFTER ESOPHAGEAL ESD: CAN WE PREVENT STRICTURE WITH STEROID INJECTION AND PGA SHIELDING?

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Introduction: Endoscopic submucosal dissection (ESD) is currently the standard method of treatment for superficial esophageal carcinoma in many countries. However, resection of more than 3/4 the circumference of the esophagus has been reported to be a risk factor for postoperative stricture after ESD. A previous pilot study has shown that combining triamcinolone injection and shielding with polyglycolic acid (PGA) sheets is effective in preventing postoperative stricture (Am J Gastro 2016). This analysis was performed to obtain more definitive evidence on the efficacy of this method, and determine factors which may induce stricture even after this method.

Aims & Methods: We have performed a retrospective analysis of patients who have undergone esophageal ESD from Jan 2002 to Dec 2018 at the University of Tokyo Hospital. 136 consecutive patients who underwent esophageal ESD for superficial esophageal squamous cell carcinoma covering over 1/2 the circumference of the esophagus were extracted. Of these, after ethics committee approval in 2013, patients have undergone either "PGA shielding" or "steroid injection + PGA shielding" following ESD. After exclusion of patients who did not undergo 12 week post-ESD follow-up, patients who underwent salvage surgery, and patients with regular oral steroid use, 111 patients (age 69.8±9.0 years) were analyzed. Multivariate logistic regression analysis was performed to evaluate risk factors associated with stricture, which was defined as the state where dilation was required for an upper gastrointestinal endoscope to pass.

Results: 82.9% (92/111) of these high-risk patients required resection of over 3/4 the circumference of the esophagus. By multivariate logistic regression analysis, location (p=0.037), resection circumference (p< 0.001), and method of prevention (p=0.020) were the only factors significantly associated with stricture. Further analyses demonstrated that stricture rates in the cervical esophagus (75.0%, p=0.040), and after total circumferential resection (83.3%, p< 0.001) were especially high.

Comparison on the efficacy of "steroid injection + PGA shielding" vs "PGA shielding" vs "control" was performed. In the relatively low-risk subgroup excluding cervical esophageal cancer and complete circumferential resection, the postoperative stricture rate was 18.9% vs 41.4% vs 51.7% respectively (p=0.014). The rate of patients requiring long-term dilation treatment was 16.2% vs 31.0% vs 28.0% respectively (p=0.320), indicating that "steroid injection + PGA shielding" is the most effective method in both preventing and alleviating stricture. However "steroid injection and PGA shielding" showed only limited effects in extremely high-risk cases with either cervical esophageal cancer or complete circumferential resection.

Conclusion: Combining steroid injection and PGA shielding is effective for preventing and alleviating postoperative stricture after esophageal ESD. There is a need for even more effective methods for cervical esophageal cancer and complete circumferential resection.

References: Triamcinolone Injection and Shielding with Polyglycolic Acid Sheets and Fibrin Glue for Postoperative Stricture Prevention after Esophageal Endoscopic Resection: A Pilot Study. Sakaguchi Y, et al. Am J Gastroenterol. 2016 Apr;111(4):581-3. doi: 10.1038/ajg.2016.60

Disclosure: Nothing to disclose

P0606 WITHDRAWN

P0607 LARGER LESIONS AND PREVIOUS CHEMORADIOTHERAPY FOR ESOPHAGEAL CANCER INCREASED THE RISK OF FAILURE OF EN BLOC RESECTION OR PERFORATION IN ESOPHAGEAL ESD

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Introduction: Endoscopic submucosal dissection (ESD) is accepted as the standard treatment for early-stage esophageal neoplasia. However, esophageal perforation may occur, leading to mediastinitis and pneumothorax, which sometimes require emergency surgery. In addition, failure of en bloc resection causes local recurrence. Until now, few studies have reported on predictors of failure of en bloc resection or perforation during ESD.

Aims & Methods: The aim of the present study is the risk factors of failure of en bloc resection or perforation in ESD for esophageal neoplasia.

This was a retrospective observational study conducted at a single institution. Between May 2004 and March 2016, 543 consecutive patients with 927 esophageal lesions were treated with ESD. Patients with metachronous esophageal neoplasia or missing data were excluded. The primary outcome was determining the predictors of failure of en bloc resection or perforation in patients who underwent esophageal ESD. Perforation was defined as a visible hole in the esophageal wall, exposing the mediastinal cavity.

Results: A total of 543 patients with 736 lesions were evaluated. Failure of en bloc resection occurred in 6 patients (1.1%) with 6 lesions, and perforation occurred in 11 patients (2.0%) with 11 lesions (1.5%). Lesion diameter [odds ratio (OR), 1.05; 95% confidence interval (CI): 1.02-1.07; p < 0.001)], wider tumor circumference (OR, 9.80, 95% CI: 1.61-59.5; p=0.01), and previous chemoradiotherapy for esophageal cancer (OR, 3.87; 95% CI: 1.19-12.53; p=0.02) were associated with failure of en bloc resection or perforation according to crude logistic regression analysis. Multivariate logistic regression analysis showed that lesion diameter (OR, 1.04; 95% CI: 1.02-1.06; p < 0.001) and previous chemoradiotherapy (OR, 5.24; 95% CI: 1.52-18.06; p = 0.009) were independent predictive factors.

Conclusion: Larger lesions and previous chemoradiotherapy for esophageal cancer increased the risk of failure of en bloc resection or perforation in patients who underwent esophageal ESD.

Disclosure: Nothing to disclose

P0608 ADENOCARCINOMA OF THE ESOPHAGOGASTRIC JUNCTION IN JAPAN: A 10-YEAR PROSPECTIVE MULTICENTER EPIDEMIOLOGICAL STUDY IN KURASHIKI, JAPAN

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Introduction: Gastroesophageal reflux disease-related diseases, such as Barrett's esophagus and adenocarcinoma of the esophagogastric junction (AEGJ), are believed to occur less frequently in Japan than in Western countries. The number of cases of these conditions reported in Japan has been gradually increasing in recent years; however, there is limited information on the epidemiology of AEGJ. Based on previously reported data (Matsueda K, et al. Dis Esophagus 2017; 30: 1-6), we decided to extend the observational period in order to conduct a long-term follow-up study.

Aims & Methods: The aim of this study was to investigate the clinicoepidemiological characteristics of AEGJ in Japan. We divided the investigation period into the following three parts: first period (2.5 years; January 1, 2008-June 30, 2010), second period (4 years; July 1, 2010-June 30, 2014), and third period (3.5 years; July 1, 2014-December 31, 2017). During the first period, 88,199 consecutive cases (48,548 males and 39,651 females; mean age, 62 years) involving upper gastrointestinal endoscopy performed at 12 hospitals in Kurashiki, Japan were recruited. The cases were prospectively followed up for 7.5 to 10 years (mean, 8.7 years). Over a 10-year period from January 2008 to December 2017, we reviewed all endoscopy reports and associated medical records. AEGJ was defined as an adeno-carcinoma of the distal esophagus (Siewert classification type I) and a true carcinoma of the cardia (Siewert type II). A new-onset patient was defined as a patient who had newly developed AEGJ, esophageal squamous cell carcinoma (SCC), and/or gastric cancer (GC) during the follow-up period. The new-onset rates of AEGJ, SCC, and GC, including Siewert type III, were calculated.

Results: During the 10-year study period, 158 patients with AEGJ were identified (131 males and 27 females; mean age, 68 years), and of these patients, 16 had Siewert type I AEGJ and 142 had Siewert type II. The incidence rate of AEGJ was 0.018%/year during the 10-years period and did not increase over the years. However, the proportion of patients with Siewert type I AEGJ significantly increased during the follow-up period (Table 1).

	First period (n=47)	Second period (n=55)	Third period (n=56)	P value
type I/type I+II	1/47 (2%)	5/55 (9%)	10/56 (18%)	< 0.05

[Table 1 The proportion of patients with Siewert type I AEGJ]

With regard to female patients, the number of cases increased from 5 (1.3 cases/year) in the second period to 13 (3.7 cases/year) in the third period. The new-onset rate of AEGJ was very low compared with that of SCC or GC, but it gradually increased from 1.1/100,000 person-years (SCC, 3.4/100,000; GC, 42.3/100,000) in the second period to 3.2/100,000 person-years (SCC, 8.8/100,000; GC, 37.7/100,000) in the third period.

Conclusion: The incidence of AEGJ is still lower in Japan than in Western countries; however, the proportion of patients with Siewert type I AEGJ and the new-onset rate of AEGJ are gradually increasing.

Disclosure: Nothing to disclose

P0609 USEFULNESS OF LINKED COLOR IMAGING IN THE EARLY DIAGNOSIS OF SUPERFICIAL ESOPHAGEAL SQUAMOUS CELL CARCINOMAS

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Introduction: Linked color imaging (LCI) installed in the FUJIFILM's LASE-REO endoscope system can highlight minor differences of color through image processing to expand the saturation and hue differences in the region of red color.
This study investigated the usefulness of LCI in SESCC.
Aims & Methods: We examined the visibility of lesions using LCI compared with that using white-light imaging (WLI) in 46 consecutive patients (29 men and 17 women; average age: 68.1 ± 9.6 years; 40 heavy drinkers and 36 smokers) with SESCC who underwent esophagogastroduodenoscopy using LCI in our department from April 2018 to November 18, 2018. The clinicopathological characteristics of the 46 cases were studied.
The average tumor diameter was 21.4±17.6 mm (5-60 mm), and the tumor stage was 0-IIc in 40 cases and 0-IIa in 6; the tumor depth was limited to the epithelium or was invading the lamina propria (EP/LPM) in 30 cases, invading the muscularis mucosa or the upper third of the submucosal layer (MM/SM1) in 12, and invading the middle third of the submucosal layer (SM2) in 4.
Changes in the visibility of the lesions were evaluated by 8 endoscopy specialists using the evaluation scale (+2: improved; +1: slightly improved; 0: equal; -1: slightly decreased; -2: decreased), and the overall score was defined as 8 or more in case of improved visibility, 7 to -7 in case of equal visibility, and -8 or less in case of decreased visibility.
Furthermore, in each lesion, the color difference between the cancerous and noncancerous areas observed by LCI was compared to that by WLI. In addition, tumor diameter, macroscopic type, depth, smoking and drinking history, and multiple lugol-voiding lesions (multiple LVLs; 10 small LVLs of the surrounding mucous membrane) were examined.
Results: The rate of change in the visibility of lesions by LCI was 41% (19/46) for improved visibility, 59% (27/46) for equal visibility, and 0% (0/46) for decreased visibility. The colors were significantly different between the cancerous and non-cancerous areas. The improved visibility was significantly different between LCI and WLI (p<0.01; two sample t-tests), but no significant differences were observed for equal visibility.
The improved visibility of the lesions by LCI had no correlations with the tumor diameter, macroscopic type, color tone, depth, or smoking and drinking history, but was significantly correlated with the presence of multiple LVLs (p<0.05; χ^2 test). The kappa value of the interobserver agreement was 0.45, which means that the observations were roughly consistent.
Conclusion: LCI for SESCC does not reduce the visibility of the lesion compared with WLI, and in particular, improves the visibility of the lesions with multiple LVLs.
Disclosure: Nothing to disclose

P0610 SCREENING FOR HEAD AND NECK SECOND PRIMARY TUMORS IN PATIENTS WITH ESOPHAGEAL SQUAMOUS CELL CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Esophageal squamous cell carcinoma (ESCC) is often accompanied by head and neck second primary tumors (HNSPTs).[1] The prognosis and survival of patients with an additional HNSPT is worse compared to patients with only ESCC (5-year survival rate of 9.2% vs. 21.0%). [2] Therefore, early detection of HNSPTs may improve the overall outcome of patients with ESCC.

Aims & Methods: The aim of this study was to investigate the yield of endoscopic screening for HNSPTs in patients with primary ESCC. Secondary aims were to investigate whether screening should be performed synchronously or metachronously, and to investigate whether there is enough evidence to justify endoscopic screening in the Western world. We conducted a systematic literature search until February 2019 to retrieve studies from all available databases. Studies were included if ESCC patients were endoscopically screened for HNSPT. The primary outcome was the pooled prevalence of HNSPTs.
Results: Twelve studies, all performed in Japan, were included in this systematic review with a total of 6483 patients (Table 1). The pooled prevalence of HNSPTs was 6.7% (95% CI: 4.9-8.4). The overall heterogeneity was high across the studies (I^2 = 89.0%, p < 0.001). The proportion of synchronous (48.2%) and metachronous (51.8%) HNSPTs was comparable. Most HNSPTs were low-stage (85.3%) and located in the hypopharynx (60.3%).
Conclusion: Based on our results, HNSPT screening could be considered in patients with primary ESCC. The majority of HNSPTs were classified as low-stage, which can be treated curatively and have an excellent prognosis. All studies were performed in Japan, it is therefore not clear if this consideration applies to the Western world.

Author	Year	Design	N	Method	Quality Score			Quality	Screening sites
					MINORS	Relevance	Total		
Abiko et al.	2018	Prospective	158	WL	18	3	21	High	Larynx
Onochi et al.	2018	Retrospective	285	WL	10	3	13	Medium	Oro-hypopharynx
Morimoto et al.	2017	Retrospective	307	WL + NBI	18	5	23	High	Oro-hypopharynx, Larynx
Kaneko et al.	2013	Retrospective	348	WL + NBI	9	4	13	Medium	Oral cavity, pharynx
Katada et al.	2012	Prospective	71	WL + NBI	16	5	21	High	Head and neck region
Muto et al.	2010	Prospective	320	WL + NBI	23	4	27	High	Head and neck region
Nonaka et al.	2009	Prospective	424	WL + NBI	19	5	24	High	Pharynx
Lo et al.	2008	Prospective	1675	WL	18	3	21	High	Head and Neck region
Watanabe et al.	2007	Prospective	1118	Lugol	10	3	13	Medium	Head and neck region
Shimizu et al.	2003	Prospective	99	Lugol	18	5	22	High	Hypopharynx, larynx
Kagei et al.	2002	Prospective	1479	WL	10	2	12	Medium	Head and neck region
Motoyama et al.	2003	Prospective	200	WL	13	4	17	High	Larynx

[Table 1. Study characteristics and quality score of all 12 studies. WL = white light, NBI = Narrow Band Imaging]

References: 1. Chuang, S.C., et al., Risk of second primary cancer among esophageal cancer patients: A pooled analysis of 13 cancer registries. Cancer Epidemiol Biomarkers Prev, 2008. 17(6): p. 1543-1549. 2. Lo, O.S.H., et al., Esophageal cancers with synchronous or antecedent head and neck cancers: A more formidable challenge? Ann Surg Oncol, 2008. 15(6): p. 1750-1756.
Disclosure: Nothing to disclose

P0611 THE PREVALENCE OF GASTRIC MUCOSAL INJURIES IN LOW-DOSE ASPIRIN USERS BY AGE

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Introduction: Low-dose aspirin (LDA) use is increasing dramatically around the world. Particularly in Japan, the number of LDA users is expected to increase rapidly due to the country's aging population. Therefore, it is an urgent issue for us to understand the features of gastric mucosal injury in patients taking LDA.

Aims & Methods: The aim of this study is to explore the generation difference in prevalence of gastric mucosal injury in LDA users. This is a case-controlled study conducted at our department. Data were extracted from the records of subjects who underwent upper gastrointestinal endoscopy at our department between April 2015 and February 2019. Of the 4,983 subjects analyzed, we focused on the subjects who did not take potassium-competitive acid blockers, proton pump inhibitors or histamine 2 receptor antagonists. We analyzed data for subjects diagnosed endoscopically with gastric erosions and ulcers. These mucosal injuries are based on the definition of ulcer classification which was defined by Murakami and Suzuki in 1971. We compared the prevalence of gastric mucosal injuries between patients taking LDA (LDA users) and taking NO LDA (nonusers) by age. Statistical analyses were performed by Mann-Whitney U test.

Results: This study included 147 subjects taking LDA (101 men, 26 women; mean age 72.5 years) and 3,362 subjects taking NO LDA (1,874 men, 1,488 women; mean age 63.1 years). In LDA users, the prevalence of gastric mucosal injury was 23.1% (3/13) (ages 39 and under), 25.0% (3/12) (ages 40-49), 40.0% (2/5) (ages 50-59), 31.8% (7/22) (ages 60-69), 23.2% (10/38) (ages 70-79), 26.3% (10/38) (80 and over). In nonusers, the prevalence of gastric mucosal injury was 17.3% (125/722) (ages 39 and under), 19.30% (96/497) (ages 40-49), 21.9% (102/465) (ages 50-59), 21.4% (183/857) (ages 60-69), 20.5% (191/232) (ages 70-79), 20.5% (79/386) (80 and over) (p=0.0039). The prevalence of gastric mucosal injury was highest in the age group 50-59 in both LDA users and nonusers.

Conclusion: We have demonstrated that the prevalence of gastric mucosal injury in LDA users was statistically significantly higher than in nonusers. In all age groups, the prevalence in LDA users was higher than in nonusers.

Disclosure: Nothing to disclose

P0612 INCIDENCE AND TREATMENT OUTCOMES OF METACHRONOUS GASTRIC CANCER OCCURRING AFTER CURATIVE ENDOSCOPIC SUBMUCOSAL DISSECTION OF UNDIFFERENTIATED-TYPE EARLY GASTRIC CANCER: JAPAN CLINICAL ONCOLOGY GROUP STUDY: SUPPLEMENTARY ANALYSIS OF JCOG1009/1010

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Introduction: Five-year cumulative incidence of metachronous gastric cancer (MGC) occurring after curative gastric endoscopic submucosal dissection (ESD) of several studies was reported in 10-16% [1]. However, most subjects of previous studies were patients undergoing ESD of differentiated-type (D-type) early gastric cancer (EGC), and little is known about long-term follow-up data of MGC occurring after gastric ESD of undifferentiated-type (UD-type) EGC.

Aims & Methods: The aim of this study was to evaluate incidence and treatment outcomes of MGC after curative gastric ESD of UD-type EGC. This study included patients who underwent curative ESD of initial solitary UD-type EGC from JCOG1009/1010, which is a multicenter single-arm confirmatory trial in Japan and showed excellent long-term outcomes in patients undergoing curative ESD of UD-type EGC [2]. Curative ESD of UD-type EGC was defined as histologically proven mucosal poorly differentiated adenocarcinoma or signet ring cell carcinoma of major histological type without ulceration nor lymphovascular invasion ≤ 20mm with free lateral and deep margin. Undifferentiated dominant-type (e.g., poorly to moderately differentiated adenocarcinoma) was also included as UD-type EGC. Surveillance endoscopy was performed biannually for the first three years and then annually. This study assessed the time to MGC occurrence after ESD, lesion characteristics, and treatment outcomes of MGC. MGC was defined as a gastric cancer that was located in a different position to the initial EGC occurring more than one year after the index ESD. Time to MGC occurrence was estimated by cumulative incidence function, regarding deaths and total gastrectomy as competing risks.

Results: A total of 198 patients undergoing curative ESD of UD-type EGC were analyzed in this study. Male/female was 96/102, and the median age was 60 (range: 23-80). Gastric atrophy (none/mild/severe) was classified 64/64/70, respectively. Eighty-five patients had *Helicobacter pylori* (*H. pylori*) infection, 59 did not have *H. pylori* infection, and 26 had successful *H. pylori* eradication at index gastric ESD (missing in 28 patients). Four patients post ESD of UD-type EGC developed MGC during a median follow up period of 5.8 years (range: 0.2-7.2). Five-year cumulative incidence function of MGC was 1.0% (95% CI: 0.2%-3.3%). The tumor location (Upper/Middle/Lower) were 1/1/2, respectively. The macroscopic type was 0-IIc in all four lesions. All MGCs were treated with ESD. Two MGCs were histologically D-type EGC, and the remaining two were UD-type EGC. The median tumor size of MGCs was 1.0 (range: 0.7-1.7) cm, and the depth of invasion (M/SM1/SM2) was 2/1/1, respectively. Three out of the four patients achieved curative resection.

Conclusion: MGC could occur less commonly after curative ESD of UD-type EGC compared with that of D-type EGC, and three out of four MGC were resected curatively with ESD.

References: 1) Abe S, et al. Metachronous Gastric Cancer Following Curative Endoscopic Resection of Early Gastric Cancer, Clin Endosc 2018 2) Takizawa K, et al. A non-Randomized Single-arm Confirmatory Trial of

Endoscopic Submucosal Dissection to Expand its Indication for Early Gastric Cancer of Undifferentiated Type: Japan Clinical Oncology Group study (JCOG1009/1010), DDW2019
Disclosure: Nothing to disclose

P0613 WITHDRAWN

P0614 METACHRONOUS MULTIPLE LESIONS DEVELOPING NEAR SCARS AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC CANCER

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Introduction: Along with the development of endoscopic submucosal dissection (ESD) for early gastric cancer(EGC), increasing numbers of patients have metachronous multiple lesions developing during follow-up after ESD. We often encounter patients in whom treatment is difficult to perform owing to the presence of metachronous multiple lesions developing near scars remaining after ESD.
Aims & Methods: We compared the incidence of metachronous multiple lesions developing near scars after ESD with that of lesions developing at other sites to examine the clinicopathological characteristics of metachronous multiple lesions developing near scars after ESD and the incidence of complications at the time of ESD.
Subjects & Methods: Among 2182 patients (2762 lesions) who underwent ESD for EGC in our hospital from September 2002 through August 2018, we studied 15 patients (20 lesions) with metachronous multiple lesions that developed near scars (group A) and 161 patients (304 lesions) with metachronous multiple lesions that developed in other regions (group B). The median follow-up period was 61 months (range, 13 to 186 months).
Results: Group A comprised 9 men and 6 women with a median age of 76 years, and group B comprised 129 men and 32 women with a median age of 73 years. In group A, 9 patients had elevated-type lesions, and 11 patients had flat, depressed-type lesions. The median lesion diameter was 10 mm. Differentiated-type lesions were found in 19 patients, and predominantly differentiated-type lesions in 1 patient.
The curability was eCuraA in 15 patients, eCuraC-1 in 2 patients, and eCuraC-2 in 3 patients. In group B, 123 patients had elevated-type lesions, and 181 patients had flat depressed-type lesions. The median lesion diameter was 13 mm. Differentiated-type lesions were found in 281 patients, differentiated-predominant mixed type lesions in 18 patients, undifferentiated-type lesions in 1 patient, and undifferentiated-predominant mixed type lesions in 4 patients.
The curability was evaluated to be eCuraA in 247 patients, eCuraB in 19 patients, eCuraC-1 in 17 patients, and eCuraC-2 in 21 patients. In group A, the site of gastric cancer was the upper part of the stomach in 1 patient, the middle part of the stomach in 13 patients, and the lower part of the stomach in 6 patients. In group B, the site of gastric cancer was the upper part of the stomach in 41 patients, the middle part of the stomach in 132 patients, the lower part of the stomach in 118 patients, and other parts of the stomach in 13 patients.
Three or more metachronous multiple lesions were found in 10 patients (67%) in group A and 50 patients (31%) in group B; this difference was significant (p< 0.01). The ESD procedure time was significantly longer in group A (110 minutes; range, 65 to 211) than in group B (78 minutes; range, 24 to 332; p< 0.01).
Complications comprised perforation in 3 patients (16.6%) and subsequent bleeding in 4 patients (22.2%) in group A and perforation in 12 patients (3.8%) and subsequent bleeding in 21 patients (5.0%) in group B. These differences were significant (both p< 0.01).
Conclusion: Patients in whom many metachronous multiple lesions develop during follow-up observation after ESD for EGC may have a higher risk of metachronous multiple lesions developing near scars. ESD for metachronous multiple lesions developing near scars requires a long

procedure time and is associated with a high incidence of complications. Treatment should therefore be carefully performed, taking into account that such lesions are technically difficult to treat.
Disclosure: Nothing to disclose

P0615 THE EFFECT OF ANTICOAGULANT THERAPY ON POST ENDOSCOPIC SUBMUCOSAL DISSECTION BLEEDING FOR GASTRIC CANCER: A PROPENSITY SCORE MATCHING ANALYSIS

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Introduction: Endoscopic submucosal dissection (ESD) has been accepted as a standard treatment for early gastric cancer (EGC). In the guideline published by the Japan Gastroenterological Endoscopy Society, it has been suggested that an anti-platelet medication should be continued throughout the peri-treatment period. However, the optimal management of anticoagulant therapy for gastric ESD remains controversial. Moreover, little is known about the effect of anticoagulant therapy on post-ESD bleeding.
Aims & Methods: In order to investigate the effect of anticoagulants for post-ESD bleeding for EGC, we retrospectively analyzed 2355 EGCs treated by ESD, including 137 lesions in patients under anticoagulants. Anticoagulant therapy included warfarin and direct oral anti-coagulants (DOACs), such as dabigatran, rivaroxaban, edoxaban and apixaban. Using propensity score matching analysis, clinicopathological findings were evaluated between lesions in patients with anticoagulant therapy and those in patients without. We used a one-to-one propensity score matching selected by age, gender, comorbidities (such as diabetes mellitus, renal failure and liver cirrhosis), tumor location, macroscopic appearance, histology, depth of tumor, ulcerative findings, procedure time, resected specimen size and perforation as parameters. Factors associated with post-ESD bleeding were analyzed with multivariable analyses with a logistic regression method.
Results: After propensity score matching, post-ESD bleeding was significantly more frequent in lesions in patients with than without anticoagulant therapy (11.7% vs 1.5%, respectively; P = 0.001). Univariate analyses revealed that anticoagulant therapy, heparin bridge therapy, undifferentiated type, deep submucosal invasion and resected specimen size were associated with post-ESD bleeding. Multivariate analysis revealed anticoagulant therapy (OR 23.1, 95% CI 3.61-147.52) and resected specimen size (OR 1.03, 95% CI 1.00-1.06) to be independent factors associated with post-ESD bleeding.
Conclusion: Anticoagulant therapy and resected specimen size were risk factors associated with post-ESD bleeding for EGC. Strategies for the prevention of post-ESD bleeding should be seriously considered for patients under anticoagulant medication.
Disclosure: Nothing to disclose

P0616 FACTOR ASSOCIATED WITH METACHRONOUS GASTRIC CANCER IN PATIENTS UNDERGOING ENDOSCOPIC SUBMUCOSAL DISSECTION OF EARLY GASTRIC CANCER

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Introduction: Risk factors for gastric cancer during continuous infection with *Helicobacter pylori (H.pylori)* have been well documented and *H.pylori* eradication is expected to suppress the occurrence of gastric cancer. However gastric cancer still remains one of the leading cancers in the world with a high mortality worldwide. In addition, the risk of developing a metachronous lesion following endoscopic resection of an early gastric cancer has been reported to between 1% and 4% per year. The gastric

mucosal atrophy has been known as the risk factor range development of metachronous gastric cancer, however no reports of bile reflux has been reported.

Aims & Methods: A retrospective study was conducted to clarify the risk factors associated with the development of metachronous gastric cancer (MGC) in patients whose early gastric cancers were treated by endoscopic submucosal dissection (ESD).

Three hundred thirty-eight patients who underwent ESD for the treatment of early gastric cancer between January 2013 and March 2018 at our hospital were enrolled in this study. The mean age was 78 years, 251 patients were male, and 87 were female. MGC was defined as secondary gastric cancer discovered after one year of endoscopic therapy of early primary gastric cancer (PGC).

The factors considered were age, gender, BMI, current cigarette smoking, current alcohol drinking, the status of *H.pylori* infection, and gastric mucosal atrophy, bile reflux into the stomach, presence of xanthoma diagnosed by endoscopy.

Results: MGC was found in 33 patients out of 338 patents (9.8%). Among them, 12 cases with MGC developed within 2 years, and 21 cases from 2 years to 5 years. Of the 33 cases of recurrence of gastric cancer, 22 cases (66.7%) were after *H.pylori* eradication. The ratio of presence of bile reflex into the stomach was significantly higher in MGC than in PGC (54.5% [18 of 33] vs 36.7% [109 of 305], P=0.039). The ratio of presence of xanthoma was higher in MGC than in PGC (51.5% [17 of 33] vs 32.9% [100 of 305], P=0.036).

Higher prevalence of current alcohol drinking (48.5% [16 of 33] vs 31.1% [95 of 305], P=0.052), and gastric mucosal severe atrophy (87.9% [29 of 33] vs 75.0% [229 of 305], P=0.055) was tended to find in MGC than in PGC. No significant differences were found in age, gender, BMI, the status of *H.pylori* infection, current cigarette smoking between two groups.

Conclusion: In the present study, the presence of bile reflex into the stomach was shown to be a candidate factor which was associated with MGC. We should perform long follow-up endoscopy carefully even after *H.pylori* eradication, with special attentions in patients with xanthoma or biliary reflux.

Disclosure: Nothing to disclose

P0617 METFORMIN USE AND RISK OF GASTRIC ADENOCARCINOMA IN A SWEDISH POPULATION-BASED COHORT STUDY

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Introduction: Whether the use of metformin decreases the risk of gastric non-cardia and cardia adenocarcinoma is unclear.

Aims & Methods: This was a Swedish nationwide and population-based cohort study in 2005-2015. Firstly, associations between metformin use and gastric non-cardia and cardia adenocarcinomas were examined within a cohort of diabetes patients using anti-diabetes medication ('diabetes cohort'). Secondly, the same associations were analysed in another cohort including metformin users and 10 times as many non-users of metformin ('matched cohort'). The non-users were frequency-matched with metformin users for sex and age. Multivariable Cox proportional hazard regression analyses provided hazard ratios (HR) and 95% confidence intervals (CI). The HRs were adjusted for sex, age, calendar year, comorbidity, *Helicobacter pylori* eradication treatment, use of non-steroidal anti-inflammatory drugs or aspirin, and use of statins.

Results: The diabetes cohort consisted of 544,130 individuals, including 407,149 (74.8%) metformin users and 136,981 (25.2%) non-users of metformin. During the follow-up, 892 (0.1%) individuals developed gastric adenocarcinoma. Compared to non-users, metformin users had no decreased risk of gastric non-cardia adenocarcinoma (adjusted HR 0.93, 95% CI 0.78-1.12) or cardia adenocarcinoma (adjusted HR 1.49, 95% CI 1.09-2.02). The matched cohort included 4,525,543 individuals, of whom 411,413 (9.1%) were metformin users and 4,114,130 (90.9%) were non-users. During the follow-up, 6,395 (0.1%) individuals developed gastric adenocarcinoma. Compared to non-users, metformin users had no decreased risk of gastric non-cardia adenocarcinoma (adjusted HR 1.30, 95% CI 1.18-1.42) or cardia adenocarcinoma (adjusted HR 1.58, 95% CI 1.38-1.81).

Conclusion: Metformin use may not prevent gastric non-cardia or cardia adenocarcinoma.

Disclosure: Nothing to disclose

P0618 EFFECTS OF HELICOBACTER PYLORI ON BIOLOGICAL CHARACTERISTICS IN EARLY GASTRIC CANCER

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Introduction: Early gastric cancer (EGC) is an early stage of gastric cancer, a curable malignant disease with a high cure rate. Finding the clinico-pathological features of early gastric cancer is an important part of its early detection and timely diagnosis and reducing the mortality rate of gastric cancer.

Aims & Methods: To elucidate the differences between the biological characteristics of tumor cells in early gastric cancer and Helicobacter pylori(HP). Of the 111 patients with early gastric cancer were enrolled in this study, of whom were divided into 4 group: 23 HP- GC patients, 47 HP+ GC patients without a history of HP eradication(U-HP+ group), 12 HP+ GC patients with a history of HP eradication(E-HP+ group), 36 HP- GC patients without a history of HP infection(U-HP- group) and 28 HP- GC patients with a history of HP infection(I-HP- group) were enrolled in this study. We compared biological characteristics of tumor between the four group.

Results: Compare with the U-HP- group, the I-HP- group was more frequently in upper one third of stomach (P = 0.01). There was no significant difference in the expression of Ki67(P > 0.05). The expression of HER2 in U-HP+ group was higher (P = 0.049) than the E-HP+ group. In addition, there was a significant increase(P = 0.002) in the expression of HER2 of the HP+ group than that of the HP- group. In the HP+ group, there was a positively correlation in HP and the expression of HER2(P=0.014).

Conclusion: HP- EGC patients without a history of HP infection more frequently occurred in the upper part of the stomach. The proliferative capacity of the cancer in different HP eradication and eradication were similar, while the neoplasm invasion in HP+ EGC were increase, especially in HP+ GC with a history of HP eradication.

Disclosure: Nothing to disclose

P0619 THE RISK FOR LYMPH NODE METASTASIS IN EPSTEIN-BARR VIRUS-ASSOCIATED GASTRIC CARCINOMA WITH SUBMUCOSAL INVASION

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Introduction: Epstein-Barr Virus (EBV)-associated gastric cancer (EBVGC) accounts for approximately 10% of gastric cancers. EBVGC is classified into one of the four molecular subtypes proposed by The Cancer Genome Atlas Research Network (Nature, 2014), and there have been reports which imply the relatively low risk of lymph node metastasis (LNM) in EBVGC with submucosal invasion (pT1b-EBVGC). However, a large cohort study is still lacking.

Aims & Methods: The present study aims to investigate the risk of LNM in pT1b-EBVGC through a multicenter study. This is a retrospective multicenter study. 5 institutes, which have pathologists specializing in the diagnosis of EBVGC, participated in this study. We reviewed medical records and extracted all pT1b-EBVGC cases diagnosed between 2001 and 2016. Lesion characteristics, patients background factors and clinical outcomes were obtained. The diagnostic criteria for EBVGC were as follows: 1) gastric adenocarcinoma with lymphoid stroma; and 2) a positive result of in-situ hybridization for EBV encoded small RNA (EBER-ISH). For surgery cases, LNM was investigated based on the histopathological evaluation of resect-

ed LNs. For endoscopic resection (ER) cases, no LNM was defined as the case where computed tomography scan did not identify any LNM during follow-up ≥ 3 years.

Results: A total of 190 pT1b-EBVGC cases were enrolled. The number of ER and surgery cases were 30 and 160, respectively. Additional surgery was performed in 25 of 30 ER cases. LNM was identified in 9 cases (4.7%), which were all surgery cases. Table 1 shows the association between LNM and various factors.

	LNM - (181)	LNM + (9)	P value
Age	64.7 ± 10.1	69.8 ± 9.9	0.141
Sex (M/F)	149/32	8/1	1.000
Lesion size (mm)	29.5 ± 17.0	36.7 ± 22.3	0.230
Macroscopic appearance (depressed/protruded/others)	122/53/6	5/4/0	0.296
Location (U/M/L)	75/87/19	4/3/2	0.367
Depth (≥ SM500/< SM500)	159/22	9/0	0.602
Ly (0/1)	160/21	3/6	< 0.001
V (0/1)	153/28	7/2	0.635

[The association between LNM and clinical factors]

Lymphatic invasion (Ly) is the only significant risk factor for LNM (p< 0.001); neither lesion size nor submucosal invasion depth (≥ 500μm/< 500μm) were significantly correlated to LNM. The present study revealed that the risk for LNM in pT1b-EBVGC without Ly was 1.8% (3/163, 95%CI; 0.6-5.3%). Moreover, as for pT1b-EBVGC without Ly and ≤ 20mm, the rate of LNM was 0% (0/62, 95%CI; 0-4.7%).

Conclusion: The present study demonstrated the relatively low risk for LNM in pT1b-EBVGC, considering that the LNM risk of all pT1b-GC is approximately 20%. This result implies that pT1b-EBVGC is a good candidate for ER or local resection.

Disclosure: Nothing to disclose

P0620 WITHDRAWN

P0621 HISTOLOGIC VALIDATION OF ARGON PLASMA COAGULATION VERSUS MONOPOLAR COAGULATION FOR GASTRIC ADENOMA WITH LOW GRADE DYSPLASIA: A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

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Introduction: Endoscopic electrocoagulation such as argon plasma coagulation (APC) or monopolar coagulation (MC) is a safe alternative treatment for gastric adenoma with low grade dysplasia (LGD). However, there was no study regarding the histologic validation of endoscopic electrocoagulation for gastric LGD.

Aims & Methods: The aim of this study was to validate the histologic complete eradication of endoscopic electrocoagulation for gastric LGD.This was a prospective randomized controlled study involving patients who diagnosed gastric LGD and underwent endoscopic submucosal dissection (ESD) after endoscopic electrocoagulation from March 2014 to December 2018. Patients were randomly assigned to either APC or MC group. The main outcome was the complete histologic eradication rate.

Results: In 68 patients, 34 patients were treated with ESD after APC and 34 patients were treated with ESD after MC. The overall histologic complete eradication rate was 33.8% (23/68). The complete eradication rate was significantly higher in the APC group than those in the MC group (55.9% vs. 11.8%, P< 0.001). In multivariate analysis, APC was the only significant predictor of histologic complete eradication. (OR 7.66; 95% CI 2.139-27.448). There were no adverse events related to the procedure in both groups.

Conclusion: Although APC is a more effective treatment option than MC in treating gastric LGD, both methods revealed disappointing results in histologic complete eradication. Therefore, endoscopic resection must be performed for curative treatment of gastric LGD.

Disclosure: Nothing to disclose

P0622 WITHDRAWN

P0623 ENDOSCOPIC ULTRASOUND-GUIDED NEEDLE-BASED CONFOCAL LASER ENDOMICROSCOPY IN GASTROINTESTINAL SUBEPITHELIAL LESIONS: A FEASIBILITY STUDY

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Introduction: Needle-based confocal laser endomicroscopy (nCLE) allows for real-time optical biopsies during endoscopic ultrasound-guided fine needle aspiration (EUS-FNA).

Aims & Methods: Little is known about the nCLE imaging of gastrointestinal subepithelial lesions (GI-SELs); therefore, we determined its feasibility. We performed nCLE during EUS-FNA in 23 consecutive patients with GI-SELs between November 2015 and May 2018. We retrospectively compared nCLE findings with pathologic findings of EUS-FNA or surgical specimens.

Results: The median number (range) of needle passes per EUS-FNA procedure was 2 (1-3). The adequate sample acquisition rate was 67.0% per needle pass and 95.7% per patient. EUS-FNA was diagnostic in 78.3% (18/23), suspicious in 4.3% (1/23), and nondiagnostic in 17.4% (4/23). The concordance rate of nCLE findings with final pathology was 95.7% (22/23), which was not significantly different from diagnostic and suspicious EUS-FNA (*P*=.2482). nCLE could differentiate GI stromal tumors from leiomyoma, in that GISTs were characterized by contrast-enhanced densely populated spindle cell tumors with unenhanced rod-shaped nuclei in 100% of 12 patients, whereas leiomyomas were characterized by narrower spindle cell tumors with fewer and smaller unenhanced nuclei in 100% of 3 patients. A desmoid tumor appeared as spindle cell tumors both with unenhanced nuclei in some parts and with fewer and smaller nuclei in other parts. In rectal metastasis from lung adenocarcinoma, some pleomorphic dark nests were observed. There were no adverse events associated with nCLE and EUS-FNA.

Conclusion: nCLE can be safe and useful for the on-site detection of abnormalities of GI-SELs.

Disclosure: Nothing to disclose

P0624 THE ROLE OF INSULIN-LIKE GROWTH FACTOR AXIS IN THE PROGRESSION AND SURVIVAL IN GASTRIC CANCER

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Introduction: Overexpression of insulin-like growth factors and its binding proteins has been reported to be associated with the progression and survival of several cancers. However, their roles in the progression of gastric cancer remain poorly understood.

Aims & Methods: We aimed to assess the impact of circulating levels of levels of insulin-like growth factors (IGF1, IGF2) and their binding proteins (IGFBP1, IGFBP2, IGFBP3) and the expression of IGFBP2 in gastric cancer issues on the progression and survival of gastric cancer. A total of 481 gastric cancer patients were enrolled in this prospective hospital-based cohort study. Another 114 subjects without gastric cancer were recruited as control group. Plasma levels of IGF1, IGF2, IGFBP1, IGFBP2, and IGFBP3 were determined by commercially available enzyme-linked immunosorbent assay or radioimmunoassay kits. Expression of IGFBP2 was assessed by immunohistochemical stains. Their impacts on gastric cancer survival were analyzed by log-rank test and Cox proportional hazards regression models.

Results: Plasma levels of IGFBP2 was significantly higher in patients with gastric cancer as compared to healthy controls (p< 0.001). Plasma levels of IGFBP2 was also significantly higher in patients with more advanced AJCC stages (p< 0.001). However, the plasma levels of IGF1, IGF2, IGFBP1,

and IGFBP3 were not significantly differed in gastric cancer patients and controls. Patients with the highest tertile of IGFBP-2 levels were associated with a worse overall survival compared to those with the lowest IGFBP2 tertile levels (Hazard Ratio =1.51, 95% CI=1.19-1.92, p=0.001) after adjustment for age, gender, location, histology type, depth of invasion, and nodal metastasis. Higher expression of IGFBP2 in gastric cancer tissues was also associated with a worse overall survival than those with lower expression of IGFBP2, after adjustment of the above variables. In contrast, the plasma levels of IGF1, IGF2, IGFBP1, and IGFBP3 were not correlated with the overall survival in gastric cancer patients.

Conclusion: IGFBP2 plasma level, but not IGF1, IGF2, IGFBP1, or IGFBP3 levels, was higher in patients with gastric cancer and correlated with stage and survival. Higher expression of IGFBP2 in gastric cancer tissues also correlated with a worse overall survival. The finding lends support that IGFBP2 is a potential therapeutic target for gastric cancer.

Disclosure: Nothing to disclose

P0625 OMENTAL FAT TISSUE PROMOTES PERITONEAL DISSEMINATION OF GASTRIC CANCER

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Introduction: Gastric cancer (GC) has a clear predilection for peritoneal metastasis that cause poor prognosis. However, the exact mechanism why peritoneal metastasis frequently occurs in GC remains unknown. Omentum is the major cite for peritoneal metastasis, which is consisted of a huge fat tissue. We hypothesize that omental adipocytes trigger GC cell toward malignant activity inducing peritoneal metastasis.

Aims & Methods: We used 2 gastric cancer cell lines that were derived from primary GC tumor without metastasis. Omental adipocyte (OmAd) was used to assess interaction with GC cells. Endothelial cells (EC) were also used for *in vitro* angiogenesis assay including EC recruitment assay and tube formation assay. Cytokine protein array and PCR array were used for comprehensive analysis to identify responsible factors, and western blot analysis and qPCR were used to determine expression level of each gene and protein.

Results: Conditioned media (CM) derived from OmAd (OmAd-CM) significantly promoted proliferation and migration of GC cells compared to control media. OmAd-CM also reinforced the ability of GC cells inducing EC recruitment and tube formation. The cytokine array identified that GRO was abundantly contained in OmAd-CM and CXCL2 is the most expressed among GRO family. Silencing CXCL2 from OmAd (siCXCL2-OmAd) inhibited OmAd-induced cell growth and migration in both GC cell lines, as well as angiogenesis. In addition, OmAd-CM induced HIF1α and VEGF-A production of GC cells through AKT phosphorylation.

Conclusion: Omental adipocytes triggers GC cells on aggressive phenotype through CXCL2 secretion, which induces angiogenesis followed by cell growth and peritoneal metastasis.

Disclosure: Nothing to disclose

P0626 HOXA11 GENE IDENTIFIED BY DNA METHYLATION PROFILING AS PROGNOSTIC MOLECULAR MARKER IN HUMAN GASTRIC ADENOCARCINOMA

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Introduction: Gastric cancer is one of the most often diagnosed cancers worldwide with over 1,000,000 new cases annually. One of the most important epigenetic mechanism in the carcinogenesis is DNA methylation with 2 main processes of hypermethylation of tumor suppressor genes and hypomethylation of oncogenes.

Multiple studies have shown the importance of these changes as possible biomarkers for the early diagnosis, treatment effectiveness and disease progression in various cancers.

Aims & Methods: The aim of this study was to assess the DNA methylation status of selected genes in gastric cancer tissues samples and evaluate the prognostic importance of these genes. Patients (99) diagnosed with gas-

tric adenocarcinoma were included in the study. All patients underwent total or distal gastrectomy. Gastric cancer tissues and adjacent healthy gastric mucosa was taken from the surgical specimen. Genomic DNA was extracted from 25 to 40 mg of frozen tissues using"AllPrep DNA/RNA Kit" according to manufacturer's recommendation.

We selected a group of genes (*RAD51B, GFRA3, AKR7A3, HOXA11, TUSC3, FLI1, SEZ6L, GLDC, NDRG*) which are involved in cellular pathways such as signal transduction, apoptosis, cell to cell communication, cell cycles and cytokine signaling, are down-regulated in cancers and may be considered as potential tumor suppressor genes or oncogenes. Specific primers for methylated and unmethylated DNA sequence were designed using ''MethPrimer''. Methylation-specific polymerase chain reaction was performed in 25 ml of total volume. The presence of a Polymerase chain reaction product signal of the correct molecular weight indicates the presence of either unmethylated or methylated alleles.

Results: Only methylation of the *HOXA11* gene (Candidate tumor suppressor) promoter was significantly more frequent in gastric cancer tumor tissue (P = 0.006) than in adjacent healthy gastric mucosa. Limited significance (P = 0.054) was observed in *SEZ6L* gene (Tumor suppressor) promoter region comparing methylation frequency between gastric cancer tissue (50.5%) and healthy gastric mucosa (29.3%). The probability to survive longer was observed only with unmethylated *HOXA11* promoter in cancer tissues 71.2 months (95% CI 57-85.3) comparing to methylated cases with survival of 44.3 months (95% CI 34.8-53.9). Moreover, survival time was significantly shorter (28.5 months(95% CI 20.8-36.2) vs. 61.2 months (95% CI 50.9-71.4)) in gastric cancer patients, when methylation was observed in adjacent healthy gastric mucosa comparing to patients with methylation in one tissue alone (healthy gastric mucosa or gastric cancer tissue). Multivariate Cox analysis revealed the *HOXA11* methylation as significantly associated with gastric cancer patients' survival (HR=2.4, 95% CI 1.19-4.86).

Conclusion: DNA methylation of *HOXA11* gene promoter is more frequent in gastric cancer tumor tissue (68.7%) than in healthy gastric mucosa (39.4%) and is associated with shorter postoperative survival in patients diagnosed with gastric adenocarcinoma. Our results suggest that *HOXA11* gene might be a prognostic molecular marker in patients with gastric adenocarcinoma.

Disclosure: Nothing to disclose

P0627 DNA REPAIR GENE POLYMORPHISMS AS GENETIC MARKERS OF PROGNOSIS IN GASTRIC CANCER

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Introduction: Repair of DNA damage is a complex and crucial process involving multiple enzymes and pathways (base excision repair, mismatch repair, nucleotide excision repair, and double strand break repair). Defi-

ciencies in this system likely lead to genomic instability affecting cancer development and prognosis. Some specific polymorphisms in DNA repair genes have been reported to play a key role in the prognosis of gastric cancer (GC). However, results are inconsistent among studies.

Aims & Methods: Since allele frequencies differ notably among ethnicities, we aimed to assess the prognostic value (overall survival) of DNA repair gene polymorphisms on GC in a Caucasian population in Spain. Six hundred and three unrelated patients diagnosed with primary GC from January 2003 to December 2010 in a network of 16 general Spanish hospitals were included in the study. Genomic DNA from GC patients was typed for a panel of 120 single nucleotide polymorphisms (SNPs) located in 52 key DNA repair pathway genes by using the Illumina platform. Overal Survival (OS) among different genotype groups was estimated using the Kaplan-Meier method and compared using the log rank test. Moreover, Cox proportional hazards models were performed to evaluate the prognostic value of DNA repair gene polymorphisms on patient's survival. *Helicobacter pylori* infection and CagA/VacA antibody status were determined in serum by western blot.

Results: The median follow-up time for all GC patients in our study was 12.5 months (range: 0.3-124). Four hundred and eighty five GC patients (80.4%) had died at the end of the follow-up period (December 2017) with a median OS of 10.07 months (CI 95%: 6.65-9.42). For censored patients, the median OS was 45.07 months (CI 95%: 36.21-53.38). Of the environmental and clinicopathologic features evaluated in this study, Cox regression analysis identified tumor stages TNM III (HR:4.32, 95% CI:2.84-6.59) and IV (HR:9.27, 95%:6.2-13.85) as prognosis factors associated with significantly reduced OS in GC patients, whereas surgical treatment (HR:0.45, 95% CI:0.36-1.57), and chemotherapy (HR:0.52, 95%:0.39-0.68) were related to a better prognosis of the disease. Concerning gene polymorphisms, only the rs1799796A>G gene variant was associated with overall survival in GC patients after correction for multiple testing. This SNP is located in the *XRCC3* gene which encodes a member of the Rad51-related protein family that participates in the double-strand break repair pathway. We found that GC patients carrying the *XRCC3* rs1799796G variant showed a significantly higher OS than non-carriers (375 days vs.184 days; HR:0.7, 95% CI:0.57-0.86). Further stratification of GC patients by age, gender, smoking habit, *Helicobacter pylori* status, tumor location, histological type, TNM stage, treatment and Charlson index, showed no effect of gene variants on patient's survival.

Conclusion: Our data show that the specific *XRCC3* rs1799796G gene variant is relevant in determining the individual prognosis of gastric cancer in Caucasians.

Disclosure: Nothing to disclose

P0628 GENETIC POLYMORPHISMS OF PG2 GENE AND PG1/PG2 RATIO PREDICT THE PRESENCE OF GASTRIC CARCINOIDS IN AUTOIMMUNE ATROPHIC GASTRITIS PATIENTS

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Introduction: Autoimmune Chronic Atrophic Gastritis (ACAG) is epidemiologically and biologically linked to the development of gastric carcinoids type I (GCs) and gastric adenocarcinoma.
ACAG is often associated to other autoimmune disorders. The aim of the study was to evaluate the incidence of GCs development and to discover potential diagnostic markers related to GCs in patients (pts) with ACAG.

Aims & Methods: 141 pts with ACAG enrolled between years 2006-2017 and were evaluated by endoscopy for the presence of GCs. Pepsinogen I (PG1), Pepsinogen II (PG2) and Gastrin 17 (G17) serum levels were quantified using an enzyme-linked immune-sorbent assay kit. Serum levels of PGs and G17 were used to discriminate among pts with ACAG and pts affected by GCs in univariant and in multivariate analysis. A panel of genetic polymor-

phisms of PG2 gene and miRNA, that are known to modulate PG2 expression (rs9471643 C/G; rs6458238 A/G; rs8111742 A/G; rs121224 C/G; rs1002765 A/G; TATA-BOX length), was tested by real time PCR.

Results: Out of the 141 ACAG pts (26 M, 115 F; mean age 54,5), 21 (15 %) (4M, 17F) presented GCs. A secondary autoimmune disorder was displayed by 98 pts (69,5%) and autoimmune tyroiditis was the most frequent (61,9%). A statistically significant difference in PG1/PG2 and G17 levels was found between ACAG pts with or without GCs (r=-0,3768 95% CI-0,5499 to -0,1726 p=0,0005).
Although it is known that PG2 levels correlate with Helicobacter Pylori (HP) infection in our series of ACAG and GCs and ACAG pts there wasn't a statistical significant difference nor in number of HP positive (+) pts nor in IgG anti HP load (HP+ GCs pts 17,6%, HP+ ACAG pts 30,2%; GCs pts IgG anti HP mean 19,42 SD: ±27,71, ACAG pts IgG anti HP mean 33,43 SD: ±41,43 p=ns). Among the 6 genetic polymorphisms, we found that rs8111742 A/G, rs121224 C/G were associated to a difference in serum PG2 levels and GCs (p=0,0016 and p=0,0051). No significant differences were found between pts with tyroiditis and GCs and pts without tyroiditis and with GCs (6,3 % and 8,5 % p=0,07).

Conclusion: GCs are often diagnosed incidentally during endoscopy. We found a higher association between GCs type I and ACAG than data present in literature and of interest we found a statistically significant difference in PG1/PG2 and G17 levels between ACAG pts with or without GCs. The identification of a different level of PGs ratio and G17 in GCs-positive ACAG could be proposed as a potential indicative marker for a further endoscopic targeted evaluation for GCs in ACAG pts.

Disclosure: Nothing to disclose

P0629 EXPRESSION OF AKT, MTOR, VEGFR2, GSK3β IN GASTRIC CANCER, PRECANCEROUS LESIONS AND CONDITIONS

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Introduction: Gastric cancer (GC) is one of the leading causes of cancer deaths worldwide[1]. Unfortunately GC is often found when it is not curable [2]. GC development is a consecutive process which is called "Correa cascade", that describes development of GC from H.pylori chronic gastritis through atrophic changes, metaplasia, dysplasia to gastric cancer [3,4,5]. Prevention of GC development and diagnostic of early GC is a very important direction in modern gastroenterology, endoscopy and anticancer programs. More and more attention is paid to the molecular processes of GC development, especially to grow factor receptor pathway. Research in this field could help to understand more about this process and to improve diagnostic systems and targeted therapy.

Aims & Methods: Biopsy from 99 patients 22-93 years old admitted to Krasnoyarsk Regional Hospital were collected during gastroscopy. After histological assessment patients were divided in 4 groups: 1st group - chronic nonatrophic pangastritis (n=27), 2nd - chronic atrophic pangastritis with intestinal metaplasia (n=31), 3rd - chronic atrophic pangastritis with dysplasia (n=11), 4th - GC (n=30) with signet ring cell carcinoma (n=15) and adenocarcinoma (n=15). Undirected imminohistochemical analysis with fluorescent marking was done in order to reveal the expression of AKT, mTOR, VEGFR2, GSK3β molecules, TUNEL method was used to asses apoptosis level.

Results: Expression of AKT was significantly increased in patients with precancerous lesions and decrease in GC group (p1-3 = 0.0007, p2-3 = 0.006, p3-4 = 0.031). mTOR expression was decreased in GC group (p_{1-4} = 0.021, p_{3-4} = 0.05). Changes in VEGFR2, GSK3β expression was not statistically significant, but the tendency with maximal value in group with dysplasia and moderate decreasing in GC group was observed. There was no difference in expression in two types of cancer inside the GC group. The highest apoptosis level was observed in gastritis with metaplastic changes and lowest in GC group (p1-4 = 0.004, p2-4 = 0.021, p3-4 = 0.00002). These changes in molecules expression could mark the stages of tumor growth such as angiogenesis, decreasing of apoptosis and proliferation.

Conclusion: Changes in AKT/mTOR/VEGFR/GSK3β pathway is an early event in gastric mucosa transformation, could happen even on stage of precancerous conditions, lesions and mark the stages of each step of Correa cascade. AKT is responsible for cell growth and proliferation and high

level of mTOR expression could explain metabolic changes, low apoptosis level and cell survival which are inherent characteristics of malignant tumor. Further research is needed to understand more about molecular processes in GC development.

References: 1. Jemal, A., et al., Global cancer statistics. CA Cancer J Clin, 2011. 61(2): p. 69-90. 2. De Angelis, R., et al., Cancer survival in Europe 1999-2007 by country and age: results of EUROCARE--5-a population-based study. Lancet Oncol, 2014. 15(1): p. 23-34. 3. Li, S., et al., Endogenous molecular network reveals two mechanisms of heterogeneity within gastric cancer. Oncotarget, 2015. 6(15): p. 13607-27. 4. Correa, P. and M.B. Piazuelo, The gastric precancerous cascade. J Dig Dis, 2012. 13(1): p. 2-9. 5. Dinis-Ribeiro, M., et al., Management of precancerous conditions and lesions in the stomach (MAPS): guideline from the European Society of Gastrointestinal Endoscopy (ESGE), European Helicobacter Study Group (EHSG), European Society of Pathology (ESP), and the Sociedade Portuguesa de Endoscopia Digestiva (SPED). Endoscopy, 2012. 44(1): p. 74-94.

Disclosure: Nothing to disclose

P0630 RELEVANCE OF TOLL-LIKE RECEPTOR GENE POLYMORPHISMS TO GASTRIC CANCER RISK AND PHENOTYPE

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Introduction: The innate immune response constitutes the first line of defense against infection by microbes such as *Helicobacter pylori* (*H. pylori*). This system senses, recognizes, and responds to bacterial components by activating a complex signaling cascade of pattern-recognition receptors (PRRs), which include the Toll-like receptors (TLRs). Several polymorphic variants in *TLR* genes have been shown to affect responsiveness to *H. pylori* infection leading to an aberrant activation of the NF-kB pathway and up-regulation of pro-inflammatory molecule expression.

Aims & Methods: Given the relevance of *H. pylori* infection and chronic inflammation in gastric carcinogenesis, we aimed to assess the role of specific *TLR* gene polymorphisms on gastric cancer (GC) risk and phenotype in a Caucasian population in Spain. Genomic DNA from 673 unrelated Spanish patients with primary GC and 673 sex- and aged- (± 5 years) matched cancer-free healthy controls was typed for 26 single nucleotide polymorphisms (SNPs) in the *TRL1* (rs10004195, rs4833095, rs4833103, rs5743551), *TLR2* (rs5743708, rs121917864, rs1898830, rs3804099, rs3804100), TLR4 (rs4986790, rs4986791, rs11536889, rs10759932, rs16906079, rs2149356), *TLR5* (rs5744168, rs5744174, rs2072493), *TLR6* (rs5743810), *TLR8* (rs1980499, rs3764880), *TLR9* (rs5743836, rs352140, rs187084), and *TLR10* (rs11466657, rs4129009) genes by using the Massarray (Sequenon) platform. Analysis of genotyping data was performed by the bioinformatic tool SNPassoc (R). *H. pylori* infection and CagA/VacA antibody status were determined in serum by western blot in patients and controls.

Results: Logistic regression analysis identified *H. pylori* infection with CagA strains (OR: 2.13; 95% CI: 1.68-2.69), smoking habit (OR: 1.82; 95% CI: 1.29-2.55) and positive family history of GC (OR: 2.83; 95% CI: 1.89-4.23) as independent risk factors for GC. Concerning gene polymorphisms, the most remarkable association was observed in the *TLR2* gene with the G allele of rs1898830 being associated with a higher risk of GC (log-additive model OR: 1.21; 95% CI: 1.06-1.42). Moreover, the *TLR1* rs10004195T>A polymorphism, previously reported to be related with *H. pylori* seroprevalence, was significantly associated with susceptibility to *H. pylori* infection in our control population (recessive model OR: 0.70; 95% CI: 0.51-0.97). No significant differences in carriage, genotype, and allele frequencies of the *TLR* gene polymorphisms were found when GC patients were categorized according to gender, age, smoking habit, *H. pylori infection*, CagA/VacA antibody status, family history of GC, tumor location, and histological subtype.

Conclusion: Our data show that the *TLR2* rs1898830A>G gene polymorphism is involved in defining the genetic basis of the risk to GC, and support the relevance of *TLR1* rs10004195 gene variant on *H. pylori*-infection susceptibility.

References: 1. Meliț LE, Mărginean CO, Mărginean CD, Mărginean MO. (2019) The Relationship between Toll-like Receptors and Helicobacter pylori-Related Gastropathies: Still a Controversial Topic. J Immunol Res. 8197048. eCollection 2019. 2. Castaño-Rodríguez N, Kaakoush NO, Mitchell HM. (2014) Pattern-recognition receptors and gastric cancer. Front Immunol. 5:336. eCollection 2014. 3. Mayerle J, den Hoed CM, Schurmann C, Stolk L, Homuth G, Peters MJ et al. (2013) Identification of genetic loci associated with Helicobacter pylori serologic status. JAMA. 309:1912-20.

Disclosure: Nothing to disclose

P0631 PLASMA LONG NONCODING RNAS PANDAR, FOXD2-AS1, AND SMARCC2 AS POTENTIAL NOVEL DIAGNOSTIC BIOMARKERS FOR GASTRIC CANCER

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Introduction: Gastric cancer is still a common cancer worldwide. Investigation of potential plasma biomarkers for gastric cancer diagnosis is essential for prevention strategies and early intervention for gastric cancer-control planning.

Aims & Methods:

Objectives: This study was aimed to explore the lncRNAs PANDAR, FOXD2-AS1, and SMARCC2 as potential novel diagnostic biomarkers for gastric cancer.

Method: 109 gastric cancer patients and 106 healthy controls were involved in this study. Plasma lncRNAs PANDAR, FOXD2-AS1, and SMARCC2 were detected by real-time PCR. Student's *t*-test, Mann-Whitney U test, and Chi-square test were used to verify the differences of clinical variables between two groups. Receiver operating characteristic curve (ROC) was used to evaluate the diagnostic value of every biomarker. Multivariable analysis of risk factors for gastric cancer was performed using logistic regression analysis.

Results: There were significant differences in age, gender, CEA, CA153 between gastric cancer and healthy controls ($P < 0.05$). Comparing with healthy subjects, the levels of plasma lncRNAs PANDAR, FOXD2-AS1, and SMARCC2 were all significantly higher in gastric cancer patients ($P < 0.05$). These lncRNAs were significantly associated with clinicopathological parameters of gastric cancer, like pathological differentiation, TNM stage, and/or lymph nodes metastasis, and/or invasion depth ($P < 0.05$). The AUC for lncRNA PANDAR was 0.767, for FOXD2-AS1 was 0.700, for SMARCC2 was 0.748, and the AUC of the combinative diagnostic value of these three lncRNAs was 0.839. Adjusted by other variables, these lncRNAs expression were significantly associated with gastric cancer.

Conclusion: Plasma lncRNAs PANDAR, FOXD2-AS1, and SMARCC2 might be appropriate diagnostic biomarkers for gastric cancer.

Disclosure: Nothing to disclose

P0632 THE OBESTATIN/G-PROTEIN COUPLED RECEPTOR 39 (GPR39) SYSTEM IS INVOLVED IN THE PROLIFERATION OF GASTRIC CANCER CELL LINES

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Introduction: Obestatin is a 23-aminoacid peptide derived from pre-proghrelin, was isolated from the stomach in 2005 and binds to the GPR39 receptor. Our group has described the expression of the obestatin/GPR39 system in healthy human stomach, as well as in gastric adenocarcinoma, where we have shown a role in both the pathogenicity and the prognosis of this tumor. The obestatin/GPR39 system regulates proliferation, epithelial-mesenchymal transition, migration capacity, invasion and metastasis in the AGS cell line, which derives from a moderately differentiated adenocarcinoma. The GPR39 expression levels found in human gastric adenocarcinomas provide the basis for including GPR39 as a prognostic marker for these tumors.

Aims & Methods: The objective of this study is to evaluate the involvement of this system in the proliferation of cell lines of human pancreatic cancer with different degrees of differentiation: the AGS cell line, a moderately differentiated adenocarcinoma; the KATO III cell line, a poorly differentiated adenocarcinoma; and the NCI-N87 cell line, a liver metastasis of a well-differentiated adenocarcinoma.

The analysis of the obestatin/GPR39 system expression in the tumor the cell lines (AGS, KATO-III and NCI-N87) was performed by using immunocytochemical techniques. In addition, cell proliferation assays were performed after obestatin treatment (100 nM) by BrdU incorporation (AGS and NCI-N87) and manual counting (AGS and KATO-III). 10% FBS was used as positive control.

Results: All the studied cell lines strongly expressed the obestatin/GPR39 system. No immunostaining was shown in negative controls incubated without primary antibody. Obestatin (100 nM) exerted a mitogenic effect in the AGS line (46,2 8,66% over control; p< 0,01), the NCI-87 cells (60,82 2,83% over control; p< 0,001) and in the KATO-III cell line (44,00 3,10% over control; p< 0,01).

Conclusion: This study offers two main findings:

1. The obestatin/GPR39 system is intensely expressed in tumor cell lines of the human stomach;

2. The exogenous obestatin treatment increased the proliferation of these cell lines, with no differences between the different cell lines. The obtained results showed that the obestatin/GPR39 system is involved in the proliferative processes in gastric cancer.

Disclosure: Nothing to disclose

P0633 WITHDRAWN

P0634 SPORADIC DUODENAL BULB NEUROENDOCRINE TUMORS - GASTRIN(G)-CELLS TUMORS ASSOCIATED TO HELICOBACTER PYLORI AND MICRONODULAR G-CELLS HYPERPLASIA

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Introduction: Sporadic duodenal neuroendocrine tumors (NETs) are relatively rare tumors of the gastrointestinal tract, but their incidence shows gradual increase in recent histopathological series. Gastrin-producing cells (G-Cells) NETs is the most frequent, though little is known about the features involved in its pathogenesis.

Aims & Methods: Considering the role of atrophic gastritis and Helicobacter pylori (Hp) infection in antral G-cells hyperplastic changes, we aimed to investigate the relationship between these factors and the development of sporadic bulb NETs. A prospective, case-control study was performed with 77 patients: 13 bulb NETs patients and 64 controls, randomly selected (28 chronic atrophic gastritis, CAG; 21 chronic superficial gastritis; and 15 normal subjects). All participants underwent upper gastrointestinal endoscopy with biopsies (antrum, corpus and bulb). Gastritis pattern was accessed. Bulb samples were evaluated for D- and G-cells quantification and G-cells hyperplastic changes. Hp infection was determined in both locations. Baseline biodemographic variables were also analysed.

Results: All NETs were G-cells tumors, small in size (median 7 mm), restricted up to submucosa, resected by mucosectomy, with no evidence of dissemination at diagnosis or during follow-up. At multivariate analysis, gastric Hp infection (OR=8,2; p=0,022), duodenal Hp infection (OR=16; p=0,027) and bulbar G-cells linear/micronodular hyperplasia (OR=79; p=< 0,001) were independent predictors of G-cells NETs development. Additionally, bulbar G-cells linear/micronodular hyperplasia had a significant association with chronic use of proton pump inhibitors (*p*=0.018). Both, NETs and G-cells hyperplasia, were not associated with body CAG.

Conclusion: Data reinforced that sporadic G-cells NETs may originate from a proliferative phase sequence. Our data suggests that Hp and related inflammation, seems the most important factor in our population. Its involvement as cause or epiphenomena in bulb G-cells hyperplasia and tumor should be further studied.

Disclosure: Nothing to disclose

H. Pylori I

10:30-17:00 / Poster Exhibition - Hall 7

P0635 PREVALENCE OF HELICOBACTER PYLORI INFECTION IN NONDIABETIC NAFLD AND IT ASSOCIATION IN SEVERITY OF FIBROSIS

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Introduction: Nonalcoholic fatty liver disease (NAFLD) is one of the most common causes of cirrhosis worldwide. A considerable amount of patients without DM still has NASH and advanced fibrosis. Helicobacter pylori (H. pylori) infection contribute to the increase in levels of pro-inflammatory cytokines which have different metabolic effects and associated with insulin resistance (IR). Therefore, H. Pylori may possibly have an effect on fibrosis progression in NAFLD in nondiabetic patients.

Aims & Methods: Investigate the prevalence of H. pylori infection in nondiabetic NAFLD patient and its association in advance fibrosis.

Nondiabetic patients who were diagnosed NAFLD by abdominal ultrasonography and/or controlled attenuation parameter (CAP) from FibroScan® were recruited for H. pylori infection testing by a 14C-urea breath test. All participants were evaluated liver fibrosis with transient elastography. They were collected standard biochemical test (eg. FPG, LDL, liver function test) and interleukin-6 to evaluate the inflammatory response. To minimized the confounding effect, we excluded patients who had BMI > 28 kg/m2 or

received steatogenic drugs. The outcome was the prevalence of H. pylori infection in NAFLD patients. We also investigated factors which independently associated with advanced fibrosis.

Results: A total of 117 NAFLD patients were enrolled. We found overall H. pylori infection in 54 patients (46%). In patients with advanced fibrosis (defined as fibrosis stage > 3 from transient elastography), the prevalence of advanced hepatic fibrosis in NAFLD patients with H. pylori infection is higher (22/54, 40.7%) than in non-infected group (18/63, 28.6%). Obesity was the variable most associated with advanced fibrosis (OR 3.18 [1.25-8.09], p-value 0.02) in univariate analysis. H. pylori infection had a marginal effect to advanced fibrosis (OR 1.72 [0.8-3.71], p-value 0.17) but no statistically significant in multivariate analysis. Other metabolic variables and interleukin-6 were not significantly associated with advanced fibrosis.

Conclusion: Prevalence of H. pylori infection in nondiabetic NAFLD patient similar to the general Thai population. Our results could not demonstrate the risk of H. pylori infection to advanced fibrosis. However, NAFLD patients with H. pylori infection tend to have a higher prevalence of advance hepatic fibrosis.

Disclosure: Nothing to disclose

P0636 STUDY OF THE HIPPO SIGNALLING PATHWAY IN GASTRIC CARCINOGENESIS INDUCED IN RESPONSE TO *HELICOBACTER PYLORI* INFECTION

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Introduction: Gastric cancer is the third leading cause of cancer-related death worldwide and *Helicobacter pylori* is recognised as its main risk factor. We have reported that *H. pylori* infection leads, through an epithelial mesenchymal transition (EMT), to the emergence of CD44+ cells with cancer stem cell (CSC) properties. The Hippo tumour suppressor pathway and its oncogenic targets YAP/TAZ control cancer initiation and progression in many cancers.

Their regulation in the context of *H. pylori*-mediated gastric carcinogenesis has not been described. We hypothesized that TAZ could be involved in the EMT process and CSC-like cells generation observed during *H. pylori* infection.

Aims & Methods: The aim of this project was to investigate the role of TAZ during the EMT and the emergence of CSC induced by chronic infection with *H. pylori* and during gastric carcinogenesis.

The consequences of TAZ inhibition were studied on *H. pylori*-induced EMT and CSC signature and properties in gastric epithelial cell lines *in vitro*. The consequences of TAZ inhibition by a siRNA strategy were studied in MKN45 and NCI-N87 gastric epithelial cell lines infected or not with the carcinogenic *H. pylori* strains 7.13 and P12 as well as *cag*A and *cag*PAI isogenic mutants. The expression of Hippo/TAZ/TEAD pathway related genes and of EMT/CSC markers was assessed by RTqPCR, western blot and immunofluorescence. TAZ/TEAD transcriptional activity was evaluated by TEAD-luciferase reporter assay. EMT and CSC functional properties were evaluated by invasion and tumorsphere assays *in vitro*.

Results: We showed that *H. pylori* infection transiently stimulates TAZ nuclear translocation and co-transcriptional activity in a CagA-dependent manner. TAZ inhibition reduced EMT markers expression, which correlated with a decrease of invasive properties induced upon *H. pylori* infection. Moreover, TAZ inhibition reduced spheroid formation which involves the CSC sub-population.

Conclusion: The Hippo/TAZ pathway is activated upon *H. pylori* infection in gastric epithelial cells and TAZ activation participates to the regulation of *H. pylori*-induced EMT and CSC invasive and tumorigenic properties.

Disclosure: Nothing to disclose

P0637 HIGH CONCORDANCE RATES OF PREMALIGNANT GASTRIC LESSIONS ASSESED BY OLGA AND OLGIM IN MONOZYGOTIC AND DYZIGOTIC TWINS

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Introduction: The development and progression of chronic *H.pylori* gastritis toward pre-neoplastic gastric lesions is a multifactorial process, which depends on interactions between environmental factors, *H.pylori* infection, gastric microbiota and host genetic factors. To date, there are no studies that would evaluate the role of shared genetic influences on susceptibility and phenotype of chronic *H.pylori* gastritis and premalignant gastric alterations in twins.

Aims & Methods: To compare histological alterations of gastric mucosa according to Sydney classification, OLGA and OLGIM staging systems in monozygotic and dizygotic twins. This prospective study included 58 individuals with 13 pairs of monozygotic and 16 pairs (11 same- sex pairs and 5 mixed- sex pairs) of dizygotic twins aged >18 years. Endoscopy for both twins was performed simultaneously on the same day. At endoscopy 5 biopsy specimens were collected: 2 from the greater and lesser curvatures of antrum, 1 from incisura angularis, 2 from the anterior and posterior walls of the corpus. *H. pylori* gastritis was assessed by histology and graded by OLGA and OLGIM staging systems.

Results: Mean age of monozygotic and dizygotic twins was 41.23 y and 38.43 y, respectively. Total prevalence of *H.pylori* was 53.4%. Among monozygotic twins, six pairs were both positive, three pairs were both negative and four pairs were discordant for the presence of *H.pylori*. Among dizygotic twins, four pairs were both positive, five pairs were both negative and seven pairs were discordant for presence of *H.pylori*. Concordance rate for chronic *H.pylori* gastritis in monozygotic twins was 69.2 % (9/13 pairs) and in dizygotic twins 62.5% (10/16 pairs), p>0.05. Concordance for antrum athrophy in monozygotic twins was 76.9 % and 75 % in dizygotic twins (p> 0.05). Concordance for corpus athrophy in monozygotic twins was 92.3% and in dizygotic twins 87.5% (p>0.05). Concordance for antrum IM in monozygotic twins was 84.6% and in dizygotic 75 % (p> 0.05). Concordance for corpus IM in monozygotic twins was 84.6 % and in dizygotic 93.7 % (p> 0.05). There was no statistical difference in concordance rates for OLGA and OLGIM stages both for monozygotic and dizygotic twins.

Conclusion: Histological gastric mucosa alterations related to *H.pylori* gastritis and premalignant lesions in monozygotic and dizygotic twins show high rates of concordance.

Disclosure: Nothing to disclose

P0638 WITHDRAWN

P0639 *HELICOBACTER PYLORI*-DERIVED MEMBRANE VESICLES MODIFY GASTRIC EPITHELIAL CELLS GENE EXPRESSION

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Introduction: The stomach-colonizing Gram-negative bacterium *Helicobacter pylori* establishes a life-long infection in humans, infecting more than half of the world population. *H. pylori* is the main etiological factor of several gastroduodenal diseases, including chronic gastritis, peptic ulcers, gastric mucosa-associated lymphoid tissue lymphoma, gastric adenocarcinoma, and more recently it has been associated with some extra-gastric diseases.

Gram-negative bacterial membrane vesicles are nanosized vesicles ranging from 20 nm to 300 nm that are secreted by virtually all bacteria. They constitute a successful strategy used by bacteria to manipulate host cell functions important for their survival, colonization, and persistence in the host with implications in bacteria-mediated pathogenesis.

Aims & Methods: The effect of bacterial membrane vesicles on host gene expression is poorly understood. Thus, the aim of this study was to investigate the impact of *H. pylori*-derived membrane vesicles uptake by gastric epithelial cells in the modulation of gene expression. Total RNA was isolated from the human gastric epithelial cell line MKN74 either unchallenged (N=3) or challenged (N=6) for 24 hours with membrane vesicles isolated from the *H. pylori* 26695 strain. A targeted RNA sequencing analysis covering 20,000 human genes was performed using the Ion Ampliseq Transcriptome kit. Differential expression analysis between unchallenged and challenged MKN74 cells was performed using the DESeq R package. Overrepresentation of gene ontology terms was determined using topGO.

Results: Our results show that ~1% (224/20,000) of the interrogated genes were differentially expressed between unchallenged and membrane vesicle-challenged MKN74 cells (adjusted P-value < 0.05), of which 99 genes were downregulated and 125 genes were upregulated. Enrichment analysis of the top forty differentially expressed genes (20 up- and 20 down-regulated) were clustered to gene ontology terms such as cytoskeleton and extracellular region for cellular components; growth factor and cytokines activity, protein binding, signalling receptor and protein kinase binding for molecular functions, and; regulation of phosphorylation, regulation of apoptotic process, signal transduction, and cell cycle regarding biological processes.

Conclusion: In summary, our findings show that *H. pylori*-derived membrane vesicles are able to modify gene expression of the gastric epithelial cell line MKN74, suggesting a role for these vesicles in the bacteria-mediated pathogenesis.

Disclosure: Nothing to disclose

P0640 Helicobacter pylori-ACTIVATED GASTRIC FIBROBLASTS INDUCE EPITHELIAL-MESENCHYMAL TRANSITION OF GASTRIC EPITHELIAL CELLS IN A TRANSFORMING GROWTH FACTOR BETA-DEPENDENT MANNER

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Introduction: Colonization of the gastric mucosa with *Helicobacter pylori (Hp)* leads to the cascade of pathologic events including local inflammation, gastric ulceration and adenocarcinoma formation. Paracrine loops between tissue cells and *Hp* have recently been implicated in the formation of gastric cancerous loci, however, the specific mechanisms underlying existence of these loops remain unknown. Here, we determined the phenotypic properties of gastric fibroblasts recently considered as the target for *Hp* (cagA+vacA+) infection and their influence on normal epithelial RGM-1 cells.

Aims & Methods: RGM-1 cells were cultured in the media conditioned with *Hp*-activated gastric fibroblasts. Their morphology and phenotypical changes associated with epithelial-mesenchymal transition (EMT) were assessed by Nomarski contrast microscopy, fluorescent microscopy and Western Blot analysis. Motility pattern of RGM-1 cells in infected and non-infected fibroblast supernatant was examined by time-lapse videomicroscopy, and by transwell migration assay. The content of TGFβ in *Hp* activated fibroblasts conditioned media was determined by ELISA.

Results: The supernatant from *Hp*-activated gastric fibroblasts caused the EMT-like phenotypic diversification of RGM-1 cells. In particular, the formation of fibroblastoid cell sub-populations was observed along with disappearance of their collective migration. These cells were characterized by efficient movement, increased transmigration potential, thick actin stress fibers developement and decreased proliferation activity. Concomitantly, we observed the downregulation of E-cadherin protein, upregulation of N-cadherin protein and the increased TGFβ level in the secretome of *Hp*-activated gastric fibroblasts. The fibroblast-CAF like transition was

manifested by increased level of α-SMA protein and its incorporation into stress fibers. The actin fibers dispersion characteristic for *Hp* (cagA+ vacA+) infection correlated with Snail mRNA upregulation.

Conclusion: Gastric fibroblasts which are one of the main targets for *Hp* infection contribute to the paracrine interactions between *Hp*, gastric fibroblasts and epithelial cells. TGFβ secreted by *Hp*-activated gastric fibroblasts prompting their differentiation towards CAF-like phenotype promotes the EMT-related phenotypic shifts in normal gastric epithelial cell populations. This mechanism may serve as the prerequisite for gastric cancer development.

Disclosure: Nothing to disclose

P0641 TLR4 RS4986791 GENE POLYMORPHISM AND *HELICOBACTER PYLORI* INFECTION IN CHILDREN

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Introduction: *TLR4* is involved in the development of *H. pylori* induced gastropathies, but also in gastric carcinogenesis.

Aims & Methods: The aim of the study was to assess the clinical, endoscopic, and socioeconomic aspects, but also *TLR4* rs4986791 gene polymorphism in children with *H. pylori* gastritis.
Methods. We performed a prospective study on 147 children admitted in a Pediatric Tertiary Gastroenterology Department from Romania, divided into 2 groups according the presence, or absence of *H. pylori* infection: group 1 - 50 children with *H. pylori* associated gastritis and group 2 - 97 children with gastritis without *H. pylori* infection.

Results: We observed that poor socioeconomic status was a significant risk factor for *H .pylori* infection (p=0.002, OR=4.03, 95% CI: [1.71; 9.50]). We found that the most frequent symptoms in patients with gastritis were epigastric pain, abdominal pain, heartburn, but without significant differences between the two groups.
We identified significant correlations between the histopathological exam and rapid urease test (p< 0.001). The variant genotype of *TLR4* rs4986791 gene polymorphism was a protective factor against *H. pylori* infection, but without statistical significance.

Conclusion: Socioeconomic status is a risk factor for *H. pylori* infection. The rapid urease test is a useful diagnostic tool for *H. pylori* infection. The variant genotype of the *TLR4* rs4986791 gene polymorphisms might be a protective factor against *H. pylori* infection in children, but further studies are necessary in order to clearly identify its role.

References: 1. Castaño-Rodríguez N, Kaakoush NO, Goh K-L, Fock KM, Mitchell HM. The role of TLR2, TLR4 and CD14 genetic polymorphisms in gastric carcinogenesis: a case-control study and meta-analysis. PLoS ONE. 2013;8(4):e60327. doi:10.1371/journal.pone.0060327 2. Meliţ LE, Mărginean CO, Mărginean CD, Mărginean MO. The Relationship between Toll-like Receptors and Helicobacter pylori-Related Gastropathies: Still a Controversial Topic. Journal of Immunology Research. doi:10.1155/2019/8197048 3. Khakzad MR, Saffari A, Mohamadpour N, et al. TLR4 and TLR2 expression in biopsy specimens from antral and corporal stomach zones in Helicobacter pylori infections. Rep Biochem Mol Biol. 2014;3(1):29-37.

Disclosure: Nothing to disclose

P0642 DETECTION OF *HELICOBACTER PYLORI* INFECTION IN GASTRIC BIOPSIES USING REAL-TIME PCR

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Introduction: *Helicobacter pylori* (*H. pylori*) is classified as a Class 1 carcinogen. Eradication of *H. pylori* is therefore imperative to prevent the natural progression of disease and help restore the gastric mucosa from peptic pathologies. Apart from non-invasive testing using breath testing and stool sampling, the use of the rapid-urease test (RUT) during oesogastroduodenoscopy (OGD) is widely practiced. Whilst previously pansensitive, there is mounting evidence showing increased resistance of *H. pylori* to standard antibiotic regimens, which has resulted in reduced eradication rates.
Aims & Methods: To compare *H. pylori* detection through real-time polymerase chain reaction (RT-PCR) to the RUT done during OGD and determine the antibiotic sensitivity for quinolones and clarithromycin.
Method: Patients above 18 years of age, scheduled for an elective OGD were considered for recruitment. Exclusion criteria included: previous *H. pylori* treatment and antibiotic usage within the preceding three months. Two biopsies from the antrum and two from the corpus were collected. All four biopsies were combined and digested with tissue-lysing buffer and Proteinase K. Automated DNA extraction was performed followed by RT-PCR for *H. pylori* DNA detection. Positive samples were tested for clarithromycin and fluoroquinolones resistance using amplification and reverse hybridization techniques. Data regarding the result of RUT performed during the OGD was also noted.
Results: 200 patients (range 20-92 years) were recruited (females = 53.1%) Real-Time PCR detected *H. pylori* in 21% of patients compared to the 29.5% detection rate by the RUT. A positive RUT and a positive RT-PCR result was observed in 17.0% of patients while 12.5% of patients had a positive RUT result but a negative RT-PCR result. Furthermore, 4.0% of patients had a negative RUT but a positive RT-PCR result. Additionally, detection of *H. pylori* was also performed using reverse hybridization techniques with determination of its antibiotic susceptibilities. *H. pylori* was detected in 19.5% of total patients using this secondary molecular technique.
Fluoroquinolone resistance was present in 21.4% of patients and 26.2% of patients exhibited clarithromycin resistance, while dual resistance to both clarithromycin and fluoroquinolones was detected in another 4.8% of patients.
Conclusion: This data demonstrates similar *H. pylori* detection rates using RT-PCR and/or reverse hybridisation techniques but lower rates than the RUT. Moreover, our data also demonstrates a high resistance rate to both clarithromycin and fluoroquinolones. Such modern techniques should be considered to replace the RUT, to avoid unnecessary antibiotic prescription due to false-positive results. This would therefore ensure the prescription of adequate antibiotic regimens when *H. pylori* infection is in fact present.
Disclosure: Nothing to disclose

P0643 WITHDRAWN

P0644 EVALUATION OF *HELICOBACTER PYLORI* POSITIVITY BY MOLECULAR-BIOLOGY METHODS IN GASTRIC BIOPSY SAMPLES FROM DISCREPANT CASES TESTED BY SEROLOGY AND HISTOLOGY

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Introduction: In gastric mucosal atrophy *H. pylori* density may be decreasing leading to false-negative histology results. Therefore, *Maastricht V* guidelines (Malfertheiner et al., 2016) accept the use of serogical tests for non-invasive *H. pylori* diagnosis.
Aims & Methods: To evaluate the presence/absence of *H. pylori* by molecular methods in subjects with discrepant histology and serology result. Individuals with discrepant serology/histology result (group 1 - positive-serology, but negative-histology, group 2 - negative-serology, but positive-histology) were selected from a GISTAR pilot-study database. Subjects having received *H. pylori* eradication therapy in life-time or reporting use of proton pump inhibitors, antibacterial medications, bismuth containing drug use one month prior upper endoscopy were excluded.
Antibodies to *H. pylori* were assessed in plasma by enzyme-linked immunosorbent assay (ELISA). *H. pylori* deoxyribonucleic acid (DNA) detection in frozen biopsy sample was performed using a real-time polymerase chain reaction (PCR) as a gold standard. Immunohistochemistry (IHC) was performed in subjects with postive-histology and negative-serology. Presence of inflammation was evaluated according to mucosal neutrophil infiltration, subjects with stage II or III in any of biopsies was considered as a group with inflammation, meanwhile 0 or I in all biopsies - as group without inflammation.
Results: The final patient sample for analysis contained data from 97 individuals: serology-positive/histology-negative cases: 81, serology-negative/histology-positive: 16. Among the first group there were approximately one fifth (21.0%) falsely positives by serology, while in the second group there were 6.3% false positives by histology. In the PCR positive group six of 15 (or 40%) gastric mucosa showed no inflammation in all biopsies but the majority (14 subjects) had ICH positive results.
The overall analysis of *H. pylori* tests' discrepant cases are shown in the Table.

Serology/ histology result	PCR result	Number of cases n/total (%)	Inflammation present in any of biopsies n/ total (%)	Inflammation absent in all biopsies n/total (%)
Serology positive, histology negative cases	PCR positive	17/81 (21.0)	1/17 (5.9)	16/17 (94.1)
	PCR negative	64/81 (79.0)	1/64 (1.6)	63/64 (98.4)
Serology negative, histology positive cases	PCR positive	15/16 (93.8)	9/15 (60.0)	6/15 (40.0)
	PCR negative	1/16 (6.3)	0/1	1/1 (100)

[Table. Analysis for total patient sample in H. pylori tests' discrepant cases.]

Conclusion: Among this high *H. pylori* prevalence middle-aged population, the majority of discrepant cases between serology and histology were rather due to false positive-serology than false-negative histology. This could be explained by possible loss of bacterium due to atrophic changes in mucosa.
Disclosure: Nothing to disclose

P0645 CLINICAL ASPECTS AND THE ROLE OF ADIPOKINES IN GALLSTONE DISEASE IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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Introduction: Close relationship between non-alcoholic fatty liver disease (NAFLD) and gallstone disease (GD) has been proved. Being aware of the specific features of the diseases the issue remains burning due to constant increase of patient number because of elevating the metabolic risk factors among the population, including obesity, overweight, diabetes mellitus type 2, dyslipidemia, etc.

Aims & Methods:
Objective: Update the comorbidity information about NAFLD and GD, evaluation of clinical and laboratory data, including insulin, leptin and adiponectin in patients with NAFLD in combination with GD.

Materials and methods: According to the design, the open comparative study with 215 patients with NAFLD was conducted. The following comparison groups were formed: group 1 (n = 94) -patients with NAFLD without GD, group 2 (n = 63) - patients with NAFLD and GD and group 3 (n = 58) - patients with NAFLD, GD and previous cholecystectomy.

Results: A high prevalence of coronary heart disease was detected in the group of patients with
GD and cholecystectomy (X_2=6.198, p≤0.05); positive, statistically significant correlation
relationships of cholelithiasis, cholecystectomy with ischemic heart disease (rs = 0.172, p≤0,05 and rs=0.241, p≤0.05, respectively). There was a statistically significant decrease in total bilirubin and total protein in patients in group 3 (H=7.376, p≤0.03 and H=6.345, p≤0.04). Insulin and leptin resistance were registered in patients with NAFLD and GD: insulin level 14.5 (7.12-35.78) mkED/ml), HOMA-IR (5.23(2.35-11.45)), leptin (14.53(9.56-28.67) ng/ml), its soluble receptors (8.03(3.98-9.45) ng/ml). There was a statistically significant increase in adiponectin (U=1106, p≤0.05) for patients with NAFLD and GD. The level of leptin was statistically significantly higher and positively interrelated with cholecystectomy (H=5.812, p≤0.05, rs=0.313, p≤0.05).

Conclusion: Patients with NAFLD, GD and previous cholecystectomy have a high incidence of coronary heart disease; the phenomenon of insulin and leptin resistance, a high level of adiponectin were determined in patients with NAFLD and gallstone disease; hyperleptinemia was registered in patients with NAFLD and GD after cholecystectomy.

Disclosure: Nothing to disclose

P0646 GASTRIC CANCER DETECTION RATES IN ACCORDANCE WITH THE INFECTION STATUS OF *HELICOBACTER PYLORI* UPON KYOTO CLASSIFICATION OF GASTRITIS BY TRANSNASAL SCREENING ENDOSCOPY

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Introduction: *Helicobacter pylori* (Hp) infection is the principal pathogenic cause of gastric cancer (GC), and eradication of Hp has been expected to decrease the incidence of GC. The recent rapid decline of Hp infection rate and global standardization of eradication therapy may affect the efficiency of GC diagnosis for screening endoscopy. We previously reported the increasing numbers of GC cases without Hp infection[1], however, the GC detection rate in accordance with Hp infection status on screening endoscopy is not elucidated.

Aims & Methods: We performed a single-center retrospective study to examine the GC incidence rate in accordance with Hp infection status for examinees of screening endoscopy from April 2014 to March 2018. All examinees were screened for GC using ultrathin endoscopes mostly inserted transnasally, and Hp infection status was also diagnosed by Kyoto classification of endoscopic gastritis into three groups as Hp-infected, Hp-past infected (mostly post Hp eradication), and Hp-uninfected. Clinical and pathological characteristics of GC cases and GC detection rate of each group were investigated.

Results: During the study period, 28894 examinees (11622 females, 40.0%) were screened. Among them, 14402 (49.8%) were under the age of 50, and 476 (16.5%) were over the age of 70. Those who were examined annually for more than 2 years were 84.9% (24532 examinees). All the examinees were diagnosed into three groups as Hp-infected (2843, 9.8%), Hp-past infected (8239, 28.5%), and Hp-uninfected (17812, 61.6%), based upon Kyoto classification of endoscopic gastritis. Forty-eight GC cases (0.17%) were detected consisting of 16 cases of Hp-infected, 14 of Hp past-infected, and 18 of Hp-uninfected. All GC cases were treated endoscopically or surgically, and 46 cases were early cancers. Accordingly, CG detection rate in accordance with Hp infection status was 0.56% for Hp-infected, 0.17% for past-Hp infected, and 0.10% for Hp-uninfected. Both the past-Hp infected and the Hp-uninfected groups showed significantly lower detection rates of GC (p< 0.001, chi-square tests) than the Hp-infected group.

Conclusion: Our study elucidated that Hp eradication could decrease the incidence of GC drastically. However, unignorable numbers of early GC cases were also detected among the Hp-past infected and Hp-uninfected examinees, indicating that the screening intervals should be optimized in accordance with the Hp infection status. Our study has limitations because of the single-center study and of a large proportion of repeated examinees.

References: 1) Gastroenterology, Vol. 152, Issue 5, S260-S261

Disclosure: Nothing to disclose

P0647 THE EFFICACY OF LOW-DOSE RADIATION THERAPY IN PATIENTS WITH *HELICOBACTER PYLORI*-NEGATIVE OR ERADICATION THERAPY-RESISTANT LOCALIZED GASTRIC MUCOSA-ASSOCIATED LYMPHOID TISSUE LYMPHOMA

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Introduction: Gastric mucosa-associated lymphoid tissue (MALT) lymphoma is considered to be closely related to *Helicobacter pylori* (*H. pylori*) infection. Although eradication of *H. pylori* is the mainstay of treatment for patients with gastric MALT lymphoma, 20% of them cannot be cured by eradication therapy. And treatment for patients with *H. pylori*-negative or eradication therapy-resistant gastric lymphoma has not yet been established.

Aims & Methods: The aim of this study is to assess the efficacy of low-dose radiation therapy on *H. pylori*-negative or eradication therapy-resistant MALT lymphoma. We enrolled patients with gastric MALT lymphoma from January 1994 through April 2018. The diagnosis was made based on morphological and immunophenotypic analysis of biopsies obtained from gastric lesions on esophagogastroduodenoscopy (EGD) in accordance with the current WHO classification. Patients with localized (stages I and II) gastric MALT lymphoma according to the Lugano classification were eligible for enrollment. Patients were also examined to confirm *H. pylori* infection status. Those with *H. pylori* infection received eradication therapy. And patients who were not cured by eradication therapy were categorized into eradication therapy-resistant cases. Patients with *H. pylori*-negative or eradication therapy-resistant MALT lymphoma received low-dose radiation therapy. A total dose of 30 Gy was administered and the fraction size was 1.5 Gy for 20 days. Response assessment was carried out every 3-6 months by EGD, various imaging techniques, and clinical examination. Patients with no endoscopic abnormality and no atypical lymphocytes detected by biopsy at endoscopic follow-up were considered to have achieved complete remission (CR). Patients with atypical lymphocytes detected by biopsy were diagnosed as having partial remission (PR).

Results: A total of 112 patients with gastric MALT lymphoma were enrolled. The median follow-up period was 76.4 months. 67 of them had *H. pylori* infection. 54 of those *H. pylori*-positive patients were successfully cured

by eradication therapy. 40 patients with *H. pylori*-negative or eradication therapy-resistant MALT lymphoma received radiation therapy. Of the 40, 32 patients had *H. pylori*-negative gastric MALT lymphoma and 8 patients were eradication therapy-resistant. 36 of them achieved CR (90.0%). 29 survived event-free. Two patients with CR were diagnosed with other diseases; one was diagnosed with primary gastric cancer while the other with follicular lymphoma. Distant recurrence was detected in five patients with CR during follow-up. 2 of them died. One of the two died from primary lung cancer while the other died from metastases to the cervical lymph nodes and bone marrow from primary MALT lymphoma. One of the patients with distant recurrence in the rectum was diagnosed with primary gastric cancer. 4 patients only achieved partial remission. One of them died because of the transformation of the disease to diffuse large B-cell lymphoma while the remaining 3 sustained survival.

Conclusion: Low-dose radiation therapy may be effective in treating *H. pylori*-negative or eradication therapy-resistant MALT lymphoma. However, careful systemic follow-up for distant involvement and second malignancy in the field of radiation is warranted. To monitor lymphoma and detect transformation at its earliest stages is crucial because transformation to diffuse large B-cell lymphoma is one of the leading causes of death in patients with gastric MALT lymphoma.

Disclosure: Nothing to disclose

P0648 CLOSE ASSOCIATION OF ENDOSCOPIC SCORES FOR GASTRIC CANCER RISK ACCORDING TO "KYOTO CLASSIFICATION OF GASTRITIS" WITH SERUM RISK CLASSIFICATION KNOWN AS "ABC METHOD"

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Introduction: In Japan, endoscopic examination has been approved for a population-based gastric cancer screening program since 2016. Kyoto classification of gastritis provides the information of *Helicobacter pylori* infection, a major cause of gastric cancer, i.e., non-gastritis, no history of *H. pylori* infection; active gastritis, current infection with *H. pylori*; and inactive gastritis, past infection. "ABC method", a blood test examining serum *H. pylori* antibody and pepsinogen, has been also accepted as non-invasive and alternative method to assess *H. pylori* infection status and gastric cancer risk.

Aims & Methods: In this study, we aimed to clarify whether endoscopic evaluation of gastritis according to "Kyoto classification" helps to judge the risk of gastric cancer in the setting of population-based gastric cancer screening program. A prospective case registration study was conducted (UMIN000028629). Data were collected from 1784 participants who underwent both of endoscopic screening for gastric cancer at Kurashiki Central Hospital Health Managing Center from September 2017 to June 2018. We compared the endoscopic score for gastric cancer risk according to "Kyoto classification of gastritis" with the results of "ABC method", and evaluated the association between them by using Spearman's correlation coefficient.

Results: Endoscopically, non-gastritis was diagnosed in 1315 (73.7%) participants, active or inactive gastritis was diagnosed in 446 (25%), and judgement was difficult in 23 (1.3%). In the ABC method, 1312 (73.5%) were classified into group A, and 472 into group B-D. The average endoscopic scores of each ABC group were as follows: group A, 0.11 ± 0.6; group B, 2.5 ± 2.1; group C, 4.7 ± 1.6; and group D, 4.4 ± 2.1. The endoscopic score based on the Kyoto classification correlated well with the risk classification of ABC method (correlation coefficient, 0.80).

ABC method	Group A	Group B	Group C	Group D
H. pylori antibody (≧3U/mL)	-	+	+	-
Pepsinogen (PG I≦70 and PG I/II≦3)	-	-	+	+
Gastric cancer risk	Minimal	Low	High	High
N (%)	1312 (73.5%)	335 (18.8)	121(6.8%)	16 (0.9%)
Endoscopic score	0.11± 0.56	2.5± 2.1	4.7± 1.6	4.4± 2.1

[Gastric cancer risk according to the ABC method and the endoscopic scores based on Kyoto classification of each group.]

Conclusion: Endoscopic scores for gastric cancer risk according to "Kyoto classification of gastritis" were highly correlated with the known risk classification as "ABC method". Our findings suggest that endoscopic evaluation of gastritis according to "Kyoto classification of gastritis" is useful to judge the risk of gastric cancer in the setting of population-based gastric cancer screening program.

Disclosure: Nothing to disclose

P0649 WITHDRAWN

P0650 WITHDRAWN

P0651 THE ROLE OF HEPATOMA-DERIVED GROWTH FACTOR (HDGF) IN RECRUITMENT OF MESENCHYMAL STEM CELLS AND GASTRIC

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Introduction: Gastric carcinoma is one of the most prevalent cancers worldwide and is the secondary leading cause of cancer-related mortality because of the poor prognosis of patients. Hepatoma-derived growth factor (HDGF) is shown to contribute to cell proliferation, anti-apoptosis and VEGF expression, lymph node metastasis and poor prognosis in human gastric carcinoma. Carcinoma-associated fibroblasts (CAFs) possess abilities to promote primary tumor growth and progression by stimulating processes of neoangiogenesis, tumor cell proliferation, survival, migration, invasion and therapy resistance. Mesenchymal stem cells (MSCs) are reported to promote tumor malignance through differentiation of MSCs toward CAFs.

Aims & Methods: HDGF is induced by co-culture experiments with *Helicobacter Pylori* strain ATCC 49503 and AGS cells. CAF markers are detected using reverse transcription and real-time PCR assays. The effect of HBMMSCs on invasive motility of gastric cancer cells is measured using transwell migration assay.

Results: In the present study, *H. pylori* infection promotes HDGF expression in human gastric cancer cells. Human bone marrow mesenchymal stem cells (HBMMSCs) treated with HDGF assume properties of CAF-like myofibroblastic phenotypes through measuring myofibroblast markers [α-smooth muscle actin (α-SMA), procollagen α1, tropomyoson I, desmin, fibroblast activation protein (FAP)], and fibroblast markers [prolyl-4-hydroxylase A1 (PHA1) and fibroblast specific protein-1 (FSP-1)/S100A4]. HDGF-recruited HBMMSCs enhances cell proliferation and invasive motility of human gastric cancer cells. Hepatoma-derived growth factor neutralizing antibody (HDGF-NAb) and serum significantly inhibit HDGF-induced recruitment and differentiation of HBMMSCs.

Conclusion: These findings suggest that HDGF might play an important factor in gastric cancer progress through stimulation of HBMMSCs differentiation to CAF-like myofibroblas cells.

Disclosure: Nothing to disclose

Small Intestinal I

P0652 A MODEL TO STUDY ISCHEMIA-REPERFUSION INJURY IN HUMAN INTESTINAL ORGANOIDS

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Introduction: Intestinal ischemia-reperfusion (IR) is a phenomenon related to a variety of pathophysiological conditions (e.g. acute mesenteric ischemia, major surgery, shock). IR leads to damage of the intestinal epithelium, which functions as a physical and immunological barrier and is therefore crucial in maintaining intestinal homeostasis. I
n order to investigate potential therapeutic targets to protect the epithelium during intestinal IR and promote a regenerative response, we aim to validate a model to study IR in human intestinal organoids. Intestinal organoids have been shown to closely resemble self-renewal kinetics, 3D architecture, and cell-type composition of the intestinal epithelium *in vivo*.
Aims & Methods: A well-established human experimental model to study IR was used for temporal expression profiling of the *in vivo* intestinal response to IR. The top perturbed pathway was further validated using qPCR. Intestinal epithelial organoids were cultured from crypts isolated from surgical specimens of normal human small intestine. To simulate IR, organoids were subjected to 12 hours of hypoxia (1% O_2) followed by 30 and 120 minutes of reoxygenation. Activation of the UPR response was assessed by qPCR for CHOP, GADD34, BiP and XBP1 splicing, and, in addition, signs of endoplasmic reticulum (ER) stress were evaluated using electron microscopy (EM).
Results: The unfolded protein response (UPR) was the top perturbed pathway during reperfusion of the ischemically injured human small intestine *in vivo*.
Subjecting small intestinal organoids to 12 hours of hypoxia followed by 30 minutes of reoxygenation significantly increased expression of UPR-related genes CHOP and GADD34 and splicing of XBP1 mRNA compared to organoids not subjected to hypoxia. In addition, EM showed dilated ER after reoxygenation which is indicative of ER stress.
Conclusion: In line with findings in the *in vivo* human IR model, revealing the response to unfolded protein as a highly regulated process during reperfusion, hypoxia-reoxygenation in intestinal organoids induces significant activation of the UPR. Intestinal organoids can be used to improve insight in the pathophysiology of epithelial IR injury and regeneration, which could lead to new therapeutic targets.
Disclosure: Nothing to disclose

P0653 OPEN STUDY OF THE ASSOCIATION COLIMYCINE / GENTAMYCIN IN THE TREATMENT OF BACTERIAL OVERGROWTH OF THE SMALL INTESTINE IN PATIENTS WITH IRRITABLE BOWEL SYNDROME

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Introduction: Small intestinal bacterial overgrowth (SIBO) is a disorder whose diagnosis can be made directly by quantitative cultures (jejunal suction fluid) or indirectly by respiratory tests. Different treatment are proposed in this indication, but not available in all countries.
Aims & Methods: The purpose of this study is to evaluate in patients with Rome III irritable bowel syndrome (IBS) and a SIBO, the effectiveness of antibiotic treatment COLIGENTA (COLIMYCINE / GENTAMYCINE) on digestive symptoms and SIBO diagnosed by lactulose breath test.
In 99 consecutive patients with Rome III IBS (16 IBS-Constipation, 45 of type IBS-Diarrhea, 12 Mixed IBS, and 26-non-specific IBS), a SIBO was diagnosed by lactulose breath test. After a 72 hours no-residue diet, the test consisted of a hydrogen breath test with samples every 10 minutes during 3 hours after ingestion of 10 g of LACTULOSE. The test was positive when the H2 production was greater than 20 ppm within the first 90 minutes after ingestion of lactulose. Treatment with COLIGENTA (3 capsules

daily for 10 days, each capsule containing 135 mg COLIMYCINE, 100 mg of GENTAMYCINE, AP-HP) was established. Four weeks after the treatment, a new lactulose breath test was performed.
Results: Four weeks after treatment, an overall improvement in symptoms was observed in 92 patients (93%). There was also a significant decrease in expired H2 (P < 0.001) for all times. And a normalization of breath tests was registered in 42 patients (43%).
Age, gender, BMI, IBS subtypes, duration of illness were not associated with breath test normalization after antibiotic therapy. Only a lower concentration of hydrogen expired at times 70 and between time 140 to 180 min was predictive of a positive response to treatment (P0.001).
During treatment, an increase in diarrhea was observed in 13 patients and increased abdominal pain in 10 patients.
Conclusion: In IBS patients, this study shows that COLIGENTA can be used for the treatment of SIBO. The reported clinical improvement (93%) was not systematically associated with standardization of respiratory tests (42%). These results prompt to perform a double-blind study with a period longer evaluation.
Disclosure: Nothing to disclose

P0654 SPY GLASS'S APPLICATION IN ENDOSCOPIC RETROGRADE APPENDICITIS THERAPY FOR THE MANAGEMENT OF ACUTE APPENDICITIS

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Introduction: To evaluate the feasibility of Spy Glass applied in endoscopic retrograde appendicitis therapy (ERAT) for the management of acute appendicitis.
Aims & Methods: An electronic colonoscope (CFHQ290I, Olympus) with a cone-shape transparent cap was inserted into ileocecum to observe appendix orifice. After Inserting Spy Glass through the electronic colonoscopic tunnel, the guide wire lead Spy Glass to the appendix cavity for observation. The appendiceal cavity was observed and treated accordingly (removal of fecal stones, flushing, biopsy if necessary) . This was done without X-ray or ultrasound guidance during the whole procedure.
Results: Spy Glass could enter into appendix cavity and completed ERAT successfully.
Conclusion: By using Spy glass ERAT can be successfully performed without guidence of X-ray or ultrasound, avoiding the hazard of radiation.
Disclosure: Nothing to disclose

P0655 WITHDRAWN

P0656 PREDICTIVE FACTORS AND CLINICAL IMPACT OF "DEEP REMISSION" IN CELIAC DISEASE

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Introduction: Despite the usefulness of serology in the follow-up of patients with celiac disease, the ultimate indicator of adherence to the gluten-free diet is the demonstration of mucosal healing, although this may not occur even in compliant patients.
However, the need for duodenal reassessment biopsies is a controversial subject among "experts".
Aims & Methods: The aim of this study was to evaluate patients who underwent histological reevaluation after starting a gluten-free diet, in order to identify those with histological improvement, including complete mucosal healing and associated factors.
Starting from a dedicated consultation celiac disease consultation, patients with apparent clinical remission with normalization of antibody titres after at least twelve months of diet, were evaluated and who agreed to a proposed histological reassessment through upper endoscopy with bi-

opsies were included. The data needed to perform this investigation were obtained from the electronic clinical records, later aggregated into a SPSS database, which was subsequently subjected to treatment and statistical analysis.

Results: A total of 69 patients were included, 79.7% (n = 55) of the female sex, with a mean age of 22.5 years, in 36.2% of the cases diagnosed at pediatric age. In 68% of cases, the diagnosis was made in the context of "classic" clinical presentations, 17% in the context of "non-classical" presentations and 15% in latent phase. In most patients (79.2%) the diagnosis was initially suspected by serology. At endoscopy 11.8% of the patients did not present macroscopic features suggestive of celiac disease, and a histological grade of Marsh 3a-c was observed in 72.5% of all cases. A minority of patients (7%) had concomitant diagnosis of other autoimmune diseases.

Four of the patients developed complications of the disease, including refractory disease (n = 1), ulcerative jejunitis (n = 1), and osteoporosis (n = 2). Eight patients (11.6%) underwent reassessment endoscopy within 24 months of starting the diet, and the remainder after 24 months. The histological findings were normalized in 37.7% (n = 26), which was associated with the presence of lower Marsh score values at diagnosis (p = 0.014) and the presence of other autoimmune conditions (p = 0.046).

A histological improvement over baseline was observed in 55 patients (79.7%), of two or more grades in 37 cases, which was related to the initial transferrin saturation (p = 0.027), and with higher values of the Marsh score at diagnosis (p = 0.005).

Conclusion: Even under a gluten-free diet, normalization of the histological findings of celiac disease is difficult to obtain and appears to be independent of most clinical and serological findings at diagnosis. Patients with less severe histologic levels at diagnosis reach remission more easily, but only represent the minority of the population.

Disclosure: Nothing to disclose

P0657 HISTOLOGICAL, IMMUNOHISTOCHEMICAL AND RNA GENE EXPRESSION RESPONSES IN COELIAC DISEASE PATIENTS CHALLENGED WITH GLUTEN

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Introduction: There is an unmet need for novel treatments, such as drugs or vaccines, adjunctive to or replacing a burdensome life-long gluten-free diet for coeliac disease. Hence, several phase 1 and 2 clinical trials are in progress to investigate whether novel treatment attenuates or prevents gluten-induced mucosal injury in coeliac disease. The gold standard for successful treatment is a healed small intestinal mucosa, and therefore, the outcome measures in proof-of-concept studies should be based on evaluation of small intestine biopsies.

Aims & Methods: We evaluated quantitative morphometric (both architectural and inflammatory), immunohistochemical and mRNA gene expression in coeliac disease patients challenged with gluten using PAXgene fixed paraffin-embedded specimens.

Fifteen coeliac disease patients were challenged with 4 grams of gluten per day for 10 weeks and twenty-eight non-coeliac patients served as disease controls.

Results: Digitally measured duodenal biopsies showed significant gluten-induced morphological (villus height: crypt depth ratio) and inflammatory changes (intraepithelial CD3+ T-lymphocyte and lamina propria CD138+ plasma cell densities). Stainings for γδ T cells and IgA deposits, where previously frozen samples have been needed, were successful in PAXgene fixed paraffin-embedded samples. Molecular morphometry, using the mRNA expression ratio of villous epithelium-specific gene APOA4 to crypt proliferation gene Ki67, showed a similar significant distinction between paired baseline and post-gluten challenge biopsies as quantitative histomorphometry.

Conclusion: Rigorous histologic and molecular markers suitable for gluten challenge studies can be obtained from a single paraffin-embedded biopsy specimen. In addition, molecular morphometry seems to be a promising new tool to be further developed.

Disclosure: Nothing to disclose

P0658 COELIAC DISEASE - OLDER PATIENTS HAVE THE MOST EXTENSIVE SMALL BOWEL INVOLVEMENT ON CAPSULE ENDOSCOPY

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Introduction: The relationship between symptomatology, serology and findings on small bowel capsule endoscopy (SBCE) in patients with coeliac disease (CD) remains unclear. Clarifying such associations will help determine if symptoms and serology can predict severity and extent of disease on SBCE.

Aims & Methods: Patients with newly diagnosed CD (villous atrophy on duodenal histology and positive CD serology) were recruited. Patients underwent a SBCE at the time of diagnosis. Information on SBCE was recorded. Signs and symptoms at presentation, serological markers, histological classification of disease in the duodenum were noted.

Results: Sixty patients with newly diagnosed CD (mean age 44.9 years SD±17.4, 17 - 76) were included in this study. Older patients (p=0.025) and patients presenting with iron deficiency anaemia had more extensive small bowel (SB) involvement (p=0.026). Patients presenting with weight loss were more likely to have SB involvement beyond the duodenum (p=0.027). Patients presenting with iron deficiency anaemia (p=0.038) and weight loss (p=0.009) were significantly older at diagnosis. Serum albumin was lower in those patients diagnosed later in life (p=0.007).

There was no significant association between anti-tissue transglutaminase antibody (p=0.396) and extent of affected SB mucosa.

Patients with more severe Marsh classification of disease on histology from the duodenal bulb had more extensive SB involvement (p=0.017).

Conclusion: This is the largest study on newly diagnosed CD and SBCE. Older patients are likely to have more extensive disease on SBCE at diagnosis. Symptoms and serology had no impact on the findings on SBCE apart from weight loss and iron deficiency anaemia.

Disclosure: Nothing to disclose

P0659 CAPSULE ENDOSCOPY IN ESTABLISHED COELIAC DISEASE: CLINICAL SYMPTOMS, EXTENT OF DISEASE AND SMALL BOWEL TRANSIT

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Introduction: Patients with established coeliac disease (CD) can present with recurrent symptoms requiring further investigations including small bowel capsule endoscopy (SBCE). There is paucity of data on the relationship between the extent, severity of disease and small bowel transit (SBT) on capsule endoscopy in relation to histology, clinical and serological parameters.

Aims & Methods: Hundred patients with CD and 200 controls were recruited. All of these patients underwent a SBCE because of symptoms, abnormal serology or a suspicion of complications. Extent of disease SBCE and SBT were studied in relation to symptomatology, serology and severity of histology from the duodenum.

Results: In patients with CD, 30 (30.0%) had a normal SBCE, 56 patients (56.0%) had proximal small bowel (SB) involvement, 7 patients (7.0%) had proximal and mid SB involvement and 7 patients (7.0%) had diffuse disease. SBT was shortest in controls (275.0; range 60.0 - 981.0 minutes), followed by those with established CD but a normal SBCE (260.0; range 104.0 - 467.0 minutes) and those with established CD and macroscopic evidence of CD on SBCE (286.0; range 60.0 - 981.0 minutes) (p=0.0001). Age at time of SBCE (p=0.006), serum albumin (p=0.004) and haemoglobin (p=0.0001), Marsh score of histology from the duodenal bulb (D1)

(p=0.0001) and the second part of the duodenum (p=0.0001), the presence of RCD features on histology correlated significantly with the percentage of affected mucosa on SBCE on univariate analysis. On multiple regression analysis, serum albumin level (p=0.036) and Marsh score of histology taken from the duodenal bulb (D1) (p=0.019), serum vitamin B12 (p=0.001) and folic acid levels (p=0.008) were statistically significant.

Conclusion: Patients with CD have a persistently prolonged SB transit even if there is no evidence of disease on SBCE. This is the first study showing correlation between extent of disease and severity of duodenal histology according to the Marsh classification.

Disclosure: Nothing to disclose

P0660 NON-RESPONSIVE AND REFRACTORY COELIAC DISEASE: THE LARGEST UK EXPERIENCE FROM THE NHS ENGLAND RARE DISEASES COLLABORATIVE NETWORK

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Introduction: Non-responsive coeliac disease (NRCD) is defined by persisting symptoms or laboratory abnormalities in patients with coeliac disease (CD), and affects up to 30% of CD patients on a gluten-free diet (GFD). Causes of NRCD are heterogeneous, with refractory CD (RCD) being associated with poor prognosis.

Aims & Methods: The aims of this study were to identify the aetiologies for persisting symptoms in patients with NRCD referred to a national UK centre for CD, and to assess and compare mortality in each group. Data on all CD patients, including those with persisting symptoms and tertiary referrals, was collected prospectively from 1998-2018. Patients were systematically investigated to establish the aetiology of their continued symptoms. They were also referred to a specialist coeliac dietitian to identify any lapses in GFD adherence or gluten cross-contamination. A repeat duodenal biopsy was performed and compared to previous biopsies where possible to check for histological remission. Colonoscopy, lactose hydrogen breath test, glucose hydrogen breath test, SeHCAT scan, CLO testing, faecal elastase, faecal calprotectin, stool culture, immunohistochemistry and γ-TCR clonality were performed where appropriate to establish a final diagnosis. Data on follow-up and outcomes was then collected for each group and survival analyses performed.

Results: A total of 2,356 patients with suspected CD were seen in this time period (121 were tertiary referrals). Of these, 157 were excluded from analysis due to unconfirmed diagnosis. Of the remaining 2,199 patients with confirmed CD, 2,123 had both villous atrophy and positive IgA-EMA/TTG, and 76 had seronegative CD. Of the 2,199 patients with confirmed CD (67% female, mean age at diagnosis 42.8 ± 18.5), 292 (13.3%) had persisting symptoms. The leading causes for persisting symptoms in patients without evidence of RCD (73% female, mean age at diagnosis 35.7 ± 19.2) were: gluten contamination (24%), functional/irritable bowel syndrome (20%), pancreatic exocrine insufficiency (7%), reflux dysmotility (5%), and microscopic colitis (5%). Of a total of 74 patients who were identified with RCD (26% of all NRCD), 56 were diagnosed with RCD I (71% female, mean age at CD diagnosis 41.8 ± 19.0) and 18 RCD II (33% female, mean age at CD diagnosis 55.4 ± 13.3). Eighteen patients (6% of all NRCD) had developed further complications consisting of enteropathy associated T-cell lymphoma (EATL) (4), B cell lymphoma (4), ulcerative jejunitis (3), small bowel adenocarcinoma (3), oesophageal adenocarcinoma (2), cutaneous T cell lymphoma (1), and neuroendocrine carcinoma of small bowel (1). Higher age at diagnosis of CD was a predictor for having RCD in patients with persisting symptoms (p< 0.001). Patients diagnosed with RCD II were significantly older at CD diagnosis (p=0.003), had a shorter delay between CD and RCD diagnosis (p=0.002) and were more likely to be male (p=0.006) compared to those diagnosed with RCD I. After a median follow up of 40.5 months (IQR 21.8-73.3), mortality was 7% in the RCD I group, compared to 39% in the RCD II group (p=0.019), with a five-year survival of 68% in patients with RCD II.

Conclusion: This is the largest UK study of NRCD and RCD. The contemporary mortality data in RCD II remains poor. Management of this group is challenging, and more evidence is required. Patients with suspected RCD should be referred to the National Centre for consideration of novel therapies such as IL-15 and Stem Cell Transplant.

Disclosure: Nothing to disclose

P0661 ASSESSING GLUTEN FREE DIET ADHERENCE USING CDAT AND BIAGI QUESTIONNAIRES IN PATIENTS WITH COELIAC DISEASE

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Introduction: The gold standard currently for assessing adherence in individuals with coeliac disease (CD) is via duodenal biopsies, which is invasive and costly. There is currently no reliable non-invasive surrogate marker to detect gluten ingestion and persisting villous atrophy in CD patients.

Aims & Methods: In view of this, our aim was to assess the utility of the CDAT and Biagi questionnaires for non-invasive assessment of gluten free adherence. Patients with an established diagnosis of coeliac disease, referred for further evaluation of dietary adherence and disease remission were assessed between January 2016 to December 2018. Patients were prospectively recruited, and completed CDAT and Biagi questionnaires at their endoscopy appointment, with at least 4 duodenal biopsies taken from D2 in addition to at least one biopsy from the duodenal bulb. The presence (Marsh 3a or above) or absence (Marsh 0-II) of villous atrophy was used to determine the sensitivities of the questionnaires in detecting persisting villous atrophy.

Results: A total of 151 patients were recruited, 101 females (66.9%), median age 55.0 years, median duration of GFD of 72.0 months. The sensitivities of CDAT, Biagi, and combined CDAT & Biagi were 52.0% (95% CI 37.6-66.1), 22.4% (12.2-37.0), 61.2% (46.2-74.8) respectively, compared to 30.6% (18.7-45.6) and 34.3% (26.7-42.7) for IgA-TTG and EMA. Specificity of CDAT, Biagi and combined CDAT & Biagi were 69.8% (60.9-77.5), 93.1% (85.6-97.0), and 69.3% (60.5-77.2) respectively, compared to 91.6% (83.6-96.0) and 92.5% (84.8-96.7) for IgA-TTG and EMA.

Conclusion: The sensitivity of the CDAT questionnaire was not superior to IgA-TTG for predicting villous atrophy in patients with coeliac disease. However, the use of a combination of both Biagi and CDAT had a greater sensitivity than IgA-TTG and IgA-EMA (p< 0.05), but lower specificity (p< 0.05). Duodenal biopsy remains the gold standard, although these scores remain useful tools in the assessment of dietary adherence.

Disclosure: Nothing to disclose

P0662 PREDICTORS OF PERSISTENT VILLOUS ATROPHY IN ADULTS WITH COELIAC DISEASE AND STRICT CONTROL OF GLUTEN-FREE DIET ADHERENCE: A MULTICENTER PROSPECTIVE STUDY (CADER STUDY)

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Introduction: Several studies have shown that a substantial proportion of adult CD patients on a gluten-free diet (GFD) exhibit persistent villous atrophy (VA) on follow-up duodenal biopsy, suggesting that the most frequent cause was poor adherence to the GFD.

Aims & Methods: To evaluate VA persistence after 2 years on a GFD in adult CD patients with strict control of diet adherence.
Symptomatic adult CD patients were prospectively included at diagnosis and started on a GFD. CD diagnosis was done according to established guidelines. A 2-year follow-up was carried out with clinical visits and di-

etary surveillance at 6 weeks and after every 6 months. Dietary adherence was assessed using the validated CD adherence test questionnaire (Leffler 2009). In each visit clinical status, serum anti-tTG2 and faecal gluten immunogenic peptides (f-GIP) were checked. For f-GIP, two faecal samples in different days of the week prior each visit were obtained and stored at -80ºC until processing. The concentration of GIP in stools was analysed by ELISA using the iVYLISA GIP stool (Biomedal S.L., Seville, Spain), considering positive values >80 ng GIP per g faeces. Duodenal follow-up biopsy was performed at 2 years. Biopsies were blindly evaluated by two expert pathologists, in case of disagreement, a consensus was achieved. Mucosal recovery was defined as the absence of VA. A sample size of 90 patients was calculated to estimate a persistent VA rate of 40%, loss of follow-up of 15%, with an accuracy of 10%. We examined age, gender, educational attainment, marital status, employment situation, clinical and serological remission, and positive f-GIP to determine predictors of persistent VA.

Results: 95 patients were included, three were excluded for not presenting VA and one one for age < 16 years. Fifteen of 91 (16%) did not ended the follow-up. Therefore, 76 patients finalized the study (36.5±1.6 years, 73% women). Follow-up duodenal biopsy showed persistent VA in 40 patients (53%, 95% CI, 41-63%) (Marsh 3a, 75% and Marsh 3b-c, 25%). Of the 40 patients, 72.5% were asymptomatic and 75% had negative serology. There were no differences in the f-GIP+ rate among patients with persistent VA and those with recovery, which in general indicated weak gluten transgressions. On multivariate analysis only older age was an independent predictive risk factor of persistent VA (32% for 16-30 yrs; 60% for >30 yrs; p=0.016).

Conclusion: Persistent VA rate after 2 years on a GFD was high in adult patients with CD, despite a strict control of diet adherence and that there were no differences in f-GIP values between persistent VA and recovery. There was an effect of increasing age on the frequency of persistent VA that was not related to dietary noncompliance and social differences.

Disclosure: Nothing to disclose

P0663 USE OF CAPSULE ENDOSCOPY IN SERONEGATIVE VILLOUS ATROPHY: DOES IT CLARIFY OR CLOUD THE PICTURE?

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Introduction: Seronegative villous atrophy (SNVA) on duodenal histology can be secondary to coeliac disease (CD) or other causes such as medications or infections. The introduction of small bowel capsule endoscopy (CE) has enabled us to study this condition further and to establish whether these patients develop complications.

Aims & Methods: The CEs of patients (128) with SNVA on duodenal histology were retrospectively analysed for features of CD (fissuring, scalloping, mosaic pattern, nodularity, villous atrophy, ulcers). Extent of affected SB mucosa was determined. 3 categories of patients were identified: group 1: no identifiable cause for SNVA, group 2: histological response to gluten free diet (GFD), group 3: alternative cause for SNVA.

Results: Overall, 49 (38%) patients had a positive CE. Patients with more severe histological pattern on duodenal biopsies were more likely to have a positive CE (partial villous atrophy (PVA) 21, 26%, subtotal villous atrophy (SVA) 12, 60% total villous atrophy (TVA) 13, 59%, p=0.001). More extensive SB disease corresponded to a more severe histological pattern (PVA 1%, SVA 15%, TVA 17%, p=0.001).

Patients with alternative causes for SNVA had the least extensive SB involvement (group 1: 9.13 (+/-25.2), group 2: 9.77 (+/-23.5), group 3: 0.025(+/-0.13)% p=0.038). Most patients had proximal SB disease (40, 82%).

These patients were followed up for up for a median of 5 years (1 - 18 years).

Group 1: 43% (55) had no identifiable cause for SNVA. 40% (22) of these patients had a positive CE. 71% (39) had spontaneous resolution of SNVA without any intervention. The other patients received a trial of GFD to which none responded. Further treatment included steroids +/- immunosuppressants in 10 patients. CE at diagnosis was positive in 8 (20.5%) of those with spontaneous resolution of SNVA, 14 (87.5%) patients with persistent SNVA (p=0.0001).

Group 2: 27% (35) patients had a histological response to a GFD. 5 of these patients (14%) were IgA deficient. 49% (17) patients had a positive CE. 7 patients eventually developed complications. All of them had a positive CE at the time of diagnosis (p=0.022). They also had more extensive SB disease than those patients who did not develop complications (50% vs 1% p=0.002). 3 patients developed refractory coeliac disease (RCD) I, 2 developed RCD 2. 2 patients developed RCD 2 and ulcerative jejunoileitis.

Group 3: 37 patients (29%) had alternative causes for SNVA. 10 (27%) patients had positive CEs (2, 60% - NSAIDs, 2, 15% - H pylori positive, 4, 67% - Giardia, 1, 33%) - angiotensin receptor blocker, 1 - Crohn's disease, p=0.125).

Conclusion: CE can be useful in patients with an unknown cause for SNVA as more extensive disease on CE at diagnosis can predict those with persistent SNVA. In SNVA-CD, more extensive disease on CE at diagnosis can be a predictor of development of complications. These patients need to be monitored more closely.

Disclosure: Nothing to disclose

P0664 IS THERE A CORRELATION BETWEEN DUODENAL HISTOLOGY AND DISEASE SEVERITY ON CAPSULE ENDOSCOPY IN PATIENTS WITH VILLOUS ATROPHY?

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Introduction: There is a lack of uniformity of reporting on features of coeliac disease (CD) on small bowel capsule endoscopy (SBCE). This makes determining extent of disease and comparison of severity of disease between SBCEs challenging even for experts in the field.

Aims & Methods: The de-identified SBCEs of 300 patients with CD (78; 26%), antibody negative villous atrophy (18, 6%) and control patients (204; 68%) with normal duodenal histology were reviewed by 2 expert SBCE reviewers. All patients had duodenal histology taken 2 weeks from undertaking SBCE. The degree of agreement between identifying CD features (fissuring, villous atrophy, scalloping, mosaicism, nodularity, ulcers) and determining extent of disease was then assessed. Multiple regression analysis was carried out to determine the correlation of CD features with extent of abnormal small bowel (SB). Ranks were then used to optimise the odds ratio obtained for each factor using an inbuilt function in SPSS. This resulted in the formulation of a score for each factor in each SB tertile.

Results: The overall kappa co-efficient for all CD features for reviewers 1 and 2 was 0.67. The intraclass correlation co-efficient for percentage extent of affected SB mucosa was 0.97 (p=0.0001). Percentage of extent of affected SB mucosa correlated with overall severity of disease as classified by each reviewer (p=0.0001) and with histology from the second part of the duodenum (p=0.0001). The multivariate regression analysis resulted in statistically significant odds ratios of CD features correlating with extent of affected SB mucosa for both reviewers 1 and 2. These were then utilized to generate a score for features of CD in the SB. The overall scores for each patient correlated with extent of affected SB mucosa for reviewer 1 (Pearson correlation co-efficient 0.662, p=0.001) and 2 (Pearson correlation co-efficient 0.838, p=0.001). The median overall scores of patients increased significantly according to the independent classification by reviewers: mild (34, 0-254), moderate (50, 27-133), severe (96, 69-128) (p=0.0001).

Conclusion: The good correlation of CD scores between expert reviewers confirms the validity of CD features on SBCE. An objective score of CD features in the SB might be useful in the follow up of patients with CD and serology negative villous atrophy.

Disclosure: Nothing to disclose

P0665 SYSTEMIC ABSORPTION, MICROBIOME METABOLISM AND SYMPTOMS FOLLOWING ORAL FRUCTOSE IN PATIENTS WITH FUNCTIONAL GASTROINTESTINAL DISORDERS

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Introduction: Fructose intolerance (FI), i.e. symptoms following ingestion of fructose, is common in patients with Functional Gastrointestinal Disorders (FGID). Malabsorption of fructose resulting in intestinal distension and fermentation is generally assumed to be the underlying mechanism. Malabsorption can be indirectly characterized by measurement of intestinal gases exhaled in breath (e.g. hydrogen, methane), or by quantifying the systemically absorbed fructose and its metabolites. We have previously shown that FI is not characterised by changes in expression of the main intestinal fructose transport proteins, GLUT5 and GLUT2 (1). Consequently, the cause of malabsorption in FI remains unclear.

Aims & Methods: We aimed to investigate malabsorption as a cause for symptoms in FGID patients following ingestion of fructose. Plasma concentrations of fructose and fructose metabolites, short-chain fatty acids (SCFA), and the gaseous fermentation products hydrogen and methane were used as measures of fructose absorption. Thirty-one male or female patients with FGID (Rome III) ingested either 35g fructose or water in a randomised, blinded, crossover study in Switzerland (2). Plasma fructose and its metabolites (glucose, alanine, lactate, glycerate) and SCFAs (acetate, propionate, butyrate, isobutyrate, valerate, isovalerate, and caproic acid) were quantified via liquid chromatography tandem mass spectrometry from blood samples drawn at 0, 0.5, 1 and 2 hours post-dosing. Breath hydrogen and methane concentrations were measured and GI symptoms recorded at the same times. The aggregate GI symptom score, the sum of 8 GI symptoms graded by intensity as 0=none, 1=mild, 2=intense, was used to classify patients regarding FI (defined as increase of >2, maximum score of 16). Analyses were performed using areas-under-the-curve of the variables for the first 2 hours post-dosing (AUC_{0-2h}).

Results: AUC_{0-2h} of fructose and metabolite plasma concentrations were similar in the 15 patients with and the 15 patients without FI (p>0.05), and did not correlate significantly with AUC_{0-2h} of aggregate GI symptom scores (r=-0.007). However, the AUC_{0-2h} of symptoms correlated positively with AUC_{0-2h} of hydrogen (r=0.73) and methane (r=0.62) concentrations. Patients with FI produced significantly more hydrogen and methane than fructose-tolerant patients (both p=0.04). The AUC_{0-2h} of the concentration of the SCFA valerate correlated positively with breath hydrogen (r=0.34) and methane (r=0.45), but negatively with plasma fructose (r=-0.41) concentrations.

AUC of parameters	FI n=15	Non-FI n=15	p-values
Fructose (µM·h)	573 ± 134	547 ± 91	0.53
Hydrogen (ppm·h)	58.5 ± 49.2	26.6 ± 22.5	0.03
Methane (ppm·h)	20.1 ± 10.6	12.9 ± 6.9	0.04
Aggregate GI symptoms (score·h)	8.57 ± 4.88	0.45 ± 0.54	<0.0001

[Study parameters in fructose-intolerant (FI) and non-FI subjects (means±SD, independent t-test)]

Conclusion: In patients with FGID, fructose intolerance is not correlated with decreased post-ingestion plasma fructose and its metabolites as indicators of malabsorption, consistent with our findings on intestinal transporter expression (1). Instead, FI appears to be associated with changes in the intestinal microbiome metabolism of fructose, arising from altered composition or activity of the intestinal microbiome in these patients.

References: 1. Wilder-Smith C et al. United European Gastroenterol J. 2014;2:14-21 2. Wilder-Smith C et al. Neurogastroenterol Motil. 2019;31:e13497

Disclosure: Nothing to disclose

P0666 VALIDITY AND GENERALIZABILITY OF THE NEWLY DEVELOPED ADULT CARBOHYDRATE PERCEPTION QUESTIONAIRE (ACPQ)

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Introduction: Breath tests are extremely popular in clinical practice to determine *carbohydrate malabsorption.* Guidelines recommend assessment of symptoms which are more relevant for clinical management (1) to diagnose *carbohydrate intolerance.* We have recently developed a test-specific perception questionnaire for the assessment of carbohydrate induced gastrointestinal symptoms, the adult Carbohydrate Perception Questionnaire (aCPQ).

Aims & Methods: Our aim was to validate the aCPQ for the assessment of carbohydrate related perception by internal-, cross- and external validation.
The aCPQ is a VAS-based questionnaire for the assessment of the presence and the severity of five complaints before and during the breath test: pain, nausea, meteorism, flatulence, diarrhoea. Criteria of internal validity were determined after the implementation of the questionnaire during lactose and fructose breath tests in 342 subjects ('Vienna-original' group). Correlation between the questionnaire and a medical interview (n=338) was determined, interviews were performed by a physician who was blinded as to the results of the questionnaire. Cross validation was performed in a follow-up patient group in the same institution ('Vienna-cross' group, n=182), external validity was assessed in a group from another university center ('Graz-external' group, n=156). NS=not significant

Results: The scale has good face validity as it is simple, easy to understand and brief. The content validity ratio according to Lawshe equales 1. Intraclass correlation coefficients for test-retest reliability (n=159; 30 minutes interval) demonstrate good repeatability (p< 0.001), Cohen's d as a measure of effect size is small (i.e. < 0.40; 0.19 or smaller for the five symptoms). Cronbach's alpha is 0.85, indicating good internal consistency. Convergent validity and discriminant validity is supported according to the multitrait-multimethod-matrix method. Moreover, the results given by the questionnaire highly correlate with the result of the medical interview (p< 0.001; Fisher exact test). Responsiveness to change has been verified during breath tests with medium to large effect sizes (p< 0.05). 146 patients were diagnosed with malabsorption, 179 patients with intolerance, among them 97 patients having both malabsorption and intolerance. The 'Vienna-cross' group included significantly more fructose tests (54%; p=0.02) and was significantly younger (43±1.3 years; p=0.05) than the 'Vienna-original' group. The percentage of patients who was diagnosed with intolerance AND malabsorption, only intolerance or only malabsorption was comparable in both 'Vienna' groups before and after correcting for age, gender and carbohydrate tested (NS). The 'Graz-external' group was significantly younger (40±1.5 years; p< 0.001) than the 'Vienna-original' group. The percentage of patients who was diagnosed with intolerance AND malabsorption, only intolerance or only malabsorption was comparable in 'Graz-external' and 'Vienna-original' before and after correcting for age, gender and carbohydrate tested (NS).

Conclusion: The adult Carbohydrate Perception Questionnaire (aCPQ) is a simple, test-specific questionnaire. It is a valid instrument with excellent psychometric properties and generalizability for the assessment of gastrointestinal symptoms after carbohydrate ingestion. The aCPQ should replace non-validated symptom assessment during carbohydrate breath tests, e.g. by interview, use of non-validated questionnaires or generic, non-test-specific instruments and allows a uniform diagnosis of carbohydrate intolerance.

References: Hammer et al. Dig Dis Sci 2018:1270

Disclosure: Nothing to disclose

P0667 GLOBAL CONSENSUS ON HISTOLOGICAL DEFINITION AND CLASSIFICATION OF NON-COELIAC GLUTEN SENSITIVITY

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Introduction: The morphological damages of intestinal Villi's/ Crypt architecture by the intraepithelial lymphocytic infiltration (IEL) in non-coeliac gluten sensitivity (NCGS) have been much less quantified compared to coeliac disease (CD).

Aims & Methods:

Aim: Morphological changes including IEL infiltration in intestinal villi's and Crypt architecture were measured in gluten induced enteropathies aiming to differentiate between NCGS, CD and controls.

Method: The study was designed at the International Meeting on Digestive Pathology, Bucharest 2017. Investigators from 22 centres, 9 countries of 4 continents, recruited CD patients with Marsh 0-II histology (n=261), NCGS (n=175), and 262 controls and used one agreed protocol to analyse the small bowel mucosa in well-oriented duodenal biopsies. Demographic and serological data were also collected.

Results: Participant countries consisted of Australia (20), Finland (20), India (25), Iran (37), Italy (239), Romania (10), Turkey (30), UK (166) and USA (151). The villus height was significantly shorter in NCGS compared to control (p< 0.001), the difference was significant even when the analysis limited to Marsh 0. Conversely, the villus height of NCGS was significantly longer than that in CD [600 (IQR: 400-705) vs 427 (IQR: 348-569), p< 0.001], the result was unchanged when analysis was limited to Marsh I-II [500 (IQR:410-629) vs 423 (IQR:349-574, p=0.009). The median Crypt depth was significantly increased in NCGS group compared to controls [296 (IQR: 205 -300) vs 222 (IQR: 158-294), p< 0.001] and it was similar to CD group [269 (IQR: 182-322), p=0.822]. Interestingly NCGS with Marsh 0, still had significantly increased crypts depth compared to controls (p< 0.001). The crypt depth value was similar in Marsh I-II for both NCGS and CD groups [273 (IQR: 180-296) vs 269 (IQR: 180-324), p=0.822)]. In addition, the ratio of villus height to crypt depth was significantly lower in NCGS compared to controls (p< 0.001), the difference was significant even when the analysis was limited to Marsh 0 (p< 0.001). In contrast, the ratio of villus height /Crypt Depth in NCGS was significantly higher than that in CD (p=0.009), the result was still significant when analysis was limited to Marsh I-II (p=0.046). The median IEL density was significantly higher 23/100EC in NCGS group compared to 14 in controls (p< 0.001) and lower than that in CD group 40/100EC (p< 0.001). When comparison was restricted to Marsh 0, NCGS still had significantly higher IEL density than controls (p< 0.001). Comparing IEL densities in Marsh I/II NGGS to Marsh I/II CD groups showed similar values (p=0.055). When the analyses were restricted to Marsh 0, the IEL density cut off scored 79% sensitivity and 55% specificity at 14/100EC for NCGS with 0.71 (95% CI: 0.64- 0.77, p< 0.001) area under curve. Similar analysis limited to Marsh I-II showed a cut-off of 25/100EC to diagnose CD and NCGS (together) from controls, with 95% sensitivity, 86% specificity and 0.94 (95% CI: 0.93-0.96, p< 0.001) area under the curve.

Conclusion: Morphometric assessment of intestinal mucosa of NCGS patients showed a range of subtle abnormalities even when the histology is reported as Marsh 0 or normal. Comparing Marsh 0 of NCGS with controls, revealed the former have significantly higher IEL density, increased crypt depth, shorter villous height and decreased villous/crypt ratio. This global morphometric assessment brings novel insight into the Marsh 0 histology spectrum that can improve the NCGS diagnostic yield as an additional biomarker.

Disclosure: Nothing to disclose

P0668 PREDICTIVE FACTORS IN CHRONIC DIARRHOEA CAUSED BY IDIOPATHIC BILE ACID MALABSORPTION

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Introduction: Most of the cases of chronic diarrhoea after excluding organic disorders are labelled as functional diarrhoea or irritable bowel syndrome (IBS). Bile acid malabsorption (BAM) is a frequently underinvestigated cause of chronic diarrhoea in adult population. In Europe the diagnosis is commonly established by the Selenium homocholic acid taurine test scan (SeHCAT). BAM is defined as mild (10-15% retention), moderate (5-10%), or severe (< 5%).

Aims & Methods: We aimed to evaluate and identify risk factors associated to MAB type 2.

Methods: We retrospectively reviewed all patients who had SeHCAT scan performed between June 2014 and October 2018 in a University tertiary referral Hospital. We excluded all patients who had known risk factors for BAM. The diagnosis of BAM was established when SeHCAT retention was inferior to 15%. We collected the following variables: demographic characteristics, IBS-D Rome III criteria, duration of diarrhoea (months), stool culture, parasitic investigation on stool specimens, *H. pylori* infection, drugs use, and HLA-DQ2/DQ8 haplotype. Univariate and multivariate

statistical analysis was performed with binary logistic regression model with analysis of successive steps forward to identify potential predictors of having a positive SeHCAT test. Variables with p < 0.1 in the univariate analysis were selected for the multivariate analysis.

Results: 298 patients referred for chronic diarrhoea underwent SeHCAT testing (109M/189F). In the whole group, the median age was 46 yo (95% C.I 44.0-50.1), the median body mass index (BMI) was 24,8 kg/m2 (95% C.I 25,4-26,8). Out of all, 75.2% met IBS-D Rome III criteria, the median duration of diarrhoea was 36 months (95% C.I 42,5-54,8), 41.9% (70/167) exhibited a history of *H. pylori* infection, and 17.5%(17/131) showed parasitic stool infestation. The percentage of positive HLA-DQ2 and DQ8 haplotypes was 52.7% (109/207) and 17.4%(36/207), respectively. SeHCAT test was positive for BAM in 47.9% (143/298): 25.2% mild, 40.6% moderate, and 34.3% severe. Patients with positive SeHCAT test exhibited higher BMI and longer periods of diarrhoea (Table 1).

	Postive SeHCAT	Negative SeHCAT	P
Gender (M;F)	68;78	41;111	<0.010
Age(yo) (median;95% IC)	43.0 (41.3-46.1)	40.0 (39.0-44.1)	0.036
BMI (Kg/m2:median;95%IC)	26.8 (26.4-28.4)	23.9 (24.0-25.7)	<0.010
Duration of diarrhoea (months; median; 95% C.I)	36.0 (44.7-65.5)	24.0 (35.9-49.2)	0.073
IBS-D Rome III criteria (%)	105/146	119/152	0.228
Blastocystis Hominis (n)	8/124	20/122	0.016
Giardia Lamblia (n)	2/124	1/122	1.000
Dientamoeba fragilis (n)	8/124	2/122	0.085
Endolimax nanas (n)	1/124	6/122	0.065
Helicobacter pylori (n)	28/74	42/93	0.349
ISRS (n)	21/145	13/152	0.144
IBPs (n)	21/145	15/151	0.286
HLA-DQ2 Haplotype (n)	49/98	60/108	0.463
HLA-DQ8 Haplotype (n)	21/98	15/108	0.199

[Demographic Characteristics]

The following variables were selected for multivariate analysis: sex, age, BMI, duration of diarrhea, previous finding of parasites in stool specimens and consumption of proton pump inhibitors. Female sex, absence of parasites in stools, and high BMI were identified as predictive factors for positive SeHCAT. The R-square of Cox and Snell, and of Nagelkerke of our model were of 11.4% and 15.2%, respectively.

Conclusion: Although we identified female sex, a high BMI and the absence of parasites in stools as independent indicators of idiopathic BAM, these factors have a low capacity to predict a positive SeHCAT test. Additional studies are needed to identify better prognostic factors indicative of idiopathic bile acid malabsorption.

Disclosure: Nothing to disclose

P0669 WITHDRAWN

P0670 PANORAMIC VERSUS AXIAL SMALL BOWEL CAPSULE ENDOSCOPY IN OVERT OBSCURE GASTROINTESTINAL BLEEDING

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Introduction: Literature comparing axial small bowel capsule endoscopy (SBCE) (Pillcam, Given Imaging) and panoramic SBCE (Capsocam, Capsovision) in obscure gastrointestinal bleeding (OGIB) is limited and contradictory (1,2).

Aims & Methods: Consecutive patients who presented with overt OGIB at a tertiary centre over a 5 year period underwent either Capsocam SBCE or Pillcam SB3 SBCE. All had negative gastroscopies and colonoscopies / CT colonographies. SBCEs were reviewed by 2 experts. Findings in the 2 groups were compared.

Results: 94 patients (39.4% Capsocam; 60.6% Pillcam; 57.4% males; mean age 64.3±18.0 years) were included. Both groups were age (p=0.174) and gender (p=0.137) matched. Severity of anaemia (p=0.053) and duration of anaemia (p=0.264) were similar in both groups.

There was no difference between groups in incomplete SBCEs (p=0.151). Diagnostic yield (DY) was comparable in both groups but Pillcam had a higher DY than Capsocam in the stomach (table 1).

Capsocam identified blood (2, 5.4%), erosions (1, 2.7%) and ulcers (1, 2.7%) in the stomach. Pillcam showed blood (4, 5.4%), erosions (11, 19.3%), ulcers (2, 3.5%), varices (1, 1.8%) and GAVE (1, 1.8%) in the stomach. Patients who underwent Capsocam examination had the following findings in the SB: 1 (2.7%) ulcer, 7 (18.9%) angioectasia, 8 (21.6%) blood, 2 (5.4%) erosions, 1 (2.7%) tumour, 1 (2.7%) diverticulum. Patients who underwent Pillcam had these findings in the SB - 10 (17.5%) ulcers, 11 (19.2%) angioectasia, 7 (12.3%) blood, 19 (33.3%) erosions, 1 (1.75%) tumour, 2 (3.51%) diverticulum, 2 (3.51%) phlebactesia, 4 (7.02%) polyps, 1 (1.75%) haemangioma, 1 (1.75%) intussusception.

	Capsocam n(%)	Pillcam n(%)	Significance (p)
Gastric DY	3 (8.1)	15 (26.3)	0.033
Small bowel (SB) DY	17 (45.9)	25 (43.9)	0.842
Colon DY	2 (5.4)	3 (5.3)	0.976

[Table 1: DY of panoramic and axial SBCE for patients with overt OGIB;]

Conclusion: SB DY was comparable between Capsocam and Pillcam groups in patients with overt OGIB but Pillcam offered a better gastric DY than Capsocam. This might be of relevance as a considerable number of lesions are missed in the upper GI tract in patients undergoing gastroscopy.

References: 1. Pioche M, Vanbiervliet G, Jacob P, Duburque C, Gincul R, Filoche B, Daudet J, Filippi J, Saurin JC, (SFED) FSoDE: Prospective randomized comparison between axial- and lateral-viewing capsule endoscopy systems in patients with obscure digestive bleeding. Endoscopy 2014, 46:479-484. 2. Zwinger LL, Siegmund B, Stroux A, Adler A, Veltzke-Schlieker W, Wentrup R, Jürgensen C, Wiedenmann B, Wiedbrauck F, Hollerbach S, et al.: CapsoCam SV-1 Versus PillCam SB 3 in the Detection of Obscure Gastrointestinal Bleeding: Results of a Prospective Randomized Comparative Multicenter Study. J Clin Gastroenterol 2018.

Disclosure: Nothing to disclose

P0671 YIELD, ETIOLOGIES AND OUTCOMES OF CAPSULE ENDOSCOPY IN PATIENTS WITH OCCULT GASTROINTESTINAL BLEEDING- A LONG TERM RETROSPECTIVE STUDY

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Introduction: Capsule endoscopy has been widely accepted as a tool to investigate chronic occult blood loss from the gastrointestinal tract as a cause of anaemia.

Aims & Methods: The aim of the study is to investigate the long term yield of capsule endoscopy (CE) for patients with occult gastrointestinal bleeding (OGIB) over 10 years in a tertiary referral hospital.

A retrospective analysis of a prospectively collected database on patients with OGIB who underwent CE to investigate persistent anemia in a tertiary referral center during 2007-2017 was performed. Medical records were reviewed. CE findings were classified as significant, suspicious/equivocal and negative. Sites of pathology were categorized into proximal, mid, distal or diffuse.

Results: A total of 644 [mean age 33.5 (range 18-88); n=432 (67%) female] had CE over this period. 174 patients (27%) with overt gastrointestinal bleeding were excluded from the study. A total of 470 patients (73%) who were suspected to have occult gastrointestinal bleeding were included into the study. Median time interval of CE after onset of anaemia was 296 days (range 1-745 days). Mean follow-up was 668.5days (range 81-1348 days). Capsules reached caecum in 459 cases (97.7%) and capsule retention was

found in 4 cases (0.9%). Small bowel pathology identified in proximal, mid, distal and throughout (diffuse) small bowel based on small bowel transit time (SBTT) were 58.6%, 9.9%, 24.1%, 9.9% and 7.3% respectively. Diagnostic yield of CE for significant pathology versus equivocal/ negative finding were 34.5% and 65.5%, respectively. Significant small bowel pathology was identified in 162 cases, of which 102 (63%) were angiodysplasia, 38 (23.5%) were inflammation or ulcers, 12(7.4%) were polyps, 9(5.6%) were tumor, 1(0.5%) was blue rubber bleb syndrome. Small bowel ulcers were significantly associated with NSAID use (46%,p=0.023). A total of 191 patients underwent a single balloon enteroscopy (172 anterograde 19 retrograde approach) with an overall diagnostic yield 109 (57.1%). 308 patients with negative CE were subsequently diagnosed with poor dietary intake of iron (n=167), heavy menstruation (n=54) hematologic disorders(n=26), colon cancer (n=2), colonic Dieulafoy's (n=1), hemorrhoid (n=1) and hemosuccus pancreaticus (n=1). A total of 56 (18.2%) had no identifiable cause detected. Survival for positive CE vs equivocal/ negative CE were 63.7% vs. 99.4% (p< 0.01).

Conclusion: Our study demonstrated that the yield of CE in persistent anemia was 34.5% and prognosis of patients with equivocal or negative CE was excellent.

References: Van de Bruaene C et al. Small bowel capsule endoscopy: Where are we after almost 15 years of use? World J Gastrointest Endosc 2015;7(1):13-36. Lopez et al. Iron deficiency anemia. Lancet 2016;387(10021):907-16. Muhammad A et al. Role of small bowel capsule endoscopy in the diagnosis and management of iron deficieny anemia in elderly: A comprehensive review of the current literature. World J Gastroenterol 2014;20(26):8416-23 Enns R. Capsule endoscopy in patients with iron deficiency. Gastroenterol Hepatol (N Y) 2012;8(12):847-9.

Disclosure: Nothing to disclose

P0672 DIAGNOSTIC YIELD OF CAPSULE ENDOSCOPY IN PATIENTS WITH OBSCURE GASTROINTESTINAL BLEEDING: A PROSPECTIVE MONOCENTRIC STUDY

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Introduction: Gastrointestinal (GI) bleeding from the small bowel is rare (5-10% of all the GI bleedings)(1). Since 2001, videocapsule endoscopy (VCE) allowed the visualization of bleeding source in most (75%) of the previous obscure GI bleedings (OGIB)(1)

Aims & Methods: In a prospective study, we aimed to assess the diagnostic yield of VCE in a cohort of consecutive patients (pts) with OGIB. Secondary endpoints was to assess the usefulness of VCE in the diagnostic work-up and management of pts with OGIB. From March 2016 to Feb. 2018, all pts with indication to perform VCE were considered. Inclusion criteria: 1) diagnosis of OGIB/iron-deficient anemia (IDA);2) age>18-≤85 yrs; 3) non-diagnostic bidirectional endoscopy; 4)Follow up ≥5mos; 5)Informed consent. Exclusion criteria:1) swallowing disorders; 2) VCE contraindications; 3) Concomitant relevant GI diseases. 4) Pregnancy. All VCE images (PillCam,Covidien plc,Dublin,Ireland) were examined by 2 independent investigators. Data were expressed as mean [range].

Results: During the study period, 50 out of the 84 pts (59.5%) referred for VCE, fulfilled the inclusion criteria (18 males [36%]; age 68 [27-83] yrs; haemoglobin 8 g/dL [4.5-12.9]). Indication for VCE: ongoing overt OGIB in 11 (22%), previous overt OGIB in 14 (28%), occult-obscure bleeding (with IDA) in 25 (50%) pts. The time interval between OGIB (or diagnosis of IDA) and VCE was 30 [3-240] days. No VCE retentions occurred. Incomplete examinations were reported in 3 (6%) pts. All VCE were discharged in ≤7 days. Ongoing treatment: single antiplatelet therapy (aspirin, ADP receptor antagonist) in 15 (30%), dual antiplatelet therapy in 7 (14%), oral anticoagulant therapy in 7 (14%), nonsteroidal anti-inflammatory drugs in 13 (26%), SSRI-drugs in 3 (6%) pts. Lesions compatible with obscure GI bleeding (positive findings) were observed in 46 (92%) pts, including (%): small bowel (SB) angiodysplastic lesions in 24 (46%), SB erosions in 20 (40%), red signs of recent bleeding in 10 (20%), blood or cloths in 8 (16%), venous ectasia in 8 (16%), mucosal or submucosal polyp/tumor mass in 5 (10%), ulcers in 1 (2%) pt. Additional findings included (%): erosive gastroduodenitis in 17 (34%), gastric/duodenal angiodysplastic lesions in 4

(8%), ulcers in 2 (4%) pts. VCE was negative in 4 (8%) pts: 1 (2%) pt with erosive gastroduodenitis (false negative), 2 (4%) pts with rectal bleeding due to rectal solitary ulcer and to hemorrhoids (true negative), respectively. In 1 (2%) pt VCE was not diagnostic. Clinically significant lesions were observed more frequently in pts with occult OGIB (24/25 [96%] pts), followed by pts with ongoing overt OGIB (10/11 [91%]) and previous overt OGIB (12/14 [85.5%]).

After VCE treatments were: medical in 30 (60%) pts; endoscopic in 7 (14%), surgical in 3 (6%), clinical observation with supportive treatments in 9 (18%) pts. After VCE, 49/50 (98%) pts were followed up for ≥5 mos (17.8 [5-28]). Bleeding resolution in these 49 pts was: complete in 31 (63.2%), partial in 9 (18.4%), absent in 9 (18.4%). Death occurred in 3 pts for non-related OGIB conditions.

Conclusion: In a prospective study, VCE use provided a high diagnostic yield in patients with OGIB, suggesting its use VCE as the first-line investigation in suspected mid-GIB. In this setting, VCE should be performed by dedicated gastroenterologists, in order to optimize the timing and the selection of patients.

References: 1) Gerson LB, Fidler JL, et al, ACG Clinical Guideline: Diagnosis and Management of Small bowel Bleeding. Am J of Gastroenterology 2015.

Disclosure: Nothing to disclose

P0673 CLINICAL FEATURES AND SOURCES OF BLEEDING IN PATIENTS WITH GASTROINTESTINAL BLEEDING OF UNKNOWN SOURCE

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Introduction: Patients having gastrointestinal bleeding (GIB) of unknown source usually presented with general clinical symptoms of blood loss and often this can only be reflected in a decrease level of hemoglobin.

Aims & Methods: The aim of the study is to analyze, evaluate and compare clinical features and identified sources of bleeding in patients with intestinal sources of bleeding.

From 14.02.2007 to 10.03.2019 there were 229 patients (m-117, f-112, mean age 52,3±18,3 years, range 17-89) who admitted to our clinics with GIB of unknown source. Obscure overt bleeding had 142 (62,0%) pts, obscure occult bleeding – 87 (38,0%) pts, that associated with severe anemia in 86 (37,5%) pts, moderate anemia – in 87 (37,9%) pts and mild anemia – in 56 (24,4%) pts. Bleeding was associated with other complaints (incl. combination of complaints in 40 pts) in 98 (42,7%) pts: abdominal pain in 50 (51,0%) pts, diarrhea in 26 (26,5%) pts, nausea/vomiting in 22 (22,4%) pts. Video capsule enteroscopy (VCE) was used for the small bowel examination in 179 (78,2%) pts. and balloon-assisted enteroscopy (BAE) – in 146 (63,7%) pts. BAE was performed after VCE in 96 (53,6%) pts.

Results: The source of GIB was found in 191 (83,4%) pts: in small bowel (SB) – in 170 (89,0%) pts; in the upper/lower GI tract – in 21 (11,0%) pts. No pathology was found in 38 (16,6%) pts. The sources of SB bleeding included vessel malformations in 65 (35,7%) pts, tumors – in 54 (29,7%) pts, erosive/ulcerative enteropathy – in 42 (23,1%) pts, diverticula – in 9 (5,3%) pts (incl. Meckel's diverticulum in 6 pts). Clinical features of the pts with SB sources of bleeding are presented in the table 1.

Conclusion: The main indication for small bowel examination is GIB of unknown source, which can have a little bit different clinical manifestations depending on the source of bleeding. All the sources of SBB tend to be recurrent, and pts mostly have severe/moderate anemia. Vessel malformations are more frequent sources of SBB in pts elder than 50 years old (p=0.008), more often presented with overt bleeding (p=0.007). Pts with tumors tend to have a long period of detection, more than 1 year; they usually have complaints of abdominal pain. Pts with enteropathy tend to have a shorter period of detection, less than 1 year, usually associated with diarrhea. All pts with SB diverticula have overt GIB, apparent with severe anemia, without any other complaints.

Disclosure: Nothing to disclose

Clinical features	Vessel malformations (n=65)	Tumors (n=54)	Enteropathy (n=42)	Diverticula (n=9)
Sex: Male/ Female	31 (47,5%)/ 34 (52,5%)	24 (44,4%)/ 30 (55,6%)	27 (64,3%)/ 15 (35,7%)	6 (66,6%)/ 3 (33,4%)
Age: <50 years/ >50 years	24 (36,9%)/ 41 (63,1%)	26 (48,1%)/ 28 (51,9%)	23 (54,7%)/ 19 (45,3%)	5 (55,5%)/ 4 (44,5%)
Bleeding: Overt (Melena/ Haematochezia)/ Occult	44 (67,7%) (28 (63,6%)/ 16 (36,4%))/ 21 (32,3%)	27 (50,0%) (17 (62,9%)/ 10 (37,1%))/ 27 (50,0%)	18 (42,8%) (9 (50,0%)/ 9 (50,0%))/ 24 (57,2%)	9 (100,0%) (3 (33,3%)/ 6 (66,7%))/ 0 (0%)
Overt bleeding in anamnesis: For the first time/ Recurrent	8 (18,2%)/ 36 (81,8%)	9 (33,3%)/ 18 (66,7%)	4 (22,2%)/ 14 (77,8%)	5 (55,5%)/ 4 (44,5%)
Anemia: Severe/ Moderate/ Mild	23 (35,4%)/ 29 (44,6%)/ 13 (20,0%)	17 (31,5%)/ 20 (37,0%)/ 17 (31,5%)	11 (26,1%)/ 14 (33,3%)/ 17 (40,4%)	5 (55,5%)/ 3 (33,3%)/ 1 (11,2%)
Other complaints: Pain/ Diarrhea/ Nausea+vomiting	5 (7,7%)/ 4 (6,1%)/ 6 (9,2%)	18 (33,3%)/ 3 (5,5%)/ 7 (12,9%)	16 (38,1%)/ 19 (45,2%)/ 8 (19,0%)	0 (0%)/ 0 (0%)/ 0 (0%)
Duration of detection the source: <1 year/ >1 year	37 (56,9%)/ 28 (43,1%)	21 (38,8%)/ 33 (61,2%)	31 (73,8%)/ 11 (26,2%)	7 (77,7%)/ 2 (22,3%)

[P0673 Table. Clinical features and the sources of SB bleeding.]

Nutrition I

10:30-17:00 / Poster Exhibition - Hall 7

P0674 LIVER FIBROSIS STAGE AT BASELINE PREDICTS OUTCOME OF METABOLIC SURGERY

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Introduction: Non-alcoholic fatty liver disease (NAFLD) and vitamin D deficiency (VDD) is highly prevalent in morbidly obese patients and can advance to non-alcoholic steatohepatitis (NASH), fibrosis, liver cirrhosis and liver cancer. Moreover, metabolic surgery might carry an increased risk for liver decompensation and mortality in cirrhotic patients. We examined the prevalence of liver fibrosis and response to metabolic surgery.

Aims & Methods: In a randomized controlled trial, baseline intraoperative needle liver biopsy was performed in 46 patients with VDD who underwent one-anastomosis gastric bypass (OAGB). Patients were followed for 12 months for non-invasive Fibroscan™ (FS) measures (M and XL probe) for the non-invasive detection of the presence of histologically advanced fibrosis and response to metabolic surgery as well as metabolic signatures and laboratory improvements. Univariate and multivariable analysis were used to test the predictive relevance of data assessed.

Results: 78% of subjects were female, mean age was 42 (SD 12) years with a BMI of 44 (4) kg/m , a waist circumference of 128 (11) cm, and a HOMA index of 6.96 (5.81). 26% suffered from diabetes, 50% from hypertension, and 26% from hyperlipidemia. 72% demonstrated NASH, 11% simple steatosis, and 17% normal liver morphology. 30% showed significant fibrosis (F≥2), 9% advanced fibrosis (F3) and 4% cirrhosis (F4).

(I) Metabolic surgery significantly improved BMI, waist circumference, HOMA Index, liver tests, and liver stiffness. Importantly, patients with F< 2 responded better. (adjusted for baseline value, age, sex, and diabetes mellitus). Of note, the groups (F< 2 vs. F>3) did not differ at baseline.

(II) FS correlated significantly (r=0.516; p< 0.001) with histological fibrosis readings and showed an AUC of 0.738 (p=0.009) to predict F≥2 and an even better AUC 0.815 (p=0.015) for F>3.

(III) Importantly, we observed a high variance in FS measurements (SD at baseline: 3.1 kPa, 1 months: 3.1 kPa, 3 months: 4 kPa, 6 months: 2.1 kPa, 12 months: 2.4 kPa,) before weight loss.

Conclusion:

(I) Metabolic surgery significantly improves liver stiffness, metabolic signatures and γ-GT. Patients with fibrosis stage < 2 responded significantly better.

(II) Fibroscan™ is a useful tool to detect patients with F≥2, demonstrating highly variable measures before weight loss (until 3 months). Hence, suggesting critical evaluation during measurement and application of novel standards such as multiple region measurements to decrease sampling error and increase accuracy in morbidly obese patients.

Fibroscan™ is an important tool to preoperatively select patients for optimal outcome and potential risk of metabolic surgery.

References: 1) Miñambres I et al. Obes Surg. 2018, doi: 10.1007/s11695-018-3562-8

2) Griffin C et al. AASLD 2018, oral Abstract #218, Hepatology 2018; 68 (S1):43A

Disclosure: Nothing to disclose

P0675 VISCERAL OBESITY MEASURED BY DUAL X-RAY ABSORPTIOMETRY AND BIOIMPEDANCE AS THE PREDICTOR FOR IBS IN OBESE PATIENTS

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Introduction: There are several studies considering obesity as the risk factor for various lower gastrointestinal symptoms. But the evidence regarding the relationship between visceral abdominal tissue (VAT) and the incidence of irritable bowel syndrome (IBS) are sparse. Moreover, the exact measurement method for VAT is still debatable. Lee. GC et.al reported VAT measurement by CT scan which is an invasive and expensive method and not appropriate in everyday usage. We aimed to measure VAT by Body composition measurements were obtained using the dual-energy X-ray absorptiometry (DXA) (Hologic Horizon W, Waltham, MA, USA) and multifrequency bioelectrical impedance analysis (BIA) (Seca mBA 515, Hamburg, Germany)and correlate the values with the presence of IBS symptoms.

Aims & Methods: The primary outcome of this study was to investigate the association between VAT and the risk of IBS. The secondary outcome is to compare two different methods for VAT measurement. Totally we enrolled 94 obese patients (76.5% F; mean age M=47,99; SD=11,8 years). In this case-control study we compare the VAT, Fatty mass (FM), Free Fatty Mass (FFM), Waist circumference (WC) between subjects with obesity and IBS (IBS group N=29; 30.9%) and controls (obese patients without IBS, non-IBS group N=65; 69.1%), who underwent obesity programme at tertiary care centre from January 2018. to January 2019. IBS was diagnosed by using Rome IV criteria questionnaire. The association between IBS and abdominal obesity was evaluated by measuring VAT, FFM, FM and waist

circumference (WC) Body composition measurements were obtained using the dual-energy X-ray absorptiometry (DXA) (Hologic Horizon W, Waltham, MA, USA) and multifrequency bioelectrical impedance analysis (BIA) (Seca mBA 515, Hamburg, Germany).

Results: The prevalence of IBS in this sample was 30.8%, (OR 0.44; 95% (CI): 0.2645 to 0.7525, P= 0.0025) among all enrolled subjects.

VAT(L) measured by bioimpedance is significant predictor for IBS in obese patients t = 2.51, df = 63.51, p< .05 (p=0.01468); Cohen's d=0.51 (moderately high) IBS (M= 4.27; SD= 2.35), non-IBS (M= 6.09; SD= 3.94).

Moreover, there is significant correlation between VAT measurement with bioimpedance and DEXA. FFM, FM and WC as well are not important predictors for IBS in obese patients. Younger obese patients are more prone to have IBS symptoms than older patients (OR 0.93; 95%(CI): 0.88 to 0.97; P=0.007).

Conclusion: Visceral adiposity measured by simple and non-invasive method is associated with an increased risk of IBS. Bioimpedance and DEXA are reliable methods for VAT measurement. However, neither FFM, FM, BMI and WC are associated with an increased risk of IBS.

References: Lee CG. Visceral abdominal obesity is associated with an increased risk of irritable bowel syndrome.Am J Gastroenterol. 2015;110(2):310-9.

Disclosure: Nothing to disclose

P0676 ENDOSCOPIC SLEEVE GASTROPLASTY VS LAPAROSCOPIC SLEEVE GASTRECTOMY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Obesity is a worldwide epidemic that continues to be pervasive and associated with significant comorbidities that can result in poor quality of life along with reduced life expectancy. Despite progress in the understanding of the complex mechanisms in obesity, bariatric surgery remains the only current treatment of obesity that demonstrates long-term effectiveness. Endoscopic sleeve gastroplasty (ESG) is a novel minimally invasive technique that was first presented in 2008 and improved upon in 2013. Data is limited in terms of the efficacy and safety of ESG, and evidence has not been synthesized in comparison to other options of bariatric surgery like laparoscopic sleeve gastrectomy (LSG).

Aims & Methods: In this study, we aim to assess and compare the outcomes of ESG with LSG by meta-analysis. We conducted a comprehensive search of several databases and conference proceedings (earliest inception to March 2019). Pooled rates of total weight loss (TWL%), excess weight loss (EWL%), and body mass index (BMI) with ESG were calculated at 1 month, 6months, and 12 months. The outcomes at 12 months with ESG were compared to the outcomes at 12 months with LSG.

Results: A total of 3713 patients were included in the analysis from 13 studies. Outcomes of ESG were analyzed from a total of 7 studies (1569 patients) and outcomes of LSG were analyzed from 6 studies (2144 patients). Baseline population characteristics were comparable between the ESG and LSG groups. The mean and/ or median age ranged from 30 years to 48 years, with predominantly female population (75%). Mean range of BMI (kg/m2) was 33.3 to 38.9 in ESG cohort and 37.4 to 48 in LSG cohort. The pooled rates of TWL at 1m, 6m, and 12m were 8.5 (95% CI 7.7-9.3, I²=87.9), 15.4 (95% CI 13.8-16.9, I²=94.7), and 17.5 (95% CI 15.3-19.7, I²=94.6) respectively. The pooled rates of EWL at 1m, 6m, and 12m were 30.1 (95% CI 22.1-38.2, I²=96.6), 57.8 (95% CI 48.6-66.9, I²=93.5), and 64.1 (95% CI 51.9-76.4, I²=92.7) respectively. The pooled rates of BMI at 1m, 6m, and 12m were 32.6 (95% CI 30.4-34.8, I²=97.5), 30.9 (95% CI 29.1-32.6, I²=96.7), and 31.3 (28.2-34.3, I²=98) respectively. At 12 months, the pooled rates of TWL, EWL, and BMI with LSG was 46.3 (30.9-61.7, I²=99), 69.9 (95% CI 59.4-80.5, I²=99), and 27.9 (95% 25.2-30.6, I²=98.9) respectively. LSG demonstrated

statistically superior TWL when compared to ESG with a statistical p-value of 0.02. EWL and BMI change with LSG and ESG were comparable with a statistical p-value of 0.5 and 0.13 respectively.

Conclusion: ESG, as a minimally invasive treatment modality, demonstrates successful clinical outcomes in patients with obesity, in terms of TWL% EWL%, and BMI. Outcomes at 12 months are similar to LSG, except for TWL that was statistically superior with LSG when compared to ESG. This study was limited by heterogeneity and indirect comparison. Well-conducted large scale studies with adequate follow-up time are needed to establish the role of ESG in the treatment of obese patients.

Disclosure: Nothing to disclose

P0677 PERINATAL PROGRAMMING OF INTESTINAL HOMEOSTASIS FOLLOWING EXPOSURE TO A HIGH FAT DIET IN MALE RATS OFFSPRING

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Introduction: Perinatal period is characterized by phases of development with high sensitivity to the environmental factors. Among the risk factors, malnutrition or maternal obesity are now recognized to program children's metabolism and promote the occurrence of obesity or type 2 diabetes during postnatal life. This study aims to identify the effects of maternal perigestational exposure to an obesogenic diet in offsprings. This exposure might increase the occurrence of obesity, associated with metabolic disorders, inflammation and disturbances of digestive function in male offsprings.

Aims & Methods: 8 female Wistar rats were fed a HFD, and 8 control female rats a standard diet (controls), supplemented or not with inulin.

Female rats were exposed to these experimental conditions during a 4-months pre-gestational period as well as during the gestation and lactation periods.

After weaning, 50 male pups were studied at young adulthood (D60), without any treatment during the experiment. Different segments of the digestive tract were studied for histological analysis, metabolic assays, inflammation and intestinal permeability.

Results: Rats from mothers fed a HFD have a higher weight than control pups at weaning time (p< 0.001), and the inulin appears to limit this weight gain (HFD *vs* HFDi p< 0.05), phenomenon still present at d60 (C *vs* HFD p< 0.01; HFD *vs* HFDi p< 0.01). Lipid and glycemic assays did not show significant differences. FITC assays didn't show any perturbation of the paracellular intestinal permeability. LPS and pro inflammatory cytokines assays (IL6, IL1β, TNFα) didn't reveal any tissue inflammation.

Conclusion: Our results indicate that pups from mothers fed an obesogenic diet are overweight at both weaning and young adulthood. Interestingly, inulin limits weight gain in these animals.

The obesogenic diet of the mother promotes the occurrence of obesity in male offsprings and an inulin-based dietary supplement could help limiting these deleterious effects. This hypothesis remains to be confirmed after analysis of the intestinal barrier tight junction proteins expression, other inflammatory markers and morphological alterations of the digestive system.

Disclosure: Nothing to disclose

P0678 ENDOSCOPIC SLEEVE PLICATION (ESP) FOR TREATMENT OF OBESITY I-II. PRELIMINARY RESULTS OF 2 SITES WITH THE NEW PATTERN FOR GASTRIC EMPTYING DELAY

Turro R.[1], Espinós Pérez J.C.[2], Lopez Nava G.[3], Mata Bilbao A.[4], Abu Dayyeh B.[5], Uchima H.[6], Rosinach M.[7], Ble Caso M.[8], Michelena J.[8], Turro J.[9]

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Introduction: Obesity is major disease in our society. Intragastric balloon is the endoscopic gold standard on short time weight loss. Endoscopic plicature can offer us better middle long term results than balloon for its durability.
Aims & Methods: This is a multi-center, prospective pilot study intended to evaluate the safety and efficacy of the Gastric Endoscopic Sleeve Plication procedure (mid & distal body plications) (GESP).
Study was Ethics approved at institutions. Written consent obtained. Indications have been obesity grade II. Use of the Incisionless Operating Platform (IOP)™ (USGI Medical, San Clemente, CA, USA) with a defined new pattern of disposition of the transmural plications with the g-cath™ EZ suture anchors in the greater curvature shortening and tubulizing the stomach to potentially delay gastric emptying and reduce gastric volume / accommodation for an enhanced physiological effect.
Follow up data will be obtained prospectively every 2 weeks initially for the first 2 months and then monthly for the next 10 months on as part of our long term follow-up program that also emphasized changes in unhealthy eating/lifestyle habits.
Gastric emptying studies previously to the intervention, 2 months after and 6 months after intervention are scheduled. Satiety test are also scheduled during the follow up, basal, 2 months and 6 months after the intervention. Liver test with analytics and fibroscan are also done in those patients basal, 2 months and 6 months.
Results: 39 operations in 39 patients were successfully performed (M: 17 F: 22). Mean BMI 36.9 (Range 31.2 - 40.3). Mean number of anchors placed was 18.3. All patients were discharged ≤ 24 hours. No serious adverse events (SAE). % Mean Total body weight loss at 5 months for the 34 patients was 13.93 ± 4.14 Kg.
Conclusion: The GESP procedure seems to be a safe intervention without significant adverse effects to date. Initial results in weight loss are encouraging. However, long term follow-up and further study remains necessary to assess its value in treating the etiology of obesity.
Disclosure: USGI Consultant Aspire Consultant Allurion Travel Grant

P0679 TRANSLATABLE MODEL OF METABOLIC SYNDROME AND LIVER DISEASE IN SMALL ANIMALS USING PRECLINICAL ULTRASOUND

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Introduction: Diagnostic ultrasound (US) using general US imaging devices can be effectively used for preclinical studies in small animals providing dynamic life-time control [1], furthermore, can enhance drug delivery and therapeutic effects with visual treatment monitoring (theranostic).
Aims & Methods: The aim was to develop model of metabolic syndrome in small animals using general US machines for longitudinal in vivo observation and screening large numbers of cases for facilitating further translation.The modeling of metabolic syndrome performed in compliance with the ethical standards and includes conducting an experiment on laboratory animals (mice, rats, murine) with the introduction of high calorie diet

or industrial fat-enriched diet; and further US monitoring using 5-20 MHz probes of diagnostic US machines in grey scale, Doppler, sonoelastography, M-mode detecting tissue movement, US-guided interventions, injection US contrast agents:
1) for precise diagnosis transabdominal US detecting signs of metabolic syndrome via detailed **imaging of internal organs:** liver size, echogenicity, stiffness, kidneys size, structure, Doppler measuring resistance index (RI) on segmental renal arteries, spleen size, muscle thickness at midfemoral level, assessment of visceral vessels, systemic hemodynamics, etc.;
2) for screening all involved animals we measured the visceral fat thickness (threshold considered as 1.5 mm in mice) on sagittal probe position and collected records of panoramic abdominal scans (in sagittal and transverse probe positions) and measured the largest longitudinal liver size (via subcostal approach). Weight, body size, laboratory indices (cholesterol, uric acid, glucose, etc.), microbiome, genetic markers were also determined. After sacrificing we evaluated studied organs.
Results: The model was successfully applied to study effects of new drugs: probiotic strains on high calorie-induced obesity model in BALB/c during 21 days [2] and prebiotic effect on high-calorie diet-induced obesity in rats [3]. US detected development metabolic syndrome, endogenous intoxication syndrome, visceral obesity and liver and kidney dysfunction in mouse and rats. Ultrasound data showed visceral obesity, injury of the liver and organs in all experimental animals. We revealed nephropathy signs (thinning, increasing echogenicity of kidney parenchyma, detecting increasing RI in renal arteries (over 0.7) was feasible in rats. Studies using the models demonstrated efficacy of studied strains, substances improving parameters during experiment. All observed changes were confirmed post mortem.
Conclusion: The method of modeling is reliable, allows to monitor metabolic syndrome signs with high translation potential reflecting development disease in humans.
References: 1. Bubnov RV. The use of ultrasound equipment of general use for in vivo study of cerium dioxide nanoparticles introduction in mice. Ultrasound Med Biol. 2011, 37 (8): 1-S162. https://doi.org/10.1016/j.ultrasmedbio.2011.05.750 2. Bubnov RV, et al. Comparative study of probiotic effects of lactobacillus and bifidobacteria strains on cholesterol levels, liver morphology and the gut microbiota in obese mice. EPMA J. 2017;8(4):357-76. https://doi.org/10.1007/s13167-017-0117-3. 3. Konopelniuk VV, et al. Efficacy of Fenugreek-based bionanocomposite on renal dysfunction and endogenous intoxication in high-calorie diet-induced obesity rat model−comparative study. EPMA J. 2017. https://doi.org/10.1007/s13167-017-0098-2
Disclosure: Nothing to disclose

P0680 ASSESSMENT OF METABOLIC SYNDROME IN INFLAMMATORY BOWEL DISEASE REVEALED FTO VARIANT RS9939609 AS A NOVEL GENETIC MARKER OF CROHN'S DISEASE

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Introduction: Metabolic syndrome (MeS) and inflammatory bowel disease (IBD) share common pathophysiological features including chronic inflammation in visceral adipose tissue, but the interplay still remains unrevealed. Great interest has been recently devoted to the association of FTO gene and obesity, although the biological function is still unclear. FTO is a member of a superfamily of Fe (II)-and 2-oxoglutarate-dependent dioxygenases and presents a nucleic acid demethylase. The proposed FTO pathophysiological mechanism includes alterations of methylation-demethylation states of genes expression in metabolically active tissues.
Aims & Methods: Newly diagnosed 94 Crohn's disease (CD) and 98 ulcerative colitis (UC) patients and 91 non-IBD controls with parameters of MeS were analyzed for FTO rs9939609 variant using PCR-ARMS (Polymerase Chain Reaction - Amplification Refractory Mutation System) method.
Results: We analyzed distribution of genetic variant FTO rs9939609, previously associated with obesity, in our study population. The genotype distribution was in Hardy-Weinberg equilibrium in each and total analyzed group. Results showed that FTO AA genotype was more frequent in CD

than UC and control group, 29.8%, 23.5% and 14.3%, respectively. It has been demonstrated that AA genotype was significant predictor of CD occurrence (p = 0.01), adjusted for age and gender in the logistic regression model. Compared to TT and TA carriers, carriers of AA genotype had 2.6 higher odds for CD development (OR = 2.6 95% CI [1.2 - 5.4])

Conclusion: The nutrigenetic approach in IBD could improve understanding of obesity-associated complex diseases and contribute to better risk stratification, considering that genetic markers are not influenced by confounding factors such as education, physical activity, social-economic status and diet. Association of FTO variant with CD could direct further nutrigenomic studies in IBD research.

Disclosure: Nothing to disclose

P0681 MICROBIOTA CHANGES INDUCED BY MICROENCAPSULATED SODIUM BUTYRATE

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Introduction: Inflammatory bowel disease (IBD) is characterized by severe inflammation of the small bowel and/or the colon leading to recurrent diarrhea and abdominal pain. Butyrate represents one of the final product of saccharolytic fermentation of complex and nondigestible polysaccharides by anaerobic bacteria and has shown anti-inflammatory and regenerative properties, providing symptomatic relief when orally supplemented in patients suffering from a various range of colonic diseases(1). Limited data are available on butyrate effectiveness in patients with IBD due to the difficultines of proving an adequate concentration of butyrate in the colon.

Aims & Methods: We investigate the effect of a microencapsulated form of sodium Butyrate (MSB, Butyrose[R], SILA, Noale, Italy) on the faecal microbiota of patients with IBD. In this prospective-randomized-placebo-controlled study, 49 IBD patients, 19 CD and 30 UC with mild-to-moderate clinical activity were enrolled . Eighteen volunteers were recruited to provide a healthy microbiota model of the local people. Patients with extensive surgery were excluded. After stratification by clinical assessment, colonoscopy, and fecal calprotectin (FC) levels, the patients were randomized to oral administration of MSB (1800 mg/die) or placebo for 2 months, in addition to conventional therapy. Clinical activity was defined according to HBI in case of Crohn's Disease (CD) and Mayo score in case of ulcerative colitis (UC). Before (T0) and after (T1) butyrate treatment, stool samples were collected for faecal microbiota assessment analysis by 16S ribosomal RNA Illumina MiSeq sequencing. Patients completed the quality of life questionnaire in IBD (IBDQ) on T=0 and T=1

Results: We confirmed the evidence of a significant difference (p< 0.001) between the microbiota of healthy controls and IBD patients. MSB induced similar changes in the microbiota of IBD patients by increasing the bacteria able to produce shortchain fatty acids (SFCA). However, an increased abundance of butyrogenic colonic bacteria (including genera Butyricicoccus and Subdoligranulum) were observed in CD patients, whereas in UC patients we observed a major increase of Lachnospiraceae (sPLSDA analysis). Clinically, when only patients with calprotectin levels above 250ug/g for CD and 150ug/g(2) for UC were considered, a 30% decrease of calprotectin levels were observed in 67% of CD patients treated with MSB versus 33.3% in those treated with placebo. Subjective improvement in QoL based on IBDQ was significantly observed either in the treatment (p=0.0046) and in placebo (p=0.039) group. However, a greater effect was observed among the UC patients.

Conclusion: Microencapsulated sodium butyrate supplementation showed an increase of butyrogenic and SCFA bacteria stimulating growth with a mimicking prebiotic effect increasing the production of endogenous and physiological SCFAs with a marked improvement of QoL and reduction of the level of inflammatory markers.

References: [1] Duncan L.P., et al., (2004), Restricted distribution of the butyrate kinase pathway among butyrateproducing bacteria from the human colon., J Bacteriol , 2099-106 [2] Lin JF,et al., (2014), Metaanalysis: fecal calprotectin for assessment of inflammatory bowel disease activity, Inflamm Bowel Dis, 1407-15

Disclosure: Nothing to disclose

P0682 PERINATAL PROGRAMMING OF INTESTINAL HOMEOSTASIS FOLLOWING EXPOSURE TO LOW DOSE OF CHLORPYRIFOS IN MALE RATS OFFSPRING

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Introduction: Perinatal period is characterized by phases of development with high sensitivity to environmental factors. Among the risk factors, pesticide exposure are now recognized to program children's metabolism and promote the occurrence of obesity or type 2 diabetes. This study purposes the peri-gestational exposure of mothers (animal model: rat) to a low dose of pesticide (chlorpyrifos, CPF). This exposition might increase the occurrence of obesity, associated with metabolic disorders and disturbances of digestive function in male offsprings.

Aims & Methods: 8 female Wistar rats were exposed to CPF, and 8 female rats to its vehicle (controls) , supplemented or not with inulin. Female rats were exposed to these experimental conditions during a pre-gestational period of 4 months as well as during the gestation and lactation periods. After weaning, 56 male pups were studied at young adulthood (D60), without any treatment during the experiment. Different segments of the digestive tract were studied for histological analysis, metabolic assays, inflammation and intestinal permeability.

Results: Rats from mothers exposed to CPF have lower birth weights than control pups (p< 0.05), but this difference appears to decrease at young adult age (J60). Lipid and glycemic assays did not show significant differences. We noticed a decrease of IGF1 (p< 0.01) and leptin plasma levels but not significantly in animals from CPF-exposed mothers. FITC assays didn't show any perturbation of the intestinal permeability. LPS and pro inflammatory cytokines assays (IL6, IL1β, TNFα) didn't show any tissue inflammation.

Conclusion: Preliminary results reveal that pups from mothers in contact with a pesticide during the peri-gestational period have developmental disabilities characterized by a lower birth weight, but also a decrease in plasma levels of factors involved in growth and metabolism (IGF1 and leptin).

We suggest that the pesticide slows down fetal and postnatal development. This hypothesis remains to be confirmed after analysis of tight junction proteins of the intestinal barrier, other inflammatory markers and morphological alterations of the digestive system.

Disclosure: Nothing to disclose

P0683 RIBOFLAVIN SUPPRESSES INFLAMMATION AND ATTENUATES CROHN'S DISEASE SYMPTOMS (RISE-UP STUDY)

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Introduction: Crohn's disease (CD) is characterized by chronic intestinal inflammation and dysbiosis in the gut. Riboflavin (vitamin B_2) has anti-inflammatory, anti-oxidant and microbiome-modulatory properties. Here, we analyzed the therapeutic potential of riboflavin in CD and its effect on markers of inflammation, oxidative stress and the gut microbiome.

Aims & Methods: In this prospective clinical intervention study, 70 CD patients were included and divided into one group with low and one group with high disease activity at baseline (defined by faecal calprotectin (FC)

cut-off value: 200 μg/g). Patients received 100 mg riboflavin (DSM, Nutritional Products Ltd.) daily for 3 weeks. Clinical disease activity (Harvey-Bradshaw Index: HBI), serum biomarkers of inflammation and redox status (plasma free thiols), and gut microbiome taxonomical composition and functionality (fluorescent *in-situ* hybridization, FISH, and metagenomic shotgun sequencing, MGS), were analyzed before and after riboflavin intervention.

Results: Riboflavin supplementation significantly decreased serum levels of inflammatory markers. In patients with low disease activity IL-2 decreased, while in patients with high disease activity C-reactive protein (CRP) and tumor necrosis factor-α (TNF-α) were reduced, and free thiols significantly increased after supplementation. Moreover, HBI was significantly decreased by riboflavin supplementation. Riboflavin supplementation led to decreased *Enterobacteriaceae* in patients with low FC levels as determined by FISH, however, MGS analysis showed no effects on diversity, taxonomy or metabolic pathways of the gut microbiome.

Conclusion: Three weeks of riboflavin supplementation suppresses systemic inflammation and attenuates systemic oxidative stress in CD, concomitant with relief of clinical symptoms. FISH analysis showed decreased *Enterobacteriaceae* in quiescent CD, though this was not observed in MGS analysis. Our data demonstrates that riboflavin supplementation has beneficial effects in CD.

Disclosure: Nothing to disclose

P0684 ZN DEFICIENCY CORRELATES WITH DISEASE ACTIVITY OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Zinc (Zn) is an essential micronutrient involved in processes of transcription and synthesis of nucleic acids and proteins. Zn deficiency may lead to modulation of the immune system, resulting in the decrease of cytokine levels, interleukins and IFN-γ. Patients with inflammatory bowel disease (IBD) may have micronutrient deficiency more common than assumed. In previous studies Zn deficiency in IBD patients was in correlation with reduced food intake, enteric loss of nutrients and malabsorption.

Aims & Methods: We aimed to assess Zn levels in IBD patients as well as healthy individuals, and to examine is there a correlation of Zn levels with disease activity.

Complete medical records of all patients with histologically diagnosed IBD were evaluated. As a control group we analyzed medical records of age and sex matched healthy volunteers, who had done their annual health check up. A case-control study was preformed among 45 newly diagnosed IBD patients and the same number age, sex matched healthy controls. All patients underwent a total colonoscopy with ileoscopy. Complete blood count was obtained in addition to inflammatory markers (CRP, erythrocyte sedimentation rate-ESR). Serum levels of Zn were measured spectrophotometrically. Mayo score, UCEIS and CDAI respectively were calculated for each patient.

Results: Serum levels of Zn were significantly lower (P< 0.05) in IBD patients than controls. Moreover serum levels of Zn negatively correlated with younger age at the time of diagnosis, CRP, sedimentation levels and TIBC, whereas we found positive correlation of Zn and Iron levels. Additionally Zn levels negatively correlated with CDAI, UCEIS and Mayo score (P< 0.05)

Conclusion: Our results suggest that Zn deficiency may be potential noninvasive indicator of disease activity in IBD patients as well as the necessity of additional supplementation in these patients, which could potentially affect the disease course.

Disclosure: Nothing to disclose

P0685 DOES GASTRIC LEPTIN PLAY A KEY ROLE IN CONTROLLING FOOD INTAKE?

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Introduction: Patients with obesity maintain high levels of leptin (anorexigenic hormone) generate from amount of fat cells, which is called leptin resistance [1]. Recent research in mice suggested that gastric leptin secreted from chief cells into the stomach could control satiety during eating [2].

This study investigated whether the gastric leptin levels in human changed due to eating as mice and there were the differences between in normal body weight subjects and in obese subjects.

Aims & Methods: Twelve patients with obesity and 5 volunteers of normal weight were enrolled in this study from February 2015 to October 2018. Visceral and subcutaneous fat volumes were evaluated by a CT scan before starting the bariatric therapy and at 6 months. The leptin levels in the serum were measured by radioimmunoassay before a meal and at 15 and/ or 30 minutes after beginning the meal.

The co-relations between the leptin level, the volume of adipose tissue and the stimulation of gastric leptin secretion during eating were evaluated statistically.

Results:
1) The co-relation coefficients between the sera leptin levels at hunger and subcutaneous fat volume was 0.83 and it is less co-related to visceral (0.21) or total (0.40) fat volume individually.
2) The leptin levels were not co-related to data of insulin, liver function and cholesterol.
3) The leptin levels were highly correlated with body weight loss by bariatric therapy.
4) Increases in leptin levels were observed in the normal subjects and in the patients with obesity only after eating more amount of food than threshold level.
5) Dietary stimulation of gastric leptin secretion was available to regulate appetite in a short term only for people without hyperleptinemia.

Conclusion: The leptin level was associated with the volume of adipose tissue in the long term but it was not clear whether gastric leptin regulated appetite shortly after eating.

References: [1] Zhou Y "Leptin signaling and leptin resistance" Front Med. 2013 June; 7(2) 201-22 [2] Cammisotto P " A review on gastric leptin" Anat Cell Biol 2012;45:1-16

Disclosure: Nothing to disclose

P0686 INTESTINAL LUMEN OMEGA-3 POLYUNSATURATED FATTY ACID LEVELS AFTER ORAL SUPPLEMENTATION

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Introduction: The omega-3 polyunsaturated fatty acids (O3PUFAs), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) display anticolorectal cancer (CRC) activity. Oral administration of mixed O3PUFAs in healthy volunteers is associated with changes in the intestinal microbiome in favour of short-chain fatty acid (SCFA) producing bacteria [1].

However, it remains unclear whether this anti-CRC activity is mediated through direct exposure of O3PUFAs in the gut lumen and/ or via systemic bioavailability. We tested whether EPA and DHA levels increase in the distal small bowel after oral supplementation with mixed O3PUFAs.

Aims & Methods: Patients with a temporary ileostomy following anterior resection for colorectal cancer were studied. Ileostomy fluid (IF) and red blood cell (rbc) membrane EPA and DHA levels were measured by liquid chromatography-tandem mass spectrometry before (V1), a few hours after the first dose (V2), and a few hours after the final dose (V3), following 28 days of daily oral supplementation with 4g mixed EPA/DHA triglycerides

(1:1) as capsules with food. The primary end-point was the change in relative amount (% total fatty acid) and absolute concentration of EPA and DHA in IF and rbcs.

Results: Eleven patients (8 male:3 female) with a median age of 63 years (range 42-81) completed the study. The ileostomy was present for a median 9 months (range 2-18) prior to enrolment. Individual compliance with capsules (pill counting) was 100% (range 50-107) over 28 days (range 1-33). Overall, the median relative amount of EPA (V2 0.53%; V3 0.36%) and DHA (V2 0.67%; V3 0.51%) in IF rose post-treatment compared to baseline values (V1; 0.19% and 0.23% for EPA and DHA, respectively). The median absolute concentration (µg/ml) in IF also increased for EPA (V2 1.53; V3 1.13) and DHA (V2 2.62; V3 1.33) from baseline values (V1; 1.06 and 0.79 for EPA and DHA, respectively). Only four patients (36%) displayed a statistically significant increase (Mann Whitney U test, p=0.006) of O3PUFAs in IF after the first dose of capsules. At V2, this group displayed a higher relative amount of EPA (range 6.1 - 22.3%) and DHA (range 7.2 - 23.6%) in IF, compared with the other seven patients (range 0.1 - 1.07% and 0.3 - 1.21% for EPA and DHA, respectively).

However, there was no significant inter-individual variation in levels of O3PUFAs in IF when measured at an equivalent amount of time (V2 median 2 hrs, V3 median 2 hrs) after the final dose of capsules (V3). There was no significant difference in the time interval between oral dosing and IF/rbc sample collection, or frequency of stoma bag changes in the previous 24 hours for V2 and V3. As expected, the relative amount of O3PUFAs in rbc increased after 28 days daily dosing compared to baseline values (EPA: V1 1.19%, V2 1.08%, V3 2.76% and DHA: V1 4.61%, V2 4.50%, V3 6.88%), in keeping with previous studies.

Conclusion: Intestinal lumen O3PUFA exposure is variable after oral consumption. Reduction in luminal O3PUFA concentrations after 28 days dosing suggests intestinal adaptation in individuals who displayed high O3PUFA levels after the first dose of oral O3PUFA supplementation. Knowledge of EPA and DHA concentrations in ileostomy fluid can be used to study changes in the microbiome and metabolome (SCFA) associated with O3PUFA treatment.

References: 1 - Watson H, Mitra S, Croden FC, Taylor M, Wood HM, Perry SL, et al. A randomised trial of the effect of omega-3 polyunsaturated fatty acid supplements on the human intestinal microbiota. Gut. 2017 Sep 26;gutjnl-2017-314968

Disclosure: Nothing to disclose

Paediatric: Upper GI I

10:30-17:00 / Poster Exhibition - Hall 7

P0687 SELECTIVE MICROBIOTA TRANSPLANTATION IS EFFECTIVE FOR CONTROLLING TOURETTE'S SYNDROME

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Introduction: Emerging scientific data support the significant role of microbiota in the modulation of the central nervous system. The reconstitution of gut microbiota might be a potential option to treat Tourette's syndrome (TS).

Aims & Methods: This study aimed to evaluate the role of selective microbiota transplantation on TS. Patients aged 7 to 60 years old with TS and a Yale Global Tic Severity Scale (YGTSS) -total tic score ≥ 25 were enrolled in this open-label clinical trial. Participants received 200ml selective microbiota suspension (mixed species of cultured bacteria) daily through the nasojejunal transendoscopic enteral tubing (TET) tube for 3 days. Clinical evaluations before, 1, 4 and 8 weeks after SMT were assessed with the YGTSS, the Adult Tic Questionnaire (ATQ)/the Parent Tic Questionnaire (PTQ), the Gilles de la Tourette Syndrome Quality-of-Life Scale (GTS-QoL) and the Clinical Global Impression (CGI)-Severity. 16S rRNA stool analysis were performed to assess associated microbial changes. The urinary metabolic profiles of those patients were generated using nuclear magnetic resonance (NMR) spectroscopy. Safety was assessed in all patients after treatment.

Results: Eleven males aged 19.2 ± 7.4 years old finished the study and were analyzed. SMT led to a significantly decrease on the YGTSS-total tic score from baseline to week 4 (46.2 ± 11.9 to 35.7 ± 17.9, *p* < 0.05). 45.5% (5/11),

45.5% (5/11) and 36.4% (4/11) of patients achieved improvement (≥ 30% reduction in YGTSS -total tic score) at week 1, week 4 and week 8 after mini-FMT, respectively. The significant improvement in quality of life was demonstrated by a decreased GTS-QoL score from 42.1±19.5 to 25.5±19.6 at week 8 after treatment (*p* = 0.024).

Patients with gastrointestinal symptoms (n = 5, such as diarrhea, constipation or flatulence) seemed show better response to SMT than others, although there was no significant difference [80% (4/5) vs. 16.7% (1/6), *p* = 0.080].

Microbiota analysis showed that SMT altered the composition greatly. SMT induced significant alterations in urinary metabolic profiles. No severe adverse events related to SMT occurred during treatment and follow-up.

Conclusion: SMT improves quality of life and symptoms of TS by altering microbiota and metabolic mechanism.

Disclosure: Nothing to disclose

P0688 CLINICAL, ENDOSCOPIC AND HISTOLOGICAL CHARACTERISTICS OF ARMENIAN CHILDREN WITH RECURRENT ABDOMINAL PAIN AND DYSPEPSIA

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Introduction: Recurrent abdominal pain and dyspepsia are among the most common complaints in paediatric patients. They are often related to gastroduodenal disease (GDD), functional dyspepsia (FD) and other gastrointestinal disorders.

Aim of the study was to analyze clinical, endoscopic and histological characteristics of Armenian children with recurrent abdominal pain and dyspeptic symptoms.

Aims & Methods: 150 patients aged 2-18 years (70 males and 80 females, mean age 9.2±3.9 years) with recurrent abdominal pain and dyspepsia were involved in the study. All patients underwent EGDS with biopsies: 2 from the antrum (1 for rapid urease test and histology, 1 for Hp culture), 1 from the duodenal bulb and 1 from the distal esophagus. Histology was assessed according to the updated Sydney system. Gastric and duodenal biopsy specimens were stained by Giemsa modification for Hp infection. 1antral biopsy was cultured in Hp selective media.

Results: The patients were divided into 2 groups: 1st groupGDD- 70 (46.7%) (presence of erosions or ulcer in the stomach and/or duodenum, proven Hp infection by 2 invasive tests) and 2nd group FD -80 (53.3%) (no lesions in the stomach and duodenum, proven or excluded Hp infection by 2 invasive tests).

The most common complaints in both groups were recurrent epigastric pain, nausea and vomiting. Night time pain wasmore prevalent in patients with GDD in comparison to FD group (6.25% vs 17.1%)[Fisher 0.04, χ2-4.41 (< 0.05)]. Heartburn was almost equally observed in both groups (10 patients, 14.3% vs 8 patients, 10%). By endoscopy in the 1st group 4 patients had nodular gastritis (5.7%), 55 aphtous erosions in the stomach and/or duodenum (78.6%) and 11 had PUD (15.7%). 74 (58.7%) FD patients were Hp positive.

By histological examination in the 1st group normal stomach mucosa was seen in 2 patients (2.8%), chronic active gastritis in 8 (11.4%), chronic non-active gastritis in 60 (85.7%), normal duodenal mucosa in 25 (35.7%), chronic active duodenitis in 4 (5.7%), chronic non-active duodenitis in 38 (54.2%) and acute duodenitis in 3 (4.3%) patients.In the 2nd group distribution of histological changes was: normal gastric mucosa in 28 (35%), chronic active gastritis in 2 (2.5%) and chronic non-active gastritis in 50 (62.5%) patients, normal duodenal mucosa in 52 (65%), chronic active duodenitis in 4 (5%), acute duodenitis1 (1.25%), chronic non-active duodenitis in 23 (28.75%).In 36 (24%) patients esophagitis was diagnosed: 9 by endoscopy (2 proven by histology) and 27 only by histological investigation: 20 (28.6%) in the GDD group and 16 (20%) in FD group.

A certain number of serious histologic lesions (22 patients, 14%) was noticed in patients with GDD and FD, respectively: gastric metaplasia in 0 (0%) and 2 (2.5%), gastric dysplasia in 1 (0.7%) and 2 (2.5%), gastric atrophy in 4 (2.8%) and 1 (1.25%), gastric metaplasia in duodenum in 8 (11.4%) and 3 (3.75%), duodenal glandular dysplasia in 1 (0.7%) and 0 (0%).

Conclusion:

- Functional dyspepsia was diagnosed in 53.3%, and GDD in 46.7% of children with recurrent abdominal pain and dyspepsia.
- Heartburn and nausea were equally observed in both groups of patients: 14.3% with GDD and 10% withFD.
- A certain number (22 patients, 14%)of serious histologic lesions was noticed in both groups: 3.5% with GDD and 6.25% children with FD.
- EGDS with biopsies might be recommended inpatients with FD to exclude serious histological changes even in case of macroscopically normal mucosa.

Disclosure: Nothing to disclose

P0689 MALNUTRITION IN PAEDIATRIC PATIENTS WITH EOSINOPHILIC ESOPHAGITIS

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Introduction: Patients with Eosinophilic Esophagitis (EoE) may be at nutritional risk due to their own disease, to low dietary intake because of symptoms or to elimination diets. The aim of our study was to screen the presence of malnutrition in paediatric patients with EoE.

Aims & Methods: We conducted a prospective observational study from November 2018 to February 2019 in a Paediatric tertiary referral centre. We included patients with EoE younger than 18 years. Patients with a previous diagnosis of other chronic disease were excluded. Demographic and anthropometric data, as well as medical history were recorded. The anthropometric assessment was made measuring weight (W), height (H) and obtaining Z-scores according to the WHO definitions for malnutrition in children ≤5 years and according to local growth charts (Hernandez et al 1988[1]) in those >5 years. Acute malnutrition was considered severe when W/H < -3 SD and mild when W/H < -2 SD; chronic malnutrition was considered severe if H/age < -3 SD, mild if H/age < -2 and acute superimposed on chronic if H/age < -2 SD and W/H< -2. Children ≤ 5 years were considered overweight if W/H> 2 SD and obese if W/H> 3 SD. Children>5 years were considered overweight if W/H> 1 SD and obese if W/H> 2 SD. SPSS 20 was used for statistical analysis.

Results: We included 33 patients with a median age of 15 years (range 10,7-17), 24 (72,7%) were male. 16 (48,5%) had asthma and 22 (66,7%) Ig E-mediated food allergies. Most patients (81,2%) were on an elimination diet: 15 because of their IgE-mediated food allergy, 4 as a dietary treatment for their EoE and 7 secondary to both indications. The median diet duration was 4 years (1,6-9,8) and the median of group foods excluded per patient was 2 (1-4). In 16 (48,5%) patients, 2 or more group foods were excluded. The food groups most commonly excluded were: milk (12), nuts (14), fruits (8), egg (7), fish and shellfish (6), gluten (5) and legumes (4). 22 (41,5%) patients received medical treatment for their EoE: 11 swallowed topical steroids (STS) and 11 proton pump inhibitors (PPI). Almost half of the patients (15, 45,5%), had active EoE in their last endoscopy and 8 (15,1%) referred symptoms in the moment of the assessment.

Malnutrition was found in 9 (27, 2%) patients: acute mild malnutrition in 1 (3%), chronic mild malnutrition in 1 (3%), obesity in 4 (12, 1%) and isolated growth retardation in 3 (9,1%). Of those with malnutrition, 8 (88, 9%) patients were on an elimination diet (p=0.4), with a median of 3 (1-6) food groups excluded per patient and a median of diet duration of 4,8 years (3,3-10,8). A third of those patients received previous nutritional supplements with elemental formulas. No statistical differences were found between the presence of malnutrition and the number of food groups excluded (p=0.4), nor in relation to diet duration (p=0.2). Nevertheless, we found a trend towards statistical difference between the duration of the disease since diagnosis and the presence of malnutrition (p=0.08). No statistical differences were found in relation to existence of Ig-E related food allergies nor in relation to medical treatment: 2 of the patients with isolated growth retardation received treatment with PPI and 1 with STS; 3 of the obese patients received medical treatment (2 PPI and 1 STS).

Conclusion: Up to 27% of patients with EoE presented malnutrition. Most of them were on exclusion diets of prolonged duration and had multiple food groups excluded. Patients with a longer duration of their EoE tend to present malnutrition in a higher frequency.

References: 1 Hernández. Castellet J, Narvaiza JL, Rincón JM, Ruiz I, Sánchez E, Sobradillo B, Zurimendi A. Curvas y Tablas de Crecimiento. Instituto de investigación sobre crecimiento y desarrollo. Fundación F. Orbegozo. Ediciones Garsi, Madrid, 1988.
Disclosure: Nothing to disclose

P0690 GENETIC STRUCTURE OF HELICOBACTER PYLORI IN RELATIVES: RESULTS FROM A FAMILY STUDY

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Introduction: Ways of transmission of Hp-infection cause the possibility of the existence of its family tanks and transmission to close relatives of the infected person. The risk of developing Hp-associated diseases of the upper digestive tract largely depends on the genetic structure of Hp. It is known that the most pronounced inflammation in the gastric mucosa is observed during colonization by its highly pathogenic strains of Hp. Chronic gastritis associated with low pathogenic strains of Hp is more often characterized by a superficial process of initial manifestation without signs of atrophy of the gastric mucosa. These facts are important to consider when deciding on the appointment of therapy for Hp-infected family members of the patient.

Aims & Methods: To determine the genetic structure of HP in close relatives of patients with HP-associated chronic gastritis.

Patients and methods. Among 120 children aged 8-15 years with verified chronic HP-associated gastritis, 16 patients with severe widespread inflammation in the gastric mucosa were selected. All patients underwent gastroscopy with the morphological study of materials of gastrobiopsy. In them using the polymerase chain reaction has identified 16 factors of pathogenicity of Hp: genes of the CagA, CagC, CagE, CagF, CagH, CagM, CagT, VacAs1, VacAs2, IceA, BabA, hpaA, OipA, AlpB and genes encoding the urease subunit B (UreB) and I (UreI). Next, we conducted serologic screening with the definition of class G antibodies to HP antigens among close relatives (parents and sibs of DM). The two and a large excess of antibody titers above the reference values, all of them conducted a similar survey (n = 38).

Results: All children and their relatives were diagnosed with moderate or severe chronic inflammation in the gastric mucosa. Morphological signs of its atrophy were revealed in 75 % of children and 90 % of their parents and sibs. Every fourth adult patient was diagnosed with intestinal metaplasia. Highly pathogenic HP strains were found in 81.3 % of children and 90 % of their close relatives. Statistical analysis showed that the genetic structure of HP in most families (12 out of 16) is almost identical. The highest reproducibility in families is characteristic for such factors of HP pathogenicity as, BabA, hpaA, VacA, Cag E, CagM, CagH, AlpB и UreB.

Conclusion: The identity of the genetic structure of HP in children and their close relatives with chronic gastritis is established. Highly pathogenic strains of HP cause a pronounced inflammatory process in the gastric mucosa. In endoscopic verification of this process, serological screening among close relatives of the patient is recommended. In patients with high titers of antibodies to HP antigens, an in-depth examination with an assessment of their genetic structure of HP is necessary.

Disclosure: Nothing to disclose

P0691 THE INFLUENCE OF THE GENETIC STRUCTURE OF HELICOBACTER PYLORI ON THE CLINICAL AND MORPHOLOGICAL MANIFESTATIONS OF CHRONIC GASTRITIS IN ADOLESCENTS

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Introduction: The genetic structure of Helicobacter pylori (Hp) is one of the most important factors determining the severity of chronic inflammation in the gastric mucosa. This makes it important to study the genome of Hp in diseases of the upper digestive tract.

Aims & Methods: To establish the features of clinical manifestations and pathomorphology of gastric mucosa in Hp-associated chronic gastritis in adolescents, depending on the genetic characteristics of Hp.

Patients and methods: 133 adolescents aged 15-18 years with Hp-associated chronic gastritis were examined. In material of gastrobiopsy, using the polymerase chain reaction has identified 16 factors of pathogenicity of Hp: genes of the CagA, CagC, CagE, CagF, CagH, CagM, CagT, VacAs1, VacAs2, IceA, BabA, hpaA, OipA, AlpB and genes encoding the urease subunit B (UreB) and I (UreI).

Results: In Hp-associated chronic gastritis in adolescents in 60,9 % of cases there is a colonization of the gastric mucosa with highly pathogenic strains of Hp. Almost all these patients (98,5 %) there is a combination of several genes of the island of pathogenicity, including 60,2 % of cases simultaneously 10 and more. Most often identified factors, promote adhesion of Hp on the epithelial cells and the formation of biological films: hpaA - 76,7 %, OipA - 62,8 %, AlpB - 79,1 %. There were allocated 2 group of patients: the main group - teenagers, which identified highly pathogenic Hp strains (n = 81) and comparison group - patients associated with low pathogenic Hp strains (n = 52). Analysis of clinical syndromes of Hp-associated chronic gastritis in adolescents have not found the dependence of the symptoms of the disease from the structure of the genome of Hp. At the same time, the presence of highly pathogenic strains of Hp according to the morphological study is associated with high rates of contamination, increased inflammation, the appearance of signs of atrophy of the gastric mucosa.

Conclusion: The genetic structure of Hp does not affect the clinical manifestations of chronic gastritis in adolescents, but determines the severity of the inflammatory process and athrophy in the gastric mucosa.

Disclosure: Nothing to disclose

P0692 THE EFFECTIVENESS OF THERAPY OF HELICOBACTER PYLORI IN CHRONIC GASTRITIS IN ADOLESCENTS, DEPENDING ON THE GENETIC STRUCTURE OF HELICOBACTER PYLORI

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Introduction: Features of the genetic structure of the Helicobacter pylori (Hp) can have a significant impact on the nature of changes in the gastric mucous of the upper digestive tract and on the development, course, prognosis of gastroduodenal pathology, as well as the effectiveness of therapy.

Aims & Methods: To establish the dynamics of pathomorphological changes in the gastric mucosa in adolescents with chronic gastritis associated with high and low pathogenic strains of Hp, after a course of anti-Helicobacter pylori therapy.

Patients and methods. 40 adolescents aged 15-17 years with chronic Hp-associated gastritis were examined. The polymerase chain reaction in material of gastrobiopsy determined the Hp virulence factors: CagA, VacAs1, IceA, BabA and the gene encoding the urease subunit I (I Ure). All patients were examined twice: before and after 6 months a course of anti-Helicobacter therapy.

Results: There were allocated 2 group of patients: the main group - teenagers, which identified highly pathogenic Hp strains (n = 27) and comparison group - patients associated with low pathogenic Hp strains (n = 13). In repeated morphological study found that after a course of anti-Helicobacter therapy expressed colonization of gastric mucosa Hp in the main group was found in 33,3 % of cases in the comparison group of only 7,7 %, p < 0,05. In the main group, moderate and severe inflammation of the gastric mucosa of 92,6 % versus 31,8 %, p < 0,005. More than half of the patients of the main group in the morphological study retained signs of atrophy of gastric mucosa; significantly, more often revealed areas of hyperplasia and microerosis.

Conclusion: Colonization of the gastric mucosa with highly pathogenic Hp strains is a factor preventing eradication of infection in chronic Hp-associated gastritis in adolescents. The majority of these patients 6 months after a course of anti-Helicobacter therapy remains moderate or severe degree of inflammation in the gastric mucosa.

Disclosure: Nothing to disclose

Liver & Biliary II

09:00-17:00 / Poster Exhibition - Hall 7

P0693 EATING BEHAVIOR CORRECTION IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE DEPENDING ON POLYMORPHISMS OF THE PPARG2 AND ADRB2 GENES

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Introduction: According to the World Health Organization, the health of the population is 68-74% dependent on lifestyle and 18-20% on genetics. At the present stage in the treatment of patients with non-alcoholic fatty liver disease (NAFLD) not enough attention is paid to the study of the individual characteristics of eating behavior (EB) and nutrigenetiki. At the same time, EB violations are a modifiable risk factor, the correction of which can positively modulate nutrigenic features - a possible metabolic response to the use of certain nutrients. Personalized approach is a priority in improving the effectiveness of treatment of patients with NAFLD. The study of nutrigenetics and its application in practice in the correction of nutrition is an important step towards personalized medicine.

Aims & Methods: Fifty patients (26 men and 24 women) with NAFLD were examined. The control group consisted of 30 practically healthy patients reciprocating by sex and age. All patients studied the characteristics of EB (DEBQ questionnaire), anthropometric indicators, lipid and carbohydrate metabolism, the degree of liver steatosis, the area of visceral adipose tissue (CT scan), nutrigenetic features (definition of 5 polymorphisms: Pro12Ala of the PPARG2 gene (rs1801282), Gln27Glu of the ADRB2 gene (rs1042714), Arg16Gly of the ADRB2 gene (rs1042713), Trp64Arg of the ADRB3 gene (rs4994) and Thr54Ala of the FABP2 gene (rs1799883), associated with the risk of metabolic disorders. Patients were prescribed individual nutritional correction for 12 months, taking into account the identified polymorphisms associated with EB violation, namely: carriers of the Pro12Ala genotype of the polymorphism of the PPARG2 gene were prescribed a therapeutic diet with moderate fat intake of 1.1-1.2 g / kg / day and carbohydrate restriction of 2.5-3 g / kg / day, Pro12Pro genotype carriers - diet with restriction of fats up to 1.0 g / kg / day and moderate consumption of carbohydrates up to 3.5-4 g / kg / day.

Results: After 12 months after individual correction, significant positive dynamics of the main anthropometric and laboratory-instrumental indicators were observed: a decrease in body mass index and waist circumference by a factor of 1.2 (p < 0.05), a decrease in the level of total cholesterol and low-density lipoproteins of 1.5 and 1.3 times, respectively (p < 0.001), the level of triglycerides, 2.1 times (p < 0.001) and the increase in high-density lipoproteins by 1.4 times (p < 0.001)), a decrease in HOMA-IR in 2.2 times (p < 0.001), liver samples (reduction of alanine aminotr nsferase 2.4 times and aspartate aminotransferase 2.5 times (p < 0.05)), CT scan - signs of steatosis (35% increase in liver x-ray density (p < 0.001)) and indicators of visceral obesity (a decrease of 2.1 times the area of visceral adipose tissue ((p < 0.001). In addition, during the control questionnaire, normalization of EB was observed in 86% of patients and a decrease in the degree of eating disorders in 14% of patients compared with baseline indicators (p < 0.001).

Conclusion: Thus, the appointment of individual correction of EB taking into account nutritional features for at least 12 months contributes to a significant improvement in metabolic parameters associated with the risk of development and progression of NAFLD, the formation and stabilization of proper eating habits, which improves the effectiveness of treatment of patients with NAFLD.

Disclosure: All authors have declared no conflicts of interest.

P0694 A NEW METHOD OF TREATMENT FOR DECOMPENSATED LIVER CIRRHOSIS: ENDOSCOPIC ULTRASOUND-GUIDED TRANSGASTRIC, TRANSHEPATIC INTRAPORTAL AUTOLOGOUS BONE MARROW TRANSPLANTATION

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Introduction: Stem cell therapy recently has been explored extensively as a promising treatment for decompensated liver cirrhosis. However, the genomic instability of cultured stem cells and the low efficiency in obtaining them hindered the progress of stem cell transplantation. Moreover, it is pivotal to optimizing transplantation routes by which the stem cells can be delivered effectively. Here we report the novel Endoscopic ultrasound (EUS)-guided transgastric and transhepatic intraportal autologous bone marrow transplantation to achieve therapeutic goals in patients with decompensated liver cirrhosis.

Aims & Methods: To investigate the effects of EUS-guided intraportal autologous bone marrow transplantation in decompensated liver cirrhosis, five patients with decompensated liver cirrhosis were recruited. All patients were successfully performed autologous bone marrow transplantation through EUS-guided portal vein (PV) access using the transgastric and transhepatic approach. Regular revisiting was conducted every 1 month and now in 6 months follow-up.

Results: Clinical symptoms of patients underwent portal vein transfusion of autologous bone marrow were improved obviously, while no side effects and complications were observed within 6 months follow-up. Specifically, albumin levels, ascites degree, and Child-Pugh score were significantly ameliorated in 1 month, and all follow-up data indicated the continuing improvement irrespective of postoperative time.

Characteristic	Baseline	1st month	P value (1st month vs Baseline)	6th month	P value (6th month vs Baseline)
Albumin, g/L	27.58±4.91	35.76±5.87	0.044	38.68±8.98	0.041
Tbil, umol/L	22.08±10.99	24.48±11.92	0.749	22.58±13.40	0.951
PT, sec	16.02±1.73	14.48±1.11	0.132	14.36±1.60	0.153
No ascites	0% (0/5)	20% (1/5)	-	60% (3/5)	-
Mild ascites	40% (2/5)	40% (2/5)	-	20% (1/5)	-
Moderate and large ascites	60% (3/5)	40% (2/5)	-	20% (1/5)	-
Child-pugh class A	20% (1/5)	40% (2/5)	-	80% (4/5)	-
Child-Pugh class B	60% (3/5)	60% (3/5)	-	20% (1/5)	-
Child-Pugh class C	20% (1/5)	0% (0/5)	-	0% (0/5)	-

[Characteristics of patients]

Conclusion: EUS-guided intraportal transplantation of autologous bone marrow improves both clinical symptoms and liver function for patients with decompensated liver cirrhosis. It may thus provide a safe, effective, non-radioactive, and minimally invasive treatment.

Disclosure: Nothing to disclose

P0695 GENETICALLY MODIFIED HSCS STIMULATES LIVER REGENERATION AND COULD BE A NEW PERSPECTIVE APPROACH FOR DEVELOPMENT LIVER DISEASE TREATMENT

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Introduction: Mortality from chronic liver disease is rising exponentially. Nowadays a lot of effort is made to find new approaches to stimulate liver regeneration and to develop new methods for liver diseases treatment. Cell and gene therapy methods, which are based on using regional stem

cells seems to be perspective. Currently a particular interest is paid to hepatic stellate cells (HSCs). Besides, it's known that HSC is the only source of hepatocyte growth factor (HGF) and fibroblast growth factor 4 (FGF4) in the liver - growth factors, which play a key role in hepatocytes differentiation during embryogenesis and liver regeneration. It is assumed that using genetically modified HSCs (gmHSCs) that express these growth factors could enhance their therapeutic potential.

Aims & Methods: The aim of our work was to study gmHSCs properties *in vitro* and their influence on liver regeneration after transplantation into the rats after partial hepatectomy (PH). HSCs were isolated from Wistar rat's liver, genetic modification was carried out by adenovirus Ad5-optH-GF-optFGF4-RFP, which contained HGF, FGF4 and reporter gene of Red Fluorescent Protein (RFP). At first, we have studied gmHSCs phenotype *in vitro*, then we have injected gmHSCs into the rats' portal vein during PH operation (experimental group-EG). Control group (CG) of animals received HSCs, transdused by Ad5-RFP vector, which contains only RFP. The animals were sacrificed on 1, 2, 3, 5, 7, 10, 14 and 21 days after HSC transplantation. Paraffin slices were stained immunohistochemically with antibodies to RFP (reporter), α-FP (hepatoblasts) and α-SMA (myofibroblasts).

Results: The results demonstrated that *in vitro* gmHSCs expressed hepatoblast marker α -FP earlier than native HSCs and the gene expression level (by RT-PCR) was also significantly higher in gmHSCs group than in native one. This means positive influence of HGF and FGF4 on gmHSCs differentiation in hepatocyte direction *in vitro*. *In vivo* transplanted HSCs saved their viability and migrated to liver parenchyma. A large number of RFP+hepatocyte-like cells were detected even on the 1st day after transplantation (4,94±2,37 %) in the EG, then their number increased to 8,57±5,15 % by the 2nd day. After that, RFP+ cells quantity gradually decreased to 4,82±3,64 % by the 14th day. In the CG dynamics was the same, but the average number of cells was less. α-FP+ hepatocytes were also detected in both groups, but in the EG α-FP+ cells amount was significantly higher than in the CG. In all the groups α-SMA+ myofibroblasts, responsible for liver fibrosis, were not detected.

Conclusion: gmHSCs transplantation had more intensive repopulating effect on hepatocytes during the transplantation. It proves the positive effect of the inserted HGF and FGF4 genes on the liver regeneration process. Thus, gmHSCs transplantation stimulates liver regeneration and contributes to hepatocytes repopulation without risk of liver fibrosis.

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Disclosure: All authors have declared no conflicts of interest.

P0696 THE EFFECT OF MESENCHYMAL STEM CELLS DERIVED MICROVESICLES TRANSPLANTATION ON LIVER REGENERATION AFTER PARTIAL HEPATECTOMY IN RATS

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Introduction: There are numerous studies of stimulation of liver regeneration by transplantation of mesenchymal stem cells. Their effect is explained by direct intercellular interactions and paracrine communications. One of the alternative ways to influence on liver regeneration is injection of microvesicles. Microvesicles are extracellular vesicles that contain growth factors and cytokines and play a major role in intercellular paracrine communications. It is said, that in compare to cells microvesicles transplantation is not accompanied by risk of metaplasia and mutations, because they do not contain any genetic information.

Aims & Methods: To study the effect of transplantation of mesenchymal stem cells microvesicles derived from adipose fat tissue on liver regeneration after partial hepatectomy in rats.

Mesenchymal stem cells, isolated from visceral rat fatty tissue (adMSC), were treated by Cytochalasin B to derive microvesicles. These microvesicles were transplanted into portal vein of rats after partial hepatectomy. Control group of rats after partial hepatectomy received injection of PBS. On 2, 5, 7 and 14 days after operation rats were sacrificed. Functional parameters of liver were analyzed by biochemical tests, morphological changes were studied by immunohistochemical staining of liver slices with antibodies to desmin (HSC marker), Ki-67 (proliferation marker), α-SMA (myofibroblasts marker), CK-19 (cholangiocytes marker).

Results: According to immunohistochemistry results injection of microvesicles: 1) inhibits activation of HSC - there were 20% less desmin+ cells; 2) there were no transformation of HSC into α-SMA+ myofibroblasts and no risk of liver fibrosis; 3) inhibition of cellular proliferation. So, Ki-67+ hepatocytes number (area of portal tract and central vein) decreased in compare to control group. Number of Ki-67+ nonparenchymal cells in portal tract area was 2 times less, than in control. 4) there were no differences in CK-19 expression in experimental and control groups. As far as the cellular proliferation and thus liver regeneration was inhibited, we`ve seen higher numbers of ALT levels in experimental group. Decreased regeneration could be also visualized by lower triglycerides and cholesterol levels, there were less, than normal values. Blood urea nitrogen normalized in control group on the 4th day, but in experimental - by the 7th day already.

Conclusion: Injection of adMSC microvesicles inhibits general cellular response to partial hepatectomy. Inhibition of hepatocytes activation and proliferation slows down liver regeneration, that is proved by biochemical tests. Inhibition of HSC activation means also lesser risk of their transformation into myofibroblasts and fibrosis development. Thus microvesicles transplantation is not for stimulation of liver regeneration. Probably these inhibitory effects could be applied for treatment of liver fibrosis, that needs to be studied.

References: Work supported by Program of Competitive Growth of KFU.

Disclosure: All authors have declared no conflicts of interest.

P0697 HUMAN DUODENAL SUBMUCOSAL GLANDS CONTAIN STEM CELLS WITH POTENTIAL FOR LIVER AND PANCREATIC REGENERATIVE MEDICINE

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Introduction: Regenerative medicine of liver and pancreas has a paramount importance. Common precursors for liver, biliary tree and pancreas exist at early stage of development in the definitive ventral endoderm forming the foregut (1).

Aims & Methods: Therefore, the aims of the present study were:

i) to evaluate whether adult human duodenal submucosal glands (SGs) contain cells expressing stem cell traits,

ii) to establish a protocol for isolating these cells based on their anatomical and phenotypic traits,

iii) to characterize self-renewal properties of duodenal SG cells and their potency to generate functional liver and β-pancreatic cells.

Human duodenum (N=15) were obtained from deceased adult organs and analyzed by immunohistochemistry and immunofluorescence (2). The entire duodenum was processed through a chemical dissolution of the mucosa layer that preserved the sub-mucosa, which was successively digested mechanically and enzymatically (2). Isolated cells were immune-selected for the markers of pluripotent stem cells Tra-1-60+ SG cells and successively cultured in self-renewal or differentiation media (2). Parallel experiments were conducted in vivo through injection of Tra-1-60 + cells in the spleen of immunocompromised mice, or in streptozotocin-induced diabetic mice, or in Krt19CreTdTomatoLSL C57BL6/J mice (1, 2).

Results: In human duodenum, SGs contain cells expressing stem cell markers and with a phenotype which differs from intestinal crypts. Uniquely, duodenal SGs contained Ck7+ and Tra-1-60+ cells which are not present in intestinal crypts. Lineage tracing study in mice demonstrates homeostatic

self-renewal of SGs, which is not supported by duodenal crypt cells. In vitro, SG cultures were composed of cells expressing Ck7, Sox9, EpCAM, Lgr5, and pluripotency markers (Sox2, Tra-1-60, Tra-1-81). SG cells have self-renewal properties, form organoids, and differentiate towards hepatic and pancreatic lineages with distinctive functional properties. In vivo, transplanted cells engraft into livers of severe combined immunodeficient (SCID) mice and differentiate to mature liver cells; in experimentally induced diabetes, insulin-positive cells appear within duodenal SGs.

Conclusion: Actual candidate cell sources for regenerative medicine of liver and pancreas are mature cells (hepatocytes and islets) with poor success in literature or reprogrammed cells with the related limits of cell manipulation and tumorigenic risk. Duodenal SGs could represent an easily available cell source for regenerative medicine of ventral endoderm organs with no need of reprogramming.

References: 1) Lanzoni G, Cardinale V, Carpino G. The hepatic, biliary, and pancreatic network of stem/progenitor cell niches in humans: A new reference frame for disease and regeneration. Hepatology. 2016 Jul;64(1):277-86. 2) Carpino G, Cardinale V, Gentile R, Onori P, Semeraro R, Franchitto A, Wang Y, Bosco D, Iossa A, Napoletano C, Cantafora A, D'Argenio G, Nuti M, Caporaso N, Berloco P, Venere R, Oikawa T, Reid L, Alvaro D, Gaudio E. Evidence for multipotent endodermal stem/progenitor cell populations in human gallbladder. J Hepatol. 2014 Jun;60(6):1194-202.

Disclosure: The authors declare no competing interests with exception of V.C., G.C., E.G., D.A., and L.R. who have submitted a provisional filling on isolation method for duodenal submucosal gland stem cells.

P0698 FIBROSCAN AS A TOOL TO IMPROVE CARDIOVASCULAR DISEASE STRATIFICATION: TRUTH OR MYTH?

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease worldwide. Transient elastography (TE, Fibroscan) with controlled attenuation parameter (CAP) has already been proven as an accurate measure for hepatic fibrosis and steatosis. However, its role in stratifying cardiovascular (CV) risk is unknown.
Aims & Methods: Cohort, retrospective, single center study, including consecutive NAFLD patients that underwent Fibroscan. Patients were followed at least a year.
Co-variables were chosen bearing in mind clinical relevance and literature evidence.
The correlation towards the outcome variable (Cardiovascular event) was assessed with univariate and multivariate analysis, using SPSS - p value < 0.05 was considered statistically significant
Results: We assessed 96 patients with NAFLD, of whom 64 (66,7%) were female, with a mean age of 51,6 years old, all Caucasian. From our cohort, 55.2 % of the patients met criteria for metabolic syndrome.
Several variables had statistical significance towards cardiovascular events incidence on the univariate analysis. (Cardiac failure; Hypertension; dyslipidemia, diabetes mellitus, metabolic syndrome, body mass index, CAP higher 290 db/m, Framigham score and some therapeutics, hypocoagulation agents, antiplatelet agents, statins, antihypertension agents.)
We report 14 (14,4%) cardiovascular events during follow up, the CAP mean in this subgroup was 318,4 db/m.
For CAP values superior to 290 db/m (decibels per meter), the odd of incidence of cardiovascular events were 4,2 times higher, for each unit of cap increase (Odds ratio crude 4,250; p value 0.05). Adjusting the regression multivariate model with previous significant variables, the association trend to statistically non-significance.
Framingham score was not correlated statistically with CAP values.
Conclusion: We were able to stablish a correlation between CAP and incidence of cardiovascular disease events. Meaning that, a CAP increase is associated with increase of incidence on CV events, mainly in high cap values, over 290 db/m. However, this correlation is diluted adjusting to another CV risk predictor covariables. Fibroscan is easy to apply, safe and a cost-effective method to evaluate NAFLD. CAP values are related to CV events, nevertheless, further studies are needed to identify properly the subpopulation that would most benefit from this feature.
Disclosure: Nothing to disclose

P0699 DIETARY INTAKE OF PHENOLIC ACIDS IS INVERSELY ASSOCIATED WITH LIVER STEATOSIS AND INSULIN RESISTANCE IN THE GENERAL POPULATION

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Introduction: The inverse association between NAFLD and diet rich in fruit and vegetables has been demonstrated, but the specific compounds that may be responsible for this association need to be elucidated.
Aims & Methods: The aim of this study was to test the association between phenolic acids (PA) consumption, liver steatosis, liver fibrosis, and insulin resistance (IR). This was a cross-sectional study among general population, included in a metabolic screening program. Liver steatosis was evaluated by ultrasonography to determine NAFLD and quantified by the HepatoRenal Index (HRI); fibrosis was assessed by FibroTest; IR by the sample upper quartile of HOMA score. Nutritional intake was measured by food frequency questionnaire (FFQ). Phenolic acids food content was calculated according to Phenol Explorer.
Results: A total of 789 subjects were included (52.6% men, age 58.83±6.58 years). Higher (above the upper median) phenolic acids intake was inversely associated with the presence of NAFLD, higher HRI and IR (OR=0.69, 95%CI 0.49-0.98, P=0.036; OR=0.64, 95%CI 0.45-0.91, P=0.013; OR=0.61, 95%CI 0.42-0.87, P=0.007, respectively), adjusting for age, gender, BMI, dietary and lifestyle factors. Considering specific classes of PA, higher hydroxybenzoic acids intake was independently associated with lower odds of NAFLD, higher HRI and fibrosis (OR=0.72, 95%CI 0.51-0.99, P=0.049; OR=0.63, 95%CI 0.45-0.89, P=0.008; OR=0.28, 95%CI 0.12-0.64, P=0.003, respectively). Higher hydroxycinnamic acids consumption was independently associated with lower odds of IR (OR=0.63, 95%CI 0.44-0.90, P=0.012).
Conclusion: Phenolic acids may represent food compounds that are protective against insulin resistance and NAFLD-related liver damage.
Disclosure: Nothing to disclose

P0700 WITHDRAWN

P0701 RISK OF METABOLIC SYNDROME IN SUBJECTS WITH NORMAL ALANINE AMINOTRANSFERASE LEVEL: A POPULATION-BASED NATIONWIDE STUDY

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Introduction: This study aimed to investigate the risk of metabolic syndrome in subjects with normal ALT level for the general population.
Aims & Methods: A cross-sectional study was conducted using nationally representative samples from the Korean National Health and Nutrition Examination Survey 2007-2015. A total of 43,402 adults (men: 17,535 and women: 25,867) with ALT ≤40 U/L and no history of hepatitis B, hepatitis C, liver cirrhosis, and liver cancer were analyzed. The risk of metabolic syndrome were evaluated according to ALT level (men: < 15 U/L, 15~30 U/L, and 30~40 U/L / women: < 10 U/L, 10~20 U/L, 20~40 U/L). Metabolic syndrome was defined by updated National Cholesterol Education Program Adult Treatment Panel III standards.
Results: The prevalence of metabolic syndrome is significantly increased as ALT increases regardless of sex. The proportion of metabolic syndrome in men is 12.6%, 25.2%, and 39.7% in ALT < 15 U/L, 15~30 U/L, and 30~40 U/L, respectively (*p*< 0.001) and that of metabolic syndrome in women is 7.2%, 23.3%, and 44.7% in ALT < 10 U/L, 10~20 U/L, and 20~40 U/L, respectively (p< 0.001). There is an ALT-dependent relationship in the risk of metabolic syndrome within normal ALT level adjusting age, alcohol intake, and body mass index.

The adjusted odds ratios (ORs) of metabolic syndrome in men are 1.55 (95% confidence interval [CI]: 1.38-1.74), and 2.48 (95% CI: 2.16-2.85) in ALT 15~30 U/L, and 30~40 U/L, respectively (*p*< 0.001). And, the adjusted ORs of metabolic syndrome in women are 1.58 (95% CI: 1.35-1.86), and 2.67 (95% CI: 2.26-3.15) in ALT 10~20 U/L, and 20~40 U/L, respectively (*p*<0.001).

Conclusion: The risk of metabolic syndrome is increased as ALT increases within normal ALT level. Even if the ALT level is within normal range, it may be a useful marker to evaluate metabolic syndrome.

Disclosure: Nothing to disclose

P0702 VITAMIN E AND C INTAKE IS INVERSELY ASSOCIATED WITH LIVER DAMAGE IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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Introduction: Evidence is limited regarding to the association between dietary intake of antioxidants and non-alcoholic fatty liver disease (NAFLD) and steatohepatitis (NASH).

Aims & Methods: The aim was to test the association between dietary vitamins E and C intake and NAFLD, NASH and fibrosis markers. This was a cross-sectional study of general population. NAFLD was evaluated by ultrasonography and presumed steatosis, NASH and fibrosis by FibroMax. The level of steatosis was defined using SteatoTest, significant NASH defined ≥2 and borderline-significant fibrosis ≥F1-F2. Nutritional intake was measured by food frequency questionnaire (FFQ).

Results: Overall, 789 subjects were included (52.6% men, age 58.83±6.58 years), 714 had reliable FibroMax. Adjusting for BMI, dietary and lifestyle factors, the upper tertile of vitamin E intake/1000 Kcal was associated with lower odds of NASH (OR= 0.64, 0.43-0.94, P= 0.024). There was an inverse association between reaching the recommended vitamin E intake and NASH (OR= 0.48, 0.30-0.77, P= 0.002). The upper tertile of vitamin C intake/1000 Kcal was associated with lower odds of NAFLD and NASH (OR = 0.68, 0.47-0.99, P= 0.045; OR= 0.57, 0.38-0.84, P= 0.004, respectively). Both vitamins were related with the level of steatosis according to SteatoTest.

Conclusion: Vitamin E and C intake may be protective from NAFLD related liver damage.

Disclosure: Nothing to disclose

P0703 PREVALENCE AND RISK FACTORS OF NONALCOHOLIC FATTY LIVER DISEASE IN A RURAL COMMUNITY OF SOUTH ASIA

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Introduction: The prevalence and risk factors of nonalcoholic fatty liver disease (NAFLD) varies in different populations. Although nonalcoholic fatty liver disease (NAFLD) has been reported high from the Western and affluent Asian countries, there is paucity of such data from less developed countries, particularly rural areas where most of the people live in Asia. Hence, we undertook a study on the epidemiology of NAFLD among the general population in a rural community of Bangladesh.

Aims & Methods: All the adult persons (≥18 years) of a defined area of three villages (Charcharia and Churian, Dhaka District, Kharrah, Munshi-ganj District) identified by manual census were interviewed by a door-to-door survey using a structured questionnaire by trained field research assistants in this cross sectional study. Clinical examination and anthropometric measurements were done by the investigators. Biochemical tests on blood were done after overnight fasting and ultrasonography were done by experienced radiologist on every subject. BMI was categorized by WHO standards and metabolic syndrome (MetS) was defined by Adult Treatment Panel III.

Results: Of the total 1682, 1353 subjects responded (response rate 80.44%). In the final analysis1305 subjects (mean age 41.28 ± 15.10, female 908, 69.6%) were included after exclusion of forty eight subjects for any amount alcohol consumption, HBsAg or Anti-HCV positivity. On ultrasonography, NAFLD was present among 242 (mean age 46.10 ± 12.30, male 93, female 149) subjects with an overall prevalence of 18.5 % (male 23.40% vs female 16.4%, p=0. 003). Among subjects with underweight, normal weight, overweight and obesity, NAFLD was present in 0/161(0%), 57/643 (8.9 %), 119/383 (31.1%) and 66/118(55.9%) respectively. NAFLD was more common among subjects aged 40 years or more [153/667, 24.4% vs 89/678, 13.1%; odds ratio (OR) 2.13, 95% confidence interval (CI):1.60-2.85]; DM (82/168,48.8% vs 160/1137, 14.1%; OR=5.82; 95% CI:4.12-8.23, <p=0.001), abdominal obesity (134/365,36.7 % vs 108/940, 11.5 %; OR=4.45, 95% CI:3.34-5.99, <p=0.001) and MetS (163/373, 43.7% vs 79/932 ,8.5 %; OR=8.38, 95% CI: 6.16-11.41). Table 1 compares the significant key parameters of MetS among subjects with and without NAFLD.

Additionally, elevated ALT (>40U/L) was present among 53/242(22.0%) subjects with NAFLD. On binary logistic regression analysis, male sex, fasting hyperglycemia or pre-existing DM, higher SBP, abdominal obesity, BMI>25 kg/m², presence of MetS and higher serum triglyceride were found to be risk factors for NAFLD.

Characteristics	Subjects with NAFLD (mean ±SD)	Subjects without NAFLD (mean ±SD)	P value
SBP	126.84±19.76	113.82±17.65	<0.001
DBP	82.19±11.46	75.54±10.56	<0.001
Fasting blood glucose (mmol/L)	6.40±3.13	4.90±1.41	<0.001
S. Total cholesterol (mg/dl)	210±82.12	188.08 ±56.22	<0.001
S.LDL-C (mg/dl)	187.85±41.24	122.22±51.84	0.115
S.HDL-C (mg/dl)	37.62± 9.51	38.84±10.91	0.109
Fasting S. triglyceride (mg/dl)	226.84±140.12	142.48±93.01	<0.001
BMI (kg/m2)	27.93±4.04	22.87±4.06	<0.001

[Comparisons of metabolic syndrome parameters between subjects with and without NAFLD]

Conclusion: NAFLD imposes a great burden of liver disease in the rural community of Bangladesh. Male sex, DM, higher SBP, abdominal obesity, BMI>25, presence of MetS and higher serum triglyceride are found to be risk factors for NAFLD.

Disclosure: Nothing to disclose

P0704 HIGH PREVALENCE OF COLONIC ADENOMAS IN PATIENTS WITH NONALCOHOLIC FATTY LIVER DISEASE: ALGERIAN PROSPECTIVE STUDY

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Introduction: Epidemiologic data suggest that colonic adenomas have an increased tendency to occur in patients who are obese, or have a positive family history of colon cancer, or diabetes mellitus. Recent data suggest that impaired glucose tolerance, dyslipidemia, and metabolic syndrome are associated with a higher risk for colonic adenomas. Patients with non-alcoholic fatty liver disease (NAFLD) often share several of the aforementioned risk factors for colonic adenomas. However, data are lacking about the relationship between NAFLD and colonic adenomas.

Aims & Methods: The aim of this study was to systematically evaluate whether NAFLD is an independent risk factor for colonic adenomas.

A prospective study. Setting University central hospital of army with case recruitment from the community and clinics. Patients Subjects aged 30-70 years were recruited for colonoscopic screening from two study cohorts: (1) community subjects; and (2) consecutive patients with biopsy proven NAFLD. In the community cohort, hepatic fat was measured by fibroscan. Main outcome measures Prevalence of colorectal adenomas. Advanced colorectal neoplasm was defined as cancer or adenomas with villous architecture or high grade dysplasia.

Results: NAFLD patients (n=203) had a higher prevalence of colorectal adenomas (34.7% vs 21.5%; p=0.043) and advanced neoplasms (18.6% vs 5.5%; p=0.002) than healthy controls (N=201). Thirteen of 29 (45%) NAFLD patients with advanced neoplasms had isolated lesions in the right sided colon. Among patients with biopsy proven NAFLD, patients with non-alcoholic steatohepatitis (N=49) had a higher prevalence of adenomas (51.0% vs 25.6%; p=0.005) and advanced neoplasms (34.7% vs 14.0%; p=0.011) than those with simple steatosis (N=86). After adjusting for demographic and metabolic factors, non-alcoholic steatohepatitis remained associated with adenomas (adjusted OR 4.89, 95% CI 2.04 to 11.70) and advanced neoplasms (OR 5.34, 95% CI 1.92 to 14.84). In contrast, the prevalence of adenomas and advanced neoplasms was similar between patients with simple steatosis and control subjects.

Conclusion: Non-alcoholic steatohepatitis is associated with a high prevalence of colorectal adenomas. The adenomas are found more commonly in the right sided colon. Colorectal cancer screening is strongly indicated in this high risk group.

References: Nadege T. Touzin, Kelvin N.V. Bush. Prevalence of colonic adenomas in patients with nonalcoholic fatty liver disease. Ther Adv Gastroenterol (2011) 4(3) 169176

Disclosure: Nothing to disclose

P0705 RESULTS OF LIFE STYLE MODIFICATION ON WEIGHT LOSS AND FACTORS OF FAILURE IN NAFLD

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Introduction: Treatment of non-alcoholic fatty liver disease (NAFLD) is essentially based on life style modification:diet and physical activity and managing risk factors. Weight loss of at least 3-5% has proven to improve steatosis and 7-10% to improve fibrosis.
Aims & Methods: To assess weight loss after 3 and 6 months of life style modification
Prospective study conducted over one year (December 2017 to December 2018) including all patients followed for NAFLD. All patients have been educated about diet and physical activity , and have been informed about complications and risks of the metabolic syndrome.
Results: We included 58 patients: 46 women and 12 men (sex-ratio =0.2) with an average age of 49.4 years [14-81 years]. Type 2 diabetes was found in 22 patients (37.9%), high blood pressure in 20 patients (34.5%) and dyslipidemia in 24 patients (41.4%). The average body mass index was 32.6 Kg/m2 [20-55 kg/m2]. Seventeen patients (29.1%) were overweight and 35 (60.6%) patients were obese. The average waist circumference was 104.24 cm [67-138cm]. Android obesity was objective in 46 patients (79.3%) and hepatic cytolysis was found in 9 patients (15.5%).
The average weight loss at 3 months was 1.26% [0.8-10%] and at 6 months was 2.33% [0.9-13.6%].
After 6 months of follow-up: 38 patients (65.5%) lost weight, 13 patients (22.4%) gained weight and 7 patients (12.1%) maintained a stable weight. Only 8 patients had a weight loss ≥5%.
Normalization of hepatic cytolysis was noted in 66.6% of patients who lost weight and had initial cytolysis.
Ischemic heart disease, gonalgia and advanced age were factors of non-adherence in patients who had not lost weight.
Conclusion: Life style modification allowed weight loss in 65.5% of patients and normalization of hepatic cytolysis in 65.5% of cases. Non-adherence to the treatment was related to the impossibility to perform regular physical activity.
Disclosure: Nothing to disclose

P0706 OCTREOTIDE AMELIORATES ENDOPLASMIC RETICULUM DYSFUNCTION IN A NONALCOHOLIC STEATOHEPATITIS MICE MODEL

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Introduction: Nonalcoholic fatty liver diseases (NAFLD), from simple steatosis to progressive nonalcoholic steatohepatitis (NASH), fibrosis and cirrhosis, are most common chronic liver diseases in the world. Somatostain (SST), a kind of neuroendocrine hormone, can suppress the release of gastrointestinal peptide, including cytokines. Octreotide, longer half-time somatosatin analog, is used as a replacement of somatostain due to similar effects.
Aims & Methods: We aim to explore the relationship between endoplasmic reticulum and nonalcoholic steatohepatitis and octreotide effects. A total of 30 male C57BL/6J mice were assigned to normal chow (NC), high fat and high cholesterol diet (HFHC), HFHC + octreotide (HFHC+O) groups. After 16-week feeding, mice received i.p. injection of either octreotide (60μg/Kg/12h) or saline for 4 weeks. Body weight, food intake, liver weight, serum and hepatic lipid levels, serum insulin, glucose tolerance test were measured, and serum and hepatic inflammatory cytokines were analyzed with ELISA. Hepatic histology was investigated with H&E staining, Oil red O staining, Sirius red staining and immunohistochemical (IHC) staining. Expression of endoplasmic reticulum function related molecules were measured with RT-PCR and western blot, respectively.
Results: In contrast to NC group, Mice with HFHC showed significant increased liver weight, ALT and AST levels, serum cholesterol and inflammatory cytokines, hepatic triglyceride and cholesterol levels, accompanied by aggregated fat deposition in hepatocytes and infiltrated inflammatory cells around hepatocytes, which were attenuated by octreotide treatment. Compared with NC mice, HFHC mice demonstrated increased F4/80 and α-SMA expression in IHC staining, and elevated expression of inositol requiring enzyme 1 (IRE-1α), activating transcription factor 6 (ATF 6) and spliced X-box binding protein 1 (sXBP-1) with RT-PCR and western blot, while octreotide treatment reversed these changes.
Conclusion: Octreotide can attenuate hepatic inflammation and lipid metabolism in a NASH mice model, probably by improving endoplasmic reticulum dysfunction. The further underlying mechanisms are under investigation.
Disclosure: Nothing to disclose

P0707 FIRST REPORT ON THE DIFFERENCES BETWEEN NON-ALCOHOLIC FATTY LIVER DISEASE PATIENTS AND HEALTHY SUBJECTS BASED ON THE DUODENAL MICROBIOME

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is a multifactorial disease. Among others, the interaction of gut microbiome with the host has been proposed as potential mechanism of NAFLD pathogenesis and progression. However, data about the composition of duodenal microbiome of these patients is scarce.
Aims & Methods: We aimed to characterize the duodenal microbiome (DM) of NAFLD patients and compare it to that of healthy controls. Patients with histological, biochemical or radiological diagnosis of NAFLD underwent upper gastrointestinal endoscopy and duodenal juice (2cc) was aspirated

from the 3rd-4thpart of duodenum in sterile traps. Patients without liver disease, undergoing gastroscopy due to gastroesophageal reflux disease, comprised the control group. DNA was isolated using the MagAttract PowerSoil DNA Kit. Microbiota was analyzed by 16S rRNA metagenomic sequencing in MiSeq platform (Illumina). Operational Taxonomic Units (OTU) clustering and taxonomic analysis were performed with CLC Microbial Genomics Module v. 2.5. A Negative Binomial GLM model was used to obtain maximum likelihood estimates for an OTU's fold change between the two groups, and the Wald test was used to determine significance.

Results: 19 subjects with NAFLD (7 females; age 57.1±11.2 yrs) and 12 controls (7 females; age 45±17.6 yrs) had their DM fully mapped. Principal Coordinate Analysis (PCoA) of the UniFrac distance generated from taxon abundance (beta-diversity) revealed important differences in the DM profile of subjects with NAFLD when compared to controls, resulting in two distinct clusters on PCoA plots.Intriguingly, the α-diversity indexes of subjects with NAFLD were similar when compared to controls (Total number, P=0.2520; Simpson's index, P=0.8320). The DM of control subjects was characterized by high relative abundance (RA) of the Firmicutes phylum (68%), followed by Bacteroidetes, Actinobacteria and Fusobacteria (14%, 7%, and 5% respectively).Comparatively to controls, the DM of subjects with NAFLD was also characterized by high RA of the Firmicutes phylum (63%, P=0.346), but the RA of the Actinobacteria phylum was increased in these subjects (Fold change (FC)=1.60, P=0.02). Interestingly, the relative abundance of the TM7 phylum was also increased in subjects with NAFLD when compared to controls (FC=1.91, P=0.02). At order level, the RA of specific taxon from Actinobacteria and TM7 phyla were also increased in subjects with NAFLD when compared to controls, including the Bifidobacteriales order (FC=6.96, P=0.03) and CW40 order (FC=4.86, P=0.02) respectively. Additionally, the Bacillales order from Firmicutes phylum and the Enterobacteriales order from Proteobacteria, were also increased in NAFLD subjects when compared to controls.

Conclusion: The duodenal microbiome of NAFLD patients is different at phylum and order level compared to that of controls. A deeper assessment of the small bowel microbiome in this population may lead to clues to the development of NAFLD.

Disclosure: Nothing to disclose

P0708 NON-INVASIVE SCREENING OF ESOPHAGEAL VARICES: A MULTICENTER STUDY EVALUATING THE BAVENO CRITERIA AND PROPOSING AN ALTERNATIVE APPROACH

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Introduction: Variceal bleeding is a common complication of patients with cirrhosis that can mark the transition from compensated advanced liver disease (cALD) to decompensated cirrhosis. Therefore, endoscopic screening for high-risk varices (HRVs) was initially proposed for all cirrhotics. In an effort to avoid unnecessary endoscopies, the Baveno VI workshop proposed criteria that would identify cirrhotics with low risk of having HRVs. According to these criteria, in patients with cALD, platelet count > 150000/µl and liver stiffness measurement (LSM) < 20 kPa, screening endoscopy could be avoided.

Aims & Methods: Aim of this study is to validate the Baveno VI criteria and explore other possible parameters that can be used for the non-invasive screening of esophageal varices. Patients with advanced liver disease (defined as LSM > 12 kPa) were prospectively enrolled. Patients with splanchnic vein thrombosis, use of beta-blockers and esophageal varices were excluded. The study participants were evaluated according to the Baveno criteria, undergoing LSM, laboratory tests and esophagogastroduodenoscopy (EGD) which was conducted within six months of liver stiffness and laboratory measurements.

Results: One-hundred and seven consecutive patients were enrolled in the study and underwent LSM and screening endoscopy. Fifty-one patients (47.7%) had portal gastropathy or normal endoscopic findings (F0), 34 patients (31.8%) exhibited small varices without red spots (F1), and 22 patients (20.5%) had HRVs (F2/F3). Thirteen patients met the Baveno VI criteria, none of which had HRVs. The Baveno VI criteria achieved 100% sensitivity and negative predictive value (NPV) while decreasing the number

of endoscopies by 12.1%. Additional parameters were examined, among which the quotient PLT / LogkPa exhibited the larger area under the curve. By setting a cut-off of ≤122000 µl^{-1} • kPa^{-1}, this method maintained 100% sensitivity and NPV, managing at the same time to increase the percentage of endoscopies avoided to 20.6%. An additional cut-off of ≤ 92000 µl^{-1} • kPa^{-1}was examined due to its capability to further increase this percentage to 44.9%. However, this happened at the expense of an increased percentage of missed HRVs (6.3%).

Conclusion: The Baveno VI criteria are validated in our study population. The new criteria developed in this study succeed in further decreasing the number of screening EGDs and appear as a legitimate alternative to the Baveno VI criteria. More studies are required, in order to verify their effectiveness.

References: De Franchis R, Abraldes JG, Bajaj J, Berzigotti A, Bosch J, Burroughs AK, et al. Expanding consensus in portal hypertension Report of the Baveno VI Consensus Workshop: Stratifying risk and individualizing care for portal hypertension. J Hepatol. 2015;63:743-52. DOI:10.1016/j.jhep.2015.07.001

Disclosure: Nothing to disclose

P0709 CHRONIC RENAL DISEASE AFTER THE FIRST EPISODE OF ACUTE KIDNEY INJURY IN CIRRHOTIC PATIENTS – A REALITY WE SHOULD KEEP IN MIND

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Introduction: Acute kidney injury (AKI) is frequently identified in cirrhotic patients and associates with bad prognosis. Recent studies suggest that after the first event, a non-neglectable percentage of patients evolves to chronic kidney disease (CKD).

Aims & Methods: We aimed to asses risk factors for progression to CKD and its' impact on patients' prognosis.

Unicentric, retrospective study, including patients with cirrhosis admitted for acute decompensation with AKI. Excluded patients with previous CKD (glomerular filtration rate (GFR) < 60mL/min/1.73m^2 for >3 months), patients who died before 3 months of follow-up and patients without adequate electronic records. Assessed GFR 3 months after the initial event and several outcomes.

Results: Included 87 patients. Three months after de initial event, 34.5% of patients had CKD. Patients who developed CKD were more frequently under proton pump inhibitors (66.7% vs 36.8%, p=0.008), had higher basal creatinine levels (1.1±1.1mg/dL vs 0.8±0.3mg/dL, p< 0.001) and reached higher maximum creatinine levels in the first AKI episode (1.8±1.1mg/dL vs 1.4±0.7, p=0.004). On multivariate logistic regression, only basal creatinine level significantly associated with of progression to CKD (p=0.006, OR 28.7, IC 95% 2.6-315.8).

Regarding outcomes, patients who devolved CKD showed higher rates of new AKI episodes (90.0% vs38.6%, p< 0.001) and had higher mortality rates at 6 months, 1 and 2 years (40.0% vs 10.5%, p=0.001; 53.3% vs 15.8%, p< 0.001 and 56.7% vs 29.8%, p=0.015, respectively).

Conclusion: After the first AKI episode over one third of patients evolve to CKD and these patients have not only higher rates of new episodes of AKI but also higher mortality rates at 6 months, 1 and 2 years. Basal creatinine level was the only independent predictor of progression to CKD.

Disclosure: Nothing to disclose

P0710 ESTIMATION OF GLOMERULAR FILTRATION RATE (GFR) IN CIRRHOTICS: EVALUATION OF EQUATIONS CURRENTLY USED IN CLINICAL PRACTICE AND VALIDATION OF ROYAL FREE HOSPITAL CIRRHOSIS GFR (GFR-RFH)

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Introduction: Many studies have stressed that the equations used currently for the estimation of GFR may overestimate renal function in cirrhotics. The GFR-RFH equation was developed in order to accurately estimate GFR in this population.
Aims & Methods: Aim of this study was to evaluate the use of widely available equations (CKD-EPI, MDRD-4, MDRD-6) and the GFR-RFH equation to correctly estimate the measured GFR of patients with cirrhosis. We retrospectively analyzed data from cirrhotic patients that were evaluated for liver transplantation. These patients were submitted to somatometric tests, laboratory tests and measurement of GFR with the use of ^{51}Cr-EDTA (GFR-M). The CKD-EPI, MDRD-4, MDRD-6 and GFR-RFH equations were calculated, while bias, precision and accuracy were estimated for each one of them and then compared with paired t-tests. Bias was defined as the mean difference between the GFR-M and the result of each equation; precision was defined as the standard deviation of the differences and accuracy was defined as the square root of the mean squared error (mean of the squared differences). Higher values are associated with higher bias and smaller precision/accuracy.
Results: One-hundred and thirty four cirrhotic patients were included (95 male, 39 female). Twenty-one patients were Child-Pugh A, 66 Child-Pugh B and 47 Child-Pugh C. The patients displayed mean GFR-M: 72.36 ±23.52, CKD-EPI:78.28 ± 23.53, MDRD-4: 75.5 ± 25.7, MDRD-6: 71.45 ± 25 and RFH-GFR: 54.3 ± 17.96. Bias was estimated for CKD-EPI, MDRD-4, MDRD-6 and GFR-RFH at -5.91, -3.13, 0.92 and 18.24 respectively. Statistically significant differences were observed between all equations separately (p < 0.001 for all comparisons). Precision was estimated at 18.47, 20.81, 18.86 and 16.6, respectively. Only the comparison between MDRD-4 and GFR-RFH yielded a statistically significant result (p= 0.037). Finally, accuracy was estimated at 19.32, 20.97, 18.81 and 24.61, respectively. CKD-EPI and MDRD-6 exhibited statistically better accuracy than GFR-RFH (p =0.006 and 0.001).
Conclusion: GFR-RFH fails to provide a better estimation of renal function in cirrhotics in our sample, in comparison to the equations used in clinical practice. Among equations that are widely used in a clinical setting, MDRD-6 seems to achieve the best overall result (smaller bias, equal precision, better accuracy) in patients with cirrhosis.
Disclosure: Nothing to disclose

P0711 SOLUBLE CD163 IS ASSOCIATED WITH PORTAL HYPERTENSION AND PREDICTS SURVIVAL IN PATIETS WITH HEPATITIS C AND ALCOHOL-INDUCED LIVER CIRRHOSIS

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Introduction: Clinically significant (CSPH) and severe portal hypertension (SPH) increase the risk for decompensation and life-threatening complications in liver cirrhosis. The search for non-invasive markers capable of predicting portal hypertension and patient survival is ongoing. Soluble CD163, a marker of Kupffer cell activation, has been associated with viral hepatitis, cirrhosis and portal hypertension. Additional data would aid in creating new non-invasive diagnostic and even treatment approaches in this field.
Aims & Methods: In this study we aimed to evaluate plasma levels of soluble CD163 in patients with liver cirrhosis, CSPH, SPH and biomarker potential to predict CSPH and SPH as well as patient survival. We prospectively investigated 100 patients with hepatitis C virus and alcohol-induced liver

cirrhosis with characterized hepatic venous pressure gradient (HVPG) and 30 healthy controls. Plasma levels of CD163 were determined by enzyme-linked immunosorbent assay. Patients were observed for follow-up period of 24 months. Associations of CD163 with Child- Pugh score, HVPG, CSPH (HVPG ≥ 10 mHg), SPH (HVPG ≥ 12) and patient survival were assessed.
Results: Plasma CD163 levels were significantly higher in cirrhotic patients than in healthy controls (p<0.0001) and increased with disease severity (Child-Pugh class A 1.3; Child-Pugh class B 1.5; Child-Pugh class C 1.8 mcg/ml; p=0.004). There was a moderate correlation between CD163 and HVPG (r= 0.377; p<0.0001). Higher levels of CD163 predicted CSPH and SPH independently from Child-Pugh class. AUC for the diagnosis of CSPH was 0.731 (p< 0.0001) and for the diagnosis of SPH 0.7 (p=0.001). A total of 15 patients died during the follow-up period. Plasma levels of CD163 higher than 1.55 mcg/ml were associated with increased mortality (24 month survival: 76% vs. 98%, p<0.0001). When stratifying patients according to this cut-off value, the OR for death in 24 months was 15.5 (p=0.01).
Conclusion: Higher plasma levels of CD163 predicted CSPH, SPH and mortality in patients with hepatitis C and alcohol-induced liver cirrhosis. Biomarker could be used as a surrogate marker for long-term survival in this patient population.
Disclosure: Nothing to disclose

P0712 ENDOGENOUS MOTION OF THE LIVER CORRELATES WITH THE SEVERITY OF PORTAL HYPERTENSION

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Introduction: Portal hypertension (PH) causes life threatening complications in patients with liver cirrhosis, therefore timely diagnosis of clinically significant (CSPH) is of utmost importance. Hepatic venous pressure gradient (HVPG) measurement remains the gold standard to assess the severity of portal hypertension, however the procedure is invasive and is only performed in specialized centers. Non-invasive assessment using elastography techniques has been successfully introduced, however these techniques have certain limitations. The search for non-invasive, accurate and applicable methods for the evaluation of portal hypertension is ongoing.
Aims & Methods: In this study we aimed to evaluate the performance of the radiofrequency ultrasound signal analysis algorithm based on endogenous motion of the liver in predicting CSPH.The study included 36 patients with hepatitis C virus or alcohol- induced liver cirrhosis with characterized HVPG measurements. All patients underwent ultrasound examination using a research dedicated ultrasound scanner Ultrasonix SonixTouch. Raw B scans forming radiofrequency signals (record duration - 7.62 s) were acquired and stored for off-line analysis. The signal analysis algorithm was developed for the assessment of liver motion induced by cardiovascular activity. The statistical analysis of endogenous displacement and strain parameters was performed.
Results: Three parameters showed statistically significant weak to moderate correlation with HVPG measurement - d_{retro} (maximal amplitude of the displacements backward, μm; r=0.39; p=0.02); $\sigma_{ROI[0...10Hz, 2 \times 2 cm]}$ (standard deviation of strain [0...10 Hz, 2 × 2 cm] μm/cm; r=-0.41; p=0.01); $\mu_{ROI[0...10Hz, 1 \times 1 cm]}$ (average strain [0...10 Hz, 1 × 1 cm] μm/cm; r=-0.34; p=0.04). The median values of parameters were significantly higher in patients with CSPH (p=0.005, p< 0.05 and p< 0.01 respectively). AUC for the diagnosis of CSPH for d_{retro} was 0.84 (p< 0.0001); with a cut-off value of 0.72 μm providing 100%sensitivity and 73% specificity. AUC for the diagnosis of CSPH for $\sigma_{ROI[0...10Hz, 2 \times 2 cm]}$ was 0.71 (p=0.036); with a cut-off value of 0.48 μm/cm providing 76% sensitivity and 72% specificity. AUC for the diagnosis of CSPH for $\mu_{ROI[0...10Hz, 1 \times 1 cm]}$ was 0.78 (p=0.0024); with a cut-off value of 0.57 μm/cm providing 76% sensitivity and 81% specificity.
Conclusion: The new algorithm estimating endogenous strain of the liver provides reliable parameters which can predict the presence of CSPH.
Disclosure: Nothing to disclose

P0713 NON-INVASIVE SCREENING OF ESOPHAGEAL VARICES – IS IT TIME TO EXPAND THE BAVENO VI CRITERIA?

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Introduction: The role of non-invasive methods for detecting liver fibrosis has been investigated in the identification of esophageal varices. The Baveno VI consensus states that in patients with compensated cirrhosis, liver stiffness by transient elastography (TE) < 20 kPa and platelets >150.000, screening endoscopy may be dispensed, given the very low probability of having high-risk varices with indication for prophylaxis or treatment (small varices with red wale marks and medium-large varices).

Aims & Methods: We aimed to apply the Baveno VI criteria in a cohort of cirrhotic patients and see how they performed in real life clinical practice. Retrospective study of all patients evaluated between January 2017 and December 2018 with a liver stiffness by TE compatible with cirrhosis and platelet count and upper endoscopy performed up to 6 months after TE. Patients with history of esophageal varices or decompensated cirrhosis were excluded.

Results: If the Baveno VI recommendations had been applied to this cohort, endoscopy would have been avoided in 47 (41.2%) patients, none of them with high-risk varices: specificity 100%, sensitivity 2.1%, positive predictive value 100%, and negative predictive value 47% for absence of varices requiring treatment (Table 1). Additionally, both platelet count (AUROC=0.894; p-value=0.0) and TE (AUROC=0.780; p-value=0.001) were individually effective in predicting absence of high-risk varices. However, considering all patients eligible for endoscopy, 53 (79.1%) did not have varices with therapeutic indication.

	Patients who would avoid endoscopy (n=47)	Patients eligible for endoscopy (n=67)
No high-risk varices	47 (100.0%)	53 (79.1%)
High-risk varices	0 (0.0%)	14 (20.9%)

[Table 1]

Conclusion: The Baveno VI criteria effectively identified a group of cirrhotic patients without varices requiring treatment in whom screening endoscopy could have been safely avoided. All patients with high-risk varices would be screened. The major drawback of the Baveno VI criteria seems to be the high number of futile screening endoscopies. With the greater availability of non-invasive methods of liver fibrosis, in the future we will probably be able to safely avoid endoscopy in a greater number of patients. Studies are needed to confirm this findings and explore cutoffs or other variables to safely dispense endoscopy in a larger number of patients.

References: Franchis R, et al. Expanding consensus in portal hypertension Report of the Baveno VI Consensus Workshop: Stratifying risk and individualizing care for portal hypertension. Journal of Hepatology 2015 vol. 63, 743-752.

Disclosure: Nothing to disclose

P0714 LONG-TERM EFFECT ON HEPATIC RESIDUAL FUNCTION AFTER SIMULTANEOUSLY COMBINED BALLOON-OCCLUDED RETROGRADE TRANSVENOUS OBLITERATION WITH PARTIAL SPLENIC EMBOLIZATION FOR GASTRIC VARICES

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Introduction: Balloon-occluded retrograde transvenous obliteration (B-RTO) has been widely adopted for the management of gastric fundal varices (GV). There are only several reports that B-RTO leads to the improvement of the hepatic residual function in the mid- and long-term. We have performed partial splenic embolization (PSE) simultaneously combined with B-RTO for the purpose of reduction of portal venous blood pressure.

We retrospectively investigated the long-term effect on hepatic residual function and the prognosis of the patients who had underwent B-RTO.

Aims & Methods: We have performed B-RTO in 60 patients with GV since 2005 at a single institute. Concomitant PSE underwent in 46 of those patients. We examined the parameters of hepatic functional reserve such as encephalopathy, ascites, total bilirubin, albumin, prothrombin time, and Child-Pugh score in the follow-up period 3, 6, 12, 24, and 36 months after B-RTO. We analyzed the survival curve using Kaplan-Meier method, and investigated the preoperative factor which affected a prognosis independently with multivariate analyses. The study was approved by the Ethics Committee of Niigata City General Hospital. The study protocol conformed to the ethical guidelines of the Declaration of Helsinki.

Results: GVs were well-embolized in 57 patients (95.0%), and GV disappeared in all patients successfully treated by B-RTO. The serum albumin levels were significantly elevated from 3.3 to 4.0 g/dL (p= 0.0076) and Child-Pugh scores decreased significantly from 7.0 to 5.7 (p= 0.4333) after B-RTO in three years. The median survival was of all cases was 2207 days, and the survival rate was 86.3 % at 1 year, 80.5 % at 3 years, 63.5 % at 5 years. Multivariate analyses revealed that "with the cancer" and "preoperative Child-Pugh B-C grade" were the predictors of poor prognosis.

Conclusion: B-RTO for GV has the long-term favorable effect on hepatic functional improvement. The addition of the PSE inhibits exacerbation of EV after B-RTO without increasing invasiveness.

Disclosure: Nothing to disclose

P0715 PLATELET INDICES REFLECT DYNAMIC CHANGES IN EXTRACELLULAR MATRIX. THE OBSERVATION OF ALCOHOLIC LIVER CIRRHOSIS AND NON-ALCOHOLIC FATTY LIVER DISEASE PATIENTS

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Introduction: Platelet (PLT) indices have been proposed as potential markers in numerous pathologies for several years. Their role was also highlighted in the assessment of liver fibrosis and exacerbation of liver failure.

Aims & Methods: The aim of our study was to verify PLT indices in the evaluation of liver fibrosis in the course of alcoholic liver cirrhosis (ALC) and non-alcoholic fatty liver disease (NAFLD) and to compare them with serological: indirect and direct markers of liver fibrosis. Another goal was to assess the relationship between PLT indices and clinical progression of liver failure in ALC (MELD score). Three hundred and two persons were enrolled to the study: 142 patients with ALC, 92 with NAFLD and 68 healthy volunteers in control group. Hematological indices were measured in each participant: mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT). Indirect markers of liver fibrosis were also assessed: AAR [aspartate aminotransferase (AST) to alanine aminotransferase (ALT) ratio], APRI (AST to PLT Ratio Index), FIB-4 (Fibrosis-4) and GPR (γ-glutamyl-transferase to PLT ratio). Among direct indices of liver fibrosis, procollagen I carboxyterminal propeptide (PICP), procollagen III aminoterminal propeptide (PIIINP), platelet-derived growth factor AB (PDGF-AB), transforming growth factor-α (TGF-α) and laminin were obtained. The assessment of clinical progression of liver failure in ALC patients was done with MELD score. NAFLD fibrosis score and BARD score were calculated in NAFLD patients. Achieved results were compared to controls and between ALC and NAFLD groups. Then a correlation between evaluated indices was performed. Diagnostic value of each assessed parameter together with proposed cut-off in research group were measured with AUC (area under the curve).

Results: PDW value in ALC group was significantly higher in comparison to controls (p< 0.0001), level of PCT was significantly lower (p< 0.0001) and MPV value did not differ significantly. PLT indices correlated positively with indirect indices of liver fibrosis: MPV with: APRI, FIB-4 and GPR (p< 0.001), PDW with: APRI and FIB-4 (p< 0.0001). There were also negative relationships between PCT and both: APRI and FIB-4 (p< 0.0001). Strong positive correlations were noted between PCT and direct markers of liver fibrosis: PDGF-AB (p< 0.001) and TGF-α (p< 0.05). MELD score correlated with PLT indices; positively with: MPV and PDW (p< 0.001) and negatively with PCT (p< 0.05). MPV and PDW values in NAFLD group were significantly higher (p< 0.0001 and p< 0,01, respectively) and PCT - lower (p<

0.01). PDW correlated positively with indirect markers of liver fibrosis (APRI and FIB-4; p<0.05) and PCT - negatively (APRI - p<0.01, FIB-4 - p<0.0001). There was a strong negative relationship between PCT and NAFLD fibrosis score (p<0.0001) and a weaker one between PCT and laminin (p< 0.05). MPV and PDW were significantly higher in ALC group compared to NAFLD patients (p<0.0001 and p<0.001, respectively); PCT level was significantly lower in ALC group (p<0.0001). AUC values and proposed cut-offs for MPV, PDW and PCT in ALC patients were: 0.458 (>11.1 fl), 0,764 (>59.3 %) and 0,839 (<0.17 %), respectively. AUC values and proposed cut-offs for MPV, PDW and PCT in NAFLD patients were: 0,808 (< 7.9 fl), 0,643 (>52.8 %) and 0,622 (<0.23 %), respectively.

Conclusion: Hematological indices are closely related to serological markers of liver fibrosis. They reflect clinical progression of ALC. PCT in ALC and MPV in NAFLD were found to have the greatest clinical accuracy.

References: 1. Saremi Z, Rastgoo M, Mohammadifard M i wsp. Comparison of platelet number and function between nonalcoholic fatty liver disease and normal individuals. J Res Med Sci. 2017; 22: 75. 2. Coskun BD, Dizdar OS, Baspınar O i wsp. Usefulness of the neutrophil-to-lymphocyte ratio and platelet morphologic parameters in predicting hepatic fibrosis in chronic hepatitis C patients. Ann Clin Lab Sci. 2016; 46: 380-6. 3. Wang LR, Zhou YF, Zhou YJ i wsp. Elevation of plateletcrit increasing the risk of non-alcoholic fatty liver disease development in female adults: a large population-based study. Clin Chim Acta. 2017; 474: 28-33.

Disclosure: Nothing to disclose

P0716 RED BLOOD CELL DISTRIBUTION WIDTH AND ITS DERIVATIVES AS PREDICTORS OF FIBROSIS AND CLINICAL OUTCOME IN ALCOHOLIC LIVER CIRRHOSIS AND NON-ALCOHOLIC FATTY LIVER DISEASE PATIENTS

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Introduction: Higher values of red blood cell distribution width (RDW) and RDW to platelet ratio (RPR) have been proposed as predictors of poor survival in cirrhotic patients, recently. RDW to lymphocyte ratio (RLR) has been only proved to correlate positively with advanced liver fibrosis in primary biliary cholangitis patients and clinical manifestation of hepatitis E in the field of hepatology, so far.

Aims & Methods: The aim of our survey was to assess the utility of RDW, RPR and RLR in the evaluation of liver fibrosis in alcoholic liver cirrhosis (ALC) and non-alcoholic fatty liver disease (NAFLD) patients. We also aimed to assess a relationship between above-mentioned parameters and clinical progression of ALC. 302 persons were included to the study: 142 patients with ALC, 92 with NAFLD and 68 volunteers in control group. Hematological indices (RDW, RPR and RLR) were obtained from each participant. Indirect markers of liver fibrosis were also measured: AAR [aspartate aminotransferase (AST) to alanine aminotransferase (ALT) ratio], APRI (AST to PLT Ratio Index), FIB-4 (Fibrosis-4) and GPR (γ-glutamyl-transferase to PLT ratio). Among direct indices of liver fibrosis, procollagen I carboxyterminal propeptide (PICP), procollagen III aminoterminal propeptide (PIIINP), platelet-derived growth factor AB (PDGF-AB), transforming growth factor-α (TGF-α) and laminin were obtained. The assessment of clinical progression of liver failure In ALC patients was done with MELD score. NAFLD fibrosis score and BARD score were calculated In NAFLD patients. Achieved results were compared to controls and between ALC and NAFLD groups. Then a correlation between evaluated indices was performed. Diagnostic value of each assessed haematological parameter together with proposed cut-off in research group were measured with AUC (area under the curve).

Results: RDW, RPR and RLR values were significantly higher in ALC patients compared to controls (p< 0.0001). There were strong positive correlations between RPR and indirect markers of liver fibrosis – FIB-4 and RPR (p< 0.0001). RDW and RPR correlated also negatively with PDGF-AB (p< 0,01 and p< 0.0001, respectively). Positive relationship was observed between RPR and MELD score (p< 0.01). RDW, RPR and RLR values were significantly higher in NAFLD patients compared to controls (p< 0.05, p< 0.0001, p< 0.0001, respectively). RDW correlated positively with FIB-4 (p< 0.05) and RPR – with APRI (p< 0.0001). There was also a strong rela-

tionship between RPR and NAFLD fibrosis score (p< 0.0001). RDW, RPR and RLR values were significantly higher in ALC patients compared to NAFLD group (p< 0.0001). AUC values and proposed cut-offs for RDW, RPR and RLR in ALC patients were: 0.912 (>14.2 %), 0,965 (>0.075) and 0.914 (>8.684), respectively. AUC values and proposed cut-offs for RDW, RPR and RLR in NAFLD patients were: 0.606 (>12.8%), 0.724 (>0.047 %) and 0,691 (>6.25 %), respectively.

Conclusion: RDW and its derivatives seem to be powerful diagnostic markers of liver fibrosis especially in ALC patients. They might also reflect a decompensation of liver function in this group.

References: 1. Turcato G, Campagnaro T, Bonora A i wsp. Red blood cell distribution width independently predicts 1-month mortality in acute decompensation of cirrhotic patients admitted to emergency department. Eur J Gastroenterol Hepatol. 2018; 30: 33-38. 2. Fan X, Deng H, Wang X i wsp. Association of red blood cell distribution width with severity of hepatitis B virus-related liver diseases. Clin Chim Acta. 2018; 482: 155-60 3. Wu J, Zhang X, Liu H i wsp. RDW, NLR and RLR in predicting liver failure and prognosis in patients with hepatitis E virus infection. Clin Biochem. 2019; 63: 24-31

Disclosure: Nothing to disclose

P0717 EFFICACY AND SAFETY OF ANTICOAGULANT TREATMENT IN PORTAL VEIN THROMBOSIS ASSOCIATED WITH CIRRHOSIS: RESULTS OF A COHORT OF 43 PATIENTS

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Introduction: An increase risk of portal vein thrombosis (PVT) in cirrhotic patients is more reported, without the true impact of PVT being properly assessed. PVT in cirrhotic patients can lead to complications in both liver function and portal hypertension.

Aims & Methods: The aim of the study was to evaluate efficacy and safety of anticoagulants in patients with cirrhosis and portal vein thrombosis without hepatocellular carcinoma. It was a prospective, single-center study including 43 patients with portal vein thrombosis recruited among 580 cirrhotic patients between January 2009 and June 2017. Existence, extension and cruoric aspect of the thrombotic obstruction were established in all cases by Doppler ultrasound and angio-CT scan. Anticoagulant treatment was initiated in case of symptomatic portal vein thrombosis or identification of a pro-thrombotic disease. 28 patients (65.1%) received anticoagulants (group G1) and 15 patients did not (group G2). The endpoints were: patency of the splanchnic venous system and evaluation of liver function based on the Child score: improvement was defined as a decrease of at least 2 points; deterioration by an increase of at least 2 points, liver function was unchanged if stability or decrease of less than 2 points.

Results: The mean age was 47.4 years [37-81] and sex ratio 0.6. Diagnosis of cirrhosis was already known in 22 patients and clinical manifestations of portal vein thrombosis revealed in 21 (48.8%) patients. Thrombosis was revealed by: ultrasound in 14 (32.5%) patients, complications of portal hypertension in 19 (44.2%) patients, acute abdominal pains in 7 patients and signs of intestinal ischemia in 3 patients. Seventeen patients presented at least one pro-thrombotic factor. Mean follow-up was 30.2 [21-62] months. Complete permeability of the venous portal system was achieved in 57.1% of treated patients (n=16) at the end of the study. Further, in G1 compared to G2, improvement of Child score and absence of hepatic insufficiency worsening were respectively recorded in 46.4% vs 0% and 21.4% vs 53.3% of cases, with p< 0.01. Moreover, no significant side effect of anticoagulants was observed.

Conclusion: Anticoagulation therapy for portal vein thrombosis in cirrhotic patients is a safe and effective treatment. It improves the hepatic function and the prognosis of patients.

Disclosure: Nothing to disclose

P0718 AN INSUFFICIENT PORTOSYSTEMIC PRESSURE GRADIENT REDUCTION AFTER TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT IS ASSOCIATED WITH INCREASED RISK OF VARICEAL REBLEEDING

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Introduction: Transjugular intrahepatic portosystemic shunt (TIPS) markedly reduces portosystemic pressure gradient (PPG). A hepatic venous pressure gradient (HVPG) < 12 mm Hg is the most consistent threshold that is protective from having recurrent complications. However, PPG after TIPS may be incoordinate to predict variceal rebleeding due to the inescapable impact of artificial portosystemic shunt. This study aimed to evaluate the incidence, clinical outcomes and predicting factor of insufficient PPG reduction after TIPS.

Aims & Methods: The present study retrospectively analyzed the data of 192 patients in whom a TIPS was indicated by the prophylaxis of variceal rebleeding and control of acute bleeding between June 2015 and April 2018. and. The PPG was measured before and after TIPS placement. The patients with PPG ≥ 12 mm Hg were divided into group A, and the rest into group B. The primary endpoint was recurrent rate of variceal hemorrhage, and other clinical outcomes were also evaluated during the follow-up.

Results: Forty-seven patients (24.5%) had an insufficient reduction of PPG (≥ 12 mm Hg) after TIPS implantation. PPG significantly decreased from 26.5±4.4 mm Hg to 15.5±3.4 mm Hg (P < 0.001) in group A and from 21.0±5.2 mm Hg to 7.6±2.5 mm Hg (P < 0.001) in group B. The median follow-up period was 422 days (range, 45-1082 days). During the follow-up period, 8 patients (17.0%) in group A and 10 patients (6.9%) in group B had recurrent variceal bleeding (P = 0.039).But there was no significant difference of variceal rebleeding rates among patients in different PPG grades (P = 0.785). The 1-year and 2-year probability of remaining free of variceal bleeding rates were 83.6% and 73.6%, respectively. Mortality was higher in group A than group B (14.9% vs 4.1%, P = 0.011), while the overt hepatic encephalopathy rate (27.7% vs 32.4%, P = 0.541) between two groups showed no significant difference.

	Overall (n=192)	Group A (n=47)	Group B (n=145)	P value
PPG before TIPS, mm Hg	22.3±5.6	26.5±4.4	21.0±5.2	<0.001
PPG after TIPS, mm Hg	9.5±4.4	15.5±3.4	7.6±2.5	<0.001
12-15 mm Hg, n (%)		28 (60)		
16-19 mm Hg, n (%)		11 (23)		
≥20 mm Hg, n (%)		8 (17)		
Reduction in index pressure gradient, mm Hg (%)	12.8±5.5	11.0±5.0	13.4±5.5	0.039
Variceal rebleeding, n (%)	23 (12)	8 (17)	10 (7)	0.039
Overt hepatic encephalopathy, n (%)	60 (31)	13 (28)	47 (32)	0.541
Mortality, n (%)	13 (7)	7 (15)	6 (4)	0.011

[Comparison of clinical outcomes between two groups]

Conclusion: PPG declines to < 12 mm Hg after TIPS creation is necessary to protects patients from variceal rebleeding. Stent-graft with adequate diameter should be chosen carefully to achieve sufficient reduction of PPG, otherwise endoscopic and (or) pharmacological therapy should be combined.

References: 1. Krajina A, Hulek P, Fejfar T, Valek V. Quality improvement guidelines for Transjugular Intrahepatic Portosystemic Shunt (TIPS). Cardiovasc Intervent Radiol, 2012;35:1295-1300. 2. Mollaiyan A , Bettinger D, Rossle M . The underdilation of nitinol stents at TIPS implantation: Solution or illusion? European Journal of Radiology, 2017;89(Complete):123-128.

Disclosure: Nothing to disclose

P0719 LIVER STIFFNESS MEASURED BY SHEAR WAVE ELASTOGRAPHY FOR PREDICTING ESOPHAGEAL VARICES IN PATIENTS WITH HEPATITIS B VIRUS RELATED CIRRHOSIS

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Introduction: Variceal bleeding is one of the most fatal complication in patients with liver cirrhosis. A screening esophagogastroduodenoscopy (EGD) is recommended in all patients with cirrhosis to detect those patients at risk of variceal bleeding. However, this technique is invasive, uncomfortable and costly. Therefore, to find reliable noninvasive methods for predicting varices is crucial for clinic.

Real-time shear wave elastography (SWE), which is a new method for measuring liver stiffness, has been developed. It has been confirmed that SWE has a higher technical success rate and a better diagnostic value for evaluating clinically significant portal hypertension than transient elastography [1]. However, there was also no coincident cut-off value for predicting varices, and only several studies about SWE evaluating the varices risk in compensated liver cirrhosis, and with all etiology cirrhosis patients [2, 3]. Different etiology of cirrhosis would affect the LS values, especially, alcohol and cholestasis. Therefore, to evaluate LS values of different etiology's cirrhosis respectively is valuable. Hepatitis B virus (HBV) related cirrhosis was the biggest part of cirrhosis patients in China. To our knowledge, no published study has examined the efficacy of SWE for predicting esophageal varices in HBV related liver cirrhosis. The purpose of this retrospective study was to investigate the diagnostic performance of SWE for predicting the presence of esophageal varices and high-risk varices in patients with HBV related cirrhosis.

Aims & Methods: To investigate liver stiffness of shear wave elastography (SWE) for predicting the presence of esophageal varices and high-risk varices in patients with hepatitis B virus (HBV) related cirrhosis. Clinical data from 135 patients with HBV virus related cirrhosis who underwent SWE and endoscopy were collected consecutively. Liver stiffness (LS) was measured by SWE. The time interval between SWE and endoscopy examination no more than 3 months. Comparisons of the accuracy of prediction between groups were made by areas under the receiver operating characteristic curves (AUROCs), and regression analyses were performed for the multiple variables related to the presence of esophageal varices and high-risk varices.

Results: The optimal cutoff values for predicting the presence of esophageal varices and high-risk varices were 12.95 and 13.05 kPa, respectively. AUROC of LS (0.883) was higher than platelet count (PLT) (0.805), APRI (0.809), FIB-4 (0.0.814), portal vein diameter (PVD) (0.739) and spleen vein diameter (SVD) (0.738) for predicting the presence of esophageal varices. AUROC of LS (0.901) was also higher than platelet count (0.755), APRI (0.767), FIB-4(0.767), PVD (0.742) and SVD (0.742) for predicting high risk varices. LS, albumin (ALB) and SVD were independent factors for predicting the presence of esophageal varices and high-risk varices. AUROCs of patients without ascites for predicting presence of esophageal varices and high-risk varices were 0.863 and 0.879. LS combined ALB and SVD with AUROCs 0.934 and 0.966 for predicting the presence of esophageal varices and high-risk varices, respectively.

Conclusion: LS of SWE, or LS combines albumin and SVD improves the diagnostic accuracy are reliable factors for predicting presence of esophageal varices and high-risk varices in patients with HBV-related cirrhosis. In addition, SWE is a reliable noninvasive tool for predicting esophageal varices with ascites.

References: 1. Elkrief, L., et al., Prospective comparison of spleen and liver stiffness by using shear-wave and transient elastography for detection of portal hypertension in cirrhosis. Radiology, 2015. 275(2): p. 589-98. 2. Kim, T.Y., et al., Diagnostic Performance of Shear Wave Elastography for Predicting Esophageal Varices in Patients With Compensated Liver Cirrhosis. J Ultrasound Med, 2016. 35(7): p. 1373-81. 3. Petzold, G., et al., Evaluation of liver stiffness by 2D-SWE in combination with non-invasive parameters as predictors for esophageal varices in patients with advanced chronic liver disease. Scand J Gastroenterol, 2019: p. 1-8.

Disclosure: Nothing to disclose

P0720 INFECTION AS A PREDICTOR OF MORTALITY IN PATIENTS WITH DECOMPENSATED LIVER CIRRHOSIS: EXPLORING THE RELATIONSHIP TO SEVERITY OF LIVER FAILURE

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Introduction: To evaluate predictive value of infection on 30-day and overall medium-term mortality in patients with decompensated liver cirrhosis and to explore its relationship with severity of liver failure.

Aims & Methods: We retrospectively reviewed medical records of patients with decompensated liver cirrhosis hospitalized at a single center between 1st March 2014 and 31st December 2017. The primary outcome was 30-day mortality after the 1st hospitalization. Secondary outcome was overall medium-term mortality: patients were tracked (direct contact, medical records) until death, liver transplantation, loss of contact or 31st December 2018 (censoring). Presence of infection was documented and classified as Healthcare associated (HCA) or community acquired (CA). Patients were evaluated for the Child-Pugh, MELD and CLiF OF score.

Results: Of the 155 included patients (77% males, median age 62 years), 90 had an infection (HCA n=42, CA n=48), mostly urinary tract infection, 53% G+ strains, with multidrug resistant bacteria in 23.8% of HCA and 4.2% CA infections. Thirty-day mortality was 10.8% in patients without infection, 22.9% in patients with CA and 31.0% in patients with HCA infection. With adjustment for Child-Pugh score, age, platelet count and hemoglobin levels, infection (HCA&CA combined) was independently associated with higher 30-day mortality (OR 2.73, 95%CI 1.07-6.94). The association disappeared after adjustment for the CLIF OF or the MELD score (higher scores associated with higher 30-day mortality).

However, infection was also independently associated with higher CLiF OF (b=0.99, 95%CI 0.50-1.48) and higher MELD ((b=3.81, 1.92-5.70) scores. Mediation analysis revealed an indirect association between infection and 30-day mortality that was mediated through its association with higher CLiF OF/MELD scores.

Infection "added" to risk of 30-day mortality at each level of liver failure: adjusted estimated probabilities of 30-day mortality in models with infection*Child-Pugh class (or CLiF OR or MELD score) interactions, were (i) 7.1% with Child-Pugh class B, 13.3% with Child-Pugh class C, 9.3-10.6% with CLiF OF scores 6, 8 and 10, respectively, and 9.3%-10.7% with MELD scores increasing form 10 to 30 if no infection, and (ii) 12.2% and 32.1% (Child-Pugh B and C), 4.9%-44.4% (CLiF OF 6-10) and 5.0% – 40.3% (MELD scores 10-30) in patients with infection.

As for the overall medium-term mortality, HCA infection, but not CA infection, was independently associated with 2.0 to 2.8-times higher risk of death irrespective of whether CLiF OF or MELD scores were accounted for (HR=2.77, 1.67-4.62 if accounting for neither, HR=2.07, 1.21-3.59 if accounting for CLiF OF and HR=2.13, 1.24-3.65 if accounting for MELD).

Conclusion: In patients with decompensated liver cirrhosis, infection is associated with higher 30-day mortality. It is also associated with worse liver function scores hence the association with mortality appears to be both direct and indirect via the level of liver failure.

Disclosure: Nothing to disclose

P0721 LIRER SCORE - A NEW PROGNOSTIC TOOL IN HEPATIC CIRRHOSIS DECOMPENSATION

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Introduction: The liver-renal-risk (LIRER) score was developed to predict adverse outcomes in cirrhotic patients with Model for End-stage Liver Disease (MELD)< 18, helping the allocation to liver transplantation in this population.

Aims & Methods: Aim: To assess the prognostic performance of LIRER compared to other prognostic scores in patients with hepatic cirrhosis decompensation, stratifying them in MELD< 18 e MELD≥18.
Methods: Retrospective, unicentric study that included patients admitted for initial decompensation of cirrhosis between January 2010 and February 2017. The LIRER, Child-Pugh (CP), MELD and MELD-Na scores were calculated at admission.

Results: 146 patients were included, 65.1% with MELD< 18. In the performed analysis, LIRER was a predictor of in-hospital mortality (p=0.02), at 30 days (p=0.04), 1 year (p=0.001), 2 years (p< 0.001) and overall mortality (p=0.007). The ROC curve analysis showed that LIRER (0.699, 0.719,0.689) was superior to CP (0.614; 0.642; 0.614), MELD (0.625; 0.639; 0.572) and MELD-Na (0.668; 0.670; 0.580) to predict 1 year, 2 years and overall mortality, respectively. Stratifying patients in MELD< 18 and MELD≥18, LIRER was found to be an independent predictor of 1 year, 2 years and overall mortality only in patients with MELD< 18 (0.674; 0.702; 0.723). The LIRER score was superior to the other scores to predict 30-day hospitalar re-admission (AUC 0.748), and the only significant in both groups (MELD< 18: 0.728; MELD≥18: 0.736), with patients with LIRER>15.9 having a significantly higher probabilityto be readmitted at 30 days (sensibility 69.6%, specificity 77.0%).

Conclusion: The LIRER score is a better predictor of overall, at 1 and 2 years mortality than CP, MELD and MELD-Na scores, in the decompensation of cirrhosis in patients with MELD< 18. LIRER is therefore an important tool to predict medium-long-term outcomes in this population. Besides, it allows predicting the 30-day readmission probability in overall patients.
Disclosure: Nothing to disclose

P0722 SURGICAL RISK ASSESSMENT IN CIRRHOSIS

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Introduction: Patients with cirrhosis are living longer, with more advanced disease because of improved medical management. As a result, they are at an increase risk for other diseases and may require emergent or elective surgical procedures other than liver transplantation. Nevertheless, the adequate selection of these patients to surgery is still challenging due to previous reports of high mortality rate and postoperative complications.

Aims & Methods: Our goal was to review the clinical performance of cirrhotic patients who underwent surgery in our hospital and to identify risk factors for mortality. A retrospective analysis of patients with cirrhosis who underwent abdominal or non-abdominal (orthopedics, vascular, ENT) surgery between 2016 and 2018 was performed. Primary outcomes were mortality, hospitalization length and need to hospital readmission.

Results: A total of 49 patients were included (91.8% male, mean age 61.1 ± 10.1 years, CHILD A 69.4% (34/49), CHILD B 30.6% (15/49), CHILD C 0). ASA classification was the following: 32.7% ASA II, 49% ASA III and 18.4% ASA IV. The majority of the patients was submitted to an abdominal surgery (63.3%) and 40.8% (29/49) underwent an urgent procedure. Mortality rate was 10.2%. Median time of hospitalization was 3 [1-70] days, with 10% of patients needing readmission. MELD Na (OR 1.33 IC 95% [1.02-1.49], p=0.03), ASA > III (OR 1.18 IC 95% [1.02-1.36], p=0,0049) and urgent surgery (OR 1.33 IC 95% [1.03 - 1.72], p=0.004) were associated with a higher postoperative mortality. Hospital readmission was higher in patients with MELD Na > 13 (3/6 vs 2/38, p=0.04). Urgent procedures (1 vs 13 days, p < 0.001), ASA > III (1 vs 5 days, p=0.004), albumin < 3.5 (1 vs 6 days, p=0.01) and MELD Na > 13 (2 vs 7 days, p=0.03) were associated with longer hospital stay.

Conclusion: In this cohort of CHILD A and B cirrhotic patients, the postoperative mortality rate was 10.2%. MELD Na, ASA > III and urgent procedure were independent associated with a higher mortality risk.

References: 1 - Northup PG, Friedman LS, Kamath PS. AGA Clinical Practice Update: Surgical Risk Assessement and Periperative Management in Cirrhosis: Expert Review. Clinical Gastroenterol Hepatol 2019 17(4):595-566 2 - Mokdad AA, Lopez AD, Shahraz S, et al. Liver cirrhosis mortality in 187 countries between 1980 and 2010: a systematic analysis. BMC Med 2014;12:145.

Disclosure: Nothing to disclose

P0723 E-CADHERIN AND ITS TRANSCRIPTIONAL REGULATORS IN ASSESSING CHRONIC HEPATITIS C VIRUS ACTIVITY AND CO-MORBIDITIES

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Introduction: Hepatitis C virus (HCV) infection poses a great health problem to the world today, affecting hundreds of millions of people, and millions more are infected every year. Because HCV typically takes years, if not decades, to progress, the burden it places on healthcare systems will inevitably increase in the coming years despite the currently available therapy. Chronic HCV infection is one of the main causes of hepatic fibrosis, which if untreated for years, will cause distortion of hepatic architecture and progression to liver cirrhosis with its serious complications e.g. hepatocellular carcinoma (HCC). The mechanisms of HCV-induced liver fibrosis and hepatocarcinogenesis are not yet well-recognized. E-cadherin is a cell surface glycoprotein that retains the stability of intercellular adhesion and cellular polarity, maintaining the epithelial barrier integrity. Its down-regulation, as a result of up-regulation of its transcriptional repressors including twist, snail (snail1), and slug (snail2), may induce epithelial-mesenchymal transition (EMT), a mechanism that is involved in HCC development and progression. The identification of molecular factors that promote EMT in HCV infection may provide valuable targets to prevent or to treat its fatal complications.

Aims & Methods: This study was designed to determine the role of E-cadherin and the transcription factors snail, slug, and twist2, which are the major regulators of EMT, in assessing chronic HCV activity and its associated fibrosis and carcinogenesis. Selected patients were subjected to thorough clinical examination and were assessed by:

(a) laboratory investigations

(b) abdominal U/S and triphasic CT.

Fifty-nine liver biopsies were examined by histopathology and by immunohistochemistry for E-cadherin, snail, slug, and twist2 expression. Grading of hepatitis activity (A) and staging of fibrosis (F) were evaluated using the METAVIR scoring system.

Results: E-cadherin expression showed a significant progressive decline with increased stage of fibrosis and with hepatic carcinogenesis ($p < 0.001$). In contrast, snail and slug were positively associated with fibrosis staging and with HCC ($p < 0.001$). However, twist2 wasn't affected by the degree of hepatitis activity, the stage of fibrosis, or by the development of HCC.

	E-cadherin	Snail and Slug	Twist2
Low activity (A1 and A2) (n=24)	50.41±3.23	17.62±3.07	53.83±5.17
High activity (A3) (n=22)	51.13±4.24	20.13±4.74	63.63±6.13
Low fibrosis (F1 and F2) (n=36)	59.16±2.01	13.08±2.03	61.77±5.21
High fibrosis (F3 and F4) (n=10)	20.50±4.24[b]	39.50±9.95**	46.80±9.61
Hepatocellular Carcinoma (n=13)	10.61±2.4[a, b]	65.76±4.59*,**	59.61±3.82

Results are expressed as mean±SEM.
[a]Significant decrease than low and high hepatitis activity and than high fibrosis (p<0.001).
[b]Significant decrease than low fibrosis (p<0.001).
*Significant increase than low and high hepatitis activity and than high fibrosis (p<0.001).
**Significant increase than low fibrosis (p<0.001).

[Table: E-cadherin, snail and slug, and twist2 expression patterns in hepatitis activity grades, liver fibrosis stages, and hepatocellular carcinoma]

Conclusion: E-cadherin and its transcriptional regulators; snail and slug are potential indicators for assessing the stage of HCV-induced liver fibrosis and carcinogenesis but not for assessing the degree of hepatitis activity. Therefore, the snail family could be a promising target for designing effective preventive and therapeutic strategies for chronic HCV infection serious co-morbidities.

References:
1. Thrift AP, El-Serag HB, Kanwal F. Global epidemiology and burden of HCV infection and HCV-related disease. Nat Rev Gastroenterol Hepatol. 2017; 14(2):122-132.
2. Gloushankova NA, Rubtsova SN, Zhitnyak IY. Cadherin-mediated cell-cell interactions in normal and cancer cells. Tissue Barriers. 2017; 5(3):e1356900.
3. Sharma G, Raheja H, Das S. Hepatitis C virus: Enslavement of host factors. IUBMB Life. 2018; 7 0(1):41-49.
4. Zhou JJ, Meng Z, He XY, Cheng D, Ye HL, Deng XG, et al. Hepatitis C virus core protein increases Snail expression and induces epithelial-mesenchymal transition through the signal transducer and activator of transcription 3 pathway in hepatoma cells. Hepatol Res. 2017; 47(6):574-583.

P0724 CAN SPLEEN STIFFNESS MEASUREMENT REPLACE THE UPPER ENDOSCOPY TO PREDICT OESOPHAGEAL VARICES IN CHRONIC LIVER DISEASE B?

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Introduction: The upper endoscopy is the gold standard method to search oesophageal varices, signes of portal hypertension. But, it is an invasive and non-risk-free examination. Few studies have investigated other non-invasive tools that can replace the upper endoscopy in predicting portal hypertension.

Aims & Methods: A total of 84 patients with viral Chronic B liver disease (28 liver cirrhosis, 56 chronic hepatitis) were prospectively randomised; all patients underwent TE for measurement of LSM/SSM and upper endoscopic examination for the diagnosis of OV.

Results: 53 men and 31 women were included, with a mean age of 49.04 ± 12.80 years. 42.86% of patients had no OV (V0); 14.27% had OV grade I (V1) and 28.57% had large oesophageal varices (OV grade II and III). Patients were divided into two groups, those with non varices and those with OV (42.86%). Spleen stiffness showed higher values in liver cirrhosis as compared with chronic hepatitis B patients (58.79KPa versus 26.93KPa; p< 0.001) and in patients with OV as compared to those without OV (52.09KPa versus 26.64KPa; p< 0.001). The median value of SSM for patients with V1 was 29.92 KPa (12.90 - 75KPa) , 61.27KPa (13.90 - 75KPa) for patient with V2 (OV grade II) and 65.85 KPa (35.50-75KPa) for patients with V3 (OV grade III). A significant difference of SSM was observed between V1,V2 ,V3 subgroups (p=0.005) .But, there was no significant difference between Vo and V1. For a SSM higher than 33.1KPa, we managed to predict the presence of OV with an area under ROC (AUROC) at 0.795, a sensibility (ss) at 72.2% , a specificity (sp) at 77.1% and a negative predictive value (NPV) at 63%. For a SSM higher than 43KPa, we manage to predict the presence of large oesophageal varices with an AUROC at 0.906, a ss at 83.3%, a sp at 83.3% and NPV at 81%. The SSM was more interesting in predicting the presence of large OV than the presence of OV (AUROC 0.906 versus 0.795).To increase the performance of SSM, we calculate the arithmetic sum of SSM and LSM and we found that SSM+LSM was better than SSM to predict the presence of OV and large OV with AUROC at 0.824 and 0.937 respectively.

Conclusion: The SSM seems to be an interesting non invasive tool to predict the presence of large OV requiring primary prophylaxis of varicose haemorrhage in order to reduce the number of screening endoscopy. The Association LSM+SSM may be considered as the first line non-invasive tool to predict the presence of OV in patients with viral chronic B liver disease.

Disclosure: Nothing to disclose

P0725 DIRECT ACTING ANTIVIRAL TREATMENT DECREASES INHIBITORY TIM-3 IMMUNE CHECKPOINT RECEPTOR EXPRESSION ON NK CELLS IN PATIENTS WITH CHRONIC HCV HEPATITIS

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Introduction: In chronic HCV hepatitis immune cells have increased expression TIM-3 checkpoint inhibitor receptor that downregulates T cell activation, resulting T cell exhaustion. In contrast to immune dysfunction of adaptive immune response high levels of TIM-3 expression on NK cells was associated with an activated phenotype towards cytotoxicity. Elimination of hepatitis C virus with direct-acting antiviral (DAA) treatment may modify host immune response via changing TIM-3 immune checkpoint molecule expression.
Aims & Methods: In this prospective study we aimed to analyse changes in TIM-3 receptor expression by peripheral blood mononuclear cells in chronic HCV hepatitis patients during DAA treatment. Phenotype distribution and expression of TIM-3 by peripheral blood CD3+, CD4+, CD8+ T cells, regulatory T cells, NK, NK dim, NK bright, NKT cells and monocytes were determined by multicolor flow cytometry in 14 patients with chronic hepatitis C pretreatment and after 12 weeks of dasabuvir, ombitasvir, paritaprevir/ritonavir combination treatment. Blood samples were collected baseline (BL), at the end of treatment (EOT) and at 12 weeks after EOT (SVR12) All patients achieved sustained virological response (SVR12).
Results: While the percentage of NK bright cells significantly decreased during DAA therapy (BL: 3,1%, SVR12: 1,7%), the percentage of peripheral blood CD3+ T lymphocytes was significantly higher at SVR12 compared to baseline values (BL: 47 % vs SVR12: 56,3%). TIM-3 expression by NKT (BL: 4,9% vs SVR12: 3,5%) and by NK bright cells (BL: 64% vs SVR12: 50,4%) decreased significantly after treatment.
Conclusion: Sustained virological response was associated with increased percentage of peripheral cytotoxic T cells and also with decreased inhibitory TIM-3 checkpoint inhibitor expression by NKT and NK bright cells. Our data suggest that DAA therapy via decreasing the expression of TIM-3 immune checkpoint molecules on NK cell subpopulations may induce the modulation of NK cell cytotoxicity against T cells and contribute to the recovery of exhausted adaptive immune responses.
Disclosure: Nothing to disclose

P0726 MOLECULAR CHARACTERIZATION OF GENOTYPIC PROFILE OF HEPATITIS D VIRUS IN LIBYA

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Introduction: Hepatitis D virus (HDV) is a hepatotropic virus that is dependent on the hepatitis B virus (HBV) and supplies the viral envelope containing the surface antigen of hepatitis B. An estimated 15-20 million people are co-infected with HBV and HDV worldwide; with areas of high endemicity in the Middle East, and the Mediterranean region. Viral genetic diversity is related to the geographical origin of the isolates, and there are at least eight genotypes that are referred to as HDV-1 through HDV-8. Data on molecular characterization of HDV in Libya are lacking.
Aims & Methods: This study aims to assess the HDV genotypic of patients infected with HDV in Libya. was genotyped by nested PCR-RFLP and sequencing from serum samples of 10 patients with HDV infection whom found to be positive in a cohort of 400 patients with hepatitis B infection. The genotypes were correlated with the clinical characterics presented by patients with HBV/HDV infection.
All HDV strains belonged to genotype 1, with a wide distribution within the HDV-1 group. They all share the African amino acid marker, a serine at position 202 of the large hepatitis D virus protein.

Results: All HDV strains belonged to genotype 1, with a wide distribution within the HDV-1 group. They all share the African amino acid marker, a serine at position 202 of the large hepatitis D virus protein.
Conclusion: HDV genotype-1 is the only genotype found, with a high diversity within this group. Further studies are needed in order to better characterize and manage the HBV/HDV-infected patients according to the genetic variability of the viral strains.
Disclosure: Nothing to disclose

P0727 HEPATITIS C PATIENTS WITH SUBSTANCE MISUSE ATTEND AND ENGAGE BETTER WITH A COMMUNITY-BASED OUTREACH CLINIC COMPARED TO A TRADITIONAL HOSPITAL-BASED CLINIC

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Introduction: In June 2017, a hepatitis C (HCV) clinic was established in the local substance misuse service (SMS) as an outreach clinic from the local hospital. The clinic initially operated once a month, but due to demand, fortnightly clinics were commenced in March 2018. The objective of the clinic was to provide HCV care (including work-up and treatment) to clients who, because of their substance misuse, might not attend hospital clinics.
Aims & Methods: The aim of this study was to assess whether the outreach clinic improved attendance and engagement among these patients compared to hospital-based clinics. The outreach clinic database was used to identify individuals who were offered an appointment between June 2017 and December 2018. The hospital electronic booking system was then used to review historic appointments made for these patients in secondary care. Attendance and engagement with the hospital and outreach clinics were compared.
Results: 51 individuals were referred to the SMS clinic between June 2017 and December 2018. 31 of these (61%) had, at some point (dating as far back as the early 2000s), been referred to secondary care for assessment of their HCV. Among those referred, 12 (39%) never attended an appointment, 18 (58%) attended at least once but were subsequently lost to follow-up and 1 (3%) was initiated on HCV treatment but was subsequently transferred to the SMS clinic once established on treatment. In comparison, of the 51 referred to the SMS clinic, 17 (33%) never attended an appointment, 12 (24%) attended at least once but were then lost to follow-up while 22 (43%) remained engaged with the outreach clinic.
Conclusion: This study demonstrates that, compared to a hospital setting, an outreach clinic in the community substantially improves attendance and engagement among HCV patients with substance misuse. Contributory factors may include reduction in barriers with SMS oriented care, and ease of access as these patients regularly attend the SMS centre.
Disclosure: Nothing to disclose

P0728 HEPATITIS B VIRUS INFECTION - IS MIGRATION STATUS A RISK FACTOR?

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Introduction: HBV infection is one of the most common infectious diseases worldwide. Chronic infection may be complicated by cirrhosis and or liver cancer. Despite the introduction of a vaccine several decades ago, this disease is still widely prevalent. The prevalence of HBV infection varies according to geographic location, with relatively low rates in Western Europe (< 1%). Overall trends in incidence in this region have improved, however, increasing immigration from countries with higher prevalence has impacted the problem.
Aims & Methods: This epidemiological study was carried out to determine trends in incidence of chronic HBV infection in Malta, a country which has recently recorded the highest rate of immigration in the European Union. HBV infection was defined as the presence of positive hepatitis B surface antigen (HBsAg) and/or positive total antibody to hepatitis B core protein (anti-HbC). Patients infected with hepatitis B between 2008 and 2017 were identified through the Virology laboratory and Molecular Diagnostics (Infectious Diseases) which caters for all patients within the Maltese National

Health Service. Demographic and clinical data were recorded, including age, gender, ethnic and racial group, viral hepatitis markers, radiology as well as histology results. Statistics on the Maltese population were obtained from the Eurostat database.

Results: Four hundred and forty-one patients were noted to suffer from HBV infection. With an average population of 425,000 during the period studied, the calculated prevalence of known chronic HBV infection was 0.1%. The proportion of non-migrants suffering from HBV infection was 0.06% (n=245) of the average non-migrant population in Malta (n=398,604). The equivalent statistic for migrants was 0.6% (n=164) of the average migrant population (n=27,162). A third of HBV-infected patients were aged 34 years or less, 74% of these being migrants (see Table). The proportion of infected migrants was lower in older age groups where correspondingly lower rates of migrants prevail. The most prevalent race was Caucasian (78%, n=321) and the main ethnic group was non-Hispanic (97.5%, n=399). Cirrhosis was present in 20% of patients, while 6% (n=26) had hepatocellular carcinoma. None of the patients studied had documented Hepatitis C or HIV co-infection, while one (5%) had previous exposure to Hepatitis A.

Conclusion: The prevalence demonstrated in our population is similar to that found in other countries in Western Europe. The risk of HBV infection was found to be 10-fold in the migrant population, hence emphasizing migrant status as a risk factor for infection. Rates of infection in individuals aged 34 years or less were much higher in the migrant population, most of which were presumably not protected by vaccination. Identification of specific patient characteristics allows for appropriate planning of public health initiatives, hence contributing to the success of eradication programs. The results obtained in the course of this investigation suggest the need for screening and treatment of migrants, while ensuring that all children are vaccinated.

Age	% of Total	Proportion of Migrants
< 34	33%(n=146)	74%
35-44	16.6%(n=73)	66%
45-54	13.9%(n=61)	25%
55-64	19.4%(n=86)	2%
65-74	6.2%(n=24)	1%
>75	2.1%(n=12)	0%
Unknown	11.1%(n=49)	Unknown

[Percentage of hepatitis B virus infected patients stratified by age group]

References: European Commission. Eurostat Population Data (Demography, Migration and Projections). Cited April 2019. Available from: https://ec.europa.eu/eurostat/web/population-demography-migration-projections/data

Disclosure: Nothing to disclose

P0729 DETERMINATION OF LIVER FIBROSIS BY BIOCHEMICAL SCORES IN COMPARISON TO TRANSIENT ELASTOGRAPHY IN PATIENTS WITH CHRONIC HEPATITIS C - A PORTUGUESE REAL LIFE COHORT

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Introduction: Noninvasive methods for estimation of liver fibrosis may help to avoid liver biopsy in many contexts. In chronic hepatitis C (CHC), guidelines recommend transient hepatic elastography (TE) prior to initiation of treatment. The validation of biochemical scores (BQS), such as APRI and FIB-4, may contribute to the simplification of treatment.

Aims & Methods: The aim of this study was to compare the diagnostic accuracy of TE in comparison to BQS in staging of fibrosis in CHC. Cross-sectional study of patients with CHC followed at a Hepatology Unit, from February/2015 to February/2019, with baseline TE, determined with Fi-broScan: F0-F1 < 7; 7£F$_2$< 9.5; 9.5£F3< 12.5; F4≥12.5. APRI and FIB4 scores were calculated at the TE date and the respective cut-offs were calculated (Youden index) to define F0-F1, F2-F3 and F4, as well as sensitivity, speci-

ficity, positive predictive value (PPV) and negative (NPV) and diagnostic accuracy expressed using the area under the receiver operating curve (AU-ROC).

Results: 405 patients, 68% men; mean age 53.17 ±9.10 (15-81). TE fibrosis stage: F0-F1 48%, F2 18.6%; F3 10.1%, F4 23.3%. The diagnostic accuracy, sensitivity and specificity of the BQS, as well as cut off, PPV and NPV are shown in Table 1.

Conclusion: In the present real-life cohort, APRI and FIB-4 had diagnostic accuracy between 83.4 and 84.6% for cirrhosis, using TE as a reference, mainly because of its high NPV of 93% for APRI (cut off < 0.883), and for FIB-4 (cut off < 1.902). The BQS were less accurate than TE in the detection of intermediate stages of fibrosis.

	Score	AUROC	Sensivity	Specificity	Cut off	PPV	NPV
F0-F1	APRI	0.806	0.771	0.743	0.558	0.764	0.750
	FIB-4	0.789	0.686	0.773	1.539	0.766	0.694
F2-F3	APRI	0.582	0.759	0.489	0.506	0.374	0.834
	FIB-4	0.550	0.724	0.444	1.185	0.344	0.800
Cirrhosis	APRI	0.834	0.808	0.809	0.883	0.562	0.933
	FIB-4	0.846	0.798	0.813	1.902	0.563	0.930

[Table 1]

References: 1- Ragazzo TG, Paranagua-Vezozzo D, Lima FR Accuracy of transient elastography-FibroScans, acoustic radiation force impulse (ARFI) imaging, the enhanced liver fibrosis (ELF) test, APRI, and the FIB-4 index compared with liver biopsy in patients with chronic hepatitis C. Clinics (Sao Paulo). 2017 Oct;72(9):516-525. 2- Omar H, Said M, Eletreby R Longitudinal assessment of hepatic fibrosis in responders to direct-acting antivirals for recurrent hepatitis C after liver transplantation using noninvasive methods. Clin Transplant. 2018 Aug;32(8):e13334. 3- Zhao Y, Thurairajah PH, Kumar R, et al Novel non-invasive score to predict cirrhosis in the era of hepatitis C elimination: A population study of ex-substance users in Singapore. Hepatobiliary Pancreat Dis Int. 2018 Dec 6. pii: S1499-3872(18)30268-6. 4- Knop V, Hofmann WP, Buggisch P, et al Estimation of liver fibrosis by noncommercial serum markers in comparison with transient elastography in patients with chronic hepatitis C virus infection receiving direct-acting antiviral treatment. J Viral Hepat. 2019 Feb;26(2):224-230.

Disclosure: Nothing to disclose

P0730 WITHDRAWN

P0731 IMPROVEMENT OF SEROLOGICAL MARKERS OF FIBROSIS IN PATIENTS WITH CHRONIC HEPATITIS TREATED WITH DIRECT ACTION ANTIVIRALS

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Introduction: The new direct-acting antiviral (DAA) achieve rates of sustained virological response (SVR) in patients with chronic hepatitis C that exceed 95%. Achieving SVR has been shown to prevent progression to liver disease final stages.

Aims & Methods: The aim of this study is to evaluate changes in liver fibrosis by non-invasive serological methods after achieving SVR with new therapies in patients with chronic hepatitis C.

A unicenter retrospective observational study of patients with chronic hepatitis C treated with DAA between 2014 and 2016 was carry out. Basal fibrosis assesment was performed by transitional elastography (TE). Advanced fibrosis was defined as > 9,5 KpA. Serological markers of fibrosis (FIB-4 / APRI) were determinated before treatment and 24 weeks post-treatment.

Results: We found that among the sample 419 of 438 patients achieved SVR. Two hundred and seventy-eight patients (66,3%) were men with a median age of 55 years (48-64). One hundred and fifty-three patients (36,5%) were hypertensive and seventy-five (17,9%) were diabetic. Fifty-three percent of the patients presented genotype 1b and 10,7% showed genotype 3.

According to ET 285 patients (68%) had advanced fibrosis. The median fibrosis stage before treatment was 11,7 KpA (8,35; 19,3) by ET 2,23 (1,3;

4,22) and 0,86 (0,49; 1,82) according to FIB-4 and APRI, respectively. This measurements 24 weeks after treatment were 1,35 (0,93; 2,16) and 0,30 (0,21; 0,47) by FIB-4 and APRI, respectively (p < 0,001).

Serological markers	Basal	Week 24	p-valor
Advanced ET: >9,5 KpA			
FIB-4	2,87 (1,75; 5,31)	1,57 (1,1; 2,76)	<0,001
APRI	1,21 (0,64; 2,39)	0,34 (0,24; 0,61)	<0,001
No advanced TE: < 9,5 KpA			
FIB-4	1,4 (0,94; 2,01)	0,99 (0,73; 1,28)	<0,001
APRI	0,58 (0,36; 0,88)	0,22 (0,18; 0,30)	<0,001

[Table 1]

Conclusion: Patients with hepatitis C virus infection who achieved a SVR after received DAA showed a significant regression of the validated serological markers of fibrosis. This findings accomplish in patients with and without advanced fibrosis.

It is probably that these changes allow us to select patients who do not beneficit themselves from a long-term follow-up. Nevertheless, to consolidate this, prospective studies with a larger patients number and follow-up time are needed.

Disclosure: Nothing to disclose

P0732 EFFECTS OF HCV ERADICATION ON CARDIAC FUNCTION IN PATIENTS WITH CIRRHOSIS: INITIAL RESULTS FROM A COHORT STUDY

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Introduction: Hepatitis C Virus (HCV) infection is one of the leading causes of cirrhosis worldwide and is associated with an increased risk of cardiovascular events (stroke, acute coronary syndrome) [1]. Furthermore, these patients can develop cirrhotic cardiomyopathy (CCM) defined by a blunted adaptative response of the myocardium to stress. [2] Direct-acting antivirals (DAAs) are a new class of drugs with very high efficacy for the treatment of HCV. We aimed to assess the impact of HCV eradication on the cardiac profile of cirrhotic patients.

Aims & Methods: This is an initial report from an ongoing prospective observational study. 17 consecutive patients with HCV cirrhosis were included before undergoing treatment with DAAs for a period of 3/ 6 months. Exclusion criteria were pre-existent cardiovascular disease, obesity and chronic alcohol intake (above 80mg/day in the last 5 years). Routine blood tests, standard 12-lead electrocardiogram, N-terminal pro-brain natriuretic peptide levels and contrast enhanced echocardiography examination with tissue Doppler imaging were performed in all patients at baseline and after 1 year of follow-up. CCM was diagnosed by echocardiography showing systolic dysfunction (SS, left ventricle ejection fraction < 55%) and/or diastolic dysfunction (DD, at least 2 out of 3 of the following: age-corrected E/A< 1, IVRT> 80ms and DT>200 ms) [3]. The main outcome was change in cardiac function after viral clearance assessed by echocardiography.

Results: 17 patients were enrolled between july 2017-march 2018, of whom 4 were lost to follow-up, 2 did not receive treatment and 1 was excluded due to presence of atrial fibrillation. 2 patients had decompensated cirrhosis based on Child-Pugh score. CCM was diagnosed in 8 out of 10 patients based on the presence of isolated DD in 6 and mixed systolic and diastolic dysfunction in 2.

There was a significant statistical improvement in thrombocyte count, albumin, INR and total bilirubin following treatment, but not for the Child or MELD score. There was a significant decrease in the lateral mitral annular systolic velocity (9.24 vs 8.52 cm/sec, p=0.05, Wilcoxon test), an increase in late velocity flow (A and VA waves) and a significant increase in mean arterial pressure (92 vs 106 mmHg, p=0.018). NT-proBNP, corrected QT and incidence of SD/DD did not significantly differ before and after viral eradication.

There were 2 new cases of CCM based on DD and 1 case with normalisation of diastolic function. One patient developed exertional dyspnea during treatment with sofosbuvir/ledipasvir and the follow-up echocardiography showed a marked difference in pulmonary artery pressure before and after treatment (26 vs 53mmHg), with the exclusion of pulmonary or left cardiac diseases. Right heart catheterization ruled out severe arterial pulmonary hypertension.

Conclusion: Eradication of HCV may influence cardiac function in patients with cirrhosis. Alterations in cardiac parameters in our cohort potentially due to viral clearence indicate that further study is warranted.

References: 1. Petta S. Hepatitis C virus and cardiovascular: A review. J Adv Res. 2016;8(2):161-168. doi:10.1016/j.jare.2016.06.001 2. EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis. Angeli, Paolo et al. Journal of Hepatology 2018 , Volume 69, Issue 2, 406 - 460 3. Moller S, Henriksen JH. Cardiovascular complications of cirrhosis. Gut 2008;57:268-278 4. Voiosu AM, Daha IC, Voiosu TA, Mateescu BR, Dan GA, Baicus CR, et al. Prevalence and impact on survival of hepatopulmonary syndrome and cirrhotic cardiomyopathy in a cohort of cirrhotic patients. Liver Int 2015;35:2547-2555.

Disclosure: Nothing to disclose

P0733 ASSESSMENT OF CARDIAC FUNCTIONS BEFORE AND AFTER TREATMENT OF EGYPTIAN CHRONIC HEPATITIS C PATIENTS USING DIRECTLY ACTING ANTIVIRALS

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Introduction: Hepatitis C virus (HCV) infection is one of the main causes of chronic liver diseases worldwide. HCV infection has been associated with numerous extra-hepatic manifestations. Also, up to 50 percent of patients with advanced cirrhosis have features of cardiac dysfunction. Treatment for chronic HCV infection is evolving from interferon-based therapy to direct-acting antiviral agents. Previous interferon-based anti-HCV therapies were mostly not tolerated by patients with advanced heart failure and had limited elimination efficacy. Those new highly anti-HCV-specific drugs lack the complex unspecific side effects upon cardiac. However, new regimens comprised of DAAs that target different steps in the HCV life cycle are in development and some have received breakthrough therapy status by the U.S. Food and Drug Administration. Also, recent retrospective studies, case reports and post marketing reports suggest that those drugs may cause a toxic cardiomyopathy.

Aims & Methods: The aim of the study is to assess the effect of treatment of naïve Egyptians chronic hepatitis C patients on cardiac functions using direct acting antivirals. This study is a prospective cohort study that was conducted on 90 treatment-naïve adult patients with chronic hepatitis C infection. Patients were divided in 2 groups :

Group 1: 45 non cirrhotic patients received treatment with Sofosbuvir + Daclatasvir for 12 months.

Group 2: 45 cirrhotic patients received treatment with Sofosbuvir + Daclatasvir + ribavirin for 12 months.

All patient achieved sustained virological response at week 12 (SVR12)

All patients were assessed at week 0 (start of treatment) and week 12 (SVR 12) with laboratory studies including level of NT- Pro BNP, ultrasonography, Echocardiography.

Results: Assessment of LV systolic functions using EF % revealed no significant difference between the studied groups regarding EF before and after treatment (P value 0.266 ,0.169 respectively) Change in EF was significantly higher in non-cirrhotic group (P value 0.024) . EF significantly increased in non-cirrhotic group after treatment(P value 0.003). Assessment of diastolic function using E/A ratio revealed no significant difference between the studied groups regarding E/A ratio before and after treatment(P value 0.752, 0.881 respectively) . E/A ratio was non-significantly changed in both groups(P value 0.202, 0.108 respectively) . Assessment of mean pulmonary artery pressure (MPAP) revealed No significant difference between the studied groups regarding MPAP before and after treatment (*P value* 0.466, 0.923 respectively) . MPAP was non-signifciantly changed in both groups(*P value* 0.693, 0.479 respectively) . Regarding serum level of NT-Pro BNP , it was significantly increased in both groups after treatment (*P value*

< 0.001 in both groups) with no significant difference between the studied groups before and after treatment (*P value* 0.058, 0.099 respectively). Also, there was no significant changes in ECG findings in both groups and there was also no significant difference between the studied groups.

Conclusion: Treatment of chronic HCV infection using DAAs (Sofosbuvir, Daclatasvir, Ribavirin) has no clinicaly significant effect on cardiac functions.However, some sort of sub-clinical myocardial affection can occur for further analytical studies.

Disclosure: Nothing to disclose

P0734 HEPATITIS C ELIMINATION IN THE NETHERLANDS (CELINE): A NATIONWIDE STUDY RETRIEVING LOST TO FOLLOW-UP CHRONIC HEPATITIS C PATIENTS

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Introduction: Hepatitis C virus (HCV) infection prevalence in the Netherlands is estimated at 0.16%[1]. As of November 2014, direct-acting antiviral (DAA) therapy is reimbursed in the Netherlands for everyone with health insurance. Unfortunately, up to 30% of the diagnosed population has been lost to follow-up (LTFU) before receiving proper treatment[2,3]. Around 320 patients in the Netherlands die annually as a result of HCV infection[4]. The Hepatitis C Elimination in The Netherlands (CELINE) project is a nationwide retrieval project that aims to retrieve and re-evaluate HCV patients who are LTFU, and link them to care. The ultimate goal is to eliminate HCV in the Netherlands, in line with the WHO goals[5].

Aims & Methods: This multicentre cohort study aims to include patients from all 47 Dutch hepatitis treatment centres. Patients are identified based on laboratory records (HCV antibodies, immunoblot, RNA and genotype). Subsequently, patient records are reviewed to identify current HCV-positive but untreated patients. The Municipal Personal Records Database is used to obtain current addresses, which accords with privacy legislations. Patients are contacted for an assessment of current HCV status, liver disease severity and if needed DAA treatment. The primary endpoint of the study is the number of LTFU patients who have been successfully linked to care. Secondary endpoints are number of patients already cured, the total number of LTFU patients, reasons for being LTFU, transmission route and liver fibrosis severity of the LTFU population.

Results: CELINE started mid-2018 and is scheduled to finish mid-2021. So far, four hepatitis treatment centres have finished the identification phase and initiated the retrieval phase. Of 3054 potential ever chronically infected patients, 61% (n=1852) have already been cured and 10% (n=298) were LTFU and eligible for retrieval (alive and current address information available).

Currently, 74 patients have been invited for outpatient clinic evaluation. Of these 74 patients, 24% (n=18) were already (being) treated, 7% (n=5) had too severe comorbidity or were deceased, 19% (n=14) refused to be re-evaluated and in 41% (n=30) contact is not yet established.

So far, seven patients (9%) have successfully been linked to care. The reasons for being LTFU were: no indication or options for therapy (n=4), LTFU during therapy (n=2) and no consequence given to HCV test (n=1). Probable transmission routes were intravenous drug use (n=4) and blood transfusion (n=3). For other patient characteristics see Table 1.

Conclusion: These interim results show the first step in reaching HCV elimination in the Netherlands. As the retrieval phase is ongoing in four hospitals and soon to start in several other hospitals, we expect to increase the number of patients linked to care in the short term.

Results are in line with those of the CELINE pilot project (REACH), which retrieved 16% of LTFU patients (n=47)[3]. CELINE can be used to serve as a blueprint for retrieval projects in other countries.

Patient characteristic (n=7)	
Age at last contact in years (median, IQR)	50 (43-58)
Male gender (n, %)	7 (100)
Years since last contact (median, range)	13 (4-20)
Treatment experienced (n, %)	4 (57)
RNA-positive at re-evalution (n, %)	3 (43)
LSM RNA-positive patients ≥9.5 kPa (n, %)	1 (33)
Treatment initiated (n, %)	3 (100)

IQR: interquartile range, n: number, LTFU: lost to follow-up, LSM: Liver Stiffness Measurement

[Table 1. Characteristics of patients linked to care]

References: 1. Koopsen et al. Chronic hepatitis B and C infections in the Netherlands: estimated prevalence in risk groups and the general population. Epidemiol Infect. 2019 Jan;147:e147. 2. Beekmans et al. Re-evaluation of chronic hepatitis B and hepatitis C patients lost to follow-up: results of the Northern Holland hepatitis retrieval project. Hepatol Med Policy. 2018;3:5. 3. Kracht et al. Retrieval And cure of Chronic Hepatitis C (REACH): Results of micro-elimination in the Utrecht province. Liver Int. 2019;39(3):455-62. 4. Hofman et al. Mortality due to chronic viral hepatitis B and C infections in the Netherlands. Ned Tijdschr Geneeskd. 2016;160:D511. 5. World Health Organization. Combating hepatitis B and C to reach elimination by 2030. Geneva, 2016.

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P0735 RECURRENCE OF HEPATOCELLULAR CARCINOMA IN CHRONIC HEPATITIS C PATIENTS TREATED WITH DIRECT ACTING ANTIVIRAL AGENTS (DAAS): A SINGLE CENTER EXPERIENCE

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Introduction: Chronic HCV infection is a leading risk factor for HCC worldwide. Some recent studies have shown an unexpected high rate and aggressive pattern of tumor recurrence following successful therapy of HCV with DAAs. It has been suggested that disruption of immune surveillance may facilitate the emergence of metastatic clones.

Aims & Methods: To assess recurrence of HCC after successful therapy in a cohort of Egyptian patients with chronic hepatitis C genotype 4 treated with Direct-Acting Antiviral agents (DAAs). Methods: This retrospective cohort study included 100 patients with HCV-induced cirrhosis who were treated with DAA therapy between December 2015 and December 2016. Patients were categorized into 2 groups: Group (I): included 50 patients with liver cirrhosis without any evidence of HCC. Group (II): included 50 patients with successfully treated HCC on top of HCV-induced liver cirrhosis.

According to the guidelines of National committee for control of viral hepatitis (NCCVH) released in November 2015, these patients were included in the study only four weeks after successful intervention for HCC aiming at cure, with no evidence of activity by dynamic imaging. All patients were

treated with Sofosbuvir, Daclatasvir with or without Ribavirin. Abdominal ultrasound (U/S) and abdominal (CT) were performed for groups I and II patients respectively at 12 weeks intervals during treatment and follow up period. Triphasic (CT) was ordered in group I patients if suspicious focal lesion was detected by U/S or raising in AFP values was observed.

Results: Most patients in both groups were males (74% in group I and & 78% in group II) with a mean age of 56.38±8.1& 57.9±6.2 years in groups I and II respectively. Treatment modality prior to DAA therapy was radiofrequency ablation (RFA) in 30 patients (60%), percutaneous ethanol injection (PEI) in 15 patients (30%) and liver resection in 5 patients (10%). Forty-one patients (82%) had undetectable HCV RNA at the end of treatment. Two patients in group I developed HCC during follow up period. Eleven patients (22%) in group II showed active nodules of HCC on repeated follow up. Of these patients with HCC activity, five patients (45.5%) developed local recurrence of a previous focal lesions, while six patients (54.5%) developed de-novo focal lesions. Two patients (18.2%) had vascular invasion and one patient (9.1%) had bone metastasis.

Conclusion: Treatment with a Sofosbuvir-based regimen was associated with a high recurrence of HCC in a cohort of Egyptian patients with HCC associated with chronic hepatitis C genotype 4. Patients with HCC should be properly evaluated prior to antiviral therapy with DAAs and followed up carefully during and after therapy.

Disclosure: Nothing to disclose

P0736 HCV MICROELIMINATION: INTERVENTIONAL STUDY IN DIAGNOSED PATIENTS WITHOUT ACCESS TO THE SYSTEM (TWO PHASE STUDY)

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Introduction: According to national data, 117.453 patients with chronic Hepatitis C (CHC) have been treated in Spain until September 2018. However, there is an important group of patients that have not got access to the system. The introduction of the one-step diagnostic process tries to improve referral in patients with detectable viral load, but, in our system, this is only applied to new diagnoses, so those previous positive serologies that have not fullfilled the diagnostic process may be excluded.

Aims & Methods: The aim of this study is to confirm CHC infection in patients with positive HCV-antibodies who have never been referred to a gastroenterologist / hepatologist and to recover patients with CHC infection who have not completed treatment due to not attendance to medical visits/ loss of follow-up.

This was a retrospective (first phase) and interventional (second phase) single center study in which we included all positive HCV antibodies between January 2013 and May 2018 in Virgen Macarena's health area (Seville-Spain), prior to the implementation of the one-step diagnosis of HCV infection.

In the first phase, we identified subjects who had never been referred and those who, after being referred, had lost follow-up. In a second phase, after contacting with primary care to establish a direct circuit for simplified referral, a specific Hepatitis C consultation was created. Later, patients were contacted by letter or phone call and blood tests, viral load and transient *elastography* (*Fibroscan*) were performed. Patients with confirmed viral load were summoned to a second visit where they were offered treatment.

Results: 1329 patients with positive HCV antibodies were included. 55,75% of them had a previous positive serology.

PHASE I (Table 1)

PHASE I	Retrospective
Global referral rate	1040/1329 = 78.3 %
Non-referral rate	289/ 1329 = 21.7%
HCV-antibodies diagnostic rate	914/1040 = 87,8%
Active infection rate	658/914 = 72%
Unnecessary referral rate	256/1040 = 24.6%
Treatment rate	451/658 = 68.5%

[Table 1. Phase I.]

Loss / non-attendance rate 231/1040 = 22.2%
PHASE II (PRELIMINARY DATA)
Lost / non-attendance clinical visits = 231:
We were able to contact 51.7% of them. The additional 17.1% did not answer phone calls/ did not have a valid telephone number, and 3% refused to attend consultations.
At the moment, viral load determination was requested in 87 patients. Active infection was confirmed in 82.8% of them. 57.1% of these patients were ex-ADVP; 14% were active drug users and 10% had a significant alcohol consumption, 37.9% presented advanced fibrosis (fibroscan> 9.5Kpa) and 4.6% had space-occupying lessions in ultrasound.
Never referred:
Of those patients, we were able to contact 40.6%. Until now, viral load determination was requested in 81 patients, 50% confirmed active infection, 22.9% spontaneous resolution, 27.1% SVR of previous treatments. 63% of patients knew they had HCV. 55.1% of these patients were ex-ADVP; 11% were active drug users, 30% presented advanced fibrosis.

Conclusion:
- One-step diagnosis of CHC infection avoids unnecessary referral of patients. However, there is an important group of patients who might get lost in the system.
- Simplied referral system with primary care allows high rates of diagnosis and treatment.
- A high percentage of patients who were lost in the system have advanced liver fibrosis and need long-term follow-up.

Disclosure: Nothing to disclose

P0737 HBEAG-NEGATIVE CHRONIC HBV INFECTION: IS HBSAG QUANTIFICATION HIGHER THAN 1000 IU/ML INFLUENTIAL IN THE PROGNOSIS?

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Introduction: Patients with HBeAg-negative chronic infection by hepatitis B virus (HBV) (previously inactive carriers) are expected to have a stable clinical course.

Aims & Methods: The aim of this study was to compare the clinical evolution of these patients regarding to HBsAg levels. Retrospective and unicentric study with assessment of patients with HBeAg-negative chronic HBV infection (EASL criteria), in a reference centre. Demographic characterization and assessment prognostic determinant factors.

Results: A total of 89 patients were included, 51% of female gender, with mean age of 53±16 years. Most of patients (83%) had mild or no fibrosis. The initial HBsAg quantification median was 949UI/mL (IQR 129-4208) and patients with HBsAg >1000IU/mL (48%) presented lower age (mean 49±15 years; p=0.032). During a median follow-up of 8 years (IQR 4-9), HBsAg negativation was achieved in three cases, as well as a paired decrease in HBsAg levels [median 0.30log10IU/mL (IQR 0.02-0.62);p< 0.001]. A decrease HBsAg>1log10IU/mL was more frequent if initial HBsAg < 1000UI/mL (p=0.029). Five patients needed to start antiviral therapy, after a median time of 6 years (IQR 3-8), one due to intrahepatic cholangiocarcinoma; however, an association with HBsAg >1000UI/mL wasn't verified (7vs 4%). The median initial HBV-DNA was 409IU/mL (IQR 49-1290) and the higher median viremia in follow-up was 1070IU/mL (IQR 158-3489). Initial HBsAg >1000 IU/ml was associated to higher viremia in follow-up (p< 0.001), including HBV-DNA >2000IU/mL (p< 0.001) e HBV-DNA>20.000 IU/mL (p=0.023).

Conclusion: Patients with HBsAg>1000IU/mL were associated to a lower age and higher viremia, which can be related with a shorter period of HBV infection. Generally, the prognosis was benign with significant HBsAg reduction during a long term follow-up; a decrease >1log10IU/mL was less frequent if HBsAg>1000 UI/mL. However, one hepatobiliar neoplasm was diagnosed and 4 patients presented progression to chronic hepatitis, which highlights the needed of surveillance.

Disclosure: Nothing to disclose

P0738 SCHEDULED SUSPENSION OF ANTIVIRAL THERAPY IN SELECTED CASES OF CHRONIC B HEPATITIS: HIGH SUSTAINED RESPONSE AND HBSAG LEVELS REDUCTION

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Introduction: EASL guidelines consider antiviral therapy suspension in selected cases of chronic B hepatitis, under rigorous monitoring. In this study, we intend to evaluate the clinical course of chronic B hepatitis patients after scheduled suspension of therapy.
Aims & Methods: Retrospective, monocentric and longitudinal study, from a prospectively registered cohort. Adults patients with diagnosis of chronic B hepatitis, without advanced fibrosis, with at least 4 years of undetectable viremia were included. After informed consent antiviral therapy was suspended. The cases that didn't presented criteria for retreatment (EASL guidelines) were considered as sustained response. Demographic characterization of population, evaluation of sustained response and HBsAg levels.
Results: A total of 26 patients were included (62% of woman, with mean age of 59±13 years). Antiviral drugs were tenofovir in 58% of cases, entecavir in 35% and lamivudine in 8%.
The mean time of HBV undetectably until antivirals suspension was 8.8±2.5 years.
A sustained response was observed in 54% of patients, during a mean follow-up of 24±9 months, after treatment suspension. It wasn't possible to identify predictive response factors. Most retreatments (67%) were due to increasing viremia and ALT; two patients developed jaundice, with complete reversion. The most used therapy was tenofovir (67%) and viral suppression was observed with a mean time of 6±3 months. Although HBsAg levels were previously stable, a significant reduction in HBsAg after treatment suspension was observed [0.6log10UI/mL (0.19-1.5)], independently of sustained response (p< 0.001).
Conclusion: In this study, a high rate of sustained response was observed, which may be related to a long duration of viral suppression; however, two cases of jaundice were observed, highlighting the relevance of a rigorous surveillance. A significant decrease in HBsAg levels suggests that there may be a benefit, in therapeutic suspension, even in patients without sustained response; these facts should be assessed with a longer follow-up period.
Disclosure: Nothing to disclose

P0739 LONG-TERM IMPACT OF DIRECT-ACTING ANTIVIRALS IN PATIENTS WITH HEPATITIS C AND ADVANCED FIBROSIS

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Introduction: The introduction of direct-acting antivirals (DAAs) have revolutionized the treatment of Hepatitis C (HCV), achieving cure rates above 95% (SVR). However, the long-term impact of treatment on clinical complications and mortality in patients with advanced fibrosis is not currently known.
Aims & Methods: The aim of our study is to describe long-term decompensations in patients with advanced fibrosis treated with DAAs.
This is a retrospective observational study of patients with chronic HCV and advanced fibrosis (Fibroscan>9.5Kpa and/or APRI>1) treated with DAAs from 2014 to 2016 in the Virgen Macarena Hospital and followed up to December 2018. We collected demographic variables, pre-treatment decompensations, response to treatment, post-treatment decompensations (ascites, encephalopathy, variceal upper gastrointestinal bleeding, development of hepatocellular carcinoma HCC) and mortality (hepatic or non-hepatic cause).
Results: A total of 298 patients were included, 67.8% (202) men, with a mean age of 57 (± 12) years, and a median follow-up of 37 months (range) (30; 43). 41.9% (125) had high blood pressure, 23.5% (70) were diabetic,

and 15.1% (45) had pre-treatment alcohol consumption. The predominant genotype was 1b in 51.3% followed by genotype 3 in 13.8%. 96% (286) reached SVR. Table 1 shows the pre and post-treatment decompensation.

Pre-treatment % (n)	Post-treatment % (n)
Ascites 8,7% (26)	Ascites 2,3% (7)
Variceal gastrointestinal bleeding 3,7% (11)	Variceal gastrointestinal bleeding 2,7% (8)
Spontaneous bacterial peritonitis (no cases)	Spontaneous bacterial peritonitis 0.3% (1)
Hepatic encephalopathy 2,7% (8)	Hepatic encephalopathy 1,7% (5)

[Table 1. Pre and post-treatment decompensation.]

During follow-up, 3.4% (10) of the patients developed HCC. The median time to development of HCC was 12.5 months (6.7; 21), and all cases occurred in patients with fibroscan >12.5kPa (F4). Additionally, 3 cases occurred in patients who did not reach SVR, and 4 cases had a previous diagnosis of HCC with a good response to local treatment (radiofrequency). The post-treatment mortality was 6.4% during the follow-up: 5.4% (16) of hepatic cause and 1% (3) of non-hepatic cause.
Conclusion: SVR after treatment with DAAs decreases the risks of decompensation in patients with chronic HCV and advanced fibrosis, although they do not eliminate them. This fact, along with the presence of associated comorbidities, implies a greater mortality risk and so means that long-term follow-up is necessary.
Disclosure: Nothing to disclose

P0740 HEPATITIS C SCREENING IN HOSPITALIZED SUBJECTS. A PROSPECTIVE STUDY IN THE VENETIAN AREA (NORTH-EAST OF ITALY)

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Introduction: The World Health Organization (WHO) recommends the implementation of strategies for the identification of HCV affected subjects for a "test-and-treat" approach in order to achieve HCV elimination in the next years. The best strategy to bring out the hidden chronic HCV infection remains uncertain. Current guidelines recommend screening in high risk populations. Hospitalized patients may represent an ideal population for HCV screening and for referral to treatment, but few data are available in this specific setting of subjects.
Aims & Methods:
Aim: of this study was to determine the prevalence of HCV infection in hospitalized subjects in the Venetian area, North-east of Italy, in order to plan an extensive treatment strategy.
Methods: All patients consecutively admitted to the surgical departments of the "dell'Angelo" Hospital, Venezia-Mestre, from 01/01/2017 to 31/12/2017, were tested for anti-HCV antibodies (CMA Abbott laboratories). In case of borderline values, a confirmatory RIBA test (INNOLIA HCV) was carried out. Positive patients were tested for HCV-RNA (RT-PCR Abbott laboratories) and HCV-genotype.
Results: Overall, 6981 patients were tested at admission (2821 males, 4160 females). 142 subjects resulted anti-HCV positive, with a prevalence of 2.0%. The prevalence was significantly higher in men (2.5%) than in women (1.7%) and increased with age (from 0.6% in 15-30 years patients to 2.7 % in 51-60 and over 70 years patients). The highest prevalence was observed in Vascular Surgery (3.6%), Traumatology (3.4%) and Neurosurgery (2.6%), the lowest in Gynecology (1.0%) and Urology (1.6%). HCV-RNA was detectable in about two-thirds of patients and the most represented genotype was genotype 1 (80%). The large majority of subjects (76%) was unaware of its status and is now recruiting for the treatment.
Conclusion: Our data show a significant prevalence of HCV infection in hospitalized subjects, two to three time higher than that expected in the general population of the Veneto region. Screening for HCV infection in

this specific setting of subjects may thus represent an useful and simple strategy to identify hidden HCV-infection and to facility HCV treatment, in order to achieve HCV elimination.
Disclosure: Nothing to disclose

P0741 THE RETREATMENT EFFICACY OF ALL-ORAL DIRECT ANTIVIRAL THERAPY FOR PATIENTS WITH HEPATITIS C VIRUS INFECTION

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Introduction: Direct-acting antiviral (DAA) therapy for hepatitis C virus (HCV) shows high sustained virologic response (SVR) rates. However, patients who have failed DAA therapy acquire resistance-associated substitutions (RASs). Glecaprevir + Pibrentasvir (GLE/PIB) therapy is approved for DAA failure patients in Japan. We therefore evaluated the efficacy of DAA retreatment and the factors associated with retreatment failure.
Aims & Methods: A total of 60 patients with HCV infection who had failed all-oral DAA therapy in the past were introduced to DAA retreatment. We evaluated the factors associated with retreatment failure. NS5A Q24, L28, R30, L31, P32, A92 and Y93 RASs at baseline and virologic failure were investigated by direct sequencing.
Results: The patient age ranged from 54 to 87 years (mean, 71), 17 patients (28%) were male, 25 (42%) patients had cirrhosis, and 12 patients (20%) had a history of hepatocellular carcinoma therapy.
Fifty-five patients had received Dacratasvir + Asunaprevir, three had received Sofosbuvir + Ledipasvir (SOF/LDV), and one each had received Ombitasvir + Paritaprevir and Sofosbuvir + Ribavirin (SOF/RBV).
Thirty-three patients were retreated with SOF/LDV, 2 were retreated with Elbasvir + Grazoprevir (EBR/GZR), and 25 were retreated with GLE/PIB. The SVR rates were 81.8% with SOF/LDV retreatment, 0% with EBR/GZR retreatment, and 87.0% with GLE/PIB retreatment.
Eleven patients did not achieve an SVR. Six and two patients failed SOF/LDV and EBR/GZR retreatment, respectively, and seven of these patients had coexisting NS5A Q24, L28, and/or R30 RASs, L31 RAS and Y93 RAS, while the other had P32L and A92K RASs at baseline. However, no marked change in the RASs between baseline and virologic failure were noted. Four patients who had initially failed DCV/ASV and SOF/LDV achieved an SVR on retreatment with GLE/PIB.
However, one patient re-treated with EBR/GZR did not achieve an SVR. Of the three patients who failed GLE/PIB retreatment, two had Q24, L28, R30 and A92 RASs, and the other had P32 deletion RAS at baseline. In those who failed GLE/PIB retreatment, the R30Q or A92T RASs at baseline changed to R30E or A92K at virologic failure. Interestingly, 10 of 11 retreatment failure patients had an interleukin 28b single nucleotide polymorphism (IL28b SNP) minor allele.
The SVR rate of patients with an IL28b SNP minor allele was significantly lower than in those with a major allele (58.3% and 95.2%, respectively; p=0.004). Furthermore, the SVR rate of patients with ≥2 NS5A RASs was lower than those with ≤1 RAS (73.2% and 100%, respectively; p=0.014). In addition, all patients who had an NS5A Y93 RAS achieved an SVR with GLE/PIB retreatment, even if they had coexisting NS5A RASs, such as Q24, L28, R30 or L31.
Conclusion: DAA retreatment with GLE/PIB resulted in a high SVR rate for patients with the NS5A Y93 RAS. However, viral factors, such as Q24, L28, R30 and A92 RASs, and host factors, such as the IL28b SNP, may influence the therapeutic effect of DAA retreatment.
Disclosure: Nothing to disclose

P0742 THE GLOBE SCORE IN ASSESSING PROGNOSIS OF PRIMARY BILIARY CHOLANGITIS WITH CONCOMITANT SJOGREN'S SYNDROME

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Introduction: Sjögren's syndrome (SS) is a systemic autoimmune chronic epithelitis that mainly affects the salivary and lacrymal glands. The coexistence of SS and primary biliary cholangitis (PBC) is not an uncommon condition, but remains poorly studied in the literature. In fact the influence of SS on the clinical outcomes of PBC patients remains unclear.
Aims & Methods: The aim of the study was to determine the prevalence and the prognostic value of SS during PBC. A retrospective study was conducted including all patients followed for PBC at our department between 2000 and 2018. SS was systematically sought.The diagnosis was done when at least 4 of the following criteria was met: dry eye for >3 months, dry mouth for >3 months, positive Schirmer test, abnormal salivary gland scintigraphy findings, diagnostic minor salivary gland biopsy, and positive anti-Ro (SS-A) or anti-La (SS-B) antibodies.
In subgroup analysis, PBC patients were classified into 2 groups: with concomitant SS or without SS. The response to UDCA therapy was evaluated according to Paris-2 criteria at 1 year of the treatment. The Globe score, a prognostic tool predicting survival without transplantation, was calculated for the 2 groups.
Results: Overall, 53 patients were included with mean age of 55 years (range 19-78 years). There was naturally a female predominance with a sex ratio F/M = 5.6 .The median follow-up was 6 years. SS was diagnosed in 14 patients. The prevalence of SS in PBC patients was 26%. There were no significant differences in age, sex, and levels of albumin, international normalized ratio, creatinine, alanine aminotransferase, alkaline phosphatase, gamma-glutamyl transferase, total bilirubin or platelet count between the 2 groups. In the PBC-SS subgroup, the mean age was 50 years. The circumstances of discovery of PBC were: cholestasis with pruritus (61%), jaundice (30%), asthenia assessment (6%) and exploration of celiac lymph nodes (3%).
At one year of UDCA therapy, a biochemical remission according to Paris II criteria was noted in 38% of PBC-SS patients and 36% in PBC-only patients (p>0.05). The mean value of the Globe score in PBC-SS patients was 1.4 versus 1.6 in PBC patients without SS (p> 0.05). The presence of SS was not significantly correlated with a poor therapeutic response, nor the prognosis of PBC.
Conclusion: To our knowledge, this is the first study to investigate the prognostic value of SS in patients with PBC using the globe score. Although their association does not appear to affect the course of PBC, screening should be systematic to improve the quality of life of the patients. Further validation of these findings in prospective studies with a larger population of patients is needed.
Disclosure: Nothing to disclose

P0743 ADD-ON STATINS IMPROVE RESPONSE TO URSODEOXYCHOLIC ACID IN PATIENTS WITH PRIMARY BILIARY CHOLANGITIS

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Introduction: Ursodeoxycholic acid (UDCA) is the standard therapy for primary biliary cholangitis (PBC); however, the proportion of non-responders to UDCA is as high as 40-50%. Non-response to UDCA is related to progression of the disease and bad prognosis.
Aims & Methods: To identify risk factors related to treatment failure with UDCA in patients with PBC.
A case-control study nested in a cohort, which included patients with PBC in whom the response to treatment with UDCA was evaluated according to Barcelona criteria. We compared characteristics between responders and non-responders to UDCA, and to evaluate risk factors related to treatment failure we performed univariate and multivariate logistic regression analyses. A *P*< 0.01 value was considered significant. Patients with self-reported non-adherence to UDCA were excluded (n=15).

Results: 119 patients with PBC, 98.3% women, the mean age was 49.9±11.4 years-old. All received UDCA (dose= 13-15 mg/kg/day), all reported adherence to therapy; nevertheless, according to Barcelona criteria, 49 (41.2%) were classified as non-responders. In the univariate analysis, albumin (mg/dL) and platelets count (cell/10^9/L) (U/L) were lower in non-responders than in responders: 3.5(range=2.0-4.8) vs. 4.0(range=2.6-4.8), P< 0.0001; 118 (range=52-518) vs. 200 (78-436), P< 0.0001, respectively. Bilirubin (mg/dL) and alkaline phosphatase (U/L) were higher in non-responders: 1.9 (range=1.0-6.4) vs. 1.6 (range=1.0-3.0), P< 0.0001; and 666 (range=143-1445) vs. 480 (range=170-1556), P=0.01, respectively. Non-responders had a higher proportion of advanced fibrosis/cirrhosis (83.7% vs. 25.7%; P< 0.0001; OR=14.8, 95%CI=5.8-37.4); obesity (81.6% vs.31.4%; P< 0.0001; OR=9.7, 95%CI=4.0-23.4); overlap with autoimmune hepatitis (AIH) (42.9% vs. 7.1%; P< 0.0001; OR=9.8, 95%CI=3.3-28.5); and longer course of the disease: 5-10 years (44.9% vs. 38.6%; P=0.004; OR=4.3, 95%CI=1.6-11.5), and >10 years (40.8% vs. 8.6%; P< 0.0001; OR=17.6, 95%CI=5.2-59.6). The add-on of statins enhanced the response to UDCA (60% vs. 16.3%; P< 0.0001; OR=0.1, 95%CI=0.05-0.3). Fibrates did not have any effect (47.1 vs. 46.9%; P=0.98; OR=1.0, 95%CI=0.5-2.1). Age, AST, ALT, GGT, cholesterol and INR were not different between groups. The results obtained in the multivariate analysis are shown in Table 1.

Variable	OR (95% CI)	P
Bilirubin (> 2.0mg/dL)	4.4 (1.1 - 17.0)	0.03
Fibrosis F3 or F4	7.1 (1.9 - 26.6)	0.004
Obesity	4.9 (1.4 - 17.9)	0.015
AIH overlap	20.8 (3.1 - 137.6)	0.002
Add-on statin *	0.08 (0.02 - 0.4) *	0.002
Time of evolution (5-10 years)	1.2 (0.3 - 5.4)	0.78
Time of evolution (>10 years)	6.1 (1.0 - 38.3)	0.05

AIH autoimmune hepatitis; CI confidence interval; F3 advanced fibrosis; F4 cirrhosis; OR odds ratio; PBC primary biliary cholangitis; UDCA ursodeoxycholic acid. * = protective factor. Multivariate analysis: Binary logistic regression.

[Multivariate analysis contrasting factors related to treatment failure to UDCA in patients with PBC according with Barcelona criteria]

Conclusion: Statins improved the response to UDCA. The overlap with AIH, the presence of advanced fibrosis/cirrhosis, bilirubin >2.0mg/dL, and obesity are factors related to treatment failure with UDCA according to Barcelona criteria.
Disclosure: Nothing to disclose

P0744 PHENOTYPIC AND GENETIC SPECTRUM OF ABCB4 GENE DEFICIENCY IN ADULT PATIENTS: A CASE SERIES

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Introduction: Mutations in the ABCB4 gene initially described as responsible for Progressive Familial Intrahepatic Cholestasis Type 3 (PFIC3), presenting in childhood, are increasingly associated to a wide and heterogeneous spectrum of cholestatic liver diseases in adults, such as Intrahepatic Cholestasis of Pregnancy (ICP), Low Phospholipid Associated Cholelithiasis syndrome (LPAC), Hormone-induced Cholestasis, Drug-induced liver injury and sporadic cases of cryptogenic biliary cirrhosis.
Aims & Methods: Characterization of the phenotypic and genetic features of patients with ABCB4 mutations diagnosed between 2015 and 2019 in a Hepatology outpatient clinic. Data from 14 patients was retrospectively collected and analysed.
Results: Fourteen patients from seven families were included (11 female, mean age of 41.3 years, 17-69 years). Nine patients presented with recurrent elevated serum liver tests, of which three had a gama-glutamil transferase (GGT) 10 times the upper limit of normal, five had a previous diagnosis of ICP and six with cholelithiasis and cholecystectomy at a young age (mean age of 27 years), two patients with intra-hepatic stones, and one case of drug-induced liver injury. ABCB4 gene screening identified six different mutations. Two patients with mutation in a homozygous state, c.504C>T(p.N168N) and 12 with heterozygous mutations. Two patients are compound heterozygotes with missense mutations, c.959C>T (p.S320F) and c.1529A>G (p.N510S). Heterozygous missense variants were found in

seven patients, c.959C>T (p.S320F) in five cases, c.3082A>G (p.Met1028Val) in one case and c1529A>G (p.Asn510Ser) in another case. Three patients have nonsense mutations detected, C.874A>T (p.Lys292) in two cases and nonsense deletion c.1181delT (p.L394fs*18) in another case. Liver biopsy was performed in three patients and revealed mild macrovesicular steatosis in two of these and portal fibrosis, ductopenia and mild necroinflammatory activity was found in one of the patients with heterozygous compound mutation.
Conclusion: Although, phenotype-genotype relationships have not been clear defined, an early diagnosis of genetic variants, namely heterozygous compound states, may have an important role in management decisions and patient outcomes. To our knowledge, we describe a not previously reported deletion (c.1181delT) in ABCB4 gene. The c.504T>C polymorphism, although a silent mutation at the protein level has been previously described as associated with predisposition to ICP.
Disclosure: Nothing to disclose

P0745 QUANTITATIVE SERUM AND BILIARY PROTEOMICS AS MARKERS FOR SCREENING AND DIAGNOSIS OF PRIMARY SCLEROSING CHOLANGITIS

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Introduction: Primary sclerosing cholangitis [PSC] is a chronic inflammatory disease of biliary epithelium leading to strictures of intra- and extrahepatic bile ducts causing cholestasis and biliary cirrhosis (1). PSC is associated with markedly increased risk of cholangiocarcinoma [CCA] (2), SIR ranging from 161 to 973 (2-3), with the lifetime risk around 10% (4-5). CCA is the most common reason for death among patients with PSC (6,7). Most of the CCA's are diagnosed within first year after diagnosis of PSC warranting diagnosis of PSC in much earlier state. For the moment, no good screening tests are available for PSC, except elevated P-ALP. Bile proteomic analysis has previously been demonstrated to discriminate benign conditions from CCA in patients with PSC (8,9).
Aims & Methods: Aims: To evaluate the proteomic profiles in serum and bile samples in controls and PSC patients to find new noninvasive markers for screening and diagnosing PSC.
Patients and methods: In total, 79 patients with confirmed PSC referred for ERC for diagnosis and surveillance of the disease were included (48 females). During ERC bile sample was aspirated using balloon catheter and then stored in -80oC. Brush cytology (BC) was collected both from extra- and intrahepatic bile ducts for Papanicolaou staining for grading dysplasia. Cholangiographic findings are scored according to modified Amsterdam score (Helsinki score). Serum samples are collected at the time of ERC. 18 serum and 6 bile samples from healthy controls were included Label -free quantitative proteomics from serum and bile from the same individuals was performed UDMSE mode in Synapts G2-Si, nUPLC-TRIZAIC C18 tile as previously described.
Results: Quantitative serum proteomics from 79 patients with PSC, but not dysplasia or CCA were compared to 18 serum from healthy controls. 112 significantly (Mann-Whitney) differentially expressed proteins were found with a maximal fold change of 2.8. The Ingenuity network analyses showed enriched expression on Protein synthesis, Cell morphology and Tissue development functions. Concomitantly the bile proteomics from same set of patients expressed 64 differentially expressed proteins, but here the fold changes were much higher, up to 128. The Ingenuity network analyses showed enriched expression on Cell morphology, Free radical scavenging and Infections diseases.
Conclusion: We show in a large set of clinical serum and bile specimens that PSC alters significantly the proteomic profiles and further analyses could identify putative novel biomarkers for screening and detection of PSC in its early, asymptomatic phase.
References: 1. Dyson JK et al Lancet. 2018. dx.doi.org/10.1016/S0140-6736(18)30300-3. 2. Bergquist A, et al. J Hepatol. 2002;36:321-7. 3. Manninen P, et al. Scand J Gastroenterol. 2015;50:423-8. 4. Boberg KM, et al. Scand

J Gastroenterol 2002; 37: 1205-11. 5. Claessen MM. J Hepatol. 2009;50:158-64. 6. de Valle et al. Liver Int. 2012;32:441-8. 7. Lewis JT, et al. Am J Surg Pathol. 2010;34:27-34. 8. Lankisch T, et al. Hepatology 2011;53:875-84. 9. Navaneethan U et al. Gastroenterology Report 2015;3:136-43
Disclosure: Nothing to disclose

P0746 ISOLATED ELEVATION OF ANTIMITOCHONDRIAL ANTIBODIES (AMA): PERSONALIZED FOLLOW-UP ACCORDING TO THE RISK OF PROGRESSION

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Introduction: The presence of AMA in patients with elevation of alkaline phosphatase (ALP) allows the diagnosis of primary biliary cholangitis (PBC). Without cholestasis however is insufficient for the diagnosis. The European Association for the Study of the Liver (EASL) recommends annual follow-up for these patients in order to detect liver disease, with a low evidence level.

Aims & Methods: Characterize the population with isolated AMA elevation and further identification of group risks for the progression of CBP. Observational study of a prospectively maintained database of AMA positive patients between January 2010 and December 2018. A positive AMA was considered by indirect immunofluorescence reactivity testing (≥1: 40). Exclusion criteria: previous diagnosis of PBC, cirrhosis, any upper limit of normal (ULN) of the reference level for ALP (120 U/L). Baseline levels were defined with simultaneous collection of AMA. When applicable, liver blood tests were collected annually. Statistical analysis was performed with SPSS (v.23). Significance level was set at < 0.05.

Results: 49 patients were included in this study of which 93,9% were female and the median age was 51 years (40,5 - 62,5). 36,7% had a diagnosis of systemic autoimmune disease. Baseline median values of ALP, gamma-glutamyl transferase (GGT) and total bilirubin (TBil) were 76 U/L (59 - 86,5), 29,7 U/L(18,7 - 58,3) and 0,5 mg/dl (0,4 -0,7), respectively. Only 28,6% of patients were submitted to annual biochemical follow-up. 5 patients fulfilled PBC EASL criteria in the follow-up. These patients had higher baseline cholestasis levels than those who did not develop PBC (median ALP U/L 88 vs. 70, p=0.007; GGT U/L 118 vs. 27 p=0.002; TBil mg/dl 1,3 vs. 0,45, p=0.002, respectively). ALP, GGT and TBil had an area under the curve (AUC) for predicting PBC of 0.854, 0.958 and 0.933, respectively (p< 0.05). An ALP value of > 86,5 U/L had a 75% sensibility and 80% specificity in predicting the development of PBC.

Conclusion: Patients with higher baseline cholestasis levels, in the normal range (86-120 U/L) may have a higher risk for developing PBC. The further categorization of a risk group suggests a personalized rather than a generalized follow-up.

References: Invernizzi P, Marzioni M, Corpechot C, et al. EASL Clinical Practice Guidelines: The diagnosis and management of patients with primary biliary cholangitis. J Hepatol 2017;67(1):145-72.

Disclosure: Nothing to disclose

P0747 MANAGEMENT OF PRIMARY BILIARY CHOLANGITIS: EXPERIENCES FROM A DISTRICT GENERAL HOSPITAL

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Introduction:
- Primary biliary cholangitis (PBC) is an uncommon but important cause of chronic liver disease which undiagnosed will often lead to cirrhosis and its associated complications.
- Lifelong Ursodeoxycholic acid (UDCA) therapy at a dose of 13-15 mg/kg/day remains the mainstay of treatment, with biochemical response indices at one year invaluable in predicting long term outcomes (1).
- HCC surveillance should be undertaken in patients with overt cirrhosis identified on baseline ultrasonography as part of risk stratification for PBC (1).

Aims & Methods: Aims:
- To assess if the optimum dose of UDCA is utilized in our PBC cohort.
- To assess if HCC surveillance is being carried out in PBC patients with cirrhosis.
Methods:
- 318 Anti-mitochondrial antibody (AMA) positive patients over a 10 year period (January 2008 - December 2017) were identified via a laboratory search.
- Those with a clinical diagnosis of PBC, defined by AMA positivity accompanied by unexplained cholestatic liver enzymes were included in this study.
Results:
- The sample size (n=74) consisted of 68 female patients (91.9%), with a median age of 65 years at diagnosis in this cohort.
- 16 subjects (21.6%) were on the recommended UDCA dosage of 13-15mg/kg/day with 4 patients (25%) having their biochemical response assessed after 12 months of therapy.
- Overt cirrhosis was diagnosed in 20 patients (27%) via ultrasonography, from which 15 (75%) were assimilated into the HCC screening programme.
- Among the non-cirrhotic cohort, 42 subjects (77.8%) remained on surveillance.
Conclusion:
- This audit emphasises the importance of raising awareness regarding the correct dosing of UDCA in the treatment of PBC in order to maximise therapeutic response.
- Disease staging should be driven by the use of transient elastography over ultrasonography in light of its diagnostic accuracy, which will minimize the need for unnecessary surveillance in patients without advanced disease.

References: 1. Hirschfield GM, et al. Gut 2018;0:1-27. doi:10.1136/gutjnl-2017-31525
Disclosure: Nothing to disclose

P0748 WITHDRAWN

P0749 DONOR-RECIPIENT GENDER AND AGE MATCHING IMPACT IN DE NOVO NEOPLASMS AFTER LIVER TRANSPLANTATION

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Introduction: De novo neoplasms (DNN) after liver transplantation (LT) have been reported as one of the major causes of mortality in liver recipients, being the most common cause of death after the second decade after LT. Current post-LT surveillance strategies are based largely on data collected on general population, but should be customized in the light of risk factors specific to LT recipients. The influence of donor-recipient sex and age matching on long-term survival after liver transplant is controversial, and data on the possible effect on DNN risk are lacking

Aims & Methods: A cohort study was conducted using data collected in 9 Italian centres between 1985 and 2014. Patients were excluded if: ≤18 years old, follow-up shorter than 90 days after LT, cancer diagnosis done within 90 days after LT. Person-years (PYs) at risk for DNN were computed from 90 days post-LT to the date of death, date of cancer diagnosis or end of follow-up, whichever came first.

A competing risk approach was applied to estimate 5-year cumulative cancer incidence by time since LT. Hazard ratios for DNN and the corresponding 95% confidence intervals (CIs) were obtained using Cox models adjusted for recipient gender, age at transplant, calendar year at transplant, and aetiology of liver disease

Results: A total of 1927 patients (75.5% males, median age at LT 53 years-old) were transplanted during the study period (85% after year 2000) receiving an organ from a deceased donor in 95.5% of cases. Distribution of LT recipients according to recipient/donor gender and donor age is shown in Table 1. Cumulative cancer incidence at 5 years after LT for all recipients was 5.4%, with no differences when the results were stratified by donor gender (male 5.8 vs females 4.6%, p=0,45). Considering both donor gender and age, among male patients receiving a graft from a male donor, the 5-year cumulative incidence was higher when donor was ≥60 years-old (p=0.03) (Figure 1). In the multivariate analysis, donor age or gender were not associated with DNN risk. However, considering their joint effect, at elevated donor age (≥60 years), the risk of DNN increased for patients receiving an organ from male donors (HR=2.00, 95% CI: 1.02-2.50). Conversely, among patients receiving an organ from female donors, the risk did not vary according to donor age. When the associations were examined in strata of recipient gender, a similar pattern of risk emerged among male only (HR=2.26; 95% CI: 1.05-4.87 for those receiving an organ from male donors ≥60 years vs < 35 years)

Conclusion: In our cohort the risk of DNN occurrence was increased in male patients receiving a liver graft from older male donors, irrespectively from patients' age at transplant. Gender and age differences in liver donor could influence DNN risk due to both patients' and donors' biologic and lifestyle factors. These results, if confirmed in other studies with different cohorts' characteristics, could be useful to further guide post-LT DNN screening-personalization and risk stratification

Disclosure: Nothing to disclose

P0750 ANGIOTENSIN II RECEPTOR BLOCKERS MIGHT BE PROTECTIVE AGAINST NON-ALCOHOLIC FATTY LIVER DISEASE AFTER LIVER TRANSPLANTATION

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Introduction: Renin-angiotensin system (RAS) has been proposed to be involved in pathogenesis of non-alcoholic fatty liver disease (NAFLD). Some evidences suggest that angiotensin II receptor blockers (ARBs) are effective for treatment of NAFLD. This study aimed to investigate association of treatment with angiotensin II receptor blockers (ARBs) after liver transplantation and occurrence of NAFLD in liver transplant recipients.

Aims & Methods: Study population were recruited from Shiraz Liver Transplant Registry (SLTR). All liver transplant recipients between March 2014 and March 2017 who were treated with ARBs for hypertension were included. These patients were matched to a group of liver transplant recipients on age, sex, diabetes and hypertension not treating with ARBs. NAFLD was defined as presence of hepatic steatosis diagnosed by ultrasound and exclusion of secondary causes of hepatic steatosis. Data were analyzed using Student's t-test and by Chi-square test. Independent variables associated with NAFLD were analyzed by logistic regression method.

Results: Totally, 81 patients were included. 26 patients treated with ARBs were compared to 55 patients not treated with these medications. No adverse effects were reported with ARBs treatment.

Univariate				Multivariate analysis		
	NAFLD (+)	NAFLD (−)	P-Value	OR	95 % CI	P-value
Age (years)	51.7 ± 8.27	53.8 ± 11.28	0.330			
PTDM (yes/no)	32/14	17/13	0.251	1.68	0.58-4.90	0.336
Weight (kg)	81.18 ±15.39	75.78 ± 15.42	0.127	1.017	0.98-1.05	0.335
ARBs	20 %	50 %	0.005	3.62	0.096-0.793	0.017
Hyperlipidemia (yes/no)	31/18	18/14	0.528			
NODAT (yes/no)	18/29	9/19	0.591			
Triglyceride (mg/dL)	236.7 ±150.2	178.7± 89.05	0.05	1.003	0.998-1.008	0.188

[Clinical characteristics of patients with and without NAFLD after liver transplantation]

Age, sex, hypertension and diabetes were not statistically different between two groups (P>0.05). NAFLD was diagnosed in 10 patients (38.4 %) among those who were treated with ARBs versus in 39 patients (70.9 %) among those who were not treated with ARBs (OR: 3.9; 95 % CI: 0.96-0.684; P-value= 0.005).

In univariate analysis, higher serum triglyceride level was associated with NAFLD after liver transplantation (P=0.05). In regression analysis patients treating with ARBs were less likely to develop NAFLD after liver transplantation (OR: 3.62; 95 % CI: 0.096-0.793; P-value= 0.017).

Conclusion: NAFLD is less likely to be diagnosed in liver transplant recipients treating with ARBs after liver transplantation. ARBs can be considered for treatment of hypertension after liver transplantation especially in those who are at risk for development of hepatic steatosis.

References: 1. Musso G, Saba F, Cassader M, et al. Angiotensin II Type 1 Receptor rs5186 Gene Variant Predicts Incident NAFLD and Associated Hypertension: Role of Dietary Fat-Induced Pro-Inflammatory Cell Activation. Am J Gastroenterol. 2019 Apr;114(4):607-619.

Disclosure: Nothing to disclose

P0751 THE EFFECT OF BASILIXIMAB INDUCTION WITH REDUCED TACROLIMUS EXPOSURE ON MEASURED GFR AFTER LIVER TRANSPLANTATION: A REAL-LIFE EXPERIENCE

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Introduction: Chronic kidney disease (CKD) is a frequent complication after liver transplantation that leads to increased mortality and decreased quality of life. CKD has a multifactorial etiology, and is in part related to calcineurin inhibitor exposure (e.g. tacrolimus). The immunosuppression protocol at Sahlgrenska University Hospital was revised in 2010 to comprise basiliximab induction with reduced and delayed tacrolimus exposure; the effects of this revised protocol on kidney function has not been studied.

Aims & Methods: We aimed to retrospectively evaluate the effect of reduced and delayed (R&D treatment) tacrolimus exposure on kidney function after liver transplantation in a real-life setting. 624 liver transplantation recipients received immunosuppression with either conventional dose tacrolimus (target trough level M0-2: 10-15 µg/L, 5-10 µg/L thereafter) + corticosteroids (conventional treatment, n=201) or basiliximab induction with reduced-dose (target trough level M0-3: 5-8 µg/L, 3-5 µg/L thereafter) tacrolimus delayed until post-operative day 3 and mycophenolate mofetil (MMF) (R&D treatment, n=342). The primary end-point was measured glomerular filtration rate (mGFR, Chrome-EDTA or iohexol) 12 months after transplantation. Secondary endpoints included 3-month mGFR, graft and patient survival. A subgroup analysis was performed by baseline mGFR (< 60 ml/min/1.73m²). Statistical analyses were performed using the Student's t-test, linear regression and Kaplan-Meier survival analysis.

Results: Baseline characteristics were comparable between the conventional and R&D treatment groups. Through univariate linear regression age, sex, malignancy or alcohol as primary indication, baseline mGFR, intraoperative blood loss, ischemia time, bilirubin at waitlist, creatinine at waitlist, INR at waitlist, hemodialysis on transplantation day and waiting list time were relevant confounders that were adjusted for. Mean mGFR at 12 months after transplantation was significantly higher in the R&D treatment group after adjusting for relevant confounders (adjusted mean 69.7 vs 58.6 ml/min/1.73m²; P< 0.001). Mean mGFR 3 months after transplantation was also significantly higher in the R&D treatment group (adjusted mean 64.2 vs 56.4; P=0.003).

Five-year graft survival was higher in the R&D treatment group (85% vs 75%, P=0.013) and five-year patient survival rates were comparable between the groups (88% vs 84%, P=0.125). A subgroup analysis in patients with baseline mGFR < 60 ml/min showed significantly higher 12-month mGFR in the R&D treatment group(unadjusted mean 53.9 vs 45.5 ml/min; P=0.046) and higher 3-month mGFR (unadjusted mean 48.7 vs 41.5; P=0.034).

Conclusion: In a real-life setting, induction with basiliximab and reduced and delayed tacrolimus exposure and MMF is associated with less perioperative kidney damage and similar survival compared to conventional tacrolimus exposure in liver transplantation recipients.
Disclosure: Nothing to disclose

P0752 THE ROLE OF ALCOHOLIC LIVER DISEASE AS RISK FACTOR FOR THE DEVELOPMENT OF *DE NOVO* METABOLIC SYNDROME AFTER LIVER TRANSPLANTATION: A PROSPECTIVE LONGITUDINAL STUDY

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Introduction: *de novo* metabolic syndrome (MS) is an emerging complication after liver transplantation (LT), resulting in an increased cardiovascular morbidity and mortality. This prospective study aimed to assess the incidence of MS post-LT and its possible associated risk factors.
Aims & Methods: LT patients between April 2013 and October 2016 were prospectively included. Patients with pre-LT MS were excluded. General and metabolic variables were collected at LT and at 6 months, 1 and 2-years post-LT as well as donor variables. Post-LT MS was evaluated according to the modified NCEP-ATP III criteria.
Results: 42 liver transplanted patients were included. The most common indications to LT were HCV (38%) and alcoholic liver disease (ALD) (36%). Six-month, 1- and 2-year incidence of de novo MS was 43%, 57% and 71% respectively. The incidence of post-LT MS at 6 months, 1 and 2 years post-LT was significantly higher in patients transplanted for ALD compared to patients transplanted for other causes (80%, 86.7% and 93.3% vs. 22.2%, 40.7% and 59.3% respectively; p<0.001).
Considering the individual metabolic variables, patients transplanted for ALD presented a significantly higher incidence of obesity (33.3%, 46.7% and 53.3% vs. 0.3%, 14.8% and 18.5%; p=0.012), hypertension (66.7%, 73.3% and 73.3% vs. 18.5%, 25.9% and 33.3%; p=0.006) and hypercholesterolemia (40%, 60% and 66.7% vs. 18.5%, 29.6% and 33.3%; p=0.034) compared to non-ALD liver transplanted patients, whereas no differences were found in the incidence of diabetes or hypertriglyceridemia.
No differences were found in terms of anthropometric and metabolic variables pre-LT between these two groups. At multivariate analysis ALD remained a risk factor significantly associated with *de novo* MS (HR 2.35, 95%CI 1.06-5.19; p=0.035).
Conclusion: *de novo* MS is a frequent complication post-LT showing a progressive increase overtime. A strict metabolic follow-up is mandatory starting early after LT, particularly for patients transplanted for ALD.
Disclosure: Nothing to disclose

P0753 THE APPROPRIATENESS OF MRCP REQUESTS TO INVESTIGATE SUSPECTED COMMON BILE DUCT STONES - SINGLE CENTRE CLINICAL AUDIT

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Introduction: The approach to patients with suspected choledocholithiasis requires careful consideration. Missed common bile duct stones (CBDS)

pose a risk of recurrent symptoms, pancreatitis, and cholangitis. However, the morbidity and cost from indiscriminant and/or invasive biliary evaluation should also be minimized. Utilizing resources for CBDS identification in efficient way is of utmost importance. MRCP is the recommended investigation for patients with intermediate likelihood of common bile duct stones (CBDS) following first line investigations -ultrasound scan (USS) and liver function tests (LFTs). In accordance with American Society of Gastrointestinal Endoscopy (ASGE) and British Society of Gastroenterology (BSG) Guidelines MRCP prior to scheduled endoscopic or surgical duct clearance is not mandated in strong likelihood of CBDS.
Aims & Methods: The clinical audit was set up to evaluate current practice of CBDS stone diagnosis prior to endoscopic biliary duct clearance procedures against recommendations of the ASGE and BSG Guidelines in the UK's general district hospital. Data was collected retrospectively. All MRCPs requests during the period of 01/07/2017 - 01/07/2018 in UK's district general hospital were reviewed. Cases of MRCP requests for suspected CBDS were identified.
Electronic records were reviewed for clinical indications and rational to suspect CBDS. Identified patients were stratified into low, intermediate and high risk of CBDS as per ASGE guidelines. Cases with incomplete data, paediatric patients, MRCP requested after bile ducts draining procedure were excluded.
Results: In 28.9% of performed MRCPs there was no justification for requesting MRCP for suspected CBDS. The most common reasons for unjustifiable MRCP requests were: strong likelihood of CBDS (hence should have gone directly to bile ducts clearance procedure), low likelihood of CBDS and/or suboptimal clinical details for MRCP, failure to perform first line investigations prior to requesting MRCPs.
Conclusion: MRCPs to diagnose CBDS are frequently made without rational, and hence do not result in change in management. Results of the singe centre audit are likely to represent situation on a larger scale. This may be partly because there is no agreed pan-European guidelines for the management of moderate and high risk of CBDS and/or agreed set threshold for determining likelihood of CBDS.
Establishment of pan-European registry or international snap shot audit on diagnostic strategies and further management in moderate and high likelihood of CBDS will enable to identify degree of variability in practises across different sites as well as gives opportunity to derive trends in clinical outcome depending on different approaches in diagnosis and management. Large scale pan-European audit will aid in developing pan-European guidelines on the role of MRCP in management of CBDS.
Disclosure: This abstract is submitted for abstract/oral presentation to the Annual Conference of the Royal College of Radiologists (UK)

P0754 MEASUREMENT OF LIVER STIFFNESS WITH 2D-SHEAR WAVE ELASTOGRAPHY (2D-SWE) IN BARIATRIC SURGERY CANDIDATES REVEALS ACCEPTABLE DIAGNOSTIC YIELD COMPARED TO LIVER BIOPSY

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is common among severely obese patients. Two-dimensional shear wave elastography (2D-SWE) has been validated as a noninvasive diagnostic tool for liver stiffness measurement. However, the technical feasibility and accuracy of this method in severely obese patients are still under debate.
Aims & Methods: We aimed to assess the diagnostic accuracy of 2D-SWE in bariatric surgery candidates in comparison with the gold standard liver biopsy.
Methods: 90 severely obese candidates for bariatric surgery were included. Liver stiffness was measured using 2D-SWE fourteen days before liver biopsy. Liver biopsy was taken on the day of surgery. The area under the receiver operating curve (AUROC) was calculated for the staging of liver fibrosis.
Results: 2D-SWE was performed in 97.3% of patients successfully. Histologic stages of fibrosis (F0-F4), were detected in 34.2%, 36%, 6.3%, 3.6%, and 0.9% of patients, respectively. The AUROC for 2D-SWE was 0.77 for

F1, 0.72 for F2, 0.77 for F3, and 0.70 for F4. In univariate analysis, 2D-SWE values were correlated with BMI, waist circumference, NAFLD activity score (NAS) and steatosis, whereas these components did not affect liver stiffness in multivariate analysis.

Conclusion: Two-dimensional shear wave elastography of the liver can be feasible and has good accuracy in severely obese candidates for bariatric surgery. Therefore, 2D-SWE may be a good option for assessing liver fibrosis, especially in the early stages of fibrosis to lessen complications of surgery in this population. However, this method should be applied on a larger scale for late stage of fibrosis.

Disclosure: Nothing to disclose

P0755 [11C]CHOLINE AS A NOVEL PET/CT BIOMARKER OF LIVER CIRRHOSIS: A PROSPECTIVE PILOT STUDY

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Introduction: Choline is a quaternary ammonium base serving as an essential nutrient in all mammalian cell membranes, including hepatocytes. Its metabolism is cell- and tissue-specific [1,2]. Choline plays a role in hepatic mitochondrial impairment, oxidative stress and DNA methylation levels of genes involved in lipid metabolism [3].

Aims & Methods:

Aim: The aim of this study was to compare findings between patients with liver cirrhosis and subjects with a normal liver on a [11C]choline PET/CT.

Methods: This prospective pilot study was conducted between the years 2012-2016. The cohort included 14 patients with prostate cancer (reference group) and 11 patients with cirrhosis attending a tertiary medical center. Demographic, clinical and laboratory data were obtained from the medical files. All participants underwent a dynamic [11C]choline PET/CT (Discovery ST, GE Medical Systems, Milwaukee WI). We compared the maximal standard uptake values (SUVmax) and the area under the curve (AUC) at 1110 seconds in both groups.

Results: The mean age of the cirrhosis group (63.4% men) was 68.4 ± 10.7 and the control group, 69.7 ± 7.3 years. The mean SUVmax was significantly higher in the cirrhosis group than in the controls (right lobe, 10.06 ± 12 vs. 6.3 ± 1.6, $p=0.011$; left lobe, 8.6 ± 11.6 vs. 5.4 ± 0.9, $P=0.024$; spleen 17.99 ± 27.8 vs. 13.4 ± 2.6, $P=0.027$; kidney, 35.9 ± 59.5 vs. 19.3 ± 4.8, $P=0.025$). The corresponding AUC values at 1110 seconds was significantly distinguished between the groups (right lobe, 13538 ± 20020 vs. 8427.3 ± 1557.9, $p=0.026$; left lobe 12304 ± 18871 vs. 6878.9 ± 1294.3, $p=0.024$; spleen, 12875 ± 17930 vs. 8263.9 ± 1279.2, $p=0.023$; kidney, 24623 ± 36025 vs. 13667 ± 3873.9, $P=0.032$).

No correlations were found between the clinical characteristics and the imaging-derived parameters in the patients with cirrhosis.

Conclusion: Our findings suggest a role for [11C]choline PET/CT as a non-invasive biomarker of cirrhosis. Further larger-scale studies are needed to confirm these observations

References: 1. Li Z, Agellon LB (2005) Phosphatidylcholine homeostasis and liver failure. J Biol Chem 280: 37798-37802. 2. Zeisel SH (2006) Choline: critical role during fetal development and dietary requirements in adults. Annu Rev Nutr 26: 229-250. 3. Zhu J, Wu Y, Tang Q, Leng Y, Cai W (2014) The effects of choline on hepatic lipid metabolism, mitochondrial function and antioxidative status in human hepatic C3A cells exposed to excessive energy substrates. Nutrients 6: 2552-2571.

Disclosure: Nothing to disclose

P0756 EVALUATION OF HEPATIC FIBROSIS ASSESSED BY SEROLOGICAL MARKERS AND SHEAR WAVE ELASTOGRAPHY: PILOT STUDY

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Introduction: Chronic liver diseases are a major health problem. The detection of initial stages of liver fibrosis allows an adequate handling oh these patiens. This could change the natural evolution, delaying descompensation in advanced stages.

Recently, the comparability between non-invasive methods and liver biopsy for assessment of fibrosis has been demostrated.

Aims & Methods: The aim of this study was to correlate the values of fibrosis determined by non-invasive methods, serological markers (APRI and FIB-4) and ultrasound shear wave elastography (SWE) in patients with chronic liver disease.A unicenter retrospective study was carry out. All liver disease patients who underwent SWE (ITACHI US) for any indication in the University Hospital Virgen Macarena between June 2017 and November 2018 were selected.

Serological fibrosis markers were calculated for all etiologies with close analytics (< 3 months) to the performance of the test. To classify the stage of fibrosis we used the accepted cut points of advanced fibrosis: APRI> 1 and FIB-4> 2.67.

Results: Two hundred thirty nine cases were included. Thirty patient presented advanced fibrosis according to serological markers. The area under the curve for advanced fibrosis by SWE was 0,803 (CI 95%). The best cut-off point to determine advanced fibrosis was ≥ 7.55 with a sensitivity of 83.3% and a specificity of 66.8%. A negative predictive value (NPV) of 96.5% was obtained.

Table 1 shows the diagnostic capacity of advanced fibrosis according to SW and serological markers by etiology.

	Advanced fibrosis (APRI/FIB4)			Advanced fibrosis (SWE)		
	Yes	No		Yes	No	
	N (%)	N (%)	p-valor	N (%)	N (%)	p-valor
Viral	11 (36,7)	116 (55,%)	0,028	43 (45,7%)	84 (57,9%)	<0,001
Enolism	7 (23,3%)	21 (10,1%)	0,028	23 (24,5%)	5 (3,4%)	< 0,001
NASH	7 (23,3%)	57 (27,4%)	0,028	18 (19,1%)	47 (32,4%)	< 0,001
Autoim-mune	5 (16,7%)	14 (6,7%)	0,028	10 (10,6%)	9 (6,2%)	< 0,001

[Table 1]

Conclusion: SWE had an adequated diagnostic ability for determinating advanced fibrosis in patients with chronic liver desease compared with serological markers.

A cut-off point SWE lower than 7.55 predicts with high probability the absence of advanced fibrosis.

Prospective studies are needed to support our results and compare them with other types of elastography-based imaging techniques or transient elastography.

Disclosure: Nothing to disclose

P0757 FIBROSIS SCREENING IN PATIENTS WITH NAFLD USING A SIMPLE POINT SHEAR WAVE ELASTOGRAPHY TECHNIQUE

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Introduction: Nonalcoholic Fatty Liver Disease(NAFLD) has recently been recognized as the most prevalent liver disease worldwide, fibrosis stage being the strongest predictor for disease-specific mortality. Non-invasive assessment of liver fibrosis has been increasingly used instead of liver biopsy. ElastPQ is a point Shear Wave Elastography(pSWE) technique that has good accuracy for staging liver fibrosis(1).

Aims & Methods: The aim of this study was to assess the value of ElastPQ as a screening tool for liver fibrosis in NAFLD patients. The study group included 420 consecutive patients with NAFLD evaluated in daily outpatient practice over a period of 18 months. The diagnosis of NAFLD was made by the presence of hepatic steatosis on ultrasound("bright liver" with posterior attenuation and increased hepato-renal index), after excluding significant alcohol consumption. Liver fibrosis was assessed by means of pSWE(ElastPQ; Affinity 70, Phillips). Valid liver stiffness values were defined as the median of 10 liver "non-zero" measurements in a homogenous area of liver parenchyma. Reliable liver stiffness measurements were defined as the median value of 10 measurements with an IQR/M < 30%. To discriminate between ElastPQ fibrosis stages we used the following cut-off values: F≥ 2: 6.9 kPa; F≥ 3: 8.4 kPa and for F=4: 12.4 kPa(2).

Results: NAFLD consisted of 42.4% (420/990) of cases evaluated by liver elastography in daily outpatient practice. We enrolled 414 consecutive patients with NAFLD with reliable liver stiffness measurements, mean age 48.6±12.6 years, 70% male, 30% female. After applying the cut-off values proposed, we found out that 86.4% (358/414) of patients where below the cut-off value of significant < F2 fibrosis, while advanced fibrosis F≥ 3 was found in 6% (25/414) of patients.

Conclusion: NAFLD was the most frequent indication for performing ElastPQ in daily outpatient practice. ElastPQ is a good and reliable point of care tool for fibrosis screening that could rule out significant fibrosis in the majority of patients and help identify patients with advanced fibrosis related to NAFLD and prioritize them for referral and treatment of their liver disease.

References: 1. Lee J et al. Non-invasive Assessment of Liver Fibrosis with ElastPQ: Comparison with Transient Elastography and Serologic Fibrosis Marker Tests, and Correlation with Liver Pathology Results. Ultrasound Med Biol. 2017;43(11):2515-2521. 2. Roccarina Davide et al. SAT-322-Comparison of point shear wave elastography (ElastPQ-pSWE) and FibroScan Transient Elastography (F-TE) for liver fibrosis staging in patients with NAFLD, Journal of Hepatology, Volume 70 , Issue 1 , e780.

Disclosure: Nothing to disclose

P0758 INTRA- AND INTEROPERATOR REPRODUCIBILITY OF A TIME HARMONIC ELASTOGRAPHY AND THE IMPACT OF ULTRASOUND EXPERIENCE IN ACHIVIENG RELIABLE RESULTS

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Introduction: The aim of this paper was to evaluate the inter-and intraobserver reproducibility of the new time-harmonic elastography diagnostic system (THED) (1) and the impact of ultrasound (US) experience in acquiring reliable measurements, since no official recommendations are available for this system.

Aims & Methods: Elastographic measurements (EM) were obtained in 27 consecutive subjects using THED. Three examiners with different levels of experience in US and US-based elastography, performed 10 valid EM on each subject.

We defined their experience as follows: E1- no experience in elastography and less than 50 ultrasound (US) examinations, E2: more than one year elastographic experience and more than 500 US examinations and E3: more than 1000 US examinations, without any experience in elastography. We used the intraclass correlation coefficient (ICC), inter-rater agreement (Kappa coefficient) and concordance correlation coefficient to assess the inter- and intraobserver reproducibility

Results: We did not find significant differences between the means of EM obtained by the examiners overall and across study group [1.66 (E1) vs 1.66 (E2) vs 1.65 (E3), p=0.76]. The overall agreement between examiners was excellent: 0.94 (95% CI: 0.89-0.97). There was at least a good agreement between examiners (E1 vs. E3: k=0.80, 95% CI:0.67-0.94; E1 vs. E2: k=0.81, 95% CI:0.69-0.94), and good to excellent in E2 vs. E3: k=0.89, 95% CI:0.82-0.96. The intraobserver reproducibility for each of the examiners was excellent, however the ICCs were higher in more experienced examiners in US: E1- 0.92, (95% CI:0.82-0.96) vs. E3-0.94 (95% CI:0.87-0.97) vs. E2-0.97 (95% CI:0.95-0.99). The concordance correlation coefficients were similar: E1 vs. E3-0.84, E1 vs. E2-0.89 and E3 vs. E2-0.89.

Conclusion: The good ICCs and Kappa coefficients for the mean values show that THED is a reproducible method. Ultrasound experience did not significantly influence the results.

References: (1) Tzschätzsch H, Nguyen Trong M, Scheuermann T, Ipek-Ugay S, Fischer T, Schultz M, Braun J, Sack I. Two-Dimensional Time-Harmonic Elastography of the Human Liver and Spleen. Ultrasound Med Biol 2016;42(11):2562-2571.

Disclosure: Nothing to disclose

P0759 DIAGNOSTIC ACCURACY OF A POCKET-SIZE ULTRASOUND DEVICE IN IDENTIFYING LIVER SURFACE NODULARITY FOR FIBROSIS STAGING IN CHRONIC LIVER DISEASE

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Introduction: In chronic liver disease fibrosis is the key prognostic factor. Liver biopsy, the reference standard for hepatic fibrosis assessment, is an invasive procedure with a small but significant risk of life-threatening complications. Many non-invasive tests have been evaluated as alternatives. Liver surface nodularity (LSN) is the highest-accuracy ultrasonographic sign to detect advanced liver fibrosis (F3-F4) [1–3].

Pocket-size Ultrasound Devices − with their small size, low cost and ease of use − have been assessed in several clinical settings, but never in CLD.

Aims & Methods: Our cross-sectional study evaluated PUD feasibility, reproducibility and accuracy in identifying LSN.

Between September 2017 and January 2019 we enrolled all consecutive consenting adults referred for liver parenchymal biopsy.,.

LSN was evaluated by 2 independent operators using PUD (Vscan® Dual Probe GE Healthcare, UK), and by an operator using standard GIUS. Transient elastography (TE) and liver biopsy were performed on all patients.

PUD reproducibility was evaluated by κ coefficient. PUD, GIUS and TE results were compared with histology (METAVIR). The estimated pre-test probability of severe fibrosis was 35%. Sensitivity, specificity, positive/negative likelihood ratios, and post-test probability were calculated.

Results: For 72 patients (31 M, age 47±28 years, NAFLD/NASH 35%, AIH 25%, PBC/PSC 14%, HBV/HCV 12%,, other 14%) PUD reproducibility (κ 0.82, 95% CI 0.68–0.96) and concordance between PUD and GIUS (κ 0.78, 95% CI 0.64–0.94) were excellent. In diagnosing F≥3 PUD achieved: 87% sensitivity, 91% specificity, LR+ 9.7, LR- 0.14, PPV 84%, NPV 93% against GIUS (95% sensitivity, 93% specificity, LR+ 13.5, LR- 0.05, PPV 88%, NPV 97%) and TE (67% sensitivity, 96% specificity, LR+ 16, LR- 0.35, PPV 89%, NPV 86%).

Conclusion: PUD proved feasible, with excellent reproducibility. PUD performed very well in diagnosing advanced compensated CLD, and comparably to GIUS and TE. PUD is deployable as first-line screening to select patients for more invasive techniques, thus shortening clinical decision times.
References: References 1) Colli et al. Radiology 2003, 2) Paggi J Hepatol 2008, 3) Lee et al. Korean J Hepatol. 2010
Disclosure: Nothing to disclose

P0760 2D-SHEAR WAVE ELASTOGRAPHY WITH ESAOTE (QELAXTO) COMPARED TO 2D-SHEAR WAVE ELASTOGRAPHY WITH AIXPLORER SUPERSONIC IMAGINE (SSI) FOR THE ASSESSMENT OF LIVER STIFFNESS IN PATIENTS WITH LIVER DISEASES

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Introduction: To date no study has ever explored the potential role of a new 2-dimensional Shear Wave Elastography (2D-SWE) technique that has been recently implemented on Esaote MyLab Nine devices. The aim of our study was to evaluate the agreement between 2D-SWE with Esaote MyLab Nine (QElaXto) and 2D-SWE with Aixplorer Supersonic Imagine (SSI) as the reference standard.
Aims & Methods: Data was collected prospectively from November 2018 to February 2019 on patients who were scheduled to undergo liver elastography as requested by our Hepatology Unit. Exclusion criteria were HCC/malignant liver nodules, severe extra-hepatic comorbidities and liver stiffness (LS) >50kPa. LS was sampled from the same intercostal space with both QElaXto and SSI when possible. Values were tested with correlation coefficient analysis and Bland-Altman analysis (B&A); agreement between the two elastography techniques was assessed with Spearman correlation.
Results: The study included 130 patients (42[32%] HCV and 26[20%] NAFLD; 96% Child-Pugh A). Failure of LS measurements occurred in only one patient for both elastography techniques (BMI >40) and another patient was excluded from the analysis because of LS>50 kPa. Correlation coefficient was very good at 0.951; B&A analysis showed a mean of 1.4 kPa, with limits of agreement at -1.5 and 4.3 kPa. Spearman's rho correlation of SSI versus QElaXto was 0.885. The relationship became less strong in the higher range of LS (≥14 kPa), corresponding to patients with liver cirrhosis.
Conclusion: There is an overall excellent degree of concordance of QElaXto as compared to the "reference standard" SSI, with the first method showing lower LS results as compared to the latter. Further studies are warranted in order to validate this new technique in comparison or in combination with other non-invasive methodologies and liver biopsy.
Disclosure: Nothing to disclose

P0761 EARLY DETECTION OF CARDIOMYOPATHY IN PATIENTS WITH LIVER CIRRHOSIS USING MYOCARDIAL STRAIN IMAGING AND ITS CORRELATION TO LIVER STIFFNESS AND SEVERITY OF LIVER DISEASE - A PILOT STUDY

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Introduction: The prevalence of cardiomyopathy in cirrhotics remains unknown because of its latent nature, characterized by blunted contractile responsiveness to stress, altered diastolic relaxation, and electrophysiological abnormalities.
Aims & Methods: Our aim was to detect early myocardial dysfunction using new echocardiography technologies in cirrhotic patients and correlating them to liver stiffness (LS) and severity of liver disease.
Consecutive patients with liver cirrhosis without structural heart disease, portal vein thrombosis, hepatocellular carcinoma outside Milan criteria, transjugular intrahepatic portosystemic shunt (TIPS) and with optimal acoustic echocardiography window in order to assess the myocardial strain were included. Conventional and speckle-tracking echocardiography (Vendor GE, EchoPAC PC software) were performed by a single investigator (EACVI TTE certified). Subclinical myocardial dysfunction of left ventricle was defined as average global longitudinal strain (GLS) < -18 % (Lang RM, et al. J Am Soc Echocardiogr 2015;28:1-39).
LS was assessed by transient elastography (TE, Fibroscan®, Echosens) and share wave elastography (SWE) from Hitachi (Arietta V70). Reliable results were defined as median value of 10 valid measurements with an IQR/Med < 30 % and expressed in kPa. The presence of ascites, esophageal varices, splenomegaly and/or thrombocytopenia were considered as sign of portal hypertension.
Results: We evaluated 60 patients, but 10 did not fulfilled the inclusion criteria (1 portal vein thrombosis, 2 coronary artery disease, 1 cor pulmonale, 4 patients with valvular dysfunction and 2 with suboptimal acoustic echocardiography window). The final analysis included 50 patients, with mean age of 58.3 ± 10.5 years (66% males).
Compensated cirrhosis (Child-Pugh A) was present in 60% of patients, 24% were classified as Child-Pugh B and 16% as Child-Pugh C.
LS could be evaluated in 76 % of cases by TE and in all patients by Hitachi SWE.
Slightly reduced left ventricular ejection fraction (EF) was observed in 4% of patients. Subclinical systolic dysfunction as assessed by GLS was present in 16 % of cases. The presence of systolic dysfunction seems to correlate with LS assessed by Hitachi SWE (Table).

Parameter	GLS < -18% or reduced EF (n=10)	GLS ≥ -18% and normal EF (n=40)	p value
LS by TE (kPa)	43.1±26.2	33.2±20.5	0.16
LS by SWE (Hitachi)(kPa)	10.8±3.8	14.2±5.7	0.002
MELD	9.9±3.8	11.3±4.5	0.36
Child-Pugh: compensated (A), decompensated (B+C)	A:7(70%), B+C:3(30%)	A:24(60%), B+C:16(40%)	A: 0.82, B+C: 0.82
Portal vein velocity (cm/s)	17.1±3.9	15.3±3.2	0.15
Signs of portal hypertension	6 (60%)	31 (77.5%)	0.46
Etiology: alcoholic (A), other etiologies (B)	A:5 (50%), B:5 (50%)	A:27(67.5%), B:13(32.5%)	A:0.50, B:0.50
Age (years)	61.5±12.2	57.2±10.1	0.29
Gender: male (A), female (B)	A:5(50%), B:5(50%)	A:28(56%), B:12(44%)	A: 0.98, B: 0.98
CO-Cardiac output (ml/min)	5.9±1.3	5.6±1.7	0.55

[Table Correlation between myocardial dysfunktion and liver stiffness and severity of liver disease]

Conclusion: Clinical or subclinical left ventricular dysfunction was identified in 20% of cirrhotic patients and this seems to correlate with LS assessed by Hitachi SWE, but not with the severity of liver cirrhosis.
Disclosure: Nothing to disclose

P0762 THE POTENTIAL OF RIGHT HEPATIC VEIN DIAMETER AS SENSITIVE MARKER FOR LIVER REMODELING IN PATIENTS WITH VIRUS C RELATED CIRRHOSIS WHO HAVE ACHIEVED SUSTAINED VIROLOGIC RESPONSE AFTER THE ADMINISTRATION OF DIRECT-ACTING ANTIVIRALS TREATMENT

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Introduction: Cirrhosis is a major cause of morbidity and mortality worldwide.

The rapid progress of medicine has transformed the representation of the hepatitis C virus infection, in no more than three decades, from an unknown disease to a safe and simple to treat one, with virologic cure in most patients.

Advances in understanding of HCV molecular biology have created the opportunity to develop designed drugs that target specific steps in the infection and replication of HCV. This breakthrough has led to the development of direct-acting antivirals (DAAs) and, from this, to the rapid approval of HCV treatment and the possibility for disease elimination.

For a long period of time, cirrhosis was considered an irreversible end stage of liver disease, mostly due to lack of treatment possibilities. Today, this irreversibility is no longer a "dogma". There are some research studies showing the potential for liver remodeling, at least at microscopic level, with regression of fibrosis after the removal of causative agents in both patient and experimental fibrosis models.

The main question is what happens next with liver, remaining in a frozen status with some degree of microscopical changes or improvements are visible at the macro level, detectable by sectional imaging tools such as CT. Our hypothesis is based on improvements in the features of cirrhosis seen on CT scan that can suggest the reversibility of liver fibrosis/cirrhosis after the achievement of sustained virologic response (SVR) in HCV related cirrhotic patients.

Aims & Methods: The purpose of this study is to evaluate the capability of CT examination to identify changes in hepatic morphology, able to demonstrate the liver remodeling after obtained SVR in patients with HCV related cirrhosis.

CT examinations of 45 patients with HCV related cirrhosis were performed before and after the administration of a direct-acting antivirals (DAAs) treatment. The liver changes were assessed by measuring volume, caudate right hepatic ratio, hepatic vessel diameters, periportal widening space and right posterior notch. There have been measured the portal vein trunk, splenic and superior mesenteric veins and the volume of the spleen as part of portal hypertension assessment.

Results: The significant variations were detected in the right hepatic vein showing a statistically significant widening after the treatment (Mdn=8.12), compared to the diameters recorded before treatment (Mdn=6.35), z=-3.894, p< 0.001, r=-0.20. The liver volume of the patients prior to the treatment was significantly higher (Mdn=1786.77) than the estimated volume subsequent to the treatment (Mdn=1716.44), z=-1.970, p=0.049, r=-0.20. The volume of the spleen before (Mdn=564.79) the treatment was significantly higher than the volume determined after the treatment (Mdn=474.44), z=-2.500, p=0.012, r=-0.269. The other parameters showed no improvement.
Conclusion: The sectional imaging techniques such as CT can be used to demonstrate the improvement of hepatic status after treatment. The most sensitive parameters are the right hepatic vein diameter and the splenic volume reduction, followed by liver volume reduction.
Disclosure: Nothing to disclose

P0763 HEPATIC PORTAL VENOUS GAS: ITS CLINICAL FEATURES AND OPTIMAL MANAGEMENTS

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Introduction: Hepatic portal venous gas (HPVG) is generally recognized to indicate poor prognoses in patients with serious intestinal damage. Although surgical removal of the damaged portion is only considered an effective therapy, some of the patients can recover with non-surgical conservative treatments.
Aims & Methods: To establish diagnostic algorithm for determining an optimal treatment, we reviewed our experienced cases of HPVG and attempted to clarify their clinical features. Thirty-five cases of HPVG [34 patients (19 women and 15 men); ages 34-99 yr (median, 85 yr)] diagnosed at Takatsuki General Hospital from April 2012 to February 2019, were included in the present retrospective study. Their most common complaint was abdominal pain (28 cases). Necessity for surgical treatment had been determined mainly by computed tomography (CT) findings, namely, abdominal free-air, lack of contrast enhancement of the intestinal wall, and intestinal emphysema. The patients' data including clinical backgrounds, physical examination findings, blood test results, CT images, and treatment outcomes were analyzed separately of surgical patients and non-surgical patients. Fisher`s exact test and Mann-Whitney U-test were used for statistical analysis, and p< 0.05 was considered to be significant.
Results: 1) Eight cases were surgically treated. Seven (87.5%) of them survived and one (12.5%) died. Intestinal necrosis was confirmed in all cases during surgery, and the necrotic portions were removed. Final diagnoses were non-occlusive mesenteric ischemia (n=4), clostridium difficile enteritis (n=1), strangulation ileus (n=1), superior mesenteric artery thrombosis (n=1) and gastric perforation (n=1; a fatal case).
2) Twenty-seven cases were treated conservatively (non-surgical patients). Thirteen of them had needed surgical operations to be cured but operations were abandoned because of their poor general conditions, such as extremely low performance status (ECOG PS 4; n=9). However, three (23%) of these 13 patients survived. The remaining 14 of 27 patients were diagnosed as being able to be sufficiently cured by conservative treatments. Of these 14 patients, only one patient (7%) died.
3) To identify potential prognostic factors in the non-surgical patients, comparative analyses were performed between the fatal (n=11) and the surviving (n=16) cases. Ascites (82% vs 31%), signs of peritoneal irritation (80% vs 6%), and shock (55% vs 0%) were significantly frequent in the fatal cases. Compared with the surviving cases, base excess was lower (median -5.5 vs 1.8 mEq/L) in the fatal cases. Percentage of patients fulfilling SIRS criteria (80% vs 37.5%) and plasma levels of CRP (median 10.22 vs 2.09 mg/dL) and lactic acid (median 39 vs 26 mg/dL) tended to be higher in the fatal cases, but the differences were not significant.
Conclusion: HPVG has a high mortality rate, that of our hospital was 34%. If intestinal necrosis is suspected, surgical removal of the necrotic portion should be considered. In non-surgical patients, ascites, signs of peritoneal irritation, shock, and low base excess were closely associated with poor prognoses. Conversely, absence or fewness of these findings may predict recovery from the life-threatening condition with conservative treatments.
Disclosure: Nothing to disclose

P0764 WITHDRAWN

P0765 BUDD-CHIARI SYNDROME: WHICH EPIDEMIOLOGIC PROFILE? A MOROCCAN EXPERIENCE

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Introduction: The Budd-Chiari syndrome (BCS) is an uncommon illness of the liver whose incidence is estimated at 0.9 /million/ year and results from the obstruction of the hepatic venous drainage whatever is the site of the obstacle, from the hepatic venules until the final part of the lower vena cava. The goal of our work was to trace the epidemiologic profile of this syndrome.

Aims & Methods: It is a descriptive retrospective study including all the patients presenting a BCS over a 14-year period (from January 2001 to December 2015). We studied the epidemiologic, clinical, biological, radiological, etiologic and evolutionary data of the patients.

Results: During the 14-year period, we collected 1323 portal hypertension cases (PHT), of which 3.9% (N=52) patient presented a Budd-Chiari syndrome. The median age of the patients was 35 years [15-75 years], with a slight female prevalence (52% of the cases). The ascites was the most revealing symptom in 48% of the cases. Radiological exploration had shown a primitive origin of the SBC on thrombosis of the hepatic veins known in 71%, thrombosis of the retro-hepatic lower vena cava in 10% and the association of both in 15% of the cases. The thrombosis of the portal vein was associated with 15% of the cases. The secondary origin of the BCS was found in two cases (4%): the first case was secondary to a compression by a hepatic mass and the second by a cyst hydatic.

The fiberscope has materialised Esophageal varices in 59.6% of the cases. The etiology of the Budd-Chiari was related to a deficit in antithrombin III in 9.6% of the cases, and a deficit out of protein S and C in 11.5% of the cases, a myélofibrose in 0.5% of the cases and two cases (4%) for each following etiology: a agenesis of the IVC, a secondary compression, a cœliaque disease and a disease of Behcet. The anticoagulants were managed in 90% of the cases. The evolution was marked by the development of a carcinoma hépatocellulaire in 4% of the cases, the hemorrhagic decompensation in 10%, the refractory ascites in 19% and hepatic encephalopathy in 12%. Intrahospital mortality was of 11.5%.

Conclusion: In our series the Budd-Chiari accounted for 3.9% of the PHT, it interested primarily the young subject of the female sex. The hepatic thrombosis of the veins known accounted for 71% of the patient with an assessment of thrombophilia disturbed in 21% of the cases and intrahospital mortality rather important of 11.5% of the cases

Disclosure: Nothing to disclose

P0766 EFFICIENCY GAINS ASSOCIATED WITH A NEW CHRONIC HEPATITIS C TREATMENT PARADIGM IN PORTUGAL

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Introduction: The current paradigm (CP) of chronic hepatitis C (CHC) treatment in Portugal is characterized by a lengthy process between diagnosis and treatment. The number of patients lost to follow-up (LTFU) within that period is a barrier to hepatitis C virus (HCV) elimination by 2030.

Aims & Methods: The objective of this analysis was to quantify the efficiency gains that could be obtained by changing to a new paradigm (NP) that minimizes time between diagnosis and treatment considering the population to be treated in the next 5 years in Portugal. A Microsoft Excel® model was developed to simulate patients' pathway from diagnosis to end of treatment, quantifying time elapsed, LTFU, disease progression and costs (excluding HCV treatment costs) from the societal perspective. Four groups of patients were considered: people who inject drugs (PWID), incarcerated (INC), men who have sex with men (MSM) and general population (GP). Model inputs, specific to each subgroup, were obtained from the literature complemented by an expert panel. All patients were assumed to be treated for 12 weeks. The CP was compared to two scenarios: a simplification of complementary diagnosis tests at the specialist level (NP1) and NP1+a streamlined path to the specialist after a positive rapid HCV test.

Results: A total of 3,500 patients were estimated to be treated per year in the next 5 years. The majority were PWID (58.5%) followed by 23.5% from GP, 11.0% from MSM and 7.0% being incarcerated individuals. The CP comprised of 17 steps, 15 of which require the patient to physically attend a health care facility. LTFU in the CP was highest among PWID (40%) followed by INC (33%). The simplification of the CP would reduce the number of patient visits to 9 (NP1) or 6 (NP2). Out of 1,104 patients who would be LTFU per year under the CP, 7% would be retained in the NP1 1 and 71% in the NP2. Summary results comparing CP to NP1 and NP2 in terms of health outcomes and cost reductions, are detailed in Table.

Endpoint	Current Paradigm [CP]	New Paradigm 1 [NP1]	New Paradigm 2 [NP2]
Total process time from diagnosis to end of treatment	67 weeks	58 weeks	45 weeks
Proportion LTFU	32%	29%	7%
Patient time used (3,500 patients per year, 5 years)	23 years	15 years (-34%)	11 years (-55%)
Cirrhosis cases over 5 years	94	86 (-9%)	32 (-66%)
Total costs over 5 years	20.4 million €	15.8 million € (-23%)	14.6 million € (-29%)

[Results of simplifying the process from diagnosis to treatment]

Conclusion: Simplification of the current CHC treatment paradigm results in efficiency gains in terms of LTFU, reduction of advanced liver disease cases, reduction in medical costs and productivity gains.

Disclosure: This analysis received financial support from Gilead Sciences, Portugal.

P0767 ESTIMATING PROPORTION OF CIRRHOSIS AND HEPATOCELLULAR CARCINOMA ATTRIBUTABLE TO HEPATITIS B AND C IN CLINICAL CENTRES IN SOFIA (BULGARIA) AND LISBON (PORTUGAL) - RESULTS FROM A EUROPEAN PILOT

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Introduction: WHO set target to reduce mortality attributable to hepatitis B (HBV) and hepatitis C (HCV) by 65% by 2030. While national mortality data from cirrhosis (CIR) and hepatocellular carcinoma (HCC) exist, proportion of cases due to HBV and/or HCV are unknown. A study protocol was developed to calculate the attributable fraction of HBV, HCV and other risk factors for CIR and HCC in a standardised way and piloted in Sofia (Bulgaria) and Lisbon (Portugal).

Aims & Methods: All patients presenting with CIR and/or HCC at the national reference centre in Sofia during 2016-2017 and the first 100 sequential patients with CIR and 100 with HCC presenting at national reference centre in Lisbon during 2015-2016 were included. Cases with CIR and HCC were identified based on ICD-10 codes in Sofia and on clinical criteria in Lisbon. Patients diagnosed with both CIR and HCC were classified as HCC. HBsAg and anti-HCV positivity were considered markers for chronic HBV and HCV, respectively. When markers for both HBV and HCV were present, HCV-RNA existence defined the case as being attributable to HCV. When viral markers were absent, excessive alcohol consumption (>30 grs/day) or non-alcoholic-fatty liver disease (NAFLD) were considered main risk factors for CIR or HCC.

Results: Data for 518 CIR, 84 HCC cases were collected in Sofia and 100 CIR and 100 HCC in Lisbon. 70% of CIR and 80% of HCC cases in Sofia and 78% of CIR and 82% of HCC in Lisbon were males. 38% of CIR, 68%

of HCC in Sofia and 53% of CIR and 71% of CIR in Lisbon were ≥60 years. In both sites, distribution of CIR and HCC cases did not differ by gender (p Sofia =0.07, p Lisbon =0.48) but patients with HCC were significantly older (p Sofia =0.00, p Lisbon =0.03). In Sofia the main risk factors for CIR were: alcohol 46%, HBV 18%, HCV 16% and NAFLD 4% and for HCC: HBV 37%, HCV 25%, alcohol 8%, NAFLD 8%. In Lisbon main risk factors for CIR were: alcohol 56%, HCV 25%, HBV 6%, NAFLD 6% and for HCC: alcohol 46%, HCV 37%, HBV 9%, NAFLD 3%. Considerable overlap between risk factors was observed.

Conclusion: Viral hepatitis B and C were important risk factors for liver morbidity in both centres. The pilot demonstrated the feasibility of collecting data on viral hepatitis prevalence that can be used to estimate mortality attributable to HBV and HCV for monitoring elimination. Further consideration should be given to representativeness of samples collected from reference centres, assessment of cases with overlapping risk factors, data collection simplification.

Disclosure: Nothing to disclose

P0768 A RETROSPECTIVE ANALYSIS OF NAFLD REFERRALS TO A PORTUGUESE TERTIARY HOSPITAL

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Introduction: Nonalcoholic Fatty Liver Disease (NAFLD) is a common cause for increased values in liver blood tests and abdominal ultrasound findings, in the primary care (PC) setting. Advanced fibrosis is a significant predictor of long-term complications and mortality. Accordingly, a major focus of clinical care for patients with NAFLD should be the determination of those at highest risk for the complications of advanced liver disease, pointing out the PC critical role for identification, risk stratification and adequate referral.

Aims & Methods: The purpose of this paper is to assess the referral letters for Hepatology appointments of NAFLD patients in a tertiary hospital. In Portugal, referral letters are in the form of an electronic free text paper.

Retrospective assessment of referral letters (RL) for first Hepatology appointments between January 2016 and December 2018.

Results: A total of 975 patients were referred to Hepatology appointments, with 121 NAFLD diagnosed (12.4%), a growing number in the three years of this study.

Within NAFLD patients, 52.9% are men, with an average age of 56. The main reasons for NAFLD patients referrals were: *altered liver blood tests and steatosis on abdominal ultrasound* (31.4%); *altered liver blood test* (23.9%); *steatosis in abdominal ultrasound* (12.4%). Only 5 RL (4%) made reference to the calculation of the NAFLD Fibrosis Score (NFS) and none mentioned the Fibrosis-4 (FIB4). Immunologic and virologic studies were mentioned on 12.4% RL.

Upon first observation in the Hepatology appointment, 63.3% of patients had a NFS predicting absence of significant fibrosis, 26.5% an undetermined NFS and 10.2% with an NFS predicting advanced fibrosis. Liver biopsy was performed in 27 patients, with findings of fibrosis score F3-F4 in 12 of them (10% of the population).

Currently, 61.4% maintain follow-up in Hepatology appointments and 33% were discharged to the PC setting. From the ones discharged, 24.2% had a normalization of the blood tests after risk factor management. The average number of appointments was 2.69 and 4% were discharged on the first appointment.

Conclusion: In a population of NAFLD patients referred to Hepatology appointments in a tertiary hospital, most had a NFS predicting low risk fibrosis. Only a small percentage of RL mentioned this, which may translate an overuse of speciality appointments.

As the growing prevalence of NALFD, an effective hospital response for clinical management of NAFLD implies a communication within the medical community for the development of significant transformations. Using stratification methods such as NFS was shown cost-effective and as such it should be increasingly used in the PC setting. Creating referral protocols is an efficient way of promoting the use of such tools.

Disclosure: Nothing to disclose

P0769 FIBROBLAST GROWTH FACTOR 19 STIMULATION BY THE FARNESOID X RECEPTOR AGONIST EYP001 IN HUMAN ILEAL EXPLANTS

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Introduction: The farnesoid X receptor (FXR) is expressed in the liver and intestine at high levels. Among its actions, it is important in regulating multiple steps in the enterohepatic circulation of bile acids which are important for cholestatic diseases and in bile acid diarrhoea. It has previously been demonstrated that transcription of fibroblast growth factor 19 (FGF19) is one of the most potently stimulated effects regulated by FXR. Ileal FGF19 is important for the regulation of hepatic bile acid synthesis. EYP001 is a selective, synthetic, non-bile acid FXR agonist, which is being developed for several liver and intestinal diseases. EYP001 has been shown to be safe and well-tolerated and to stimulate serum FGF19 levels, together with inhibition of markers of hepatic bile acid synthesis and bile acid levels.

Aims & Methods: The aim of this study was to determine the FXR-dependent effects of EYP001 in human ileum. Normal human ileal mucosal biopsies were obtained at routine ileo-colonoscopy. Incubations were performed for 6h with EYP001 or with negative or positive (chenodeoxycholic acid, CDCA) controls. RNA was extracted and transcript expression measured by QRT-PCR. FGF19 protein was measured in the culture fluid by ELISA.

Results: FGF19 transcripts were potently stimulated by EYP0011 (50 µmol/L) with a median 1400-fold increase (p=0.012, n=8). This was 1.2x more potent than CDCA (50 µmol/L). EYP001 at 10 µmol/L was about 25% as active; 100 µmol/L was not more potent. Expression of other FXR-responsive genes SHP, OSTα and FABP6 was increased about 4-fold by EYP001, much less than the 1000-fold changes found with FGF19. ASBT was not significantly affected. FGF19 protein was also stimulated significantly by EYP001.

Conclusion: These studies have shown that EYP001 is a potent FXR agonist in human ileal mucosal explant culture, stimulating FGF19 transcript levels and protein production. These findings justify further studies of EYP001 in human diseases where a response to FXR agonists is predicted such as in bile acid diarrhoea.

Disclosure: PRR, RD, PS, EM, JV are employed by Enyo. FS and JW have received grant funding from Enyo

P0770 THE INFLUENCES OF EST AND ANTIBIOTIC TREATMENT ON THE BILIARY MICROBIOTA OF CHOLEDOCHOLITHIASIS PATIENTS

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Introduction: The number of samples involved in previous studies of the bile duct microbiota in choledocholithiasis patients is relatively small, thus a comprehensive understanding of the biliary microbiota is still lacking. In addition, the influences of endoscopic sphincterotomy (EST) and preoperative use of antibiotics on the biliary bacterial community still remain unclear.

Aims & Methods: Bile samples (obtained by ERCP from the common bile duct) and clinical data of 121 patients were collected. The samples were divided into 4 groups (NN: with no antibiotic use and no history of EST, n = 31; NE: with no antibiotic use but with a EST history, n = 20; AN: with antibiotic use but no EST history, n = 55; AE: with antibiotic use and EST history, n = 15). Based on 16S rDNA sequencing method, the putative impacts of EST and antibiotics on the biliary microbiota were investigated.

Results: The NN samples had a distinguished bacterial profile from those of the NE group, with 20 genera having differential relative abundances among the two groups, which thus might be related with relapse of the common bile duct stones.

Moreover, the history of EST could affect the beta-diversity rather than alpha-diversity of the biliary microbiota of patients without antibiotic treatment. The predicted KEGG pathways were also altered in NN and NE

samples, of which the majority were related with metabolic pathways. Antibiotic treatment had diverse effects on the composition of the biliary microbiota, which were characterized by different or fluctuant variance patterns of some specific genera. Regardless of the antibiotic type and treatment course, a panel of bacterial taxa, including *Escherichia/Shigella*, *Fusobacterium*, *Neisseria*, *Haemophilus*, *Aeromonas* and *Porphyromonas*, were always observed to have differential relative abundances in the samples receiving antibiotics relative to those without preoperative treatment. Notably, after antibiotic treatment, the alpha-diversity indexes were significantly increased in treated samples than the rest ones, which was different from the results obtained from the gut microbiota. Meanwhile, the potential interactions among biliary bacteria as well as the predicted profiles of KEGG orthologies were also affected by the introduction of antibiotics.

Conclusion: The compositions of the biliary bacterial community could be impacted by both routine EST operation and the use of antibiotics, which suggested the possibility of optimizing the therapy methods. And further in-depth exploration of the pathogenic mechanism of the biliary bacterial flora in choledocholithiasis should benefit the treatment of patients.

Disclosure: Nothing to disclose

P0771 THE INVESTIGATION OF THERAPEUTIC IMPLICATIONS OF MAST CELL STABILIZER CROMOLYN SODIUM ON CHOLESTASIS AND CHOLESTATIC PRURITIS IN BILE DUCT LIGATION MODEL OF EXPERIMENTAL CHOLESTASIS

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Introduction: Cholestasis can present with jaundice and intense pruritus, the pathophysiology of which is unclear. Data from the relevant studies indicated that hepatic mast cells have potential roles in progression of cholestasis and cholestasis induced itch such as elevated total blood histamine concentration in bile duct ligation (BDL) models of cholestasis, activation of mast cells by bile acids, increased skin mast cell accumulation in jaundiced animals and decreased biliary hyperplasia in cholestatic rodents after mast cell stabilizer; cromolyn sodium administration. In this study, we aimed to compare the effects of cromolyn sodium and other various therapeutic agents on serum biochemistry, serum histamine, total bile acids, autotaxin levels, liver histopathology and mast cell distribution in the liver, skin and peritoneum in experimental cholestasis induced by BDL in rats. We also aimed to investigate its efficacy on cholestatic pruritus and to compare the effectiveness with a group of therapeutic agents used in this area.

Aims & Methods: Sixty-nine male rats of Spraque Dawley, weighing between 193-296 grams, were randomly divided into 8 groups. We weighed the rats preoperatively and applied the determined treatment every day consecutively for 10 days after the surgery. The BDL was not performed during the laparotomy and no medical treatment was given to the sham group (n =9). The control group (n=12) underwent BDL and intraperitoneal (ip) saline was given as the treatment. BDL was applied to the other 6 groups. Group 1 (n=9) received ip cromolyn sodium, group 2 (n=8) received ip chlorpheniramine maleate, group 3 (n=8) received oral sertraline, group 4 (n=8) received ip ondansetron, group 5 (n=7) received oral ursodeoxycholic acid and lastly group 6 (n=8) received ip naloxone. On the fifth and tenth days of the experiment, subjects were observed for 5 minutes in terms of itching behavior. After 10 days, the rats were weighed and blood samples were taken under general anesthesia. Lastly, tissue (skin-subcutaneous, peritoneal membrane, liver) samples were taken for histopathological studies with sacrification.

Results: Other than groups 2 to 6, the significant decreases in all parameters including serum histamine and autotaxin levels, plasma total bile acids, total and direct bilirubin concentrations, alkaline phosphatase and gamma-glutamyl transpeptidase measures were observed only in group

1 compared to the control group (p<0.05). When liver specimens were evaluated histopathologically; portal inflammation, lobular inflammation, bile duct proliferation, necrosis and fibrosis were significantly improved in group 1 and 3 (p< 0.05). We identified increased mast cell accumulation in the liver, the skin and the peritoneum in the control group. Only in group 1, liver and peritoneal mast cells were significantly decreased compared to the control group (p=0.003, p=0.004, respectively), whereas the decrease in skin mast cells was not significant (p=0.09). On the fifth and tenth days of the experiment, the mean duration of the rat's itching was significantly lower in all groups compared to the control group (p<0.05). Duration of the itching was observed to increase in the control group from day 5 to 10 and the itching period was detected to decrease in Group 1, 2, 4 and 5.

Conclusion: Our study has shown that cromolyn sodium has promising anti-pruritic efficacy and has provided biochemical and histopathological recovery in the relevant parameters of cholestasis in the animal model.

Disclosure: Nothing to disclose

P0772 UTILITY OF SEHCAT SCAN IN EVALUATION OF CHRONIC DIARRHEA

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Introduction: SeHCAT scan, is an essential diagnostic modality for bile acid malabsorption (BAM). The British Society of Gastroenterology (BSG) recommends use of this test for identifying BAM in diarrhoea-predominant irritable bowel syndrome (IBS-D) and people with Crohn's disease (CD) without ileal resection.[1] However, its use for evaluation of chronic diarrhoea and its cost-effectiveness to the National Health Service (NHS) is subject to further evidence. We aim to demonstrate the utility of this investigation in patients with chronic diarrhoea classifying them into different associated gastrointestinal (GI) conditions.

Aims & Methods: We retrospectively analysed SeHCAT scans done over a period of 1 year. This data was further classified based on their association with diarrhoea predominant irritable bowel syndrome (IBS-D), Crohn's disease (CD), ulcerative colitis (UC), post-cholecystectomy, celiac disease and chronic pancreatitis (CP). The patients with CD were further sub-categorised and analysed.

Results: Total patients included were 122 with 72.1% (n=88) females, average age 49.6 years (range 81 -17). BAM was present in 50% (n=61) of those evaluated. Positive cases were classified as mild (21.3%, n=13), moderate (23%, n=14) and severe (55.7%, n=34). On analysis of prevalence of BAM based on associated GI conditions it was found 70.3% of 37 patients with CD had the condition. Similarly the prevalence of BAM noted in other groups were 42.3% of 26 IBS-D, 55.5% of 27 Post-cholecystectomy, 33.33% of 6 UC, 60% of 5 CP. We had only one patient with celiac disease and was found to have BAM. There were 16 patients who did not have a GI diagnosis but were evaluated for chronic diarrhoea with a SeHCAT scan. Three of these were diagnosed to have BAM. Of the 37 CD patients 18 had CD without ileal disease, 72.2% (n=13) having BAM. Nine had ileal involvement (Montreal L1 or L3) and 66.7% (n=9) with BAM. Seven of the CD patient had previous ileal resection and 71.4%(n=5) were positive for BAM. Similarly 3 CD patients had other colonic surgery and BAM was noted in 66.7% (n=2).

Conclusion: We noted that SeHCAT scan is a useful test for evaluation of chronic diarrhoea in conditions with high pre-test probability. If done earlier in suspected cases it saves the cost of undergoing more investigations for chronic diarrhoea. Our analysis also indicated that in inflammatory bowel disease (IBD), especially CD, regardless of the location phenotype and surgical history, BAM was noted with equal prevalence. Further studies with larger dataset are needed to identify the utility and cost-effectiveness of SeHCAT scan in diagnostic algorithm for chronic diarrhoea.

References: 1. Arasaradnam, R.P, et al., 2018. Guidelines for the investigation of chronic diarrhoea in adults: British Society of Gastroenterology. Gut, pp.gutjnl-2017.

Disclosure: Nothing to disclose

P0773 THE IMPORTANCE OF 24 BILE ACIDS IN LIVER BILE OF BENIGN AND MALIGNANT BILIARY STENOSIS

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Introduction: Differential diagnosis of benign and malignant biliary stenosis might be difficult. Histology of bioptic specimens is often indeterminate. Laboratory markers (serum bilirubin > 75 μmol/L, CA 19-9 > 400 U/mL) and the length of stenosis (> 15 mm) can be helpful but not specific enough (ref. 1). Only one study of altered bile composition has been published so far. Bile salts, phospholipids and cholesterol were significantly lower in 14 patients who developed non-anastomotic biliary strictures after liver transplantation (ref. 2).

Aims & Methods: The aim of our prospective study was to investigate 24 different bile acids in liver bile of patients with benign and malignant biliary stenosis and controls without stenosis.

A total of 73 patients entered the study: 7 subjects with benign biliary stenosis (6 men, 1 woman; 68±13 years old), 21 with malignant biliary stenosis (15 men, 6 women; 72±14 years old) and 45 patients without biliary stenosis (22 men, 23 women; 70±13 years old), out of those 25 subjects with and 20 without choledocholithiasis. Serum total bilirubin and C-reactive protein were investigated before ERCP. Samples of hepatic bile were collected from the common hepatic duct endoscopically (prior to contrast media use) and immediately frozen at -80 ºC until the analysis. Twenty-four different bile acids were investigated by high-performance liquid chromatography / mass spectrometry: lithocholic, ursodeoxycholic, hyodeoxycholic, chenodeoxycholic (CDCA), *deoxycholic, alfa- and beta-muricholic,* hyocholic, obeticholic, glycolithocholic (GLCA), glycoursodeoxycholic (GUDCA), glycohyodeoxycholic, glycochenodeoxycholic (GCDCA), glycodeoxycholic (GDCA), glycocholic (GCA), glyohyocholic, taurolithocholic (TLCA), tauroursodeoxycholic (TUDCA), taurohyodeoxycholic, taurochenodeoxycholic, taurodeoxycholic (TDCA), tauromuricholic (TMCA), trihydroxycholestanoic (THCA), taurocholic (TCA) and cholic (CA) acid.

Results: Serum total bilirubin was significantly higher in patients with malignant biliary stenosis compared with non-stenotic controls (p = 0.005). Significant relationship (r > 0.7) was found between several pairs of bile acids (GLCA-GDCA; GLCA-TLCA; GCDCA-GDCA; GCDCA-GCA; CDCA-CA; GUDCA-TUDCA; GDCA-TDCA; TCDCA-TCA; TMCA-THCA). Significantly lower bile acids concentrations in malignant biliary stenosis compared with controls without stenosis were found for GLCA (median 12.4, IQR 0 - 44.7 vs 32.1, 4.1 - 260.1 μmol/L; p = 0.032), GUDCA (median 123.7, IQR 2.6 - 319.9 vs 259.2, 38.0 - 1247.0 μmol/L; p = 0.032), GCDCA (median 4995.0, IQR 2404.9 - 9474.5 vs 2642.0, 308.7 - 5746.8 μmol/L; p = 0.006), GDCA (median 381.0, IQR 8.9 - 1497.8 vs 1110.5, 135.9 - 4421.3 μmol/L; p = 0.031), GHCA (median 8.0, IQR 2.7 - 14.6 vs 16.4, 10.3 - 33.8 μmol/L; p = 0.005), TUDCA (median 19.2, IQR 0 - 58.8 vs 58.9, 9.5 - 152.8 μmol/L; p = 0.044) and TDCA (median 118.3, IQR 7.1 - 321.6 vs 377.5, 79.8 - 930.7 μmol/L; p = 0.036). Significant difference between benign and malignant stenosis was found for CA (median 97.8, IQR 5.8 - 465.9 vs 0, 0 - 20.4 μmol/L; p = 0.022). Other results did not reach statistical significance.

Conclusion: Analysis of bile acids might be helpful in the differential diagnosis of malignant and benign biliary stenosis. However, more patients must be enrolled in the study in order to be able to evaluate the real diagnostic yield of bile acids monitoring.

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References: 1. Can J Gastroenterol 2000; 14(5): 397-402. 2. J Hepatol 2009; 50(1): 69-79.

Disclosure: Nothing to disclose

P0774 REAL-TIME DEEP IMAGING OF BILIARY EXCRETION TO THE INTESTINAL TRACT BY USING NEAR-INFRARED PHOSPHORS

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Introduction: Biliary excretion from the liver to the intestinal tract, an excretion route in addition to the renal clearance via glomerular filtration, is an important biomedical phenomenon related to health and diseases such as jaundice, gallstone formation, and excretion of therapeutic drugs. We hypothesized that an emerging fluorescence imaging system in the wavelength range of over-thousand-nanometre (OTN) near-infrared (NIR), which allows deep bioimaging with high spatial resolution due to its less scattering by biological tissues [1-4], may be available to monitor the dynamic change of the biliary excretion.

Aims & Methods: The aim of the present study was to investigate the possibility of real-time monitoring of the biliary excretion using the *in vivo* deep OTN-NIR fluorescence imaging system in a non-clinical experimental (mouse) model. An OTN-NIR fluorescence dye IR-1061 (Sigma-Aldrich) was loaded into micelle nanoparticles (MNPs) composed of an amphiphilic polymer N-(carbonyl-methoxypolyethyleneglycol 2000)-1,2-distearoyl-sn-glycero-3-phosphoethanol-amine ($DSPE-PEG_{2k}$) by a simple 'one-pot' procedure as described previously [5] with minor modifications.

The particle size of the prepared OTN-NIR fluorescence MNPs (OTN-MNPs) was 9 nm. The OTN-MNPs emit OTN-NIR fluorescence peaked at 1100 nm under 980-nm excitation.

After intravenous injection of the OTN-MNPs into 6-week-old mice under anesthesia, OTN-NIR fluorescence images of mice were observed by a portable NIR fluorescence *in vivo* imaging system SAI-1000 (Shimadzu). All animal care and experiments were carried out according to the guidelines on care and use of laboratory animals as stated by Tokyo University of Science.

Results: Following intravenous injection of the OTN-MNPs into mice, whole-body blood vessels were visualized using the proposed system. The OTN-MNPs were trapped by the reticuloendothelial system and mostly distributed to the liver within 60 min post-injection. The mice were fed a high-fat diet to enhance bile secretion, and after 90-180 min, OTN-NIR fluorophores are excreted from the liver with bile to the duodenum. We successfully imaged time-dependent dynamic change of distribution of the fluorophores encapsulated by the MNPs in the hepatobiliary route of live mice.

Conclusion: The OTN-MNP is useful for *in vivo* real-time imaging of hepatobiliary excretion with the OTN-NIR fluorescence imaging technique. This technique is useful for screening hepatobiliary excretion of administered substances and for monitoring of the bile excretion from the liver through the intestinal tract.

References: [1] Smith A.M. et al., Nat. Nanotechnol., 4 (2009) 710-711. [2] Soga K. et al., J. Photopolym, Sci. Technol., 25 (2012) 57-62. [3] Hemmer E. et al., Nanoscale, 5 (2013) 11339-11361. [4] Jaque D. et al., Adv. Opt. Photon., 8 (2016) 1-103. [5] Kamimura M. et al., Polym. J., 49 (2017) 799-803.

Disclosure: Nothing to disclose

P0775 THE BILE ACID AGONIST TGR5 INDUCES INTESTINAL GROWTH IN A GLP-2 DEPENDENT MANNER AND AMELIORATES INTESTINAL INJURY IN MICE

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Introduction: Enteroendocrine L cells express the bile acid receptor Takeda-G-protein-receptor-5 (TGR5). Activation of TGR5 triggers the release of glucagon-like peptide 1 (GLP-1) and glucagon-like peptide 2 (GLP-2). Treatment with GLP-2 analogues, and to a lesser extent GLP-1, results in intestinotrophic effects and ameliorates intestinal injury in rodents.

Aims & Methods: In this study, we aim to investigate the contributions of the TGR5 receptor to glucagon-like peptide secretion and the impact on the intestinal architecture and healing response.

Female mice (n=8) were treated with the orally bioavailable TGR5 agonist RO5527239 (30 mg/kg) or vehicle twice daily for ten days and the intestinal parameters explored; including intestinal weight, morphometry and gut hormone analysis. In a subsequent study, GLP-2r KO mice (n=12) and their wild type littermates were either treated with RO5527239 (30 mg/kg) or vehicle twice daily for ten days and small intestinal weight was recorded. Finally, female mice (n= 8) received a single injection of the chemotherapy 5-fluorouracil (5-FU) (400 mg/kg) or saline and were treated with RO5527239 (30 mg/kg) or vehicle twice daily until sacrifice 72 h after 5-FU. Body weight and intestinal parameters were explored.

Results: Agonist treatment resulted in a significant increase in relative small intestinal weight (p< 0.0001). Morphological changes were primarily located proximally leading to an increase in mucosa cross-sectional area and villus height in the duodenum (p< 0.01). The large intestine was structurally unaffected but the concentration of intact GLP-1 and GLP-2 was increased in colonic tissue (p< 0.01).

Agonist treatment resulted in an increase in relative small intestinal weight (p< 0.01) in the wild type mice, which was not present in the GLP-2r KO mice. Agonist treatment of 5-FU treated mice resulted in an increase in villus height (p< 0.05), crypt depth and a decrease in histological severity score.

Conclusion: This study shows that activation of the TGR5 resulted in small intestinal growth and the increased secretion of GLP-1 and GLP-2 from the colon. Additionally, TGR5 activation produced a growth response in the small intestine in a GLP-2 dependent manner and ameliorated 5-FU mucositis in mice. Taken together, this work suggests TGR5 as a potential target for alleviating intestinal injury through the stimulation of GLP-2 secretion.

Disclosure: Nothing to disclose

P0776 COMPARISON OF THE CLINICAL OUTCOMES OF SUPRAPAPILLARY AND TRANSPAPILLARY STENT INSERTION IN UNRESECTABLE CHOLANGIOCARCINOMA WITH BILIARY OBSTRUCTION

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Introduction: To prevent stent migration, transpapillary stent placement has been recommended for the endoscopic treatment of malignant hilar biliary stricture. However, placement above the papilla is currently favored because it is believed to prevent reflux of duodenal contents and prolong stent patency.

Aims & Methods: The aim of the current study was to compare the efficacies and safety aspects of transpapillary and suprapapillary stent placement. In addition, success rates of stent revision were evaluated with respect to stent location.

The medical records of 73 hilar cholangiocarcinoma patients that underwent endoscopic metal stent insertion between January 2005 and December 2015, were retrospectively reviewed. Patients were allocated by stent location to a suprapapillary group (S group; N=44) or a transpapillary group (T group; N=29). Clinical outcomes, durations of stent patencies, adverse events related to stent placement, and revision success rates in the two study groups were compared.

Results: Suprapapillary stent placement was performed in 44 patients and transpapillary placement was performed in 29. Patency periods were similar in the two groups (group S, 140 days; group T, 157 days; P =0.476). Rates of stent obstruction in the S and T groups were 38.4% and 21.9%, respectively (P=0.470). An adverse event related to stent insertion occurred in 15 (20.5%) of the 73 study subjects with no significant intergroup difference. The success rate of endoscopic revision was significantly higher in the T group (P = 0.01), and the time required for revision tended to be shorter in the T group.

Conclusion: The effectivenesses and safeties of suprapapillary and transpapillary stent insertion were found to be similar, but the success rate of endoscopic revision was significantly higher for transpapillary stent inser-

tion. Therefore, we recommend transpapillary stent placement be considered for patients with hilar cholangiocarcinoma and biliary obstruction.

Disclosure: Nothing to disclose

P0777 A POSITIVE LYMPH NODE RATIO-BASED NOMOGRAM STAGING SYSTEM TO PREDICT CANCER-SPECIFIC SURVIVAL FOR PATIENTS WITH RESECTED GALLBLADDER CANCER

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Introduction: Gallbladder cancer (GBC) is one of the most aggressive malignant tumors with a poor long-term prognosis worldwide, and there is no effective and convenient method for predicting cancer-specific survival (CSS). Positive lymph node ratio (pLNR), but not the location or number of invaded nodes, independently predicts the surgical outcomes of patients who have undergone curative resection. We aim to analyze the significance of pLNR in GBC patients and develop a novel staging system based on a formulated nomogram for CSS.

Aims & Methods: A total of 1,356 patients with resected GBC were divided into a training set (n=904) in an earlier period and a validation set (n=452) thereafter. We used a univariate Cox regression analysis to screen for risk clinicopathological factors for CSS in the SEER discovery set. We further performed stepwise multivariate Cox regression analysis to screen for important independent factors for CSS. A competing risk model based on risk factors was evaluated by Cox multivariate analysis to ensure that they were related to CSS. A novel nomogram based on the pLNR for predicting CSS at 1 and 3 years was formulated with the other identified independent important factors. The SEER internal testing set was used to evaluate the predictive reliability and accuracy of the nomogram. The concordance index and calibration plots were used to evaluate model discrimination. The predictive accuracy and clinical value of the nomograms were measured by decision curve analysis (DCA). The CSS nomogram was further validated in an internal validation set.

Results: The 1-, 2- and 3-year CSS rates were 54.94%, 29.65%, and 15.12%, respectively, in the entire SEER cohort. The optimal cutoff value for pLNR determined by the maximum Youden index of the ROC curve was 0.08. According to the survival analysis, patients in the pLNR≤8% group had a poorer CSS than those in the pLNR>8% group in the discovery set. pLNR was associated with histologic type, histologic grade, tumor size, tumor extension, N classification, M classification, TNM staging system, and distant organ metastasis (including bone, brain, liver and lung) by statistical significance. The pLNR was an independent prognostic factor for CSS based on Cox regression analyses. A prognostic nomogram that combined T classification, pLNR, M classification, histologic grade, live metastasis and tumor size was formulated with a c-index of 0.763 (95% CI, 0.728-0.798), while the c-indexes for the staging system of AJCC 8th, the AJCC 7th, and the AJCC 6th for CSS prediction were 0.718, 0.718, and 0.717, respectively. The calibration curves showed perfect agreement. The DCA showed that the nomogram provided substantial clinical value. The nomogram (the AUCs of time-dependent ROC curve analysis for one, three, and five years were 0.693, 0.716, and 0.726, respectively) showed high prognostic accuracy.

Conclusion: Based on the clinical risk factors identified in a large population-based cohort, especially the pLNR, a robust prognostic predictor of CSS for resected GBC patients, we established the first practical formulated nomogram staging system that includes the T classification, pLNR, N classification, tumor size, histologic grade and liver metastasis. Moreover, the internal cohort validation results demonstrated that these nomograms performed very well and showed excellent discrimination compared with the AJCC 7th and 8th edition staging systems. Our nomograms were demonstrated to be clinically useful in a DCA, and they should therefore help clinicians generate better risk stratifications and formulate individual treatments.

Disclosure: Nothing to disclose

P0778 SUFFICIENT TISSUE ACQUISITION RATE OF PERORAL CHOLANGIOSCOPY-GUIDED FORCEPS BIOPSY

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Introduction: Peroral cholangioscopy (POCS)-guided forceps biopsy (FB) is a commonly used method for diagnosing indeterminate biliary lesions and for the preoperative identification of the exact perihilar and distal margins of biliary tract cancer (BTC). However, POCS-FB may result in the acquisition of an insufficient amount of specimen at times. Therefore, we evaluated the sufficient tissue acquisition rate (TAR) and the factor affecting the sufficient TAR of POCS-FB for the biliary tract.

Aims & Methods: Patients who underwent POCS-FB for biliary disease between September 2016 and October 2018 at our hospital were enrolled retrospectively. We evaluated the sufficient TAR of POCS-FB for biliary lesion and that for non-stenotic bile duct. Sufficient tissue was defined as a specimen that allowed the evaluation of the histological finding of the biliary epithelium. A specimen that contained only interstitial tissue was deemed insufficient. Moreover, the factors affecting sufficient TAR of POCS-FB were evaluated. Subgroup analyses of age, sex, malignant biliary disease, the location of the biliary lesion, length of biliary stricture, macroscopic types of BTC, presence of acute cholangitis, level of serum total bilirubin, level of CEA, level of CA19-9, procedure time, EST, biopsy site, and previous biliary stenting before POCS were assessed to determine the sufficient TAR of POCS-FB. We carried out univariate analyses to assess the sufficient TAR, and factors with $P < 0.1$ were included in the multivariate logistic regression analyses. The pathological diagnostic ability for BTC and the adverse event of the POCS-FB were also evaluated.

Results: We enrolled 47 patients with biliary disease and performed POCS-FB for biliary lesion and POCS-FB for non-stenotic bile duct in 40 and 36 patients, respectively. The malignant group included 12 patients with perihilar cholangiocarcinoma (CCA), 14 patients with distal CCA, one with intrahepatic CCA and one with cystic ductal carcinoma. The benign group included 9 patients with benign biliary strictures, 3 patients with immunoglobulin G subclass 4-associated sclerosing cholangitis, 3 patients with primary sclerosing cholangitis, 2 patients with drug-induced cholangitis, one with intraductal papillary neoplasm of the bile duct, and one with a peribiliary cyst. The sufficient TAR of POCS-FB for biliary lesions and that for non-stenotic bile duct were 86.4%, and 68.9%, respectively.

In the multivariate logistic regression analyses, age < 65 years old (odds ratio 0.170, 95% Confidence interval [CI] 0.044-0.649, $P = 0.004$) and previous biliary stenting before POCS (odds ratio 0.199, 95% CI 0.053-0.756, $P = 0.017$) were the significant factors affecting the sufficient TAR of POCS-FB for biliary lesion. For non-stenotic bile duct, the biliary lesion in the distal bile duct (odds ratio 0.322, 95% CI 0.139-0.744, $P = 0.008$), procedure time in 75 minutes or less (odds ratio 3.012, 95% CI 1.092-8.312, $P = 0.033$), and EST (odds ratio 7.041, 95% CI 2.117-23.421, $P = 0.002$) were the significant factors affecting the sufficient TAR of POCS-FB. Sensitivity, specificity, and accuracy of POCS-FB for BTC were 76.2%, 94.7%, and 85.0%, respectively. The adverse event rate of POCS-FB was 17.0%, including acute pancreatitis (8.5%), infection (cholangitis, 6.4%), and hemorrhage (2.1%).

Conclusion: The previous biliary stenting was a factor affecting low TAR of POCS-FB for biliary lesion. In the POCS-FB for non-stenotic bile duct, the presence of the lesion in the distal bile duct, the POCS-FB without EST, and the long procedure time of POCS were factors affecting low TAR.

Disclosure: Nothing to disclose

P0779 EFFECTS OF SARCOPENIA AND BACKGROUND FACTORS ON ELDERLY BILIARY CANCER PATIENTS RECEIVING CHEMOTHERAPY

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Introduction: Recently, as the number of elderly biliary tract cancer patients has increased, the opportunities for administering chemotherapy to these patients has also increased. On the other hand, sarcopenia is an important prognostic factors in various types of carcinoma, and it is possible that it may influence the treatment effectiveness. However, clinical trials of chemotherapy for biliary tract cancer often target patients up to the age of 75 years, but too few studies have been done on chemotherapy for the elderly with sarcopenia.

Aims & Methods: The aim of this study was to investigate the effects of sarcopenia and other background factors on treatment and prognosis in elderly biliary cancer patients who received chemotherapy. A retrospective analysis was performed on 46 patients aged 65 years or older who underwent chemotherapy for unresectable biliary tract cancer at two related institutions between November 2012 and April 2018. Sarcopenia was assessed by measurement of the psoas muscle index (PMI). PMI at the third lumbar spine level was calculated from prechemotherapeutic computed tomography images. Treatment-related factors included age, sex, medical history (hypertension, diabetes, dyslipidemia, cholelithiasis), Eastern Cooperative Oncology Group performance status (ECOG PS), tumor site, metastatic site, postoperative recurrence, chemotherapy regimen, body mass index, body fat composition, laboratory data (white blood cell, albumin, hepatobiliary enzymes, lactate dehydrogenase, C-reactive protein (CRP), serum tumor markers (CA19-9, CEA)). We also used the modified Glasgow Prognostic Score (mGPS), Platelet-Lymphocyte Ratio (PLR), and the CRP/Albumin Ratio (CAR) as an indicator of nutritional status. The associations between these clinical factors and overall survival (OS) and time to treatment failure (TTF) were determined using univariate and multivariate analysis.Furthermore, stratification was performed based on the presence or absence of sarcopenia, and the influence of sarcopenia on OS and TTF was similarly examined.

Results: The mean age of the patients was 75.9±5.5 years at the start of chemotherapy.

The univariate analysis showed that the significant factors affecting OS included sarcopenia, PS, lung metastasis, liver metastasis, CA 19-9, PLR, and CAR (p< 0.05).

Next, a multivariate analysis using Cox proportional hazards regression showed that independent significant results were obtained for sarcopenia (HR 5.55 : 95%CI 1.96~15.94 : P=0.0013) and CAR (HR 3.04 : 95%CI 1.23~7.50 : P=0.016). Similarly, in TTF, the significant factors included sarcopenia, PS, CA 19-9, PLR, and CAR in univariate analysis, and independent significant results were obtained for sarcopenia (HR 2.85 : 95%CI 1.20~6.80 : P=0.018) in multivariate analysis. Finally, as a result of stratification according to the presence or absence of sarcopenia, significant differences from univariate analysis were seen in PS, lung metastasis, CRP, CA19-9, mGPS and CAR in OS, and PS, CRP, CA 19-9, mGPS and CAR in TTF.

Conclusion: In chemotherapy of elderly biliary tract cancer patients, the presence or absence of sarcopenia and the nutritional status are related to the treatment effect, and should be considered as potential markers to predict the outcome of chemotherapy. We suggest that maintenance of muscle mass and improvement of nutritional status may affect the effect of chemotherapy.

References: [1] Arai H, Akishita M, Kuzuya M, et al. Clinical Guidelines for Sarcopenia. Geriatrics & Gerontology Int 2018;18:1-44. [2] Kurita Y, Kobayashi N, Tokuhisa M, et al. Sarcopenia is a reliable prognostic factor in patients with advanced pancreatic cancer receiving FOLFIRINOX chemotherapy. Pancreatology 2019;19:127-135.

Disclosure: Nothing to disclose

P0780 DEVELOPMENT OF A BILIARY MULTI-HOLE SELF-EXPANDABLE METALLIC STENT FOR BILE TRACT DISEASES

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Introduction: Uncovered stents used for malignant obstructions in the biliary tree, especially in the hilar area, are prone to obstruction by tumor ingrowths. In comparison, however, covered stents may block bile duct branches and are at risk of migration. We have developed a Multi-Hole Self-Expandable Metallic Stent (MHSEMS), with a hole in each cell, to prevent the obstruction of bile duct branches. In addition, the holes may prevent migration due to small ingrowths by reducing the tension of the membrane.

Aims & Methods: A MHSEMS has a hole in each stent cell on its covering membrane. When the stent is positioned in a junction connected by side branches, bile flows inside the stent through the holes in its covering membrane. Tumors may grow through these holes but may become suppressed due to the size of the ingrowth. As a result of low membrane tension caused by the holes, the placed stent becomes fixed to surrounding tissues and is prevented from migrating. Presently, the MHSEMS is available with two types of hole sizes: small and large.

In addition, a lasso attached to the distal end of the MHSEMS is helpful for stent removal. Even if an obstruction by a tumor ingrowth does occur, the silicone cover will protect the surrounding tissue and enhance any ablation effect, such as during endobiliary radiofrequency ablation (RFA), allowing the patient to be a candidate for such treatment. Using MHSEMS, we treated six patients with malignant biliary obstruction and one case with uncontrolled post-endoscopic sphincterotomy bleeding.

Results: We had a 100% success rate for stent deployment. Stent patency was also 100% successful. In addition, jaundice improved in all patients with a malignant stricture, while complications such as pancreatitis, bleeding and cholangitis did not occur. The mean patency duration was found to be 274 days. None of the six cases showed any stent migration. For post-endoscopic sphincterotomy bleeding, complete hemostasis was achieved and the stent was successfully removed after 2 weeks.

Conclusion: MHSEMS may be considered a hybrid-type stent, with characteristics that fall between those of UCSEMS and CSEMS. Thus, MHSEMS may be regarded as a promising new treatment option for benign and malignant bile duct strictures.

Disclosure: Makoto Kobayashi has a patent on the Multi-Hole Self-Expandable Metallic Stent (MHSEMS) with royalties paid by M.I.Tech Co., Ltd.

P0781 PERORAL SINGLE OPERATOR CHOLANGIOSCOPY FOR INDETERMINATE BILIARY STRICTURES IN CLINICAL PRACTICE OF A TERTIARY REFERRAL CENTER: INSUFFICIENT DIAGNOSTIC ACCURACY AND A LIMITED CLINICAL IMPACT

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Introduction: Peroral single operator cholangioscopy (pSOC) is considered to be a valuable diagnostic modality for indeterminate biliary strictures 1. Nevertheless, the chosen measures of diagnostic accuracy for pSOC vary and the impact on patient management is scarcely reported. The aim of this study was to estimate diagnostic accuracy of pSOC visual assessment and targeted biopsies for indeterminate biliary strictures. Additional aims were to compare diagnostic accuracy pSOC with sequentially taken brush cytology and to assess the clinical impact of pSOC outcome on patient management.

Aims & Methods: A retrospective single center open label cohort study was performed for patients of 18 years and older who underwent pSOC for indeterminate biliary strictures between November 2007 and May 2017 with the Spyglass® or Spyglass DS® system. Indeterminate biliary strictures were defined as strictures of the intra- or extrahepatic bile duct without a mass detectable on abdominal imaging, in which conventional workup

was non-diagnostic and a clear explanation from the clinical context was lacking (e.g. no recent trauma or biliary surgery)[2,3]. Endoscopy and pathology reports were reviewed for results of brush cytology and pSOC visual impression and targeted biopsies. Diagnostic accuracy of pSOC was defined as sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) and compared to same parameters of brush cytology. Clinical impact was assessed by review of medical records and was classified in three categories; change, confirmation or no influence in patient management.

Results: A total of 76 patients were included, with primary sclerosing cholangitis being present in 40%. In 87% of patients prior ERCP was performed, combined with brush cytology in 59%. In 55% of patients a biliary stent was in situ and removed prior to pSOC procedure. A malignant stricture was diagnosed in 22 patients (30%), including 17 cholangiocarcinoma. The sensitivity, specificity, PPV and NPV for pSOC visual impression was 64%, 61%, 42% and 83%. For pSOC targeted biopsies, the sensitivity, specificity, PPV and NPV was 15%, 63%, 75% and 67%. In contrast, sequential brush cytology yielded a sensitivity, specificity, PPV and NPV of 47%, 92%, 73% and 81%. The clinical impact of pSOC outcome on patient management was limited, as it had no influence on management in 33% of patients and only resulted in change of management in 13% of patients.

Conclusion: In a population with a high prevalence of primary sclerosing cholangitis and prior biliary stents in situ, the diagnostic accuracy of pSOC for indeterminate biliary strictures was found to be inferior to brush cytology and had low impact on patient management.

References: 1. Chen YK, Parsi MA, Binmoeller KF, et al. Single-operator cholangioscopy in patients requiring evaluation of bile duct disease or therapy of biliary stones (with videos). Gastrointest Endosc. 2011;74(4):805-814. doi:10.1016/j.gie.2011.04.016 2. Levy MJ, Baron TH, Clayton AC, et al. Prospective evaluation of advanced molecular markers and imaging techniques in patients with indeterminate bile duct strictures. Am J Gastroenterol. 2008;103(5):1263-1273. doi:10.1111/j.1572-0241.2007.01776.x 3. Bowlus CL, Olson KA, Gershwin ME. Evaluation of indeterminate biliary strictures. doi:10.1038/nrgastro.2015.182

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P0782 ROLE OF PERORAL CHOLANGIOSCOPY FOR DIAGNOSIS AND STAGING OF BILIARY TUMORS

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Introduction: In the approach to biliary strictures it is important to establish a histopathological diagnosis. On the other hand, in the preoperative evaluation of malignant biliary lesions, intraductal extension may condition therapeutic approach. Peroral cholangioscopy (POC) has shown to be a useful diagnostic procedure in the evaluation of biliary strictures, however its role on preoperative staging has not been established.

Aims & Methods: The aim of our study was to evaluate POC role in the diagnosis and preoperative intraductal staging of extrahepatic biliary cancer. Retrospective cohort study that included all patients who underwent POC with *SpyGlass™ Direct Visualization System* (Boston Scientific) for diagnosis of biliary strictures or preoperative evaluation of extrahepatic biliary tumors, between January 2015 and January 2019, in a single tertiary center. The primary endpoint was to assess the accuracy, sensitivity and specificity of *SpyGlass* visual findings and *SpyGlass*-guided biopsy findings in the diagnosis of patients with biliary strictures. A final diagnosis of malignancy was made based on positive histopathology of *SpyGlass*-guided biopsy/other tissue sampling procedures or evidence of disease progression consistent with malignancy during at least a 6 months follow-up. The secondary endpoint was to evaluate the ability of POC to detect mucosal cancerous extension preoperatively in possibly resectable peri-hilar cholangiocarcinoma (CCA) and the changes on surgical approach based on findings. In all malignant cases, we compared previous imagiologic anatomic classification with that accessed with POC. Anatomic classification was based on Bismuth-Corlette Classification (BCC).

Results: Forty-three patients were included, 63% male with a median age of 62 years (IQR 53-72). Thirty-eight (88.3%) underwent POC due to indeterminate biliary strictures, 3 (7%) due to bile duct filling defect and 2 (4.7%) for intraductal staging of perihilar CCA. In the follow-up, a final

diagnosis of malignancy was established in 56%. Visual impression accuracy with *SpyGlass* was 95% (100% sensitivity and 90% specificity). *SpyBite* biopsies accuracy was 81% (67% sensitivity and 100% specificity).

In the 19 patients with a final perihilar CCA diagnosis, intraductal evaluation with *SpyGlass* altered anatomic classification (BBC) defined by previous imagiologic findings in 8 (42.1%) patients (BCC 3a to 4, n=3; BCC 2 to 4, n=3; BCC 2 to 3a, n=2). In 2 cases, a resectable BCC type 2 was a type 3a based on *SpyGlass* examination, which modified the surgical approach from a bile duct resection (BDR) to a BDR with right hepatic lobectomy. In 3 cases, a previous BCC type 2 lesion was reclassified as BCC type 4 on *SpyGlass* approach and in two of these cases the lesions were considered irresectable.

The remaining 3 patients were previous classified as a BCC type 3a based on imagiologic findings and were actually a BCC type 4 on *SpyGlass* examination. One patient previously considered candidate for surgical resection was deemed irresectable.

Although, TNM data was missing in another, was considered irresectable and was referred for palliative biliary stent. The remaining case was irresectable, so there was no change on therapeutic approach after POC.

Conclusion: POC was useful in the diagnostic evaluation of biliary stenosis. Its use in potentially resectable cases of CCA was important to stablish best therapeutic approach. In the future, preoperative staging of perihilar CCA with POC combined with imagiologic evaluation of vascular extension of the lesions may optimize surgery results.

Disclosure: Nothing to disclose

P0783 DIGITAL CHOLANGIOSCOPIC INTERPRETATION: WHEN NORTH MEETS THE SOUTH

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Introduction: Digital single-operator cholangioscopy (DSOC) (SpyGlass DS™, Boston Scientific, MA, USA) allows for high-definition imaging of the biliary tree. The superior visualization has led to the development of two different sets of criteria to evaluate and classify indeterminate biliary strictures: the Monaco criteria and the criteria in Carlos Robles-Medranda's publication (CRM). Our objective was to assess the interrater agreement (IA) of DSOC interpretation for indeterminate biliary strictures using the two newly published criteria.

Aims & Methods: 40 de-identified DSOC video clips were sent to 15 interventional endoscopists with experience in cholangioscopy. They were asked to score the videos based on the presence of Monaco Classification criteria: stricture, lesion, mucosal changes, papillary projections, ulceration, white linear bands or rings, and vessels. Next they scored the videos using CRM criteria: villous pattern, polypoid pattern, inflammatory pattern, flat pattern, ulcerate pattern and honeycomb pattern. The endoscopists then diagnosed the clips as neoplastic or non-neoplastic based on the criteria. Intraclass correlation (ICC) analysis was done to evaluate interrater agreement for both criteria sets and final diagnosis.

Results: Clips of 26 malignant lesions and 14 benign lesions were scored. The IA using both the Monaco criteria and CRM criteria ranged from poor to excellent (range 0.1 to 0.76) and (range 0.1 to 0.62) respectively.; Within the Monaco criteria, IA was excellent for lesion (0.75) and fingerlike papillary projections (0.74); good for tortuous vessels (0.7), mucosal features (0.62), uniform papillary projections (0.53), and ulceration (0.58); and fair for white linear bands (0.4). Within the CRM criteria, the IA was good for villous pattern (0.62), flat pattern (0.62), and honeycomb pattern; fair for ulcerated pattern (0.56), polypoid pattern (0.52) and inflammatory pattern (0.54). The diagnostic IA using Monaco criteria was good (0.65), while the diagnostic IA using CRM was fair (0.58). The overall diagnostic accuracy using the Monaco classification was 61% and CRM criteria was 57%.

Conclusion: The IOA and accuracy rate of DSOC using visual criteria from both Monaco Criteria and CRM are similar. However, some criteria from both sets suffer from poor IA, thus affecting the overall diagnostic accuracy. More formal training and refinements in visual criteria with additional validation are needed to improve diagnostic accuracy.

Disclosure: Drs. Michel Kahaleh, Amy Tyberg, Amrita Sethi, Prashant Kedia, Paul Tarnasky, Divyesh Sejpal, Douglas G. Adler and Raj Shah are consultants for Boston Scientific. Drs. Isaac Raijman, Paul Tarnasky are speakers for Boston Scientific.

P0784 TREATMENT OUTCOME OF ENDOSCOPIC PAPILLECTOMY ON AMPULLARY TUMORS WITH HIGH-GRADE ADENOMA OR EARLY ADENOCARCINOMA

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Introduction: Endoscopic papillectomy is widely used for the curative treatment of ampulla of Vater tumors replacing surgical resection. However, there are scarce data on the treatment outcome in tumors with high-grade adenoma or early adenocarcinoma. The aim of this study was to evaluate the outcome after endoscopic papillectomy of ampullary tumor with high-grade adenoma or early adenocarcinoma.

Aims & Methods: From January 2005 to December 2018, all the patients underwent endoscopic papillectomy as an initial curative treatment for ampullary high-grade adenoma or early adenocarcinoma at Seoul National University Hospital were retrospectively reviewed. The patients who were confirmed with high-grade adenoma or early adenocarcinoma were recommended to undergo subsequent surgical resection. Patients who refused to undergo surgery were followed up at 1 month with endoscopy. If residual tumor was identified at follow up endoscopy, it was considered as incomplete resection, and progression free survival of patients without incomplete resection was evaluated.

Results: A total of 230 endoscopic papillectomy were performed during study period. Among them, 80 were high-grade adenoma or adenocarcinoma (46 high-grade adenoma and 34 adenocarcinoma). One patient with adenocarcinoma was died after the procedure related complication (massive hemorrhage). Within 1 month after the procedure, 13 patients received subsequent surgical resection and presence of residual tumor on surgical specimen was 9 of 13 (69.2%). 21 patients had residual tumor on follow up endoscopy (incomplete resection rate of 35%) and 6 patients were lost to follow up. Total recurrence was 13 cases during the follow up period. Median progression free survival of patients without incomplete resection (n = 39) were 963 days (95% confidence interval, 525 - N/A).

Conclusion: Incomplete resection rate and probability of remaining tumor in surgical specimen were remarkably high after the endoscopic papillectomy of ampullary high-grade adenoma or early adenocarcinoma. In addition, tumors recurred frequently in long-term follow-up even after the complete resection. Endoscopic papillectomy should be cautiously applied in ampullary tumor with high-grade adenoma or early adenocarcinoma.

Disclosure: Nothing to disclose

Pancreas II

09:00-17:00 / Poster Exhibition - Hall 7

P0785 9-(N-METHYL-L-ISOLEUCINE)-CYCLOSPORIN A (NIM811) REDUCE THE SEVERITY OF ACUTE PANCREATITIS VIA INHIBITION OF THE MITOCHONDRIAL TRANSITION PORE

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Introduction: Mitochondrial dysfunction has crucial role in the development of acute pancreatitis (AP), however the accurate molecular mechanism is not known yet.
Aims & Methods: In this study we investigated a possible molecular target – the genetic and pharmacological inhibition of mitochondrial transition pore (mPTP, which has a regulator unit; the Cyclophilin D (*Cyp D*)) in the aspect of AP. Pancreatic ducts (PD) and acinar cells were isolated by enzymatic digestion from Bl/6 wild type or *Cyp D* knock out (*Cyp D* KO) mice. In vitro measurements were performed by confocal and microfluorometry. AP was induced by cerulein (10x50μg/kg) or taurocholic acid (2ml/kg,4%). As a non immunsupressant pharmacological inhibitor of *Cyp D :* NIM811 were used (in vitro -2μM, in vivo - 5mg/kg or 10 mg/kg NIM811).
Results: Genetic and pharmacologic inhibition (NIM811, cyclosporinA) of *Cyp D* significantly reduced the loss of ΔΨ (in PD and acinar cells) and protected PDs HCO_3^- secretion during the administration of 500μM chenodeoxycholic acid (CDC) or 100 mM ethanol (EtOH) and 200μM palnitoleic acid (PA) treatment (p< 0.05). Immunfluorescence meaurements revealed a significant difference in the amount of the mitochondrial protein TOM20 levels between the CDC and the EtOH+PA treated WT and mPTP inhibited (*Cyp D* KO or CYA/NIM811) groups (PD and acini). We detected significantly reduced apoptosis, necrosis levels in *Cyp D* KO and NIM811 treated groups compared to WT controls (PD and acinar cells).
Significantly reduced oedema, necrosis, leukocyte infiltration, serum amylase and in vivo ductal fluid secretion levels were detected in samples from *Cyp D* KO animals or NIM811 treated animals (p< 0.05)compared to WT controls in vivo.
Conclusion: Our data highlights a potencial new pharmacon; the NIM811 which reduced the severity of AP in mice. Our results also revealed that protecting mitochondrial homeostasis have a central role in the function of pancreatic ductal epithelial cells presumably by providing ATP for fluid and ion secretion. These data suggests that NIM811 could open up new perspectives in the treatment of AP.
Disclosure: Nothing to disclose

P0786 NOCICEPTIN RECEPTORS AS A NOVEL TARGET FOR THE TREATMENT IN ACUTE PANCREATITIS

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Introduction: The pathophysiology of experimental acute pancreatitis (AP) consists of the activation of pancreatic enzymes within acinar cells, the release of the activated enzymes in the interstitium, the autodigestion of the pancreas, and the release of activated pancreatic enzymes and other factors into the circulation that result in the development of multiple organ dysfunction. Current treatment options are limited, and predominantly aimed at supportive therapy. Better understanding of the underlying pathophysiology of AP may lead to more targeted therapeutic options, potentially leading to improved survival. In general, the effects mediated by the nociceptin receptors (NOP) on gastrointestinal functions resemble those of classic analgesic opioid agonists and nociceptin, the endogenous NOP agonist, has been reported to play an important role in the regulation of pancreatic exocrine secretion.

Aims & Methods: The primary aim was to examine the potential role of NOP in AP.
The AP mouse model was induced by the intraperitoneal (i.p.) administration of the L-arginine solution followed by second i.p. injection after 1h (dose 400mg/100g body weight (BW)). After 12h from the first L-arginine i.p. injection, mice were divided into 3 experimental groups: AP mice treated with a potent and selective NOP agonist (SCH 21510, i.p. injection every 12h; 1 mg/kg BW), AP mice treated with a potent and selective NOP antagonist ((±)-J 113397, i.p. injection every 12h; 12 mg/kg BW), and non-treated AP mice (injected with equivalent volume of 0.9% NaCl every 12h). Control mice were injected with equivalent volume of 0.9% NaCl. Mice were kept under observation, allowed free access to feed and water, and sacrificed at 72h. Pancreatic and lung tissues were collected for histology in 10% buffered formalin or snap frozen in liquid nitrogen for myeloperoxidase (MPO) analysis.
Results: Treatment of mice with SCH 21510 did not influence histopathological changes or the MPO activity in pancreas and lungs while (±)-J 113397 reduced pancreatic injury and MPO activity, as well as inhibited pancreatitis-associated lung injury.
Conclusion: The results of the present study showed that the modulation of NOP through selective NOP antagonist (±)-J 113397 significantly decreased AP symptoms and for that reason may be considered as a novel treatment target in AP.
Disclosure: Nothing to disclose

P0787 THE FUNCTION OF CFTR CL⁻ CHANNEL IN THE EXOCRINE/ENDOCRINE PANCREAS UNDER PATHOLOGICAL CONDITIONS

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Introduction: The exocrine and endocrine pancreas work in close interaction with each other in which the CFTR Cl⁻ channel plays an essential role by regulating ductal secretory processes and, as shown by some studies, β-cell insulin secretion. The role of the channel under certain pathological conditions is not completely known, therefore our aim in this study was to investigate the exocrine and endocrine functions in diabetes- or pancreatitis-induced wild-type (WT) and CFTR knock out (KO) mice.
Aims & Methods: Intra-interlobular pancreatic ductal fragments were isolated from WT and CFTR KO mice by enzymatic digestion. Pancreatic ductal fluid and HCO_3^- secretion was measured by in vivo fluid secretion measurements and fluorescence microscopy. Islet functions during i.p. glucose tolerance test were investigated by serum insulin and glucagon measurements. Pancreas tissue sections were prepared and immunhistologically stained against insulin, glucagon and CFTR to observe islet and ductal morphology. Pancreatitis was induced by i.p. injection of cerulein and disease severity was assessed by evaluation of histological sections and serum amylase measurements. Diabetes was induced by i.p. administration of streptozotocin and disease development was confirmed by glucose tolerance test.
Results: Pancreatic ductal fluid and HCO_3^- secretion significantly increased in diabetic and decreased in pancreatitis induced mice. Serum levels of insulin decreased in diabetic animals, whereas the serum levels of glucagon were elevated. The absence of CFTR decreased ductal fluid and HCO_3^- secretion and resulted in lower serum insulin and higher glucagon levels. Immunhistological staining of insulin and glucagon in pancreas tissue sections revealed a morphological change in CFTR KO islets with higher content of α-cells that localized towards the center. Diabetic animals did not show difference in CFTR expression compared to the control group, whereas mice with pancreatitis showed less staining of intercalated and intralobular ducts.
Conclusion: Our results suggest that CFTR Cl⁻ channel plays a key role in ductal HCO_3^- secretion and has a direct or indirect role in islet function and structure.

Disclosure: Nothing to disclose

P0788 AZATHIOPRINE AND 5-AMINOSALYCILIC ACID IMPAIR DUCTAL EPITHELIAL TRANSPORTER FUNCTIONS IN MICE

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Introduction: Numerous case-reports and observational studies suggest that several medications, such as azathioprine (AZA) and 5-aminosalycilic acid (5-ASA), can induce acute pancreatitis. The important role of pancreatic ducts in the pathomechanism of acute pancreatitis has been highlighted recently. Pancreatic ductal functions are essential for the homeostasis and integrity of the pancreas. Toxic factors, such as alcohol or bile acids, can impair the ductal HCO_3^- secretion which can ultimately lead to pancreatic injury. Our knowledge about pancreatic ductal functions in drug induced pancreatitis is, however, limited. Since medications can also act as toxic factors, we wanted to investigate what effects do AZA and 5-ASA have on pancreatic ductal functions and HCO_3^- secretion.
Aims & Methods: For investigation of *in vivo* effect of drugs C57BL6 mice were fed daily with 15 and 150 mg/kg AZA, as well as 50 and 500 mg/kg 5-ASA by gastric feeding needle for one and four weeks. Control mice received 10 ml/kg 0.9% NaCl solution. Mice were euthanized and pancreatic ductal segments were isolated with microdissection technique. Changes in intracellular pH was estimated using a fluorescent dye, BCECF-AM. Cells were incubated with 2 µM BCECF-AM in standard Hepes solution for 30 min at room temperature. To determine HCO_3^- secretion rates and activity of basolateral transporters (NHE and NBC), we used the ammonium pulse method. Pancreatic ducts from non-treated animals were also isolated and HCO_3^- secretion was assessed under normal conditions and under acute perfusion with solutions containing different concentrations of AZA and 5-ASA.
Results: In the presence of either 1 or 10 µg/ml AZA or 5-ASA the regeneration from alkalosis was significantly lower compared to control ducts, which means that either AZA or 5-ASA in 1 and 10 µg/ml concentrations can inhibit HCO_3^--secretion across the apical membrane of the ductal cells. We found similar results in case of regeneration from acidosis with the exception of 1 µg/ml AZA. Administration of 10 µg/ml AZA or 5-ASA and 1 µg/ml 5-ASA significantly decreased the regeneration of acidosis in pancreatic ducts, which suggests that 10 µg/ml AZA or 5-ASA and 1 µg/ml 5-ASA can inhibit HCO_3^--influx across the basolateral membrane. However, 1 µg/ml AZA caused no significant changes in regeneration from acidosis in isolated pancreatic ducts. Per os treatment of mice both with AZA and 5-ASA for one week caused no changes in HCO_3^--secretion in either concentration. Treatment with AZA caused significantly lower basolateral transporter activity compared to control animals in a dose dependent manner, while treatment with 5-ASA showed no effect. After four weeks of treatment both drugs impaired the ductal HCO_3^--secretion rates. No correlation to 5-ASA doses was to be observed, while treatment with 150 mg/kg AZA proved to be lethal after 12-14 days. Basolateral transporter activity was only impaired after treatment with 15 mg/kg AZA.
Conclusion: Both azathioprine and 5-aminosalycilic acid can impair ductal HCO_3^--secretion under acute exposure. Per os treatment for a longer time-period with both drugs can also reduce the ductal functions. This effect might explain the relatively high number of acute pancreatitis cases in patients treated with these medications. In order to understand the exact molecular mechanisms further investigations are highly needed.
Disclosure: Nothing to disclose

P0789 VX-770 AND VX-809 RESTORE THE ALCOHOL-INDUCED CFTR EXPRESSION DEFECT IN PANCREATIC DUCTAL CELLS

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Introduction: Our research group previously showed that ethanol (EtOH) increases the severity of acute alcohol-induced pancreatitis by disrupting level and function of the cystic fibrosis transmembrane conductance regulator (CFTR). It is well known that Ivacaftor (VX-770) and Lumacaftor (VX-809) can correct the impaired CFTR function and expression in cystic fibrosis (CF) patients.
Aims & Methods: The main aim of the study is to test the effect of these compounds on the CFTR expression during EtOH exposure.
Intact guinea pig pancreatic ducts (PDs) and Capan-1 cells were treated with different concentration of EtOH (30, 50 and 100 mM) alone and in combination with VX-770 (10 µM) and/or VX-809 (10 µM) for 12 hours. CFTR expression was evaluated by immunofluorescent staining and our images were captured by confocal microscopy.
Results: Exposure of Capan-1 cells and guinea pig PDs to EtOH dose-dependently decreased the plasma membrane expression of CFTR. 10 µM VX-770 and VX-809 alone had no significant effect on the channel's expression, however, both of the compounds dose-dependently prevented the EtOH-induced CFTR damage that could be observed even after 2 hours of treatments. Co-administration of VX-770 and VX-809 also prevented the EtOH-induced (30 and 50 mM) decrease in CFTR expression, however was not able to prevent the effect of 100 mM EtOH. In addition, combination of the two drugs did not potentiate each other's effect.
Conclusion: Our findings suggest that VX-809 and VX-770 can restore the CFTR expression defect caused by alcohol. These data suggest that correcting CFTR function or expression could have therapeutic benefits in pancreatitis.
Disclosure: Nothing to disclose

P0790 PITFALLS IN AR42J-MODEL OF CERULEIN-INDUCED ACUTE PANCREATITIS

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Introduction: AR42J are immortalized pancreatic adenocarcinoma cells that share similarities with pancreatic acinar cells. AR42J are often used as a cell-culture model of cerulein (CN)-induced acute pancreatitis (AP). Nevertheless, it is controversial how to treat AR42J for reliable induction of AP. Also, gene knockout or overexpression often remains challenging. In this study, we provide evidence for optimized CN-induced AP in AR42J and high transfection efficacy using glyoxalase-I (Glo-I) as target of interest.
Aims & Methods: Effect of dexamethasone (dexa) and CN on cell morphology and amylase secretion was analyzed via ELISA of supernatant. Effect of CN on IL-6 and TNF-alpha and NF-κB-p65 was measured via qRT-PCR, ELISA and Westernblot (WB). Transfection efficacy was measured by WB, qRT-PCR and immune fluorescence of pEGFP-N1-Glo-I-Vector and Glo-I-siRNA
Results: Treatment of AR42J with 100nm dexamethasone is mandatory for differentiation to an acinar cell like phenotype and amylase production. CN resulted in secretion of amylase but does not influence amylase pro-

duction. High levels of amylase secretion were detected between 3 and 24 hours of incubation. Treatment with LPS alone or in combination with CN did not influence amylase secretion. CN led neither to increased secretion nor production of TNF-alpha. No CN-induced elevation of IL-6 was observed. CN-induced stimulation of NF-κB was found to be highest on protein level after 6h of incubation. Only cells up to a passage of 35 should be used for experiments. DNA-amount of 2.5μg was sufficient to induce Glo-I overexpression on protein and mRNA levels with highest effect after 12 to 24 hours. Knockdown was achieved by using 30pM of Glo-I-siRNA leading to effective reduction of protein levels after 72 hours. AR42J cell passages of 35 or more should not be used for CN-induced AP.
Conclusion: CN-induced AP in AR42J cells is a reliable *in-vitro* model of AP but specific conditions are mandatory to obtain reproducible data.
Disclosure: Nothing to disclose

P0791 GLYOXALASE-I IS UPREGULATED IN ACUTE CERULEIN-INDUCED PANCREATITIS: A NEW MECHANISM IN PANCREATIC INFLAMMATION?

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Introduction: Inflammation caused by oxidative stress (ROS) is an essential mechanism for initiation and deterioration of acute pancreatitis (AP). An important source for ROS comprises the reactive compound methylglyoxal (MGO) itself and the MGO-derived formation of advanced glycation end-products (AGEs). AGEs bind to RAGE and activate NF-κB leading to production of proinflammatory cytokines. MGO is detoxified by glyoxalase-I (Glo-I). The importance of Glo-I has been shown in different models of inflammation and carcinogenesis. Nevertheless, the role of Glo-I and MGO in AP has not been evaluated so far. This study analyzed Glo-I in cerulein (CN)-induced AP and determined the effects of Glo-I knockdown, -overexpression and pharmacological modulation.
Aims & Methods: AP was induced in C57BL/J6 mice by 10 i.p. injections of 50 μg/kg b.w. CN. Glo-I was analyzed in explanted pancreata by Western-blot (WB), qRT-PCR and immunohistochemistry. AR42J cells were differentiated by dexamethasone and an AP was induced *in-vitro* by 100nM CN. Cells were co-treated with ethyl pyruvate (EP) and BrBzGSHCp2, two Glo-I modulators. Knockdown and overexpression of Glo-I was achieved by transient transfection with Glo-I siRNA and pEGFP-N1-Glo-I-Vector. Amylase secretion, TNF-α production (ELISA), Expression of Glo-I, RAGE and NF-κB (WB) were measured.
Results: Glo-I was significantly upregulated on protein and mRNA levels in CN treated mice. In AR42J cells, treatment with EP and BrBzGSHCp2 resulted in significant reduction of CN-induced amylase secretion. CN-induced NF-κB expression was attenuated by BrBzGSHCp2 but not EP. Overexpression of Glo-I resulted in significant reduction of CN-induced amylase levels. Glo-I knockdown was accompanied by consecutive increase of amylase-secretion. Interestingly, Glo-I knockdown but not overexpression reduced NF-κB expression via decrease of RAGE.
Conclusion: Glo-I is overexpressed in a model of CN-induced AP. Pharmacologic modulation and overexpression of Glo-I reduced amylase secretion in AP *in vitro*. Targeting Glo-I in AP could be an innovative therapeutic approach for future *in vivo* studies.
Disclosure: Nothing to disclose

P0792 FEATURES OF HYPERTRIGLYCERIDEMIA-INDUCED ACUTE PANCREATITIS FROM A GLOBAL MULTICENTER COHORT STUDY OF 22 CENTERS (APPRENTICE)

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Introduction: Severe hypertriglyceridemia is an important, well-known cause of acute pancreatitis (AP). Existing data on clinical characteristics of hypertriglyceridemia-induced acute pancreatitis(HTG-AP) are very limited.
Aims & Methods: The aim of this project was examine prevalence, patient characteristics and clinical outcomes of HTG-AP patients compared to other etiologies from a large, international cohort study.
Acute Pancreatitis Patient Registry to Examine Novel Therapies In Clinical Experience (APPRENTICE) is a global, multicenter, cohort study. AP patients were prospectively enrolled in 22 international centers. Data were collected via standardized questionnaires and registered in REDCap (Research Electronic Data Capture). Revised Atlanta Classification definitions were used to determine severity. Primary HTG-AP was confirmed when common etiologies were excluded and serum triglycerides were>500mg/dl. Pearson's chi-squared test and t-test were used to compare categorical and continuous variables, respectively. Multivariable logistic regression model was used with severe/moderate condition as the outcome.
Results: 1478 patients were prospectively enrolled, of whom 69 diagnosed with HTG-AP (prevalence=4.6%). Compared to the other etiologies, HTG-AP patients were younger (40.4 vs 50 years; p< 0.0001) had higher BMI (30.4 vs 27.5kg/m²; p=0.0002) and more frequent alcohol use (70.6% vs 48.9%;p< 0.0001), were more likely diabetics (59.4% vs 15.3%; p< 0.0001), and had more frequently recurrent AP (RAP) (40.6% vs 24%; p=0.002). Median TG level for HTG-AP patients was 1675 mg/dl and 133 mg/dl for the others. In terms of clinical outcomes, ICU admission was more frequent in HTG-AP patients (26.1% vs 16.4; p=0.036), but no significant difference was found in terms of rate of moderate/severe AP, length of hospital stay, or mortality. At the multivariable logistic regression, male sex and increasing BMI were associated with risk of moderate/severe AP while HTG-AP was not. Within the HTG-AP population, no differences were found in terms of patient and hospitalization features based on magnitude of HTG levels.
Conclusion: HTG-AP accounts for 4.6% of AP cases, affects younger, overweight and diabetic patients, and those who use alcohol, require ICU and have RAP more often compared to other etiologies. This suggests that HTG-AP has a higher cost compared to other etiologies. However, no difference was found in terms of severity, length of stay or mortality. Also, basal HTG levels do not seem to affect the clinical outcome of these patients.
Disclosure: Nothing to disclose

P0793 A BEDSIDE SCORE PREDICTING COMMON BILE DUCT STONE IN PATIENTS WITH ACUTE BILIARY PANCREATITIS

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Introduction: Gallstones are considered the most common cause of acute pancreatitis. Despite that most of the stones are expelled spontaneously through the papilla due to their small size; about 20% to 30% of patients with acute biliary pancreatitis (ABP) will have persistent CBD stones. Therefore, the identification of retained common bile duct stone after an acute episode of biliary pancreatitis is of paramount importance since stone extraction is mandatory.
Aims & Methods: We aimed to generate a simple non-invasive scoring model to predict the presence of CBD stones in patients with biliary pancreatitis. We performed a retrospective study at Galilee Medical Cen-

ter including patients with an established diagnosis of pancreatitis with suspected CBD stone. One hundred and fifty-four patients were included, among them thirty-three patients (21.5%) were diagnosed with CBD stone by endoscopic ultrasound (US).

Results: In univariate analysis, age (OR 1.048, P=0.0004), aspartate transaminase (OR 1.002, P=0.0015), alkaline phosphatase (OR 1.005, P=0.0005), gamma-glutamyl transferase (GGT) (OR 1.003, P=0.0002) and CBD width by US (OR 1.187, P=0.0445) were significantly associated with CBD stone. In multivariate regression analysis, three parameters were identified to significantly predict CBD stone; age (OR 1.062, P=0.0005), GGT level (OR 1.003, P=0.0003) and dilated CBD (OR 3.685, P=0.027), with area under the curve of 0.8433. We developed a diagnostic score that included the 3 parameters that were significant on multivariate analysis, with assignment of weights for each variable according to the co-efficient estimate. A score that ranges from 51.28 to 73.7 has a very high specificity (90% - 100%) for CBD stones, while a low score that ranges from 9.16 to 41.04 has a high sensitivity (82% - 100%). By performing internal validation, the NPV of the low score group was 93%

Conclusion: We recommend incorporating this score as an aid for stratifying into patients with acute biliary pancreatitis with low or high probability for the presence of CBD stone

Disclosure: Nothing to disclose

P0794 INFECTED PANCREATIC NECROSIS IN THE COURSE OF SEVERE ACUTE PANCREATITIS: CAN WE PREDICT CATHETER DRAINAGE FAILURE AND NEED FOR ADDITIONAL NECROSECTOMY?

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Introduction: Recent guidelines advocate the step-up approach for the management of infected pancreatic necrosis (IPN). Nearly half of patients will require secondary necrosectomy after drainage. A previous study (1) identified 4 risk factors of catheter drainage failure: male gender, multiple organ failure, percentage of necrosis and heterogeneous collection, leading to propose a nomogram with an area under receiver operating characteristic (ROC) curve of 0.76. Our primary objective was to validate this novel nomogram. Our secondary goals were to explore others potential predictors of failure of catheter drainage.

Aims & Methods: We retrospectively studied 72 consecutive patients admitted in 3 university hospitals for suspected IPN requiring interventions by catheter drainage first between 2012 and 2016 . All computed tomography (CT) examinations performed prior to the first drainage procedure were reviewed by a single blinded radiologist. Drainage success or failure rates were assessed. Success was defined by survival without any additional necrosectomy, while failure was defined by death and/or additional necrosectomy after the drainage procedure because of lack of improvement. ROC curve of predictors of drainage failure according to Hollemans nomogram and area under the curve (AUC) were also calculated.

Results: Catheter drainage alone achieved success in 44.4% of patients. Nomogram predicted catheter drainage failure with an area under the ROC curve of 0.71. Scores ≤ 8 (low) or 40 (maximum) resulted in 100% success or failure rates of primary catheter drainage, respectively. In multivariate analysis, catheter drainage failure was independently associated with body mass index (BMI) (OR: 1.14; 95% CI: 1.01-1.29; *P*: 0.02), heterogeneous collection (OR: 18.84; 95% CI: 2.02-175.86; *P*: 0.01) and respiratory failure 24 hours prior catheter drainage (OR: 16.76; 95% CI: 1.94-144.4; *P*: 0.01).

Conclusion: More than half of patients required necrosectomy because of failure of radiological catheter drainage. However, Hollemans nomogram can be useful to predict catheter drainage failure, especially for extreme values. Heterogeneous collection on CT and respiratory failure 24h prior to drainage were strongly associated with catheter drainage failure. Early identification of patients at risk of drainage failure alone might help improving their management and reducing antibiotics duration.

References: Hollemans RA, Bollen TL, van Brunschot S, Bakker OJ, Ahmed Ali U, van Goor H, et al. Predicting Success of Catheter Drainage in Infected Necrotizing Pancreatitis. Ann Surg. avr 2016;263(4):787-92.

Disclosure: Nothing to disclose

P0795 REDEFINING THE ROLE OF ANTIBIOTICS IN INFECTED PANCREATIC NECROSIS DURING SEVERE ACUTE PANCREATITIS: AN OBSERVATIONAL STUDY OF 137 MICROBIOLOGICAL SAMPLES

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Introduction: Recent guidelines ruled out prophylactic antibiotics to prevent IPN and advocate the step-up approach for the management of IPN. Emerging drug resistant bacteria is a rising problem among SAP and ICU patients. However, there is no recommendation regarding antimicrobial therapy management for IPN (molecules and duration). In real life, many patients will have culture levied under broad spectrum antimicrobial therapy. Our primary objective was to determine the impact of prior antibiotherapy on samples cultures collected during interventions for a suspected infected pancreatic necrosis (IPN) among patients admitted for severe acute pancreatitis (SAP) and to determine if prior antibiotic therapy negatively affects the results of the culture. Description of microbiological species and their patterns of resistance were our secondary goals.

Aims & Methods: We retrospectively studied 62 consecutive patients admitted in ICU for suspected IPN requiring interventions. We collected data about microbiological samples, as well as antimicrobial therapy type and duration before and after intervention for suspected IPN. We classified species according to the definitions proposed by Magiorakos et al.

Results: IPN was confirmed for 48 patients, with 137 samples collected during interventions. 57% of positive cultures were levied under efficient antibiotherapy, previous antibiotherapy did not influence cultures results (p=0.84). 1/3 of samples were polymicrobial. Half of the patients developed multi and extensively drug resistant bacteria. Prolonged antibiotics did not sterilized collections or necrotic tissues for extensively drug resistant bacteria that were founded into necrotic collection even after several weeks of adapted antibiotics.

Conclusion: Previous antibiotherapy did not influence microbiological culture results and prolonged adapted broad-spectrum antibiotics did not allow sterilizing necrotic tissue or fluid collections. Our results showed a 50% prevalence of drug resistant bacteria. Negative cultures among patients under antibiotics should question the diagnosis of IPN and antibiotics discontinuation. Strategies to reduce antimicrobial therapy use and exposure in the course of SAP are needed. Futures prospective studies should determine the optimal antimicrobial therapy duration.

References: Magiorakos A-P, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis. mars 2012;18(3):268-81.

Disclosure: Nothing to disclose

P0796 THE PROGNOSTIC ROLE OF FATTY LIVER DISEASE IN ACUTE PANCREATITIS: A META-ANALYSIS

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Introduction: Acute pancreatitis (AP) is a life-threatening condition with an average mortality of 2-5%, which can rise up to 30% in severe cases. Tremendous efforts were made to identify factors that can predict diseases course. A potential predictor may be pre-existing fatty liver disease (FLD).

Aims & Methods: The aim of this study was to perform a meta-analysis on the prognostic role of FLD in AP.
We performed a systematic search in seven medical databases for cohort studies reporting on adult AP cases with and without FLD of any origin proven by cross-sectional imaging and/or histology. The primary outcome was in-hospital mortality, secondary outcomes included AP severity,

length of hospital stay (LOH), necrotizing AP and systemic inflammatory response syndrome (SIRS). We calculated risk ratio (RR) for categorical variables (i.e., mortality, AP severity, and necrosis) and weighted mean difference (WMD) for LOH with 95% confidence intervals (CIs) with the random effect model. Heterogeneity was tested with I^2-statistics.

Results: Twelve studies containing data on 6233 patients were eligible for meta-analysis. Patients with FLD were more likely to die (RR=3.24, CI: 1.65-6.34, p=0.001; I^2=41.6%), to develop severe (RR=2.27, CI: 1.9-2.7, p< 0.001; I^2=0.0%), and necrotizing AP (RR=2.37, CI: 1.92-2.92, p< 0.001; I^2=30.4%) compared to those not having pre-existing FLD. The presence of systemic complications affecting at least one organ (RR=2.03, CI: 1.54-2.67, p< 0.001; I^2=68.1%) and SIRS (RR=1.94, CI: 1.64-2.29, p< 0.001; I^2=34.4%) was significantly higher in the FLD group. There was a tendency for longer LOH with FLD (WMD=2.08 days, CI: 1.09-3.07, p< 0.001; I^2=0.0%).

Conclusion: Our results showed that fatty liver disease is a risk factor of mortality, severe disease course, necrosis, systemic complications and longer length of hospitalization in AP; therefore, we suggest the incorporation of FLD into the prognostic tools in AP.

Disclosure: Nothing to disclose

P0797 LOCAL ADMINISTRATION OF ANTIBIOTICS THROUGH NASOCYSTIC CATHETER FOR THE TREATMENT OF INFECTED PANCREATIC NECROSIS (IPN)

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Introduction: IPN is associated with a high morbimortality. Current treatment of IPN is based on minimally invasive methods, mainly endoscopic or percutaneous drainage and necrosectomy. We designed a step-up protocol for the treatment of IPN based on local administration of antibiotics with drainage previous endoscopic necrosectomy (Pancreatology 2016;16:719-25).

Aims & Methods: Aim of our study was to analyse the proportion of patients requiring necrosectomy in our step-up protocol for IPN. Methods: Retrospective, observational and descriptive study of patients with acute pancreatitis (AP) admitted to our department between January 2015 and December 2018. Cases with pancreatic necrosis (PN) and IPN (defined as positive culture of the necrosis) were evaluated. The number of patients who responded to each of the three steps of our protocol were analysed: Step 1, systemic antibiotics; step 2, endoscopic transmural drainage + local administration of antibiotics; step 3, endoscopic necrosectomy. Transmural drainage was performed by endoscopic ultrasound, by using plastics and/or metal stents. During the same procedure, a nasocystic catheter was placed deep in the necrotic cavity through metal stents or in parallel to plastic stents. Endoscopic necrosectomy was performed when previous steps failed. Data are shown as percentage.

Results: 1158 patients with AP were included. 110 patients (8.4%) suffered from necrotising pancreatitis, and 48 of them (42.6% of necrotising pancreatitis) had IPN and were treated with systemic antibiotics. Nineteen patients (39.6% of IPN) responded to systemic antibiotics. Six patients with IPN on systemic antibiotics died within the first 4 weeks of disease before a second therapeutic step could be applied. Three patients underwent urgent surgical necrosectomy within the first 4 weeks of disease with a 100% mortality. The remaining 20 patients underwent endoscopic transmural drainage and local antibiotic administration through nasocystic catheter. Nine of them (47.4%) did well and 9 needed endoscopic necrosectomy (45% of all IPN). Two patients died before necrosectomy could be performed. Overall mortality of the total cohort of AP was 2.53%.

Conclusion: Addition of local infusion of antibiotics through a nasocystic catheter to endoscopic transmural drainage avoids the need of necrosectomy in half of patients with IPN, who did not respond to systemic antibiotics. These data justify a randomized controlled trial to evaluate this approach.

Disclosure: Nothing to disclose

P0798 WITHDRAWN

P0799 ALCOHOL CONSUMPTION AND SMOKING SYNERGIZE WITH EACH OTHER AND INCREASE THE RISK OF LOCAL COMPLICATIONS AND SEVERITY IN ACUTE PANCREATITIS

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Introduction: Both alcohol consumption and smoking have been reported to be harmful to the pancreas and these addictions often go together.

Aims & Methods: Our aim is to epidemiologically characterize smoking and alcohol consumption habits and evaluate their independent and joint clinical effects in acute pancreatitis (AP).

A total of 1435 adult patient with the diagnosis of AP from 28 healthcare centers were enrolled between 2012 and 2017 by the Hungarian Pancreatic Study Group. Four groups of patients were retrospectively formed: non-smoker-non-drinker (NS-ND), smoker-non-drinker (S-ND), non-smoker-drinker (NS-D) and smoker-drinker (S-D).

Results: 693 (48.7%) of the patients were ND-NS, 119 (8.4%) S-ND, 334 (23.5%) NS-D and 278 (19.5%) were S-D. The average age of onset of AP was significantly lower in the S-ND, NS-D and S-D groups as compared to the NS-ND group (51.7±15.1, 54.9±16.0 and 46.3±11.9 years respectively vs. 61.1±17.6, p< 0.001). The male/female ratio was 0.6 in the ND-NS group, 0.9 in the S-ND, 3.2 in the NS-D and 6.0 in the S-D groups. Drinking alone had no effect on the BMI (NS-ND: 28.3±5.9, NS-D: 28.2±5.1), but smoking in addition to drinking was associated with lower BMI (S-ND: 27.5±6.5 and S-D: 25.7±5.3, p< 0.001).

There are fewer mild cases and more moderately severe cases in the NS-D and S-D groups as compared to the NS-ND group of patients. To reason this change, we can observe an increase in the rate of local complications (ND-NS: 34.4%, NS-D: 37.5%, S-D: 44.1%) including fluid collection (28.3%, 31.3%, 35.5%), pseudocyst (9.0%, 9.2%, 13.3%) and necrosis (8.8%, 11.0%, 11.5%).

Drinking and smoking together also elevate the risk for recurrent AP (RAP). 18.9% of the patients had RAP in the NS-ND, while 23.5% in the NS-D and 31.9% in the S-D groups.

Concerning on admission serum blood parameters, smoking together with drinking has a significant synergic moderating effect on amylase and lipase levels. The amylase in the S-D group was significantly lower than in the NS-ND group (710 vs. 1309, p< 0.05). Smoking and alcohol consumption together are associated with higher levels of C-reactive protein (CRP) but has no effect on white blood cell count.

Conclusion: Drinking and smoking together result in the onset of pancreatitis 15 years earlier, in addition, it elevates the risk of recurrent disease. Drinking and smoking synergize with each other and increase the rate of local complications and moderately severe cases.

Disclosure: Nothing to disclose

P0800 ENDOSCOPIC TRANSGASTRIC DRAINAGE AND NECROSECTOMY FOR WALLED-OFF PANCREATIC NECROSIS HAS BENEFICIAL LONG-TERM OUTCOMES

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Introduction: Although endoscopy is a cornerstone in the treatment of walled-off pancreatic necrosis (WON), long term outcomes are unclear.

Aims & Methods: We performed a retrospective cohort study of patients with WON who have been treated with transgastric drainage and necrosectomy (ETDN) in a tertiary referral center. Primary outcomes were development of exocrine- or endocrine insufficiency, use of analgesics, number of WON- and non-WON related re-admissions, and need for endoscopic intervention during follow-up due to main pancreatic duct (MPD) abnormalities. From Jan. 2010 to Dec. 2018, 215 patients with WON underwent ETDN in our center. We excluded patients who underwent ETDN more than 90 days from the onset of acute pancreatitis (n=35), patients with known chronic pancreatitis (n=4), patients who died during admission (n=29) and during follow-up (n=18), and patient with missing data (n=7). We registered patient characteristics including the development of exocrine (need for pancreatic enzyme replacement therapy) and endocrine insufficiency (need for peroral antidiabetics or insulin), number of WON-related re-admissions, use of analgesics, and need for endoscopic therapy on MPD during follow-up.

Results: We included 122 patients (68 males, median age 57 years). Gallstones were the main etiology (52%). Median time from onset to index intervention was 33 days (range 11-88). ETDN was performed primarily due to infection (81%). Median computer tomography severity index (CTSI) and modified CTSI scores were 7 and 9, respectively. Median follow-up time was 52 months (range 11-112 months).

During follow-up, 21 (17%) patients developed exocrine insufficiency and 33 (27%) developed endocrine insufficiency, ten patients (8%) needed potent opioids and ten patients needed mild opioids. The median number on WON-related readmissions was 0 (range 0-16) and 18 (15%) patients needed endoscopic therapy on MPD during follow-up.

Presence of diabetes at index endoscopy (OR 7.57; 95% CI, 2.54-22.55; p< 0.001) and endoscopic therapy on MPD during follow-up (OR 7.67; 95% CI, 2.55-23.09; p< 0.001) both predicted development of exocrine insufficiency in univariate regression analyses. In multivariate analysis, only endoscopic therapy on MPD predicted development of exocrine insufficiency (OR 7.98; 95% CI, 2.37-26.83; p< 0.001). CTSI (OR 1.55; 95% CI, 1.23-1.97; p< 0.001) and modified CTSI (OR 1.71; 95% CI, 1.25-2.34; p< 0.001) predicted development of endocrine insufficiency both in univariate and multivariate analysis.

Conclusion: This study reports long-term data on patients with WON treated with ETDN. The proportion with endocrine and exocrine insufficiency was relatively small as was the proportion with opioid requiring pain. WON-related readmissions were rare.

This suggests that the treatment has beneficial long-term outcomes. The risk of developing exocrine and endocrine insufficiency is correlated to main pancreatic duct abnormalities and imaging severity index, respectively.

Disclosure: Nothing to disclose

P0801 PROGNOSIS OF ACUTE PANCREATITIS ASSOCIATED WITH HIGH SERUM TRIGLYCERIDES MANAGED IN A TERTIARY CENTER OF GASTROENTEROLOGY

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Introduction: After alcohol and gallstones, hypertriglyceridemia (HTG) is the third most common cause of acute pancreatitis (AP). Data in the literature regarding correlation between level of serum tryglicerides (TG) and disease severity is at variance.

Aims & Methods: The objective in our study was to analyze the prognosis of AP in patients who associated high level of serum TG. Data was collected in a retrospective manner and included all cases of AP admitted in our clinic between 1st of January 2014 and 31st of December 2018. Revised Atlanta Classification was used to define severity. Levels of TG were measured at admission and 48 hours afterwards - the first value obtained during day 3 to 7 of hospitalization was considered. They were recorded according to the definition of the National Cholesterol Education Program/Adult Treatment Panel III (NCEP/ATPIII) as high - 200-499 mg/dL and very high - > 499 mg/dL respectively.

Results: There were 123 cases of AP admitted in our center during the 5-year study period. We found no correlation between abnormal TG levels and severity, mortality rate, admission duration and local complications rate, defined as mentioned. High TG at admission and persistent high TG during hospitalization were significantly associated with occurrence of systemic complications, at a similar rate (27 .8%, p = 0.03 and 27.3%, p = 0.04 respectively). Acute kidney injury was more prevalent in those with high TG at admission (16.7 %, p = 0.02), while sepsis occurred more often in those with persistently high TG (13.6 %, p = 0.01). Only persistently high TG levels correlated with necessity (27%, p = 0.05) and a longer duration (p = 0.03) of Intensive Care Unit (ICU) admission. Presence of very high TG level at admission correlated with length of ICU stay. No correlations were found between persistence of very high TG during hospitalization (8, 6.5%), and other registered variables.

Conclusion: In our study HTG was significantly associated with an increased incidence of systemic complications in AP. Nevertheless need for ICU admission and length of stay were only correlated with persistent HTG longer than 48 hours after admission. Mortality and severity of AP were not impacted by presence of HTG in our group.

Disclosure: Nothing to disclose

P0802 LEFT VENTRICULAR ASSIST DEVICE (LVAD) USE IS ASSOCIATED WITH ACUTE PANCREATITIS: A MULTICENTER RETROSPECTIVE COHORT

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Introduction: Case series suggest that left ventricular assist devices (LVAD) increase the risk of acute pancreatitis. Hemolysis and ischemia have been proposed as putative mechanisms. Cardiac transplant recipients also have perioperative ischemia and medications that can potentially cause pancreatic inflammation.

Aims & Methods: We aim to compare the incidence of acute pancreatitis in patients receiving advanced heart failure therapies. Our secondary goal is to identify potential risk factors associated with acute pancreatitis in the same population.

A retrospective cohort of patients with advanced heart failure (NYHA class III and IV) was followed from 2012 to 2018 in three referral hospitals. Three groups were compared: LVAD recipients (final destination), transplant recipients (with LVAD as a bridge for transplant, or direct transplant recipients) and controls that refused or did not qualified for advanced therapies. Patients were enrolled the day they had an AICD placed (or the day they presented to our heart failure clinic).

Demographics, body mass index (BMI), tobacco and alcohol use, baseline ejection fraction, history of gallstone disease and development of hemo-

lysis were recorded. Log-rank test and adjusted hazard ratios compared pancreatitis incidence between groups. Kaplan Meier curves were elaborated.

Results: 1,344 patients were included in the cohort: 407 with LVAD as final destination, 589 with transplant (233 with LVAD bridge and 356 transplanted directly) and 348 controls. 987 (73.4%) patients were male, mean age was 60.9 ±14.3 years, average BMI was 28.4 ±5.9Kg/m². 701 (55.3%) patients had previous alcohol use, and 263 (21.5%) had history of gallstones. Mean follow-up was 85.7 ±61.2 months. 423 (31.5%) patients died during cohort follow-up.

A total of 39 cases of acute pancreatitis were reported. Annual incidence was 6.7 cases per 1000 LVAD patients, 2.3 per 1000 transplant recipients, 4.1 per 1000 patients on bridge therapy (after receiving a heart transplant) and 3.2 per 1000 controls (log-rank test for equality p=0.03). Combined, the annual incidence of acute pancreatitis was 5.6 cases per 1000 LVAD users and 2.7 cases in 1000 nonusers (p=0.009).

Unadjusted hazard ratio for acute pancreatitis in LVAD was 2.4 (95%CI 1.2-4.6) and 2.0 (95%CI 0.7-5.5) after adjusting for gender, age, BMI, ejection fraction, alcohol use, smoking, history of gallstones disease and hemolysis. History of gallstone disease had the highest effect on developing acute pancreatitis (adjusted hazard ratio 4.0, 95%CI 1.6-9.9).

Among the patients who developed pancreatitis, 4 (10.5%) had history of significant alcohol use and 19 (48.7%) moderate use; 17 (46.9%) had history of smoking, 21 (55.3%) had history of gallstone disease and 14 (36.8%) hemolysis.

Prevalence of gallstone disease was similar in patients with or without LVAD (21.0% vs. 22.0% p=0.6). History of hemolysis was significantly higher in patients with LVAD (6.0% vs. 35.0%, p< 0.001).

Abdominal imaging showed a spectrum of disease including a normal pancreas (17.9%), edematous pancreatitis (44.7%), small fluid collections (17.9%) and hemorrhagic/necrotic pancreatitis (5.3%).

Conclusion: Patients with LVAD have twice the risk of developing acute pancreatitis compared to heart transplant recipients and heart failure controls. The effect of LVAD seems to dissipate once patients undergo cardiac transplantation and gallstone disease likely plays an important effect in pathogenesis. Studies that elucidate the mechanisms behind pancreatic injury in advanced heart failure and interventions to prevent them are strongly suggested.

Disclosure: Nothing to disclose

P0803 SERUM TRIGLYCERIDE LEVEL DOSE-DEPENDENTLY ELEVATES THE RISK OF LOCAL OR SYSTEMIC COMPLICATIONS IN ACUTE PANCREATITIS: A MULTICENTER INTERNATIONAL COHORT ANALYSIS OF 716 PATIENTS

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Introduction: Hypertriglyceridaemia (HTG) is the third most common cause of acute pancreatitis (AP) and opposite to the other etiologies, most often moderate or severe AP develop. Unfortunately, only small amount of data are available concerning its dose-dependency.

Aims & Methods: Our aim was to investigate the dose-dependent effects of serum triglyceride levels on AP. Data of 716 patients were retrospectively analyzed from the prospectively collected, international, multicenter AP registry operated by the Hungarian Pancreatic Study Group (HPSG). AP patients over 18-year-old, who underwent triglyceride measurement within the first three days were included from 31 centers and 12 countries. Six groups were created based on the highest triglyceride level of the initiating three days (< 1.7 mmol/l, 1.7-2.19 mmol/l, 2.2-5.59 mmol/l, 5.6-11.19 mmol/l, 11.2-22.39 mmol/l, >22.4 mmol/l). HTG was indicated above 1.7 mmol/l.

Results: The total data quality was 81%. 30.6% (n=219) of the patients presented with HTG. The ratio of male gender in the whole cohort was 59% (n=421) and was significantly elevated in the HTG group, compared to

patients with normal triglyceride level (p< 0.001). BMI and diabetes in the personal history correlated with the hypertriglyceride level (p=0.001, p< 0.001). Triglyceride dose-dependently and above 22.4 mmol/l significantly (p=0.003) elevated the risk for severe pancreatitis. HTG above 11.2 mmol/l was significantly related to a higher risk for local complications (p< 0.001), local fluid collection (p=0.004), pancreas necrosis (p=0.02) and HTG above 5.6 mmol/l was significantly related to a higher incidence of diabetes as complication (p=0.008). Risk for systemic organ failure was significantly elevated above 22.4 mmol/l triglyceride (p=0.002).

Conclusion: Serum triglyceride has a dose-dependent effect on the risk for local and systemic complications and severity of AP.

Disclosure: Nothing to disclose

P0804 MUTATIONS IN THE 5' UPSTREAM REGION OF CHYMOTRYPSINOGEN C GENE ARE NOT ASSOCIATED WITH CHRONIC PANCREATITIS

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Introduction: Chymotrypsinogen C (*CTRC*) plays a significant role in regulating trypsinogen activation. Early activation of trypsinogen inside the pancreas is a key molecular mechanism in the pathogenesis of pancreatitis that results in self-digestion and local inflammation of the organ. Loss-of-function mutations in the *CTRC* gene encoding Chymotrypsinogen C impair either the catalytic activity or the expression of the enzyme. Impaired expression of *CTRC* might be caused by variants in the 5' upstream region, however, this region of the gene was not investigated yet.

Aims & Methods: Our aim was to sequence the 5' upstream region of the *CTRC* gene in patients and controls in order to identify variants that may predispose to chronic pancreatitis. We selected 117 patients with non-alcoholic (NACP), 147 patients with alcoholic chronic pancreatitis (ACP) and 263 controls recruited by the Hungarian Pancreatic Study Group (HPSG - www.pancreas.hu). Mutations within the ~1.4 kb CTRC 5' upstream region were analyzed by Sanger sequencing.

Results: We found 2 common polymorphisms (c.-913A>G and c.-811G>A) and 4 further variants (c.-993G>T, c.-314AAAT[5], c.-92C>T and c.-59C>T) in the ~1.4 kb long 5' upstream region of the *CTRC* gene. However, we found that the variant c.-913A>G slightly accumulated in patients compared to controls, genotype and allelic distribution of the identified variants were generally comparable between each group of patients and controls.

Conclusion: Based on our preliminary results, the identified mutations in the 1.4 kb long 5' upstream region of the *CTRC* gene are not associated with chronic pancreatitis.

References: Hegyi E, Sahin-Tóth M. Genetic Risk in Chronic Pancreatitis: The Trypsin-Dependent Pathway. Dig Dis Sci. 2017;62(7):1692-1701.

Disclosure: Nothing to disclose

P0805 CHARACTERIZATION OF THE PATHOMECHANISM OF SMOKE-INDUCED PANCREATIC DAMAGE

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Introduction: Smoking represents an independent risk factor for the development of chronic pancreatitis (CP). It is well documented that secretion of pancreatic ductal alkaline fluid (which is regulated mostly by the anion exchanger and cystic fibrosis conductancia regulator- CFTR) is diminished in CP. Earlier we demonstrated that cigarette smoking significantly diminishes fluid and HCO_3^- secretion, and CFTR activity in guinea pig pancreas, however, the underlying mechanisms are unknown. The aim of this study was to understand the pathomechanism of smoke-induced pancreatic ductal cell damage.
Aims & Methods: CFTR function was measured in non-smoker and smoker patients with, or without chronic pancreatitis based on Cl^- concentrations in sweat. The effect of smoking on CFTR expression was analysed by RT-qPCR, immunofluorescence staining. Pancreatic ducts were isolated from guinea pig pancreas. Cigarette smoke extract (CSE) was prepared by smoking of 15 cigarettes into 10 ml distilled water. Intracellular pH, Ca^{2+} concentration and ATP levels were evaluated by fluorescence microscopy. Mitochondrial membrane potential was measured by using confocal microscopy.
Results: Cl^- concentrations increased in sweat samples from patients from CP and further elevation was detected in a smoker group. Smoking significantly decreased the membrane expression of CFTR in human tissue samples. CSE incubation decrease CFTR mRNA and protein expression on Capan 1 cells. Smoking CSE incubation also decreases HCO_3^- secretion in guinea pig pancreatic ducts via inhibition of the Cl^-/HCO_3^- exchanger, Na^+/H^+ exchanger and Na^+/HCO_3^- cotransporter. CSE pretreatment decreased the amplitude of carbachole-induced Ca^{2+} signal in pancreatic ducts, suggesting that cigarette smoking alters Ca^{2+} signaling pathways in some way. CSE incubation was reduced mitochondrial membrane potential in guinea pig pancreatic ducts.
Conclusion: The inhibition of CFTR and other ion transporters by CSE could play a crucial role in the development of ductal insuffiency and chronic pancreatitis. This study was supported by OTKA, MTA, SZTA and ÚNKP.
Disclosure: Nothing to disclose

P0806 THE GUT MICROBIOTA CAN COMPENSATE ENZYMATIC ACTIVITY IN PATIENTS WITH PANCREATIC EXOCRINE INSUFFICIENCY

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Introduction: Pancreatic exocrine insufficiency (PEI) is an inflammatory condition of the pancreas in which the fibrosis development and loss of pancreatic parenchyma lead to an alteration of the endocrine and exocrine function. Genetic predisposition is one of the main common causes of PEI development, although malformations, autoimmunity, alcohol and nicotine are other predisposing factors, especially the interaction among several of them. The possible involvement of certain microbial groups in scenarios where the disease and inflammation have control needs to be elucidated.
Aims & Methods: The objective of this work was to explore the state of the intestinal microbiota in search of some indicative bacteria that allow us to differentiate healthy individuals from an PEI population.
Two cohorts were included in this study at Hospital Dr. Josep Trueta (Girona, Spain): 11 patients with PEI and 6 low risk, healthy (i,e.,non-smokers and non-drinkers) subjects. Patients with PEI had fecal elastase values <

15 µg/g or between 15 and 200 µg/g and values below 29% of C^{13}-triglycerides in the breath test. Patients brought a sample of feces from which 17 bacterial markers representing the main physiological and ecological phyla were analyzed. Two different indexes were defined according to the different functional groups of microorganisms based on the enzymatic activities of amylase, lipase and protease. In addition, 1 index indicative of eubiosis was also defined. The indexes were calculated by adding the relative abundance of the bacterial markers. The relative abundance was calculated according to the total bacterial load (Eubacteria). Therefore, the lower the value of the index the greater the abundance of the markers that constitutes it.
Results: When analyzed separately, the different bacterial markers did not present significant differences between the patients with PEI and the healthy subjects. However, significant differences were observed when comparing PEI and healthy subjects when the all bacterial indexes were combined. The 2 indexes based on enzymatic activity were significantly higher in healthy controls than in PEI patients (*p*-value=0.044, *p*-value=0.032, respectively). In contrast, the eubiosis index was significantly higher in PEI patients than in healthy controls (*p*-value=0.039).
Conclusion: Patients suffering from PEI have lower (log)-ratios indexes defined according to amylase, proteolytic, and lipase bacterial activities and an increase in the eubiosis. Since no clinical/physiological implications were derived from these enzymatic activity differences, the results suggest a possible involvement of the bacteria present in the digestive tract to compensate the lack of enzymatic activity characteristic of PEI.
Disclosure: Prof. Garcia-Gil, Dr. Aldeguer, Dr. Serra-Pagès, Dr. Ramió-Pujol, Ms. Oliver are employees from GoodGut, company who has received private and public funding. Prof. Garcia-Gil, Dr. Aldeguer, Dr. Serra-Pagès, Dr. Ramió-Pujol, Ms. Oliver report grants from MINECO and from CDTI, during the conduct of the study. Prof. Garcia-Gil, Dr. Aldeguer and Dr. Serra-Pagès are also GoodGut shareholders, outside the submitted work. The rest of the authors have nothing to disclose.

P0807 WITHDRAWN

P0808 ROLE OF COMMON CASR VARIANTS IN CHRONIC PANCREATITIS

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Introduction: The calcium sensing receptor (CASR) plays an essential role in maintaining mineral ion homeostasis and is also expressed in human pancreatic acinar and ductal cells. Over the past years, the possible involvement of common *CASR* variants in chronic pancreatitis (CP) has emerged, however, their role in the pathogenesis of CP remains controversial due to the lack of large case-control studies.
Aims & Methods: Our aim was to analyze the clinically frequent *CASR* variants in an ethnically homogenous group of Hungarian CP patients and healthy controls. 257 CP patients (cases) and 183 controls with no pancreatic disease from the Hungarian National Pancreas Registry were enrolled. As the most common *CASR* variants are located in exon 7, we PCR amplified and sequenced this exon with its flanking intronic regions.
Results: We identified three common exon 7 variants in our cohort: c.2956G>T (p.A986S), c.2968A>G (p.R990G) and c.3031C>G (p.Q1011E). No significant differences were found in allele frequencies of these variants in cases compared to the control group: p.A986S (19.26% vs 18.58%, OR=1.05, p=0.8), p.R990G (7.8% vs 6.3%, OR=1.26, p=0.4) and p.Q1011E (3.7% vs 4.1%, OR=0.9, p=0.8). However, genotype distribution analysis revealed, that the p.A986S variant in homozygous state was overrepresented

in patients relative to controls (3.5% vs 1.1%, OR=3.3, p=0.13). Although this difference was not statistically significant, there is a clear trend which warrants extension of the studies to a larger cohort in the future.

Conclusion: The homozygous c.2956G>T (p.A986S) variant is overrepresented in the Hungarian cohort of chronic pancreatitis patients relative to the control group. Our results strengthen the previous findings in a French cohort (Masson E, 2015) and support the possible pathogenic role of the homozygous p.A986S variant in chronic pancreatitis.

Disclosure: Nothing to disclose

P0809 ASSOCIATION BETWEEN ENDOSCOPIC ULTRASONOGRAPHY FINDINGS AND PATHOLOGY/BLOOD BIOCHEMICAL FINDINGS IN CHRONIC PANCREATITIS

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Introduction: Endoscopic ultrasonography (EUS) diagnostic categories for changes indicating early chronic pancreatitis were formulated as the Rosemont classification. Japan was the first in the world to introduce diagnostic criteria for "early-stage chronic pancreatitis," centered on EUS imaging diagnostics, in the Japanese Clinical Diagnostic Criteria for Chronic Pancreatitis 2009. However, EUS findings and diagnostic factors for chronic pancreatitis are often inconsistent. This study aimed to investigate the usefulness of EUS by conducting a statistical analysis of EUS findings in patients with chronic pancreatitis diagnosed on the basis of EUS findings and the volume of alcohol consumption, presence of diabetes, history of acute pancreatitis, and blood biochemical findings, and by comparing EUS and pathological findings.

Aims & Methods: Between February 2014 to December 2017, 54 patients with repeat episodes of upper abdominal pain or abnormalities in pancreatic blood enzymes who had been diagnosed with early-stage chronic pancreatitis or chronic pancreatitis on the basis of EUS testing at our hospital were categorized into confirmed, probable, and early-stage chronic pancreatitis cases in accordance with the Japanese Clinical Diagnostic Criteria for Chronic Pancreatitis 2009. Statistical analysis was conducted for each group on the association with the volume of alcohol consumption, presence of diabetes, history of acute pancreatitis, blood biochemical findings, and Rosemont classification.

Results: The 54 study participants were comprised of 37 men and 17 women, with a mean age of 58.0 years. Of the cases, 24, 5, and 25 were confirmed, probable, and early-stage chronic pancreatitis, respectively. The mean alcohol consumption (pure alcohol by grams per day) tended to be higher in the confirmed cases (89 g/day) than in the probable (27.5 g/day) or early-stage chronic pancreatitis cases (30.1 g/day; p=0.08). No significant differences were observed among the groups for the presence of diabetes, history of acute pancreatitis and blood biochemical findings. When the EUS and pathological findings were compared, the imaging results were consistent with the EUS fibrosis findings and irregular pancreatic duct images.

Conclusion: Our study showed no association between the clinical diagnosis of chronic pancreatitis based on EUS findings and the presence of diabetes, history of acute pancreatitis, or blood biochemical findings. One previous report suggested a tendency of anomalous EUS findings to increase in patients aged ≥60 years. Thus, at present, whether EUS findings of chronic pancreatitis, considered to be representative of histological fibrosis, are changes due to aging is difficult to determine, which makes careful diagnosis vital to avoid overdiagnosis of the condition.

References: Raimondi S et al. Best Practice & Research Clinical Gastroenterology 2010;24:349-58. Gibo J et al. a Journal of Technical Methods and Pathology 2005
 Rajan E et al. Gastrointest Endosc 2005

Disclosure: Nothing to disclose

P0810 WHAT IS THE OPTIMAL MANAGEMENT OF PARADUODENAL PANCREATITIS? SURGERY IS ASSOCIATED WITH HIGHER INCIDENCE OF DIABETES BUT SIMILAR QUALITY OF LIFE AND PAIN CONTROL

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Introduction: Paraduodenal pancreatitis (PP) is a focal form of chronic pancreatitis that affects the groove area between duodenum and the head of the pancreas. Consensus regarding surgical or non-surgical management as the best treatment option still is lacking.

Aims & Methods: We retrospectively evaluated all patients managed for PP at The Pancreas Institute of the University of Verona Hospital. The outcomes of surgical vs. medical treatment with regards to pain control, quality of life (QoL) and pancreatic insufficiency were evaluated through specific questionnaires.

Results: The final study population consisted of 75 patients: 62.6% underwent surgery and 37.4% were managed without surgery. All surgical procedures consisted of pancreaticoduodenectomy. The median follow-up from the diagnosis of PP was 60 (12 - 240) months. Patients who underwent surgery experienced a similar incidence of steatorrhea (44.7 vs. 52.6%; p= 0.4) but a significant higher incidence of diabetes (59.6 vs. 10.7%; p< 0.01) when compared to those managed without surgery. There was no difference in terms of reported chronic pain (Graded chronic pain scale, median 0 vs. 1; p= 0.1) and QoL (Pancreatitis QoL Instrument, median 82 vs. 79; p=0.2). However, surgical patients reported a worse level of self-care activities associated with glycemic control (Diabetes self-management questionnaire, median 20 vs. 28, p=0.02).

Conclusion: In patients affected by PP, surgery and medical therapy seem to obtain similar results in terms of QoL and pain control. However, surgery is associated with an increased prevalence of postoperative diabetes with consequent relevant issues in the self-care management.

Disclosure: Nothing to disclose

P0811 WITHDRAWN

P0812 CHRONIC PANCREATITIS IS ASSOCIATED WITH INCREASED CARDIOVASCULAR MORTALITY: A POPULATION-BASED ANALYSIS

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Introduction: Chronic pancreatitis (CP) is associated with high morbidity and mortality. Chronic inflammatory changes leading to systemic atherosclerosis can cause ischemic heart disease (IHD). Studies observing this relationship are limited, particularly describing associated epidemiological relationships, mortality rates, and the role of statin therapy. This study aims to analyze variables that pose a risk of IHD development in patients with chronic pancreatitis, and report the role of statin use.

Aims & Methods: A population-based study was conducted using a cloud-based, HIPPA-enabled web platform called Explorys (IBM, New York) to collect aggregated de-identified electronic health records. At the time of

the study, Explorys had access to over 62 million unique records. Data was obtained using ICD-9 code criteria for chronic pancreatitis, ischemic heart disease, and HMG-CoA reductase inhibitors (statins). Patient characteristics and all-cause mortality rates were compared with patients of IHD after a diagnosis of CP as a first time event using relative risk (RR) with 95% confidence interval (CI) in a random-effect model.

Results: Chronic pancreatitis was found in 81,820 patients, of which 14,500 (17.7%) had subsequent development of IHD. The RR of IHD was significantly higher in patients with prior CP vs. the control population in our registry [RR 7.50 (95% CI: 7.37-7.63), P< 0.0001]. Family history of cardiac disease, tobacco use, obesity, and aspirin use were higher in the CP with IHD population. Patients that were elderly (> 65), male, and African-American were at higher risk of IHD with prior CP. Also, there was a higher rate of all-cause mortality in patients with CP and IHD vs. patients with CP alone. The younger population (18 - 65) and African-Americans with CP on statins had a beneficial effect in the prevention of IHD. Statins did not affect all-cause mortality in patients with CP and IHD vs. patients on statins with CP with subsequent IHD (P=0.3338).

Characteristic	Chronic Pancreatitis [n=81,820]	Chronic Pancreatitis with subsequent IHD [n=14,500]	Relative Risk [95% CI]	P
Age, n [%]				
18-65	53,640 [66]	6,870 [47]	0.47 [0.46, 0.49]	< 0.0001
>65	27,740 [34]	7,590 [52]	2.14 [2.08, 2.20]	< 0.0001
Male, n [%]	42,390 [52]	8,290 [57]	1.24 [1.21, 1.28]	< 0.0001
Ethnicity, n [%]				
Caucasian	58,240 [71]	10,340 [71]	1.01 [0.97, 1.04]	0.7039
African-American	16,670 [20]	3,500 [24]	1.24 [1.20, 1.29]	< 0.0001
Hispanic	4,390 [5]	740 [5]	0.95 [0.89, 1.01]	0.1246
Cormorbidities, n [%]				
FH of Cardiac Disease	11,620 [14]	2,410 [17]	1.20 [1.16, 1.25]	< 0.0001
History of tobacco use	31,770 [39]	6,450 [44]	1.26 [1.23, 1.30]	< 0.0001
BMI > 30	47,300 [58]	11,210 [77]	2.48 [2.40, 2.58]	< 0.0001
Aspirin use, n [%]	32,600 [40]	10,710 [74]	4.26 [4.12, 4.42]	< 0.0001
All-cause Mortality, n [%]	10,670 [13]	3,160 [22]	1.86 [1.80, 1.92]	< 0.0001

[Baseline characteristics]

Conclusion: Patients at higher risk of IHD post CP diagnosis include being elderly, male, and African-American. Mortality is significantly increased in patients with CP and IHD vs. CP alone. Statins had a beneficial effect in decreasing the rates of IHD in patients that were less than 65 and African-Americans.

Disclosure: Nothing to disclose

P0813 QUALITY OF LIFE ASSESSMENT IN PATIENTS WITH PANCREATIC DISORDERS AND EXOCRINE INSUFFICIENCY RECEIVING ENZYME REPLACEMENT THERAPY

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Introduction: With disease progression and complications appearance patients with pancreatic disorders complain of impaired overall quality of life (QoL). Nowadays the QoL assessment is adopted as part of the monitoring strategy of the treatment and the patients' outcome.

Aims & Methods: The aim of this study was to investigate QoL in patients with pancreatic disorders, receiving pancreatic enzyme replacement therapy due to pancreatic exocrine insufficiency. Study enrolled 142 patients (88 males, mean age 52years): 82 patients had chronic pancreatitis (CP), 30- acute pancreatitis (AP), 30- pancreatic cancer/pancreatic resection (PC/PR). QoL was evaluated by the European Organization for Research and Treatment of Cancer QoL questionnaire (QLQ-C30), containing 30 questions. The QLQ-C30 is composed of both multi-item scales and single-item

measures. These include five functional scales, three symptom scales, a global health status / QoL scale, and six single items. Each of the multi-item scales includes a different set of items - no item occurs in more than one scale. Severity of CP was assessed by M-ANNHEIM classification. We evaluated nutritional status (prealbumin and retinol binding protein (RBP) by immunonephelometry, fat-soluble vitamins A, D, E by HPLC and LC-MS/MS. Statistical analysis was performed via SPSSv22.

Results: Patients with pancreatic cancer had shown worst QoL, including all functional scales, symptomatic scales (fatigue, nausea, pain), dyspnoea, loss of appetite and diarrhoea. Mean levels of scale scores of physical functioning (p=0.013), role functioning (p=0.06) and dyspnoea (p=0.032) were significantly lowest in patients with PC/PR. We demonstrated significant worsening of mean levels of scale scores according to global health status and almost all functional scales and symptomatic scales/items (except of cognitive functioning, dyspnoea, insomnia, constipation, and diarrhoea) with progression of CP with significant lowest QoL in patients with advanced CP. Patients with AP without walled-off necrosis had significant overall better QoL scale scores compared to those with walled-off necrosis. In all groups of patients (CP, AP, PC/PR) we observed a tendency to better QoL assessment with nutritional status normalization. Significant differences were found mainly in the protein markers prealbumin and RBP in patients with CP and PC/PR.

Conclusion: An effort should be point at multidisciplinary approach for up-to-date strategy for patients with pancreatic disorders, focusing not only on the improvement of symptoms and nutritional status, but also on social well-being. Questionnaires on quality of life are useful clinical tools that would identify patients at risk who to be provided with therapeutic education and physical rehabilitation, behavioral support and medication.

Disclosure: Nothing to disclose

P0814 ATTAINING MORE THAN 90% PANCREATIC STONE DISINTEGRATION RATE BY USING A NEW THIRD-GENERATION SHOCKWAVE LITHOTRIPTER WITH ADDITIONAL ENDOSCOPIC LITHOTOMY

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Introduction: Multiple case reports and case series describe the successful management of pancreatic duct stones with mechanical lithotripsy (ML), electrohydraulic lithotripsy (EHL), and extracorporeal shock wave lithotripsy (ESWL). Combining ESWL with ERCP may increase the rate of complete main pancreatic duct (MPD) clearance. However, no randomized studies have compared the efficacy of ESWL with other lithotripsy modalities for MPD clearance.

Aims & Methods: To evaluate the adequate methods of pancreatic stone treatments and compare the abilities of lithotripters to fragment pancreatic stones, we retrospectively evaluated 161 cases from June 2012 to December 2018 that were performed by 8 well-trained pancreaticobiliary physicians. For the preparation management of ESWL, endoscopic pancreatic sphincterotomy (EPST) was routinely performed with ERCP. Cases complicated by abdominal complaints (exacerbation of pancreatitis, pseudocysts, and fistula), endoscopic nasal pancreatic drainage (ENPD) or endoscopic pancreatic stent (EPS) placement were initially possible. Pancreatic stones treated with endoscopic monotherapy were excluded in this study. ESWL was continued until the stone disintegration was observed. If sufficient effect was not achieved, endoscopic electrohydraulic lithotripsy (EHL) or endoscopic lithotomy using basket or grasping forceps was additionally performed. For ESWL, we used a third-generation electromagnetic shock wave lithotripter (Lithoskop, Siemens, Erlagen, Germany; group 1) from 2008 to 2016 and Modulith SLX-F2 (Storz Medical AG, Tagerwilen, Switzerland; group 2) from 2017 to 2018. ESWL disintegration and additional endoscopic lithotomy rates were evaluated and compared between the two lithotripters.

Results: In this study, 161 patients (169 stones; Lithoskop, 129 cases and Modulith, 40 cases) were evaluated. The ENPD/EPS placement success rates were 43.9% and 45.7% in groups 1 and 2, respectively, showing no significant difference between the ESWL preparations. No significant dif-

ferences were also found between the stone characteristics (stone size, computed tomography value, and number and location of stones). For the 144 stones in the MPD head, the success rates of the initial ESWL procedure were 68.1% in group 1 and 78.6% in group 2, showing no significant difference between the two lithotripters. The overall success rate with additional endoscopic lithotomy was decreased to 66.7% in group 1 and increased to 92.9% in group 2, showing a higher stone lithotomy rate using Modulith SLX-F2 and additional endoscopic treatments (p < 0.05). For the 25 stones in the MPD body, the success rate after the initial ESWL procedure was 53.9% in group 1 and 83.3% in group 2, respectively, showing no significant difference between the two lithotripters. The overall success rate with additional endoscopic lithotomy was increased to 61.5% in group 1 and 91.7% in group 2, showing no significant difference between the two treatment methods (p = 0.07). MPD head stricture was significantly associated with factors of unsuccessful additional stone lithotripsy and was the only factor of unsuccessful stone lithotripsy.

Conclusion: No significant differences were found in the disintegration rates between the two lithotripters. However, pancreatic stone disintegration rate attained more than 90% by using a Modulith SLX-F2 lithotripter with additional endoscopic lithotomy.

Disclosure: Nothing to disclose

P0815 UTILITY OF A 21-GAUGE MENGHINI TYPE BIOPSY NEEDLE FOR AN ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE BIOPSY FOR THE HISTOPATHOLOGICAL DIAGNOSIS OF AUTOIMMUNE PANCREATITIS

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Introduction: The pancreatic histology is a cardinal factor influencing a diagnosis of autoimmune pancreatitis (AIP), but the International Consensus Diagnostic Criteria (ICDC) state that it should be assessed only using surgical or core biopsy specimens. We evaluated the utility of pancreatic tissue collection using a 21-gauge Menghini type biopsy needle with an endoscopic ultrasound-guided fine needle biopsy (EUS-FNB) for the diagnosis of AIP.

Aims & Methods: From January 2015 to December 2018, 14 patients at our institution who had been diagnosed with definitive type 1 AIP (n=13) or not-definitive type 1 AIP (n=1) based on pancreatic imaging, serum IgG4 levels, and other organ involvement according to the ICDC underwent an EUS-FNB using a 21-gauge biopsy needle (EUS Sonopsy CY®; HAKKO, Nagano, Japan) originally made for a liver biopsy. No patients had type 2 AIP. After the enlarged lesion in the pancreas had been punctured, the needle was pushed forward quickly with aspiration under 10 mL of negative pressure, and then the handle of the needle was turned until the tip of the needle was confirmed to be rotated in the lesion. To reduce the contamination of blood, this procedure was repeated only three times. The male-to-female ratio of patients was 11:3, and the median age was 71 (range: 50-79) years old. Diffuse enlargement and segmental or focal enlargement of the pancreas was present in 10 (71%) and 4 (29%) patients, respectively.

Results: Adequate specimens were obtained in all patients, with a median of 4.5 (range: 2-6) punctures. Regarding the histopathological findings based on the ICDC, lymphoplasmacytic infiltration, IgG4-postive plasmacyte infiltration (>10/high-power field), storiform fibrosis, and obliterative phlebitis were detected in 9 (63%), 9 (63%), 4 (29%), and 0 patients, respectively. Consequently, 9 patients (63%) were histopathologically diagnosed with AIP (level 1 and level 2 criteria of lymphoplasmacytic sclerosing pancreatitis met by 4 [29%] and 5 [36%] patients, respectively). This histological finding contributed to a diagnosis of definitive type 1 AIP in a patient who had had not definitive type 1 AIP. Two patients (14%) who had undergone endoscopic pancreatography on the same day had procedure-related pancreatitis.

Conclusion: The 21-gauge Menghini type biopsy needle may be useful for the histopathological diagnosis of AIP because of its high recovery rate of pancreatic tissue with relatively little blood contamination.

Disclosure: Nothing to disclose

P0816 IMMUNOGLOBULIN G SUBTYPES-1 AND 2 (IGG1 AND IGG2) CAN DIFFERENTIATE BETWEEN AUTOIMMUNE PANCREATITIS WITH ASSOCIATED CHOLANGIOPATHY AND PRIMARY SCLEROSING CHOLANGITIS

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Introduction: Autoimmune pancreatitis (AIP) type 1 is part of a larger systemic disease defined by fibrosclerotic processes and elevated IgG4 and hence called IgG4-related disease (IgG4-RD). Primary sclerosing cholangitis (PSC) is a chronic cholestatic liver disease characterized by progressive destruction of the bile ducts and eventually development of biliary cirrhosis. IgG4 associated cholangiopathy (IAC) may be present at the time of AIP type 1 diagnosis or occurs later in the disease course. IgG4 is considered reliable but not ideal marker for diagnosis of AIP type 1 with reported sensitivity between 71 to 81%. It is essential to differentiate sclerosing cholangitis with AIP from primary sclerosing cholangitis (PSC) as the treatment and prognosis of the two diseases are totally different.

Aims & Methods: Based on circumstantial evidence on other IgG subclasses found elevated in autoimmune rheumatologic diseases the aim of this study was to test all IgG subclasses to assess their usefulness to differentiate AIP with IAC from PSC as the other chronic and autoimmune disease of the bile ducts. We performed retrospective analysis of patients with AIP at our outpatient clinic. Patients from the PSC registry were taken as a control group. Blood samples for the measurement of all IgG subclasses were analyzed at the time of diagnosis before the patients received corticosteroid/immunosuppressive therapy.

Results: From our patient registries, we included 142 patients where all IgG subclasses were measured, 69 with AIP type 1and 73 with PSC. Patients with AIP and IAC had higher values in IgG2 when compared to AIP alone or PSC with a high specificity (97%) and high positive predicted value (PPV=91%). In patients with normal or low IgG2 or IgG4, a high IgG1 indicated PSC.

Conclusion: IgG1 and IgG2 can distinguish patients with AIP-related cholangitis (IAC) from those with PSC. High serum IgG2 in those who are IgG/IgG4 positive and elevated IgG1 in those who have low or normal IgG2 and IgG4 indicating PSC in this context can be considered an additional aid in establishing the one condition and/or excluding the other.

Disclosure: Nothing to disclose

P0817 LUNG INVOLVEMENT IN PATIENTS WITH AUTOIMMUNE PANCREATITIS

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Introduction: Immunoglobulin G4-related disease (IgG4-RD) is a systemic immune-mediated disease characterized pathologically by the infiltration of IgG4-bearing plasma cells into involved organs. Autoimmune pancreatitis (AIP) is a form of chronic pancreatitis with a heavy lymphocytic infiltration and two distinct histopathological subtypes: lymphoplasmacytic sclerosing pancreatitis (AIP type 1) and idiopathic duct-centric pancreatitis (AIP type 2). Pulmonary involvement (including lung, pleura and mediastinum) has been reported in 12% of patients with systemic IgG4-RD presentations. Most of the epidemiological data is coming from Japan and there is a lack of information from Europe, especially from Scandinavian countries. We are presenting first results on lung involvement in patients with AIP in European population.

Aims & Methods: We performed a single-center retrospective study on a prospectively collected cohort of patients diagnosed with AIP at the outpatient clinic of the Department for Digestive Diseases at Karolinska University Hospital in Stockholm, Sweden from 2004 to 2018. Demographic and clinical data were collected from the medical charts.

Results: Eighty-seven patients with AIP were included in the study; 56.3% male and 43.7% female, average age of 50.3±19.2 years. Patients were followed for 51.7±40.6 months after the diagnosis of AIP. Majority were never smokers (60.7%). Lung involvement was diagnosed in 17 (19.5%) patients: 13 patients with asthma, 5 patients with nodular lesions, 2 patients with granulomatosis with polyangiitis and 2 patients with mediastinal lymphadenopathy (in 4 patients combination of mentioned clinical conditions were presented).

Conclusion: Lung involvement was diagnosed in 17 (19.5%) patients in AIP. Compare with other studies, our patients were younger, presentation of OOI was more often and the proportion of female was higher. There was no connection with environmental factors such as occupation of patients.

Disclosure: Nothing to disclose

P0818 IL1R1 GENE POLYMORPHISMS IN IGG4-RELATED DISEASE PATIENTS ARE ASSOCIATED WITH IGG4-RELATED PERIAORTITIS/PERIARTERITIS

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Introduction: Immunoglobulin G4-related disease (IgG4-RD) is a systemic condition characterized by high serum immunoglobulin G4 (IgG4) concentration and IgG4-bearing plasma cell infiltration in affected organs. Recently, IgG4-RD has been recognized to affect the cardiovascular system as the IgG4-related periaortitis/periarteritis,which includes the inflammatory aneurysms, lymphoplasmacytic aortitis, and aortic dissection. IgG4-related periaortitis/periarteritis show adoventia and/or tunica media thickness by IgG4-postitive plasma cells. Nearly half of the inflammatory abdominal aortic aneurysms leading to surgical treatment might be classified into IgG4-related. Therefore, it is important to predict the onset of vascular lesions at the time of diagnosis of IgG4-RD. However, the factors of onset of IgG4-related periaortitis/periarteritis are unclear.

Aims & Methods: In this study, we performed GWAS screening analysis for 124 cases of IgG4-related disease. And the association analysis was performed between in the groups with vasculitis (41) and without vasculitis (83). The vasculitis was detected by imaging findings using contrast-enhanced CT.

Results: Some SNPs in candidate genes (*CAMK2A*, *VPS13B*, *IL1R1*) showed a statistically significant correlation to the onset of vasculitis. Among them, we focused in investigation of *IL1R1* gene involved in various immune responses. We performed fine mapping of additional 8 SNPs (rs3917225, rs2287049, rs3917273, rs2160227, rs951192, rs3917318, rs7582198) with Taq-Man assays. 3minor alleles of rs951192, rs3917318 and rs7582198 showed significant correlation (p< 0.0009, OR>4) with the vasculitis group as the additive model.

Conclusion: These results suggest that *IL1R1* gene polymorphisms are related with the onset of IgG4-related periaortitis/periarteritis.

Disclosure: Nothing to disclose

P0819 PREDICTION OF PANCREATIC ATROPHY AFTER STEROID THERAPY AND THE EXACERBATION OF DIABETES USING EQUILIBRIUM CONTRAST CT IMAGING IN AUTOIMMUNE PANCREATITIS

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Introduction: Previously we reported pancreatic atrophy after the beginning of steroid therapy was associated with diabetes control worsening and incidence of new onset of diabetes in patients with autoimmune pancreatitis (AIP). However, the predictor for pancreatic atrophy and the exacerbation of diabetes after steroid therapy remains unknown.

Aims & Methods: To evaluate the role of equilibrium computed tomographic (CT) imaging for the prediction of pancreatic atrophy after steroid therapy. Forty-six steroid treated AIP patients, who underwent CE-CT examinations before and after steroid therapy, were included in this study during December 2005 to December 2017. CT attenuation (Hounsfield units [HU]) values in noncontrast (NC) and equilibrium phase (EP) images were measured by placing three regions of interest (ROIs) from the pancreas swelling at the diagnosis of AIP. The incidence of the pancreatic atrophy and diabetes exacerbation after steroid therapy was estimated by the following three parameters in CE-CT before steroid therapy:

1) HU values in NC images;

2) HU values in EP images; and

3) subtracted HU values between NC and EP images.

Pancreatic atrophy after steroid therapy was defined to be present when the width of the pancreatic body was less than 10 mm. Pancreatic volume of whole pancreas was measured in CE-CT before and after steroid therapy, and volume reduction rate was also calculated.

Results: Pancreatic atrophy was observed in 14 patients and not in 32 patients after the steroid therapy. The volume of the whole pancreas after steroid therapy correlated with the diameter of the pancreatic body (r=0.59, P<0.0001). Volume reduction rate of whole pancreas was also correlated with pancreatic body diameter (r=-0.49, P=0.001). Pancreatic atrophy was associated with the thickness of pancreatic body on HU values in EP and subtracted images (114.5±12.8 vs 99.5±11.1; P=0.0002, 70.9±14.72 vs 57.2±13.1: P=0.003) before steroid therapy, but not with HU values in NC images (P=0.42). HU values in EP and subtracted images were correlated with exacerbation of diabetes (P=0.0085, P=0.04). In addition, pancreatic body diameter, pancreas volume, and volume reduction rate after steroid therapy were associated with the exacerbation of diabetes (P=0.0003, P=0.002, P=0.0006).

Conclusion: Equilibrium contrast and subtracted CT imaging at the diagnosis of AIP would be a potential predictor for pancreatic atrophy and the exacerbation of diabetes after steroid therapy.

Disclosure: Nothing to disclose

P0820 RITUXIMAB FOR THE TREATMENT OF 15 PATIENTS WITH RECURRENT TYPE 1 AUTOIMMUNE PANCREATITIS

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Introduction: Autoimmune pancreatitis (AIP) is an immunemediated fibro-inflammatory disease of the pancreas. It frequently shows an incomplete response to glucocorticoids and immunosuppressants. Bcell depletion is

an effective treatment for type 1 AIP. Rituximab (RTX) seems to be an appealing alternative to conventional therapies for nonresponder or relapser patients.

Aims & Methods: The aim of this study was to assess the efficacy of RTX in type 1 AIP in a prospective panel study.15 patients with relapsing type 1 AIP after conventional steroid therapy and not responding or intolerant to Azatioprine, were treated with 4 doses of RTX (1000 mg each) from February 2013 to December 2017. Diagnosis of type 1 AIP was achieved with ICDC criteria. 14 of them had extrapancreatic involvement. Disease response was measured by IgG4Related Disease Responder Index (IgG4RD RI) and by serum IgG4 levels.

Results: Disease remission was achieved by 14 of the subjects (93%). The baseline IgG4RD RI declines from a mean of 13.4 (range 721) to 1.5 (range 110) 6 months after the treatment (p< 0.001). Serum IgG4 levels decreased from 492 mg/dl (range 1181260) to 92.5 mg/dl (range 37180) (p< 0.001). The 36% of patients relapsed (5/15) after 28 months of followup (range 1539). The follow up was significantly lower in patients in complete remission (10, range 320) compared with those who relapsed (36, range 1746) (p=0.005). Two mild adverse infuse reactions associate with the use of RTX were reported (13%).

Conclusion: RTX seems to be effective in type 1 AIP. Overall, RTX treatment was well tolerated with minimal side effects. We need more trials to evaluate the long term safety profile.

Disclosure: Nothing to disclose

P0821 PANCREATIC ATROPHY AND DIABETES MELLITUS IN PATIENTS WITH AUTOIMMUNE PANCREATITIS

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Introduction: Autoimmune pancreatitis (AIP) is an inflammation of the pancreas which was first described in 1961 but received its current name in 1995. Since it was detected there have been several different diagnostic criteria for AIP, the most recent being the International Consensus Diagnostic Criteria (ICDC) for AIP which were proposed in 2011. The first-line treatment for AIP typically consists of a steroid treatment; a response to steroid treatment also forms part of the diagnostic criteria for AIP. Pancreatic atrophy has been observed in several patients with AIP and it has been discussed whether the development of atrophy is aggravated by the treatment with steroids. Another disease which has been associated with AIP is diabetes mellitus (DM), the prevalence ranging from 12%-83.3%. Although AIP can be seen as a type of chronic pancreatitis (CP) and patients with AIP also can develop signs of CP, there have only been very few studies that have compared the course of the two diseases with each other.

Aims & Methods: Aim of our study was to compare these two groups with each other in regard to the rate at which these patients developed pancreatic atrophy and DM. For this study we collected the data of 105 patients who had come to the Gastrocentrum of the Karolinska University Hospital for AIP and CP and who in the course of time had developed an atrophy of the pancreas. Two patients were excluded because they lacked follow-up. The imaging which best coincided with the patients time of diagnosis was determined as month zero and all follow-up imaging evaluated to determine when the patient developed an atrophy, classified as first or second degree. Furthermore we determined if and when the patient had developed DM and looked at the measures of fecal elastase 1(FE-1) as parameter for the exocrine function.

Results: The study showed that patients with AIP developed pancreatic atrophy significantly faster than patients with CP. Furthermore, the patients with AIP who had received steroid treatment had a significantly quicker development of atrophy 2nd degree compared to patients with AIP who did not receive steroid treatment. We also found that the time to development of DM was significantly shorter in the group of patients with AIP when compared with CP. Furthermore, at the time of diagnosis, patients with AIP had significantly lower values of fecal elastasis-1 than patients with CP.

Conclusion: Patients with AIP develop pancreatic atrophy and DM significantly quicker than patients with CP of other etiology. Steroid treatment may aggravate the development of pancreatic atrophy in patients with AIP.

Disclosure: Nothing to disclose

P0822 SURVIVAL OF RESECTABLE PANCREATIC CANCER: THE IMPACT OF POST-OPERATIVE CHEMOTHERAPY

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Introduction: Surgical resection with chemotherapy remains the preferred treatment for pancreatic ductal adenocarcinoma (PDA). Data remains limited regarding survival rates for resectable PDA with adjuvant chemotherapy treatment when managed by a multidisciplinary team. The objective of this study is to assess survival rates and outcomes of adjuvant chemotherapy for resectable PDA following presentation at a multidisciplinary pancreas conference (MDPC).

Aims & Methods: All patients presented at a tertiary care center from April 2013 to August 2016 with PDA were discussed at the MDPC and were followed prospectively until November 2018. Patients were included in the study if the MDPC determined they had resectable PDA. Resectable PDA was defined as no involvement or abutment of regional vascular structures and no extra-pancreatic disease as determined by radiologic imaging. Patients underwent attempted upfront surgery and were followed until the end of the study timepoint.

Results: A total of 278 patients were presented at the MDPC during the study period. The MDPC determined that 91 patients met criteria for resectable disease and 70 were fit for surgery. A total of 64 patients underwent successful surgery, as 6 patients had metastatic disease upon laparotomy (91.4% resection rate). Of the 64 patients that underwent surgery, 37 (58%) started adjuvant chemotherapy with only 16 (25%) completing treatment. Patients who completed their adjuvant chemotherapy had a significantly prolonged survival time versus those who did not complete all cycles (36.9 months vs. 18.8 months, P = 0.014) (Figure 1). Reasons for patients who did not receive adjuvant chemotherapy included debilitation and post-operative complications (Table 1). Patients receiving any adjuvant chemotherapy had a median overall survival of 34.8 months versus a median overall survival of 17.1 months for those that did not (P = 0.43). Each additional cycle of chemotherapy conferred a relative survival advantage of 13.7% (P = 0.016).

Reasons for Not Starting Chemotherapy	Number of Occurrences
Post-Op Complications	7
Debilitation/Not Tolerating	5
ICU Admission	3
Metastatic Disease	3
Loss of follow-up	2
Prolonged Recovery	1
Surgically Curative	1
Unknown	5
Reasons for Not Completing Chemotherapy	Number of Occurrences
Side effects	8
Metastatic Disease	4
Debilitation	3
Not Tolerable	1
Unknown	5

[Failed Chemotherapy]

Conclusion: Our data suggest that successful completion of adjuvant chemotherapy has better survival outcomes, specifically for those who completed 4-6 cycles versus those that completed 1-3 cycles. Each successive

cycle following resection provides a significant survival advantage of nearly 14%. Given that only 25% of patients in this study completed adjuvant chemotherapy due to debilitation, operative complications, family issues, etc., consideration should be given for optimizing fitness or providing preoperative neoadjuvant therapy in resectable PDA. Further studies are warranted.

Disclosure: Nothing to disclose

P0823 MR DIFFUSION-WEIGHTED IMAGING FOR PANCREATIC TUMOR SCREENING – SENSITIVITY, SPECIFICITY AND IMPROVEMENTS IN COMBINATION WITH MRCP

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Introduction: Although application of MR diffusion-weighted imaging (DWI) for pancreatic cancer diagnosis has spread in recent years, its sensitivity and specificity for pancreatic tumors has not been elucidated. Furthermore, results of its use in combination with magnetic resonance cholangiopancreatography (MRCP) remain unclear.
Aims & Methods: We attempted to clarify sensitivity and specificity, as well as positive and negative predictive values of DWI for pancreatic tumors. In addition, each of those 4 factors were examined with MRCP, and combined use of DWI and MRCP. Of 671 cases that underwent DWI and MRCP examinations from June 2017 to March 2019 at our hospital, 203 also evaluated by a pathological examination or contrast-enhanced endoscopic ultrasound sonography were retrospectively reviewed. Those included a case with a solid pancreatic mass in which both endoscopic ultrasound fine-needle aspiration biopsy (EUS-FNA) and surgery were rejected. Therefore,202 patients were eligible for this study. Cases positive for a pancreatic tumor were defined based on pathological diagnosis following surgical excision, or EUS-FNA or pancreatic fluid cytology findings. On the other hand, those negative for a pancreatic tumor were defined when no solid tumor was detected by contrast-enhanced EUS, or cases with a solid mass detected by contrast-enhanced EUS ultimately denied based on EUS-FNA or pancreatic juice cytology findings. DWI was performed with a b-value of 800 and cases with high signal were defined as DWI-positive. MRCP-positive was determined when localized main pancreatic duct stenosis accompanied by caudal pancreatic duct dilation were detected by MRCP.
Results: Among the 202 cases, 15 had pancreatic tumors (invasive ductal carcinoma, 11; PanIN-3, 1, intraductal papillary mucinous neoplasia high grade (IPMN HGD), 3; neuroendocrine tumor (NET) G1, 1). DWI showed a sensitivity of 93.3%, specificity of 94.1%, positive predictive value of 56.0%, and negative predictive value of 99.4%, while those values for MRCP alone were 86.7%, 98.9%, 86.7%, and 98.9%, respectively, and for the combination of DWI and MRCP were 100%, 94.1%, 57.7%, and 100%, respectively. Of the 15 cases with a pancreatic tumor, all but 1 (PanIN-3) were revealed by DWI, including a 5-mm NETG1 tumor. The PanIN-3 case not seen in DWI findings was visualized by MRCP as localized main pancreatic duct stenosis with dilation of the caudal main pancreatic duct.
Conclusion: For pancreatic tumor diagnosis, DWI was found to be more sensitive than MRCP, while those in combination resulted in increased sensitivity. DWI was able to reveal lesions at the edge of the pancreas not shown by MRCP. Based on our findings, we consider that the combination of DWI and MRCP is a rational protocol. However, the positive predictive value of DWI is low and false positive findings are often noted, thus additional imaging methods such as EUS and contrast-enhanced CT are necessary for qualitative diagnosis.
Disclosure: Nothing to disclose

P0824 PROGRAMMED DEATH-LIGAND 1 STATUS PROVIDED BY ENDOSCOPIC ULTRASOUND-GUIDED FINE-NEEDLE BIOPSIES AS A PREDICTOR OF PROGNOSIS IN PATIENTS WITH PANCREATIC DUCTAL ADENOCARCINOMAS (SUCCESS)

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Introduction: Pancreatic ductal adenocarcinoma (PDAC) has a suboptimal response to systemic treatments with an impact on survival due to its power to evade host immune surveillance (1). The binding of Programmed-cell Death 1 (PD-1) to its ligand Programmed-cell Death Ligand 1 (PD-L1) gives rise to a major immune tolerance mechanism (2). Thus, PD-L1 hyper-expression induced by tumor cells generates T cell apoptosis, escaping the tumor from immune surveillance. In addition, evaluation of MMR-D status is equally important, considering FDA approval of PD-1 inhibitor, pembrolizumab, for the treatment of unresectable or metastatic, microsatellite instability-high (MSI-H) or MMR-D PDAC that have progressed following prior treatment (3).
Aims & Methods: Considering that PDAC PD-L1 expression quantification is limited to surgical resection due to the current IHC test requirement for a histologic rather than a cytologic evaluation, (4) the objectives of the project include the assessment of tumor PD-L1/MMR-D expression in patients with PDAC using Endoscopic Ultrasound-Fine Needle Biopsy (EUS-FNB) samples.
Results: At this moment, in this prospective, non-randomized, single-arm, interventional study we
enrolled 20 patients with suspicion of pancreatic masses who performed EUS-FNB for
confirmation of diagnosis. All patients have had a confirmed diagnosis of PDAC and
subsequently IHC was made for PD-L1/MMR-D testing. Through EUS-FNB, PD-L1/MMR-D
status was determined in all cases. PD-L1 positive rate measured by immunohistochemistry was 20% while MMR-D mutation was absent in all cases. In addition, PD-L1 status was positive in 2 patients with a PDAC T4 stage.
Conclusion: EUS-FNB can successfully determine primary pancreas malignancy PD-L1/MMR-D status. PD-L1 expression levels represent a poor prognosis factor in PDAC patients
References: 1.Delitto D, Perez C, Han S, et al. Downstream mediators of the intratumoral interferon response suppress antitumor immunity, induce gemcitabine resistance and associate with poor survival in human pancreatic cancer. Cancer Immunol Immunother 2015;64(12):1553-1563. 2. Sloot S, Chen YA, Zhao X, et al. Improved survival of patients with melanoma brain metastases in the era of targeted BRAF and immune checkpoint therapies. Cancer 2018;124:297-305. 3. Yamaki S, Yanagimoto H, Tsuta K, et al. PD-L1 expression in pancreatic ductal adenocarcinoma is a poor prognostic factor in patients with high CD8+ tumor-infiltrating lymphocytes: highly sensitive detection using phosphor-integrated dot staining. Int J Clin Oncol 2017;22:726-733. 4. Tessier-Cloutier B, Kalloger SE, Al-Kandari M, et al. Programmed cell death ligand 1 cut-point is associated with reduced disease specific survival in resected pancreatic ductal adenocarcinoma. BMC Cancer 2017;17:618.
Disclosure: Nothing to disclose

P0825 PANCREATIC CANCER IN LIVER TRANSPLANT RECIPIENTS

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Introduction: The chronic use of immunosuppressive agents in liver transplant recipients increases the long-term risk of malignancy (including gastrointestinal cancers), compared with that of general population.

Aims & Methods: The purpose of our study was to investigate incidence and characteristic of pancreatic cancer in liver transplant recipients. We performed a retrospective analysis of medical records of all adult patients who underwent liver transplantation in our center between years 1996 and 2017. All patients were treated by combination of calcineurin inhibitors and mycophenolate mofetil with or without concomitant corticosteroids.

Results: In examined period, one thousand, three hundred fifty-two adult patients underwent liver transplantation in our center; the median follow-up was 60 (1-276) months. Adenocarcinoma of the pancreas was diagnosed in five patients (0.4%, SIR 1.76), four men and one woman. Average age of patients diagnosed with pancreatic cancer was 61 (56-67) years, the mean period between liver transplantation and occurrence of malignancy was 54 (26-136) months. Indications for liver transplantation were alcoholic liver cirrhosis (2x), overlap syndrome of primary sclerosing cholangitis and autoimmune hepatitis, liver cirrhosis due to chronic HCV infection and secondary sclerosing cholangitis. Four of five patients were non-smokers; the only smoker had tumor duplicity (lung cancer). Two patients were diabetics; one of them was diagnosed with new-onset DM six months prior to finding of cancer. One patient had chronic pancreatitis. One patient was diagnosed with stage IB cancer, all the others with stage IIB. Three patients underwent surgical treatment. Median overall survival was 3 (1-30) months, in resected group it was 12 (1-30) months.

Conclusion: In our study, liver transplant recipients had higher incidence of pancreatic cancer compared to that of general population. They were diagnosed in younger age and with earlier stage of the disease. Despite that, the prognosis was unfavorable.

Disclosure: Nothing to disclose

P0826 SIGNIFICANCE OF IN VITRO PHOTODYNAMIC CYTODIAGNOSIS USING 5-AMINOLEVULINIC ACID IN SOLID PANCREATIC TUMORS EXTRACTED BY ENDOSCOPIC ULTRASOUND-GUIDED FINE-NEEDLE ASPIRATION

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Introduction: Recently photodynamic diagnosis using 5-aminolevulinic acid (5-ALA) has been gaining attention in diagnosing neoplastic diseases in the field of urology.

In the present study, *in vitro* method of photodynamic cytodiagnosis (PDCD) using the reagent 5-ALA in the cytodiagnosis of solid pancreatic tumors was attempted to develop and the accuracy of PDCD for malignancy was assessed.

Aims & Methods: EUS-FNA was performed for patients with solid pancreatic tumors at Osaka Rosai Hospital from September 2015 to March 2018. Samples were diagnosd independently by conventional cytology and PDCD. The definitive diagnosis of benign or malignant diseases was evaluated with the histopathological examinations on surgical specimens. In patients who did not undergo surgery, the final diagnosis was evaluated with the clinical, radiological, and serological evaluation during follow-up over 6 month as well as the histopathological examinations on cell blocks. ALA is the natural precursor in the heme biosynthetic pathway that induces the intracellular accumulation of endogenous protoporphyrin IX (PPIX) when provided exogenously in large excess. It is metabolized into PPIX in the mitochondria and is characterized by excessive intracellular accumulation in cancer cells. Because PPIX is overproduced in cancer cells, when stimulated by blue light, ALA-induced PPIX can be applied as a red fluorescence detection marker for photodynamic diagnosis (PDD).

Results: A total of 53 patients with solid pancreatic tumors (35 males and 18 females, average age: 70.2 years old [range, 38-89 years old]) were enrolled. The definitive diagnosis were 7 benign lesions (2 with chronic pancreatitis and 5 with autoimmune pancreatitis) and 46 malignant lesions (41 with pancreatic ductal carcinoma, 4 with pancreatic acinar cell carcinoma, and 1 with neuroendocrine tumor). With regard for malignant patients with class 4 and 5 disease, the diagnoses of conventional cytology had a sensitivity of 93.5% (43/46), a specificity of 85.7% (6/7), a positive predictive value of 97.7% (43/44). By *in vitro* PDCD method, the reddish fluorescence was detected in the cell samples, which was judged as cancer cells. PDCD showed a sensitivity of 91.3% (42/46) and specificity of 100%

(7/7), while conventional cytology showed a sensitivity of 93.5% (43/46) and specificity of 85.7% (6/7). Two patients are successfully diagnosed as malignancy by only PDCD method, while four patients were false-negative, two of which had pancreas cancer with formy gland pattern. In formy gland cells, PPIX is poorly produced since there are no mitochondria in these cells.

Conclusion: *In vitro* PDCD performed using the 5-ALA method can effectively and safely identify a diagnosis of pancreatic cancer without requiring an expert pathologist. The sensitivity of this technique could be increased in the diagnosis of pancreatic malignancy by combining it with the conventional method.

Disclosure: Nothing to disclose

P0827 DEPRESSION AND PANCREATIC CANCER, HELP IS ON ITS WAY!

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Introduction: Pancreatic cancer (PaC) is the third leading cause of all cancer related deaths with a high mortality rate and poor prognosis. Identifying risk factors and symptoms help improve the clinical management and outcomes of PaC. Depression often occurs in patients diagnosed with cancer, and is prevalent in up to 50-78% of patients with PaC. This study aims to evaluate demographical trends and mortality rates in patients diagnosed with PaC with preceding and subsequent depressive disorder. Additionally, the role of mental health professionals and its effect on survival is observed.

Aims & Methods: A longitudinal population-based study, using an IBM platform called Explorys was used to collect de-identified data. Over 60 million patients, spanning nationally in over 40 healthcare systems' electronic medical records are in this cloud-based, HIPPA-enabled platform. Data was obtained using SNOMED and ICD-9 code criteria with search terms "malignant tumor of the pancreas" and "depressive disorder." A temporal relationship was established to delineate relationship of depression diagnosis with PaC. Demographical data, mortality rates, depressive disorder symptoms and the role of mental health professionals (psychiatrist, psychologist, and behavioral professional) was observed and reported.

	Depression and PaC [N = 11,730]	Control [N = 5,290,190]	Odds Ratio [95% CI]	P
Male, n [%]	4,890 [41.7]	1,707,420 [32.3]	1.50 [1.45, 1.56]	< 0.0001
Race, n [%]				
Caucasian	9,440 [80.5]	4,187,610 [79.2]	1.09 [1.04, 1.14]	0.0004
African-American	1,420 [12.1]	548,350 [10.4]	1.19 [1.13, 1.26]	< 0.0001
Hispanic	90 [0.8]	50,910 [1]	0.80 [0.65, 0.98]	0.0310
Age, n [%]				
18-65	4,030 [34.4]	3,674,020 [69.4]	0.23 [0.22, 0.24]	< 0.0001
> 65	7,650 [65.2]	1,523,850 [28.8]	4.63 [4.46, 4.81]	< 0.0001
Findings, n [%]				
Anxiety	5,080 [43.3]	2,200,320 [41.6]	1.07 [1.03, 1.11]	0.0002
Sleep Disorder	4,470 [38.1]	1,613,450 [30.5]	1.40 [1.35, 1.46]	< 0.0001
Agitation	170 [1.4]	40,270 [0.8]	1.92 [1.85, 1.99]	< 0.0001
Suicidal Thoughts	380 [3.2]	388,670 [7.3]	0.42 [0.41, 0.44]	< 0.0001
Weight Loss	3,580 [30.5]	353,210 [6.7]	6.14 [5.92, 6.37]	< 0.0001
Fatigue	5,470 [46.6]	1,463,100 [27.7]	2.29 [2.20, 2.37]	< 0.0001

[Depression Preceding Pancreatic Cancer]

Results: A total of 58,140 patients were found to have diagnosis of PaC, of which 11,730 (20.2%) had prior diagnosis of depression, and 11,690 (20.1%) had subsequent diagnosis of depression. Incidence was higher in females, Caucasians, African-Americans, and younger patients (18 - 65). All-cause mortality was higher in patients with depressive disorder and PaC vs. PaC

patients without depression (P < 0.001). Patients with PaC and depressive disorder that were referred to a mental health professional had a lower rate of all-cause mortality when compared to patients without a referral (P = 0.009). Additionally, 83.1% of patients had a diagnosis of PaC within 6 months of their depressive disorder diagnosis. Over 90% had diagnosis of PaC within 3 years. Preceding symptoms of anxiety, sleep disorder, agitation, and weight loss were strongly associated with higher rates of PaC.

Conclusion: Identifying and treating symptoms of PaC potentially helps improve outcomes and survival. This study shows that depressive disorder is under diagnosed in PaC and leads to higher mortality. Identifying clinical signs and symptoms of depression may help diagnose PaC earlier, and treatment improves survival. High vigilance is encouraged within the first 3 years of depressive disorder diagnosis for those at risk of pancreatic cancer. Referral to mental health care professionals improves survival in patients with PaC, therefore referrals or screenings should be considered as part of a multidisciplinary team management in pancreas cancer.

Disclosure: Nothing to disclose

P0828 TREATMENT AND SURVIVAL OF PANCREATIC CANCER RECURRENCE IN THE NETHERLANDS - PRELIMINARY RESULTS OF A NATIONWIDE ANALYSIS

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Introduction: Despite the high rate of recurrence after resection of pancreatic ductal adenocarcinoma (PDAC), Dutch and European guidelines for standardized follow-up are lacking. This has led to different surveillance strategies in daily clinical practice. In this context, data on the exact incidence, symptomatology, treatment and survival following PDAC recurrence in the Netherlands are lacking.
Aims & Methods: A multicenter retrospective observational cohort study was performed in 17 Dutch pancreatic cancer centers. Data from the first 10 centers were used for preliminary analyses. All patients registered in the prospective Dutch Pancreatic Clinical Audit who underwent PDAC resection (2014-2016) were included. Additional data on follow-up and treatment of PDAC recurrence were collected. Mean survival was evaluated using Kaplan-Meier curves. Multivariable Cox regression was performed to compare survival rates between patients who underwent treatment for recurrence and patients who received best supportive care. Survival analyses were stratified for symptomatic and asymptomatic patients.
Results: 401 resected patients with a median follow-up of 15 months (IQR 9-25 months) were analyzed. A total of 305 patients (76%) developed PDAC recurrence at a median follow-up of 9 months (IQR 6-15 months). Median overall survival in these patients was 13 months (IQR 9-21 months). In total, 91 patients (30%) underwent treatment for PDAC recurrence. Treatment was independently associated with longer survival, in both symptomatic patients (HR0.16 (95%CI 0.09-0.30); P< 0.001) and asymptomatic patients (HR0.16 (95%CI 0.04-0.63); P=0.01). Of 57 patients with asymptomatic recurrence, 25 patients (44%) received palliative treatment, as compared with 63 (29%) of 214 symptomatic patients (P=0.04).
Conclusion: Treatment of both asymptomatic and symptomatic PDAC recurrence seems independently associated with improved survival. As these results are subjected to confounding by indication, lead-time bias and guarantee-time bias, prospective studies are needed to determine the true value of standardized follow-up and treatment of PDAC recurrence, accounting for psychosocial and economic aspects.
Disclosure: Nothing to disclose

P0829 REDUCTION OF ROCK2 GENE EXPRESSION CORRELATES WITH LIVER METASTASIS AS AN INDEX OF METASTASIS FOR INVASIVE DUCTAL CARCINOMA OF THE PANCREAS

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Introduction: Although resections for invasive ductal carcinoma of the pancreas (IDCP) are expected to leave no residual carcinoma (R0), the 5-year survival rate is only 37.4% [1]. The cause of the poor prognosis after surgical resection of IDCP is recurrent carcinoma. Recurrent sites after pancreatic resection of IDCP are usually found in the liver and local site. Notably, survival of patients with liver metastasis (LM) is significantly shorter than that of patients with local site recurrences [2]. Effective diagnosis and treatment of LM are primary steps to improve IDCP prognoses. We found that the median numbers of invaded veins and percentage of invaded veins/total number of veins in the IDCP area were significantly higher in the LM group (UEGW 2016, [3]). However, there remains the need to identify gene mutations related to liver metastasisfor possible gene therapies. Various studies have shown that RNA microarray analysis improves the diagnosis and risk stratification of many cancers, but few studies have investigated the potential for liver metastasis of IDCP. In this study, we analyzed potential gene mutations involved in liver metastasis of IDCP by RNA microarray. Furthermore,immunohistochemistry wasperformed using diagnosed sections.
Aims & Methods: Of 402 patients who were diagnosed with IDCP, 21 (5.2%) had tumors with pTS1. The follow-up period of the 21 patients was 6 monthsto 25 years. All patients underwent anR0 resection. Handling of the surgical specimensand assessment of vascular permeation by the carcinoma were performed as described previously [4]. Clinicopathological factors were assessed according to the Classification of Pancreatic Carcinoma(4th English edition)by the Japan Pancreas Society. Messenger RNA was obtained from formalin fixed, paraffin-embedded pancreatic sections. RNA harvested from resected pancreatic cancers was hybridized to RNA microarrays. Immunohistochemical staining was also performed. The antibody clone and dilution were ROCK2 (Gene Tex, USA) and 1:500, respectively.
Results: The small tumour group (n=21) included 12 malesand ninefemale-saged 51-80years. Five patients died because ofliver metastasis (LM group, n=5), and 12 patients survivedwithout recurrence. The other patients died of non-pancreatic desease. We searched for gene mutation groups correlated to liver metastasis of IDCP, such as the vascular smooth muscle contract group, pathway in cancer group, Wnt signal group,and focal adhesion group. Significant reduction of ROCK2 gene expressionwas a common occurrence inthe four groups (p=0.013). Moreover, reductionof ROCK2 expression indiagnosed sectionswas foundin all cases of LM, but not in non-LM patients (p=0.009).
Conclusion: IDCP patients with reductionof ROCK2 gene expression have thepotential for liver metastasis regardless of R0 resectioning of IDCP.
References: [1]Pancreatic cancer registry report 2007. Japan Pancreas Society http://doi.org/10.2958/suizo.22.e239-e247 [2]Westerdahl J, Andrén-Sandberg A, Ihse I. Recurrence of exocrine pancreatic cancer-local or hepatic? Hepatogastroenterology 1993; 40: 384-7 [3] Hamada Y, Nakayama Y. Aggressive venous invasion in the area of carcinoma correlates with liver metastasis as an index of metastasis for invasive ductal carcinoma of the pancreas. Pancreatology 17; 951-955: 2017 [3] Nakayama Y, Inoue H, Hamada Y, et al. Intraductal tubular adenoma of the pancreas, pyloric gland type: a clinicopathologic and immunohistochemical study of 6 cases. Am J Surg Pathol. 29 ;607-616: 2005
Disclosure: Nothing to disclose

P0830 INITIATION OF ORAL FEEDING EARLY POSTOPERATIVELY DOES NOT INCREASE THE INCIDENCE OF COMPLICATIONS AFTER PANCREATODUODENECTOMY FOR PANCREATIC CANCER

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Introduction: Pancreatoduodenectomy (PD) is associated with significant incidence of morbidity, including postoperative pancreatic and biliary fistula (POPF and POBF), delayed gastric emptying (DGE), and other major and minor postoperative complications. These affecting the need and modality of nutritional support and prolongs hospital stay.[1,2] The reluctance to initiate early oral feeding arises from the fear of an increased risk for postoperative complications.[3,4]

Aims & Methods: Aim of this study was to evaluate the influence of early per oral food intake on development of postoperative complication after PD. This prospective observational study included 72 patients underwent PD due to pancreatic cancer. Patients were divided in 2 groups regarding time of initiation of solid per oral food intake (group 1 from 3-5 and group 2 >5 postoperative day). The groups were compared in relation to the occurrence of POPF, POBF, DGE and the Clavien-Dindo (CD) grade.

Results: The group 1 included 24(33%), and the group 2 48(67%) patients. There were no difference in age (p=1), gender (p=0.99), ASA score (p=1) and intraoperative blood loss (p=0.74) between groups. Duration of surgery was shorter in the group 2 (p=0.02), where 39(81%) patients underwent pylorus preserving PD versus 9(37%) patients with standard Whipple procedure in group 1 (p=0.001). POPF (grade A to C) occurred in 15(20%) patients, and clinical relevant POPF (grade B and C) occurred in 7(9.7%) patients. POBF occurred in 6(8%) patients and DGE was present in 16(22%) patients, respectively. POPF (grade A to C) developed in 5(21%) patients in group 1 and 10(21%) patients in group 2, (p=1). POPF (grade B and C) developed in 3(12.5%) patients in group 1 and 4(8.3%) patients in group 2, (p=0.62). POBF occured in 0 patients in group 1 and 6(12%) patients in group 2, (p=0.17). One (4%) patient in group 1 experienced DGE and 15(31%) patients in group 2, (p=0.001). CD grade ≥3 had 4(17%) patients in group 1 and 21(44%) patients in group 2, (p=0.001). The presence of CD grade ≥3 was associate with delayed initiation of per oral food intake (p=0.009). Significant correlation between CD grade and time of initiation of per oral food intake was found (p< 0.001).

Conclusion: Early initiation of oral feeding in patients underwent PD had no impact on POPF and POBP occurrence. Delayed initiation of per oral food intake was associated with the presence of DGE and CD grade ≥3.

	Total n=72	Group 1 (n=24)	Group 2 (n=48)	P
POPF n(%)	15 (20)	5 (21)	10 (21)	1.000
POBF n(%)	6 (8)	0	6 (12)	0.169
DGE n(%)	16 (22)	1 (4)	15 (31)	<0.001
CD grade n(%)				
0	27 (38)	16 (66)	11 (23)	<0.001
1	14 (19)	3 (13)	11 (23)	0.002
2	6 (8)	1 (4)	5 (10)	0.017
≥3	25 (35)	4 (17)	21 (44)	<0.001

[Table 1. Difference in postoperative complications between groups]

References: 1. Gerritsen A, Wennink RA, Besselink MG, van Santvoort HC, Tseng DS, Steenhagen E, Borel Rinkes IH, Molenaar IQ. Early oral feeding after pancreatoduodenectomy enhances recovery without increasing morbidity. HPB (Oxford). 2014 Jul;16(7):656-64 2. Braga M, Pecorelli N, Ariotti R, Capretti G, Greco M, Balzano G, Castoldi R, Beretta L. Enhanced recovery after surgery pathway in patients undergoing pancreaticoduodenectomy. World J Surg. 2014 Nov;38(11):2960-6 3. Lassen K, Coolsen MM, Slim K, Carli F, de Aguilar-Nascimento JE, Schäfer M, Parks RW, Fearon KC, Lobo DN, Demartines N, Braga M, Ljungqvist O, Dejong CH; ERAS® Society; European Society for Clinical Nutrition and Metabolism; International Association for Surgical Metabolism and Nutrition. Guidelines for perioperative care for pancreaticoduodenectomy: Enhanced Recovery After Surgery (ERAS®) Society recommendations. Clin Nutr. 2012 Dec;31(6):817-30 4. Wu W, Hong X, Fu L, Liu S, You L, Zhou L, et al. The Effect of Pylorus Removal on Delayed Gastric Emptying after Pancreaticoduodenectomy: A Meta-Analysis of 2,599 Patients. PLoS ONE 2014;9(10): e108380.
Disclosure: Nothing to disclose

Endoscopy and Imaging II
09:00-17:00 / Poster Exhibition - Hall 7

P0831 SAFETY AND EFFICACY OF THE THULIUM AND ERBIUM LASER SYSTEM ON BLEEDING VASCULAR LESIONS OF THE GI TRACT: RESULTS FROM THE FIRST REAL-LIFE MULTICENTRE STUDY

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Introduction: Recent pilot studies assessed the feasibility of the Thulium and Erbium laser system (TELS) for endoscopic haemostasis, ablation and resection. Herein, we investigated for the first time ever, the safety and efficacy of endoscopic treatment with TELS in patients with gastrointestinal bleeding due to vascular lesions.

Aims & Methods: Consecutive patients treated with TELS for chronic gastrointestinal bleeding with moderate/severe anaemia due to vascular lesions were enrolled in two Italian centres between March 2016 and October 2018.

Technical success and safety as established by the ASGE Lexicon, were defined as primary endpoints.

As secondary endpoints, we assessed the biological success comparing the lowest haemoglobin values ±1 month prior to and after treatment, along with the need of packed red blood cells (PRB) transfusions ±6 month prior to and after treatment. For gastric antral vascular ectasia (GAVE), a new scoring system was proposed to evaluate pre/post-treatment endoscopic severity by assessing both mucosal involvement (< 30%=+1, 30-50%=+2, >50%=+3), and presence of bleeding (traces of blood=+3, active=+5). For each procedure, image/video documentations and TELS technical parameters (i.e., lasing time, power output, energy employed) were digitally recorded. Student paired t-test was performed.

Results: Twenty-six patients (20 men; range 48-91 years) underwent 32 endoscopic TELS sessions for the treatment of angioectasias (14/26), GAVE (9/26), and RP (3/26). All procedures resulted in a complication-free technical success, thereby reaching the primary study endpoints. Haemoglobin values showed a significant rise along with a decreased need of PRB transfusions. The median value of GAVE endoscopic severity remarkably improved within a six-month follow-up.

TELS endoscopic treatments (for each vascular lesion type)	32 (13 for GAVE; 14 for Angioectasia; 5 for RP)
Complication-free (any degree of adverse event) technical success	32/32
Δ Lowest Hb ± 1month (30/32 procedures*)	+1.58 g/dl (95%CI = 0.93-2.23, p-value <0.001)
Δ PRB ± 6months (30/32 procedures*)	-1.8 units (95CI% = -2.8--0.8; p-value <0.001)
GAVE endoscopic severity (9/14 procedures*)	5 to 2

[Results - Ongoing follow-up data*]

Conclusion: This multicentre study conducted in real-life setting suggests that TELS is a safe and effective tool for the endoscopic treatment of patients with gastrointestinal bleeding caused by various types of superficial vascular lesions.
Disclosure: Nothing to disclose

P0832 PERCUTANEOUS TRANSESOPHAGEAL GASTROTUBING (PTEG) –THREE WAYS OF PROCEDURE

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Introduction: Percutaneous transesophageal gastrotubing (PTEG) was established as an alternative route to access the gastrointestinal tract for the patients that Percutaneous Endoscopic Gastrostomy was contraindicated. PTEG will be an ideal method for tube feeding and decompression. There are three ways of procedure, and a similar effect is expected.

Aims & Methods: The aim of this study is to evaluate the clinical usefulness of PTEG for the patients who need tube feeding or decompression from gastrointestinal tract. A rupture-free balloon (RFB) catheter is inserted into the upper esophagus. Percutaneous balloon puncture with a specialized needle is then performed from the left side of patient's neck under ultrasonographic control. A guide wire is inserted through the needle into the RFB, followed by a dilator and sheath. A placement tube is then inserted through the sheath, and the sheath is removed. Conventional procedure supported by fluoroscopy was classified in group A, Group B was supported by endoscopy. Double Balloons equipped Over tube type RFB were used instead of primary RFB under endoscopic support was classified in group C that the puncture needle is punctured into the over tube trough the balloon. We perform PTEG in a total of 185 patients (115men and 70women, mean age 71.3 years) in whom PEG was not feasible. PTEG was performed for nutrition in 104 patients and for decompression in 81.

Results: The number of patients was 30 in group A, 117 in group B, and 38 in group C respectively. Satisfactory results were achieved in all 185 patients. Median follow-up was 327.0 days in those who received nutrition and 66.0 days in patients who received decompression. Nine of the 30 patients who were started in the fluoroscopically assisted (Group A) needed endoscopic assistance to complete the procedure. Two of the 117 patients in the endoscopic assistance(Group B) required fluoroscopy because of the tube insertion into the jejunum. All patients could free from nasal tube prior insertion. Six of 104 patients for nutrition were able to free from tube feeding due to PTEG tube feeding support. Oral ingestion could be achieved in 44.0% and home care could achieved in 66.0% of decompression group patients. Major complications were bleeding in two patients required blood transfusion and one patient had tracheal penetration, which was managed conservatively. Other complications were minor oozing bleeding in thirteen patients that did not require blood transfusion, subcutaneous emphysema in two patients, which were managed conservatively. Complication rate of each group was 16.7%,11.1%,15.7%,respectivery. No patient required surgical treatment or died after PTEG.

Conclusion: PTEG is safe and useful for long-term nutrition and/or decompression for the patient who is contraindicated to PEG. PTEG is a suitable procedure of the patients having an eating disorder and/or the malignant disease as tubal feeding and palliative care. Same result is achieved in any way of procedure.

Disclosure: Nothing to disclose

P0833 FEASIBILITY AND EFFECTIVENESS OF IRREVIRSIBLE ELECTROPORATION APPLIED BY ENDOSCOPIC CATHETERS ON GASTROINTESTINAL TRACT: AN EXPERIMENTAL ANIMAL STUDY

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Introduction: Irreversible Electroporation (IRE) is an ablation technique that induces apoptosis by applying an electric field. IRE has several advantages over other ablation techniques. Recently, ablation therapy studies have been performed on Barrett's esophagus and gastrointestinal tumors, and they are becoming popular as next ablation therapy in various cancers. The purpose of this study was to investigate the possibility of applying IRE therapy to gastrointestinal tract using newly designed endoscopic ablative catheters.

Aims & Methods: After a pig was anesthetized, the esophagogastroduodenoscope was approached into the stomach of the pig. We inserted the IRE catheters into the channel of the endoscope. Then the DC generator was connected to the IRE catheter and applied electrical stimulation to the target of duodenum, stomach, and esophagus. The conditions of electrical stimulation are as follows; amplitude ranged from 500V to 2000V, pulse number ranged from 20 to 60, pulse duration was 100us, pulse length was 100ms. Pigs were sacrificed after 24 hours later and ablated tissues were analyzed by H & E staining and TUNEL assay.

Results: Result from H & E staining, there was no damage at 500 V in all the organs. On the contrary, erosion and necrosis occurred in mucosa at 1000V, and inflammation occurred in submucosa at 1500V in both stomach and duodenum. At 2000V, extensive hemorrhage and inflammation occurred in the submucosa. However, submucosal inflammation was also developed in pulse number 80. In the esophagus, epithelial seperation occurred at 1000V and epithelial erosion occurred at 1500V. It was the 2000V that inflammation of submucosa occurred. Secondly, TUNEL assay was used to confirm apoptosis, and as the voltage and pulse became larger, the area in which apoptosis was induced was wider.

Conclusion: Tissue apoptosis was successfully induced by using the IRE catheter. Our newly designed IRE catheters showed feasibility and effectivenss on GI tract.

Disclosure: Nothing to disclose

P0834 LONG TERM SURVIVAL OF EARLY GASTRIC CANCER WITH SUBMUCOSAL INVASION AFTER ESD

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Introduction: Clinical outcome of early gastric cancer (EGC) with submucosal (SM) invasion after endoscopic submucosal dissection (ESD) is not fully elucidated. Additional surgery may decrease the mortality by lymph node metastasis, but can be an overtreatment for some patients with SM invasion gastric cancer. We investigated the clinical outcome for SM invasion gastric cancer after ESD.

Aims & Methods: We investigated the clinical outcomes for EGC with SM invasion after ESD and validity of Japanese guideline

Methods: ESD was performed for 1196 patients (1637 lesions) of EGC at our hospital between July 2006 and December 2018. 148 patients (153 lesions) were histopathologically diagnosed as tubular adenocarcinoma with SM invasion. Based on the Japanese guideline, we recommended the patients to undergo radical surgery or be followed up without additional treatment after ESD. Concretely, the patients whose histopathological findings revealed SM invasion depth were shallower than 500μm, lymphatic and venous invasion were negative, horizontal and vertical margin, ulcerative findings were negative, and tumor size were 3cm or smaller, pathological findings were undifferentiated type were followed up without additional treatment. Other patients were recommended to undergo radical surgery. Patients were divided into radical surgery group (n=78) and no additional treatment group (n=70). We retrospectively analyzed the disease-specific survival (DSS) and disease-free survival (DFS) in both groups, and risk factors of lymph node metastasis in surgical specimen or recurrence after ESD.

Results: 3 year and 5 year DSS are 98 % and 98 % in radical surgery group, and 98 % and 98 % in no additional treatment group. 3 year and 5 year DFS were 97 % and 97% in radical surgery group, and 96 % and 93 % in no additional treatment group, respectively. There are no statistically significant differences between the radical surgery group and no additional treatment group in DSS and DFS. In radical surgery group, six patients had lymph node metastasis in surgical specimen. Two patients who had not have lymph node metastasis recurred afterwards. On the other hand, three patients who were recommended to undergo radical surgery but didn't do it had a local recurrence in no additional treatment group. The rate of lymph node metastasis in surgical specimen or recurrence were 13.4%

(11/82) in the subgroup of histopathologic findings with deep submucosal invasion (SM deeper than 500µm), 40% (6/15) with venous invasion, 20.6% (7/34) with lymphatic invasion, 21.2% (7/33) with ulcerative findings, 15% (6/40) with large tumor size (>30mm) , 10%(2/20) with vertical margin positive or unclear and 14.3% (2/14) with undifferentiated histological type , respectively. Multivariate analysis revealed that venous invasion and ulcerative finding were independent risk factors of lymph node metastasis in surgical specimen or recurrence (odds ratio: 3.9, 3.7 95% confidence interval 1.13 to 14.4, 1.10-14.4; p=0.03,p=0.03 , respectively).
Conclusion: This study demonstrates that the patients of gastric cancer with SM invasion after ESD revealed long term survival. Venous invasion, and ulcerative finding seemed to be significant risk factors of lymph node metastasis in surgical specimen or recurrence.
References: Japanese gastric cancer treatment guideline 2018(ver. 5)
Disclosure: Nothing to disclose

P0835 CLINICAL OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR GASTRIC HETEROTOPIC PANCREAS WITH RECURRENT PANCREATITIS

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Introduction: Gastric heterotopic pancreas (GHP) is generally asymptomatic and rarely has complications such as pancreatitis, pseudocysts, gastric outlet obstruction, upper gastrointestinal bleeding, obstructive jaundice, or intussusception. We investigated clinical outcomes to determine the feasibility and effectiveness of ESD for GHP with recurrent pancreatitis.
Aims & Methods: Subjects who underwent ESD for GHP with recurrent pancreatitis at Asan Medical Center between 2003 and 2017 were eligible. The clinical features of patients and tumors, image finding, histopathologic characteristics, adverse events, results of ESD, and long-term outcome were investigated. We diagnosed with acute gastric heterotopic pancreatitis when the patient with GHP has recurrent severe abdominal pain and meets more than one of the following criteria. (1) increased size of GHP on endoscopic ultrasonography (EUS) or CT during the pain; (2) increase of serum pancreatic enzyme with normal pancreas on image; (3) no more abdominal pain after ESD.
Results: A total of 5 patients had undergone ESD for acute gastric heterotopic pancreatitis after conservative management. The median age was 32 years (interquartile range [IQR]: 28-37 years), and 2 was male. All lesions were located on greater curvature of antrum and 3 out of the lesions had a typical central indentation. On EUS, all lesions involved muscularis mucosa, submucosa and muscularis propria. The median tumor size was 20 mm (IQR: 18-35 mm), and the median procedure time was 26 minutes (IQR: 17-27 minutes). There were no procedure-related complications such as delayed bleeding or stricture. The 4 patients had increased in size of GHP on EUS or CT during the pain, one of them accompanied by elevation of serum pancreatic enzymes and had a complication of pseudocyst formation. In 1 patient, there was no increase in size of GHP but continued severe abdominal pain and had elevation of amylase. He resolved the recurrent abdominal pain after ESD. All patients had no recurrent abdominal pain during the follow-up period after ESD (mean follow-up period: 24.8±12.3 months).
Conclusion: ESD appears to be a feasible and effective alternative option to surgery for the treatment of GHP with recurrent pancreatitis, based on the favorable clinical outcomes.
Disclosure: Nothing to disclose

P0836 CLINICAL OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR GASTRIC LESIONS USING A NOVEL DIATHERMY KNIFE WITH SUCTION FUNCTION FOR BLEEDING CONTROL ASSISTANCE

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Introduction: The Endosaber (Sumitomo Bakelite, Tokyo, Japan) is a newly developed, inexpensive multi-functional, needle-type knife with four tiny channels at the tip of the sheath capable of both suctioning and injecting. The equipped feature distinct from conventional endoscopic devices is the suction function, which enables clear visibility of the bleeding point during hemostasis. The tip of the sheath can come directly in contact with the bleeder, and with suction, clear the field at the same time. The aim of this study was to evaluate the clinical outcomes and safety of ESD using Endosaber for gastric lesions.
Aims & Methods: We included patients who underwent ESD for gastric lesions between June 2018 and August 2018 in this retrospective study. Lesions treated with ESD using a novel diathermy knife with suction capability,Endosaber (ESD-E) and conventional ESD (ESD-C) were compared. The endpoints were the treatment outcomes of ESD (en bloc resection rate, total procedure time, the procedure speed of specimen, the rate and procedures of using hemostatic therapies, the adverse events and the cost-effectiveness.
Results: Thirty-six gastric lesions in 33 consecutive patients (25 male, 8 female) were analyzed. ESD-E group consisted of 12 gastric lesions and ESD-C group consisted of 24 gastric lesions. The mean age was 68.2±10.6 years. There were no significant differences between the two groups with age, gender, location of lesions, morphology, and operator level. There were no significant differences in the average size of lesions between the two groups (17.2±10.7mm in ESD-E vs.12.8±10.1 mmin ESD-C (p=0.24).
Treatment outcomes of ESD showed an en bloc resection rate of 100% in both groups in gastric ESD; complete resection rate of 100% in ESD-E group vs. 97.0% in ESD-C group (p=1). With respect to adverse events, there was one micro-perforation observed in ESD-C group. There were no significant differences in the average time of ESD between the two groups (34.8±19.9 min in ESD-E vs. 37.8±22.5 minin ESD-C (p=0.70)). In the procedure speed of ESD specimens there were no significant differences between the two groups (30.0 mm²/min in ESD-E group vs. 19.3 mm²/min in ESD-C group(p< 0.20)). However multivariate regression analysis with operator level that was variables potentially affecting clinical outcomes identified using Endosaber as significantly correlated with gastric ESD.In rate of using hemostatic therapies there were no significant differencesbetween the two groups (44.4% in ESD-E group vs. 47.1% in ESD-C group (p=1)). Fewer hemostatic procedures using the hemostatic forceps were performed in ESD-E group than in ESD-C, although the difference was not significant (0.9±1.7 in ESD-E group vs. 1.9±2.6 in the ESD-C group (p=0.3)). Then the cost of devices in ESD was significantly different between the two groups (338.6±155.9 EURin ESD-E group vs. 414.5±0 EUR in ESD-C group (p< 0.05)).
Conclusion: ESD using Endosaber was safe and comparable to conventional ESD in gastric ESD. Using Endosaber appears to be faster than ESD-C significantly. Moreover, using Endosaber significantly lowered the ESD cost compared to conventional ESD. Further prospective studies are needed, but the sufficient utilization of the suction function might reduce the use of hemostatic forceps.
Disclosure: Nothing to disclose

P0837 ENDOSCOPIC SUBMUCOSAL DISSECTION OF ESOPHAGEAL, GASTRIC AND COLORECTAL TUMORS: EXPERIENCE OF CAMPINAS STATE UNIVERSITY/GASTROCENTRO – BRAZIL, BETWEEN THE YEARS 2008 TO 2018

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Introduction: Endoscopic resection has become a therapeutic option for the treatment of gastrointestinal(GI) tumors with or without superficial submucosal invasion. Endoscopic Submucosal Dissection(ESD) is a technique developed for en bloc resection of GI tumors that has been consolidated as safe, effective and with few complications, allowing adequate tumoral staging and improving rates of curative resections.

Aims & Methods: To describe the experience of a tertiary center for endoscopic treatment of esophageal, gastric and colorectal tumors by the ESD. A retrospective study evaluate patients with esophageal, gastric and colorectal tumors submitted to ESD from 2008 to 2018. Indication criteria for ESD were based on Guidelines of the Japanese Society and European Society. All resection products were sent for histopathological analysis.

Results: Ninety-two patients underwent ESD: 10 esophageal, 40 gastric and 42 colonic. In relation to esophageal tumors, mean age was 58(45-71)years, 90% male, being 9 squamous cell carcinomas(SCC) and 1 adenocarcinoma(ACA). Average size of tumors: 30.5 (20-40)mm and mean procedure time: 114(60-160)min. Complication rate: 20%, with 2 cases of perforation successfully treated endoscopically. Resection en bloc was possible in 9 patients. Histopathological analysis: 7 SCC intramucosal (m1=3;m2=1;m3=2)and 3 submucosal tumors (Sm1=1;Sm2 = 2). Nine cases had free deep resection margin; 2 had lateral margin invasion and 1 case the margins evaluation was not possible (peacemeal resection). Cure rate: 40%. About gastric tumors, mean age was 58(53-88)years, 57.5% male, with 25 ACA and 15 adenomas. Mean size: 30.4(15-60)mm and mean procedure time: 124(60-240)min. Complication rate: 8.5%, with 1 perforation and 2 late bleeding(1 of them elderly, with liver disease and blood dyscrasia that evolved to death). Resection en bloc was possible in 33 patients. Histopathological study showed: 15 cases pre-diagnosed as adenomas, 8 were ACA. Twenty five pre-diagnosed as ACA, 22 confirmed ACA and 3 showed adenomas with high-grade dysplasia(HGD). Among the ACA, 20 were intramucosal(m1=5;m2= 6;m3 = 9)and 10 with submucosal invasion(Sm1=8;Sm2=2). All cases had free deep resection margins, 2 with lateral focal involvement and 3 with vascular invasion. In 1 case, there was recurrence 3 months after ESD and the patient underwent gastrectomy. Cure rate: 90%. Regarding colorectal tumors, the mean age was 61(34-85)years, 57.1% female. Twenty six(62%) classified as granular laterally-spreading tumor(LST-G) and 16(38%) as non-granular LST(LST-NG), according to Kyoto Classification. The mean lesion size was 29.7(20-100)mm, with 20 located in the rectum, 3 sigmoid, 6 ascending, 6 transverse, 6 descending and 4 in the cecum. Mean duration of the procedure: 150 min(60-420 min). Histological diagnosis evidencied 28 adenomas: 19 with HGD, 8 with low grade dysplasia(LGD), 3 serreted with LGD. Twelve ACA: 11 mucosal invasion(m1=4;m2=4;m3=3)and one with submucosal invasion(Sm2). Among the LST-G (26), 7 had histological diagnosis of ACA, 12 adenomas with HGD and 7 with LGD. In relation to the LST-NG(16), 5 had diagnosis of ACA, 5 adenomas with HGD and 6 adenomas with LGD. Deep margins were all free of lesion, and in 3 cases(7.1%) lateral margin was compromised. There were 6 complications(14.3%): 2 minor bleedings without hemodynamic instability and 4 perforations, treated with conservative measures(clinical support and placement of endoscopic clips), all with good evolution. Cure rate: 98%.

Conclusion: ESD was safe, effective method, curative in gastric and colorectal tumors with few complications.

Disclosure: Nothing to disclose

P0838 DIAGNOSTIC ACCURACY OF ENDOFASTER COMPARED TO HISTOLOGY FOR CHRONIC ATROPHIC GASTRITIS IN HYPO-ACHLORHYDRIC PATIENTS USING NARROW BAND IMAGING TARGETED BIOPSIES: A REAL-TIME PROSPECTIVE STUDY

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Introduction: NISO Biomed EndoFaster is a medical device which automatically analyzes gastric juice in real time through its aspiration during upper gastrointestinal endoscopy. The operating principle of the device is based on determining the pH of gastric juice allowing the detection of hypo-achlorhydric conditions.

Aims & Methods: The aim of this study was to compare the diagnostic accuracy of EndoFaster with histological examination as gold standard for chronic atrophic gastritis through narrow band imaging (NBI) targeted biopsies.

Prospective study on consecutive adult patients undergoing to gastroscopy for the suspect of chronic atrophic gastritis (anemia, dyspepsia), in a single unit of Digestive Endoscopy (University Hospital Sant'Andrea, Rome) in the period between April and November 2018 were included. Patients in therapy with proton pump inhibitor in the previous 4 weeks, gastric surgery and/or known gastric neoplasia were excluded. At the beginning of the endoscopic examination, a sample of gastric juice (2 ml) was aspirated and analyzed by EndoFaster in real time (15 seconds). Endoscopists were blinded for the report of the device. Evaluation of gastric mucosa in high resolution white light (HR-WL) was firstly performed, then with narrow band imaging (HR-NBI) allowing to perform targeted biopsies where the suspicion of intestinal metaplasia was present. In case of normal gastric mucosa with NBI, biopsies were performed randomly using the Sydney System protocol.

Results: Overall, 124 patients were included (64% F; 56 (18-80) years). Chronic atrophic gastritis was present in 42% of patients. Endofaster showed an accuracy for atrophic gastritis of 87.1% and a sensitivity, specificity, PPV and NPV of 77.4%, 94.4%, 91.1% and 84.9%, respectively. The pH value measured by Endofaster showed a positive correlation with the grade of atrophy (r = 0.67, 95% CI 0,73 to 0,81, p < 0.0001). NBI showed an accuracy of 90% and a sensitivity, specificity, PPV and NPV of 90%, 89.7%, 83.7% and 93.8%, respectively, for the diagnosis of intestinal metaplasia. Endofaster allowed to diagnose atrophic gastritis in 3.0% of patients negative to NBI (atrophic gastritis without intestinal metaplasia).

Conclusion: Endofaster seems a promising tool to diagnose chronic atrophic gastritis. The evaluation of hypo-achlorhydria during gastroscopy can also address bioptic sampling in chronic atrophic gastritis patients without metaplasia.

Disclosure: Nothing to disclose

P0839 FINAL RESULTS OF A PROSPECTIVE STUDY COMPARING CONFOCAL LASER ENDOMICROSCOPY WITH STANDARD BIOPSIES IN THE ASSESSMENT OF PERSISTENT OR RECURRENT INTESTINAL METAPLASIA/NEOPLASIA AFTER ENDOSCOPIC TREATMENT OF BARRETT'S ESOPHAGUS RELATED NEOPLASIA

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Introduction: Patients after endoscopic treatment of Barrett's esophagus (BE) related neoplasia (BORN) should undergo regular endoscopic surveillance with biopsies to detect persistent or recurrent intestinal metaplasia (IM) or neoplasia (N). Probe-based confocal laser endomicroscopy (pCLE) offers detailed examination of cellular structures and may examine larger

areas compared to standard biopsy. The role of pCLE in the surveillance of patients after endoscopic treatment of BORN has not been systematically assessed.

Aims & Methods: The aim of this prospective study was to evaluate the efficacy of pCLE (vs. standard biopsies) in detection of persistent/recurrent IM/neoplasia in patients after endoscopic treatment of BORN.

This is a single center, prospective, controlled and pathologist-blinded study in patients undergoing surveillance endoscopy after endoscopic treatment of BORN. pCLE images were obtained from the neo-Z-line (in few cases including macroscopically visible tongues), the cardia and the esophagus. Thereafter, standard biopsies were taken and sent for histopathological analysis (minimally 4 biopsies from macroscopically normal neo-Z-line, 2 biopsies from the cardia and the esophagus and targeted biopsies from visible abnormalities, if present).

Intestinal metaplasia (IM) on pCLE was defined by the presence of regular capillaries in upper and deeper parts of the mucosal layer along with identification of dark ("non-refractile") mucin in goblet cells in columnar-lined mucosa. The dysplastic BE was characterized by black cells with irregular borders and shapes, and irregular leaking capillaries in the mucosa.

Results: We examined 52 patients, from these 22 patients (42%) had the initial diagnosis of low-grade intraepithelial neoplasia (LGIN), 10 patients (19%) had high-grade intraepithelial neoplasia (HGIN) and 20 patients (39%) had an early adenocarcinoma (EAC). Eight patients (15%) underwent endoscopic resection (ER) only, 25 patients (48%) underwent ER or ESD of all visible lesions followed by radiofrequency ablation (RFA), and 19 patients (37%) had RFA as a single treatment modality.

Persistent/recurrent IM was detected only at the level of neo-Z-line in 12 patients (23%, 12/52 pts) by both standard biopsies and pCLE.pCLE but not biopsies detected persistent/recurrent IM in 4 patients (8%, 4/52), another 2 patients had IM present in biopsies but not in pCLE (4%, 2/52).

pCLE (but not biopsies) diagnosed one patient with recurrent LGIN in a macroscopic visible tongue arising from neo-Z-line, no other recurrences of BORN occurred.

Sensitivity and specificity of pCLE in detection of persistent/recurrent IM was 87.5% (95% CI 61.7 - 98.5) and 90.5% (95% CI 77.4 - 97.3), respectively, with a positive predictive value of 77.8% (95% CI 57.5 - 90.1) and a negative predictive value of 95.0% (95% CI 83.8 - 98.6). Agreement of pCLE and histopathological findings was 90%.

Conclusion: pCLE is comparable to standard biopsies in detection of persistent/recurrent IM after endoscopic treatment of BORN.

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Disclosure: Nothing to disclose

P0840 DEVELOPMENT OF NEAR-INFRARED HYPERSPECTRAL IMAGING ENDOSCOPY

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Introduction: In recent years, Near-Infrared Hyperspectral Imaging (NIR-HSI) has been attracting attention. HSI data includes spectral information in each pixel that is handled as images of any wavelength band[1]. The spectral signature of each pixel in the images enables the HSI to identify various pathological conditions. The HSI system can cover NIR spectral ranges (700-2,500 nm) which can penetrate biological tissues more efficiently than visible light because the tissues scatter and absorb less light at longer wavelengths[2]. On the other hand, to analyze big data of NIR-HSI, machine learning is useful for recognizing and extracting the feature of NIR-HSI[3]. Therefore, NIR-HSI with machine learning provides great advantages for supplying diagnostic support information to detect tumor beneath a normal mucosa such as gastrointestinal stromal tumor (GIST).

Aims & Methods: The aim of this study was to establish the method of diagnosis of GIST covered by normal mucosa by using NIR-HSI machine learning. The subjects were surgically resected gastric GIST specimens at our hospital from April 2016 to March 2018. Before fixation, NIR-HSI images of specimens were captured from the mucosal surface side with an NIR hyperspectral camera, Compovision (Sumitomo Electric Industries, Ltd., CV-N800HS). On the obtained NIR-HSI images, the area of GIST regions was defined by a pathologist to prepare training data for GIST and normal regions. The GIST specimens for analysis were selected using the following criteria: (i) GIST was covered with normal mucosa, (ii) normal mucosa existed around GIST in surgical resected specimen, (iii) GIST with a certain size capable of spectral extraction. For each selected specimen, the spectra were extracted from the pixels which were labelled as normal and GIST regions to prepare training data. The number of extracted spectra from the normal and GIST regions was the same to prevent the occurrence of bias in the training data. Then, one of the machine learning systems, support vector machine (SVM), was employed to predict normal and GIST regions from spectral data of each pixel in the NIR-HSI and the prediction accuracy was analyzed by leave-one-out cross-validation.

Results: Images of 14 specimens were captured with Compovision and four specimens that met the criteria mentioned above were selected to use for the analysis. For each specimen, the number of extracted spectra from the normal and GIST regions as training data was 1700 to 3000 pixels, respectively. At wavelength between 1000 and 1600 nm, average accuracy, sensitivity and specificity were 86.9% (95% CI, 81.5-92.2%), 91.7% (95% CI, 81.6-101.8%) and 80.2% (95% CI, 70.5-89.9%), respectively.

Conclusion: GIST diagnostic system with NIR-HSI and machine learning could identify GIST regions covered by normal mucosa with high accuracy. Applying this system to a flexible scope that can be inserted into the forceps channel can enable us to use it in clinical setting.

References: 1. Kumashiro R, et al. Integrated Endoscopic System Based on Optical Imaging and Hyperspectral Data Analysis for Colorectal Cancer Detection. Anticancer Res. 2016; 8: 3925-32. 2. Smith, A. M., et al. Bioimaging: second window for in vivo imaging. Nat Nanotechnol, 2009; 11: 710-1. 3. Melgani F, et al. Classification of Hyperspectral Remote Sensing Images with Support Vector Machines. IEEE Trans Geosci Remote Sens. 2004; 42: 1778-90.

Disclosure: Nothing to disclose

P0841 CLINICAL OUTCOME AND PREDICTING FACTORS OF SEVERE NON-HEMORRHAGIC ESOPHAGEAL ENDOSCOPIC URGENCIES: THE EXPERIENCE OF A TERTIARY REFERRAL CENTER

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Introduction: Caustic and foreign body ingestion represent a significant part of endoscopic urgencies. They can lead to critical conditions and severe complications that may need a multidisciplinary approach. A correct use and interpretation of diagnostic findings at admission is mandatory for risk stratification and subsequent clinical decision.

Aims & Methods: Aim of this retrospective single center study was to evaluate predicting factors of clinical outcome of inpatients with esophageal non-hemorrhagic urgencies, especially Foreign body ingestion (FBI) and caustic ingestion (CAI). All consecutive cases of esophageal non-hemorrhagic urgencies admitted as inpatients in the tertiary Referral University Hospital São João in Porto were collected, in a period between 2000 and 2019. Type of urgencies and clinical history were evaluated together with clinical records regarding preliminary exams (blood tests, EGDS, TC), length of hospitalization, complications and outcome.

Results: Sixty-seven patients were included (M/F: 1.79, mean age 54.3±13.3 years): 44 cases of FBI (most frequently animal bones), 22 cases of CAI (most commonly Sodium Hypochlorite) and 1 case of other substances ingestion (polyurethane). The Charlson Comorbidity score index had a mean value of 3, with no significant difference between FBI and CAI groups. Twenty-seven patients (40%) were affected by psychiatric disease, in particular alcoholism and depression. Psychiatric disease was strongly associ-

ated with CAI and intentional ingestion (p < 0.0001). Among all patients, 66 had a mean length of hospitalization (LoH) of 15 days (CAI Vs FBI, 24.9 Vs 11.3 days, p 0.05) while only 1 patient died after 5 days from caustic ingestion. Blood tests at first day showed a mean value of C-reactive protein (CRP) of 68.9 mg/L in FBI group and 27.2mg/L in CAI group with a significant difference (p=0.036) and significantly associated with LoH in the FBI group (p>0.001), but not in CAI group. WBC had a mean value of 10,3 x10^9/L in FBI and 11.3x10^9/L with no significant differences between FBI and CAI (p 0.28) and no significant association with LoH (p 0.37). EGDS was performed in the majority of cases within the first 24h. In the CAI group, esophageal involvement was complete in the 65% of the cases. Zargar classification showed a significant association with LoH in CAI group (p 0.042). In the FBI group, lacerations were recognized in 41.5% of the cases, while perforation was present in 29.3%, with no significant association with outcome.

Among the findings of CT scan, edema of the esophageal wall was the most common finding in CAI group (p 0.02) and perforation in FBI group (p 0.006). In the CAI group, CT scan Severity Index was significantly associated with LoH (p 0.01), while the presence of perforation was the most significant factor in the FBI group (p 0.06).

Conclusion: EGDS with Zargar Classification is useful for risk stratification in patients with caustic ingestion. CT scan Severity Index for caustics and the presence of perforation for foreign body ingestion are associated with severity of the condition.

CRP at admission is an excellent and inexpensive predictor of clinical outcome in foreign ingestion cases. However, in caustic ingestion patients, it may underestimate the severity of the clinical picture.

	EGDS - Zargar classification	EGDS - presence of perforation	CT scan- caustic ingestion severity index	CT scan - presence of perforation	C-reactive protein at admission	White blood count at admission
Caustic Ingestion group- Length of hospitalization	p= 0.042	p= 0.38	p= 0.01	p= 0.38	p= 0.36	p= 0.2
Foreign object group- Length of hospitalization	na	p= 0.37	na	p= 0.006	p= 0.0001	p= 0.8

[Table 1: risk factors and clinical outcome]

References: - Faz, Athena Alipour, et al. "Epidemiologic features and outcomes of caustic ingestions; a 10-year cross-sectional study." Emergency 5.1 (2017). - Zhong, Qian, et al. "Esophageal foreign body ingestion in adults on weekdays and holidays: a retrospective study of 1058 patients." Medicine 96.43 (2017).
Disclosure: Nothing to disclose

P0842 DIAGNOSTIC YIELD OF ENDOSCOPY FOR PREDICTION OF ACUTE GRAFT VERSUS HOST DISEASE IN THE UPPER GASTROINTESTINAL TRACT

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Introduction: Intestinal graft-versus-host disease (GvHD) is a frequent complication after hematopoietic progenitor cell transplantation (HSCT) and biopsies are recommended for diagnosis. However, the best biopsy sites have yet not been clearly established and final histology results are often delayed as specific staining is required.
Aims & Methods: Aim: We aimed to assess the diagnostic yield of endoscopy for prediction of GvHD of the upper gastrointestinal tract. In addition, we aimed to determine the best sites for obtaining biopsies for diagnosis of GvHD.
Material and methods: A large scaled retrospective cohort study was conducted. Patients diagnosed with acute GvHD in the upper gastrointestinal tract were included. Details included symptoms at time of referral for endoscopy, type of procedure performed, macroscopic findings on endoscopy, and histologic findings of biopsies obtained. Biopsies were graded with the Lerner score. Sensitivity, specificity, positive predictive value (PPV), and negative predictive values (NPV) were calculated.
Results: : A total of 101 patients (mean age 50.24, 44%female) underwent upper endoscopy and were diagnosed with intestinal GvHD. Mean Lerner-score was 2.0, 1.5, 1.5, and 1.8 for the esophagus, antrum, corpus and duodenum, respectively.
Sensitivity, specificity, PPV and NPV for endoscopic prediction of GvHD were inconclusive and not significantly (P>0.05) different between the esophagus (Sensitivity=54%, Specificity=62%, PPV=45%, NPV=70%), antrum (Sensitivity=53%, Specificity=66%, PPV=42%, NPV=75%), corpus (Sensitivity=50%, Specificity=54%, PPV=40%, NPV=64%) and duodenum (Sensitivity=58%, Specificity=83%, PPV=83%, NPV=58%).
Conclusion: The diagnostic yield of endoscopy for prediction of acute GvHD in the upper gastrointestinal tract is considerable low and cannot replace histopathological evaluation. No specific biopsy side showed superior prediction of GvHD. Therefore, we recommend a stepwise biopsy-protocol for patients undergoing upper endoscopy for diagnosis of GvHD.
Disclosure: Nothing to disclose

P0843 EVALUATION OF ENDOSCOPIC RESECTION COMBINED WITH CRYOBALLOON ABLATION SYSTEM FOR ESOPHAGUS IN PORCINE MODELS

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Introduction: Endoscopic resection (ER) is a standard treatment for superficial esophageal squamous cell carcinoma (SESCC). Metachronous development of SESCC due to field cancerization is a major issue to be solved even with a high en bloc resection rate of endoscopic submucosal dissection (ESD). Furthermore, ER for lesions on the post ER scar is difficult in technique, and new therapeutic options are necessary to develop.
The Cryoballoon Ablation system (CBAS), (HOYA Pentax Medical), is a new endoscopic ablation therapy. Operation using CBAS is simple and fast, and high efficacy and safety for patients with dysplastic Barrett's esophagus or SESCC are reported. While CBAS might be a good candidate for additional treatment after ER or salvage treatment for lesions on post ER scar.
Aims & Methods: The study objective was to evaluate the technical feasibility and tissue damage of combination treatment of ER and CBAS in porcine models.
In this study, feasibility of combination therapy were evaluated in three pigs (pigA,B,C). All ER procedure were performed by EMR using Cap method(EMR-C). The detail of combination therapy for each pigs were as follows;
a) Simultaneous EMR-C and CBAS(CBAS was performed for post EMR-C mucosal defect ; ER+CBAS) for pig A, EMR-C+CBAS were performed at two sites on the first day, and at other two sites on the 28 days later.,
b) CBAS for post EMR-C scar for pig B, EMR-C was performed at two sites on the first day, and CBAS was performed for two sites of EMR-C scars and two sites of normal mucosa at 28 days after EMR-C. c) EMR-C for post CBAS scar for pig C, CBAS was performed in two sites on the first day, and 28 days later EMR-C was performed at two sites on post CBAS scar and two normal sites.
All pigs were euthanized at 32 days after initial procedure and evaluated tissue damage. EMR-C specimens were evaluated pathologically. The outcome parameters, the occurrence of any bleeding or perforation, weight loss were evaluated in all pigs.
Results: All endoscopic procedures were as schedule. In pig B, CBAS was performed for EMR-C scars without any technical difficulty. In Pig C, only a mild scar was observed with endoscopy at the site after CBAS at 28 days. And, lifting with submucosal injection was smooth and resection was technically easy in EMR-C for CBAS scars. All pigs did not experience anorexia, rapid weight loss, bleeding and perforation during the observation period and was euthanized at 32 days after initial endoscopic procedure. Pathological evaluation of EMR-C specimens showed only mild fibrosis in the lamina propria mucosae after CBAS compared to EMR-C specimens in normal areas. Tissue damage of treatment against pig A B were as shown

in table1. There was no significant difference between CBAS alone and combination with ER. While the tissue damage of CBAS or EMR-C+CBAS spread throughout the entire esophageal wall at 4 days after treatment, only mild fibrosis was observed in the lamina propria mucosa at 28 days after treatment.

Animal number	treatment	Ablation duration (seconds)	Time to euthanasia from treatment (days)	Maximum depth of ablation damage (wall layers)
pigA	EMR+CBAS	8	4	adventitia
pigA	EMR+CBAS	8	4	muscularis propria
pigB	CBAS for EMR sca	8	4	muscularis propria
pigB	CBAS for EMR sca	8	4	submucosa
pigB	CBAS	8	4	adventitia
pigB	CBAS	8	4	submucosa

[Histological damage of treatment against pig A, B]

Conclusion: Combination treatment of endoscopic resection and CBAS can be technically feasible, and there was no significant difference of tissue damage comparing with CBAS alone.
Disclosure: Nothing to disclose

P0844 APPLICATION OF CONVOLUTIONAL NEURAL NETWORKS FOR STRATIFICATION OF THE DEGREE OF ENDOSCOPIC ATROPHY ON ENDOSCOPIC IMAGES

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Introduction: Histologic assessment of atrophy or intestinal metaplasia, or serum pepsinogen are reportedly useful for risk stratification of gastric cancer. However histologic assessment requires biopsy, and pepsinogen levels are affected by *Helicobacter pylori* eradication therapy. Endoscopic atrophy gradually proceed from the distal part of the stomach to proximal, and the degree of endoscopic atrophy using Kimura-Takemoto classification is reported useful even after eradication, but Kimura-Takemoto classification is unfamiliar outside Japan.
Aims & Methods: In this study, we constructedconvolutional neural network (CNN), and evaluated its ability to classify the degree of the endoscopic atrophy. We performed standard esophagogastroduodenoscopy (EGD) and captured esophagogastroduodenal mucosal images. Clinical diagnosis ofthe degree of endoscopic atrophy using Kimura-Takemoto classification as reference standard was established by board certified endoscopists of Japanese gastroenterological endoscopy society. Endoscopic images were classified into four categories according to the location of the stomach, "antrum", "body (antegrade view)", "body (retroflex view)", and "cardia or fundus". A deep CNN was pre-trained and fine-tuned on a dataset of 11497 images (4373 with atrophy and 7124 without atrophy; 4294 are body (downward view), 4003 body (retroflex view), and 3200 "antrum") obtained from 2016 to 2018. Images of cardia or fundus were excluded from the training data set. A separate test data set (3124 images from 92 patients (34 no atrophy, 14 mild (C1, C2), 26 moderate (C3, O1) and 18 severe atrophy (O2, O3)) obtained from January to February 2019 was evaluated by the CNN.
Results: The trained CNN output a continuous number between 0 and 1as the probability index for the presence or the absence of atrophy, and location of the stomach per image. If the number of images diagnosed as atrophy are equal or larger than no atrophy in each location classified by the CNN, the location was judged as atrophic. Either the body (antegrade view) or the body (retroflex view) is judged as atrophic, it is classified as moderate to severe atrophy. On the other hand, both of the body (antegrade view) and the body (retroflex view) are judged as non-atrophic, it is classified as none to mild atrophy. Among 48 none to mild atrophy diagnosed by endoscopists, the CNN "correctly" diagnosed as none to mild in 41 cases (85%). And among moderate to severe atrophy diagnosed by endoscopists, the CNN "correctly" diagnosed in 33 case (75%). Time needed to diagnose 3124 images was 84 seconds.

Conclusion: The degree of endoscopic atrophy could be diagnosed based on endoscopic images using CNN in a considerably short time. It was suggested that the CNN can be introduced to risk stratification of gastric cancer based on endoscopic images.
Disclosure: Nothing to disclose

P0845 WITHDRAWN

P0846 CLINICAL OUTCOMES OF PER-ORAL ENDOSCOPIC TUMOR RESECTION FOR SUBMUCOSAL TUMORS IN THE ESOPHAGUS AND GASTRIC CARDIA

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Introduction: The clinical success of per-oral endoscopic myotomy (POEM) has led to the development of a new field of 'submucosal endoscopy'. This study aimed to evaluate the safety, efficacy, and limitations of per-oral endoscopic tumor resection (POET) in the management of submucosal tumors (SMTs) in the esophagus and the gastric cardia.
Aims & Methods: POET was performed in 47 patients from January 2011-December 2017. Indication for POET was SMT< 30mm in size in minor axis. Patient and tumor characteristics (age, gender, tumor location, size, and histology), operative and clinical results of POET (procedure time, procedure completion rate, en bloc resection rate, length of hospitalization, adverse events, recurrences) were collected prospectively and analyzed retrospectively.
Results: POET was successfully completed in 43 patients (91.5%) without any major adverse events (Clavian-Dindo IIIb-IV). Four patients required conversion to an open surgical procedure due to suboptimal visualization during POET. Two patients had a piecemeal resection of their SMTs. Median follow-up was 44 months (10-96 months), during which time there were no incidences of recurrence. Tumors in which the minor axis was >30mm or if the product of the major and minor axes, termed tumor mass index (TMI) was greater than 1000, had a high likelihood of being converted to surgical resection.
Conclusion: POET is a safe and effective treatment for SMTs. However, in patients where the minor axis is greater than 30mm or the TMI>1000, surgical excision should be considered. Furthermore, application of POET for SMTs with malignant potential should be carefully considered to ensure optical oncologic outcomes.
Disclosure: Inoue H is an advisor of Olympus Corporation and Top Corporation. He has also received educational grants from Olympus Corp., and Takeda Pharmaceutical Co. Bechara R is a consultant of Olympus Corporation. Onimaru M, Tanabe M, Abad MRA, Shimamura Y, Ueno A, Sumi K, Ikeda H, Ito H have no conflict of interests to declare.

P0847 MEASUREMENT OF MUCOSAL MITOCHONDRIAL OXYGEN DURING UPPER ENDOSCOPY AS A POTENTIAL NOVEL TEST FOR THE DIAGNOSIS OF MESENTERIC ISCHEMIA

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Introduction: Chronic mesenteric ischemia (CMI) is a grave and debilitating condition. Variability of symptoms and abundant collateral circulation, makes diagnosing CMI challenging, especially in single vessel disease. Functional tests such as tonometry and visible light spectroscopy are used to detect mucosal ischemia, but both have their limitations(1).

An easy-to-use and accurate functional test to diagnose CMI is highly desired. Protoporphyrin IX-triplet state lifetime technique (PpIX-TSLT) is a novel method used to measure oxygen in mitochondria(2). After administration of aminolevulinicacid (ALA) mitochondrial PpIX increases. Green light is used to excite PpIX, causing light emission by delayed fluorescence. After collision with oxygen molecules PpIX returns to its ground state, halting light emission. The duration of light emission is measured. When few mitochondrial oxygen is present, collisions are less likely to occur resulting in a longer duration of light emission. *In vivo* measurements of mitochondrial oxygen have been performed in skin and liver, but this technique has never been applied to perform *in vivo* endoscopic mucosal oxygen measurements(3,4).

Aims & Methods: Aim of the current study was to verify the feasibility of measuring mucosal mitochondrial oxygen during upper endoscopy. Mitochondrial oxygen measurements were performed in six healthy volunteers during 10 upper endoscopies, 4 hours after oral administration of ALA. The ALA dose administered was 0, 1, 5 or 20mg/kg. Measurements were conducted at 3 mucosal spots in the antrum, duodenal bulb and descending duodenum. Measurements were performed with the catheter close to the mucosa and while applying pressure in order to induce local ischemia by compromising capillary circulation. Measurements are reported as 1 divided by duration of light emission in microseconds, whereby high values represent high oxygen content.

Results: Measurements proved easy to perform and were successful in all volunteers. ALA dose of 5 mg/kg showed adequate signal-to-noise ratio values of >20 in duodenal bulb and descending duodenum, without occurrence of side effects. Median and interquartile ranges (IQR) of the measurements without application of pressure were 0.092 (0.061-0.132) in antrum, 0.041 (0.032-0.049) in duodenal bulb and 0.016 (0.011-0.026) in descending duodenum. Values decreased significantly (p< 0.001) at all locations when pressure was applied. Median (IQR) during pressure in the antrum was 0.052 (0.032-0.069), in the duodenal bulb 0.013 (0.010-0.022) and in the descending duodenum, 0.009 (0.008-0.011).

Conclusion: Endoscopic measurement of mucosal mitochondrial oxygen is technically feasible and demonstrated to be oxygen dependent, with an optimal ALA dose of 5mg/kg. *In vivo* endoscopic mucosal mitochondrial oxygen measurements are a possible novel functional test for the diagnosis of CMI.

References: 1. van Noord D, Kolkman JJ. Functional testing in the diagnosis of chronic mesenteric ischemia. Best Pract Res Clin Gastroenterol. 2017;31(1):59-68. 2. Mik EG. Special article: measuring mitochondrial oxygen tension: from basic principles to application in humans. Anesth Analg. 2013;117(4):834-46. 3. Mik EG, Johannes T, Zuurbier CJ, Heinen A, Houben-Weerts JH, Balestra GM, et al. In vivo mitochondrial oxygen tension measured by a delayed fluorescence lifetime technique. Biophys J. 2008;95(8):3977-90. 4. Romers LH, Bakker C, Dollee N, Hoeks SE, Lima A, Raat NJ, et al. Cutaneous Mitochondrial PO2, but Not Tissue Oxygen Saturation, Is an Early Indicator of the Physiologic Limit of Hemodilution in the Pig. Anesthesiology. 2016;125(1):124-32.

Disclosure: Nothing to disclose

P0848 EFFICACY AND SAFETY OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR SUPERFICIAL PARA-AMPULLARY DUODENAL EPITHELIAL TUMORS

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Introduction: Endoscopic submucosal dissection (ESD) has been developed as an option for treatment of esophageal, gastric and colorectal lesions. Recently, in Japan, endoscopic submucosal dissection (ESD) for the duodenal tumors has come to be treated. Meta-analysis for superficial non-ampullary duodenal epithelial tumors (SNADETs) reported that ESD might achieve higher en bloc and complete resections at the expense of a greater perforation rate compared to endoscopic mucosal resection. However, the high incidence rate of complications involving bleeding, perforations, and postoperative leakages require mainly high invasive surgery. Some studies

were reported that prophylactic defect closure using Over-The-Scope Clips (OTSCs) was useful for preventing postoperative complications. Therefore, ESD for the duodenal tumors is increasing gradually.

In such a situation, we have recently detected the lesions near ampulla of Vater. Those lesions make it the most technically difficult to perform endoscopic submucosal dissection and also perform combined laparoscopic and endoscopic surgery due to the location. In this study, we investigated the clinical outcomes for SNADETs located within 10 mm from the ampulla of Vater which were defined as para-ampullary tumors (PA) compared to non-ampullary tumors (NA).

Aims & Methods: We enrolled the patients with duodenal tumors that received ESD in June 2016 to October 2018. 3 patients as PA and 35 patients as NA were included in this study. All SNADETs were performed ESD using the pocket-creation method. The post-ESD mucosal defect was closed using OTSC or conventional clip. We examined the clinical outcomes of PA compared to NA.

Results: Clinical characteristics were male / female (PA/NA 3:0/23:12), mean age (PA/NA 64.3/61.7 years), mean tumor diameter (PA/NA 30.0/16.9 mm), tumor morphology (PA/NA I:IIa:IIb:IIc 1:1:0:1/3:22:0:10). All of the SNADETs were completely removed by ESD with all the scissors forceps. We performed prophylactic defect closure using OTSCs and clip by clipping. Endoscopic retrograde biliary drainage was also placed in all PA, because the ampulla of Vater was included in the resected area. The mean procedure time and closure time were 97 and 45minutes in PA and 70 and 22 minutes in NA respectively. The complete defect closure was achieved in 100% in PA and 97.1% in NA respectively. R0 resection rate and en bloc resection rate were 100 and 100% in PA and 94.3 and 100% in NA, respectively. There was no complication in PA and there were 2 cases in NA. 1 case was delayed bleeding and other was postoperative perforation. Perforation occurred in only one patient who did not have successful closure of the defect. Delayed bleeding was detected in one patient who occurred the bleeding from the mucosal surface sutured in OTSC. Lesions consisted of 1 adenocarcinoma and 2 adenomas in PA and 30 adenocarcinomas, 1 adenoma and others in NA. Although the tumor size was significantly larger in the PA group (30 vs 16mm, respectively p = 0.02) and the treatment time and the closure time were longer due to ERBD placement, (97+45min vs 62+22min, respectively), complete closure was possible and there was no significant difference in the treatment results.

Conclusion: ESD with prophylactic defect closure using OTSC and conventional clip for para-ampullary tumors was as efficient and safe as that for non-ampullary tumors regardless of technical difficulties.

Disclosure: Nothing to disclose

P0849 THE USE OF SPRAYABLE WOUND DRESSING COMPRISING MULTIFUNCTIONAL HYDROPHOBIZED MICROPARTICLES DURING GASTRIC ULCER HEALING FOLLOWING ENDOSCOPIC SUBMUCOSAL DISSECTION: A MINIATURE SWINE MODEL

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Introduction: Methods for preventing complications following endoscopic submucosal dissection (ESD) have recently been investigated; however, currently, there is no available method to efficiently prevent scar contracture after ESD. We have reported that usage of high-adhesion gelatin porous films reduce inflammation and tissue contraction during gastric ulcer healing following ESD in a swine model.

However, the sheet had a complication that the lesion to stick was limited and the operability was poor. We changed the dosage form from sheet type to spray type.

Sprayable wound dressing comprises multi-functional hydrophobized microparticles (hMPs) that possess the abilities for tissue adhesiveness in wet environments, acceleration of blood coagulation, enhancement of epithelialization, and enhancement of angiogenesis.

Aims & Methods: In the present study, we aimed to determine the effects of hMPs on the healing of gastric ulcers following ESD in miniature swine model. The gastric ulcers were generated by performing ESD. Following

ESD (Day 0), the artificial ulcers were either sprayed with hMPs (hMPs group, n = 4) or left unsprayed (control group, n = 4). Macroscopic and microscopic examinations were performed on Day 14 following ESD.
Results: Infiltration of inflammatory cells in the submucosal layers were significantly reduced (p = 0.034). Expressions of alpha-SMA-positive cells and Type I collagen were significantly suppressed (p = 0.002 and p = 0.019, respectively), indicating that hMPs suppressed fibrosis after ESD. The numbers of VEGF-positive cells and microvessels were not significantly different between the groups, whereas the number of cells positive for vWF were significantly increased (p = 0.016). Furthermore, there was a significant reduction in the atrophy and fibrosis score (p = 0.024), which reflects the degree of atrophy or fibrosis of the muscularis propria.
Conclusion: The use of hMPs reduced the degree of inflammation, fibrosis, and tissue contraction during the gastric ulcer healing process following ESD. hMPs can be easily delivered using clinically-available air pump devices and can be tightly localized. Therefore, hMPs would contribute to reduce the burden on operators and patients by reducing operation times and ensuring an accurate procedure. Specifically, hMPs may offer successful treatment of wounds without stricture after ESD procedures and also provide a novel therapeutic modality for wound treatment after ESD.
Disclosure: Nothing to disclose

P0850 SURVIVAL IN PATIENTS WITH MISSED UPPER GASTROINTESTINAL CANCER DURING OESOPHAGOGASTRODUODENOSCOPY

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Introduction: According to a recent meta-analysis the rate of missed gastric cancer during upper endoscopy is approximately 10% (1). While risk factors for missed upper gastrointestinal cancer have been identified in retrospective studies, the effect of missed upper gastrointestinal cancer on long-term survival is not clearly documented.
Aims & Methods: We aimed to identify risk factors associated with missed upper gastrointestinal cancer and to compare survival between missed and non-missed upper gastrointestinal cancer. This is a single centre, retrospective cohort study. All upper endoscopies performed at our department between January 2007 and December 2015 were included in the study. The endoscopy database was cross-referenced with the Slovenian Cancer Registry Database. Missed cancers were defined as those diagnosed within 36 months since the last upper endoscopy. We excluded patients with a history of previous upper gastrointestinal cancer and those who were in surveillance program due to high risk conditions for the cancer development (Barrett's oesophagus, intestinal metaplasia with OLGIM stage ≥ 3). The association of demographic and endoscopic characteristics was analysed with multivariable logistic regression, categorical data were compared using the chi-squared test. Survival analysis was performed with the Kaplan-Meier method.
Results: During the study period 29,617 upper endoscopies were performed and 663 upper gastrointestinal cancers were diagnosed; 164 (24.7%) patients were excluded because of previous upper gastrointestinal cancer, further 10 (1.5%) were excluded because their cancer was diagnosed during surveillance for precancerous conditions. In the final cohort of 489 upper gastrointestinal cancers, 37 were missed (7.6 %; esophagus: 3.8%; gastric: 8.0%; duodenum: 23%) (Table 1).

	Diagnosed cancer (n=443)	Missed cancer (n=37)	P value
Age, mean (SD)	69 (12)	69 (12)	0.92
Female, n (%)	138 (31.2)	12 (32.4)	0.87
Alarm symptoms at index endoscopy	379 (85.5)	20 (54.1)	<0.0001
Stage at diagnosis, n (%)			0.714
limited to organ	74 (16.7)	5 (13.5)	
locally advanced	199 (44.9)	16 (43.2)	
metastatic	126 (28.4)	10 (27.0)	
incomplete data	44 (9.9)	6 (16.2)	
Treatment with curative intent	210 (47.4)	13 (35.1)	0.278

[Characteristics of missed and non-missed upper gastrointestinal cancers in the study cohort.]

Conclusion: Median survival of patients with missed upper gastrointestinal cancer during upper endoscopy was shorter compared to non-missed upper gastrointestinal cancer.
References: Pimenta-Melo AR, Monteiro-Soares M, Libânio D, Dinis-Ribeiro M. Missing rate for gastric cancer during upper gastrointestinal endoscopy: a systematic review and meta-analysis. Eur J Gastroenterol Hepatol. 2016 Sep;28(9):1041-9.
Disclosure: Nothing to disclose

P0851 THE PREDICTIVE FACTORS OF ENDOSCOPIC FINDINGS FOR CANCER OF SUPERFICIAL DUODENAL EPITHELIAL TUMORS

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Introduction: Superficial duodenal epithelial tumors (SDETs) are rare, and there is no report of detailed endoscopic diagnosis of many SDET cases.
Aims & Methods: We investigated the relationship between endoscopic findings and final histopathological diagnosis of a large number of SDETs. Four hundred fifty-six SDETs in 434 patients who underwent endoscopic resection was retrospectively reviewed in this study, including 195 prospectively registered SDETs in 186 patients who underwent magnified endoscopic examination with image-enhanced endoscopy (IEE-ME). We investigated the location, size, macroscopic type, and color of SDETs and confirmed IEE-ME findings including surface structures (closed- or open-loop structure) and presence of white opaque substance (WOS) in these SDETs. We performed histopathological diagnosis based on the Vienna classification (VCL) and divided the lesions into category 3 (C3) and beyond category 4.1 (C4/5).
Results: The proportion of VCL C4/5 cases decreased from 30% for lesions of lesions in the duodenal bulb to 12.4% for lesions in the horizontal portion (P=0.0087) and increased with lesion size (P < 0.0001). Based on IEE-ME findings, lesions with closed-loop structure and negative WOS were significantly more frequently diagnosed as VCL C4/5 (P=0.0222, and 0.0038, respectively). In multivariate analysis, tumor size (odds ratio (OR), 20.39; 95% confidence interval (CI), 2.23-186.40; P < 0.0093) and negative WOS (OR, 5.81; 95% CI, 1.24-27.18; P < 0.0268) were significant predictors of VCL C4/5 of SDETs.

Factor	Odds ratio	95% CI	P value
Size (per cm)	20.39	2.17-198.68	0.0093
WOS (negative)	5.81	1.23-28.35	0.0268

[Multivariate analysis of predictors of duodenal cancer]

Conclusion: We found that negative WOS by IEE-ME and lesion size were independent predictors of VCL C4/5 in SDETs. These factors may help us select more appropriate therapeutic strategies for SDETs.
Disclosure: Nothing to disclose

P0852 OUTCOMES OF A NOVEL BARIATRIC STENT IN THE MANAGEMENT OF SLEEVE GASTRECTOMY LEAKS: A MULTICENTER STUDY

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Introduction: The management of laparoscopic sleeve gastrectomy (LSG) leaks remains a challenge. This can be treated with placement of self-expandable metal stents, which are most effective in the acute and early settings. However, migration is a frequent adverse event (AE). Novel fully covered stents with a larger proximal flare to limit migration designed specifically to treat post-sleeve leaks were recently introduced.

Aims & Methods: The aim of this study is to evaluate the safety and efficacy of a novel stent specifically designed for post-sleeve leaks treatment.
This is a multicenter retrospective study, including patients with acute and early post-LSG leaks, treated with a large bariatric stent. The outcomes include technical success, clinical success, and safety profile. A multivariable regression was performed to assess predictors of success.

Results: Thirty-seven patients were included (10 acute and 27 early leaks), with 30 stents in the post pyloric (POST) and 7 in the pre-pyloric (PRE) position. Technical success was 100%. Mean stent dwell time was 29.08 days. Clinical success was achieved in 78.37%. Leak duration, leak size and stent dwell time did not correlate with clinical success. During follow-up, 8 patients had stent migration (21,62%) and all were in a POST position. AE post stent removal were also evaluated (PRE:57.14% vs POST:33.3%, p=0.45). There was no difference between PRE and POST position in the severe AE analysis.

Conclusion: This novel large-caliber fully-covered stent specifically designed for sleeve leaks appears to be effective at treating acute and early leaks.
However, the large flanges and long stent length do not appear to reduce migration rate, and may be associated with higher overall adverse event rates. Additionally, avoiding placement in the post-pyloric position may help mitigate migration risk.

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P0853 AN ANALYSIS OF NEWLY DETECTED GASTRIC NEOPLASM IN PATIENTS WITH ALREADY DIAGNOSED GASTRIC NEOPLASM

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Introduction: Recently, synchronous multiple early gastric cancers are being increasingly reported due to the aging society and development of endoscopy techniques.

Aims & Methods: We usually perform reexamination of esophagogastroduodenoscopy (re-EGD) for the patients who have a gastric adenoma or adenocarcinoma before ESD, and sometimes detect the another lesion. We evaluated the clinicopathological findings of those lesions.
Between January 2014 and December 2018, we performed re-EGD for 1299 patients in our hospital. The lesions which were detected anew in re-EGD were extracted, then we investigated their clinicopathological characteristics retrospectively.

Results: 76 patients with 83 lesions were detected in re-EGD. The location is cardia/ gastric body/ angle/ pylorus: 7/ 30/ 36/ 20, and les/ ant/ gre/ pos: 29/ 15/ 19/ 20. The average diameter was 9.1mm(2-40mm). The pathological diagnosis were 18 adenoma, 46 differentiated adenocarcinoma, and 1 undifferentiated adenocarcinoma. The invasion depth was all intramucosal cancer. Their H.pylori infection status was 29 were positive, 46 were after eradication, and 1 was negative. The degree of atrophy was 1 was mild(C-1, 2), 19 were moderate (C-3, O-1), and 56 were severe(O-2, 3). On the other hand, with respect to the 83 lesions which were detected from the beginning, the average diameter was 14.8mm, and pathological diagnosis were 5 adenoma, 76 differentiated adenocarcinoma, and 2 undifferentiated adenocarcinoma. The lesions which were detected in re-EGD were significantly smaller than those were detected from the beginning (p< 0.01), and ratio of adenocarcinoma is lower than those (p< 0.01). With respect to the location, 64/83 (77%) of the lesion were located in the same area of the lesions which were detected previously.

Conclusion: The patients with a gastric cancer often have the another lesion synchronously. The lesions which were detected newly tend to be smaller than the lesions which were already detected, and located in same area of those frequently.

Disclosure: Nothing to disclose

P0854 MULTICENTRE, RETROSPECTIVE, COHORT STUDY OF 55 PATIENTS WITH BURIED BUMPER SYNDROME TREATED ENDOSCOPICALLY WITH A NOVEL DEDICATED DEVICE

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Introduction: Buried bumper syndrome (BBS) is an uncommon complication of percutaneous endoscopic gastrostomy (PEG) placement; its incidence is 1%. Several techniques for endoscopic management of BBS have been described, given the absence of a dedicated device to date.

Aims & Methods: This was a retrospective, international multicentre, cohort study involving 15 Endoscopy Units across Europe between December 2016 and February 2019. Patients with BBS treated endoscopically with a novel, sphincterotome-like, dedicated device were included. A total of 55 cases were retrospectively analysed. The primary endpoint was success rate of buried bumper endoscopic removal with the dedicated device. A median follow-up of 96 days was performed in 38 patients and complications rate were registered.

Results: The study group included 42 men (76%) and 13 women (24%) with a median age of 66 years (range 17-94). Diagnosis of BBS was suspected through clinical assessment and confirmed through endoscopic

examination. Radiological examinations were performed in only 7 cases (12.7%). Patients underwent PEG placement 859.5 days (range 49-4380) before the removal of the buried bumper, due to cerebrovascular disease (16 patients, 29%), cerebral palsy (9 patients, 16.4%), head and neck cancer (9 patients, 16.4%), Parkinson's disease (4 patients, 7.3%), neurological diseases and psychomotor retardation (4 patients, 7.3%), amyotrophic lateral sclerosis (4 patients, 7.3%), multiple sclerosis (2 patients, 3.6%), cancer (2 patients, 3.6%), cerebral tumor (1 patient, 1.8%), head injury (1 patient, 1.8%), oesophageal cancer (1 patient, 1.8%), poly-trauma (1 patient, 1.8%), miscellaneous (1 patient, 1.8%). Nine patients had a clinical history of previous BBSs (16%), treated with a different therapeutic approach. The buried bumper was located in the gastric body in 46 patients (83.6%) and in the gastric antrum in 9 patients (16.3%). The use of additional devices was applied in 40 procedures (72.7%). In this regard, a wire was used in 14 patients (25.4%), a snare in 14 patients (25.4%), a forceps in 8 patients (14.5%), a knife in 2 patients (3.6%) and a balloon in two patients (3.6%). The median time for the endoscopic removal of the buried bumper, recorded in 42 patients, was 22 minutes (range 5-60). The buried bumper was successfully removed in 53 cases (96.4%). Peri-procedural endoscopic complications occurred in 7 procedures (12.7%). Significant bleeding, in particular, occurred in 4 patients (7.3%), a small perforation in 2 patients (3.6%) and in one patient (1.8%) a slight laceration of the gastro-oesophageal junction occurred during the PEG extraction. Two patients (3.4%) developed a post-procedure sepsis that was successfully treated with antibiotics. In 44 patients (80%) a new PEG was placed during the same procedure of removal of the buried bumper, through the same site of the gastric wall in 35 patients (80%), while a new gastrostomy was required in 9 patients (20%). In 5 patients (9.1%) a second PEG was placed after a median time of 4.5 days (range 2-14), all the times through a new site of the gastric wall. A median follow up of 96 days (range 1-593) was performed in 38 patients (69.1%), during which no significant complications occurred and one patient died of unrelated condition (encephalitis).

Conclusion: To the best of our knowledge this is the first international multicentre study regarding the endoscopic management of BBS with a dedicated device. Based on our preliminary data it appears to be user-friendly, safe, quick and effective for minimally invasive, endoscopic management of BBS.

Disclosure: Dr Despott and Dr Murino receive research/ education support from Aquilant Medical, Fujifilm, Olympus, Pentax Medical, Boston scientific and GI supply. All others authors have no conflicts of interest to disclosure.

P0855 EYE TRACKING FOR ASSESSMENT OF PROFICIENCY IN ENDOSCOPIC SUBMUCOSAL DISSECTION

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Introduction: Endoscopic submucosal dissection (ESD) has recently become widely acceptedas the ideal minimally invasive curative treatment for early stage gastrointestinal cancer. However, the safety and success of ESD depends on doctors' skill levels. There are no established training systems to overcome this difficulty, with the level of proficiency still being dependent on the skill of the individual doctor.

Aims & Methods: The aim of this study was to use an eye tracking device to measure endoscopic skill, assess the differences between experienced and novice endoscopists, isolate commonalities between experienced endoscopists, and identify elements required for ESD. Three endoscopists who were experienced in ESD (Group E) and threewho were novices (Group N) each performed ESD on an ex vivo porcine stomach model while wearing eye-tracking glasses. Eye tracking is technically to measure the point of gaze or measurement of eyes activity. We measured the area of distribution of gazeand compared between two groups.

Results: The area of distribution of gazewas significantly smallerfor Group Ethan for Group N (P=0.021). We divided into three phases; prediction, incision and dissection phase. In terms of prediction and dissection phase, there was significantly smaller for Group E than for Group N.

Conclusion: The experienced endoscopists in this study were able to predict their next step in advance and their movements were consistent. This showed that not only endoscopic skills but also the knowledge required

to predict the next movement is important in ESD. The development of a training system based on this analysis could make ESD a safer and more efficient procedure.

Disclosure: Nothing to disclose

P0856 ENDOSCOPIC HAND SUTURING CONTRIBUTES TO FASTER HEALING OF THE MUCOSAL DEFECTS AFTER GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION: A HISTOLOGICAL ANALYSIS IN IN VIVO PORCINE MODELS

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Introduction: Endoscopic hand suturing (EHS) is one of closure techniques for mucosal defects after endoscopic submucosal dissection (ESD) using a curved needle with absorbable suture and a trough-the-scope needle holder[1]. However, it is unclear whether EHS can keep post-ESD mucosal defects closed and promote healing. Furthermore, the histologic healing process of the sutured defects is also unknown.

Aims & Methods: To evaluate how EHS contributes to the mucosal healing, we investigated histological analyses of the sutured defect after ESD in in vivo porcine models.

We conducted this study using two live pigs. Under general anesthesia, the first pig underwent gastric ESDto create two 2 cm-mucosal defects (one on the anterior wall (AW) and another on the posterior wall (PW), respectively). The defect on PW was closed by EHS (a sutured group), and that on AW was left open as a control group. On postoperative week (POW) 1 and 2, the previously-created sites were observed endoscopically, and subsequently the same procedure as mentioned above was conducted to create new lesions (one for ESD plus EHS, another for ESD only), respectively. In the second pig, the control groups were set on PW and the sutured groups were set on AW. On POW 3, the pigs were killed for histology after endoscopic observation. In each session, the size of the mucosal defects was endoscopically estimated and recorded.

When the mucosal defects were replaced with scar tissue or remained closed by EHS without dehiscence, they were recorded as zero. For histological assessment, the width of absent epithelium in hematoxylin and eosin stain and the width of absent muscularis mucosae in alpha-smooth muscle actin (αSMA) stain were measured in each treated sites. In addition, fibroblast, which contributes to the healing process of ulcers, was defined as the area of positive αSMA in submucosa of the treated areas. It was measured in 3 fields (×400 magnification) for each slice using software ImageJ with the IHC profiler plugin. The endoscopically-estimated size of the mucosal defects and the histologically-measured the widths and the area were compared between the two groups. Furthermore, histological morphology of the mucosal layer in the sutured group was assessed.

Results: The endoscopic average size of the mucosal defects (mm) (n = 6 on POW 1, 4 on POW 2, 2 on POW 3) were 15 ± 2.6, 6.3 ± 2.8, 2.0 ± 2.0 in the control group and 0, 0, 0 in the sutured group (p = 0.001, 0.004, 0.21), respectively. The histologic average width of absent epithelium (mm) (n = 2 on POW 1, 2 on POW 2, 2 on POW 3) were 10.7 ± 2.2, 4.2 ± 3.5, 1.1 ± 1.1 in the control group and 0.88 ± 0.30, 0, 0 in the sutured group (p = 0.023, 0.18, 0.21), respectively. The histologic average width of absent muscularis mucosae (mm) (n = 2 on POW 1, 2 on POW 2, 2 on POW 3) were 13.2 ± 2.6, 8.2 ± 2.9, 7.5 ± 1.0 in the control group and 2.8 ± 0.7, 0, 0 in the sutured group (p = 0.030, 0.054, 0.009), respectively.

The area of fibroblast (μm²) (n = 2 on POW 1, 2 on POW 2, 2 on POW 3) were 7079, 16963, 19656 in the control group and 9728, 6577, 4908 in the sutured group (p = 0.21, 0.0001, 0.0003), respectively. In the histological assessment of the sutured sites on POW 2 and 3, the muscularis mucosae fused to each other, and the connected epithelium covered on it in line without inversion.

Conclusion: EHS may contribute to faster healing of the post-ESD mucosal defects without dehiscence in the porcine models. Histologically, layer-to-layer healing seems to be obtained in the sutured mucosa by EHS as with a natural healing process of the mucosal defect after ESD.

References: 1. Goto O, Sasaki M, Akimoto T, et al. Endoscopic hand-suturing for defect closure after gastric endoscopic submucosal dissection: a pilot study in animals and in humans. Endoscopy 2017; 49: 792-7
Disclosure: Nothing to disclose

P0857 INTERNATIONAL MULTICENTER EXPERT SURVEY ON ENDOSCOPIC TREATMENT OF UPPER GASTROINTESTINAL ANASTOMOTIC LEAKS

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Introduction: Upper gastrointestinal (UGI) anastomotic leaks have a high risk of morbidity and mortality. A variety of endoscopic techniques are currently available; however, no definite consensus exists on the most appropriate therapeutic approach. Knowledge of current practices is important for the design of prospective studies.
Aims & Methods: To explore the current practices on the management of UGI anastomotic leaks. A survey questionnaire consisting of 35 opinion-probing questions and 4 short clinical cases was distributed among international expert therapeutic endoscopists regarding management of UGI anastomotic leaks.
Results: A total of 44% of 163 surveys were returned. Majority (69%) were gastroenterologists and 56% had >10 years of experience. A third of respondents treat between 10-19 patients annually. Stent placement is the technique most frequently used (average ranking [AR]: 6.3), followed by endoscopic internal drainage (EID) (AR: 4.7), OTSC (AR: 4.6) and endoscopic vacuum therapy (EVT) (AR: 4.1). Regarding stents, 56% use FC-SEMS as their usual first option. The vast majority (80%) utilize techniques to minimize migration (suture: 33%); 4 weeks was the most common (49%) reported stent dwell time. The majority of respondents perform epithelial ablation prior to OTSC placement (62%) and suturing (61%). Regarding EVT, 75% change the sponge every 3-5 days and 56% perform balloon dilation and intracavitary EVT in patients with large cavities but small leak defects. Regarding endoscopic septotomy, 56% consider a minimal interval of 4 weeks from surgery and 90% consider the need to perform further septotomy sessions, with a median of 11 days between treatments. Regarding EID, 82% prefer to place two plastic stents and 62% shorter stents (*Table 1*). Persistent inflammation with clinical sepsis was the definition most commonly (55%) reported for endoscopic failure. Regarding clinical cases,

EVT and stent placement, with or without percutaneous/surgical drainage, were the therapeutic options most often chosen by respondents in patients with previous oncologic surgery; EVT and EID were the therapeutic options most often chosen in patients with previous bariatric surgery.
Conclusion: There is a wide variation in the management of patients with UGI anastomotic leaks, even among experts. Future prospective studies are needed to move from an expert- to an evidence- and personalised-based care.
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P0858 HYBRID ARGON-PLASMA-COAGULATION VERSUS RADIOFREQUENCY ABLATION IN BARRETT'S ESOPHAGUS AFTER ENDOSCOPIC RESECTION OF NEOPLASTIC LESIONS: A RANDOMIZED TRIAL AT A TERTIARY CENTER

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Introduction: Neoplastic Barrett esophagus (BE) is usually treated by a combination of endoscopic resection for (visible) neoplasia followed by ablation of the remaining Barrett's mucosa with the aim to eradicate the entire BE. Different ablation techniques have been established in clinical routine for this therapy approach. Radiofrequency ablation (RFA) and argon-plasma -coagulation (APC) are most frequently used. There is some evidence that prior injection to APC (Hybrid-APC) lowers stricture rates in these patients. There is only very rare data comparing APC and RFA in a randomised trial setting and no study comparing H-APC with RFA so far.
Aims & Methods: The Aim of this study is to compare the two major ablation techniques in a large group of patients. The study was planned as a non-inferior trial. All patients who have been treated for neoplastic lesions in Barrett's esophagus and were planned for subsequent ablation were randomized to RFA or H-APC. Time of deviation, complications and postinterventional pain (1-10 on scale, duration) were measured. All patients are planned for follow-up gastroscopy after 3,6,12 and 24 months with chromoendoscopy and biopsies at the Z-line.
Results: 64 patients (60 males, 4 females, mean age 64,9 years) have been included to the study with N=28 randomized to RFA and N=38 to H-APC group. N=28 patients have completed ablation and short-term follow-up (3 or 6 months). 114 ablative interventions have been performed so far. In mean 1,8 ablations (min 1 max 5) were needed for successful Barrett's

Ideal patient characteristics						
	Stent	OTSC	EVT	Suture	Septotomy	EID
Time of leak Acute Chronic No experience No information	93.8% (n=60) 17.2% (n=11) n=2 n=5	96.8% (n=61) 19% (n=12) n=6 n=2	48.7% (n=19) 71.8% (n=28) n=27 n=5	89.5% (n=34) 31.6% (n=12) n=32 n=1	3.2% (n=1) 100% (n=31) n=38 n=2	54.3% (n=25) 65.2% (n=30) n=22 n=3
Leak size 0 - 1cm 1 - 2cm 2 - 3cm >3cm No experience No information	54.1% (n=33) 63.9% (n=39) 55.7% (n=34) 42.6% (n=26) n=2 n=8	77% (n=47) 47.5% (n=29) 9.8% (n=6) - n=6 n=4	25% (n=10) 40% (n=16) 67.5% (n=27) 77.5% (n=31) n=27 n=4	64.7% (n=22) 50% (n=17) 47.1% (n=16) 35.3% (n=12) n=32 n=5	51.9% (n=14) 63% (n=17) 51.9% (n=14) 63% (n=17) n=38 n=6	63.6% (n=28) 65.9% (n=29) 45.5% (n=20) 38.6% (n=17) n=22 n=5
Leak location Intra-thoracic Intra-abdominal No experience No information	93.2% (n=55) 45.8% (n=27) n=2 n=10	64% (n=32) 92% (n=46) n=6 n=15	92.5% (n=37) 60% (n=24) n=27 n=4	58.6% (n=17) 96.6% (n=28) n=32 n=10	25% (n=7) 92.9% (n=26) n=38 n=5	66% (n=31) 83% (n=39) n=22 n=2
Associated collection Yes No No experience No information	11.3% (n=7) 88.7% (n=55) n=2 n=7	7% (n=4) 93% (n=53) n=6 n=8	95.2% (n=40) 4.8% (n=2) n=27 n=2	11.1% (n=4) 88.9% (n=32) n=32 n=3	90% (n=27) 10% (n=3) n=38 n=3	97.9% (n=46) 2.1% (n=1) n=22 n=2
Previous surgery Bariatric Oncologic No experience No information	78.6% (n=44) 75% (n=42) n=2 n=13	87.8% (n=43) 71.4% (n=35) n=7 n=15	81.6% (n=31) 84.2% (n=32) n=27 n=6	96.6% (n=28) 72.4% (n=21) n=32 n=10	100% (n=27) 25.9% (n=7) n=38 n=6	95.5% (n=42) 59.1% (n=26) n=22 n=5

[P0857 Table. Ideal patient characteristics for each endoscopic technique]

eradication. There was no significant difference in Barrett's length between the two groups. The mean length of BE before ablation was 3,7cm (H-APC) and 4.9cm (RFA).

Barrett's eradication rate after 6 months follow-up was 90% in the RFA group and 78 % in the hybrid- APC group. Except of non-healers (10.1 %) all Barrett remnants were localized at the neo-Zline. However, the post interventional pain was significantly higher in the RFA group: mean 3.7 /10 and duration of 7.3 days, whereas patients in H-APC group complained about pain for 3.3 days in mean and severity of 1.9/10.

Conclusion: Bothe ablation techniques have good results in eradication rate with slightly better outcome for the RFA group. The pain severity and duration therefore were significantly higher in the RFA group. Combination of H-APC in the tubular esophagus und RFA at the Z-Line might lead to a better outcome for Barrett's eradication and patients discomfort.

Disclosure: Nothing to disclose

P0859 ENDOSCOPIC FULL THICKNESS RESECTION FOR TREATMENT OF GASTRIC SUBEPITHELIAL TUMORS

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Introduction: Submucosal tunnel endoscopic resections (STER) had been increasingly performed for treatment of gastric subepithelial tumors. One of the limitations for STER is the risk of incomplete tumor resection due to close dissection and bridging of tumor capsule. Endoscopic full thickness resection (EFTR) allowed complete resection of the tumor with margins to prevent recurrence. This study aimed to review the techniques and outcomes of EFTR for treatment of gastric subepithelial tumors.
Aims & Methods: Patients who received endoscopic resection for gastric subepithelial tumors were recruited. The gastric subepithelial tumors were considered eligible for endoscopic resection with size < 40mm. All patients received preoperative assessments including EUS and CT scan to define the extend of tumors and the proportion of extra and intraluminal components. All the procedures were performed under general anesthesia with CO2 insufflation. EFTR started after injection with mucosal incision up to 50% of tumor circumference, followed by submucosal dissection to identify tumor margin. Further dissection was performed using ESD devices. After adequate exposure of lateral margins, incision into muscularis propria was performed to achieve full thickness resection. Luminal defects were closed by either clips, clip-loop crown method or Overstitch suturing.
Results: From 2012 to 2019, 18 patients received EFTR for gastric subepithelial tumors. The mean age was 60.6 years, and 6 were male. The GIST were located at greater curvature (4), cardia (6), lesser curve (4) and antrum (2). The mean size was 21.9mm (10 - 50 mm). Half of the EFTR were performed in operation theatre while half were done at endoscopy. The mean hospital stay was 4.2 days, and mean operative time was 92 minutes (34-180 mins). There was one conversion to laparoscopic resection. Closure of luminal defect were performed with clips (7), Overstitch endoscopic suturing (7) and clip and loop crown closure (3). Most patients resumed full diet on day 3, and all the pathologies confirmed GIST tumors with clear resection margins.
Conclusion: Endoscopic Full Thickness Resection is technically feasible and safe procedure for treatment of gastric GIST. Future research should focus on refining the techniques of EFTR and closure of the defect.
Disclosure: Nothing to disclose

P0860 ENDOSCOPIC STENT PLACEMENT FOR TREATMENT OF SLEEVE GASTRECTOMY LEAK: A SINGLE INSTITUTION EXPERIENCE WITH FULLY-COVERED STENTS

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Introduction: Laparoscopic sleeve gastrectomy (LSG) is one of the most commonly performed bariatric procedures for treatment of morbid obesity. Despite its popularity, it is not without risks, the most serious of which is the staple line leak. Staple line leaks are difficult to manage and require significant resources in the form of surgical, radiological and endoscopic interventions, resulting in long hospital and intensive care stays and significant morbidity.
Aims & Methods: The objective of this report is to describe our single-institution experience in managing SG staple-line leaks with fully-covered self-expanding metal stents (SEMS) across the leak sites.
Data for all patients who underwent endoscopic stent placement for an SG leak between 12/2016 and 02/2019 at a single academic institution were retrospectively reviewed. Patient medical history, perioperative information, stent placement details, outcomes, and subsequent interventions were recorded.
Results: Twenty-six patients with SG staple-line leaks treated with fully-covered endoscopic stents were identified. Leaks were detected at a median of 11.5 days post-procedure (range, 1-31 d). Stents remained in place for an average of 44.8 ±10.8 days. Complete migration occurred in three (12%) and partial migration (1 - 4 cm) in five (20%) of the stent placements. One patient was lost to follow-up, and 22 of the remaining 25 patients (88%) healed after stent placement. Two patients (8%) ultimately required operative revision with partial gastrectomy and Roux-en-Y oesophagojejunostomy for management of persistent leakage.
Conclusion: Endoscopic management using fully-covered SEMS for staple-line leaks after SG is effective in the majority of patients. However, migration is the limiting factor for optimal management. Algorithms are needed for the management of chronic staple-line leaks, which are less likely to heal after stent placement. Our data indicate that earlier use of SEMS seems to reduce the time until closure and the length of the total hospital stay.
Disclosure: Nothing to disclose

P0861 THE ROLE OF ENDOSCOPIC HEMOSTATIC POWDER IN NON-VARICEAL GASTROINTESTINAL BLEEDING: A SYSTEMATIC REVIEW AND META-ANALYSIS WITH IMPLICATION ON CLINICAL PRACTICE

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Introduction: Acute non-variceal upper gastrointestinal bleeding (NVUGIB) is a common medical problem that results in high morbidity and mortality. Endoscopic hemostasis has been widely accepted as first-line management for patients with NVUGIB. Hemostatic nanopowder is a novel therapy used to treat patients with upper gastrointestinal bleeding. Hemostasis is achieved by adhering of the powder to the bleeding site, which leads to a mechanical barrier. The powder has been shown to enhance clot formation and shortens coagulation time. It is delivered through a catheter and sprayed onto the bleeding site under direct endoscopic guidance, without direct tissue contact. The reported success rate of homeostatic nanopowder in patients with NVUGIB ranges between 75 to 100%, with the re-

bleeding rate of 10-49%. This systematic review and meta-analysis aimed to assess the effectiveness of hemostatic powder in achieving initial hemostasis, either as primary monotherapy, or as a part of salvage therapy in treating patients with NVUGIB.

Aims & Methods: We performed a comprehensive literature search of PubMed, EMBASE, Web of Science, and Cochrane Library through November 2018. Studies with more than ten patients were selected according to predefined criteria and analyzed to generate pooled data. Weighted pooled rate (WPR) for initial hemostasis, rebleeding rate for primary monotherapy or salvage therapy, and post-procedure complications were calculated for overall studies. Heterogeneity was quantified using the I-squared measure. Meta-analysis with Fixed effects model was performed to calculate data for initial hemostasis, rebleeding rate, and complications.

Results: Out of 1379 studies obtained from the initial database search, 16 studies with a total of 688 patients met the inclusion criteria and were included in the meta-analysis. Most of the patients were treated for peptic ulcer bleeding (62.5%). Hemostatic powder was used in 473 (68.8%) patients as primary monotherapy and in 215 (31.2%) patients as a salvage therapy. The weight pooled rate (WPR) for initial hemostasis as primary monotherapy was 93% (95% CI: 0.93-0.90) and 95% (95% CI: 0.91-0.97) as a salvage therapy. The rate of rebleeding after initial hemostasis in monotherapy was 19% (95% CI: 0.16-0.23) and salvage therapy was 31% (95% CI: 0.25-0.13) respectively. The WPR for post-procedure complications was 4% (95% CI: 0.02-0.07).

Conclusion: Hemostatic nanopowder appears to be a safe and effective therapeutic option for the management of acute non-variceal upper gastrointestinal bleeding. This study represents the first meta-analysis that demonstrates the success of the hemostatic nanopowder in those patients. Further trials should clarify the ideal setting for the use of hemostatic powder.

References: 1. Yau AH, Ou G, Galorport C, et al. Safety and efficacy of Hemospray(R) in upper gastrointestinal bleeding. Can J Gastroenterol Hepatol 2014;28:72-6. 2. Sulz MC, Frei R, Meyenberger C, et al. Routine use of Hemospray for gastrointestinal bleeding: prospective two-center experience in Switzerland. Endoscopy 2014;46:619-24. 3. Masci E, Arena M, Morandi E, et al. Upper gastrointestinal active bleeding ulcers: review of literature on the results of endoscopic techniques and our experience with Hemospray. Scand J Gastroenterol 2014;49:1290-5. 4. Sung JJ, Luo D, Wu JC, et al. Early clinical experience of the safety and effectiveness of Hemospray in achieving hemostasis in patients with acute peptic ulcer bleeding. Endoscopy 2011;43:291-5. 5. Changela K, Papafragkakis H, Ofori E, et al. Hemostatic powder spray: a new method for managing gastrointestinal bleeding. Therap Adv Gastroenterol 2015;8:125-35.

Disclosure: Nothing to disclose

P0862 FOURTH-GENERATION ENDOCYTOSCOPY FOR IN-VIVO DIAGNOSIS OF SUPERFICIAL SQUAMOUS CELL CARCINOMA: DIAGNOSTIC ACCURACY OF NON-EXPERTS

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Introduction: Fourth-generation endocytoscopy (EC; GIF-H290EC; GIF-Y0074 [prototype], Olympus., Tokyo, Japan) was newly developed to provide high-definition images with ultrahigh magnification (×520 fold) allowing in-vivo histologic assessment of gastrointestinal lesions by visualizing the cellular nuclei and cytoplasm.

Aims & Methods: This study aimed to evaluate the diagnostic accuracy of EC in the diagnosis of superficial esophageal squamous cell cancer between non-expert endoscopists. A single-center, retrospective study of prospectively collected data of all squamous esophageal EC examinations was conducted. The double staining method using crystal violet and methylene blue was applied to all lesions. Two endoscopists with expertise in EC collected images of 57 esophageal lesions, whose histology was established between June 2015 and April 2018. The image quality was assessed by these experts and poor quality images were discarded. Two non-experts endoscopists with no experience in EC and blinded to white-light and narrow-band imaging findings as well as histopathologic diagnosis, independently reviewed and diagnosed all endocytoscopic images after

one hour lecture of EC. EC diagnosis was made based on the new simplified criteria that we modified from a previously reported classification (Inoue H, et al. Gastrointest Endosc Clin N Am. 2004). The classification is based on the density and size of the nucleus, the shape of the cells, and the frontline of cellular border: EC 1a: normal; EC 1b: inflammation; EC 2: intraepithelial neoplasia (IN); and EC 3: squamous cell carcinoma (SCC). The diagnostic performance of fourth-generation EC was assessed while using the gold standard histopathology as a reference and the interobserver agreement by using the κ value.

Results: EC images of 47 lesions (82.4%) were were selected for image review. The histopathology of the 47 lesions were as follows: normal 2; inflammation 14; intraepithelial neoplasia 4; and SCC 27. The sensitivity, specificity, and overall accuracy of EC for esophageal cancer diagnosis (EC1+2 vs EC3) were 82.1% (95%CI:64.4-92.1), 78.9% (95%CI:56.7-91.5), and 80.9% (95%CI:67.5-89.6) by endoscopist A; and 100.0% (95%CI:87.9-100.0), 68.4% (95%CI:46.0-84.6), and 87.2% (95%CI:74.8-94.0) by endoscopist B. The inter-observer agreement, $Kappa$ statistic= 0.68 (95%CI:0.47-0.89), was good.

Conclusion: Fourth generation endocytoscopy using a new simplified classification yielded optimal diagnostic accuracy for the diagnosis of superficial SCC in endoscopists without previous expertise in EC. EC aids in the diagnosis of early esophageal cancer and can be applied in clinical settings after minimal training.

Disclosure: Nothing to disclose

P0863 MUSCULOSKELETAL INJURY AMONG ENDOSCOPY PHYSICIANS, NURSES AND TECHNICIANS

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Introduction: Ergonomics is the study of physical and cognitive demand of a task in accordance with an individual's capacity, to minimize injury and maximize efficiency. Studies have suggested a high prevalence of musculoskeletal injuries among endoscopists and ancillary staff. Survey-based studies estimate a 37% to 89% prevalence of musculoskeletal pain among gastroenterologists.

There is paucity of data especially of endoscopists from eastern populations.

Aims & Methods: Assess the frequency and severity of musculoskeletal injury among endoscopy staff who are involved in endoscopic procedures To assess the effect of musculoskeletal injury on quality of work in endoscopy

A questionnaire was developed based upon the recommendation of the present guidelines. The data will be collected by the self-administered questionnaire, focusing on eleven components, covering demographics, musculoskeletal injury and working hours and duration.

Results: A total of 47 participants, 30 (63.8%) male, 39 (83%) had right hand dominance and 8 (12.8%) had left hand dominance. There were endoscopists, trainees and ancilliary staff, 13 (27.7%), 9 (19.1%) and 29(53.2%) respectively. Assessing level of activity, 18(38.3%) had no regular exercise, 11 (23.4%) exercised less than 150 minutes per day, 13 (27%) more than 150 minutes.

23 (48.9%) of the participants had been doing endoscopies for upto 5 years, 24 (51%) had been involved in endoscopy for more than 5 years.

37 (78.7%) reported experiencing pain or numbness, of these 16 (42.6%) had neck pain, 13 (34%) lower back pain, 9(25%) shoulder pain, 7 (19.1%) hand pain, 6 (14.9%) thumb pain, 4(10.6%) elbow pain and 3(8.5%) reported carpal tunnel syndrome. 10 (27%) of those having pain attributed it to endoscopy 21 (56%) were not certain, 6 (16%) said that symptoms were not caused by endoscopy.

16(44.4%), said pain was evident during endoscopy in 12 (34.3%) were quite bothered by their symptoms. The duration of symptoms was more than 6 months in 14 (37%), in 28 (77%) symptoms were static. 11 (29.7%) had to take time off from work, 23.4% of total group. 17 (45.9%) took medications for resolution of pain.

The responders were asked if they use some modifications to prevent these injury and 11(23.4) endoscopic monitor at eye level, 3 (7%) cardiac monitor at headside, 5 (10.6) stopped to move patients 7 (14.9%) sit while performing colonoscopy, 12 (25%) use height adjustable beds.

Conclusion: There is high prevalence of musculoskeletal injury in personnel involved in endoscopy, much of which has been attributed to endoscopic practice by responders in this study. Strategies to improve the ergonomics are vital.

Raising awareness and enhancing ergonomics in endoscopy may prevent endoscopic-related injury.

Neck pain	16 (42.6%)
back pain	13 (34%)
Shoulder pain	9 (25%)
hand pain	7 (19.1%)
Thumb pain	6 (10.6%)
Elbow pain	4(8.5%)
Carpal tunnel	3 (8.5%)

[Musculoskeletal injury frequency]

References: Training the Endo-Athlete: An Update in Ergonomics in Endoscopy Singla, Manish et al. Clinical Gastroenterology and Hepatology, Volume 16, Issue 7, 1003 - 1006
Disclosure: Nothing to disclose

P0864 ENDOSCOPIC MANAGMENT OF PLUMMER-VINSON SYNDROME

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Introduction: Plummer Vinson Syndrome (PVS) also called Kelly Patterson is a rare clinical condition. It is characterized by dysphagia associated with iron deficiency anemia and upper esophageal webs in the post-cricoid region. Endoscopic esophageal dilatation is sometimes necessary. The purpose of our study was to evaluate the clinical, morphological, therapeutic features of this syndrome.
Aims & Methods: Twenty patients with PVS, diagnosed from January 2007 to December 2016, were collected. Treatment was based on endoscopic dilation associated with iron supplementation. The dilation was performed as an outpatient by Savary-Gilliard esophageal bougies with an increasing caliber from 7 to 14 mm. A new dilatation session was performed in case of recurrence of dysphagia and / or esophageal stricture.
Results: There were 20 patients (18 women (90%) and 2 men (10%)). The average age was 52 years (35-73). All patients suffered from dysphagia and anemic syndrome with an average duration of 22 months. All patients had iron deficiency anemia with an average hemoglobin level of 9.7g / dL (5.9-11) and a mean ferritin level of 11 μg / L (4-20). Twenty-three dilatation sessions were performed, on average 1.25 sessions per patient (1 to 3 sessions). One patient had 2 webs, the rest of our patients had a single web. The associated diseases were celiac disease in one case (5%), Biermer anemia in 4 cases (20%) and chronic gastritis Helicobacter Pylori negative in 3 patients (15%). No post-dilation complications occurred. The evolution was favorable marked by a disappearance of the dysphagia and a correction of the anemia in all the cases. No case of malignancy was observed during the patient follow-up with a mean follow-up of 30 months (8-60).
Conclusion: Plummer Vinson syndrome is a rare condition that affects the quality of life of patients. Its treatment is based on endoscopic dilatation and iron supplementation. Due to the progressive risk of malignancy regular monitoring is required.
Disclosure: Nothing to disclose

P0865 VALIDATION OF A SCORING SYSTEM FOR THE QUALITY OF VIEW AT UPPER GI ENDOSCOPY

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Introduction: Despite Oesophagogastroduodenoscopy (OGD) being the gold standard for visualising the upper gastrointestinal (GI) tract, there are few criteria for a successful procedure compared to e.g. colonoscopy. Post OGD upper GI cancer - failing to diagnose upper GI cancer at endoscopy up to 3 years before diagnosis - occurs in 10% of upper GI cancers. Our aim was to validate an OGD visualisation score through evaluating its reproducibility.
Aims & Methods: Subjects undergoing diagnostic OGD were prospectively recruited. The OGD was recorded, and video footage anonymised. Eight experienced endoscopists rated 16 pre-selected video recordings providing two scores for six areas (upper and lower oesophagus, upper and lower stomach, first and second part of duodenum). The first score is an adapted luminal contents score.[1,2] The second view score is based on bowel preparation quality scales. Each area was scored between 1 and 4 with 1 being excellent and 4 being poor; the best score a video could receive was 6 and the poorest was 24 (example contents and view scores - Table 1). The Intra-Class Correlation (ICC) estimate (two-way random effects model for absolute agreement of raters) was used to measure the correlation of the average ratings for both the median scores and the poorest scores for each scoring system.[3]
Results: 16 patients were included in the validation study (50% male, median age 55 (40.5-67.5) years. The median contents score was 11 (range 6-21). The highest contents score recorded by area was: 1 - 5%; 2 - 38%; 3 - 41%; 4 - 16%. The highest view score recorded by area was: 1 - 13%; 2 - 26%; 3 - 45%; 4 - 16%. The median view score was 10 (range 6-19). Both the contents and the view scores demonstrated respectable correlation between mean observer scores.[3] The contents ICC for the median score was moderate, at 0.74 (95% CI 0.48-0.89) and for the highest score, good, at 0.90 (0.81-0.96). The view score also demonstrated good ICC values for the median rating at 0.90 (0.59-0.92) and for the highest score, at 0.85 (0.70-0.93).
Conclusion: The quality of OGD visualisation scoring showed good correlation between observers and appears to be a valid tool for the assessment of OGD quality. Having validated this scoring system, a cohort study will examine the association between visualisation scores and patient and endoscopist specific factors and allow assessment of interventions to improve OGD quality.

Contents Score Description	Grade	View Score Description	Grade
No foam, mucus, bubbles, debris, food or blood	1	Full distension, allowing clear view of all 4 quadrants on withdrawal	1
Minimal foam, mucus, bubbles, food or blood that does not obscure view	2	Full distension not completely achieved resulting in some limitation of view	2
Moderate foam, mucus, bubbles, debris, food or blood obscuring view to some extent	3	Reduced distension resulting in limited mucosal views	3
Abundant foam, mucus, bubbles, debris, food or blood significantly obscuring view	4	A collapsed oesophagus that does not distend, making the mucosa very difficult to assess or impassable stricture preventing full examination or failed intubation	4

[Table 1: example scores]

References: 1: Kuo CH, Sheu BS, Kao AW, et al. A defoaming agent should be used with pronase premedication to improve visibility in upper gastrointestinal endoscopy. Endoscopy 2002;34:531-4. doi:10.1055/s-2002-33220 2: Chang C-C, Chen S-H, Lin C-P, et al. Premedication with pronase or N-acetylcysteine improves visibility during gastroendoscopy: an endoscopist-blinded, prospective, randomized study. World J Gastroenterol 2007;13:444-7. 3: Koo TK, Li MY. A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. J Chiropr Med 2016;15:155-63. doi:10.1016/j.jcm.2016.02.012
Disclosure: Nothing to disclose

P0866 AN AUDIT OF POST OGD UPPER GASTROINTESTINAL CANCERS (POUGIC): 41% ARE POTENTIALLY PREVENTABLE

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Introduction: Upper gastrointestinal (GI) cancer has a poor prognosis, with most diagnosed at a late stage and only 1 in 5 surviving beyond 5 years. Failure to diagnose a cancer during an oesophagogastroduodenoscopy (OGD) may postpone effective treatment. This study examined post OGD upper GI Cancers within two hospitals to estimate how many were potentially preventable.

Aims & Methods: Between 2016-18 all cases of upper GI cancer were identified through coding records. Electronic case files were reviewed for evidence of an OGD between 6 months and 3 years before the cancer diagnosis. An OGD that failed to diagnose upper GI cancer within this time frame was considered a post OGD upper GI cancer (POUGIC). An algorithm was developed to categorise POUGIC cases based on previous work on post colonoscopy colorectal cancer, the presence or absence of a pre-malignant or cancer associated lesion and whether the OGD procedure was adequate or not (Table 1).

Results: 324 upper GI cancer cases were identified during the study period. 66% were male and median age was 72 (IQR 64-80) years. 17 (5%) were considered POUGIC cases – 47% male and median age 71 (64-78) years. 24% were Barrett's surveillance OGDs. Sedation was used in 38% of cancer cases (35% of POUGIC) and 81% of cancer cases were recorded as being well tolerated (71% of POUGIC).

Applying the POUGIC algorithm to the 17 cases identified, adequate OGDs and sampling or follow up were found in: type 1a – 11.8%; 2a – 11.8%; 3a – 35%. For those cases with inadequate OGDs or sampling or follow up: type 1b – 11.8% (pre-malignant lesion – inadequate sampling or follow up); 2b – 17.6% (cancer associated lesion – inadequate sampling or follow up); 3b – 11.8% (possible missed lesion prior exam inadequate). In total 41% of cases were type "b" cases and potentially preventable, examples of which included Barrett's surveillance period being longer than current guidance (Type 1b), inadequate follow up of an oesophageal ulcer (Type 2b) and alternative and inferior investigations arranged when endoscopies were abandoned due to poor patient tolerance of the procedure (Type 3b).

Type 1	Premalignant lesion (Barrett's oesophagus, adenoma, hyperplastic polyp, gastric Intestinal Metaplasia or atrophy) in the same segment as cancer.
a	biopsy and surveillance adequate
b	biopsy and surveillance inadequate
Type 2	Lesion associated cancer same segment as cancer (oesophageal ulcer or stricture, grade C or D reflux oesophagitis, gastric ulcer)
a	Cancer associated lesion noted and biopsy sampling and follow up adequate
b	Cancer associated lesion noted but biopsy sampling and follow up inadequate
Type 3	No pre-malignant lesion/lesion associated cancer same segment as cancer
a	Possible missed lesion, prior exam adequate
b	Possible missed lesion, prior exam inadequate

[Table 1. POUGIC Algorithm]

Conclusion: 5% of upper GI cancer cases identified in this audit were POUGIC, which is lower than previously reported. The POUGIC algorithm used in this audit allows for the categorisation of cases into those which are potentially avoidable and unavoidable – 41 % were potentially avoidable. A focus on quality improvement of Type "b" cases is important to diagnose upper GI cancer earlier and improve outcomes in upper GI cancer.
Disclosure: Nothing to disclose

P0867 ADVANTAGES OF CAP-ASSISTED DEVICE IN THE ENDOSCOPIC MANAGEMENT OF FOOD BOLUS OBSTRUCTION IN THE ESOPHAGUS: A MULTICENTER RANDOMIZED, CONTROLLED TRIAL

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Introduction: Food bolus (FB) is a common presentation to emergency department. Endoscopic removal of FB can be challenging. Data on the use of a cap in FB is limited. This study compares the safety and advantages of cap-assisted device in removal of FB compared to conventional devices.
Aims & Methods: A randomized, prospective multicenter trial at 3 high-volume tertiary-care referral endoscopic centers in Australia was performed. Consecutive patients who underwent an endoscopy for acute food bolus were randomized into this multicenter study. Patients were randomized to use either (i) transparent cap-assisted device or (ii) conventional device/s. Food bolus retrieval time, rate of en-bloc removal, total procedure time, procedure adverse events, type, size and location of FB were studied.
Results: A total of 342 patients were enrolled into the study. The cap-assisted group had a shorter food bolus retrieval time (FBRT) (4.6+3.1min vs. 22.3+11.3mins, $P<$ 0.01) procedure time (22.9+6.1min vs. 47.7+17.1min, $P=<$ 0.01), a higher success rate of FB removal (99.4% vs 93.6%, $P=$ 0.01) a higher rate of en-bloc removal (93.0% vs. 28.1%, $P<$ 0.01), a lower rate of major adverse events (9/171 vs. 13/171, $P<$ 0.01) and a larger measured mean FB size (FB length: 17.6+2.9mm vs. 8.3+9.2mm, $P<$ 0.01 and FB width: 52.3+20.7mm vs. 26.6+27.5mm, $P<$ 0.01) compared to conventional group. The type and location of FB were comparable between the two groups, with no significant differences (p>0.05).
Conclusion: The use of a transparent cap was found to be safe and effective in removal of oesophageal FB. This technique was associated with a shorter procedure time, a higher rate of en bloc removal of FB, a lower rate of adverse events and a larger mean FB size retrieved compared to conventional technique.
Disclosure: Nothing to disclose

P0868 MUCOSAL TRANSPLANTATION FOR THE MANAGEMENT OF STRICTURE AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION

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Introduction: Endoscopic submucosal dissection (ESD) of high grade dysplasia and early esophageal cancer has gained acceptance in the last decade as an effective therapeutic option. Although the short term results of ESD are promising, a high risk of procedure related complications, including post- procedural stricture remains unresolved.
Aims & Methods: The aim of this study were to assess the effectiveness and safety of mucosal transplantation into esophagus from the stomach in preventing stricture formation after ESD in early esophageal cancer. Six patients who underwent circumferential ESD for early esophageal cancer were enrolled. After the patients underwent ESD, the mucosal patches taken from the posterior wall of the middle part of the gastric body by the ESD were placed to the ulcer site of esophagus. The guide wire was then inserted into the gastric cavity via flexible endoscopic channel to fix the patches with the stent at the ulcer site. The stent was removed after the performance with media of 7.83 days (range 7-9). All of the patients were followed up with endoscope.
Results: The graft survival rate was 83.3% with strictures occurred at a mean of 33.67 days (range 20-56) after the procedure. The median number of endoscopic balloon dilatation sessions was 5.67 (range 4-7).
Conclusion: Gastro-esophageal mucosal transplantation for stricture prevention after circumferential submucosal dissection for early esophageal cancer and or high grade dysplasia seems feasible with excellent outcome. This study opens new perspective in this field.
Disclosure: Nothing to disclose

P0869 SAFETY PROFILE OF PERORAL ENDOSCOPIC MYOTOMY (POEM)

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Introduction: Peroral endoscopic myotomy (POEM) is endoscopic method of esophageal myotomy with high clinical efficacy and safety and represents a desirable therapeutic alternative to laparoscopy as a less invasive approach. Nevertheless, POEM remains an invasive intervention carrying risk of potential complications.

Aims & Methods: The aim of our analysis was to assess the perioperative and early postoperative adverse events (AEs) in patients undergoing POEM.

We retrospectively evaluated the prospectively collected data from all consecutive patients who underwent POEM at our institution between December 2012 and May 2018 and searched for periprocedural complications.

Results: A total of 231 patients have undergone 243 POEM procedures (12x re-POEM) from which 50 procedures (20.6%) passed uneventfully while in 193 procedures (79.4%), some AE occurred. Perioperative AEs included subcutaneus emphysema (79/243; 32.5%; no treatment needed), capnoperitoneum requiring puncture (141; 58%), allergic reaction to antibiotics (2; 0.8%), anaesthesia-related complications (14; 5.8%). Postoperative AEs included pain requiring analgesics (158; 65%), fever (20; 8.2%) and pneumonia (3; 1.2%). One patient (0.4%) lost taste and smell irreversibly. A total of 10 serious adverse events occurred in 8 patients (3.3%): post-POEM leak from mucosal incision requiring endoscopic clipping in 5, pneumothorax in 2 (1 required drainage), pleural effusion requiring drainage in 1 and scrotum emphysema in 1 case. One patient died during the procedure due to cardiac arrest (the autopsy revealed unrecognized pulmonary hypertension and severe ischemic heart disease). The mean length of stay was 2.5 (±0.5) days, prolonged (≥4 days) hospitalization was required in 25 (10,8%) patients.

ASA score was available in 170 patients: I- 44/170 (25.9%), II- 90 (52.9%) and III- 36 (21.2%). In patients with ASA I, II, III no adverse events occurred in 18.2%, 17.8% and 16.7% respectively. Serious complications were diagnosed in patients with ASA I, II, III in 2.3%, 4.4% and 5.6% respectively. The correlation between severe complications and ASA score was not statistically significant (p=0.754).

Conclusion: POEM-related adverse events are rather common; however, most of them are mild. Although being quite rare, severe complications, and even fatal, may still occur. ASA score does not seem to be a significant predictor of major complications.

Disclosure: Nothing to disclose

P0870 FITTING THE QUALITY INDICATORS IN FECAL IMMUNOHISTOCHEMICAL TEST (FIT) POSITIVE COLONOSCOPY

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Introduction: Adenoma detection rate (ADR) is an important quality measure to assess the colonoscopy examination and high ADR is shown to protect against CRC. The ADR varies widely amongst endoscopist. Recently, adenoma per colonoscopy (APC) has been proposed as an additional quality measure to overcome the limitations with ADR. It was suggested that high ADR with low APC rate may reflect less thorough "remove one adenoma and done" type colonic evaluation.

We hypothesized that this may not be true and ADR consistently correlates with APC during colonoscopy. We studied the relationship of ADR and APC in FIT positive patients where adenoma prevalence is higher and compared their efficacy based on correlation with advanced adenoma detection rate (AADR).

Aims & Methods: We retrospectively studied the FIT positive database from November 2016 to October 2018 at Singapore General Hospital. Four gastroenterologist and 13 surgeons performed the colonoscopy. We excluded endoscopist who performed less than 10 cases from analysis. We defined advanced adenoma as adenoma ≥10mm in size or with villous histology or high-grade dysplasia. We included them in the ADR and APC calculation. We used descriptive and Student-t test statistics for comparison. We used Pearson's correlation and Fisher r-to-z transformation to compare the relationship between ADR and APC, ADR and AADR, and APC and AADR. We performed multivariate analysis to identify factors that predicted high ADR.Our institutional review board approved this audit.

Results: We analyzed 476 FIT positive patients who underwent colonoscopy: 118 evaluated by gastroenterologist and 358 by surgeons. The mean ± SD age was 64± 8 years and majority were females (53%). Each endoscopist performed 28 ± 14 colonoscopies. The mean Boston bowel preparation score was 6.3 ± 1.6. The caecal intubation rate was 100% and the mean withdrawal time was 11.6 ± 1.7 minutes. The overall ADR, APC and AADR was 51%, 1.06 and 16%, respectively. We found the ADR, APC and AADR was significantly higher for gastroenterologist than surgeons (45% vs. 70%, 0.8 vs. 1.8, 14 vs 22, p=0.0001). We found the overall ADR correlated strongly with APC (R=0.89, p=0.0001) and moderately with AADR (R=0.71, p=0.001). Similarly, the APC correlated significantly to AADR (R=0.61, p=0.009). We did not observe any difference in the correlation coefficient between ADR-AADR and APC-AADR (0.71 vs. 0.61, p=0.63). Age and withdrawal significantly predicted high ADR (p< 0.001) in multivariate analysis. The cancer detection rate in this entire cohort was 5%.

Conclusion: ADR was significantly higher in FIT positive patients and correlated significantly with APC and AADR. In quality assessment of colonoscopy, ADR should be used as the indicator than APC. We did not observe "remove one adenoma and done" behavior.

Disclosure: Nothing to disclose

P0871 UNDERWATER ENDOSCOPIC RESECTION FOR COLONIC LESIONS IN DIFFICULT AND CHALLENGING SITUATIONS

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Introduction: Classical endoscopic mucosa resection (EMR) creates a submucosal cushion of fluid to avoid muscle layer damage at the time of snare resection. Sometimes the submucosal injection may narrow the working space in the colon, or increase the tension of the lesion and sometimes make it harder to snare (specially nongranular lesions). Underwater endoscopic resection (UEMR), first described by Dr. Binmoeller[1], avoids the need for submucosal injection, and it may be helpful in challenging situations such as non-lifting lesions, or difficult locations.

Aims & Methods: The aims of the study were to assess the safety, utility and technical success rate of the underwater technique for the treatment of challenging colonic lesions.

Clinical, endoscopic and histological data were collected from cases of UEMR performed in 4 centers between January 2016 and July 2018. Inclusion criteria was lesions with no-lifting sign (in previous endoscopic injec-

tion) that were poor candidates for classic EMR, difficult location (ileocecal valve, diverticulum or appendix) or lesions with a previous failed attempt for EMR in an expert center. SMSA polyp score was not applied because previous attempt of EMR is not addressed by this scoring system.

Results: 60 UEMR in challenging situations were performed, of which 57 completed follow-up (mean 186 days) to date. The mean age of the patients was 66.14, being 68% men.

There were 37 (61.67%) non-lifting lesions (including recurrent/residual lesions in ICV and appendix, and non-treated lesions), 17 (28.3%) appendicular or ileocecal valve lesions not previously treated, 1 (1.6%) intradiverticular lesion, 2 (3.3%) lesions in complex sigma and 3 (5%) residual lesion including ileocecal valve.

The mean size (diameter) of the lesions was 19 mm, and the mean size (largest diameter) of the resection specimen was 15.3 mm (95% CI 13.68 - 16.99 mm) being the largest specimen of 30 mm in diameter, with En bloc resection in 34 cases (56,67%), and piecemeal resection in 2-3 fragments in 19 cases (31,67%). The histology showed pT1 in 4 cases (one low risk pT1a), HGD and intramucosal cancer in 8 cases, and no advanced histology (LGD, SSP/A withoud displasia) in the others. There was one postprocedural bleeding requiring endoscopic treatment and no major complications (no perforations). The success (complete macroscopic resection) of the technique was 98% with 3 recurrences, that were succesfully re-treated endoscopically and 4 patients underwent surgery, 3 cases due to high risk features at histology (pT1b) and 1 case of deep intraapendicular lesion.

Conclusion: Underwater endoscopic resection in the colon is a safe and useful technique for challenging colorectal lesions such as non-lifting lesions, appendiceal, ileocecal valve, diverticular, and difficult sigmoid locations.

Residual/Recurrent lesion non-lifting	27 (45%) -includes AO & ICV
Non-lifting untreated lesion	10 (16,67%)
AO untreated lesion	12 (20%)
ICV untreated lesion	5 (8,3%)
Intradiverticular untreated lesion	1 (1,6%)
Failed EMR attempt at sigmoid lesion	2 (3,3%)
Incomplete resection (re-schedule)	3 (5%) -one case ICV

[Location of the lesions]

References: 1. Binmoeller K, Weilert F, Shah J, Bhat Y, Kane S. Gastrointest Endosc. 2012 May;75(5):1086-91. doi: 10.1016/j.gie.2011.12.022.
Disclosure: This abstract was accepted as oral presentation at ESGE Days 2019

P0872 SAFETY AND FEASIBILITY OF ENDOSCOPIC FULL-THICKNESS RESECTION IN COLORECTUM USING OVER THE SCOPE CLIP. A MULTICENTER SPANISH EXPERIENCE

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Introduction: Endoscopic full-thickness resection (EFTR) using a modified over-the-scope clip (FTRD kit) in the colorectum is a technique that allows *en-bloc* full-thickness resection of lesions for selected cases (e.g. non-lifting lesions suspicious of flat malignant polyps), especially for lesions < 20mm[1].

Aims & Methods: To study the safety and feasibility of the endoscopic full-thickness resection (EFTR) in colorectal lesions using an over-the-scope-clip.

The clinical, endoscopic and histological data were collected prospectively in all cases of EFTR performed in 10 centers of Spain using the FTRD kit (Ovesco Endoscopy, Tübingen, Germany) during the period from June 2015 to July 2018.

Results: 71 EFTR were scheduled.

In 3 patients EFTR was not possible due to impossibility to pass the sigmoid with the kit. In the other 68 patients the technical success was 85.2% with en-bloc resection in 83,8%.

The mean age of the patients was 67 years (range 40-86), being men 64,79%.

Indications were: non-lifting sign recurrent lesions (46.47%), non-lifting sign untreated lesions (23.94%), incomplete resection of non-lifting sign lesions (11,26%), appendicular lesions (2.8%), suspected T1 lesion (7%), EFTR of suspicious scar (4,2%), subepithelial lesions (4.2%).

The mean diameter of the resected specimen was 21.53mm (95% CI 19.87-23,2).

Final histology: LGD adenoma (40%), HGD adenoma (23%), intramucosal adenocarcinoma (4.47%), SSP (5.87%), T1sm1 (2.9%), advanced adenocarcinoma >sm2 (13%), scar tissue (6%) and others (2.8%).

In one case the OTSC was not deployed, with intraprocedural perforation. There were 2 cases of delayed perforation and 1 case of delayed bleeding. 10 patients underwent surgery: 3 perforation, 1 intraapendicular lesion, and 6 for advanced adenocarcinoma.

During the follow-up, 3 recurrences / residual tissues were treated endoscopically (benign histology).

Conclusion: EFTR using a modified OTSC (FTRD system) for selected cases (such as failure of other endoscopic treatments in lesions < 20-25mm) is a safe and feasible technique.

Evaluation of the insertion with a long cap (e.g. "prOVE" cap) and traction of the lesion prior to EFTR is highly recommended. Special care must be taken to avoid performing the resection if the OTSC is not deployed.

References: 1. Schmidt A ,Bayna T, Schumacher B, et al. Gut 2017 . doi: 10.1136/gutjnl-2016-313677
Disclosure: Nothing to disclose

P0873 EFTR WITH OTSC IN COLORECTUM: WHAT HAPPENS WHEN THE LESION IS TRAPPED IN THE OVER-THE-SCOPE-CLIP AND IS NOT RESECTED

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Introduction: Endoscopic full-thickness resection (EFTR) using a modified over-the-scope clip (FTRD kit) in the colorectum is feasible for selected cases (e.g. suspicious of flat malignant polyps) , allowing *en-bloc* resection of lesions up to 20-25mm. But in some cases there is a risk of technical failure due to poor traction, rupture of the snare or loosing of the resection plane, and part of the lesion or the whole of it might get trapped inside the over-the-scope clip (OTSC).
Aims & Methods: Our aim was to study the outcomes of the patients with the lesion trapped in the OTSC due to technical failure.
Clinical, endoscopic and histological data were collected prospectively in all cases of EFTR performed in 10 centers of Spain using the FTRD kit (Ovesco Endoscopy, Tübingen, Germany) during the period from June 2015 to July 2018.
Cases of technical failure with part or the entire lesion trapped inside the OTSC were analyzed.
Results: 68 cases of EFTR were evaluated.
In 10 cases, the lesion was trapped in the OTSC and could not be resected properly.
The mean age of the patients was 71 years, being men 80%.
Indications were: non-lifting sign recurrent lesions (6 cases), non-lifting sign untreated lesions (1), incomplete resection with non-lifting sign (2), appendicular lesions (1).
Location were appendix (1 case), stump (1), right colon (1), transverse colon (2), left colon (2), sigma (2), rectosigmoid junction (1).
The mean diameter of the lesion was 19mm.
In 8 cases there was a partial resection of the lesion (mean diameter of the lesion 18mm), and in 2 cases only biopsies were taken.
Final histology: LGD (4 cases), HGD (2), intramucosal adenocarcinoma (1), SSP (2), advanced adenocarcinoma >sm2 (2).
In the follow-up, three lesiones underwent surgery (appendicular lesion and advanced adenocarcinoma), 3 residual lesions were treated endoscopically and in 4 cases the scar showed no residual tissue.
Conclusion: In some cases of intended EFTR , residual tissue trapped inside the OTSC might be easily treated endoscopically and sometimes might be treated by the OTSC itself, if the residual lesion is small.
Disclosure: Nothing to disclose

P0874 LONG-TERM EFFICACY AND SAFETY OF COLD SNARE POLYPECTOMY VERSUS CONVENTIONAL ENDOSCOPIC MUCOSAL RESECTION FOR 5-9 MM COLORECTAL POLYPS

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Introduction: Cold snare polypectomy (CSP) is becoming a common method for removal small or diminutive polyps without submucosal injections or electrocautery. The aim of this study was to assess long-term efficacy and safety of cold snare polypectomy versus conventional endoscopic mucosal resection for 5-9 mm colorectal polyps with well-matched patient groups.
Aims & Methods: In this retrospective analysis, 328 colorectal polyps from 187 patients were removed with CSP or endoscopic mucosal resection (EMR) in Seoul St. Mary's Hospital between March 2014 and June 2014. Resected polyps were divided into CSP group and EMR group. A 1:2 propensity case-matches analysis was used with covariates of baseline characteristics, including sex, age, polyp size, follow-up duration, and procedure-performed endoscopists. Finally, 5-9 mm sized polyps were included in this study. The recurrence rate and complication rate were compared between the matched two groups.
Results: Two groups were well balanced by propensity score matching, and 151 polyps were matched. Fifty eight polyps from 35 patients were treated by CSP and 93 polyps from 71 patients treated by EMR. In CSP group and EMR group, mean age (years, mean ± SD) was 64.8±7.6 and 64.1±9.5 (p=0.638), polyp size 5.9±0.8 cm and 6.0±0.9 cm (p=0.397), and follow-up duration 33.1±9.2 months and 32.2±10.0 months (p=0.584), respectively. While 6 of 58 polyps (10.3%) in CSP group recurred during follow-up period, 1 of 93 polyps (1.1%) recurred in EMR group (p=0.008). Serious adverse events such as delayed bleeding and perforation did not occur in either group.
Conclusion: CSP group had significantly higher recurrence rate than EMR group after resection of 5-9 mm colorectal polyps. Both methods were safe without serious adverse events. Further prospective study including a large number of patients is required.
Disclosure: Nothing to disclose

P0875 TIP-IN ENDOSCOPIC MUCOSAL RESECTION FOR LARGE COLORECTAL SESSILE POLYPS

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Introduction: Tip-in endoscopic mucosal resection (EMR) is a modified EMR technique using which en bloc resection of large colorectal sessile polyps can be performed; however, its usefulness for colorectal sessile polyps of >20 mm has not been reported. This study examined treatment outcomes of tip-in and conventional EMR for large colorectal sessile polyps of ≥20 mm.
Aims & Methods: This was a retrospective case-control study conducted at a single tertiary center in Japan. Subjects included those with large colorectal sessile polyps of ≥20 mm, excluding pedunculated-type polyps, who underwent endoscopic resection between January 2010 and January 2019. For tip-in EMR, 15-mm snare master or 20-mm spiral snare (Olympus Co., LTD, Tokyo, Japan) was used. After a sufficient local injection, the snare tip was projected by 2 mm and a mucosal incision was created on the oral side of the lesion. After this, while fixing the snare tip to the submucosal layer, the snare was expanded while gradually pulling the scope. Once the lateral margin of the lesion was completely secured, the snare was closed while de-airing, and resection was then performed. The primary outcome was endoscopic treatment outcomes when using tip-in and conventional EMR, and the secondary outcome was the local recurrence rate after endoscopic treatment.

Results: During the study period, 126 patients 126lesions (72 men and 54 women, mean age: 69.9±12 years, mean tumor size: 23.6±4.1mm) were resected using tip-in or conventional EMR. Forty-three colorectal lesions were treated using tip-in EMR and 83 using conventional EMR. Tip-in EMR had a significantly higher en bloc resection rate (90.7% vs. 50.7%, P = 0.008), and significantly shorter treatment duration (6.64 ± 0.64 min vs. 10.47 ± 0.81 min, P = 0.005) than conventional EMR. Perforation rates with tip-in and conventional EMR were 4.6% and 3.6%, respectively, indicating no significant difference (P = 0.556). All cases with perforation were successfully sutured using hemoclips, and additional surgical intervention was not required. Local recurrence was examined in 80 cases who were followed up for >6 months after endoscopic resection. The mean follow-up period was 25.7 ± 15.5 months. Recurrence rate was 0% and 7.0% in tip-in and conventional EMR cases, respectively, without significance difference (P = 0.495.)

Conclusion: Tip-in EMR showed high en-block resection rate and no residual tumor was found. This technique is a potential endoscopic treatment alternative for large colorectal sessile polyps of ≥20 mm.

References: Chien H, Imai K, Hotta K, Ito S, Yamaguchi Y, Kawata N, Tanaka M, Takizawa K, Kakushima N, Matsubayashi H, Ono H (2016) Tip-in EMR for R0 resection for a large flat colonic tumor. Gastrointest Endosc 84:743.

Disclosure: Nothing to disclose

P0876 FACTORS ASSOCIATED WITH SEDATION USE IN DIAGNOSTIC AND SCREENING PATIENTS ≥50 YEARS OF AGE: OBSERVATIONS FROM THE EUROPEAN COLONOSCOPY QUALITY INVESTIGATION QUESTIONNAIRE

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Introduction: The development of the procedure questionnaire, by the European Colonoscopy Quality Investigation (ECQI) Group, has been previously described in posters presented at United European Gastroenterology Week, 2015 and 2016.

Aims & Methods: To assess the factors associated with sedation use in diagnostic and screening patients ≥50 years of age using questionnaire responses from across Europe. Data collection is an ongoing process: we analysed data collected between 2/6/16 and 30/4/18 (n=6445).

All screening and diagnostic colonoscopies in patients aged ≥50 years were identified in our dataset (n=3365). Stepwise multivariable logistic regression analysis was conducted to determine the main factors associated with sedation use. Analysis was performed on the following variables: age in 10-year categories; body mass index (BMI) categories; gender; inpatient status; reason for procedure; time of day colonoscopy performed; previous total colonoscopy in last 5 years; Boston Bowel Preparation Score (BBPS) ≥6; retraction time categories; chromoendoscopy used; high-definition equipment used; assistive technology used; intended endpoint; and intended endpoint reached.

Results: There were 1394 procedures where the results of all selected variables were known provided by 59 practitioners from 38 institutions: 71.0% of procedures used sedation. In order, the most associated variables were:
1. Use of high-definition equipment (76.3% vs. 55.5%, p< 0.0001).
2. Use of assistive technology (59.0% vs. 72.8%, p< 0.0001).
3. Female gender (78.8% vs. 62.2% male, p< 0.0001).
4. Longer retraction time (83.9% > 10 minutes vs. 65.1% 6 - 10 minutes and 66.7% < 6 minutes, p< 0.0001).
5. Use of chromoendoscopy (76.3% vs. 69.5%, p=0.0051).
6. Younger patient age (78.0% 50 - 59 years vs. 67.6% 60 - 69, 68.1% 70 - 79, 69.4% ≥80, p< 0.0001).
7. Inpatient status (84.0% vs. 68.7% outpatient, p< 0.0001).

Conclusion: The use of sedation appears to be more associated with factors related to the equipment/techniques used during colonoscopy than patient characteristics.

Disclosure: Toth E, Agrawal A, Amaro A, Hünger M, Petruzziello L, Jover R, Ono A: Consultant & advisory board participant to Norgine. Spada C: Consultant fee from Norgine. Brink L: Consultancy & Advisory Board participant to Norgine, AMBU. Fischbach W: Consultancy & Advisory Board participant to Norgine; Speaking - Abbott, Bio Merieux, Falk; Advisory speaking - Aptalis, Fresenius Biotech, Pfizer; Advisory - Boehringer Ingelheim, med update. Kinnunen U: Consultant & advisory board participant to Norgine and Olympus (European NBI Expert Training Group). Riemann JF: In terms of ECQI, consultant to Norgine, otherwise no conflict of interest. Amlani B: Employee of Norgine. Koulaouzidis A: No relevant conflict of interest. Patai A: No conflict of interest. Pecere S: No conflict of interest.

P0877 LINKED COLOR IMAGING AND BLUE LASER IMAGING IMPROVE THE VISIBILITY AND COLOR DIFFERENCE VALUE OF COLORECTAL POLYPS IN UNDERWATER CONDITION

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Introduction: Underwater endoscopic mucosal resection (UEMR) is simple and effective technique, and recently widespread for the treatment of colorectal polyps. Although UEMR has lots of benefits compared to conventional EMR, UEMR has some problems to be solved. Especially, in underwater condition, diagnosis of the extent of the superficial colorectal lesions is sometimes difficult compared to that in conventional air fulfilled condition because chromoendoscopy is not available. Image enhanced endoscopy (IEE) such as blue laser imaging (BLI) or narrow band imaging was reportedly useful to diagnosis the lesion extent, but these IEE are not good at poor bowel preparation. On the other hand, linked color imaging (LCI) which enhances color contrast seemed theoretically useful to diagnose the lesion extent even in underwater. Thus, we evaluated which observation mode (white light imaging [WLI], BLI, or LCI) was the most effective to diagnose the lesion extent of superficial colorectal polyps in underwater condition.

Aims & Methods: Between April 2018 and December 2018, consecutive superficial colorectal polyps observed by three mode (WLI, BLI, and LCI) in underwater condition before UEMR were prospectively registered into database of our endoscopy unit, and the images were retrospectively analyzed. Observation in underwater and UEMR was conducted by using a LASEREO system (FUJIFILM, Tokyo, Japan) with an EC-L600ZP endoscope. Color values of the lesion and surrounding non-neoplastic mucosa were calculated using Photoshop (CIE L*a*b* color space). Then, color difference between the lesion and surrounding non-neoplastic mucosa (ΔE) was examined in each mode. The extent of the lesion was confirmed histologically after UEMR. The visibility score of images in each mode was also evaluated by four evaluators (2 experts and 2 non-experts, who were blinded to background and histology). The visibility score was categorized from 4 (excellent visibility) to 1 (poor visibility).

Results: In total, 73 colorectal polyps (50 adenomatous polyps [Ad] and 23 sessile serrated adenoma/polyps [SSA/P]) observed by each mode were analyzed. Median lesion size (range) was 7 (5-25) mm. Among them, 61 polyps (44 Ad and 17 SSA/P) were observed in transparent underwater condition, and 12 polyps (6 Ad and 6 SSA/P) were observed in crowdy underwater condition due to poor bowel preparation. In transparent condition, color difference between the lesion and surrounding non-neoplastic mucosa (ΔE) of 61 lesions with BLI (8.2) and LCI (7.4) was significantly higher than with WLI (5.2) ($P< .001$). The mean visibility score of BLI (3.5) and LCI (3.4) was significantly higher than that of WLI (3.4) ($P< .001$). There was no significant difference between BLI and LCI regarding color

difference and visibility score. The color difference and visibility score of 44 Ad was similar to 61 polyps as mentioned above. But, the color difference of 17 SSA/P with BLI was significantly higher than that of WLI, and there was no significant difference between LCI and WLI. In crowdy underwater condition, the mean visibility score of WLI (2.5) and LCI (2.8) was significantly higher than that of BLI (2.1) (*P=002, P< .001*, respectively). The mean visibility score of LCI was tend to be higher than that of WLI (*P=008*). Accurate measurement of color difference was impossible in crowdy condition.

Conclusion: BLI and LCI was useful to evaluate the extent of colorectal polyps in transparent underwater condition. BLI seemed to be suitable to evaluate the extent of SSA/P. In crowdy underwater condition, LCI was better to evaluate the colorectal polyps.

References: 1. Yamashina T, uedo N, et al. Comparison of Underwater vs Conventional Endoscopic Mucosal Resection of Intermediate-size Colorectal Polyps. Gastroenterology 2019 Apr 11. pii: S0016-5085(19)35685-9. 2. Binmoeller KF, Weilert F, et al. "Underwater" EMR without submucosal injection for large sessile colorectal polyps (with video). Gastrointest Endosc. 2012 May;75(5):1086-91.

Disclosure: Nothing to disclose

P0878 REVIEW OF EFFECTIVENESS OF PATIENT INFORMATION LEAFLET (PIL) IN PATIENTS UNDERGOING GASTROINTESTINAL ENDOSCOPY

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Introduction: In the United Kingdom, endoscopy services are overburdened and waiting times are long due to limited resources. To improve this, there is a national drive for increasing Straight to Test (STT) patients. An effective Patient Information Leaflet (PIL) is paramount to facilitate this. PILs are an effective patient education tool to support patients in making informed choices for their health care. Multiple factors influence the effectiveness with readability being the most important factor that directly affects patient's ability to access the information provided.(1) Effective provision of information can improve patient satisfaction, greater compliance to treatment and follow up, thereby improving patient care.

Research shows patients retain only 20% of verbal discussion with health care providers, but this improves to 50% with additional written or visual information. (2)

As per our endoscopy unit policy, all patients are provided with a paper PIL pre-procedure (updated every 3 years).

Aims & Methods: Primary aims:

1. To assess patient use and effectiveness of PIL

2. To assess effectiveness of PIL in STT patients at South Tyneside District Hospital.

Secondary aims:

1. To assess preferred formats of PIL

Methods: All consecutive patients attending the endoscopy day ward over a 10 week period were asked to fill in a questionnaire and return it prior to discharge.

Results: 206 patients returned the PIL (M=97, F=105, Prefer not to say=4). Patients underwent gastroscopy (n=79), colonoscopy (n=70), flexible sigmoidoscopy (n=12), capsule endoscopy (n=14). Majority of patients (52.7%) were aged 55-74 years.

Only 76.2% of patients read the PIL in full with women more likely than men. There is interest in electronic format and audio-visual aids despite a majority (88.1%) of patients still preferring printed PIL. 1 in 5 of patients who did not read the PIL thought an electronic PIL would be useful.

1 in 6 patients did not find the PIL useful. Issues reported were that the PIL was too long/difficult to understand/too complicated (n=8). Others felt the PIL had incorrect information or caused anxiety (n=5). Patients who did not find the PIL useful were >45 years.

Patients who had a prior discussion with their clinician or had an endoscopy pre-assessment found the PILs very or extremely useful (n=151, 85.6%). STT patients account for 10% of all patients (these patients neither had a discussion with a clinician nor a pre-assessment). Only 62% of these patients read the PIL in full and 23.5% of them did not find the PIL useful, suggesting poor understanding of the procedure.

Conclusion: Almost a quarter of patients did not read the PIL and 18% of patients found the PIL somewhat useful or not useful. This implies poor understanding of the procedure which may have legal consequences. Although our numbers are low, our results still show a significant proportion of STT patient did not find the PIL useful. In view of increasing use of STT pathway, there is a need to reinforce the use of pre-assessment clinics and to introduce newer innovations such as audio-visual aids. Use of audio-visual aids in an ophthalmology pre-operative setting has shown to meet patient information needs, improve patient satisfaction and reduce patient anxiety.(3)

Our results show a demand for electronic platforms to access patient information and healthcare providers need to adapt to this.

We aim to re-audit patient satisfaction after introduction of audio-visual aids.

References: 1. Protheroe J, Estacio EV, Saidy-Khan S. Patient information materials in general practices and promotion of health literacy: an observational study of their effectiveness. Br J Gen Pract. 2015;65(632):e192-7. 2. Gauld VA. Written advice: compliance and recall. J R Coll Gen Pract. 1981;31(230):553-6. 3. Ahmed KJ, Pilling JD, Ahmed K, Buchan J. Effect of a patient-information video on the preoperative anxiety levels of cataract surgery patients. J Cataract Refract Surg. 2019;45(4):475-479.

Disclosure: Nothing to disclose

P0879 ENDOSCOPIC SUBMUCOSAL DISSECTION FOR COLORECTAL LESIONS: OUTCOMES FROM A UNITED STATES EXPERIENCE

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Introduction: Endoscopic submucosal dissection (ESD) is an endoscopic resection technique used for removal of large non-pedunculated colorectal polyps and early (T1) colorectal cancers. This innovative modality provides an alternative to surgical resection. It allows for en bloc resection regardless of lesions size, which facilitates specimen orientation and accurate pathologic staging. The technique is also often curative as previously demonstrated by experiences showing a high R0 resection rate with low recurrence rate. While ESD is a well established technique in Asia for management of early gastrointestinal (GI) neoplasia, adoption in the western world has been limited.

Aims & Methods: \We aim to describe outcomes from a colorectal ESD program at a United States (US) academic tertiary medical center and compare this to published non-Asian and Asian experiences.

Retrospective review was performed of colonic lesions referred to the University of Chicago Medical Center for ESD from 2012 to 2019. Data collected included lesion characteristics, procedural outcomes, histology findings, and patient follow up.

Results: The study included 73 patients with a median age of 63 years (range 30-83) of which 34 were male (46.6%) and 39 were female (53.4%). The rectum was the most common location (n=47, 64.4%). Mean lesion size was 30.1 mm (SD± 18.0 mm) and most frequent Paris classification was IIa (n=21, 28.8%).

Complete ESD was achieved in 72 cases (98.6%) with 61 patients (83.6%) confirmed to have an R0 resection on histology. ESD was performed en bloc in 50 cases (68.5%). The en bloc resection rate improved from 54.1% to 83.3% from the first half of the cases to second half (p=0.007). Adenocarcinoma was present in 14 of the resected lesions (19.2%). The mean procedure time was 116.3 min (SD± 54.4). Complications occurred in 9 cases (12.3%) with 4 cases of delayed bleeding (5.5%), 4 cases of perforation (5.5%) and 1 case of perforation with delayed bleeding (1.4%).

Most complications (n=6, 66.7%) were successfully treated endoscopically. Surgery was needed in three cases of perforation. Follow up procedures were performed in 32 patients (43.8%) while the remaining 41 patients (56.2%) followed up elsewhere or are not due yet. Mean follow up interval was 7.4 months (SD± 4.1).

Follow up endoscopy showed inflamed or regenerative mucosa in almost all cases (n=31, 96.9%) with only 1 case of recurrent adenoma (3.1%). Table 1 compares these US outcomes to a recent meta-analysis[1] of pooled ESD outcomes in non-Asian and Asian countries.

	United States Center	Non-Asian Countries	Asian Countries
En Bloc Resection	68.5%	81.2%	93.0%
R0 Resection	83.6%	71.3%	85.6%
Recurrence	3.1%	5.2%	1.1%
Delayed Bleeding	6.8%	4.2%	2.4%
Perforation	6.8%	8.6%	4.5%
Need for Surgery Post ESD Complication	4.1%	3.1%	0.8%

[Colorectal ESD Outcomes at a United States Single Center Compared to Pooled Outcomes from Non-Asian and Asian Countries]

Conclusion: This study shows successful outcomes of colorectal ESD at a US tertiary center. While the en bloc resection rate was lower than in other published cohorts, there was a learning curve with significant improvement over time. Additionally, both the R0 resection rate and lesion recurrence rate were more favorable than in other Western experiences, and approach the rates seen in Asian countries. Complications were slightly higher in this study, but most were managed endoscopically. Overall, colorectal ESD is an important endoscopic advancement and effective nonsurgical treatment for early neoplasia. ESD training in the United States should be increased to optimize utilization and achieve outcomes comparable to Asia.
References: 1. Fuccio L, Hassan C, Ponchon T et al. Clinical outcomes after endoscopic submucosal dissection for colorectal neoplasia: a systematic review and meta-analysis Gastrointest Endosc 2017;8674-86.e17
Disclosure: Nothing to disclose

P0880 FEASIBILITY OF THE ENDOSCOPIC CLASSIFICATION OF FIBROSIS IN ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) FOR COLORECTAL NEOPLASMS

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Introduction: The possibility of complete curative en bloc resection is sometimes related to the presence and degree of fibrosis in the submucosal layer (SM), rather than tumor size and location. In this study, we analyzed the clinical outcomes of ESD for colorectal neoplasms accompanied by fibrosis. The aim of this study was thus to establish a safe and curative ESD procedure for colorectal neoplasms showing fibrosis in the SM layer.
Aims & Methods: ESD was performed for 1,659 epithelial neoplasms in 1,620 patients (male 906, female 714, average 66.7 years old) from January 2003 to October 2018, and was completed for 1,643 lesions. Of these cases, 359 showed SM fibrosis. These cases were divided into three groups: absence of fibrosis (A), fibrosis due to benign causes (B), and fibrosis due to cancer invasion (C). Furthermore, cases were classified as mild (grade 1), moderate (grade 2), or severe (grade 3). Clinical outcomes and pathological findings of the above-mentioned ESD cases were analyzed according to these endoscopic classifications to facilitate the safe achievement of ESD. In addition, histological validation of endoscopic diagnosis was examined for the 240 of the 359 cases with fibrosis, to clarify for differential diagnosis between Type B and C.
Results: Of the 359 cases with fibrosis, 226 cases involved benign causes (Type B), and 133 cases were considered related to cancer invasion (Type C). As the results of the validation study (n=240) for differential diagnosis between Types B and C as follows; sensitivity: 88.7%, specificity: 90.5%, accuracy: 89.2%, PPV: 96.3%, NPV: 74.0%. En bloc resection rates (n=359) were as follows: A, 97.7%; B-1: 97.1%; B-2: 88.8%; B-3: 63.3%; Type C-1: 100%; C-2: 91.4%; C-3: 61.5%. The en bloc resection rates for Types B-3 and C-3 were significantly lower (P < 0.05) than that for Type A. Similarly, R0 rates for Type B (82.8%) and C (82.9%) were significantly lower than that for Type A (93.5%). There were 12 cases (0.7%) of perforation, 5 of which (Type B) required emergency surgery. From these results, tumors accompanied by mild to moderate fibrosis become the standard indication for ESD. The tumors accompanied by severe fibrosis should be indicated as relative indications for ESD and required high quality of ESD technique to avoid perforation.

Conclusion: Accurate diagnosis of fibrosis based on the perioperative endoscopic findings appears feasible and contributes to completing the ESD procedure safely and curatively.
Disclosure: Nothing to disclose

P0881 ONLY LINKED COLOR IMAGING INCREASES COLOR CONTRAST BETWEEN COLON POLYPS AND SURROUNDING MUCOSA

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Introduction: HD-white light endoscopy (WLE) is the gold standard in the detection of colon adenoma. Virtual chromoendoscopy cannot improve adenoma detection. Recently linked color imaging (LCI) was developed which is combining special light and a post processing in one imaging modality. First study results show a better visibility and a higher adenoma detection rate using LCI.
Aims & Methods: Evaluation of color difference between colon adenoma and surrounding mucosa as a potential explanation of higher detection rate.
Results: Prospective acquisition of images from adenoma in the three light modes WLE, Blue Light Imaging (BLI) and LCI.
Transformation of the images into L*a*b* color space. Measurement of color at areas of 31 x 31 pixels, two inside the polyp and 2 in the surrounding mucosa each. Calculation of the color difference according to the Delta E (Lab) Method.
We used paired t-test for statistical analysis.
Results: In total 90 polyps were evaluated. Delta-E in WLE was lowest (12.34 ± 6.73). The highest Delta-E value was calculated for LCI (16.83 ± 10.85). The Delta-E using BLI was 14.38 ± 11.42. The difference between LIC vs BLI and BLI vs. WLE was not significant. He difference between WLE and LCI was highly significant (p=0.002)
Conclusion: Only linked color imaging leads to a significant increase of the color contrast of colon adenoma. This is a useful explanation for the reported increased adenoma detection rate using LCI.
Disclosure: JW honor. of Fujifilm

P0882 FEASIBILITY AND ACCURACY OF INNOVATIVE 3 DIMENTIONAL COLONOSCOPE IMAGE USING FIBER BRAG GRATING SENSOR

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Introduction: Colonoscopy is difficult procedure, largely due to unpredictable looping during insertion. If the endoscopist is able to see the colonoscope on the image display, fewer attempts are needed to straighten the shaft of the scope. A prototype Fiber Brag Grating(FBG) scope guided endoscopy provides a facility for continuous viewing on a monitor of the position of the colonoscope during examination. The aim of this study was to evaluate the accuracy and feasibility of the innovative 3D Colonoscope image using FBG sensor.
Aims & Methods: In the first part of the study, the FBG sensor was inserted into the working channel of a general colonoscope in the first 100 cm from the tip of the scope. Then, the scope was placed in front of the monitor to confirm movement of the scope in all three dimensions. We evaluated loop formation such as N loop, alpha loop, reverse alpha loop, with the 3D imaging monitor. In the second part of the study, 5 patients underwent colonoscopy with a FBG sensor, the colonoscope can be displayed in anteroposterior or lateral view, or in both positions together. The fluoroscopy was used in all investigations for comparison.

Results: In the first part of the study, the results showed that the shape sensor was reliable at a maximum bending curvature of 80mm-1. The average tip position error was 1.22 ± 0.82 mm, which corresponds to 0.82 ± 0.7% of the total length of the sensor. Colonoscope movement and loops were detected correctly through the monitor. The prototype FBG in the second part of the study showed a high correlation and little discrepancy with the comparative findings on fluoroscopy. During the colonoscopy, we could confirm the shape of the loop made in the body.

Conclusion: Image of colonoscopy reconstructed by FBG sensor can be successfully applied to display colonoscope configuration. This flexible, thin and almost weightless shape sensor would be a novel technique for identification of colonoscope shape.

Disclosure: Nothing to disclose

P0883 EFFECTIVENESS OF SUCTION VALVE BUTTON REMOVAL FOR POLYP FRAGMENTATION AND PATHOLOGICAL DIAGNOSIS IN EXTRACTING RESECTED COLON POLYPS ON THE BASIS OF PROPENSITY SCORE MATCHING ANALYSIS

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Introduction: When colorectal polyps were endoscopically resected, they were usually extracted by suctioning and sent for pathological examination. However, the fragmentation of polyp during extraction is one of the limitations for appropriate pathological diagnosis. Suction valve button is one of the intricating parts in construction of endoscope which may have implicit fragmentation risk.

Aims & Methods: In this study, we retrospectively evaluated the effect of removing the suction valve button during extracting polyp for fragmentation and pathological cut-end diagnosis.

We reviewed the reports of endoscopically removed polyps between September 2018 and February 2019. Cases included in this study were clinically diagnosed as neoplasm using magnifying endoscopy, collectively resected by cold snare polypectomy (CSP) or EMR, and extracted by suctioning. Endoscopic and pathologic findings listed as following were collected; patient age, sex, colonoscope (HQ-290ZI: device channel 3.7 mm, PCF-290ZI: device channel 3.2 mm, Olympus), lesion location, lesion size, resection method (CSP or EMR), removal of suction valve button during polyp extraction, and for the outcomes, polyp fragmentation rate, pathological histology, and pathological cut-end among neoplastic lesions ("negative" or "positive/imponderable"). Polyp extraction with suction valve button was the conventional method of pressing the button and retrieving the polyp into a polyp trap affixed to the suction connector of the colonoscope. For the polyp extraction without suction valve button, we removed the button from the colonoscope before suctioning the polyp and sealed the suction valve cylinder by finger to apply suction.

Fragmentation was defined as the macroscopic presence of multiple pieces of extracted polyp in the trap, all of which was double-checked by doctor and nurse, and all of the pieces were put into the formalin bottle for fixation. We used one-to-one propensity score matching method to adjust for the difference between the groups of with and without suction valve button.

Results: We selected 322 pairs of cases for analysis on the basis of propensity score matching. After matching, the difference of the variables between each group were closely balanced. The fragmentation rate was significantly different between the extraction with and without suction valve button (36,7% vs. 22.4%, $P < .001$). For histological diagnosis in each group, the rate of normal colon mucosa was 8.4% and 9.9%, whereas that of neoplastic lesion was 90.0% and 88.6%, which were not significantly different. Among the neoplastic lesions, the rate of cut-end negative was higher in button-removed group (82.8% vs 90.8%, $P = .010$). On the other hand, when we concern pathological histology of normal colon mucosa as cut-end "imponderable", the cut-end negative rate was 76.7% vs 81.8% ($P = .113$). In the multivariate analysis, suction valve button removal was the only independently associated factor for fragmentation (Odd ratio [OR] 0.496, $P < .001$) and for negative cut-end in neoplastic lesions (OR 0.505, $P = .009$). Additionally, the rate of pathological diagnosis as normal colon mucosa was independently associated with the resection method (CSP 10.4%, EMR 2.1%, OR 0.342, $P = .003$), but not with button removal (OR 1.23, $P = .453$).

Conclusion: Suction valve button removal during extracting polyps was an effective way to improve the rates of fragmentation and pathological cut-end diagnosis of neoplastic lesions.

Disclosure: Nothing to disclose

P0884 FLEXIBLE SIGMOIDOSCOPY FOR EVALUATION OF ANASTOMOTIC INTEGRITY PRIOR TO THE REVERSAL OF A LOOP ILEOSTOMY

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Introduction: Preoperative evaluation for anastomotic status has been routinely done with contrast enema (CE) before ileostomy closure. However, there are few data supporting the routine practice of examining CE prior to ileostomy closure. Actually, CE gives limited information to surgeon compared to endoscopic evaluation and even can cause colon perforation and contrast peritonitis.

Aims & Methods: The aim of this study is to evaluate the feasibility and usefulness of preoperative flexible sigmoidoscopic examination instead of contrast enema (CE) prior to ileostomy closure in rectal cancer patients who underwent anterior resection with a loop ileostomy.

We reviewed prospectively collected data of patients with rectal cancer who underwent anterior resection with a loop ileostomy from October 2008 to November 2016. We compared postoperative outcomes between patients who underwent flexible sigmoidoscopy (FS) and underwent CE study.

Results: Ninety-eight patients underwent CE examination, and 49 patients underwent FS prior to the reversal of a loop ileostomy. There was no significant difference in gender, body mass index, anastomotic type and anastomotic level between two groups except for age and time to ileostomy closure. Two patients in CE group developed anorectal suppuration after the reversal of an ileostomy. They showed intact anastomotic site on preoperative examination. Patients in FS group developed no anorectal suppuration after the reversal of an ileostomy.

Conclusion: Preoperative findings on CE could not predict postoperative anorectal problem. FS can evaluate the status of anastomotic site without increasing the postoperative anorectal problem. We suggest that CE can be replaced by FS in assessment of anastomotic integrity prior to the reversal of a loop ileostomy.

Disclosure: Nothing to disclose

P0885 ANALYSIS OF AN OPEN-ENDED COAXIAL METHOD FOR DETECTION COLORECTAL CANCER OBTAINED THROUGH COLONOSCOPY BIOPSIES: PRELIMINARY RESULTS

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Introduction: Many technological advances have been made to optimize the detection of colorectal cancer lesions. Research has shown that the electromagnetic properties of healthy and cancerous tissues differ in many biological tissues.

Aims & Methods: We aim at analyzing electromagnetic properties of healthy and pathological colon tissue and their differences with biopsies gathered from colonoscopy procedures. The dielectric constant and the conductivity of healthy and pathological colorectal samples of 70 patients were analyzed using the open-ended coaxial technique and were later correlated with their pathology results. Since these properties depend on multiple factors like tissue's temperature, system calibration and the patient itself, polyps were analyzed by computing the difference between the healthy and the pathological samples within each patient. Measurements were performed on adenocarcinomas (CRC), adenomas without dysplasia, adenomas with low-grade dysplasia, adenomas with high-grade dysplasia, hyperplastic and hamartomatous polyps.

Results: The differences obtained in dielectric constant between CRC and healthy pairs are higher than in the rest of pathologies. Within the frequency region where larger differences appear, the median of this difference is 4.8 units. Differences in conductivity are lower, having a median of 2 units. By selecting a threshold in the difference of dielectric constant that maximizes the diagnostic capability of CRC, the system showed a sensitivity of 75% and a specificity of 89% for detecting this disease (table 1).
Conclusion: Results have shown that measurements of electromagnetic properties of tissue could aid in the detection of colorectal pathologies. The variability of the results is quite large, and hence the system should be improved prior to a potential implementation.
Disclosure: Nothing to disclose

P0886 CONECCT CLASSIFICATION: A NEW CLASSIFICATION TO BEST CHOOSE THE TREATMENT IN CASE OF LARGE SUPERFICIAL COLORECTAL LESION

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Introduction: Several classifications has been developed to predict the risk of submucosal invasion in case of superficial colorectal lesion. We developed the CONECCT (COlorectal NEoplasia Classifiation to Choose the Treatment) classification that merged all existing classification (Paris, SANO, KUDO, WASP, LST, NICE) in one table to simplify endoscopic characterization. The originality of this classification is the combination of macroscopic features with mucosal pattern and vascular pattern abnormalities without using magnification.
We performed a prospective study to evaluate the performance of the CONECCT classification to differentiate adenoma (CONECCT IIA) and high risk adenoma or superficial carcinoma (CONECCT IIC: SANO IIIA or Macronodule bigger than 1 cm or ulceration or non-granular type).
Aims & Methods: Bicenter prospective study of all characterization data recorded before ESD for large superficial colorectal lesions in two European expert's centers. Sensibility (Se) Specificity (Spe) Positive predictive value (PPV) Negative predictive value (NPV) of presence of macronodule bigger than 1 cm, SANO IIIA, Paris 0-IIC (presence of ulceration) and CONECCT IIC were calculated.
Lesions were evaluated thanks to last generations endoscope: FUJIFILM series 760 or OLYMPUS series 190 without magnification or dual focus just before the ESD procedure.
Results: 515 colorectal ESDs were performed between 01/2016 and 04/2019 at 2 European expert's centers.
Results of ESD: En bloc Resection = 95,7%, R0 resection = 81%, Curative resection = 80%
466 lesions with a mean size of 57 mm that had all characterization data (Paris, SANO, KUDO, WASP, LST, NICE, CONECCT) were included. 64% of lesions were LST-G, 21% LST-NG and 15% protruded lesions. 80% of lesions were CONECCT IIc, 42% SANO IIIA, 14% had an ulceration (Paris O-IIc) and 51% had a macronodule.
Histological analysis: LGD : 147 (32%) ; HGD (Vienne 4.2 and 4.3) : 174 (37%) ; IM carcinoma: 101 (22%) ; Sm < 1000 : 22 (5%), sm > 1000:17 (4%) T2: 4 (1%)
Sensibility and specificity:
· LST with macro-nodule bigger than 1 cm:
- Submucosal cancer: Sen=74% / Spe=51% / PPV=13.6% / NPV=95,1%
· Paris IIC
- Submucosal cancer: Sen=24.4% / Spe=86.8% / PPV=15.4% / NPV=92%
· Sano IIIA
- Submucosal cancer: Sen=69.8% / Spe=60.4% / PPV=15.4% / NPV=95.1%
· CONECCT IIC
- Submucosal cancer: Sen=100% / Spe=21.1% / PPV=11.6% / NPV=100%
No difference was observed using FUJIFILM or OLYMPUS Scope (p=0,95):
FUJIFILM:
· Sano IIIA
- Submucosal cancer: Sen=66.7% / Spe=59,2%% / PPV=13.5% / NPV=94.9%

· CONECCT IIC
- Submucosal cancer: Sen=100% / Spe=23.6% / PPV=10.4% / NPV=100%
OLYMPUS:
Sano IIIA
- Submucosal cancer: Sen=78.9% / Spe=57.1% / PPV=14.6% / NPV=96.7%
CONECCT IIC
- Submucosal cancer: Sen=100% / Spe=20% / PPV=10.4% / NPV=100%
Conclusion: The CONECCT classification allows to predict with a 100% sensibility and a 100% NPV the risk of submucosal invasion with high definition scope without magnification.
PPV is always very small (around 15%) indicated that we are not able to clearly identify the submucosal cancer. However NPV of CONECCT classification is perfect (100%) indicated that we are able to exclude submucosal carcinoma using the CONECCT classification (CONECCT IIA). CONECCT IIA lesions never presented submucosal adenocarcinoma and are best target for a piece-meal resection, however en-bloc resection by ESD should be the treatment of choice for CONECCT IIC lesions.
Disclosure: Nothing to disclose

P0887 AN INTERNATIONAL POLYPECTOMY PRACTICE SURVEY

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Introduction: Polypectomy plays a key role in colorectal cancer (CRC) prevention. In recent years new polypectomy techniques, like cold snare resection, have been introduced. Ablative techniques, such as hot forceps resection and argon plasma coagulation (APC), have been associated with more complications and seemed to be losing popularity. We conducted an international survey to better understand changes in polypectomy practice patterns during recent years, uptake of cold snare polypectomy and adherence to guideline recommendations.
Aims & Methods: Colonoscopy practitioners were contacted through Gastroenterology, Colorectal Surgery and Endoscopy societies around the world and asked to participate in a Google Form online survey. The primary aim was to evaluate the uptake of cold snare polypectomy in the last 5 years and to evaluate the current predominant polypectomy approaches for colorectal polyps between 1-20mm. Secondary aims were to evaluate perceived benefits and concerns related to each specific polypectomy techniques and to evaluate adherence to recent guideline recommendations.
Results: The survey was distributed by 9 societies and completed by 808 colonoscopy practitioners around the world. Survey participants reported an 87.5 % (95% CI 85.2%-89.8%)) increase in use of cold snare during the last 5 years, with 55.3% (95% CI 51.9%- 58.7%) of survey participants reporting more than a 50% increase in its use. Cold snare was reported to be the predominant polypectomy technique for 4-5 mm polyps (67.0% (95% CI (63.7%-70.2%) and also for 6-10mm polyps (55.2% (95% CI 51.7%-58.6%). For polyps 1-3 mm, cold forceps remains the predominant utilized polypectomy technique (78.4% (95% CI (75.6%-81.3%), while hot snare polypectomy remains the predominant utilized polypectomy technique for polyps 10-20 mm (92.5% (95% CI (90.7%-94.3%)) (table 1). 54.8 % (95% CI (51.4%-58.3%) of survey participants reported having no concerns for using cold snare, which was more than for other techniques: cold forceps (29.7%), hot snare (27.0%), APC (13.1%) and hot forceps (9.5%). Cold forceps most reported concern was incomplete resection (60.6% (95% CI (57.3%-64.0%)). Hot snare most reported concerns were delayed bleeding (54.8%; 95% CI (51.4%-58.3%) and perforation (48.1%; 95% CI (44.7%-51.6%)). 66.6% (95% CI (63.3%- 69.8%) of survey participants reported never using APC and 61.5% (95% CI (58.2%-64.9%)) never using hot forceps for standard polypectomy.
Conclusion: This survey found a substantial increase in utilizing cold snare polypectomy during recent years. Cold snare polypectomy has meanwhile become the predominant polypectomy approach for 4-10mm colorectal polyps among endoscopists. For smaller (1-3mm) polyps cold forceps and for larger (10-20 mm) polyps hot snare polypectomy currently remains the

predominant polypectomy approach. Ablative techniques (hot forceps and APC) are not used anymore by the majority of endoscopist for standard 1-20 mm polypectomy. Current clinical practice patterns are well aligned with recently issued guideline recommendations.
Disclosure: Nothing to disclose

Polyp size	APC	Cold Forceps	Hot Forceps	Cold Snare	Hot Snare
1 - 3 mm	3 (0.4%)	626 (78.4%)	25 (3.1%)	140 (17.5%)	4 (0.5%)
4 - 5 mm	3 (0.4%)	188 (23.4%)	28 (3.5%)	537 (67.0%)	46 (5.7%)
6 - 10 mm	2 (0.2%)	22 (2.7%)	15 (1.9%)	442 (55.2%)	320 (40.0%)
11 - 20 mm	10 (1.2%)	3 (0.4%)	10 (1.2%)	37 (4.6%)	742 (92.5%)

[Physicians preferred resection strategy for various polyp sizes]

P0888 THE OPTIMAL IMAGING WINDOW FOR MOLECULAR FLUORESCENCE ENDOSCOPY USING A C-MET TARGETED FLUORESCENT PEPTIDE FOR THE DETECTION OF DYSPLASTIC COLORECTAL POLYPS

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Introduction: White-light colonoscopy is the gold standard for colorectal polyp detection and colorectal cancer (CRC) prevention. However, there is still a polyp detection miss-rate of up to 22%.[1] Fluorescence molecular endoscopy (FME) using EMI-137, a c-Met targeted fluorescent peptide, has the potential to guide the endoscopist and improve polyp detection rates.[2] The aim of this study was to determine the optimal dose-to-imaging interval for FME and to further evaluate the safety and tolerability of EMI-137 in a population at high-risk for CRC.

Aims & Methods: FME was performed in 15 patients with a colorectal adenoma containing at least low-grade dysplasia. EMI-137 was administered intravenously (0.13 mg/kg) to three patients at either 1, 2 or 3 hours prior to colonoscopy. The two cohorts with the most optimal target-to-background ratio (TBR), or the 1- and 2-hour cohort in case of similar TBRs, were expanded to six patients. Fluorescence was visualized and quantified *in vivo* using multi-diameter single-fiber reflectance, single-fiber fluorescence (MDSFR/SFF) spectroscopy. Fluorescence was correlated to standard histology and c-Met expression on 4mm tissue sections *ex vivo*. EMI-137 localization was assessed using fluorescence microscopy and confirmed by *in vitro* c-Met binding experiments.

Results: FME using EMI-137 appeared to be safe and well tolerated. The dose-to-imaging interval for the 1-, 2- and 3-hour cohort was 0:54 - 1:28 hour (n=6), 1:50 - 2:33 hours (n=6) and 2:41 - 3:20 hours (n=3). *In vivo* visualization and quantification of fluorescence showed significantly increased fluorescence in dysplastic versus normal tissue for the 1-, 2- and 3-hour cohorts (median intrinsic fluorescence $Qm^f_{a,x}$= 3.46·10^{-4} vs. 2.15·10^{-4} mm^{-1}, P < 0.0001; 3.28·10^{-4} vs. 2.04·10^{-4} mm^{-1}, P < 0.0001 and 3.22·10^{-4} vs. 1.94·10^{-4} mm^{-1}, P < 0.0001 respectively). *Ex vivo,* an overall median TBR of 1.62 was observed based on histological delineation of 41 tissue sections, with significant c-Met membrane overexpression in dysplasia. Fluorescence microscopy showed increased fluorescence in the proximity of the dysplastic crypts compared to normal tissue. A dose-dependent specific binding of EMI-137 was observed *in vitro.*

Conclusion: We demonstrate that FME using EMI-137 appeared to be safe and feasible within a one-to-three hour timeframe. No significant differences have been observed between the time-cohorts, although a dose-to-imaging interval of one hour was considered preferable from a clinical perspective. Future pivotal studies will study the use of EMI-137 for improved detection of colorectal polyps in screening colonoscopies of patients at average risk of developing colorectal cancer.

References: 1. van Rijn JC, Reitsma JB, Stoker J, et al. Polyp Miss Rate Determined by Tandem Colonoscopy: A Systematic Review. The American Journal of Gastroenterology. 2006 Feb;101(2):343-50. 2. Burggraaf J, Kamerling IMC, Gordon PB, et al. Detection of colorectal polyps in humans using an intravenously administered fluorescent peptide targeted against c-Met. Nature Medicine; 2015 Jul 13;21(8):955-61.
Disclosure: Nothing to disclose

P0889 USE OF THE *BOSTON BOWEL PREPARATION SCALE* IN THE REAL WORD: WHAT AFFECTS IT?

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Introduction: The adequacy of bowel cleansing is one of the quality measures for lower intestinal endoscopy, affecting both the security and the diagnostic accuracy of the procedure. The aim of this study was to evaluate the quality of bowel preparation in a series of consecutive exams and to determine its predictive factors.

Aims & Methods: Retrospective study assessing patients that underwent colonoscopy in a tertiary hospital between 01/2016 and 06/2018. For the morning procedures, the preparation was given on the day before colonoscopy and for the afternoon procedures, a split-dose bowel cleansing regimen was adopted. The *Boston Bowel Preparation Scale* (BBPS) was used to evaluate the quality of the bowel preparation - total BBPS score ≥6 was considered as adequate.

Results: A total of 4872 colonoscopies in 3839 patients [men - 51.4%, mean age - 61.2±13.9 years] were performed, by 11 endoscopists. The main indications were: surveillance for neoplastic polyps/colorectal cancer (CRC) (52.0%); family history of CRC (21.9%). In this last case, patients were educated regarding bowel preparation by the Family Risk Clinic nurses.

Cecal intubation rate was 96.2%. Inadequate bowel preparation (BBPS< 6) was observed in 32.3% of the colonoscopies, with BBPS being ≤1 in the right colon in 26.8% of cases in the right colon; 16.4% in the transverse colon, and 17.9% in the left colon.

The quality of bowel preparation was significantly associated, in univariate analyses, with gender (BBPS< 6: 37.5% men vs 26.8% women), day of the week, hour of the exam, morning/afternoon procedure (BBPS< 6: 35.0% morning vs 22.5% afternoon), endoscopist and family history of CRC (BBPS< 6: 21.8% of the exams performed because of family history of CRC vs 35.5% of the exams performed for other reasons).

On multivariate logistic regression analysis, predictive factors for quality of bowel preparation were gender (p< 0.001), day of the week (p=0.016), morning/afternoon procedure (p< 0.001) and colonoscopies performed because for family history of CRC (p< 0.001).

Conclusion: In the real world, we confirmed gender, educational interventions and split dose regimens (adopted for the afternoon procedures) as factors influencing quality of bowel preparation.
Disclosure: Nothing to disclose

P0890 EFFICACY AND SECURITY OF THE DOUBLE CLIP COUNTERTRACTION METHOD FOR RESIDUAL OR LOCALLY RECURRENT LESIONS IN COLONIC ENDOSCOPIC SUBMUCOSAL DISSECTION

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Introduction: Endoscopic submucosal dissection (ESD) for the resection of scarred colonic lesions is a feasible but challenging technique because of submucosal fibrosis. We previously reported an internal traction method using two clips and a rubber band and making ESD easier.This study

aimed to evaluate the efficacy and security of ESD using this countertraction technique (DCT-ESD) in case of residual or locally recurrent colonic lesions.

Aims & Methods: We retrospectively analyzed all residual or locally recurrent colonic lesions, DSM treated, in two french expert center, between august 2017 and february 2019. The countertraction technique has been systematically used.

The primary endpoint was the En bloc R0 resection rate. Secondary endpoints were en bloc resection rate, degrees of fibrosis, tumor diameter, procedure time, resection speed, secondary surgical treatment, and complication rate.

Results: Among the 44 patients included, there were 29 (66%) locally recurrent colonic lesions and 15 (34%) residual lesions after a primary endoscopic resection. Severe submucosal fibrosis was observed in 39 patients (88.6%) and intermediate fibrosis in 5 patients (11.4%). Mean resected specimen diameter, procedure time and resection speed were 40mm [20-65mm], 50min [6-230min], and 27mm2/min [6-95mm2/min], respectively. The en bloc resection rate was 90.9% (4 piecemeal mucosal resections conversions at the beginning of the study). This rate increases to 100% from the 11th resection due to the learning curve. Only 72.7% of all patients had negative margins (En bloc R0) often due to a hole inside the lesion. At all, 4 patients (9.1%) had needed secondary surgical treatment, three for incomplete resection and one for none curative resection criteria. Complication included three (6.8%) small intraoperative perforations endoscopic treated. There was no secondary perforation but one case of delayed bleeding. No surgery was necessary following a complication.

Conclusion: In cases with scarred colonic lesions, thanks to the double clip and rubber band countertraction method, ESD allows curative resection with low complication risk. This technique is an alternative to Full thickness resection (FTRD) particularly for large lesions over 3 cm.

References: - Lacopini F,et al. Colorectal endoscopic submucosal dissection: predictors and neoplasm-related gradients of difficulty. Endosc Int Open. sept 2017; - Matsumoto A, et al. Outcome of endoscopic submucosal dissection for colorectal tumors accompanied by fibrosis. Scand J Gastroenterol. nov 2010; - Oyama T. Counter Traction Makes Endoscopic Submucosal Dissection Easier. Clin Endosc. nov 2012 ; - Jacques J et al. Double-clip counter-traction using a rubber band is a useful and adaptive tool for colonic endoscopic submucosal dissection. Endoscopy. févr 2018;

Disclosure: Nothing to disclose

P0891 THE ROLE OF THE EDUCATIONAL PROJECT «QUACOL - QUALITY IN COLONOSCOPY» IN IMPROVING OF THE COLONOSCOPY QUALITY: RESULTS OF YAROSLAVL REGIONAL CANCER HOSPITAL STUDY

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Introduction: Suboptimal quality of colonoscopy is associated with increased risk of interval colorectal cancer. It is uncertain how quality in colonoscopy might be improved. We assessed the effect of the educational project «QuaCol» on colonoscopy quality. It was performed in Russia between trials «QuaCol 1» and «QuaCol 2». We compared results of «QuaCol 1» versus «QuaCol 2».

Aims & Methods: We examined colonoscopies performed at the Endoscopy Department of Yaroslavl Regional Cancer Hospital (YRCH) within trial «QuaCol 1» between September and December 2014 and trial «QuaCol 2» between November 2018 and February 2019. The main quality indicators such as polyp detection rate (PDR), adenoma detection rate (ADR), caecal intubation rate (CIR) and colonoscopy withdrawal time (CWT), bowel preparation were assessed. We assessed also using of split-regimen laxative. The colonoscopies were performed by the same 9 colonoscopists during «QuaCol 1» and «QuaCol 2».

Our study divided colonoscopists into 2 groups, depending on their respective ADRs within «QuaCol 1»: low-detectors (ADR ≤ 20 %) and high-detectors (ADR > 20%). Then we assessed their ADRs in «QuaCol 2» and compared results.

Results: 987 patients (F 65,9%, M 34,1%; mean age 53) were included in the trial «QuaCol 1» and 1366 patients (F 71%, M 29%; mean age 55) were included in the trial «QuaCol 2». The main quality indicators were ADR (21,2 vs 29 %, p < 0,0001), CIR (92, 3 vs 96 %, p < 0,0001), PDR (40 vs 49 %, p < 0,0001), CWT > 6 min (34 vs 41,4%, p < 0,0001), adequate bowel preparation (92 vs 94 %, p < 0,05). Split-regimen was used (83 vs 94,8 %). The ADR of low-detectors increased significantly higher (16,7 vs 24,5%, p < 0.0001) than of high-detectors (31 vs 35,4 %, p < 0,01) after performing of the educational project «QuaCol».

Conclusion: The quality of colonoscopy in YRCH within «QuaCol 1» was recognized as suboptimal to according recommendation ESGE. Then was performed the educational project «QuaCol - Quality in Colonoscopy». The educational project included some lectures about colonoscopy quality indicators, about importance of adequate bowel preparation and factors affecting on patients complains - low-volume laxative, split-regimen, low-fiber diet. Hand-on-trainings were organized for improving of the technique and skills of endoscopists. Then «QuaCol 2» was performed. According to our study, the quality of colonoscopy in YRCH Obecame is optimal after performing of the educational project «QuaCol». Our data demonstrated that ADR is increased (it was statistically valid). CIR is increased (it was statistically valid). PDR is increased (it was statistically valid). CWT > 6 min is increased (it was statistically valid). Adequate bowel preparation is slightly increased (it was not statistically valid). Our study showed the medical educational may be a key factor of improving in colonoscopy quality. The improvement of colonoscopy quality is associated with increase prevention role of colonoscopy against colorectal cancer.

References: 1. Kaminski Michal F. et al. Performance measures for lower gastrointestinal endoscopy: a European Society of Gastrointestinal Endoscopy (ESGE) Quality Improvement Initiative. Endoscopy 2017;49. 2. B. Rembacken, C. Hassan, J. F. Riemann, A. Chilton, M. Rutter, J.-M. Dumonceau, M. Omar, T. Ponchon. Quality in screening colonoscopy: position statement of the European Society of Gastrointestinal Endoscopy (ESGE). Endoscopy 2012; 44: 957-968. 3. M. Antipova, M. Burdyukov, M. Bykov, L. Domarev, E. Fedorov, S. Gabriel, K. Glebov, S. Kashin, M. Knyazev, A. Korotkevich, A. Kotovsky, I. Kruglova, V. Krushelnitsky, E. Mayat, M. Merzlyakov, D. Mtvralashvili, A. Pyrkh, O. Sannikov, E. Shitikov, A. Subbotin, A. Taran, V. Veselov, D. Zavyalov , C. Hassan, F. Radaelli, L. Ridola, A. Repici and M. Korolev. Quality of coloscopy in an emerging country: A prospective, multicentre study in Russia. Gastroenterology 2015; 148 , 4: 209-210.

Disclosure: Nothing to disclose

P0892 OUTCOMES OF COLONOSCOPIC SURVEILLANCE AND MOLECULAR PHENOTYPING IN PATIENTS AT HEREDITARY RISK OF COLORECTAL CANCER

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Introduction: An estimated 35% of cases of colorectal cancer (CRC) are due to heritable factors, and approximately 30% of the UK population has a family history of CRC. Those at hereditary risk should be effectively managed through registration, phenotypic and genotypic characterisation, and risk-stratified colonoscopic surveillance. We assessed the impact of surveillance in patients at hereditary risk of CRC managed through the Family History of Bowel Cancer Registry at West Middlesex University Hospital (WMUH). Through analysis of this registry data, we assessed the diagnostic yield of colonoscopic surveillance and assessed the role of molecular testing.

Aims & Methods: We analysed prospectively collected colonoscopic surveillance data at WMUH between 2010-2018. Patients were divided into five family history risk populations as defined by current British Society of Gastroenterology (BSG) guidelines. Patient demographics including age, gender and family history were collated, alongside colonoscopy findings, and molecular data including mismatch repair (MMR) status and germline testing. Impact of these variables on the prevalence of non-advanced adenomas (NAAs) and advanced adenomas (AAs) were assessed by logistic regression using SPSS software. Time to NAA or AA was determined by survival analysis and findings were compared between index and surveillance colonoscopy.

Results: In total, 752 colonoscopies were performed in 454 patients with 1081 years of colonoscopic follow-up. Five CRCs, 56 AAs and 204 NAAs were identified with an adenoma detection rate (ADR) of 20.01%. Time to both NAA and AA occurred at significantly earlier age in patients with LS. The prevalence of CRC, AA and NAAs in patients without Lynch syndrome (LS) was 0.46%, 7.85% and 25.04%, respectively, with no significant differences between non-LS family history populations. Although the number of affected offspring did associate with AA detection on univariate analysis (P = 0.038), only age was significantly associated with both NAA and AA detection on multivariable analysis (P < 0.001). A normal index colonoscopy was strongly associated with normal findings during surveillance (p < 0.001). A family history of MMR proficient CRC was associated with an ADR equivalent to the non-LS population (22.67%). Molecular testing significantly altered surveillance strategy in 27.6% of patients through re-categorisation of familial risk.

Conclusion: This data emphasises the strong association of colorectal neoplasia with MMR status and the need to exclude LS in patients at familial risk. Age is independently associated with colorectal neoplasia risk in this analysis, however patients often undergo colonoscopic surveillance inappropriately early. A normal index colonoscopy is associated with a low diagnostic yield in subsequent colonoscopies in this population, and this relatively low yield may influence future guideline strategies. Finally, we believe that molecular phenotyping to risk stratify patients helps to facilitate effective colorectal cancer prevention.

Disclosure: Nothing to disclose

P0893 COLONOSCOPIST KEY PERFORMANCE INDICATORS IN PATIENTS WITH A FAMILY HISTORY OF COLORECTAL CANCER UNDERGOING SURVEILLANCE

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Introduction: Colorectal cancer (CRC) accounts for over 40,000 new cases/year in the UK, and in 35% of cases CRC develops due to inherited susceptibility. Patients at hereditary risk undergo colonoscopic surveillance to reduce CRC incidence and mortality. High quality colonoscopy, measured by key performance indicators (KPIs) including adenoma detection rate (ADR), caecal intubation rate (CIR), and polyp recovery rate (PRR) may enhance surveillance outcomes.

This is particularly important for high risk patients where colonoscopy may be a one-off intervention, or where there is significant risk of interval cancers. Consequently, we assessed colonoscopy quality in a cohort at hereditary risk of CRC managed at West Middlesex University Hospital (WMUH), and determined their relationship to colonoscopist KPIs in non-surveillance cohorts.

Aims & Methods: We analysed prospective colonoscopic surveillance data through the Family History of Bowel Cancer Registry at WMUH between 2010-2019. A cohort of 454 patients at hereditary risk were divided into five risk groups based on current British Society of Gastroenterology guidelines. Patient demographics including age, gender and family history were collated alongside colonoscopist data, colonoscopy findings, and KPIs. Using linear regression on SPSS software, we compared findings to the ADR, CIR and PRR of colonoscopists in non-surveillance patients.

Results: During surveillance, 752 colonoscopies were performed by 12 clinicians. The adequacy of bowel preparation and CIR across all colonoscopists was 89.2% and 98.0%, respectively. The collective ADR during index, 1st, 2nd and 3rd surveillance colonoscopies was 19.6%, 15.9%, 29.3% and 25.8%, respectively. T

here was no difference in ADRs at Index, 1st and 2nd surveillance colonoscopy between familial risk groups. The average ADR for colonoscopists across all surveillance colonoscopies was 22.8% (8.6-38.1%). In the non-surveillance cohort ADR was 29.5% (13.3-40.7%), CIR 93.5% (78.8-95.7%) and PRR 95.2% (86.9-98.2%). Colonoscopist ADRs during surveillance correlated with both ADRs (R²0.738, P < 0.01) and PRRs (R²0.695, P < 0.01) in the non-surveillance cohort but not CIR.

Conclusion: ADR is the main indicator of efficacy during colonoscopy and a consistent independent risk factor for interval CRCs in screening colonoscopies. Colonoscopists ADRs in patients undergoing surveillance correlated with their ADRs and PRRs during colonoscopies in a non-surveil-

lance cohort. Therefore, we suggest that all surveillance colonoscopies are performed by endoscopists consistently achieving BSG colonoscopy KPI minimum standards.

Disclosure: Nothing to disclose

P0894 FREE DIET VS LOW-RESIDUE DIET IN THE QUALITY OF OUTPATIENT COLONOSCOPY: A PROSPECTIVE, RANDOMIZED, SINGLE BLIND CLINICAL TRIAL

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Introduction: Colonoscopy is the best exploration for detection of colorectal cancer (CRC) and polyps. An adequate bowel preparation, usually defined with BBPS score ≥2-2-2, is a marker of quality that should be fulfilled in at least 85% of colonoscopies. With this aim, a low-residue diet is usually recommended for outpatient colonoscopies. Compliance with bowel preparation protocol is mandatory. In this context, a free diet without restrictions may improve tolerance and adherence to the bowel cleansing protocol, especially in outpatient setting, the main scenario of colorectal cancer screening programs.

Aims & Methods: Our aim was to compare the quality of colonoscopy with two different diets: low-residue diet and a free diet without restrictions.

A prospective, randomized, single blind clinical trial was designed to evaluate the impact of low-residue diet and free diet without restrictions the day before colonoscopy for bowel cleansing. The BBPS scale was used, with a value of ≥2-2-2 defining an adequate preparation. Patients between 18 and 75 years old, scheduled for outpatient colonoscopy were included. Patients with previous colonoscopies, colorectal surgery, obesity grade II o more (BMI≥35) or severe constipation without response to conventional treatment were excluded. Participants were randomised to group A (low-residue diet the day before colonoscopy) or B (free diet, including breakfast on the day of colonoscopy). Endoscopists were blinded for diet. Sodium picosulfate/magnesium citrate was used in all patients, giving the first dose 8 hours and the second dose 4 hours before colonoscopy. Sex, age, indication for colonoscopy, BMI, diabetes, diverticula, tolerance to preparation, exploration and recuperation, time of exploration and polyp detection rate (PDR) were evaluated. Results are shown as means and percentages, and analysed by chi-square and T-student test as appropriate.

Results: Based on previous sample size calculation, 201 patients were included (52.2% women, median age 51 years, range 23-75). Main indications for colonoscopy were CCR family history (60.1%), rectal bleeding (15.9%) and abdominal pain (6.9%). Diabetes was present in 6.5% of patients. The median BMI was 26.7±3.88. Diverticula were reported in 20.8% of cases. The median procedure time was 14.5 minutes (875±360 seconds). PDR was 37.8%. 108 patients (53.7%) were included in group A and 93 (46.3%) in B. An adequate bowel preparation was observed in 96.2% in group A and 87.1% in group B (p=0.03). Only 2 procedures had to be interrupted due to poor bowel preparation, both in group A. There were no differences in age (p 0.99), sex (p 0.19), BMI (p 0.91), tolerance to preparation (p 0.20), exploration (p 0.32) or recuperation (0.93), exploration time (0.54) or PDR (0.80). No differences were observed between patients with adequate or poor bowel preparation in sex (p=0.21), age (p=0.22), BMI (p=0.17), diverticula (p=0.46), diabetes (p=0.57), amount of liquids (p=0.86).

Conclusion: In outpatient colonoscopy without risk factors for poor bowel preparation, a free diet without restrictions for bowel cleansing is associated with an adequate bowel preparation in more than 85% of patients. The impact of a low-residue diet in this setting is statistically significant, although clinically less relevant than expected.

Disclosure: Nothing to disclose

P0895 EFFICACY AND SAFETY OF SUCK-AND-SNARE EMR FOR TREATMENT OF NON-LIFTING COLORECTAL POLYPS

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Introduction: Endoscopic mucosal resection (EMR) is a well-established technique for removal of benign colorectal polyps. Submucosal fibrosis can cause non-lifting or insufficient submucosal lifting and is frequently encountered during EMR for recurrent or residual adenoma. It increases complexity of the procedure, because it is often difficult or even impossible to grasp non-lifting tissue in the snare. Suck-and-snare (SAS) is a modified adjunctive EMR technique using suction to grasp and snare the target area. Our aim was to describe the efficacy and safety of the SAS technique for non-lifting colorectal polyps.

Aims & Methods: We prospectively registered all consecutive patients in whom the SAS technique was used in the endoscopic treatment of presumed benign non-lifting colorectal polyps. With the SAS technique, the target area is suctioned into a cap (soft straight 4mm) mounted on the scope. A prepositioned snare strangulates and resects the lesion after maximum aspiration. Clinical and endoscopic data on target area, technical success, adverse events and follow-up were collected.

Results: From May 2016 until March 2019, 70 patients (mean age 69 yrs (SD ±8.8), male 66%) were included. Non-lifting was caused by fibrosis due to recurrent or residual adenoma (n=51, including 3 also known with IBD), IBD (n=5) and other reasons (n=14). The target areas were remaining island(s) (n=35) or the entire lesion (n=35), with a median size of 15 mm (range 3-42 mm). Technical success with complete removal of polyp tissue with SAS alone was achieved in 47 patients (67%). In 20 patients (28%) at least 75% of the target area could be resected, followed by adjunctive cold avulsion and/or ablative therapy. In 3 cases ≤15% of the target area could be removed with SAS. Reason for incomplete removal was inadequate grasp with the snare, together with insufficient suction into the cap in 2 cases. No polyp- or procedural factors were associated with recurrence at follow-up. Benign histology was reported in 67 cases (96%). Unexpectedly, invasive cancer was found in 3 patients, of whom 2 were referred for surgery and 1 preferred surveillance. Recurrence rate after SAS for benign lesions was 26% (16/61) after median follow-up time 7 months (range 2-20). Follow-up data is pending in 6 cases. Muscle layer injury related to SAS occurred in 6 patients (11%), including 3 transmural perforations, successfully treated with clips. Delayed bleeding in 5 cases (7.5%), all could be managed endoscopically or were self-limiting.

Conclusion: Suck-and-snare EMR is a promising adjunctive technique with an acceptable safety profile, and seems attractive in finishing endoscopic resection for benign non-lifting fibrotic colorectal polyps.

Disclosure: Nothing to disclose

P0896 ADENOMA DETECTION RATE AND PROCEDURE INDICATION: BEYOND SCREENING COLONOSCOPIES

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Introduction: Adenoma detection rate (ADR) is the most important quality measure in screening colonoscopies because it is inversely related to the development of interval cancer and mortality. Minimum standard ADR recommended according to different ESGE Guidelines is ≥25%; however, this recommendation is based in studies that evaluated the prevalence of adenomas in asymptomatic patients undergoing a primary screening colonoscopies. However, it remains unknown whether this cut-off must be the same for other colonoscopy indications.

Aims & Methods: The aim of this study was to describe the ADR based on procedure indication and to predict the ADR recommended cut-off for other indications.

An observational, multicenter and cross-sectional study was conducted between February 2016 and December 2017 in 14 Spanish centers. Four colonoscopy indications have been considered: primary screening colonoscopies (reference category), positive fecal immunochemical test (+FIT) (OC-SensorTM; cut-off level 20µg/g), post-polypectomy surveillance and gastrointestinal symptoms. The ADR was calculated by age, sex, body mass index, comorbidities and aspirin use. The ESGE Guideline published in 2017 has been considered as the reference for ADR recommendations. Logistic regression analysis was used to assessed the relationship between ADR and indications, and population proportions and its confidence intervals (95%CI) were calculated using the exact Clopper-Pearson method.

Results: A total of 14867 patients were included and the global ADR was 38%. According to procedure indications and adjusted by factors mentioned previously, statistically significant differences between ADRs were found (p-value< 0.001). The ADR in gastrointestinal symptoms was 28.1% (OR 0.67, 95%CI 0.58-0.79); 46.4% (OR 2.01, 95%CI 1.71-2.35) in FIT-based procedures; 48.2% (OR 1.41, 95%CI 1.20-1.67) in surveillance compared to 30.8% in primary screening colonoscopies. Trend lines for the ADR in each indication were calculated based on endoscopists that performed procedures in all indications and no correlation between the quality of endoscopists and the ADR was found. 95%CI calculated for ADR population proportions was 27-29.3% in symptoms, 45.1-47.7% in +FIT endoscopies, 46.1-50.3% in post-polypectomy surveillance and 28.2-33.5% in colonoscopy screening group. Finally, based in our results, we propose a formula for calculating the minimal ADR adjusted to the clinical practice of each endoscopist.

Conclusion: ADR significantly differs between colonoscopy indications. Policies addressing performance measures beyond colonoscopy screening procedures may be developed. According to population proportions results, two different cut-offs could be suggested as new minimum standard ADR recommendations: ≥25% in gastrointestinal symptoms and primary screening colonoscopies and ≥45% in FIT-based screening and endoscopic surveillance.

References: Kaminski MF, Thomas-Gibson S, Bugajski M, et al. Performance measures for lower gastrointestinal endoscopy: a European Society of Gastrointestinal Endoscopy (ESGE) Quality Improvement Initiative. Endoscopy 2017;49(4):378-97.
Disclosure: Nothing to disclose

P0897 QUALITY INDICATORS IN THE DETECTION OF COLONIC LESIONS DURING COLONOSCOPY: A SINGLE CENTRE EXPERIENCE

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Introduction: Colorectal cancer (CRC) is the third neoplastic lesion diagnosed in males and the second one in females. The mortality for this neoplasia has decreased since the widespread of the colonoscopy as a tool in the screening. The ESGE (European Society of Gastrointestinal Endoscopy) guidelines establish the quality indicators in screening colonoscopy for the detection and differentiation of colonic neoplasia.
Aims & Methods: In this study, we have evaluated the experience of a single Italian centre (ASST Spedali Civili - University of Brescia) in colonoscopy. We analysed the adenoma detection rate (ADR), polyp detection rate (PDR), serrated detection rate (SDR) in the right and left colon in our Endoscopy Unit in 2017. Moreover, we evaluated the influence of bowel preparation and endoscopist's experience in the detection and treatment of colonic lesions. We divided 3077 patients who met the inclusion criteria (full colonoscopies and no colonic resections) in 4 groups: I. age ≥ 50 years with fecal occult blood test (FOBT) positive (n=282); II. age ≥ 50 years with a different indication (n=1291); III. surveillance colonoscopy for familiarity for CRC or previous history of neoplastic colonic lesions, any age (n=1100); IV. age < 50 years, any indications (n=404). The bowel preparation was scored with Boston Bowel Preparation Scale (BBPS) and a score ≥ 6 was considered sufficient. Statistical analysis were performed with SPSS and chi-square test has been calculate.
Results: The bowel preparation was found sufficient in 259 (91,8%) patients in group I, in 1097 (84,9%) in group II, in 1013 (92,1%) in group III and 367 (90,8%) in group IV. The PDR was higher in the group I (52,1%) and group III (49,8%) compared to group II (37,4%) and group IV (18,3%). A similar pattern was observed for the ADR: higher in the group I (40,7%) and group III (34,6%) and lower in the group II (28,7%) and group IV (10,9%). However, the SDR was 5,7%, 5,4% and 5,7% in group I, II, and III, respectively; while, it was 2,0% in group IV. A sufficient bowel preparation does not improve either PDR, ADR or SDR. Regarding the differences between right and left colon, the PDR was superior in the left colon in all groups (41,1% vs 24,5%, 24,7% vs 21,6%, 31,3% vs 30,4% and 12,2% vs 8,1% in group I, II, III and IV respectively). The ADR was higher in the left colon in the group I (31,2% vs 18,1%), group II (16,2% vs 13,3%) and group IV (5,8% vs 5,3%), while in the group III it was superior in the right colon (24,2% vs 15,4%). On the other hand, the SDR was higher in the right colon compare to the left colon in all groups (3,2% vs 2,5%, 4,2% vs 1,5%, 4,4% vs 1,8% and 1,7% vs 0,7%). Between endoscopists, the PDR was from 24,9% to 51,5%; the ADR from 17,1% to 40,0% and the SDR from 1,0% to 9,4%; without any correlations with bowel preparation.

Conclusion: In our experience, the ADR, PDR and SDR were higher in patients with risk factors for having CRC (group I and III), compared to the general population (group IV). The bowel preparation does not influence these considered parameters and it is possible that they are not enough and new parameters, such as cancer interval, could be considered in a quality colonoscopy definition. ADR and PDR were superior in the left colon; while, the SDR was better in the right colon; probably, because hyperplastic polyps are more frequent in this side.
Disclosure: Nothing to disclose

P0898 PREDICTORS OF ADENOMA DETECTION RATE OF POSITIVE FIT VS SCREENING COLONOSCOPY IN A URBAN SAFETY NET HOSPITAL

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Introduction: Fecal immunochemistry test (FIT) and colonoscopy are the first-tier colorectal cancer (CRC) screening tests recommended for average risk adults aged 50 years and above in the United States.
Aims & Methods: To compare the predictors of adenoma detection rate (ADR) of Positive FIT with screening colonoscopy (SC).
Individuals ≥ 50 years, at average risk of CRC who underwent quantitative FIT or SC as part of their routine CRC screening between 09/01/2017 and 08/30/2018 were reviewed. The quality of bowel preparation was assessed by Aronchick scale and fair/ good/excellent was considered adequate. The colonoscopy findings of the individuals following a positive FIT (FITC) were compared to those who underwent SC.
Advanced adenoma was defined as polyp ≥ 10 mm in size, with villous histology or high - grade dysplasia. Lesions were categorized into proximal - cecum to splenic flexure and distal - descending colon to rectum. Demographic variables, ADR, AADR, mean size of the largest polyp, adenoma per colonoscopy (APC) were compared between the two groups using chi-square test and student's T test. p < 0.05 was determined statistically significant.
Results: 351 individuals were identified in FITC group (follow up rate was 60.16% after a positive FIT) and 1841 in SC group. The ADR was 66% in FITC and 34% in SC (odds ratio OR 3.78, CI 2.97-4.82, p< 0.0001). AADR was 35.89% in FITC and 8.64% in SC (OR 5.92, CI 4.51-7.77, p < 0.0001). The mean size of the largest polyp for FITC was significantly higher than SC (FITSC 12.09 ± 1.15 mm, SC 8.06 ± 0.56 mm, p < 0.0001) for proximal (FITC 10.03 ± 1.11, SC 7.37 ± 0.58, p < 0.0001) as well as distal lesions (FITC 12.10 ± 1.49, SC 8.89 ± 0.92, p= 0.0002). APC was also significantly higher in FITC (3.31 ± 0.50) compared to SC (1.90 ± 0.13), p < 0.0001. Individuals who had a true positive FIT (adenoma detected) were more likely men and had a history of smoking whereas individuals who had a positive SC (adenoma

Variables	FITC -Positive (ADR) (N= 232)	FITC - Negative (N= 119)	FITC - ADR Odds ratio (CI)	FITC - ADR P value	SC Positive (ADR) (N= 430)	SC Negative (N= 1411)	SC - ADR Odds ratio (CI)	SC - ADR P value	FITC - ADR vs SC - ADR Odds ratio (CI) P value
Mean Age	62.2 (61.2 - 63.2)	62.7 (61.2 - 64.1)	-	0.637	61.5 (60.7 - 62.2)	60.4 (60.0 - 60.8)	-	0.156	p =0.178
Male	51.7% (120)	38.7% (46)	1.70 (1.08 - 2.67)	0.021	40.5% (174)	43.4% (612)	0.89 (0.72 - 1.10)	0.285	1.58 (1.14 - 2.17) p= 0.005
Non- Hispanic Black	59.9% (139)	49.6% (59)	1.52 (0.97 - 2.37)	0.065	45.1% (194)	45.4% (641)	0.99 (0.80 - 1.23)	0.909	1.81 (1.31 - 2.51) p= 0.0003
Obesity	61.2% (142)	51.2% (61)	1.50 (0.96 - 2.34)	0.075	51.6% (222)	50.2% (708)	1.06 (0.85 - 1.32)	0.599	1.48 (1.07 - 2.05) p= 0.018
Smoking history	66.4% (154)	53.8% (64)	1.70 (1.08 - 2.67)	0.022	56.3% (242)	48.2% (680)	1.38 (1.14 - 1.72)	0.003	1.53 (1.10 - 2.14) p= 0.012
Diabetes mellitus 2	31.5% (73)	26.9% (32)	1.24 (0.76 - 2.04)	0.376	28.6% (123)	23.0% (324)	1.34 (1.05 - 1.73)	0.017	1.15 (0.81 - 1.62) p= 0.442
Essential hypertension	74.1% (172)	72.3% (86)	1.10 (0.67 - 1.81)	0.707	68.1% (293)	57.7% (814)	1.57 (1.25 - 1.97)	0.0001	1.34 (0.94 - 1.92) p= 0.108
Hyperlipidemia	64.2% (149)	69.8% (83)	0.78 (0.48 - 1.25)	0.301	60.7% (261)	56.1% (792)	1.21 (0.97 - 1.50)	0.094	1.16 (0.83 - 1.61) p= 0.373

[P0898 Predictors of Adenoma Detection Rate (ADR) in Positive FIT colonoscopy (FITC) and Screening colonoscopy (SC)]

detected) were more likely to have a history of smoking, diabetes mellitus type 2, hypertension and hyperlipidemia.

When individuals with true positive FIT were compared with positive SC, FIT true positives were more likely to be Non-Hispanic blacks, had a history of smoking and obesity.

Conclusion: As expected, the odds of detecting adenomas and advanced adenomas were more common in the FITC compared to the SC group. FIT requires larger size to detect adenomas compared to screening colonoscopy and the difference was more pronounced for distal lesions. Risk factors of CRC influenced FIT and screening colonoscopy ADRs differently except for smoking (increased odds of positive FITC and SC). Understanding the demographic predictors for a positive CRC screening test will help providers and patients select the most suitable screening method.
Disclosure: Nothing to disclose

P0899 DISSECTION-ENABLED SCAFFOLD ASSISTED RESECTION (DESCAR): SAFETY, FEASIBILITY, AND EFFICACY FOR RESECTION OF RESIDUAL AND NON-LIFTING COLONIC NEOPLASIAS

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Introduction: Colonic lesions referred for endoscopic mucosal resection (EMR) may not be amenable to conventional snare resection due to previous manipulation or submucosal invasion or because of flat areas of visible tissue that cannot be snared. Current methods for treating residual tissue may lead to incomplete resection or not allow complete tissue sampling for histologic evaluation. In 2018, our group initially described Dissection-enabled Scaffold Assisted Resection (DeSCAR)—a technique combining circumferential endoscopic submucosal dissection (ESD) with EMR—to be a safe technique for the endoscopic resection for removal of superficial, non-lifting or residual lesional "islands" with suspected submucosal involvement or fibrosis[1].

Our aim is to describe our expanded experience and follow up of patients undergoing DeSCAR and assess the efficacy, safety, and feasibility of this technique for endoscopic resection of non-lifting or residual colonic lesions.
Aims & Methods: Lesions referred for EMR were retrospectively reviewed. In addition to our initial cohort of 29 patients from 2015-2017, 28 additional patients from 2018-2019 were identified where lifting and/or snaring of colonic lesions was incomplete, and the DeSCAR technique was undertaken. Cases were reviewed for location, prior manipulation, rates of successful hybrid resection, adverse events, and endoscopic follow up to assess for residual lesions.
Results: 57 lesions underwent DeSCAR due to non-lifting or residual "islands" of tissue. Patients were 51% female and 49% male with an average age 69 (SD +/- 9.6 yrs). Lesions were located in the cecum (n=16), right colon (n=22), transverse colon (n=5), left colon (n=7), rectum (n=4), or in other locations defined by distance from the anus (n=4). Average lesion size was 27.7 mm (SD +/- 16.6 mm). Previous manipulation occurred in 54 of 57 cases (68% biopsy, 47% resection attempt, 18% intralesional tattoo injection). The technical success rate for resection of non-lifting lesions was 100%. There were two delayed bleeding episode (one requiring endoscopic intervention) and one small perforation (managed by successful endoscopic hemoclip closure at the time of perforation), but no other adverse events were observed. Endoscopic follow up was available in 25 patients (44%) with no residual adenoma noted in 23 patients (92% of those with surveillance).
Conclusion: Our expanded experience with DeSCAR continues to demonstrate a high safety, feasibility, and effectiveness profile as an alternative to argon plasma coagulation and avulsion for the endoscopic management of non-lifting or residual colonic lesions, providing *en-bloc* resection of tissue for histologic review. Further studies are needed to demonstrate long-term eradication and direct comparison with other currently available endoscopic techniques.
References: 1. Stier M, Chapman C, Kreitman A, Hart J, Xiao S et al. Dissection-enabled scaffold-assisted resection (DeSCAR): A novel technique for resection of residual or non-lifting GI neoplasia of the colon (with video). Gastrointest Endosc. 2018; 87(3): 843-851.

P0900 ENDOSCOPIC FEATURE OF DEPRESSED TYPE COLORECTAL NEOPLASMS IN MAGNIFYING ENDOSCOPY AND ENDOCYTOSCOPY

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Introduction: Colorectal cancers are generally recognized to develop from "polyps". This "adenoma-carcinoma sequence" theory has been in the mainstream of development of colorectal cancers. However, recently the existence of many depressed-type cancers has been revealed, which are considered to emerge directly from normal epithelium, not through the adenomatous stage. This theory is called "de novo" pathway.

Now, it is possible to presume the histology of colorectal lesions using magnifying endoscopy (pit pattern classification) and endocytoscopy (EC classification). We can observe not only the structural atypia but also the cellular atypia in vivo.
Aims & Methods: The aim is to clarify the endoscopic characteristics of depressed-type colorectal neoplasms, demonstrating the validity of pit pattern and EC classification.

A total of 32025 colorectal neoplasms excluding advanced cancers were resected endoscopically or surgically in our unit from April 2001 to February 2018.

Of these, 24704 lesions were low-grade dysplasia, 6058 were high-grade dysplasia and 1263 were submucosally invasive (T1) carcinomas. According to the developmental morphology classification, they were divided into 3 types: depressed, flat and protruded-type. We investigated the rate of T1 carcinomas and the characteristics of depressed-type neoplasms concerning pit pattern and EC classification.
Results: The rate of T1 carcinomas in depressed-type lesions reached to 62.7%, meanwhile that in flat-type and protruded-type lesions was 3.2% and 2.8%, respectively. Within less than 5mm in diameter, that was 10.1%, 0% and 0%, respectively. Most of the flat-type (92.3%) and protruded-type (94.5%) lesions showed type III_L or IV pit pattern corresponding to adenomas, whereas 91.7% of the depressed-type lesions were characterized by type III_S, V_I or V_N pit patterns corresponding to carcinomas. As for endocytoscopy, most of the flat-and protruded-type lesions showed EC2 corresponding to adenomas. In contrast, the depressed-type lesions were observed as EC3a (37.0%) and EC3b (55.6%) corresponding to invasive carcinomas.
Conclusion: This study revealed the diagnostic characteristics of depressed-type lesions. They show typically type III_S, V_I or V_N pit patterns in magnifying endoscopy and type EC3a or EC3b in endocytoscopy. These lesions tend to invade the submucosal layer even when they are small. It is important to diagnose colorectal neoplasms according to their morphology.
Disclosure: Nothing to disclose

P0901 INTERMEDIATE RISK OF APPENDICITIS FOLLOWING FULL-THICKNESS RESECTION OF ADENOMAS ARISING FROM THE APPENDICEAL ORIFICE- A RETROSPECTIVE ANALYSIS

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Introduction: Conventional endoscopic resection techniques of adenomas near the appendiceal orifice have certain limitations e.g. an increased risk for perforation. Endoscopic full-thickness resection (eFTR) is a novel technique for adenoma resection up to 20mm in diameter. As full thickness resection near the appendiceal orifice is associated with a subtotal appendectomy it remained unclear whether the risk for development of an appendicitis or mucocele is increased. We present the results of a retrospective analysis of 38 patients with adenomas involving the appendiceal orifice treated with the FTRD system (Ovesco Endoscopy, Tuebingen, Germany).
Aims & Methods: Retrospective analysis of patients treated with eFTR for adenoma near the appendiceal orifice between 2014 and 2018. 38 patients from 2 centres (Ludwigsburg, Ulm) were included, median age 68.0 (47-85) yrs., follow up-time median 11 (6-32) months. The objective was the evaluation of post treatment complications in acute and long term follow up (appendicitis, mucocele). Patients with prior appendectomy were excluded from the study.
Results: All patients received prophylactic antibiotic treatment for on average 3.7 days in a row started perintenventionally. No acute severe adverse events were reported for the eFTR procedure. Symptoms of appendicitis occurred in 9 patients (23.7%) within follow-up. In 3 cases conservative treatment was sufficient, 5 patients were transferred to appendectomy. No development of a mucocele was reported in long time follow up.
Conclusion: Based on this retrospective analysis eFTR of adenomas involving the appendiceal orifice is associated with an intermediate risk for developing appendicitis and consecutive risk for appendectomy. Therefore we conclude patients must be thoroughly informed about the risks. The reason why some patients develop appendicitis should be further elucidated.
Disclosure: Alexander Meining, Karel Caca: Consultancies for OVESCO, Germany

P0902 EFFICACY AND FEASIBILITY OF FULL THICKNESS DEFECT CLOSURE USING MODIFIED ENDOLOOPS: EX VIVO STUDY IN A PORCINE COLON MODEL

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Introduction: To ensure a safer endoscopic full-thickness resection (EFTR), a reliable defect closure system is essential. The commercially available endoloop was modified for the purposes of a more secure closure. The aim of this study was to evaluate the efficacy and feasibility of modified endoloops for defect closure.
Aims & Methods: Two prototype endoloops (Olympus, Tokyo) were studied. One was an endoloop with a double-cinch and the other an endoloop with a 3mm needle at the base of the loop. Phase 1: Full-thickness colon resections measuring 2 cm in diameter were created free-hand. The closing force for each device was compared to the gold standard of a hand-sewn defect closure using leak testing. Five different closure methods were studied: 1. conventional endoloop, 2. endoloop with a double-cinch, 3. endoloop with a needle, 4. over-the-scope clip (Padlock clip; US Endoscopy, OH), 5. free-hand suturing. Phase 2: EFTR was performed to compare the closing forces of the optimal modified endoloop identified from Phase 1 to the conventional endoloop. Using endoloops, a pseudopolyp containing the entire colonic wall was created and then resected using a hot snare.
Results: Phase 1: A total of 17 sites were resected using the free-hand model. The median maximum pressure for leak testing in hand-sewn closure was 22 mmHg compared to conventional endoloop (21 mmHg; p=0.56),

double-cinch endoloop (47 mmHg; p=0.077), endoloop with a needle (22 mmHg; p=0.86), and over-the-scope clip (40 mmHg; p=0.13). In Phase 2: EFTRs were successfully completed in 16 colonic sites (conventional endoloop, 8 sites; double-cinch endoloop, 8 sites). The median lesion size in conventional and double-cinch endoloops were 17mm (range: 14-20) and 19 mm (range: 15-22), respectively (p=0.13). The median maximum pressure for leak testing in the conventional and double-cinch endoloops were 29 mmHg (range, 20-45) and 42mmHg (range, 34-55), respectively (p< 0.01).
Conclusion: A double-cinch endoloop demonstrated a significantly higher closing force compared to conventional endoloops. The median maximum pressure for leak testing was higher with the double-cinch endoloop compared to hand-sewn closure, but did not reach significance. This simple modification to a currently available and familiar device could enhance defect closure following EFTR.
Disclosure: Nothing to disclose

P0903 ENOUGH IS ENOUGH: AN IN-VITRO DOSE-FINDING STUDY OF ANTIFOAMING EFFECTS OF SIMETHICONE

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Introduction: Simethicone is an antifoaming agent frequently added to endoscopic rinse solutions but has recently been implicated as a possible risk factor for endoscopy transmitted infections due to a potential simethicone build-up in the working channels [1-3]. However, we have previously shown that discontinuation of simethicone use has a detrimental effect on the polyp and adenoma detection rates [4, 5]. However, the build-up of a deposit in the working channels of the endoscope is likely related to the simethicone concentration in the rinse solution. Unfortunately, no data are available on the minimal effective dose of simethicone that has antifoaming effects. We therefore aimed to determine the lowest effective concentration of simethicone that retains antifoaming properties.
Aims & Methods: We developed an 'in vitro bubble model'. For this purpose six 100 mL test tubes filled with water for irrigation were prepared with a standard kitchen detergent (Fairy®, 1% v/v). One test tube served as control, while different doses of simethicone ((Infacol®, 0.02, 0.2, 2.0, 20 and 200 mg) were added to the other 5 test tubes. Oxygen was streamed for 30 seconds into the test tube at a rate of 2 L/min. After 10 seconds, digital photos were taken and the foam or bubbles that were visible on the photos rated semi-quantitatively rated (0 = no air bubbles, 1 = isolated air bubbles not impairing the visibility, 2 = air bubbles partly covering the surface, 3 = air bubbles fully covering the surface, 4 = multi-layered air bubbles) by five independent assessors blinded for the dosing of simethicone. Sufficient suppression of air bubbles was assumed when all assessors reported a score of 1 or less.
After determining the minimal effective dose of simethicone, we implemented this into routine clinical practice and compared polyp detection rates before and after introduction of the low-dose simethicone. To control for differences in the performance of endoscopists, we compared data from the same clinicians pre and post the dose change.
Results: Simethicone at doses as low as 20 mg/100 mL resulted in a complete or near complete prevention of bubble formation. Thus, doses as low as 20 mg/100 mL appear to be the appropriate minimal doses of simethicone to suppress bubble formation during endoscopic procedures. We compared polyp detection rates in 1,340 patients undergoing routine colonoscopy (606 female, age 59.6±14.9 [mean ± SD]), with 1,475 patients undergoing routine colonoscopies (655 female, age 58.3±15.2 [mean ± SD]) after implementation of the low dose simethicone protocol. In the high dose, the polyp detection rate was 56.5% (53.8-59.1% [95% CI]) and in the low dose it was 56.7% (54.2-59.3% [95% CI]).
Conclusion: While in most endoscopy units simethicone is added ad libitum to rinse solutions (e.g. 200 mg/100 mL), our data suggest that doses as low as 20 mg/100 mL are sufficient to abolish or prevent the formation of air bubbles or foam. Most importantly, this low dose of simethicone resulted in no change to our polyp detection rates, indicating that it is a clinically appropriate dose.

References: 1. Ofstead, C.L., et al., Simethicone residue remains inside gastrointestinal endoscopes despite reprocessing. Am J Infect Control, 2016. 44(11): p. 1237-1240. 2. van Stiphout, S.H., et al., Crystallization in the waterjet channel in colonoscopes due to simethicone. Endoscopy, 2016. 48(S 01): p. E394-e395. 3. Kovaleva, J., et al., Transmission of infection by flexible gastrointestinal endoscopy and bronchoscopy. Clin Microbiol Rev, 2013. 26(2): p. 231-54. 4. Bai, Y., et al., Impact of preprocedure simethicone on adenoma detection rate during colonoscopy: a multicenter, endoscopist-blinded randomized controlled trial. Endoscopy, 2018. 50(02): p. 128-136. 5. Kutyla, M., et al., Influence of Simethicone Added to the Rinse Water during Colonoscopies on Polyp Detection Rates: Results of an Unintended Cohort Study. Digestion, 2018. 98(4): p. 217-221.
Disclosure: Nothing to disclose

P0904 ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) OF EARLY RECTAL NEOPLASIA USING THE TISSUE RETRACTOR SYSTEM (TRS), A NEW ENDOSCOPIC PLATFORM FOR ENDOLUMINAL EN BLOC TISSUE RESECTION IN THE GASTROINTESTINAL TRACT – FIRST RETROSPECTIVE CASE SERIES AT A GERMAN REFERENCE CENTER

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Introduction: Endoscopic resection (ER) is the curatively intended first-line therapy for early rectal neoplasia (ERN)[1]. Prerequisite is successful R0 resection, which cannot always be achieved with lesions >20mm by endoscopic mucosal resection (EMR). In these cases, ESD is the preferred method[2]. Advantages of ESD are higher en bloc resection and lower recurrence rates, while EMR is faster to perform and shows lower perforation rates[3-5].

For safer and faster ER, stable device position and good view into the submucosal space are needed. Tissue Retractor System (TRS) was developed to enable this with help of mechanisms established in laparoscopic surgery with a conventional endoscope[6]. TRS is a novel system, consisting of flexible overtube with expandable working chamber with 2 independent instrumentation catheters. With forceps via catheters, tissue can be stretched and held in position for ER.

Aims & Methods: Primary objective: Technical success of TRS-ESD (complete resection of target lesion using TRS). Secondary objectives: En bloc, R0 and curative resections, adverse events (AEs).

Retrospective analysis of all TRS-ESD cases of ERN between June 2018 and February 2019 at a tertiary referral center in Germany.

Results: 8 patients treated with ESD using TRS were included (3 women, 5 men, mean age 67 years, range 53-82). Target lesions were therapeutic naive, located in rectum (7 distal, 1 proximal), slightly-elevated with sessile parts (laterally spreading tumors nodular mixed type) and classified as type 2a or 2b according to JNET (Japan NBI expert team) classification[7]. Mean diameter 45.6mm (20-80mm). Technical success (complete resection using TRS) was achieved in 87.5% (7/8). In 12.5% (1/8) positioning of TRS (distal rectum) was not successful for anatomical reasons.

However, all lesions were resected completely (100%). The single lesion, non suspicious of malignancy, where TRS positioning was not successful, was resected by EMR (piece-meal technique, PM-EMR); all other lesions (87.5%, 7/8) were resected by ESD en bloc using TRS. Histologically, adenomas were found in 62.5% (5/8: 2 low grade dysplasia, LGD, 3 high grade dysplasia, HGD) and adenocarcinomas (AC) in 37.5% (3/8).

Overall, R0 resection was achieved in 75% (6/8). All (3/3) carcinomas were resected en bloc, R0 and curatively. 2 of 5 adenomas were not resected R0 (1 PM-EMR of LGD-adenoma due to failed TRS-positioning, 1 en bloc resection with focal adenoma in horizontal margin). All HGD-adenomas were curatively resected. No intraprocedural or delayed AEs occurred.

Conclusion: ESD using TRS seems to be feasible and safe in the rectum. En bloc and R0 resection rates were comparable to those of conventional ESD. The rate of curative ESDs in cases of AC was high with 100%, which is less explained by the use of TRS than by adequate pretherapeutic selection of lesions. Whether use of TRS could finally be helpful reducing disadvantages of ESD cannot be answered with this work.

Although perforation rate of 0% was lower than that of conventional ESD, data is limited by the small number of cases and the retrospective analysis. Duration of intervention could not be analyzed in the current retrospective dataset, but appeared not to be shorter. A reason could be longer learning curve for this complex procedure. For final appraisal now data from large scale prospective trial is needed.

References: 1. Schmiegel W, Buchberger B, Follmann M, et al. S3-Leitlinie - Kolorektales Karzinom. Z Gastroenterol 2017;55:1344-1498. 2. Pimentel-Nunes P, Dinis-Ribeiro M, Ponchon T, et al. Endoscopic submucosal dissection: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy 2015;47:829-54. 3. Probst A, Ebigbo A, Markl B, et al. Endoscopic submucosal dissection for early rectal neoplasia: experience from a European center. Endoscopy 2017;49:222-232. 4. Probst A, Golger D, Anthuber M, et al. Endoscopic submucosal dissection in large sessile lesions of the rectosigmoid: learning curve in a European center. Endoscopy 2012;44:660-7. 5. Saito Y, Fukuzawa M, Matsuda T, et al. Clinical outcome of endoscopic submucosal dissection versus endoscopic mucosal resection of large colorectal tumors as determined by curative resection. Surg Endosc 2010;24:343-52. 6. Kantsevoy SV, Bitner M, Piskun G. New endoscopic platform for endoluminal en bloc tissue resection in the gastrointestinal tract (with videos). Surg Endosc 2016;30:3145-51. 7. Sano Y, Tanaka S, Kudo SE, et al. Narrow-band imaging (NBI) magnifying endoscopic classification of colorectal tumors proposed by the Japan NBI Expert Team. Dig Endosc 2016;28:526-33.
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P0905 A 3-DAY VERSUS 1-DAY LOW RESIDUE DIET TO IMPROVE COLONOSCOPY PREPARATION RESULT AND PATIENT TOLERABILITY, A RANDOMIZED, SINGLE-BLINDED, CONTROLLED TRIAL

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Introduction: The European Society of Gastrointestinal Endoscopy (ESGE) recommends a low-fibre diet on the day preceding the colonoscopy, although some endoscopistas suggest a 3-day diet before colonoscopy. We intended to study the influence of a 3-day (3D) versus 1-day (1D) low residue diet in bowel preparation results and the effect on patient tolerability and adherence.

Aims & Methods: Randomized controlled trial, single-centre, endoscopist single-blinded, consecutive outpatients scheduled for total colonoscopy. Bowel preparation was 4L split-dose of polyethylene glycol. Randomization in 2 groups (n = 206), D3 vs. D1. The primary outcome was the bowel cleansing quality assessment by the Boston Bowel Preparation Scale (BBPS) (adequate cleansing ≥ 2 points per segment) to achieve a reduction from 15 to 5% of inadequate preparation result with a 3-day regimen. Statistical analysis in intention to treat (ITT) and per protocol (PP) with descriptive analysis, $\chi2$ and logistic regression with 95% confidence intervals (CI). Clinical Trial register NCT02955901.

Results: 412 patients were included, and groups were homogeneous in relation to gender, age, colonoscopy indication and risk factors for inadequate preparation.

The inadequate bowel preparation rate (primary outcome), assessed by the BBPS, was not significantly different between groups: ITT analysis (n=412) D3 8.3% vs. D1 5.3%, p=0.24 and PP analysis (N=400) D3 6,5% vs. D1 3,5%, p=0.16.

Secondary outcomes, on ITT analysis, were similar between groups (D3 vs. D1): cecal intubation rate (95.1% vs. 98.1%, p=0.1), polyp detection (52.9% vs. 52.4%, p=0.92) and advanced adenomas detection (34.9% vs. 39.8 %, p=0.45). No differences were also found between groups (D3 vs. D1) regarding adverse effects / patients complaints (55.8% vs. 60.2%, p=0.37), ease in acquiring the proposed diet (5.3% vs. 6.8%, p=0.54) and willingness to repeat the regimen (77.2% vs. 80.6%, p=0.4) but difficulty in following the prescribed diet was significantly higher in D3 group: 11.7% vs. 4.4% p=0.008, OR 2.7, 95%CI 1.3-5.8.

Non-compliance with split dose (OR 30, 95%CI 7.7-120), chronic constipation (OR 3.3, 95%CI 1.3-8.8), consumption of tricyclic antidepressants (OR 3.2; 95%CI 1.1-8.8) and diabetes (OR 3.1, 95%CI 1.2-7.9) were statistically significant factors for inadequate preparation.

Conclusion: The increase for 3 days of a low residue diet prior to colonoscopy did not reduced the rate of inadequate bowel preparation; similar bowel preparation quality results are obtained with only 1 day of low residue diet within the ESGE threshold and with better adhesion and tolerability by the patient, under a split-dose preparation

Disclosure: Nothing to disclose

P0906 COMPARISON OF THE EFFECTIVENESS OF FOUR BOWEL CLEANSING PREPARATIONS BEFORE COLONOSCOPY - RANDOMIZED, SINGLE - BLIND STUDY

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Introduction: The effectiveness of bowel preparation is an essential requirement of successful colonoscopy. Polyethylenglycol is a gold standard in bowel preparation. It's main disadvantage is high volume. Oral sulfate solution (OSS), low volume PEG + ascorbic acid (2L-PEG/Asc) and sodium picosulfate + magnesium citric-acid solution (SP/MC) are low-volume preparations that might be appropriate substitution of PEG.
Aims & Methods: Comparison of the effectiveness of four bowel cleansing preparations.
Randomized, single-blind study. Patients with colonoscopy from all indications (except planned therapeutic procedure) were recruited. Instructions were provided in both verbal and written version and split-dose regimen was recommended. The bowel cleansing quality was evaluated by the experienced endoscopists blinded about the type of a bowel preparation. The effectiveness was assessed by the degree of bowel cleansing according to Boston Bowel Preparation Scale (BBPS) and polyp detection rate (PDR).
Results: In the period from 09/2017 to 03/2019 there were 439 individuals included in the study of which 6 patients eventually did not undergo colonoscopy from different reasons and 13 patients did not have total colonoscopy. The final analyzed number of patients was 420. The numbers of individuals with each preparation were as follows: 109 PEG; 108 OSS; 103 2L-PEG/Asc and 100 SP/MC. Representation of men was 51 % and average age was 58 years for whole group. Split-dose regimen was respected by 82% of patients. Adequate bowel cleansing (BBPS total score ≥ 6 and sub score ≥ 2 in each colonic segment) was comparable for all groups (95.4% PEG vs. 94.4% OSS vs. 98.1% 2L-PEG/Asc vs. 96.0% SP/MC; p = 0.600). Excellent bowel cleansing (BBPS total score ≥ 8 and sub score ≥ 2 in each colonic segment) was observed often in PEG and OSS group however the difference was not significant (86.2% PEG vs. 84.3% OSS vs. 80.6% 2L-PEG/Asc vs. 80.0% SP/MC; p = 0.580). Average value of total BBPS and average sub score for each colonic segment and preparations shows table 1. Polyp detection rate was comparable for all groups (49.5% PEG vs. 50.0% OSS vs. 36.9% 2L-PEG/Asc vs. 42.0% in SP/MC; p = 0.166). There was also no difference in detection of advanced colorectal neoplasia (≥ 10 mm, high grade dysplasia or cancer): 11.0% PEG vs. 10.2% OSS vs. 9.7% in 2L-PEG/Asc vs. 15.0% in SP/MC; p = 0.654. Average size of detected polyp was 5 mm and average number of detected polyp for each person was 2.
Conclusion: All tested low volume solutions provide comparable effectiveness of bowel preparation as polyethylenglycol and they could be considered as it's alternative.
Supported by the projects MO1012 and Progres Q28/LF1. The study is registered on ClinicalTrials.gov.(NCT03242369).

	PEG	OSS	2L-PEG/ASC	SP/MC	Total number; p - value
Number of patient	109	108	103	100	420
Excellent preparation	86.2%	84.3%	80.6%	80.0%	0.580
Adequate preparation	95.4%	94.4%	98.1%	96.0%	0.600
Average value of total BBPS (SD)	8.4 (1.1)	8.4 (1.3)	8.4 (1.0)	8.3 (1.0)	
Sub score: RC	2.6 (0.6)	2.7 (0.6)	2.7 (0.5)	2.6 (0.6)	
TC	2.9 (0.4)	2.8 (0.5)	2.8 (0.4)	2.8 (0.4)	
LC	2.9 (0.4)	2.9 (0.4)	2.9 (0.3)	2.9 (0.3)	

[Table 1.]

Excellent bowel preparation: BBPS total score ≥ 8 and sub score ≥ 2 in each colonic segment; Adequate bowel preparation: BBPS total score ≥ 6 and sub score ≥ 2 in each colonic segment; RC: right colon; TC: transverse colon; LC: left colon; SD: standard deviation.
Disclosure: Nothing to disclose

P0907 ADHERENCE TO SURVEILLANCE GUIDELINES AFTER REMOVAL OF COLORECTAL POLYPS: A MULTI-NATIONAL, MULTI-CENTER, PROSPECTIVE SURVEY

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Introduction: The rate of polyp detection and removal from the screening colonoscopy have grown tremendously in many Asian countries. However, there is a great concern for demand of surveillance colonoscopy. Despite a continuing effort to lengthen intervals for surveillance colonoscopy, a number of surveys have indicated that most doctors still recommend more frequent surveillance colonoscopy than guideline suggest. The aim of this study is to investigate the surveillance recommendations of Asian gastroenterologists after polypectomy and compare them with recommendations from international guidelines.
Aims & Methods: A survey study was performed among seven Asian countries from July 2018 and October 2018. An email invitation which a link provided was send to gastroenterologists, general internal medicine and surgeons. Participants were asked to complete a survey of eight clinical scenarios designed to evaluate their potential course of action in response to screening or follow-up colonoscopy results. The US Multi-Society Task Force on Colorectal Cancer 2012 was determined as a standard guideline. We stratified participants according to their number of colonoscopy as 1) performed ≥ 20 colonoscopies per month [high-volume (HV)] and 2) < 20 colonosopies per month [low-volume (LV)].
Results: One hundred thirty-seven doctors were invited. A total of valid response were obtained from 123 doctors (89.8%). Respondents included 40 Korean gastroenterologists and 83 physicians from other Asian countries. Majority of participants (73%) practiced in a tertiary hospital and 87% were gastroenterologists. Approximately, half of participants adhered to the guideline regardless of adenomas except a combination between adenoma ≥10 mm with tubulovillous and high grade dysplasia, in which 35% of participants adhered to the guideline. Only 12% of participants adhered to the guideline of 10 years interval for no polyp in a patients with a prior high-risk adenoma. According to the stratification by colonoscopy number, 78 (64%) participants were in HV group, and 45 (36%) were in LV group. The HV group more adhered to the guideline recommendation after removal of adenoma than LV group. The reasons for non-adherence to the guideline were concern of missed polyp (59%), low cost for colonoscopy (26%), incomplete resection (25%), and medical liability (15%).
Conclusion: This study shows a remaining discrepancy between physician's recommendation and current guideline for post-polypectomy surveillance. Physicians in LV group frequently do not adhere to the guideline, suggesting a need for appropriate control and continuing education. Concern for quality of colonoscopy and incomplete polyp resection were mainly related to non-adherence.
Disclosure: Nothing to disclose

P0908 IN PATIENTS WITH AN OVERALL CLEANSING SUCCESS THE 1L POLYETHYLENE GLYCOL NER1006 ACHIEVES MORE HIGH-QUALITY CLEANSED SEGMENTS PER PATIENT THAN THREE STANDARD BOWEL PREPARATIONS

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Introduction: Detection of all adenomas during colonoscopy is important for patient protection against colorectal cancer. At a minimum, this requires successful pre-colonoscopy colon cleansing which is usually based

on the least clean colon segment. High-quality cleansing has however been shown to improve adenoma detection. The prospective phase 3 development programme for 1L polyethylene glycol (PEG) NER1006 (studies DAYB, MORA and NOCT) is the largest to date on colon cleansing quality [1-3]. The primary analysis revealed a higher or at least as effective adequate level cleansing efficacy of NER1006 versus sodium picosulfate/magnesium citrate (SPMC), 2L PEG + ascorbate (2LPEG), and oral sulfate solution (OSS). An improved high-quality cleansing efficacy has already been shown for NER1006 at the treatment group level, but the patient level benefits remain unclear.

Aims & Methods: This post hoc analysis of 1749 patients in three randomised phase 3 trials examined if the number of high-quality cleansed colon segments per patient could improve with NER1006 versus SPMC, 2LPEG or OSS. All patients with documented segmental cleansing scores and neoplasia counts were included. Treatment-blinded central readers assessed the segmental cleansing quality using the validated Harefield Cleansing Scale (HCS) scores 0-4 based on colonoscopy videos by site colonoscopists. Patients with an overall cleansing success (HCS Grades A-B) were stratified per trial and allocated bowel preparation. The mean number of attained high-quality colon segments (HCS scores 3-4) per patient was calculated. One-sided t-tests compared the mean number of high-quality colon segments per patient using NER1006 versus the comparator in each trial.

Results: A total of 1471/1749 patients (84%) achieved overall cleansing success (Table). With comparable split dosing regimens, overall cleansing success rates reflected the primary published results [1-3]. The mean number of high-quality colon segments per patient was greater for patients using NER1006 than any of the comparators in each respective trial. Day before split dosing with NER1006 was more effective than with SPMC: 1.13 vs 0.76; P=0.005. Overnight or morning only split dosing with NER1006 was more effective than with 2LPEG: 2.52 and 2.65 vs 1.65; P< 0.001 for both. Similarly, overnight split dosing with NER1006 was more effective than with OSS: 2.61 vs 2.30; P=0.032. The additional effect size for NER1006 versus its comparators ranged from 0.31-1.00 high-quality segments per patient.

Conclusion: These results demonstrate that despite comparable or higher adequate cleansing success, this does not prevent NER1006 from being clearly more effective than SPMC, 2LPEG or OSS in delivering more high-quality cleansed segments per patient.

	DAYB		MORA			NOCT	
	NER1006	SPMC	NER1006	NER1006	2LPEG	NER1006	OSS
Split dosing regimen	Day before	Day before	Overnight	Morning only	Overnight	Overnight	Overnight
Patients with overall cleansing success (HCS grade A-B), n/N (%)	151/229 (65.9)	133/239 (55.6)	248/256 (96.9)	242/266 (91.0)	230/250 (92.0)	231/251 (92.0)	236/258 (91.5)
High-quality segments (HCS score 3-4) per patient with overall cleansing success, mean (SD)	1.13 (1.29)	0.76 (1.07)	2.52 (1.76)	2.65 (1.81)	1.65 (1.71)	2.61 (1.80)	2.30 (1.81)
Effect size	0.37	-	0.88	1.00	-	0.31	-
P-value vs comparator	0.005	-	<0.001	<0.001	-	0.032	-

[Table. High-quality segments (HCS score 3-4) per patient with overall cleansing success assessed by treatment-blinded central readers]

References: 1. Bisschops R et al. Endoscopy 2019; 51(1):60-72 2. DeMicco MP et al. Gastrointestinal Endoscopy 2018; 87(3):677-687 3. Schreiber S et al. Endoscopy 2019; 51(1):73-84

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P0909 ADENOMA PER COLONOSCOPY (APC) AND ADENOMA PER POSITIVE PARTICIPANT (APP) AS QUALITY METRICS IN SCREENING COLONOSCOPY

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Introduction: Adenoma detection rate (ADR; proportion of colonoscopies with at least 1 adenoma) is the most validated metric in colonoscopy quality. However, ADR is not free of limitations. These include the "one and done" phenomenon, in which endoscopists may be less vigilant after having detected their first adenoma. Alternative quality indicators considering the total number of adenomas have been proposed, although supported by scant evidence.

Aims & Methods: We evaluated APC (total number of adenomas divided by the total number of colonoscopies) and APP (total number of adenomas divided by the number of colonoscopies with at least 1 adenoma) as quality markers for screening colonoscopy, based on the correlation of each with the ADR and the advanced ADR (AADR; proportion of colonoscopies with an advanced neoplasm). For this purpose, consecutive screening colonoscopies conducted in a single endoscopy unit in Greece (Jan 2015-June 2018) were retrospectively reviewed. Pearson's correlation was used to evaluate the relationship between APC-ADR, APC-AADR, APP-ADR and APP-AADR.

Results: A total of 1505 colonoscopies performed by 6 endoscopists were analyzed. The ADRs ranged from 13.0% to 28.7% (mean, 22.7%), AADRs from 3.9% to 8.8% (mean, 6.6%), APCs from 0.18 to 0.45 (mean, 0.30) and APPs from 1.29 to 1.50 (mean, 1.38). APC showed a strong correlation with ADR (r=0.91, p=0.01) and AADR (r=0.89, p=0.02). Contrarily, no association could be identified between APP and both these parameters (ADR: p=0.91; AADR: p=0.37).

Conclusion: In our setting, APC, but not APP, demonstrated significant correlation with both ADR and AADR and may considered as alternative quality indicator of screening colonoscopy.

Disclosure: Nothing to disclose

P0910 SCAR ASSESSMENT AFTER PIECEMEAL ENDOSCOPIC MUCOSAL RESECTION – INTEROBSERVER AGREEMENT IN HISTOLOGICAL RECURRENCE PREDICTION

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Introduction: It is unclear whether scar assessment after piecemeal endoscopic mucosal resection (pEMR) has to include scar biopsy in the absence suspected recurrence. Histological recurrence (HR) is an important limitation of pEMR and occurs in ≤20%. Currently HR assessment is routinely performed through endoscopic evaluation and scar biopsy. Advanced imaging methods such as *Narrow-Band Imaging* (NBI) may predict HR with high acuity.

Aims & Methods: This study aims to evaluate agreement between gastroenterologists with different endoscopic experience, in the prediction of HR based on the endoscopic scar assessment.

Patients undergoing colonoscopy 3-6 months after a pEMR of 20mm or larger non-invasive colorectal lesions were included. Scar biopsy was performed and in case of suspected endoscopic recurrence residual lesion was resected.

Thirty-eight high definition images with white light (WL) or NBI were selected, of which 18 with HR and 20 without HR. 12 participants with different degrees of experience in therapeutic endoscopy performed an offline assessment of pEMR scars. The images were randomized. Participants were blinded for the randomization and histology. Each gastroenterologist classified the images as HR or without HR, and the interobserver agreement coefficient (k) was calculated.

Results: Mean age was 66±12 years, with 60.5% male (n = 23). The mean lesion size was 35±15 mm, with 60.5% 0-Is-IIa (n=23).

Endoscopic prediction of recurrence had high sensitivity (55.6%-88.9%) and specificity (85.0-95.0%). Negative predictive value (70.4%-94.1%) and positive predictive value (82.4-93.8%) were also calculated. Coefficient of agreement (k) between the different participants was 0.806 (p< 0.001). In patients with recurrence k-coefficient was 0.881 (p < 0.001). In patients without recurrence k-coefficient was 0.925 (p < 0.001). There were no significant differences between NBI (k-0.769; p < 0.001) and WL (k-0.837; p < 0.001).

Conclusion: Endoscopic prediction of recurrence based on offline scar assessment under WL and NBI showed high interobserver agreement among gastroenterologists with different degrees of experience in therapeutic endoscopy.

Disclosure: Nothing to disclose

P0911 RETROGRADE INSPECTION OF THE COLON WITH A DEDICATED RETROGRADE VIEWING ENDOSCOPE INCREASES ADENOMA DETECTION RATE

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Introduction: Adenoma detection rate (ADR) is inversely related to the incidence of interval colorectal cancers and therefore serves as a benchmark criterion for quality assessment during screening or surveillance colonoscopies. Within this study, we evaluated whether additional retrograde inspection of the colon can increase ADR and the number of adenomas per patient.

Aims & Methods: Patients undergoing screening or surveillance colonoscopies were prospectively enrolled. During colonoscopy, each segment of the colon (Cecum and ascending colon, transverse colon, descending and sigmoid colon) were inspected first with HD standard forward view (SFV) followed by inspection of the same segment in retroflected view (RFV) using a dedicated endoscope with a 210° retroflex angulation (Pentax Retro-View). Number of adenomas in each segment detected with SFV and RFV as well as withdrawal times with SFV and RFV were recorded.

Results: At the time of abstract submission, 56 patients (mean age 59.4 years, 38 male) were prospectively included. Inspection of the whole colon in retroflexion was possible in all patients. Polyp detection rate (PDR) with SFV was 36% and increased to 46% when additional RFV was performed in each segment. Likewise, ADR increased by 9% when RFV was performed (ADR SFV: 32%, ADR RFV: 41%). Adenoma per patient rate was 1.7 with SFV and increased to 2.3 with additional RV. Size of the additional adenomas found with RFV ranged from 3 to 10 mm. Withdrawal times were not significantly different between SFV and RV.

Conclusion: Additional retroflection of the colon using a dedicated endoscope can significantly increase ADR and the number of adenomas found per patients. This approach should be considered during standard colonoscopy to increase ADR and to improve the quality of colonoscopy.

Disclosure: Nothing to disclose

P0912 CLINICAL AND PATHOLOGICAL FEATURES OF DEPRESSED-TYPE COLORECTAL CARCINOMAS

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Introduction: Colorectal cancers have two development theories. One is "adenoma-carcinoma sequence".The other is "de novo" pathway, considered to emerge directly from normal epithelium, not through the adenomatous stage. We investigated clinicopathological characteristics of depressed-type colorectal carcinomas considered as"de novo"pathway.

Aims & Methods: A total of 34,276 colorectal neoplasms excluding advanced cancers were resected endoscopically or surgically in our center from April 2001 to December 2018. Of these, 1,203 lesions were T1 carcinomas. According to the morphological development classification (modified Paris classification), they were divided into 3 types: 265 lesions (22%) were depressed-type, 428 lesions (36%) were flat-type and 510 lesions (42%) were protruded-type. We investigated the clinicopathological differences of these types.

Results: Among T1 carcinomas, the rate of vessel invasion was 47% in depressed-type, 22% in flat-type and 21% in protruded-type, that of poorly differentiated or mucinous adenocarcinoma was 16%, 10% and 14%, that of massively submucosal invasion was 94%, 70% and 78%, and that of tumor budding was 48%, 26% and 30%, respectively. The rates of these pathological factors were significantly higher in depressed-type lesions than other types. The rate of adenomatous component was 5%, 55% and 52%, and the rate of polypoid growth was 14%, 56% and 96% respectively. It was significantly lower in depressed-type lesions than other types. The mean size of tumor of each type was 15mm, 30mm, and 19mm, and that of depressed-type was significantly smaller than other types. The rate of lymph node metastasis was 9%, 6% and 12%, respectively. The rate of distant metastasis or recurrence was 1% (10/1,203). Among these 10 cases, 5 cases were depressed-type lesions among which one showed a para-aortic lymph node metastasis and four showed lung metastases.

Conclusion: Depressed-type colorectal carcinomas had significantly lower adenomatous components and smaller size than flat- or protruded-types, suggesting that they follow a growth "de novo" pathway different from the "adenoma-carcinoma sequence". Depressed-type colorectal carcinomas contained worth pathological features than other types. Giving a careful attention to the morphological features is important to diagnosis the colorectal carcinomas.

Disclosure: Nothing to disclose

P0913 EFFICACY AND LONG-TERM OUTCOMES OF RECTAL NEUROENDOCRINE TUMORS AFTER ENDOSCOPIC SUBMUCOSAL RESECTION WITH A LIGATION DEVICE

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Introduction: The therapeutic strategies for the rectal neuroendocrine tumor (NET) still have not been standardized. We often use endoscopic submucosal resection with a ligation device (ESMR-L) for treatment of rectal NET. We conducted this study to evaluate the clinical outcomes of rectal NET treated by ESMR-L.

Aims & Methods: Between May 2002 and March 2018, 199 patients with 200 rectal NETs underwent ESMR-L in our hospital. Firstly, we investigated association between clinicopathological characteristics including endoscopic findings and therapeutic outcomes. Curative resection was defined as margin negative without lymphovascular invasion. Subsequently, the long-term outcomes after a 48-months follow-up period were also evaluated.

Results: The majority were male (74.5%) and the average age was 52.4 years. Most of the lesions were located at Rb (82.5%), and the average size was 4.6mm. Of the 200 lesions, 199 achieved margin negative and 125 achieved curative resection, respectively. Multivariate logistic regression analyses revealed that the tumor size ≧5mm (OR: 2.30, 95% CI: 1.24-4.26, P=0.008) and presence of central depression (OR: 3.72, 95% CI: 1.06-13.1, P=0.04) are significantly associated with non-curative resection. 13 (17.3%) of the non-curative resection underwent additional surgery, among which 2 cases (15.4%) had histological lymph node metastasis. Both of them could not detect the metastasis in preoperative period. Regarding to long-term outcomes, no case had local or distant metastases during the follow-up period. With respect to complications, 13 (6.5%) cases had delayed bleeding and one (0.5%) had perforation, but they were successfully managed conservatively.

Conclusion: ESMR-L is a feasible procedure as an endoscopic resection for rectal NET. Since there were few patients with non-curative resection who underwent additional surgery, we cannot exclude the possible presence of clinically undetectable metastatic lesions. However, considering that there was no recurrence in those cases, observation without additional surgery in a subset of cases with non-curative resection might be allowed.

Disclosure: Nothing to disclose

P0914 ENDOSCOPIC FULL THICKNESS RESECTION OF COLORECTAL LESIONS WITH THE FULL THICKNESS RESECTION DEVICE: THE FIRST GREEK EXPERIENCE

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Introduction: Endoscopic full thickness resection (EFTR) by the Full Thickness Resection Device (FTRD®) is an invasive treatment for colorectal lesions not resectable by conventional endoscopic techniques. This study presents the first Greek experience on FTRD® procedure, assessing EFTR efficacy and safety.

Aims & Methods: We conducted a retrospective analysis of 21 patients consecutively treated with FTRD® at two referral centers from October 2015 through April 2019. The indications included difficult adenomas (non-lifting and/or at difficult locations), early adenocarcinomas and subepithelial tumors.

Primary endpoints were technical success (resection in one piece and macroscopically complete) and R0 resection (negative lateral and deep margins based on histological examination).

Results: Technical success and R0 resection occurred in 17 of 21 procedures (80.9%). In 11 patients with difficult adenomas, they were achieved in 81.8%. In the subgroup with carcinomas (n=3), technical success and R0 resection rate was 66.6% while in the subgroup with subepithelial tumors (n=7) the rate was 85.7%. In general, technical success and R0 resection were decreased significantly for lesions >20mm versus ≤20mm (p=0.005). In 21 patients a total of four adverse events occurred (19%) and one of the patients underwent laparoscopic appendectomy due to EFTR around the appendix.

Conclusion: Our study showed favorable results concerning EFTR feasibility, efficacy and safety, especially for lesions ≤20 mm, non-lifting adenomas, subepithelial tumors and adenomas involving the appendix. Technical success, R0 resection and adverse events rates are comparable with data reported in literature. Larger randomized studies comparing available surgical techniques with EFTR are needed to better define the clinical benefit and long-term outcomes of EFTR in selected patients.

Disclosure: Nothing to disclose

P0915 VISUAL ESTIMATION OF COLORECTAL POLYP SIZE IN A COLON MODEL

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Introduction: Correct estimation of colorectal polyp size is important for surveillance policy, to estimate malignant potential and to plan the method of removal[1]. In relation to smaller polyps, size estimation is of major importance in the 'resect-and-discard' strategy[2]. Currently, the gold standard of polyp size determination is the pathological measured diameter, but often is relied on visual (endoscopic) rating of polyp size. Literature shows that this visual estimation is frequently inaccurate when compared to the pathological report[3,4]. We aimed to assess factors which could hypothetically influence the accuracy of visual polyp size and volume estimation in a colon model.

Aims & Methods: We created a colon model with artificial polyps of different size, shape and volume, which were photographed using an Olympus video colonoscope (Olympus EVIS EXERA III, CF-HQ190L) at fixed distances of 1, 3, and 5cm. The pictures were presented to 15 endoscopists of three different centers, who were asked to estimate polyp diameter and volume. Polyp diameters were categorized into ≤5mm, 6-9mm and ≥10mm, as these were considered clinical relevant categories[1,2]. Level of agreement

between the visually estimated diameter category and the true (measured) diameter category was assessed using the Kappa test. Agreement in volume estimation was assessed using intraclass correlation.

Results: The Kappa for agreement of the correct category of polyp diameter was 0.41 (95% confidence interval (CI) 0.33-0.48), which equals a fair to moderate agreement[5]. Agreement did not substantially improve with experience, with a Kappa of 0.42 (95% CI 0.33-0.51) in the experienced group (>48 months of endoscopic experience) versus 0.39 (95% CI 0.26-0.51) in the less experienced group. Moderate agreement was observed between estimated and true polyp volume (intraclass correlation 0.69, CI 0.63-0.74). Subanalysis showed that the best distance to estimate polyp diameter was at 3cm (Kappa of 0.45, versus 0.37 at 1cm and 0.40 at 5cm). Polyps photographed at 1cm were consequently estimated larger than those photographed at 3 and 5cm, for diameter as well as volume.

Conclusion: In this study using a colon model with artificial polyps we found fairly disappointing results in estimation of polyp size (both diameter and volume). Our data suggests that endoscopists tend to overestimate polyp size at short endoscopic distance and underestimate polyp size at larger distance. Three centimeters seems to be the ideal endoscopic distance for optimal polyp size estimation.

Novel techniques are needed to more accurately assess polyp size during endoscopy.

References: 1. Van Heijningen EM et al. Features of adenoma and colonoscopy associated with recurrent colorectal neoplasia on a large community-based study. Gastroenterology. 2013 Jun;144(7):1410-8. 2. Kandel P, Wallace MB. Should we resect and discard low risk diminutive colon polyps. Clin Endosc. 2019 Jan;Epub ahead of print. 3. Anderson BW et al. Endoscopic over-estimation of colorectal polyp size. Gastrointest Endosc. 2016 Jan;83(1):201-8. 4. Eichenseer PJ, Dhanekula R, Jakate S, Mobarhan S and Melson JE. Endoscopic mis-sizing of polyps changes colorectal cancer surveillance recommendations. Dis Colon Rectum. 2013 Mar;56(3):315-21. 5. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics. 1977;33(1):159-74.

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P0916 DELAYED BLEEDING AFTER COLONOSCOPIC TREATMENT IN PATIENTS TAKING ANTICOAGULANTS

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Introduction: Delayed bleeding after endoscopic treatment in antithrombotic therapy is still a serious complication. Japanese guidelines for gastroenterological endoscopy have recommended continued warfarin treatment in patients where the INR within therapeutic range and withdrawal of direct anticoagulants (DOACs) only on the day of treatment. However these guidelines have suggested the management of anticoagulants, the differences of the influence on delayed bleeding between warfarin and DOACs, and among each DOACs haven't been clarified yet.

Aims & Methods: The aim of this study is to clarify the effect of anticoagulants on bleeding after colonoscopic treatment. This study was three institutions retrospective cohort study based on clinical records. We assessed 265 consecutive patients with anticoagulants who underwent colonoscopic treatment from January 2013 to December 2017. 122 patients were taking warfarin and 143 patients taking DOACs, including 33 patients on dabigatran, 58 patients on dabigatran, 39 patients on apixaban and 13 patients on edoxaban. Delayed bleeding has been defined as an event requiring emergency endoscopic hemostasis or a >2g/dL decrease in hemoglobin level after colonoscopic treatment.

Results: The overall delayed bleeding rate was 4.5% (12/265), and the bleeding rate was significantly higher in the DOACs group with 7.0% (10/143) than in the Warfarin group with 1.6% (2/122) (p=0.041). In DOACs, the delayed bleeding rate of each agents were 3% in dabigatran (1/33), 8.6% in rivaroxaban (5/58), 7.7% in apixaban (3/39), 8.3% (1/13) in edoxaban. Dabigatran, as direct thrombin inhibitor, had lower delayed bleeding rates than factor Xa inhibitors, but there was no significant difference. Heparin bridge therapy (HBT) after procedure was performed more frequently in warfarin group (19%) than in DOACs group (2.8%) (p< 0.001), however, there was no association between delayed bleeding and HBT. Antiplatelet agents were combined in 45 cases (17%) and were signifi-

cantly higher in warfarin group (34% vs 9.7%, p<0.001), but combined use of antiplatelet agents was not related to delayed bleeding. There was no significant differences in tumor diameter, tumor location and procedure (ESD or Polypectomy/EMR) between the two groups. The hospitalization period was significantly shorter in DOACs group (7days vs 2days, p< 0.001). Perioperative thromboembolism occurred in 1 case of DOACs group, and the patient was improved with only slight paralysis.

Conclusion: In colonoscopic treatment, delayed bleeding was more frequent in patient with DOACs, and the DOACs effects differed in each agent. In DOACs, the possibility of rapid onset of anticoagulant effect after oral administration was considered. We have previously reported that there was less delayed bleeding rate after gastric ESD in patients taking dabigatran. A shift from factor Xa inhibitors to dabigatran could be the option to reduce the delayed bleeding in gastrointestinal endoscopic treatment.

Disclosure: Nothing to disclose

P0917 COLONIC ENDOSCOPIC SUBMUCOSAL DISSECTION USING ENDOMASTER EASE ROBOTIC SYSTEM: A PRECLINICAL STUDY

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Introduction: One of the difficulties in performing endoscopic submucosal dissection (ESD) is the lack of retraction during submucosal dissection. The development of master and slave transluminal endoscopic robot (MASTER), EndoMaster EASE System, aims to enhance safety and efficacy of ESD through two flexible robotic arms for tissue retraction and dissection. This is a preclinical animal study to evaluate performance of colorectal ESD using the latest version of the EndoMaster EASE System.

Aims & Methods: The latest version of the EndoMaster EASE System consisted of an independently designed flexible robotic platform with build-in endoscopic imaging system with working channels for the passage of 2 robotic arms and accessories. In this animal study, the outcomes measured included operating time (from starting incision to finishing dissection), completeness of resection, procedure-related complications as well as limitation of arms manipulation in narrow working space as assessed by counting the frequency of blind cutting.

Results: A total of 5 colorectal ESD procedures were performed in a 66.7kg porcine model under general anesthesia [Figure 1]. The mean operative time was 73.8 minutes, and the mean size of specimen resected was 1340 mm². There was no perforation, while profuse bleeding was encountered during one of the ESD procedures [Table 1]. Hemostasis was achieved after adequate exposure of bleeding arteriole by retracting the mucosal with robotic arm. The en-bloc resection rate was 100%

Conclusion: This study confirmed the feasibility and safety in performing ESD using the EndoMaster EASE System in porcine colon. This provides an important preclinical experience for the next clinical trial.

No	Weight (kg)	Location	OT time	Disssec-tion Time (mins)	Speci-men size (mm2)	Dissection speed (mm2/min)	Difficulty in manipula-tion	Compli-cation
1	66.7	Sigmoid (36cm)	68	46	35x35	26.63	nil	nil
2	66.7	Rectum (5cm)	46	26	50x45	86.53	nil	nil
3	66.2	Sigmoid (28cm)	30	18	25x25	34.72	nil	nil
4	58	Sigmoid (36cm)	158	100	40x50	20.00	yes	intra-operative bleeding
5	58	Sigmoid (24cm)	79	67	20x30	8.95	nil	nil

[Outcomes of Colorectal ESD using the EndoMaster EASE System in porcine model]

Disclosure: Philip Chiu serve on scientific advisory board of EndoMASTER Pte Louis Phee and Lawrence Ho are co-founder of EndoMASTER Pte

P0918 PREVALENCE AND CHARACTERISTICS OF COLONIC POLYPS AMONG PATIENTS REFERRED FOR FAST TRACK COLONOSCOPY FOR IRON DEFICIENCY ANAEMIA

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Introduction: Iron deficiency anaemia (IDA) is a common indication for fast track referral for suspected colorectal cancer. The vast majority of these patients undergo upper and lower gastrointestinal (GI) endoscopy. Most research focuses on the incidence of colorectal cancer, but there is a paucity of published data concerning colonic polyps in this patient population.

Aims & Methods: The aim of this study was to investigate the prevalence and characterisation of polyps, the histological subtype, and to identify any relationship between these and the degree of anaemia in patients referred for colonoscopy via the fast track pathway.

A dedicated, prospectively populated database of fast track referrals for endoscopy was utilised. Patient demographics, polyps and/or tumour characteristics, and haematological results at the time of referral were captured. These included haemoglobin level (Hb), mean cell volume (MCV), and markers of iron metabolism (iron, transferrin, transferrin saturation, and ferritin levels). Anaemia was defined as Hb level of < 120g/L for women and < 135g/L for men. Descriptive details of patient age, sex, referral route (if not fast track), and polyp characterisation were recorded. Data was analysed using the IBM SPSS® statistical tool.

Results: 846 patients underwent colonoscopy for anaemia at our centre over a period of 5 years (31st March 2014 to 7th April 2019). 355 patients in the cohort were found to have polyps (42.0%) and 58 had colorectal cancer (6.9%).

In cancer patients, low Hb and MCV were statistically significant (p 0.014 and 0.008 respectively). Hb had a negative predictive value of 0.92 for malignancy, being just 0.38 for polyps.

After exclusion of patients with cancer and those who did not have full haematinics data, further subgroup analysis was carried out on a total of 217 patients. Median polyp number and size were 1 (range 1-8) and 5mm (range 1-40mm) respectively. 66.4% of those patients with IDA had a pathologically confirmed adenoma, but there was no difference in measured blood results between adenoma and non-adenoma patients (p value range 0.249 – 0.935). In addition, neither polyp size nor site correlated with any of the blood tests analysed (all r²< ±0.15, p>0.3).

Conclusion: Colorectal polyps are common but incidental findings among patients who undergo colonoscopy for iron deficiency anaemia. The level of anaemia does not appear to correlate with incidence, site, or size of polyps. Further research is required to validate these findings and to investigate novel markers for patients with anaemia, as colonoscopy does not appear to identify the cause of anaemia in the majority of cases.

Disclosure: Nothing to disclose

P0919 LOW-DOSE RECTAL DICLOFENAC FOR THE PREVENTION OF POST-ERCP PANCREATITIS IN ELDERLY PATIENTS

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Introduction: According to the guidelines of the European Society of Gastrointestinal Endoscopy and Japan Gastroenterological Endoscopy Society, 50-100 mg rectal dose of nonsteroidal anti-inflammatory drugs (NSAIDs; diclofenac or indomethacin) is recommended for prophylaxis of post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis (PEP). However, little is known about the appropriate dose of NSAIDs to prevent PEP in elderly patients.

Moreover, the recommended dose is higher than the 25 mg dose that is commonly administered to Japanese patients, especially frail elderly patients with a low body weight or decreased renal function, who are more prone to adverse reactions.

Aims & Methods: The aim of this study was to evaluate the efficacy and safety of 25 mg rectal dose of diclofenac to prevent PEP in elderly patients aged over 75 years.

This was a retrospective observational study in a single institution. Between April 2013 and March 2019, 636 patients underwent 1200 ERCP procedures. Patients aged over 75 years with normal upper intestinal anatomy including Billroth I reconstruction were enrolled in this study. The exclusion criteria were as follows: 1) acute pancreatitis, 2) peptic ulcer disease, 3) contraindication to NSAIDs, 4) aspirin-induced asthma, and 5) severe kidney dysfunction with serum creatinine over 120 μmol/L. Consequently, 303 patients with 626 procedures were included in this study. They were administered with or without the rectal administration of 25 mg diclofenac 30 min before the procedure. The primary outcome was overall occurrence of PEP. Generalized estimating equations (GEE) were used to analyze repeated-measures data. The propensity score approach with inverse probability of treatment weighting (IPTW) was used to adjust for covariate imbalance between diclofenac and non-diclofenac groups.

Results: Patients were assigned to either administration of 25 mg diclofenac group (59 patients with 132 procedures) or non-diclofenac group (244 patients with 504 procedures). Their average age, body-mass index, and creatinine clearance (Ccr) were 83.5±5.5 years old, 21.2±4.2 kg/m², and 43.5±16.8 mL/min/1.73m², respectively. Patients with decreased renal function less than Ccr 60 mL/min/1.73 m² accounted for 86% (260/303). Thirty-four patients developed PEP and the incidence rate of PEP in diclofenac group (3.4%, 2/59) was significantly lower than in non-diclofenac group (13.1%, 32/244, p=0.037). The multivariate analysis using GEE revealed that prophylactic administration of low-dose diclofenac reduced the incidence of PEP (OR, 0.226; 95% CI, 0.052-0.975; p=0.046). Multivariate analysis using IPTW also showed that low-dose diclofenac was effective to prevent PEP (OR, 0.158; 95%CI, 0.029-0.872; p=0.034). After ERCP, there were no adverse events related to diclofenac such as gastrointestinal hemorrhage/ulceration and acute renal failure.

Conclusion: A 25 mg rectal dose of diclofenac was considered to be effective and safe in preventing PEP in elderly patients aged over 75 years.

Disclosure: Nothing to disclose

P0920 DOES ERCP PERFORMED FOR PATIENTS WITH ACUTE PANCREATITIS INCREASE THE RISK FOR THE COMPLICATION? A PROSPECTIVE MULTICENTRE OBSERVATIONAL STUDY

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Introduction: Complications associated with endoscopic retrograde cholangiopancreatography (ERCP) includepost-endoscopic sphincterotomy (EST) bleeding, perforation and sedation problems, in addition to post-ERCP pancreatitis. ERCP is frequently necessaryin cases of obstructive pancreatitis caused by choledocholithiasis orpancreatic cancer. However, once pancreatitis develops,complications are believedto arise owing to papillary oedema or deterioration of general condition.

In the present prospective multicentre study, we investigated whether pancreatitis beforeERCP was performed increasedthe risk of complications associated with ERCP.

Aims & Methods: We prospectively followed 3920 patients examined by performing ERCP in five high-volume centresbetween April 2015 and May 2017. The outcomemeasures were as follows: presence or absence of pancreatitis prior to the examination, patients' backgrounds, procedures, serum amylase level after the examination and complications associated with ERCP.

Results: In total, 127 (3.2%)patients hadacute pancreatitis before ERCPwas performed. Nosignificant difference was observed between the pancreatitis and non-pancreatitis groups in terms of age, sex and mean exami-

nation time. The ASA physical status classification scoreand frequency of obstructive jaundice and untreated papilla were significantly higher in the pancreatitis group (p < 0.001). We observed that the pancreatitis group had a higher frequency of cannulation, incidence of endoscopic sphincterotomy (EST), placement of biliary and pancreatic stents, pancreatography and insertion of guidewire than non-pancreatitis group (p = 0.003, p = 0.001, p < 0.001, p = 0.002 and p < 0.001, respectively). Nosignificant difference was observed in the incidence of cholangitis, cholecystitis, bleeding after EST, perforation, biliary tract injury and sedation complications. Theincidences of pancreatic duct injury were higher in the pancreatitis group than in non-pancreatitis group (p < 0.001). The frequency of post-ERCP pancreatitis was 7% (266/3650).

Conclusion: ERCP performed for patients with acute pancreatitis had an acceptable level of safety. We also found that the biliary cannulation rate was higher in patients with pancreatitis. However, care should be taken when inserting a guidewire to the pancreatic duct owing to an increased risk of pancreatic ductal injury.

Disclosure: Nothing to disclose

P0921 CLINICAL USEFULNESS OF A CONVENTIONAL GASTROSCOPE FOR ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN PATIENTS WITH SURGICALLY ALTERED GASTROINTESTINAL ANATOMY

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) in patients with surgical altered gastrointestinal anatomy (SAGA) is technically challenging. Some studies reported that ERCP using balloon-assisted enteroscope (BAE) yield better results than previous attempts of ERCP using conventional endoscopes. However, requirement for the specific endoscopic system limits the numbers of hospitals equipped with BAE. Considering the distance from the mouth to the blind end in patients with SAGA, it would be possible to perform ERCP using a conventional gastroscope instead of BAE.

Aims & Methods: The aim of this study was to assess the efficacy and safety of ERCP using gastroscope in patients with SAGA. Additionally, we identified the risk factors of failure of ERCP using gastroscope.

This was a retrospective observational study in a single institution. Between April 2013 and September 2018, ERCP procedures using the gastroscope, Q260J (Olympus, Japan, working length of 1040 mm, working channel of 3.2 mm) were performed in patients with SAGA such as post-gastrectomy with Billroth-II (B-II) and Roux-en-Y (R-Y) and post-pancreaticoduodenectomy with modified Child method (PD). Success rates of deep insertion, cholangiogram and treatment were evaluated. We estimated the predictive factors of failure of ERCP using gastroscope. Generalized estimating equations (GEE) were used to analyze repeated-measures data.

Results: Total 29 patients with 47 procedures were included, comprising B-II (10 patients with 17 procedures), R-Y (13 patients with 18 procedures) and PD (6 patients with 12 procedures). Deep insertion was successful in 41/47 procedures (87%), average insertion time was 7.7±6.4 min. Successful cholangiogram and treatments were obtained in 38/41 (93%) and 36/41 (88%) procedures, respectively. Overall average procedure time was 35.3±15.5 min. Although there was no significant difference in the success rate of deep insertion among three groups, the rate in patients with R-Y tended to be low, the rate in patients with B-II, R-Y and PD being 86% (15/17), 75% (14/18) and 100% (12/12), respectively. Complications occurred in 4/47 procedures (8.5%), and all complications were managed conservatively. There were no independent predictive factors of failure associated with our endoscopic procedures. In a separate analysis focusing on patients with R-Y, laparotomic gastrectomy was the only independent predictive factor of failure of deep insertion by multivariate logistic regression with GEE (odds ratio, 5.06; 95% confidence interval, 1.00-25.47).

Conclusion: Since ERCP using the conventional gastroscope was safe and effective in patients with SAGA, gastroscope could be used in place of BAE. However, because the success rate of deep insertion in patients with laparotomic gastrectomy with R-Y was relatively low, such patients should receive ERCP using BAE.

Disclosure: Nothing to disclose

P0922 ERCP IS MORE CHALLENGING IN CASES OF ACUTE BILIARY PANCREATITIS THAN IN ACUTE CHOLANGITIS – AN ANALYSIS OF THE HUNGARIAN ERCP REGISTRY DATA

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) is necessary in acute biliary pancreatitis (ABP) when cholangitis or common bile duct stone is present. However, the inflammation of the pancreas and the surrounding tissues might make it more difficult. This topic is not widely studied, therefore we intended to quantify this challenge for the endoscopist by analyzing 5 tertiary centers' data from the prospectively collected data of Hungarian ERCP registry.

Aims & Methods: 150 ABP cases and 243 acute cholangitis (AC) cases without ABP were included. Previous papillotomy, altered gastroduodenal anatomy and biliary stricture cases were excluded. The rate of biliary access, advanced cannulation method, adverse event rates, cannulation and fluoroscopy time, as well as subjective difficulty were evaluated.

Results: Needle-knife precut use was significantly higher in the ABP than in AC group (33% vs. 21%; p=0.013), however, no difference was found between biliary cannulation rates of the two groups (93% vs. 91%). Significantly more pancreatic guidewire manipulation (30% vs. 16%; p=0.01) and prophylactic pancreatic stent use (22% vs. 9%; p< 0.001) was seen in the ABP than in AC group. Moreover, longer cannulation time in the ABP patients (300 vs. 200 s; p=0.008) but similar fluoroscopy times (90 vs. 87 s) were measured in the two groups. There was no difference between the adverse events rate of ABP vs. AC cases (immediate bleeding: 11% vs. 9%, only one case required transfusion in the AC group, all other cases were controlled endoscopically; hypoxia: 5% vs. 7%). No significant difference was found in the subjective difficulty, however, there was a trend towards easier examinations (< 3 on a 10-point scale) in the AC group (40% vs. 51%; p=0.073).

Conclusion: ERCP in ABP cases is more challenging than in AC but does not affect the outcomes in our registry data. The increased need for pre-cutting, longer cannulation time and higher rate of pancreatic guidewire manipulations show more frequent difficult biliary cannulation in the ABP patients without worsening the biliary cannulation success rate. The level of subjective difficulty also correlates with these data. Adverse events rates were similar in the groups.

Disclosure: Nothing to disclose

P0923 PERFORATION OF THE LATERAL DUODENAL WALL CAUSED BY PLASTIC BILIARY STENT DISPLACEMENT TREATED WITH OVER-THE-SCOPE-CLIP: A PROSPECTIVELY COLLECTED COHORT

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Introduction: Duodenal perforation is a complication of ERCP in less than 1% of procedures and can sometimes be caused by the impaction of a distally migrated stent into the lateral duodenal wall. Treatment options when this occurs may include endoscopic treatment with either through-the-scope clips or over-the-scope clips (OTSC) and surgical repair.

Aims & Methods: The goal was to determine the incidence of duodenal perforation caused by plastic biliary stents displacement in our center and identify possible predisposing factors. We also wanted to evaluate the efficacy and safety of endoscopic closure with OTSC. To obtain data, we went over the database including all ERCPs performed and screened for duodenal perforation secondary to biliary plastic stents displacement from January 1st 2014 to March 31st 2019. We then collected individual data of the screened cases.

Results: Six cases of ERCP done for lateral duodenal wall perforation caused by plastic biliary stent displacement were identified during that period (0.8% of the 696 ERCPs with plastic stent placement performed over the same period). In most cases the diagnosis of perforation was done less than five days after the stent placement (4/6) and the time between stent insertion and perforation diagnosis ranged from 2 to 91 days. In the majority of these patients (5/6) biliary stenting was done with multiple double flaps straight plastic stents, in all cases the longest stent was the culprit and in most of them (5/6) the culprit stent was in the left intra-hepatic bile ducts. The length of the perforating stents ranged from 12 to 18 cm. Two patients had a history of previous stenting achieving a higher total stents diameter than what was applied at the last examination (patient 3 had a maximum total stents diameter of 18.5 Fr while the total diameter of stents in his last ERCP was of 10 Fr and patient 4 had a maximum total stents diameter of 27 Fr while the total diameter of stents in his last ERCP was of 25.5 Fr). Each patient was treated with a 12mm OTSC which permitted successful closure of all perforations (6/6; 100%) confirmed by subsequent imaging modalities. In five patients no further interventions were needed and outcome at 28 days was excellent for four of them. One patient died at day 17 after perforation closure but his death was not related to the complication. Further intervention after successful treatment was needed for another patient. This patient developed peritonitis requiring laparotomy and peritoneal lavage. The laparotomy did not show any residual leak at the perforation site but the patient eventually died of this complication at day 5 post perforation.

Patients characteristics (Gender, age)	Stenting indication	Days between stent placement and perforation diagnosis	Culprit stent informations	Immediate outcome	28 days outcome
1. M 75	Biliary leak post hepatectomy	21	Double flaps 18 cm 8,5 Fr (1/2 migrated)	Success at closure	No further interventions or complications
2. M 61	Bilioma post liver transplantation	2	BSLC 17 cm 8,5 Fr	Success at closure	No further interventions but death 17 days later (biliary sepsis)
3. F 31	Choledocholithiasis and bile duct stenosis	4	Double flaps 15 cm 7 Fr (1/2 migrated)	Success at closure	No further interventions or complications
4. M 52	Ischemic cholangitis	91	Double flaps 12 cm 8,5 Fr (2/3 migrated)	Success at closure	No further interventions or complications
5. M 72	Bile duct compression after hepatic artery embolization	2	Double flaps 13 cm 8,5 Fr (1/2 migrated)	Success at closure	Peritonitis needing laparotomy and death 3 days later
6. F 46	Anastomotic stenosis post liver transplantation	2	Double flaps 12 cm 8,5 Fr (1/2 migrated)	Success at closure	No further interventions or complications

[Table 1: Cases Summary]

Conclusion: Perforation of the lateral duodenal wall by a biliary stent is a rare complication of ERCP in a tertiary referral center. In this study, most cases were related to multiple straight plastic stents with double flaps. A history of maximal total stents diameter achieved before the last ERCP, use of longer stents (>12 cm) and placement of stent into the left intra-hepatic bile ducts could be potential risk factors. OTSC appears as an effective treatment with a closure success rate of 100% in our cohort.

Disclosure: Nothing to disclose

P0924 WHO SHOULD ADMINISTER SEDATION DURING ERCP - ANESTHESIOLOGIST, INTENSIVIST OR ENDOSCOPIST? A COMPARATIVE PROSPECTIVE STUDY

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Introduction: The proper training in sedation and who should administer it during ERCP still unknown.
Aims & Methods: To compare safety and effectiveness of sedation during ERCP (sERCP) regarding which medical doctor directs it.
A comparative prospective non-randomized study done in daily practice. Consecutive patients who underwent to ERCP were collected at two centers. January 2017 - May 2018. Sedation was directed either by an endoscopist (endoscopist-directed propofol: EDP), on Monday or by an intensivist (intensivist-administered propofol: IAP), on Wednesday or by an anesthesiologist (monitored anesthesia care: MAC), on Thursday. The safety was measured by the appearance of serious adverse events (SAE) and the effectiveness, by the cancelled ERCP rate, sedation time and patient position that determined ease of ERCP and quality of radiologic images.
Results: 454 patients (Age: 72.7 ±15.7y; women: 54.63%): 147 into EDP group, 137 IAP group and 170, MAC group. The endoscopist had the largest experience in sERCP (>100 procedures): 98%, p=0.000 and he administered only propofol in 81.9%, the intensivist administered propofol plus midazolam in 78.7% and anesthesiologist, propofol plus other agents (i.e. opioids, ketamine) in 86.2%, p=0.000. The sedation was deepest in MAC, Observers's Assessment of Alertness-Sedation score (OAAS): 5.19 ±0.6, p=0.000. The SAE rate was 8.6%, lowest in EDP: 4.8%, p=0.042. The SpO_2 < 70% was the most frequent SAE: 4.5%, highest in MAC: 6.1%, p=0.085 and it had required more respiratory resuscitation measures (chin-lift maneuver, increasing of FIO_2 or Guedel airway insertion) in MAC and IAP than EDP, p=0.003. The tracheal intubation was most frequent in MAC: 1.8%, p=0.074. Concerning effectiveness, the highest cancelled ERCP rate was observed in MAC: 2.9%, p=0.015. Similarly, in this group the lateral decubitus position was most frequent (31.6%, p=0.000), which determined the worst radiologic image (17.8%, p=0.000). The sedation time was shortest in IAP: 44.4 ±1.8 min, p=0.023. In a multivariate analysis, the shorter training on sERCP: OR =6.56 (3.18-13.54 CI95%), Obstructive sleep apnea: OR =4.34 (2.07-9.11 CI95%) and age ≥75years: OR =2.18 (1.03-4.63 CI95%) were associated to appearance of complications.
Conclusion: Our data suggest that sERCP is safer and more effective when is administered by an expert nursing team directed by an endoscopist.
Disclosure: Nothing to disclose

P0925 ENDOSCOPIC ULTRASOUND (EUS)-DIRECTED TRANSGASTRIC ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP): A SINGLE CENTER EXPERIENCE OF AN EVOLVING PROCEDURE

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Introduction: EUS-directed transgastric ERCP is an emerging technique for pancreaticobiliary intervention in patients with a history of Roux-en-Y gastric bypass (RYGB). It can allow ERCP to be performed in a minimally invasive fashion and with a high technical success rate.
Aims & Methods: The aim of this study was to analyze the safety and efficacy of EDGE procedures performed at a single tertiary care center. Patients with a history of RYGB who underwent an EDGE procedure between January 2018 and April 2019 were included in the study. Patient demographics, procedure time, technical success and complications (bleeding, infection, perforation and pancreatitis) were recorded. Total time to complete procedure and hospital length of stay was calculated by addition of the time for EUS and ERCP. Statistical analysis was performed using SPSS 23 (IBM, Armonk, NY).
Results: Eighteen patients were included in the study. Mean age was 61 +/- 11 years and 78% (n=14) were females. EDGE was performed after a failed ERCP in 22% (n=4). EDGE was performed as a same-day procedure in 33% (n=6) and access route was transgastric for 89% (n=16) vs transjujenal for 11% (n=2). Technical success was 100% (n=18). LAMS was removed during the initial ERCP for 44% (n=8), follow-up EGD for 17% (n=3), elective surgery (Whipples procedure) for 3% (n=17%), follow up ERCP for 11% (n=2), follow-up EUS for 6% (n=1) and left in place for 6% (n=1). 72% (n=13) underwent spontaneous closure of the fistula, 17% (n=3) underwent closure intraoperatively, 6% (n=1) underwent closure with endoscopic mucosal clips. Post-procedural bleeding occurred in 6% (n=1). LAMS dislodgement during the procedure with successful replacement of the LAMS occurred in 6% (n=1). The mean hospital length of stay was 1.09 +/- 0.76 days.
Conclusion: EDGE is a safe and efficacious procedure that has a 100% technical success rate and short length of stay with minimal complications.
Disclosure: Nothing to disclose

P0926 SPYGLASSDS GUIDED LITHOTRIPSY FOR PANCREATIC DUCT STONES IN SYMPTOMATIC, TREATMENT REFRACTORY CHRONIC PANCREATITIS- 12 MONTHS FOLLOW UP ON CLINICAL, TECHNICAL SUCCESS AND QUALITY OF LIFE

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Introduction: Pancreatic duct (PD) stones are a common complication in chronic calcifying pancreatitis (CCP) and contribute to pain onset and pain exacerbation. (Digital) single-operator pancreaticoscopy (d-SOP) guided lithotripsy was shown to be a promising option of therapy regarding technical success (95% ductal clearance) and short-term pain relieve. However, there is only little evidence of mid-and long-term clinical success and impact on quality of life.
Aims & Methods: Analysis of clinical success and impact on quality of life after d-SOP guided lithotripsy in CCP in ongoing follow up. A single-center, retrospective analysis of all d-SOP guided lithotripsies (n=23) of PD stones in 20 CCP patients after introduction of next generation d-SOP (SpyGlass DS) in 2015. Clinical success was determined by a systematic questionnaire regarding pain intensity and incidence as well as quality of life after 3,6 and 12 months in an ongoing follow up.
Results: After d-SOP guided lithotripsy technical success (PD decompression) was achieved in a total of 19/20 cases. Clinical success (pain reduction >50 % in numerical rating scale (NRS) pain score) was achieved in 19/20 cases. In early follow-ups 95% of the patients reported major improvement in symptoms und quality of life. In the latest (12 months) follow up 2 patients were referred to a surgeon for partial pancreatectomy, one patient was lost to follow-up. Of the 17 remaining patients clinical success - as defined above - was persistent in 11 cases and 12 patients described major improvements in symptoms and disability in daily life. There was no need of further interventional therapy except subsequent stentingin case of persistent PD strictures.
Conclusion: d-SOP guided lithotripsy was found to be safe and effective regarding technical success and clinical outcome. Beneficial effects on symptom control and quality of life seem to last in the majority of CCP patients after a 12 months follow-up.
Disclosure: Nothing to disclose

P0927 A NOVEL, SMALL J-TIPPED GUIDEWIRE REDUCE THE RISK OF POST-ENDOSCOPIC RETROGRADE CHOLANGIPANCREATOGRAPHY PANCREATITIS IN PATIENTS WITH DIFFICULT BILIARY CANNULATION

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Introduction: ESGE guideline recommends using pancreatic guidewire (PGW)-assisted biliary cannulation in patients where biliary cannulation is difficult and repeated unintentional access to the main pancreatic duct occurs. However, insertion of the GW into the pancreatic duct has a risk of post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis. Recently, J-tipped GW designed for improving luminal passage have been developed and reported to be beneficial in selective biliary cannulations. Although J-tipped GW was not applicable to pancreatic duct due to its large tip radius, the newly developed small J-tipped GW with a smaller loop has enabled pancreatic duct interventions.

Aims & Methods: The aims of this study were to evaluate the safety and efficacy of newly developed small J-tipped guidewire for PGW-assisted biliary cannulation. PGW-assisted biliary cannulation for difficult biliary cannulation with naïve papilla were performed in a total of 277 cases. We used angle-tipped GWs from January 2011 to February 2014 and small J-tipped GWs from March 2014 to September 2016. The patients were divided into two groups chronologically, according to the time period during which guidewires were used for PGW-assisted biliary cannulation: the angle-tipped GW group (from January 2011 to February 2014) and the small J-tipped GW group (from March 2014 to September 2016). Pancreatic stent was inserted after PGW-assisted biliary cannulation. The success rates and complications were evaluated.

Results: Success rates of PGW-assisted biliary cannulation were 81% in the small J-tipped GW group and 70% in the angle-tipped GW group, respectively. There was no statistical difference between the two groups (p = 0.052). The rate of post-ERCP pancreatitis was significantly lower in the small J-tipped GW group compared with that in the angle-tipped GW group (6.3% vs 19.0%, P = 0.01). Moreover, localized pancreatitis or pancreatic ductal leakage caused by injury of pancreatic duct were significantly less in the small J-tipped GW group compared to the angle-tipped GW group. Multivariate analysis showed that the use of the small J-tipped GW was the only factor reducing the risk of post-ERCP pancreatitis (OR 0.32, 95% CI 0.12-0.87, P = 0.026).

Conclusion: Newly developed small J-tipped GW reduce a risk of developing post-ERCP pancreatitis in patients with difficult biliary cannulation.
Disclosure: Nothing to disclose

P0928 NON-ALCOHOLIC FATTY LIVER DISEASE AS A RISK FACTOR FOR POST ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY PANCREATITIS

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Introduction: The prevalence of post endoscopic retrograde cholangiopancreatography pancreatitis (PEP) is variable and ranges from 5-25%. Fatty liver disease has been increasingly encountered in the last decade and it is already reported as a risk factor for several extra-hepatic diseases, however, it has not been reported as a risk factor for PEP.

Aims & Methods: We aimed to assess whether NAFLD is a risk factor for the development of PEP. We performed a retrospective multicenter study. All patients who underwent ERCP during 2014-2016 who had a diagnosis of NAFLD by abdominal imaging were eligible for inclusion. Four hundred and one patients were included, among them, thirty-eight (9.5%) were diagnosed with PEP according to clinical, laboratory and radiological criteria.

Results: The mean age in groups A (patients without PEP) and group B (patients with PEP) were 61.2 ± 20.9 and 67.6 ±19.3, respectively. Forty-five percent in group A and 44% in group B were males. The most common indication for ERCP in the two groups was confirmed CBD stones, cholangitis and obstructive jaundice. One-hundred twenty-four patients (34%) in group A had fatty liver as diagnosed by pre-endoscopic ultrasound (US) compared to 21 patients (55.3%) in group B, P=0.01.
In univariate analysis, several predictors of PEP were identified. Fatty liver (OR 2.363, 95% CI 1.211-4.614, P=0.01), AST (OR 1.008, 95% CI 1.000-1.016, P=0.04), ALT (OR 0.979, 95% CI 0.968-0.991, P=0.0007), ALP (OR 1.008, 95% CI 1.001-1.015, P=0.01), GGT (OR 1.014, 95% CI 1.006-1.021, P=0.0005) and total bilirubin (OR 1.141, 95% CI 1.039-1.253, P=0.005) were statistically significant in predicting PEP. In multivariate regression analysis, only fatty liver showed statistically significant correlation with PEP (OR 3.224, 95% CI 1.548-6.713, P=0.001), while the other parameters showed very weak association with PEP, with ROC area under the curve (AUC) of 0.8156. Notably, no patients with dilated CBD of more than 10 mm had developed PEP.

Conclusion: NAFLD was shown to be a risk factor for PEP. Therefore, we suggest to consider prophylactic pancreatic stenting and/or NSAID's suppositories among these patients.
Disclosure: Nothing to disclose

P0929 IS VASCULARITY ENOUGH TO PREDICT NEOPLASIA IN BILE DUCT LESIONS DURING PERORAL CHOLANGIOSCOPY?

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Introduction: The direct visualization of the intraductal biliary system via peroral cholangioscopy (POCS) changes the clinical management in patients with bile duct lesions. Macroscopic features have been used to determine neoplasia in bile duct lesions during POCS such as the presence of masses or irregular surfaces; however, the presence of bleeding, oozing or tortuous vessels as signs of neovasculature might be most the accurate findings for neoplasia.

Aims & Methods: To evaluate the role of neovasculature in bile duct lesions for the prediction of neoplasia during peroral cholangioscopy.
A cohort study with prospectively collected endoscopic data of patients with bile duct lesions evaluated via POCS who was aged ≥18 years. Patients with lesions but with no subsequent histological confirmation, with less than six months of follow-up, or concomitant choledocholithiasis during POCS were excluded for analysis. POCS were performed using a digital, single-operator cholangioscopy system (Spyglass®, Boston Scientific, Marlborough, MA, USA). Neovasculature was defined as the presence of irregular or spider vascularity on bile duct lesions. The neovasculature overall diagnostic accuracy was estimated considering a six months follow-up as a gold standard. Inter-observer agreement analysis was performed between two endoscopists (JO & JAV). A p-value< 0.05 was considered statistically significant. Data were analyzed in R-3.4.2 (R Foundation for Statistical Computing; Vienna, Austria).

	Total (n=95)	Neoplastic (n=52)	Non-neopastic (n=43)	p-value
Age (years), median (range)	66 (20-93)	71.2 (37-93)	61 (20-87)	<0.001
Gender (female), n (%)	51 (53.7)	26 (50.0)	25 (58.1)	0.428
Main POCS indication (Tumor suspicion/ indeterminate stenosis), n/n	50/45	42/10	8/35	<0.001
Previous ERCP, n (%)	40 (42.1)	15 (28.8)	25 (58.1)	0.039
Bile common duct localization, n (%)	61 (64.2)	30 (57.7)	31 (72.1)	0.028
Presence of neovascularity, n (%)	65 (68.4)	49 (94.2)	16 (37.2)	<0.001
Neoplastic histology, n (%)	48 (50.0)	48 (92.3)	0	<0.001

[Table 1. Baseline characteristics between neoplastic vs. non-neoplastic groups according to follow-up.]

Results: Ninety-five patients were enrolled, median age 65.6 (16 – 93) years old, 56 (55%) were female. Neovasculature signs were appreciated in 65/95 (68%) of cases. The biopsies sample were adequate in 90/95 (95%) cases. Histology confirmed neoplasia in 45/61 (74%) cases; while, follow-up in 49/65 (75%).

Table 1 summarized baseline characteristics between neoplastic vs. non-neoplastic groups according to follow-up. The vascularity for predicting neoplastic lesions reached sensitivity, specificity, positive and negative predictive value (PPV & NPV), positive & negative likelihood ratio, observed and inter-rater agreement of 94%, 63%, 75%, 90%, 2.53 (95% IC 1.71 – 3.76), 0.09 (95% IC 0.03 – 0.28), 80% and 57% (p< 0.001), respectively. The interobserver agreement analysis exhibited an excellent agreement (K>80%; p< 0.001).

Conclusion: Irregular or spider vascularity on bile duct lesions during POCS evaluation predict properly biliary neoplastic lesions.

Disclosure: Nothing to disclose

P0930 ANALYSIS OF POST-ERCP PANCREATITIS RATE IN THE TIME TO SUCCESSFUL BILIARY DEEP CANNULATION AND OPERATOR CHANGE FROM TRAINEE TO EXPERT

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Introduction: Selective biliary deep cannulation is a first step of biliary endoscopic treatment and one of the most important procedures to master for trainees. When this procedure is time-consuming, the complication risk may increase. We retrospectively analyzed the relation between biliary cannulation time and post-ERCP pancreatitis (PEP) and assumed the time to change an operator from a trainee to an expert.

Aims & Methods: Between April, 2011 and March, 2019, there are 996 patients with intact papilla [536 male, median of age 75 year old (IQR: 66-83)] in whom the selective biliary deep cannulation was mandatory for the endoscopic treatment. The diseases of the patients were benign in 765 cases (76.8%). ERC was usually commenced with conventional cannulation technique. Wire-guided cannulation, pancreatic guide wire method, or needle knife precut were allowed. The expert (EX) was H.K. who experienced more than 3000 ERCP cases and the other operators were defined as trainees (TR).

Although the operator change from TR to EX was within EX discretion, the time of operator change was principally within 15 minutes. The PEP was defined as sever epigastric pain and more than twice value of upper serum AMY level which were occurred in the patients within 24 hours after treatment. The degree of PEP severity was classified according to Cotton criteria. The rate of PEP was analyzed according to the first operator and time.

Results: The success rate of biliary cannulation was 98.9% (985/996). The median time of cannulation was 5 minutes (IQR: 2-15). PEP rate was 6.0% (60/996). The moderate PEP was noted in 5.0% (3/60) and the rest mild. The number of EX-first cases was 310 (31.1%) and that of TR-first cases 686 (68.9%). The rate of operator change from TR to EX was 31.6% (217/686). The success rate of cannulation in EX-first cases was 99.7% (309/310) and that in TR-first cases was 98.5% (676/686);(p=0.11). The median cannulation time was 3 minutes (IQR: 1-8.8) in EX-first cases and that in TR-first cases was 5.5 minutes (IQR: 2-14.8); (p< 0.001). The PEP rate in EX-first cases was 4.2% (13/310) and that in TR-first cases was 6.9% (47/686);(p=0.10). In TR-first cases, median successful cannulation time by TR alone was 6 minutes (IQR: 2-15) and median time of operator change was 10 minutes (IQR: 7-15). Comparing the PEP rate according to successful cannulation time: within 10 minutes (short time: ST) and more than 10 minutes (long time: LT), the PEP rate was 4.4% (31/700) in ST and 9.8% (29/296) in LT; (p< 0.01).

Compared between the first operators in ST cases, the PEP rate in EX-first cases was 3.6% (9/247) and that in TR-first cases was 4.9%(22/453); NS (p=0.46). In LT cases, that in EX-first cases was 6.3% (4/63) and that in TR-first cases 10.7% (25/233); NS (p=0.30). Compared in intra-operator time, in EX first cases, there was no significant difference (3.6% vs 6.3%: p=0.34) in PEP rate between ST and LT. However, compared in TR-first cases, significant increase in PEP rate was noted (4.9% vs 10.7%: p< 0.01). In operator-changed cases, total PEP rate was 6.9% (15/217). PEP rate in

ST was 4.3% (5/116) and that in LT was 9.9% (10/101); NS (p=0.10). In cases that successful cannulation was achieved by TR alone, total PEP rate was 6.8% (32/468). However, PEP rate significantly increased (p< 0.001) from 5.1% (ST: 21/412) to 19.6% (LT: 11/56).

Conclusion: In case of time-consuming, the more PEP rate increases, especially in TR-first cases. These data suggests that operator change may be considered in case that TR consumes more than 10 minutes to achieve successful deep biliary cannulation.

Disclosure: Consultant: Piolax Medical Devices Gadelius Medical

P0931 ERGONOMIC INJURIES IN ENDOSCOPISTS AND THEIR RISK FACTORS

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Introduction: Endoscopists often experience musculoskeletal pain and injury (most often in the back, neck, shoulders, hands, wrists, and thumbs) that are associated with the minute and repetitive strain that is placed on these areas during endoscopic procedures. The aim of this study is to assess the musculoskeletal injuries in endoscopists and their risk factors.

Aims & Methods: Objective: To assess frequency of ergonomic injuries in endoscopists and their risk factors, at a tertiary care hospital, Karachi.

Subject & methods: This cross sectional study was conducted at the Department of Gastroenterology, Liaquat National Hospital after informed written consent on endoscopy practitioners doing endoscopies throughout the Pakistan. Endoscopists were asked to fill-up the Performa. Chi square test was used for analysis. P-value < 0.05 was considered as significant.

Results: Out of 61 endoscopists 58 (95.1%) were male and 3 (4.9%) were female with the mean age of 44.02+7.873 years. The most common ergonomic injury noted was back pain in 25 patients (41%), leg pain in 14 (23%) and hand pain in 12 (19.7%). Ergonomic injuries were common in endoscopists with higher BMI (p< 0.004), were seen more in enodscopists performing high number of procedures (p< 0.001), more commonly noted in endoscopists with higher cumulative duration of GI practice (p< 0.001) and common in endoscposists not doing regular exercise (p< 0.030). But ergonomic injuries were not associated with mini-rests between procedures (p< 0.133), glove size of the enodoscopists (p< 0.102) and hand dominancy (right handed & left handed) (p< 0.182).

Conclusion: Among endoscopists there is a increased prevalence of injuries definitely or potentially related to endoscopy. Higher procedure volume, cumulative years performing endoscopy, BMI and lack of regular exercise are associated with more work-related injuries.

Disclosure: Nothing to disclose

P0932 PANCREATIC PARENCHYMA ATROPHY AND DILATED MAIN PANCREATIC DUCT CAN BE NEGATIVE PREDICTORS OF PANCREATITIS RELATED TO BILIARY SEMS INSERTION

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Introduction: Obstructive jaundice is crucial for the patients with pancreatobiliary malignancy. Insertion of self-expansive metallic stent (SEMS) into biliary duct is known useful to improve obstructive jaundice and quality of life (QOL) of these patients. However, post ERCP pancreatitis (PEP) after SEMS insertion across the papilla of Vater is one of the most important adverse events affect patients' QOL.

Aims & Methods: Ninety patients received biliary SEMS insertion for biliary obstruction due to malignancy in Iwata City Hospital form 2010 to 2018 were reviewed. We evaluated the relationship between incidence of PEP after biliary SEMS insertion and clinical factors, including age, sex, serum amylase level, tumor location, cause of obstruction, with/without EST, with/without pancreatography, diameter of main pancreatic duct (MPD), and thickness of pancreatic parenchyma.

Results: Mild and severe PEP were diagnosed in 11 (12.2%) and 1 (1.1%) patients, respectively. Only the thickness of pancreatic parenchyma (p< 0.001) and diameter of MPD (p< 0.001) showed significant difference between PEP and non-PEP groups. However, other factors did not show significant difference in the incidence of PEP. The incidence of PEP among patients

whose thickness of pancreatic parenchyma at the left side of corpus verte-brare were less than 10mm (1.7%) in computed tomography was quite low-er than patients whose thickness were 10mm or more (32.2%) (p< 0.001). Similarly, the wider (5mm or more) diameter of MPD (1.6%) reduced the incidence of PEP compared to narrower ones (30.0%) (p< 0.001).

Conclusion: These results imply that pancreatic parenchyma atrophy and dilated MPD are negative predictive factor of pancreatitis related to biliary SEMS insertion.

Disclosure: Nothing to disclose

P0933 PARTIALLY COVERED SELF-EXPANDABLE METAL STENTS REPLACE PLASTIC STENTS FOR MALIGNANT EXTRAHEPATIC BILIARY OBSTRUCTION: RESULTS OF A MEDICAL CENTER

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Introduction: Endoscopic biliary stenting has been well established as standard treatment of malignant biliary obstruction. Comparing with plas-tic stent, self-expandable metal stent (SEMS) has longer stent patency. However, few reports are published to compare primary SEMS placement and reintervention of SEMS to replace plastic stent.

Aims & Methods: The aim of this study was to assess the differences in stent patency and complications between patients with primary metal stent placement and reintervention to replace previous plastic stent. From Jan., 2010 to Dec., 2016, patients with malignant obstruction below the common hepatic duct (CHD) confluence undergoing biliary stenting with partially covered self-expandable metal stents (PCSEMS) were retro-spectively analyzed. Malignancy was diagnosed based on clinical, labora-tory, imaging, and pathologic studies.

Results: A total of 81 patients (43 female and 38 male; mean age 72.5±13.1 years) with PCSEMS for malignant obstruction below the CHD confluence were included. Malignancy included pancreatic cancer (n=58, 71.6%), cholangiocarcinoma (n=12, 14.8%), ampullary cancer (n=8, 9.9%), meta-static cancer (n=2, 2.5%), and gallbladder cancer (n=1, 1.2%). Strictures were located at upper (n=3, 3.7%), middle (n=12, 14.8%), and distal extra-hepatic duct (n=66, 81.5%), respectively. Average length of stricture was 21.2±9.0 mm. All patients underwent endoscopic sphincterotomy before metal stent placement. The length of PCSEMS was 40 mm (n=11, 13.6%), 60 mm (n=58, 71.6%), and 80 mm (n=12, 14.8%). The lumen diameter of PCSMS was all the same (10 mm). Twenty of 81 (24.7%) patients received chemotherapy and/or radiotherapy. PCSEMS was placed as a primary in-tervention in 21 (26 %) patients, and PCSEMS replacing plastic stent was performed in 60 (74%) patients. Overall stent patency was 210±112 days. During the period of follow-up (190.2±190.5 days), stent complications oc-curred in 25 of 81 (31%) patients and included cholangitis (n=10), stent mi-gration (n=6), cholecystitis (n=2), pancreatitis (n=2), stent occlusion (n=2), perforation (n=1), liver abscess (n=1), and hemorrhage (n=1), Although stent patency, and stent complications were lesser in reintevention (26.7%) than in primary intervention (42.9%), the differences were not statistically significant (*P* > 0.05).

Conclusion: For patients with malignant obstruction below the CHD con-fluence, primary metal stent placement and reintervention with PCSEMS showed comparable stent patency and complications.

Disclosure: Nothing to disclose

P0934 DICLOFENAC DOES NOT REDUCE THE RISK OF ACUTE POST ENDOSCOPIC RETROGRADE CHOLANGIOGRAPHY PANCREATITIS IN PATIENTS WITH PRIMARY SCLEROSING CHOLANGITIS

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Introduction: European society of gastrointestinal endoscopy (ESGE) rec-ommends (1) rectal indomethacin or diclofenac prior to endoscopic ret-rograde cholangiopancreatography (ERCP) as a prophylaxis for post-ERCP pancreatitis (PEP). Primary sclerosing cholangitis (PSC) is a chronic chole-

static liver disease characterized by intrahepatic or extrahepatic stricturing and markedly increased risk for biliary neoplasia (2). ESGE/EASL suggest (3) that ERCP can be done in PSC if MRC plus liver biopsy is equivocal or contraindicated in patients with persisting clinical suspicion of PSC and in addition ERCP is done for ductal sampling (brush cytology) and dilatation of significant strictures. The risk for PEP is approximately 7 % in PSC (4).

Aims & Methods: Our aim was to evaluate the role of rectal diclofenac as a prevention of PEP or other ERCP-related complications in PSC patients. Since November 2013 all ERCP patients without contraindications in Hel-sinki University Hospital (HUH) Endoscopy unit in Meilahti have received rectal diclofenac before ERCP procedure. This survey was a retrospective patient-control study, where we collected the clinical data from patient re-cords from 1000 consecutive ERCP procedures made for patients with PSC or suspected PSC at HUH Endoscopy unit and with administration of rectal diclofenac (procedures after November 2013). Control procedures (n=1000) were with the same indication but without administration of rectal diclof-enac (ERCP procedures before November 2013). Totally 2000 ERCPs were made for 925 patients between January 2009 and January 2018. Acute PEP and other ERCP-related complications were evaluated.

Results: PEP developed in 49 patients (4.9%) in diclofenac group and 62 patients (6.2%) in control group (p=0.241). There was no statistically sig-nificant difference between the groups in severity of PEP or in other acute complications. Risk of PEP was slightly more elevated in patients with na-tive papilla: 11.4% in diclofenac group and 8.7% in control group, p=0.294.

	Diclofenac group (n=1000)	Control group (n=1000)	p-value
Age* at ERCP	40 (16-73)	39 (16-79)	0.568
Female	370 (48.0)	401 (52.0)	0.168
BMI* (kg/m²)	25.0 (13.7-45.0)	24.5 (12.1-48.0)	0.222
Native papilla	193 (19.3)	358 (35.8)	0.000
Diverticulum	24 (2.4)	34 (3.4)	0.230
Duration of ERCP* (minutes)	26 (5-94)	26 (5-123)	0.953
Biliary papillotomy	214 (21.4)	409 (40.9)	0.000
Pancreatic papillotomy	41 (4.1)	80 (8.0)	0.000
Inflammatory bowel disease	743/975 (76.2)	478/944 (50.6)	0.000
Post-ERCP pancreatitis (PEP)	49 (4.9)	62 (6.2)	0.241
Severity of PEP			0.130
mild	34/49 (69.4)	36/62 (58.1)	
moderate	10/49 (20.4)	22/62 (35.5)	
severe	5/49 (10.2)	4/62 (6.5)	
Cholangitis	15/1000 (1.5)	28/1000 (2.8)	0.063
Bleeding	7/1000 (0.7)	2/1000 (0.2)	0.179
Perforation	6/1000 (0.6)	5/1000 (0.5)	1.000
Other	0/1000 (0.0)	1/1000 (0.1)	1.000
PEP in native papilla patients	22/193 (11.4)	31/358 (8.7)	0.294

[Table 1. Patient characteristics and ERCP complications. Numerical data are presented as median (range) or number of patients (%).**Cotton et al. (6)]*

Conclusion: In low-risk unit, diclofenac does not reduce the risk of PEP or other ERCP-related complications in patients with PSC. In addition, there is no significant difference in PEP rate in patients with native papilla com-pared to those with biliary papillotomy. The results of the present study are in line with our previous report in non-PSC-patients (5).

References: 1. Dumonceau JM et al. Prophylaxis of post-ERCP pancreatitis: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endos-copy 2014;46:799-815. 2. Dyson JK et al. Primary sclerosing cholangitis. Lancet 2018;391:2547-2559. 3. Aabbakken L et al. Role of endoscopy in pri-mary sclerosing cholangitis: European Society of Gastrointestinal Endos-copy (ESGE) and European Association for the Study of the Liver (EASL) Clinical Guideline. Endoscopy 2017;49:588-608. 4. Ismail S et al. Risk fac-tors for complications of ERCP in primary sclerosing cholangitis. Endos-copy 2012;44:1133-8. 5. Rainio M, et al. Diclofenac does not reduce the risk of post-endoscopic retrograde cholangiopancreatography pancreatitis in low-risk units. J Gastrointest Surg. 2017;21:1270-1277. 6. Cotton PB et al. Risk factors for complications after ERCP: a multivariate analysis of 11,497 procedures over 12 years. Gastrointest Endosc 2009;70:80-88.

Disclosure: Nothing to disclose

P0935 TRANSPANCREATIC SPHINCTEROTOMY: A VALUABLE TECHNIQUE TO GAIN BILIARY ACCESS

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Introduction: In cases of inadvertent pancreatic guidewire cannulation, transpancreatic sphincterotomy (TPS) is a feasible alternative to achieve biliary access. We intended to compare several aspects of TPS with the standard needle-knife precut papillotomy (NKPP) using data from the Hungarian ERCP Registry

Aims & Methods: 76 TPS and 240 NKPP cases could be analyzed from the database. Biliary cannulation success rate, postERCP pancreatitis (PEP) rate, use of prophylactic measures, cannulation time and subjective difficulty were compared.

Results: Biliary cannulation achieved more frequently after TPS (70/76, 92.1%) compared to NKPP (200/240, 83.3%, p=0.058). PEP developed at a similar rate after TPS (3/76, 3.9%) and NKPP (8/240, 3.3%). Prophylactic pancreatic stent (PPS) was inserted in 44 of 76 (57.9%) cases in the TPS group, while only in 15 of 240 (6.3%) cases in the NKPP group. Multiple pancreatic guidewire passages occurred in 26 patients in the NKPP group, but PPS was placed only in 6 (23.1%) of them. Indomethacin suppository was used in 52.6% of TPS and 49.2% of NKPP cases. Additional needle-knife precut was needed after TPS in 7 cases, 1 PEP developed in these cases. We found no statistically significant difference in the subjective difficulty on a 10- point scale between the two techniques (TPS: 5.8 vs. NKPP: 6.7) and there was also no difference in the mean cannulation time (TPS: 9.0 min vs. NKPP: 7.4 min).

Conclusion: TPS is an effective and safe technique in cases of difficult biliary access and also allows the use of preventive methods (e.g. PPS) easily. However, the Hungarian practice shows a serious deviation from international recommendations in this regard. One of the long-term goals of the registry is to improve the use of PEP prevention techniques in Hungary.

Disclosure: Nothing to disclose

P0936 ANALYSIS OF BILIARY CANNULATION ALGORITHM IN HIGH-VOLUME HUNGARIAN ERCP CENTERS BASED ON PROSPECTIVELY COLLECTED REGISTRY DATA

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Introduction: Selective biliary duct cannulation (BDC) was analysed in our current practice based on the data from five tertiary centers according to the recent evidence-based ESGE algorithm of biliary access.

Aims & Methods: The prospectively collected ERCP Registry contained 1011 cases of intact papilla with biliary indications. The rate of difficult biliary access and the usage of advanced biliary cannulation methods were analysed.

Results: Simple cannulation (659 cases, 65.2%): Deep BDC was achieved with guidewire in 305 cases (30.2%), with papillotome in 312 cases (30.9%), but failed in 39 cases (3.9%) due to anatomical obstacles. In 3 (0.3%) cases the BDC was not successful. The average cannulation time was 125 s, only 6.1% of the patient had longer than 300 s cannulation time. Twelve (1.9%) post-ERCP pancreatitis (PEP) occurred. Pancreatic guidewire (PGW) assisted cannulation (134 cases, 13.3%): BDC was achieved with double guidewire in 27, with papillotome in 3, while after prophylactic

pancreas stent (PPS) insertion in 12 cases. Pre-cutting was used after PGW or PPS insertion in 12 and 33 cases, TPS was performed in 47 cases. The average cannulation time was 481 s. Biliary access failed in 18 patients (13.4%), while PEP rate was 2.2%. Needle-knife precut (NKP) (160 patients, 15.8%): BDC failed in 28 (17.5%), while PEP developed in 7 cases (4.4%). The average cannulation time was 514 s. Needle-knife fistulotomy (NKF) (58 patients, 5.7%): BDC failed in 4 (6.9%), PEP developed in 2 cases (3.4%). The average cannulation time was 466 s. The overall failure rate of BDC in our cohort was 5.2% (53/1011) excluding anatomical reasons. 42 out of 44 initially failed procedures were successfully completed later on.

Conclusion: Advanced biliary cannulation methods were used in our tertiary centers in more than one third of the cases. NKF had the highest BDC rate and required the shortest cannulation time. The PEP rates were similar in the different groups.

Disclosure: Nothing to disclose

P0937 RECTAL VERSUS INTRAMUSCULAR DICLOFENAC IN THE PREVENTION OF POST ERCP PANCREATITIS. THE EXPERIENCE OF A GREEK TERTIARY REFERRAL CENTER

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Introduction: Acute pancreatitis is a potentially serious complication of Endoscopic Retrograde Cholangiopancreatography (ERCP). Independent patient-related and procedure-related factors increase the risk of post-ERCP pancreatitis (PEP). Non-steroidal anti-inflammatory drugs (NSAIDs) administered mainly rectally before or immediately after endoscopy, have demonstrated an efficacy in reducing the incidence of PEP.

Aims & Methods: Investigating the difference in the incidence of PEP among intramuscular (IM) or rectal (PR) administration of diclofenac before ERCP, taking into account patient-related and procedure-related factors associated with PEP, as well as the intraprocedural hemorrhage during the endoscopy. The retrospective study of our department's records revealed rectal administration of diclofenac for two years 2014-15 (N = 233) and intramuscular for the consecutive two years 2016-17 (N = 283). Data analysis was performed with the SPSS statistical package.

Results: 516 patients (294 men, 222 women) were included in the study (mean age: 72 years). The indication was either choledocholithiasis (N=351, 68%) or benign/malignant biliary/pancreatic stenosis (N=165, 32%). The diagnosis of PEP was defined by the criteria of the Atlanta Classification. The total incidence of PEP was 4.5% (N=23), with no significant differences between rectal (N = 12, 5.2%) and intramuscular (N=11, 3.9%) route of administration (p=0.633). The factor that appeared to be of significance was pre-cut sphincterotomy, since patients who had pre-cut sphincterotomy had a 2.67 fold higher probability of PEP (p=0.050). Marginal significance was also revealed for the passage of the guidewire in the pancreatic duct more than once (10.8% vs 4%) (p=0.074), as well as with the duration of cannulation attempts over 10 minutes (7.4% vs 3.3%) (p=0.069). Younger age, female gender, history of pancreatitis or PEP, non-dilated extrahepatic bile ducts, normal serum bilirubin, pancreatic injection, biliary balloon sphincter dilation and failure to clear bile duct stones did not show statistically significant results. Intraprocedural bleeding during ERCP (N=11, 2.1%) was almost twice higher in the rectal (N=7, 3%) compared to intramuscular group (N=4, 1.4%) (p=0.236). Although pancreatic stent was not placed in 21 of the 23 patients who developed PEP, it did not appear statistically significant in the prevention of PEP either alone (p=0.703) or in combination with diclofenac administration (p=0.517). The mean amylase value in PEP incidents did not show significant difference between the two NSAIDs subgroups (p=0.639), as it did not in the mean amylase value in patients who had hyperamylasemia after ERCP (p=0.172). In the multivariate analysis the only significant and independent factor for PEP was precut sphincterotomy (p=0.029), with these patients displaying 2.7 times greater probability of PEP manifestation.

Conclusion: The results of our study did not reveal any statistically significant difference between rectal or intramuscular administration of diclofenac in the prevention of PEP, despite the opposite results of the majority of the so far published studies and meta-analysis. Some of the risk factors associated with increased risk of PEP were also confirmed

References: 1. Cotton P, Garrow DA, Gallagher J, Romaqnuolo J. Risk factors for complications after ERCP: a multivariate analysis of 11497 procedures over 12 years. Gastrointest Endosc. 2009;70:80-88 2. Jean-Marc Dumon-

ceau, Angelo Andriulli, B. Joseph Elmunzer, Alberto Mariani, Tobias Meister, Jacques Deviere, Tomasz Marek, Todd H. Baron, Cesare Hassan, Pier A. Testoni, Christine Kapral. Prophylaxis of post-ERCP pancreatitis: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy 2014; 46: 799-815
Disclosure: Nothing to disclose

P0938 THE CLASSIFICATION OF BILIARY STRICTURES IN PATIENTS WITH RIGHT LOBE LIVER TRANSPLANT RECIPIENTS AND ITS RELATION WITH ENDOSCOPIC TREATMENT SUCCESS

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Introduction: Traversing the stricture with a guidewire is a prerequisite for endoscopic treatment of biliary strictures developed after living donor liver transplantation (LDLT). Percutaneous, combined (magnetic compression anastomosis) or surgical methods can be used in cases of failure. As the biliary anastomosis is performed in patients with anatomic variations, there is great diversity in the biliary strictures. In this study, we aimed to evaluate the effect of biliary anastomosis and biliary strictures on the success of endoscopic treatment and suggest a radiologic classification.
Aims & Methods: The cholangiographic findings of 125 biliary strictures developed among 104 patients (77 male, mean age:51 years) with right lobe LDLT and choledocho-choledochostomy, who underwent ERCP at two reference centers of Turkey between 2013 and 2019, were retrospectively reviewed. Patients with biliary leak (n=14), referred for stent exchange (n=76), with no biliary strictures (n=7), left lobe (n=13) or cadaveric transplantation (n=54), strictures traversed by percutaneous route previously (n=12) and those with missing data (n=9) were excluded. The effect of nine different types of anastomosis classified according to the number (1,2 or >2) and location (common bile duct, hepatic bile ducts or cystic duct) of anastomosis and crossing of anterior and posterior ducts, the angle between the proximal and distal sites of the anastomosis (0-30°, 30-60°, 60-90°, >90°), the contrast enhancement pattern of the stricture (passage of contrast and visualization of the anastomosis), and the anatomy of the proximal site of the choledochus (round, triangular, intermediate form, end to site anastomosis) on the success of traversing the anastomosis with a guidewire were evaluated.
Results: Out of 125 biliary strictures, 86 (68,8%) could be passed via endoscopic route. After excluding 6 patients in whom the strictures were traversed via percutaneous route at outside centers, the remaining 33 strictures were managed by either percutaneously (n=13; 39,4%) or magnetic compression anastomosis (n=20; 60,6%). Compared to round appearance, triangular (OR:6,5) or intermediate form (OR:17,7) of the proximal site of the choledochus and end to side anastomosis (OR:5,1) were associated with an increased chance of traversing the stricture (p< 0,001). The success of endoscopic treatment was higher in patients with passage of contrast through the stricture associated with (92%) or without (81%) visualization of the anastomosis, compared to those with no passage of contrast (20%) (p< 0,001). The success was increased as the angle between the proximal and distal sites of the anastomosis approximated to zero (0-30°:74%, 30-60°=69%, 60-90°=63%, >90°=41%). The types of anastomosis and stricture (anastomotic or non-anastomotic) and the duration passed between the transplantation and ERCP had no effect on the success of treatment.
Conclusion: The types of biliary anastomosis and stricture affect the success of endoscopic treatment in patients with biliary strictures after right lobe LDLT. These data may play role in making decision about the type of anastomosis during the surgery in suitable patients.
Disclosure: Nothing to disclose

P0939 A NOVEL TREATMENT APPROACH IN VISCERAL ARTERY PSEUDOANEURYSM: ENDOSCOPIC ULTRASOUND GUIDED THROMBIN INJECTION

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Introduction: Pseudoaneurysms usually occur after vascular injuries or erosions such as in trauma or inflammation like pancreatitis, and are associated with high morbidity and mortality. Digital subtraction angiography with coil embolization is the established treatment for aneurysm. There are limited data in literature on endoscopic ultrasound (EUS) guided thrombin injection for pseudoaneurysm.
Aims & Methods: Aim of the study is to assess the efficacy and safety of EUS guided thrombin injection in pseudoaneurysm. Prospective study was done at SMS Hospital, Jaipur from January 2018 to December 2018. All patients with symptomatic visceral artery pseudoaneurysm were enrolled consecutively. Data related to demography, laboratory parameters, radiological imaging, pseudoaneurysm and endotherapy were analyzed.
Results: Eight patients with median age 34(27-58) years, all males were studied. Etiology of pseudoaneurysm was chronic pancreatitis in 6(75%) and idiopathic in 2(25%) patients. Vessel was splenic artery in 5(62.5%), left hepatic artery 2(25%) and gastroduodenal artery in 1(12.5%) patients. Size of pseudoaneurysm was 2.9 cm x 2.6 cm (1.8x1.9- 4x5 cm). All patients were presented with history of gastrointestinal bleeding and two patients had hemobilia. Hemoglobin was 5.2 gm/dl (4.1-12.2 gm/dl) and requirement of packed red cell transfusion was 3(0-5) units. Thrombin requirement was 400 IU (200-500IU) for loss of doppler flow signals. Computed tomography and EUS after 3 months showed obliterated pseudoaneurysms in 7(87.5%) patients, while recurrence was seen in 1(12.5%) patient after 6 weeks of thrombin injection.
Conclusion: EUS-guided thrombin injection is a new option for management of pseudoaneurysm.
Disclosure: Nothing to disclose

P0940 EUS-FNB IN THE EVALUATION OF SUBEPITHELIAL LESIONS OF THE GASTROINTESTINAL TRACT: SIDE-TYPE VERSUS END-TYPE NEEDLE - WHICH ONE IS THE BEST?

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Introduction: Endoscopic ultrasonography (EUS) is the most widely used method for characterization of subepithelial lesions (SELs) arising from the gastrointestinal (GI) tract.
However, the diagnostic accuracy of fine needle aspiration (EUS-FNA) ranges widely from 46% to 93% in the evaluation of GI stromal tumors[1.] Recent studies have showed superior diagnostic accuracy of fine needle biopsy needles (EUS-FNB), comparing to the standard EUS-FNA needles. Nevertheless there have been little head-to-head comparative data between FNB needles.
Aims & Methods: The aim of this study was to compare the diagnostic yield of the side-type needles with the end-type needles in the diagnosis of SELs of the GI tract.
A retrospective cohort study was conducted, including consecutive patients with SELs of the GI tract undergoing EUS-FNB between January 2016 and November 2018. Macroscopic on-site evaluation was used to evaluate core quality and set the number of needle passages necessary to obtain a macroscopic visible core. All samples were reviewed by one experient pathologist, who was blinded to the type of needle used, and classified as diagnostic (if biopsy specimens were adequate for making a diagnosis, including immunohistochemical staining whenever necessary), suggestive (if a suggestive primary diagnosis was assigned, but a definitive final diagnosis was not achieved) and non diagnostic (if samples were primarily insufficient for diagnosis)[2]. Primary outcome was defined as the ability to provide a suitable sample allowing histological interpretation (diagnostic yield). Secondary outcome was defined as the number of needle passages required to obtain a proper macroscopic sample.

Results: A total of 21 lesions were included (stomach n=16, duodenum n=2, rectum n=2, oesophagus n=1; median of lesion size on EUS 24 mm (10-134)) from 21 patients (9 females/12 males; median age 67 years (50-79)). The procedure was technically feasible in all patients. Side-type needles were used in 10 lesions and end-type needles in 11 lesions (fork-tip needle n=3, Freensen needle n=8). Diagnostic yield was 80% (8/10) in side-type needle group and 81.8% (9/11) in the end-type needle group (pvalue 1). Median needle passages to obtain a macroscopic visible sample was 3 (IQR 1) in the side-type needle group and 3 (IQR 2) in the end-type needle group (p value 0.821). There were no intra-procedure EUS-FNB related adverse events.

Conclusion: In our study there were no significant difference in diagnostic yield between side-type and end-type needles. Number of passages to obtain a macroscopic visible sample were similar between EUS-FNB needles. The procedure was feasible and safe in all lesions.

References: 1- Faulx A, Kothari S, Acosta R et al. The role of endoscopy in subepithelial lesions of the GI tract. Gastrointestinal Endoscopy 2017. 85:1117-1132 2- Lee M, Min BH, Lee H, et al. Feasibility and Diagnostic Yield of Endoscopic Ultrasonography-Guided Fine Needle Biopsy With a New Core Biopsy Needle Device in Patients With Gastric Subepithelial Tumors. Medicine 2015. 94

Disclosure: Nothing to disclose

P0941 NEWLY DEVELOPED MODEL FOR TRAINING EUS-HGS AND PSEUDOCYST DRAINAGE PROCEDURE

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Introduction: Endoscopic ultrasonography-guided fine-needle aspiration (EUS-FNA) has become a indispensable examination in the clinical fields. Furthermore, therapeutic EUS such as pseudocyst drainage, EUS-biliary drainage, and EUS-pancreatic duct drainage, etc. have become popular year by year. Generally, it has been believed that the learning of EUS-FNA takes long time and certain number of case experiences are essential, in order to become a good endosonographer. And it is difficult to learn EUS/EUS-FNA without instructors.

Futhermore, clinical cases are not enough for training young endosonographer and hands-on training with models are able to reduce the number of performing clinical EUS-FNA on training program. Therefore, we have developed newly designed model for training therapeutic EUS-FNA procedure such as EUS-HGS and PFC drainage, and investigated its usefulness and limitations.

Aims & Methods: We have collaborated with Olympus Co. and made model for EUS-HGS by special plastic material (Century medical Co., Tokyo) and pseudocyst model by non-rupture-balloon (Sumitomo Bakelight Co., Tokyo) which is 8cm in diameter. This balloon is filled by lubricant, and these models are put into water tank. We have tried this model at Kitasato Interventional hands-on training workshop with 40 attendees. We have investigated whether all attendees can complete EUS-FNA of the pancreas and pseudocyst drainage or not? And how long does it take to complete the procedure? Furthermore, we have checked their impression of this model. We have employed UCT-260 (Olympus Co., Tokyo) ,19G EUS-FNA needles and 7Fr plastic stent as a drainage tube.

Results: Concerning about EUS-HGS, all attendee have to identify B2 and B3 branch, secondly puncture B3 with 19G needle, thirdly put in a 0.035inch guidewire, and finally deploy 7Fr stent. 96% (43/45) of attendees have completed EUS-HGS model with 7 minutes in average. Concerning about pseudocyst model, attendees have to firstly look for the good position for pseudocyst drainage, secondly attendee puncture the balloon with 19G needle, thirdly put in a 0.035 inch guidewire, push a dilator into the model, and finally put a 7 Fr drainage tube in the pseudocyst model. 89% (40/45) of attendees have completed pseudocyst drainage with 8.5 minutes in average. All balloons have not ruptured during these procedures and kept the balloon size, in spite of some leakage. According to their impression, resistance of puncture and putting in a stent is less, compared with clinical cases, however it is very useful to understand EUS-HGS and EUS-guided pseudocyst drainage.

Conclusion: We concluded that newly designed EUS-HGS and pseudocyst model is useful to train the beginner, in order to understand the procedure. Furthermore, using these models, we can do hands-on training everywhere and there is no necessity of animal laboratory because of dry model.

Disclosure: Nothing to disclose

P0942 WITHDRAWN

P0943 CELIAC GANGLIA NEUROLYSIS VERSUS BILATERAL CELIAC PLEXUS NEUROLYSIS FOR MANAGING ABDOMINAL PAIN ASSOCIATED WITH PANCREATIC CANCER

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Introduction: Abdominal pain is a common problem in patients with pancreatic cancer, present in as many as 70% to 80% of patients at the time of diagnosis. It can be difficult to treat and patients may suffer from drug-related side effects. In these patients, celiac plexus neurolysis (CPN) may be indicated.

Aims & Methods: To assess efficacy and safety of endoscopic ultrasound guided celiac ganglia versus bilateral plexus neurolysis using absolute alcohol for managing abdominal pain associated with pancreatic cancer. A prospective randomized study were conducted on 35 patients with abdominal pain due to inoperable cancer pancreas. They were randomly assigned into two groups of EUS-CPN (celiac ganglia or Bilateral technique). Then patients were followed up at 2 weeks, 6 weeks and 6 months after procedure.

Results: In Group A (23 patients; 65.7%) celiac ganglia neurolysis was done and group B (12 patients; 34.3%) bilateral technique was done. Group A & B were matched regarding age, gender, site, type of pancreatic pathology and type of analgesics used before the procedure. Both techniques achieved similar rates of successful pain relief (83.3% of patients in Group A and 82.6% in Group B) without significant difference in Visual Analogue Scale of pain at 2 weeks and 2 months post-procedure. They were also similar regarding onset on pain relief and time of pain recurrence. There were no major complications or moralities related to the procedure, however minor complications occurred in 10 patients (28.6%) as transient hypotension and self-limiting diarrhea. The rate of complication was similar in both groups.

Conclusion: EUS-guided celiac ganglia neurolysis is an easy technique more feasible and comparable with bilateral plexus neurolysis in terms of overall pain relief and reduction in dose and/or frequency of analgesics needed without increase in rate of procedure-related complications.

Disclosure: Nothing to disclose

P0944 RELATIONSHIP BETWEEN FIRST-VISIT PATIENTS WITH DIABETES MELLITUS AND ENDOSCOPIC ULTRASOUND IMAGES OF EARLY CHRONIC PANCREATITIS

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Introduction: Early chronic pancreatic is a new clinical entity. Endoscopic ultrasound (EUS) is an essential modality to diagnose patients with early chronic pancreatitis.

However, diabetes mellitus (DM) derives from a disorder of the pancreatic function, and the relationship between early chronic pancreatitis and DM is still not clear.

Aims & Methods: This prospective study was conducted for 21 patients with DM. EUS was performed before medical treatment. Diabetologist were in charge of treatment and were blind to the EUS findings. We analyzed gender, age, BMI, smoking, alcohol, family history, past history, hypertension, hyperlipidemia, HbA1c, anti-GAD antibodies, insulin secretion function, complications and therapeutic discipline. In addition, we evaluated whether the EUS findings contributed to the decision on which therapeutic method to use.

Results: 12 out of 21 cases meet the criteria for EUS findings for early chronic pancreatitis, while the others did not. Initial treatment went well for all the patients with DM.

In the univariate analysis, age, HbA1c, and therapeutic method were significant variables to differentiate between the presence or absence of EUS findings for early chronic pancreatitis. Patients without EUS findings for early chronic pancreatitis tended to be younger (p = 0.030), with a higher HbA1c (p = 0.032) and higher insulin usage (p = 0.021) than patients with early chronic pancreatitis. In the multivariate analysis, absence of EUS findings for early chronic pancreatitis was an important factor in the use of insulin for treatment (p = 0.016).

Conclusion: EUS is a valuable modality to differentiate between the presence or absence of early chronic pancreatitis in patients with DM. It seems likely that an EUS can contribute to the decision on which treatment method to use for patients with DM.

Disclosure: Nothing to disclose

P0945 NOVEL BILIARY DILATATION SWINE MODEL USING ENDOBILIARY TEMPERATURE-CONTROLLED RADIOFREQUENCY ABLATION: AN EFFECTIVE TOOL FOR EUS GUIDED-BILIARY DRAINAGES

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Introduction: EUS-guided biliary drainage procedures (EUS-BD) have been demonstrated to be effective but technically challenging and require a substantial learning curve. Both phantoms and "ex vivo" biliary dilatation models, have been described to enhance learning in this field, but they provide a limited level of realism [1,2].

Swine model is the most realistic tool for training in EUS and biliary dilatation swine models have been described. However, they provide an erratic biliary dilatation, and can also be technically cumbersome [3-6]

Aims & Methods: The aims of our study were to develop a swine biliary dilatation model using temperature-controlled Endobiliary Radiofrequency Ablation (EB-RFA) and to investigate feasibility of EUS-BD in this kind of model.

Seven fourteen-month-old mini pigs underwent ERCP and a dedicated biliary radiofrequency catheter with a distal temperature sensor (ELRA RF catheter, STARmend, Goyang, Korea) was used to deliver energy into the common bile duct.

With the end-point to obtain a biliary stricture EB-RFA energy was then delivered at 7 or 10W with a target temperature of 75 or 80°C for one or two rounds (ranging from 60 to 120 seconds each).

Two weeks after EB-RFA, EUS examination confirmed massive biliary dilatation and EUS-guided biliary drainage procedure (EUS-BD) was then attempted by performing a hepaticogastrostomy (HGS) or a cholecysto-gastrostomy (CG).

Results: EB-RFA was successfully performed in all 7 pigs into the distal or proximal CBD (distal CBD, n = 6; proximal CBD, n =1). There were no immediate post-procedural adverse events.

After two weeks all pigs were jaundiced without clinical evidence of acute cholangitis. EUS examination revealed massive intrahepatic and extrahepatic biliary dilation in all pigs and EUS-BD was attempted in the same session. HGS was performed in 6 pigs. Technical success was achieved in five of 6 pigs. Technical failure of HGS occurred during stent deployment. CG was successfully performed in one pig with both distended gallbladder and intrahepatic and extrahepatic biliary dilatation.

On the macroscopic evaluation, fibrotic tissue has been found around the CBD stricture without any sign of damage.

Conclusion: Our study demonstrates that EB-RFA is an effective minimally invasive method for creating a critical biliary stricture with associated upstream biliary dilation.

Furthermore, EUS-BD was technically feasible in this model which provides excellent level of realism in comparison to procedures undertaken in humans.

References: 1) Dhir V, Itoi T, Fockens P et al. Novel ex vivo model for hands-on teaching of and training in EUS-guided biliary drainage: creation of"Mumbai EUS" stereolithography/3D printing bile duct prototype. Gastrointest Endosc 2015; 81: 440- 446 2) Dhir V, Itoi T, Pausawasdi N et al.

Evaluation of a novel, hybrid model (Mumbai EUS II) for stepwise teaching and training in EUS-guided biliary drainage and rendezvous procedures. Endoscopy International Open 2017; 05: E1087-E1095 3)Rumalla A, Petersen BT, Baron TH, et al. Development of a swine model for benign stenosis of the bile duct by endoscopic application of intraluminal thermal injury. Gastrointest Endosc 2003; 57:73-7 4) Alcaide N, Lorenzo-Pelayo N, Ruiz-Zorrilla R, et al. Endoscopic Porcine Model of Biliary Obstruction Using Over-the-Scope Clips: Feasibility and Applicability to Training in EUS-Guided Drainage Procedures. Gastroint Endosc 2013; 77, (5S) 5) Lee TH, Choi JH, Lee SS, et al. A pilot proof-of-concept study of a modified device for one-step endoscopic ultrasound-guided biliary drainage in a new experimental biliary dilatation animal model. World J Gastroenterol 2014; 20: 5859-5866 6) Park JS, Kwon CI, Jeong S et al. Development of a swine bile duct dilation model using endoclips or a detachable snare under cap-assisted endoscopy.

Disclosure: Nothing to disclose

P0946 EVALUATION OF THE PANCREAS AND BILE DUCTS WITH A NEWLY DEVELOPED SLIM LINEAR ECHOENDOSCOPE

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Introduction: Endoscopic ultrasound (EUS) is consider as the technique of choice for the evaluation of gastrointestinal and extraintestinal lesions, mainly for pancreatico-biliary diseases. Standard linear EUS scopes have been usually thick and stiff in the tip.

Aims & Methods:

Aim of our study was to compare the maneuverability and image quality of a recently develop slim linear echoendoscope to the current standard scopes in the evaluation of pancreaticobiliary diseases.

Material and methods: Retrospective analysis of a prospectively collected endoscopy database from a referral academic center over 4 months. Patients undergoing diagnostic EUS with the slim linear echoendoscope (with a rounded and shorter distal part, together with a shorter bending section), attached to the ultrasound system HITACHI ARIETTA-V70 (Hitachi, Tokyo, Japan) were included in the study. All procedures were performed under conscious sedation. EUS-guided tissue acquisition was performed if indicated. The maneuverability and image quality were evaluated. A descriptive analysis was performed, showing results as mean ± SD or 95% confidence interval.

Results: Out of 537 EUS procedures performed in the study period, 128 (23.8%) were done with the new linear slim echoendoscope for examination of the pancreas and bile ducts, and were included in the study. Mean age was 63 years (range 22-91, 72 females). Compared with the examinations performed with the standard EUS scope, the new slim echoendoscope performed better in terms of maneuverability during esophageal intubation, pylorus traversing and accessing from duodenal bulb to the second portion. Image quality at the standard stations (esophagus, stomach, and duodenum) was also considered better with the new scope. A complete pancreatico-biliary exploration was achieved in all cases (100%). Final diagnosis was stone disease in 40 cases, chronic pancreatitis in 34, acute pancreatitis in 5, solid pancreatic tumors in 10, 9 cases with peptic ulcer disease, 1 case of retroperitoneal lymph nodes, 1 case of liver metastasis, and 17 cases presented a normal exploration. EUS-guided tissue acquisition was performed in 9 cases (7 pancreatic tumors, liver metastasis and lymph nodes), being feasible in all cases. No complications were reported.

Conclusion: The new slim echoendoscope showed improved maneuverability and image quality. A complete biliopancreatic exploration can be performed safely and effectively, including EUS guided tissue acquisition.

Disclosure: Nothing to disclose

P0947 EUS GUIDED CHOLEDOCODUODENOSTOMY WITH ELECTROCAUTERY ENHANCED LUMEN APPOSING METAL STENT: FRENCH MULTICENTRIC STUDY AFTER LEARNING CURVE

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Introduction: EUS guided biliary drainage is indicated in case of impossibility or failure of classic biliary drainage by ERCP. Recently we reported a good efficiency of EUS guided choledocoduodenostomy using the HOT-AXIOS device (Electrocautery enhanced lumen apposing metal stent) in a retrospective multicentric study. However in this study, technical success was 88.5%. Utilization of the recommended technique (direct punction of the common bile duct with the HOT AXIOS + using a 6 mm Stent + fistulotomy with a pure section current) was the only predicting factor of clinical success.
We decide to reevaluate this procedure one year after in the same centers.
Aims & Methods: French retrospective multicentric study of a prospective database including all cases of EUS guided CDS with HOT AXIOS device in the 7 centers that participate to the first study.
Primary ENDPOINT: technical success rate defined as the ability to correctly deploy the Hot Axios stent between the common bile duct and the duodenal bulb with visualization of bile flow.
Secondary endpoints: Clinical success rate (decrease in bilirubin of at least 50% at day 7 or normalization at day 30), per-procedural complication rate, short-term complications (all complications occurring between the procedure and discharge from the hospital), Recurrence of biliary obstruction during follow-up.
Results: 70 consecutive patients were included in this study between 01/09/2017 and 22/09/2018 by 11 operators in 9 centers.
Pancreatic adenocarcinoma was the etiology of biliary obstruction in 77% of cases. Failure of primary ERCP was due to duodenal stenosis in 44% of cases, tumoral infiltration of the papilla in 22% of cases, and failure of deep cannulation in 4% of cases.
95% of patient had 1 or 0 ERCP procedure before EUS-CDS.
The mean duration of the procedure was 5 min (+/- 3). The recommended technique (direct fistulotomy with HOT-AXIOS using e pure cut current + using a stent of 6 or 8 mm) was used in 98.5% of cases.
Primary Endpoint: Technical success rate was 98.5% with only one failure.
Secondary Endpoints: Clinical success rate: 98.4%.
Per procedural complication: 1.6%: one bleeding during the fistulotomy stopped by the expansion of the stent itself.
Short term complications: 0%.
Recurrence of biliary obstruction: 7 cases (11.5%) (median follow up: 151 days).
Conclusion: EUS-CDS with the HOT AXIOS is efficacious and safe in distal malignant obstruction of the common bile duct in cases of ERCP failure with impressive results once the expertise is acquired and the recommended technic is followed.
It should be the technique of choice in case of distal tumoral obstruction and failure or impossibility of ERCP. Moreover it could chanllenge ERCP in the future as a primary option for biliary drainage on case of distal malignant obstruction.
Disclosure: Jeremie JACQUES, Fabien FUMEX, Jocelyn Privat, Bertrand NAPOLEON, Romain LEGROS: Consultants for Boston Scientific

P0948 USEFULNESS OF HISTOLOGICAL DIAGNOSIS BY PROCORE 20G NEEDLE FOR PANCREATIC SOLID TUMOR

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Introduction: EUS-FNAB is widely used for pathological diagnosis of pancreatic solid tumor. EchoTip ProCore 20G needle (PC20) is a puncture needle useful for histopathology because it has a large diameter and forward bevel type of core trap. In this study, we examined the tissue diagnostic efficacy of PC20 in pancreatic solid mass.
Aims & Methods: We conducted a retrospective study of EUS-FNAB for pancreatic solid tumor that was using PC20 from the first pass performed between October 2016 and December 2018 at Kyorin University hospital.
The main outcome was to evaluate the accuracy of histological diagnosis and the positive effect that added cytology. Secondary outcome was to examine the accuracy of histological diagnosis by number of passes. In EUS-FNAB, we firstly collected specimens by suction method. In cases with bleeding, cases in that specimens were small amount to exam, and cases when the needle was broken, we added more passes, or changed to slow-pull method, or other needles. Group4,5 in histology and Class IV, V in cytology were diagnosed as malignant tumor.
Results: A total of 90 patients were enrolled this study. The final diagnosis were pancreatic ductal carcinoma in 81, metastasis pancreatic carcinoma in 3, neuroendocrine tumor in 3, autoimmune pancreatitis in 1, and the others in 2. The cytological accuracy in PC20 was 85.6% (77/90). The histological accuracy in PC20 was 95.6% (86/90), other four patients were diagnosed by the changing to other needle, the accuracy by combining histological and cytological yield was 98.9% (89/90). By adding cytology to histology, the total accuracy was risen 3.3%, but it was no significant difference in comparison to only histological yield (p=0.36).
In number of passes using PC20, the histological accuracy was 86.6% (78/90) in once, 94.4% (85/90) in twice, and 95.6% (86/90) in 3 or more times. There was significant difference between once and twice (p=0.05), but no difference between twice and 3 or more times.
Conclusion: EUS-FNAB with PC20 for pancreatic masses showed sufficient accuracy in histological diagnosis. Additional effect of passes more than twice was not proven in accuracy of histological diagnosis.
Disclosure: Nothing to disclose

P0949 SLOW-PULL COMPARED TO SUCTION TECHNIQUE FOR EUS-GUIDED SAMPLING OF PANCREATIC SOLID LESIONS: A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Introduction: The European Society of Gastrointestinal Endoscopy (ESGE) guidelines suggest to employ the suction (SU) technique for endoscopic ultrasound (EUS)-guided fine needle aspiration (FNA) of pancreatic solid lesions. However, recently some randomized controlled trials have reported that the slow-pull (SP) technique has a similar diagnostic accuracy with possibly less blood contamination. However, these results are heterogeneous and often limited to small cohorts.
Aims & Methods: The aim of the study was to perform a meta-analysis to compare sensitivity, specificity, accuracy and adequacy of the SU and SP techniques for FNA of solid pancreatic lesions.
A computerized bibliographic search was restricted to randomized controlled trials only. Pooled effects were calculated using a random-effects model and expressed in terms of pooled sensitivity and specificity and OR (95% CI) for accuracy and adequacy.
Results: Overall, 7 RCTs were included (2 conducted in the US, 2 in Korea, 1 in India, 1 in Brasil, 1 in Italy); 4 were full text publications, 3 abstracts; the RCTs investigated 646 patients (216 sampled with SP, 211 with SU, and 119

with both). The SP technique showed a slightly higher pooled sensitivity compared to SU (83.1% vs 77.2%), while specificity was similar (96.2% vs 96.4%). A non-significant superiority of SP in terms of pooled accuracy (OR 0.59; 95% CI 0.3-1.1; p=0.1) was recorded, while adequacy was similar (OR 1.17; 95% CI 0.5-2.5; p=0.6). Two studies reported data on significant blood contamination with a pooled rate of 10.8% for SP and 25.6% for SU.

Conclusion: The present meta-analysis reveals non-superiority of SU over SP, with some trend toward better performance of SP with reduced blood contamination; the current recommendations regarding preferential use of suction might need to be revised in light of these findings.

Disclosure: Nothing to disclose

P0950 EXPERIENCE WITH EUS-GUIDED BIOPSY USING THE PUNCTURE BIOPSY FORCEPS

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Introduction: Endoscopic Ultrasound (EUS) guided fine needle aspiration (FNA) can be used to obtain cytology of solid organs, lymph nodes and submucosal tumors of the gastrointestinal tract. However, there is a rising demand for histology sampling for the evaluation of tissue architecture and to perform additional diagnostics. Available needles for fine needle biopsy (FNB) can provide histology in roughly 57-89% of the cases [1-3]. Considering the poor performance of FNB and the rising demand for histology sampling, new techniques are needed to increase the diagnostic tissue histology yield [4]. Recently, a new promising device was developed to increase histology yield in EUS-guided puncturing [5], with an updated design: a Nitinol 19-gauge puncture biopsy forceps (PBF; MTW Endoskopie Manufaktur, Wesel, Germany).

Aims & Methods: We conducted a retrospective multicenter feasibility study in 2018 with one University Hospital (Radboudumc (RU), Nijmegen, The Netherlands), one general hospital (Evangelisches Krankenhaus (EVK), Düsseldorf, Germany) and two private hospitals (New Medical Centre Specialty Hospital (NH), Abu Dhabi and Thumbay Hospital (TH), Dubai, United Arab Emirates). Data were derived from pathology and doctors' reports. Primary outcome was diagnostic yield. Secondary outcomes were safety (bleeding, perforation) and technical performance.

Results: Nineteen patients were included: 4 from RU, 3 from EVK, 10 from NH and 2 from TH. The majority of patients was male (12/19, 63%), the age ranged from 34-76 years of age. The BPF was used for biopsy of the pancreas in 9, GE junction lesion in 3, lymph nodes in 2, submucosal lesion in 3 (1 duodenal bulb and 2 gastric wall) and during rectal EUS in 2 patients (perirectal lesion and thickened small bowel wall). 1-5 passes per case were performed with the PBF. In 17 patients FNA or FNB with another needle was also performed.

Primary outcome: In 68% (13/19) diagnostic histology was obtained with the PBF. In 3 cases no diagnosis could be made with either histology or cytology. In 3 cases diagnosis was made on the cytology only and in 4 on histology from the PBF only. In 9 cases both histology and cytology were diagnostic.

Secondary outcomes: No adverse events occurred in these 19 patients. The PBF was very sharp resulting in easy penetration. The forceps mechanism in the tip works well even after multiple biopsies in the same patient. The Nitinol tip facilitates good bridging possibilities. A lock mechanism on the handle prevents the PBF from opening during introduction. However, in one patient the PBF was accidently opened in the shaft. In two patients the spring mechanism failed after the first pass making it unable to continue with the same needle.

Conclusion: The PBF is a promising device that can be used for a wide range of indications. However, technical improvement of the needle is needed to prevent technical failure. The PBF can potentially be useful in cases where cytology alone is not adequate for diagnosis or when histology is desired for additional stains, genotyping or molecular analysis. To determine the value of the PBF and its position in the diagnostic field a prospective study is needed in which the PBF is compared to other routinely used device(s).

References: 1. Attili, F., et al., Performance of a new histology needle for EUS-guided fine needle biopsy: A retrospective multicenter study. Dig Liver Dis, 2018. 50(5): p. 469-474. 2. DeWitt, J., et al., Comparison of EUS-guided tissue acquisition using two different 19-gauge core biopsy needles: a multicenter, prospective, randomized, and blinded study. Endosc Int Open, 2015. 3(5): p. E471-8. 3. Bang, J.Y., R. Hawes, and S. Varadarajulu, A meta-analysis comparing ProCore and standard fine-needle aspiration needles for endoscopic ultrasound-guided tissue acquisition. Endoscopy, 2016. 48(4): p. 339-49. 4. Hebert-Magee, S., Is there a role for endoscopic ultrasound-guided fine-needle biopsy in pancreatic cancer? Endoscopy, 2015. 47(4): p. 291-2. 5. Litjens, G., et al., First experience of obtaining pancreatic tissue with a puncture biopsy forceps versus fine needle aspiration. Endoscopy, 2015. 47 Suppl 1: p. E609-10.

Disclosure: Dr. ir. E.J.M. van Geenen is advisor of MTW Endoskopie Manufaktur, Wesel, Germany. A proportion of the needles used for this study where provided free of charge by MTW Endoskopie Manufaktur, Wesel, Germany.

P0951 ENDOSCOPIC ULTRASOUND-GUIDED CHOLEDOCHODUODENOSTOMY FOLLOWED BY DUODENAL STENTING IN PATIENTS WITH MALIGNANT UNRESECTABLE BILIODUODENAL OBSTRUCTION

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Introduction: In patients with advanced pancreaticobiliary malignancy, along with biliary obstruction, gastric outlet obstruction is a frequent occurrence. Endoscopic retrograde cholangiopancreatography (ERCP), a first line modality for palliation of obstructive jaundice is often unsuccessful in patients with combined bilioduodenal obstruction, due to inability to reach the duodenal papilla and early dysfunction of biliary self-expanding metal stent (SEMS) due to the duodenobiliary reflux enhanced by duodenal stenosis.

As an alternative, Endoscopic ultrasound (EUS)-guided choledochoduodenostomy (EUS-CDS) and duodenal stent placement has been recently described with high rates of technical and clinical success, but with limited number of studies and unclear sequence of stenting (i.e. whether biliary or duodenal stenting first).

Aims & Methods: We evaluated the technical success, clinical success and safety of endoscopic ultrasound-guided choledochoduodenostomy followed by duodenal SEMS placement in patients with malignant bilioduodenal obstruction.

Medical records of consecutive patients with unresectable malignant distal biliary obstruction and gastric outlet obstruction (GOO), who required biliary drainage by EUS-CDS (because of failure of attempt at ERCP) and antroduodenal stenting were reviewed. EUS-CDS was done using 6-cm, PCSEMS (Wallflex, Boston Scientific). Technical success, clinical success [biliary stent- more than 50% reduction in total bilirubin at 2 weeks post-procedure; antroduodenal stent- improvement in Gastric Outlet Obstruction Scoring system (GOOSS)], stent patency rate and adverse events (AEs) were assessed.

Results: Between January 2015 and January 2019, 11 patients underwent combined EUS-CDS and antroduodenal stent placement. Both EUS-CDS and antroduodenal stent placement were technically and clinically successful in all patients. Median total serum bilirubin decreased from 15.8mg/dL to 5.9mg/dL at 2 weeks post procedure. Recurrence of jaundice was not seen until 2 months post double stent placement or death.

Median GOOSS improved from 0.56 to 2.3 at 4 weeks post-procedure. All patients were able to maintain weight above 90% of baseline at 4 weeks and 72.7% of patients had weight above 80% of baseline at 8 weeks post duodenal stent deployment.

GOO did not recur in patients who were alive at 2 months. In 8 (72.7%) of the 11 patients, the biliary and antroduodenal stents were patent and functioning normally at 2 months post-procedure.

Only one patient had bile leak, which resolved with therapeutic paracentesis. There were no procedure-related deaths. Most of the patients (9/11) died of advanced cancer cachexia.

Conclusion: EUS guided choledochoduodenostomy followed by duodenal stenting is safe and has high technical and clinical success for palliation of malignant bilioduodenal obstruction.

References: 1. Nakai Y, Hamada T, Isayama H, et al. Endoscopic management of combined malignant biliary and gastric outlet obstruction. Dig Endosc. 2017;29:16-25. 2. Hamada T, Isayama H, Nakai Y, et al. Duodenal invasion is a risk factor for the early dysfunction of biliary metal stents in unresectable pancreatic cancer. Gastrointest Endosc. 2011;74:548-555. 3. Ogura T, Chiba Y, Masuda D, et al. Comparison of the clinical impact of endoscopic ultrasound-guided choledochoduodenostomy and hepaticogastrostomy for bile duct obstruction with duodenal obstruction. Endoscopy. 2016;48:156-163. 4. Moon JH, Choi HJ. Endoscopic double-metallic stenting for malignant biliary and duodenal obstructions. J Hepatobiliary Pancreat Sci 2011;18:658-63 5. Kawakubo K, Isayama H, Nakai Y et al. Simultaneous duodenal metal stent placement and EUS-guided choledochoduodenostomy for unresectable pancreatic cancer. Gut Liver 2012; 6: 399-402. 6. Hamada T, Nakai Y, Lau JY, et al. International study of endoscopic management of distal malignant biliary obstruction combined with duodenal obstruction. Scand J Gastroenterol 2018;53:46-55.
Disclosure: Nothing to disclose

P0952 PREDICTORS OF ADEQUATE SAMPLING IN ENDOSCOPIC ULTRASOUND GUIDED TISSUE ACQUISITION OF SOLID PANCREATIC LESIONS IN A LARGE PROSPECTIVE COHORT OF DUTCH COMMUNITY HOSPITALS

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Introduction: Endoscopic ultrasound (EUS) guided tissue acquisition (TA) is the method of choice to establish a pathological diagnosis of solid pancreatic lesions. EUS guided TA is a complex multistep procedure involving efforts of both endosonographers and cytopathologists.

Reported outcomes on the quality and yield of EUS guided TA are skewed towards high-volume academic institutions. For community hospitals, in which the majority of these procedures are performed, these data are unknown. Rate of adequate sample(RAS) (the proportion of tissue samples sufficient for cytopathological evaluation) is the only quality indicator solely reflecting the work of the endosonography team.

Aims & Methods: The aims of this study are 1. to determine and improve the RAS of EUS guided TA in a group of community hospitals and 2. to identify determinants of RAS. From January 2015 until October 2018 five community hospitals in the Rotterdam region in the Netherlands, prospectively included procedures. The primary outcome variable was RAS. Univariate and multivariate analyses were performed to identify determinants of yield such as type and size of needle used, application of suction, presence of rapid on site cytopathological evaluation (ROSE) and the number of procedures performed by the endosonographers.

Results: Seventeen endosonographers, with individual EUS experience ranging from 1-14 years, performed 372 consecutive procedures over a period of 46 consecutive months. Overall RAS was 93% (ASGE ref standard: >85%)(ref 1). In a multivariate analysis the use of suction and number of procedures performed by endosonographers were statistically significantly and positively associated with RAS (p=0.01) and (p=0.04) respectively. No significant interaction was found between number of procedures and use of suction. No significant association was found between RAS and needle type, needle size, ROSE and number of passes. Seven endosonographers performed less than 20 procedures (median 9 (3-18)) accounting for 70 procedures in total. Within this subgroup RAS was 87%. The remaining seven endosonographers performed 302 procedures (median 56 (21-63)) yielding a RAS of 95%. Differences in RAS between "low-volume" and "high-volume" endosonographers were statistically significant p=0.01.

Conclusion: Both use of suction and higher number of procedures performed by endosonographers are associated with better outcome (RAS) of EUS guided TA in this prospective cohort in community hospitals. The quality of EUS guided TA in a community hospital may be partly influenced by the number of procedures done. However, the quality of an individual endosonographer depends on more factors than its volume alone and requires further research.

References: 1. Wani, S., et al. (2015). "Quality indicators for EUS." Am J Gastroenterol 110(1): 102-113.
Disclosure: Nothing to disclose

P0953 ENDOSCOPIC ULTRASOUND (EUS)-GUIDED LIVER BIOPSY: A COMPARATIVE STUDY IN AN EX-VIVO MODEL

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Introduction: EUS-guided biopsy is a safe and accurate method for the histological diagnosis of solid liver lesions. However, few data are available on liver parenchymal diseases.

Aims & Methods: Aim of our study was to evaluate in an ex-vivo model the ability of different EUS needles to obtain histological samples of liver tissue.

Material y Methods: 7 different types of EUS biopsy needles in an ex-vivo pig liver were tested: A1: 22G Franseen type needle; L1-L3: standard cytology needles of 25G, 22G and 19G respectively; SC1-SC3: SharckCore type needles of 25G, 22G and 19G respectively. Biopsies were performed without suction and without stylet. Two passes were performed with each needle type. Samples were collected in formalin. Samples were considered satisfactory if they were at least 1cm in length and if they included at least 10 porta spaces. Fragmentation was evaluated as well.

Results: Table shows results obtained with each of the needles used.

CASE	N.º CILINDERS	FRAGMENTATION	MEASURE (cm)	PORTAL SPACES	QUALITY
A1	8	High	0,1-0,4	2	Non-satisfactory
L1	8	High	0,1	0	Non-satisfactory
L2	4	Medium	0,1	0	Non-satisfactory
L3	9	High	0,1-0,4	0	Non-satisfactory
SC1	9	High	70,1-0,8	7	Non-satisfactory
SC2	11	High	0,1-1	11	Satisfactory
SC3	11	High	0,1-1,4	10	Satisfactory

[Table 1]

Conclusion: SharkCore needles (22G and 19G) allow obtaining a core liver biopsy in an ex-vivo model, suitable for histological evaluation. These results should be confirmed in vivo.
Disclosure: Nothing to disclose

P0954 WITHDRAWN

P0955 EUS-GUIDED PLACEMENT OF NEW GOLD FIDUCIAL MARKERS FOR STEREOTACTIC BODY RADIATION THERAPY IN LOCALLY ADVANCED PANCREATIC CANCER: PRELIMINARY RESULTS OF FEASIBILITY AND SAFETY

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Introduction: Radiation therapy has an emerging role in the multi-modal treatment of locally advanced pancreatic cancer (LAPC). Stereotactic body radiation therapy (SBRT) is an innovative radiation technique characterized by a high prescription dose delivered in only a few fractions thus increasing the local control rate. Endoscopic ultrasound (EUS)-guided fiducial placement allows for accurate tracking of target motionduring SBRT delivery.

Aims & Methods: The aim of this study is to present preliminary results on the feasibility and safety of EUS-guided fiducial placement using a new preloaded needle in patients with LAPCIn a prospective phase II study(NCT03158779), patients with LAPC treated with induction chemotherapy according to FOLFIRINOX or gemcitabine + nab-paclitaxel schedules were then treated with an ablative dose of SBRT (54Gy in 6 daily fractions). Gold markers were implanted under EUS-guidance into the tumor at opposite edges. A new dedicated EUS delivery device was used: a 22G needle preloaded with 4 gold fiducials (0.43mm width x 5mm length).Fluoroscopy was used to confirm correct fiducial deployment. Prior to fiducial placement, patients received IV antibiotic prophylaxis and rectal indomethacin. Technical aspects of the EUS procedure and fiducial visualization were scored on a predetermined 5-point Likert scale (1 = best, 5 = worst).

Results: From May 2017 to March 2019, 10 patients (mean age 65.7 years) were enrolled. Before fiducial placement, all patients received induction chemotherapy with gemcitabine + nab-paclitaxel (6 patients) or FOLFIRINOX (4 patients) for a median duration of 4.6 months (range 2-7 months). At restaging, all patients still had locally advanced tumors with no regression to resectable disease. The mean tumor size was 28.5 mm. Other characteristics are listed in Table 1.

PATIENT	AGE	GENDER	LOCATION OF NEOPLASIA	DIAMETER OF NEOPLASIA	TECHNICAL DIFFICULTIES	NUMBER FIDUCIALS	ADJUST-MENT
1	72	F	HEAD	36	MILD (HARDNESS OF TISSUE)	3	YES (< 3 MM)
2	57	M	UNCINATE	42	MILD (HARDNESS OF TISSUE)	3	NO
3	54	M	BODY	42	NO	2	NO
4	71	F	BODY	31	COLLATERAL VESSELS AROUND LESION	2	NO
5	70	F	BODY	36	NO	4	NO
6	53	F	HEAD	30	RELEASE OF TWO FIDUCIALS IN ONE SHOT	4	NO
7	75	F	UNCINATE	18	NO	2	NO
8	80	M	NECK	12	COLLATERAL VESSELS AROUND LESION	1	NO
9	72	F	UNCINATE	16	NO	2	NO
10	53	F	BODY	22	NO	3	NO

[Table 1]

A total of 26 fiducials were implanted, with a mean number of 2.6 fiducials placed per patient (range 1-4). All the fiducials were successfully deployed inside the target lesion with a technical success of 100%. In 5 of 10 patients, the procedure had no technical difficulties. In the other 5 patients, fiducial placement was characterized by minor technical difficulties due to increased hardness of lesion, interposing vessels or poor control with the first marker release. EUS, fluoroscopic and CT visualization of the fiducials was rated as excellent. Patients started the SBRT protocol 10.2 days (range 6-19) after simulation CT-scan. At the beginning of the SBRT delivery, minimal movement of one fiducial (<3 mm) occurred in one patient. No severe adverse events occurred and all procedures were performed in an outpatient setting.

Conclusion: These preliminary results demonstrate the feasibility and safety of the EUS-guided fiducial placement using a new preloaded needle in patients with LAPC. Only minor technical difficulties (mainly due to tumor hardness or collateral vessels) were encountered that did not affect the correct placement of the fiducials.

Disclosure: Nothing to disclose

P0956 SAFETY AND EFFICACY OF ENDOSCOPIC ULTRASOUND GUIDED BIOPSY USING A TRANSVASCULAR APPROACH

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Introduction: Traditionally, when performing endoscopic ultrasound (EUS) guided biopsy, target lesions beyond vascular structures were avoided due to concerns of major bleeding complications, leaving surgery as the only option for tissue sampling. There are few case reports and series published, underlining one small case series of transaortic sampling with favorable results. Furthermore, based on previous feasibility studies, the American Society of Gastrointestinal Endoscopy (ASGE) published a review on potential applications of EUS-guided portal vein interventions which seem safe and effective.

Aims & Methods: Due to the limited data available, we reviewed our experience in EUS-guided biopsy using a transvascular approach to assess its safety and diagnostic performance.

A retrospective analysis was done of 15 patients who underwent, for cancer staging, an EUS-guided biopsy with a transvascular approach from July 2007 to March 2019.

Case	Sex/Age	Punctured Structure	Needle	Nº Lesions	Nº Passes	Complications
1	M/59	Aortic Arch	25 G	1	3	No
2	F/42	Vena Cava	25 G	2	1 and 2	No
3	F/42	Portal Vein	25 G	1	5	No
4	F/59	Aortic Arch	25 G	1	2	No
5	F/55	Aortic Arch	25 G	1	3	No
6	M/53	Aorta	25 G	1	2	No
7	F/35	Aortic Arch	25 G	1	4	No
8	F/63	Aortic Arch	25 G	1	3	No
9	F/48	Aorta	25 G	1	1	No
10	M/60	Aortic Arch	25 G	1	1	No
11	F/51	Aortic Arch	25 G	1	1	No
12	F/60	Pulmonary Artery and Aorta	22 and 25 G (respectively)	2	1 and 1	Minor, self-limiting hemorrhage.
13	M/61	Aorta	25 G	1	3	No
14	F/66	Left pulmonary artery	22 G	1	1	Bronchial hemorrhage, intubation and endoscopic treatment.
15	M/55	Aortic Arch	25 G	1	3	Self-limiting periaortic hematoma.

[Table 1. Cases of EUS-guided biopsy using a transvascular approach.]

Results: The sample has a median age of 59.93 years (Table 1). With respect to medication, 26.67% were under non-steroidal anti-inflammatory drugs, 20% aspirin and 6.67% low-molecular weight heparin. The medication was temporarily interrupted if it was necessary. Eighty percent of the patients underwent general anesthesia and 20% deep sedation with intermittent bolus of propofol.

The punctured vascular structure was arterial in 86.67% of the cases, being the aorta (80%) the most punctured. The needle used in all the cases was a 25G, except in the biopsies through the pulmonary artery in which a 22G was used, with a median of 2.27 passes for lesion. (IC 95: 1.56 - 2.75). An on-site pathologist was present in all cases. The cytology report was positive for malignancy in 86.67% of the cases and negative for malignancy in 6.67% of the cases.

In 93.33% of the cases, the procedure was performed in an ambulatory fashion. Three patients had mild bleeding; one was a self-limiting peri-aortic hematoma, another one stopped bleeding with echoendoscope compression and another one required hospital admission for observation and did not need any other intervention.

Conclusion: This is one the largest case series published to date. Taking into consideration the diagnostic performance and the low complication rate, we consider the EUS-guided biopsy with a transvascular approach a feasible procedure and reasonably safe in cases in which there is no other ultrasonographic window.

Disclosure: Nothing to disclose

P0957 CUMULATIVE SUM ANALYSES GUIDING IMPROVEMENT OF TEAM PERFORMANCE IN EUS GUIDED TISSUE ACQUISITION OF SOLID PANCREATIC LESIONS IN COMMUNITY HOSPITALS

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Introduction: Endoscopic ultrasound (EUS) guided tissue acquisition (TA) is a complex multistep procedure involving efforts of both endosonographers and cytopathologists. Published outcomes on the quality and yield of EUS guided TA are skewed towards high-volume academic institutions. For community hospitals, in which the majority of these procedures are performed, these data are unknown. Rate of adequate sample (RAS) (the proportion of tissue samples sufficient for cytopathological evaluation) is the only quality indicator solely reflecting the work of the endosonography team. The ASGE guideline described a performance target of 85% for RAS (Ref 1). Cumulative SUM (CUSUM) analysis is a method that can be used for quality control (Ref 2). For EUS CUSUM has been used to evaluate learning curves of trainees (Ref 3).

Aims & Methods: The aim of this study is to investigate whether CUSUM might be a good method to visualize and evaluate the quality of daily practice EUS guided TA of solid pancreatic lesions in community hospitals.

In Rotterdam region, The Netherlands, a group of five community hospitals formed an EUS interest group (QUEST). With three annual meetings and a regional symposium the goal of QUEST is to improve the quality of EUS in community hospitals. For this particular study, in each hospital retrospective data was collected of EUS-FNA/FNB procedures performed in the year 2014. In January 2015, a prospective registration of all consecutive EUS procedures with FNA/FNB started. CUSUM was used to identify changes in quality. With CUSUM each adequate sample contributes to an upwards slope of the CUSUM curve, each inadequate sample will contribute to a downwards slope of the CUSUM curve. Two decision limits are calculated. When a curve crosses the upper limit, the quality is good, according to literature. When a curve crosses the lower limit an intervention is needed to improve the quality. When a curve stays between the decision limits the observations should be continued until the curve will cross one of the decision limits.

Results: A total of 103 retrospective procedures and 372 consecutive prospective procedures were included. Values of RAS are shown in table 1.

	RAS Hospital A	RAS Hospital B	RAS Hospital C	RAS Hospital D	RAS Hospital E	RAS Total cohort
Retrospective series	70%	95%	100%	55%	78%	80%
Prospective series	88%	89%	98%	99%	91%	93%
95% CI	0.2 - 41	-13 - 16	-13 - 9	23 - 64	-4 - 34	6 - 22
p-value	0.047	0.4	0.4	<0.01	0,1	<0,01

[Table 1. Adequate sample rates and differences between retrospective and prospective series.]

With CUSUM analysis the learning curve shows a downwards slope in 2014 (retrospective series) and crosses the lower decision limit during that year. The formation of QUEST (January 2015) marked a turning point with the curve showing an upwards slope crossing the upper decision limit in December 2017. CUSUM learning curves also revealed differences in quality between the five hospitals in QUEST showing relevant positive improvements after team formation, especially for those hospitals initially underperforming.

Conclusion: CUSUM showed to be a valid method to measure quality of EUS guided TA of solid pancreatic lesions. It provides continuous feedback on the development (or maintenance) of TA quality and can also be used to compare hospitals. We conclude that after the formation of the QUEST group, RAS of the participating community hospitals is comparable to the ASGE guideline.

References: 1. Wani S, Wallace MB, Cohen J, Pike IM, Adler DG, Kochman ML, et al. Quality indicators for EUS. Am J Gastroenterol. 2015;110(1):102-13. 2. Williams SM, Parry BR, Schlup MM. Quality control: an application of the cusum. BMJ. 1992;304(6838):1359-61. 3. Wani S, Cote GA, Keswani R, Mullady D, Azar R, Murad F, et al. Learning curves for EUS by using cumulative sum analysis: implications for American Society for Gastrointestinal Endoscopy recommendations for training. Gastrointest Endosc. 2013;77(4):558-65.

Disclosure: Nothing to disclose

P0958 FIVE FNA SPECIMENS IN ONE PASS: A DISRUPTIVE NEW NEEDLE CONCEPT

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Introduction: EUS-guided FNA and FNB have established their place for tissue acquisition. However, the procedure has been stagnating in recent years at a level of accuracy which falls short of patient and physician hopes. In recent years, needles have been redesigned to allow for core sampling, (FNB), to allow for immune-staining of specimens.

However, false negative results for malignancy range from 4% (experts centers) to 30%. Multiple needle passes are often needed, but often slide along the same tract as the first pass, limiting diagnostic yield. An FNA approach usually requires 3-5 passes, with fewer passes for the FNB needles. Furthermore, rapid on-site cytology can lower number of passes, but the majority of centers find this to be logistically and/or financially prohibitive. Needles after repeated passes bend out of shape leading to use of a second needle, which has cost implications. Tumor composition can be a mosaic of desmoplasia, necrosis, cystic areas, and malignant cells. If the needle is in the wrong plane and the endoscopist is unable to do fanning an inconclusive diagnosis can occur. We introduce a new needle concept to improve diagnostic yield and lower false negatives, with use of a device which has five needles.

Aims & Methods: A multi-pass needle has been designed which ensures five specimens will be from various sites, because the five needles are all penetrating at the same time in different planes of the lesion. This needle apparatus uses the same sheath as a standard 19 gauge needle, but within the sheath it houses a five-lumen plastic tube, which separates between the central 22g needle and the four peripheral 25g needles. The ergonomically-designed handle has a two-phase mechanism which allows the endoscopist to first place the 22g needle within the target lesion, which is the same as the process done today, and to then extrude the four 25g needles, which are pre-bent so as to spread out to a diameter of about one cm,

at a distance of about 3cm from the scope. These additional needles will each, without fanning, obtain specimens near to the central needle, and therefore a greater representation of tumor tissue will be obtained, while completing the procedure in one pass, with better accuracy due to less false negatives. The two channels for suction can be attached to either the single central needle and/or to all four peripheral needles with stopcocks facilitating the maintaining of suction when so desired. Each needle has its own stylet, these may be removed at any time desired.

Results: We present in the accompanying figure the InstaFan, a disruptive technological advance, for the delivery of better EUS biopsies. Ex vivo studies found that the 5 needles did not cause leakage from the gut or perforation of the gut wall, and that the 5 needles delivered resulted in five distinct specimens each of which was an adequate specimen for pathological diagnostic purposes using the cell block method and paraffin slices allowing immune-staining.

Conclusion: Future directions of the InstaFan will be animal in vivo animal safety study followed by first trials in humans. The goal of the InstaFan will be to reduce false negatives, thus increasing optimization of tumor diagnosis.

Disclosure: Both authors disclose financial association with the developers of this new needle

P0959 HIGH DIAGNOSTIC YIELD OF MUTATIONAL ANALYSIS ON EUS-GUIDED BIOPSIES USING A NEW FRANSEEN NEEDLE IN PATIENTS WITH LOCALLY ADVANCED PANCREATIC CANCER (LAPC)

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Introduction: Genomic analyses of pancreatic cancer display a complex mutational background with few known oncogenic events in well know cancer-related genes, and many other low prevalence mutated genes.

In order to conduct a genetic study of locally advanced pancreatic cancer (LAPC), bioptic samples of the primitive tumor are necessary. Endoscopic ultrasound-fine needle aspiration with cytology has led to some preliminary results, however, the quantity of cellsobtained may be insufficient to perform a genetic analysis.

New histology needles have been developed to obtain more material and a better preservation of the tissues for ancillary analysis such as somatic mutations analysis and immunohistochemistry.

Aims & Methods: 33 patients with naïve LAPC underwent EUS- fine needle biopsy (FNB)with the new 22GFranseen needle. Bioptic samples were sent topathological evaluation and to genetic analysis. DNA extraction was performed, and Next Generation Sequencing provided mutational profiles of the extracted DNA samples. NGS was performed with a 161 genes panel; 18 of the most prevalent genes were selected to undergo computational analysis.

Results: EUS- FNB allowed for a macroscopic core in 31 patients (94%), and pathological diagnosis was obtained in 100% of patients. Good quality DNA was extracted from 32 samples (97%), and NGS analysis confirmed the diagnosis in 30 patients (93.75%). The diagnostic yield of NGS analysis improved when combined with serum CA19.9 levels (97%). Results on DNA extraction and NGS analysis are depicted in table 1.

Genetic profiling obtained from NGS sequencing revealed pathogenic mutations in KRAS, TP53, GNAS, SMAD4 and CDKN2A, as well as a large number of mutations of uncertain significance. Preliminary data analysis revealed that the mutational burden of known oncogenes may be underestimated.

Conclusion: The tissue obtained with the new 22G Franseen FNB needle demonstrated a high diagnostic yield for the histological diagnosis of pancreatic adenocarcinoma and gave material of good quality of NGS analysis.

The ability to identify distinct mutation subsets via EUS-TA could greatly aid patient stratification and would represent a crucial step in the field of personalized medicine.

Disclosure: Nothing to disclose

	RESULTS	NOTES
DNA EXTRACTION FOR NGS ANALYSIS	32/33 PATIENTS (97%)	1/33 NECROTIC SAMPLE
KRAS	29/32 PATIENTS (91%)	MISSENSE MUTATION
TP53	13/32 PATIENTS (41%)	9 MISSENSE MUTATION 4 TRUNCATIVE MUTATION
GNAS	3/32 PATIENTS (9%)	MISSENSE MUTATION
SMAD4	2/32 PATIENTS (6%)	1 MISSENSE MUTATION 1 TRUNCATIVE MUTATION
CDKN2A	1/32 PATIENTS (3%)	MISSENSE MUTATION

[Table 1]

P0960 WITHDRAWN

P0961 THE ROLE OF SUBMUCOSAL TATTOOS DURING DEVICE ASSISTED ENTEROSCOPY ON SUBSEQUENT PATIENT MANAGEMENT

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Introduction: ESGE recommends placing a submucosal tattoo to mark an identified lesion and/or the deepest point of insertion during device assisted enteroscopy (1).

Aims & Methods: Patients who underwent a double balloon enteroscopy (DBE) during which a tattoo was placed were included. Information on repeat DBEs, second look small bowel capsule endoscopies (SBCEs) and subsequent surgeries was gathered.

Results: 283 patients (mean 57 years +/-15.5; 52.7% males) had a tattoo placed during DBE. Most underwent antegrade DBE (218; 77.0%). The most common indication was iron deficiency anaemia (IDA) (Table 1).

Indication	Frequency	Percentage
Iron deficiency anaemia	72	25.4
Ulcers	48	17.0
GI bleed	63	22.3
Polyp	27	9.5
Angioectasias	21	7.4
? Tumour	19	6.7
? Crohn's disease	18	6.4
? Stricture	18	6.4
Abnormal radiology	10	3.5
? Coeliac complication	8	2.8
Diarrhoea, weight loss, malabsorption	6	2.1
White tipped villi	2	0.7
Retained SBCE	2	0.7

[Table 1: Indications for DBE;]

Pathology was reached in 158 (55.8%) patients. Other patients (111; 39.2%) had a normal DBE with subsequent investigations ruling out any pathology. In 14 patients (4.9%), the pathology was not reached.

A repeat DBE was carried out in 47 patients. Tattoo from previous DBE was detected in 18 (38.3%) patients. 28 of these patients underwent a DBE using a different route. A tattoo was detected in only 6 (21.4%) of these patients and in 12 (63.2%) patients who underwent a DBE via the same route (p=0.006).

36 patients (12.7%) were diagnosed with a tumour, meckel's diverticulum or a stricture. 26 (72.2%) underwent surgery and 20 (76.9%) of these patients had the lesion tattooed facilitating surgery.

80 patients underwent a second SBCE after DBE to ensure pathology was

not missed. Of these, 53 (66.3%) had a tattoo identified. 21 of these patients (26.3%) had pathology detected beyond the tattoo requiring alternative procedures.

In those patients (14) where pathology was not reached, 5 underwent surgery, 4 patients were not for surgery due to the multiple carcinoid tumours identified and 5 patients were treated conservatively as the pathology was deemed to be benign on subsequent investigations.

Conclusion: Placing a tattoo can be helpful where the suspicion of pathology is high despite a negative DBE as this will help the detection of the pathology in relation to the tattoo on subsequent SBCEs. A tattoo can help pathology be localised during surgery and facilitate resection.

References: 1 Rondonotti E, Spada C, Adler Set al. . Small-bowel capsule endoscopy and device-assisted enteroscopy for diagnosis and treatment of small-bowel disorders: European Society of Gastrointestinal Endoscopy (ESGE) Technical Review Endoscopy. 2018;50:423-446.

Disclosure: Nothing to disclose

P0962 CAPSULE ENDOSCOPY, ENTEROSCOPY AND RADIOLOGY - WHERE DOES THE JIGSAW PIECE FIT FOR COELIAC DISEASE?

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Introduction: Capsule endoscopy (CE) has a useful role in patients with established coeliac disease (CD) with new symptoms or where a complication is suspected. Similarly double balloon enteroscopy (DBE) is helpful for histological diagnosis of pathology reported on CE in conjunction with radiology.

Aims & Methods: Patients with established CD who underwent DBE +/- CE +/- radiological investigations were included. Information on findings, histological results and final diagnosis were gathered.

Results: Twenty-four patients with established CD (median age 63 years, 54.2% males) underwent antegrade (83.3%) or retrograde DBE (16.7%). Patients underwent small bowel (SB) investigations because of persistent symptoms or anaemia (11, 45.8%) or to rule out complications of refractory coeliac disease (RCD) (13, 54.2%). Patients underwent a CE (23, 95.7%) and radiological investigations (13, 54.2%) prior to DBE. Findings on CE included: mass lesion (5, 20.8%), stricture (1, 4.2%), evidence of gluten enteropathy (9, 37.5%), ulcers (7, 28.3%). Findings on radiological imaging were: abdominal lymphadenopathy (3, 23.1%), thickened SB (6, 46.2%), mesenteric mass (1, 7.7%), strictures (1, 7.7%), lymphoma (1, 7.7%). Twenty-two patients (91.7%) had positive findings on DBE. In 3 of these, findings related to CD were present. However, the suggested mass / stricture on CE or radiological imaging was not seen. Histological findings were: raised intraepithelial lymphocytes (5, 20.8%), partial (5, 20.8%), subtotal (4, 16.7%) and total villous atrophy (6, 25.0%), adenocarcinoma (2, 8.3%), changes consistent with RCD 2 (1, 4.2%), enteropathy associated T cell lymphoma (EATL) (1, 4.2%). There was a good concordance between CE and DBE (K=0.646, p=0.001) and between radiological investigations and DBE (K=0.755, p=0.005). The concordance between CE and radiological studies was lower (k=0.429, p=0.070). DBE revealed more severe histological changes in the SB in 7 (n=10, 70.0%) patients compared to duodenal biopsies taken during gastroscopy (p=0.036).

CE revealed ulcers in 29.0% (7) of patients. However only 2 (28.6%) patients had the diagnosis of ulcerative jejunoileitis confirmed on DBE. One patient with adenocarcinoma had positive findings on all 3 modalities. Another patient with adenocarcinoma had positive findings on CE and DBE. The patient diagnosed with EATL had a positive MRI. DBE was confirmative of the diagnosis. CE only showed scalloping and villous blunting in the proximal SB. In another patient diagnosed with neuroendocrine tumour, both CE and CT were diagnostic.

However, the lesion was not reached during DBE.

Conclusion: CE has a high diagnostic yield as an initial investigation compared to radiological studies. DBE has a useful role in establishing a confirmative diagnosis of pre-malignant and malignant conditions. In patients with active disease on CE, DBE can be useful in obtaining histological specimens that can provide additional information to that obtained from duodenal biopsies.

Disclosure: Nothing to disclose

P0963 18F- FLUORO DEOXY GLUCOSE-LABELLED AUTOLOGOUS LEUKOCYTE POSITRON EMISSION TOMOGRAPHY/COMPUTED TOMOGRAPHY VS NEWER MRI TECHNIQUES: OPENING NEWER HORIZONS IN DETECTING INFECTION IN FLUID COLLECTIONS OF ACUTE PANCREATITIS

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Introduction: Acute pancreatitis (AP) is a significant medical and surgical problem with variable clinical course and outcomes. Severe acute pancreatitis (SAP) is one of the most dangerous Illnesses, with a significant mortality as high as 8%-39%. Infection of the pancreatic necrosis is a dreaded complication during the late course and the resulting sepsis &/or multiple-organ dysfunction syndrome (MODS) are the main causes of death. Superimposed infection in setting of pancreatitis remains both diagnostic and therapeutic challenge and may be potentially life threatening if the diagnosis is delayed. Therefore prompt non-invasive diagnosis of infection is crucial because it has pivotal influence on decision making and management. The clinical presentation, and laboratory parameters are often equivocal and the definitive proof of infection is generally obtained by performing an image guided aspiration of the collection followed by Gram's staining and culture for bacteria and/or fungal organisms.

With significant advancements in imaging techniques , we intended to explore the utility of novel imaging techniques for early non-invasive detection of infection in this clinical setting . We performed a study to evaluate the role of two newer imaging modalities i.e 18F-FDG-Labelled Autologous leukocyte PET/CT and MRI (including advanced techniques like diffusion weighted imaging (DWI), spectroscopy (MRS)) in this scenario.

Aims & Methods: To evaluate the utility of novel imaging techniques i.e 18F-FDG-Labelled Autologous Leukocyte PET/CT and MRI (including DW-MRI, MRS) in early non- invasive detection of infection in setting of acute pancreatitis.

We performed a prospective analytical study which approved by our institutional review committee in which patients of AP and suspected infection were radiologically evaluated by both 18F-FDG-Labelled Autologous Leukocyte PET/CT and advanced MRI within a span of 24-36 hrs .Targeted image guided sampling and aspiration was then performed from the suspected collection,followed by microbiological assessment.

Results: After evaluation of 32 patients of acute pancreatitis with clinical suspicion of infection in the fluid collections, positive microbiological evidence of infection were found in 14 patients and all these patients showed restricted diffusion on MRI and increased uptake on 18F-FDG-Labelled Autologous Leukocyte PET/CT. 18 patients who did not have microbiologically proven infection showed no restricted diffusion on DWI or increased uptake on PET/CT.

Conclusion: Advanced imaging techniques like 18F-FDG-Labelled Autologous Leukocyte PET/CT and DW MRI are showing encouraging results with high sensitivity for early detection of infection in setting of acute pancreatitis. Addition of these modalities to the imaging protocols may help in early diagnosis of superimposed infection thereby improving clinical outcomes. Also both these modalities have shown comparable accuracies in our study.

Disclosure: Nothing to disclose

P0964 ULTRASONOGRAPHIC ASSESSMENT IN INFLAMMATORY BOWEL DISEASE PATIENTS AND FECAL CALPROTECTIN LEVELS: EMERGING TOOLS IN MONITORING DISEASE ACTIVITY

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Introduction: Current guidelines recommend bowel ultrasound (BUS) besides gold standard endoscopic assessment in the management of inflammatory bowel disease (IBD) patients [1]. Sonographic measurements superpose with endoscopic findings and other imagistic methods (MRI) [2]. Faecal calprotectin level correlates significantly with endoscopic disease activity in IBD [3] and the test is useful in clinical practice for assessment of endoscopic activity and remission.

Aims & Methods: 42 IBD patients were included in the study (3 diagnosed with ulcerative colitis, 39 with Crohn's disease). Diagnosis was established endoscopically and histologically and both patients with active and inactive disease were included. Exclusion criteria referred to patients with superimposed infection (viral and Clostridium Difficile) and patients that had solely rectal involvement of the disease. Patients were prospectively evaluated sonographically using a 4-8 MHz micro-convex transducer and the examiner was blinded to biological data. No special preparation was needed before BUS. Data collection was performed noting 3 sonographic measurements of bowel wall thickness in each patient and the assessment of intestinal wall structure. The sonographic measurements were noted in the corresponding regions according to endoscopic observations. Mean value of BWT was calculated. Faecal calprotectin levels were obtained for each patient and the test had a cut-off value of 50 mg/kg.

Results: Strong correlations were observed for the three measurements of the bowel wall thickness (Spearman's equation, r= 0.754, r=0.787 and r=0.793, p< 0.001) and values of faecal calprotectin. A mean calculated value of the 3 measurements of BWT was highly correlated with the level of calprotectin too (r=0.802, p< 0.001). The observation that the higher the value of the faecal calprotectin the greater the disturbance of the wall stratification (CI 95% [-710.6-359.7], p< 0.001) suggested a relationship between the presence of a stratified wall appearance and calprotectin levels.

Conclusion: Sonographic findings (BWT and bowel wall structure) and faecal calprotectin levels could be used in clinical practice to evaluate disease activity in IBD patients.

References: 1. 1. Maaser C et al., ECCO-ESGAR Guideline for Diagnostic Assessment in IBD Part 1: Initial diagnosis, monitoring of known IBD, detection of complications, Journal of Crohn's and Colitis, 2018, 1-32. doi:10.1093/ecco-jcc/jjy113 2. Allocca A et al., Comparative Accuracy of Bowel Ultrasound Versus Magnetic Resonance Enterography in Combination With Colonoscopy in Assessing Crohn's Disease and Guiding Clinical Decision-making, Journal of Crohn's and Colitis, 2018, 1-8. doi:10.1093/ecco-jcc/jjy093 3. N'Haens G et al, Fecal Calprotectin is a Surrogate Marker for Endoscopic Lesions in Inflammatory Bowel Disease, Inflammatory Bowel Diseases, 2012,12: 2218-2224, https://doi.org/10.1002/ibd.22917

Disclosure: Nothing to disclose

P0965 COLITIS ON CT - DOES THIS MEAN INFLAMMATORY BOWEL DISEASE?

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Introduction: Cross sectional imaging is commonly used to assess the abdomen for a variety of symptoms. Colitis reported on CT has become a frequent indication for lower gastrointestinal endoscopy. The outcomes of performing colonoscopy for radiology reported colitis is not clearly known.

Aims & Methods: A retrospective, single centre study of patients referred for a colonoscopy with the indication of 'abnormal imaging'. Data was collected using the endoscopy software audit tool over a 12-month period (September 2017 to August 2018). Patients who had undergone an imaging modality other than CT and those with an overt colonic polyp or mass on CT were excluded from the analysis. Analyses were performed using chi-square and student t-test.

Results: 249 patients (183 CT (73.5%), 66 CTVC (26.5%)) underwent a colonoscopy for CT evidence of mural thickening (218 (87.6%)), fat stranding (88 (35.3%)), inflammation (104 (41.8%)) or local lymph nodes (37 (14.9%)); median age 68 (IQR 53 - 79); median time from CT to endoscopy 33 days (IQR 12.5 - 56.5). Initial indication for CT examination: Abdominal pain 112 (45.0%), Change in bowel habit 39 (15.7%), ?Malignancy 32 (12.9%), PR bleeding 13 (5.2%), Weight loss 9 (3.6%) and Other 44 (17.7%). 53 (21.3%) patients had completely normal lower GI endoscopy. 111 (44.6%) had uncomplicated diverticulosis, 11 (4.4%) diverticulitis, 20 (8.0%) haemorrhoids and 37 (14.9%) colorectal polyps.

20 patients (8.0%) had endoscopic evidence of colitis; 14 (6%) histological evidence of colitis. 10 (4%) confirmed IBD at 6 months follow up (4 UC, 6 CD).

	Normal (n=53)	Colitis (n=20)	Malignancy (n=21)	*p value
Age, mean	63.6	54.4	69.5	**<0.02**
Time to endoscopy (days), mean	45.3	24.5	24.9	**<0.04**
Mural thickening (%)	48 (90.1)	19 (95)	20 (95.2)	ns
Fat stranding (%)	14 (26.4)	12 (60)	9 (42.9)	**<0.03**
Inflammation (%)	16 (30.2)	12 (60)	9 (42.9)	0.06
Lymph nodes (%)	4 (5.7)	8 (40)	11 (52.4)	**<0.00006**
Haemoglobin (g/L), mean	128.0	123.8	112.2	**0.005**
CRP (mg/L), mean	29.8	55.5	68.1	**0.10, <0.05**

[Table 1. Comparison of endoscopic diagnoses according to CT features and blood results.]

Conclusion: Colitis reported on CT correlates with endoscopic colitis in only 8% of patients in this study. Less than 5% are diagnosed with IBD at 6months follow up. The correlation improves in younger patients and with shorter interval between CT and endoscopy. One in five patients had completely normal endoscopy and over 90% had a benign diagnosis. Radiological reporting of fat stranding was an independent risk factor for endoscopic colitis. Anaemia and raised CRP helps identify those at higher risk of malignancy whilst raised CRP alone shows a trend towards identifying true colitis. We conclude that the findings of 'colitis' on CT does not imply IBD in the majority.

Disclosure: Nothing to disclose

P0966 USEFULNESS OF SLIM FULLY-COVERED SELF-EXPANDABLE METAL STENT FOR UNRESECTABLE HILAR MALIGNANT BILIARY OBSTRUCTION

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Introduction: Endoscopic treatment for unresectable hilar malignant biliary obstruction is still difficult because intrahepatic biliary branches were independent of each other, and a standard treatment has not been established yet. We have been using slim fully-covered self-expandable metal stent (SFCSEMS) side-by-side placement method, and examined the usefulness of this method.

Aims & Methods: A retrospective study was conducted on unresectable hilar malignant biliary obstruction in which SFCSEMS (6mm in a diameter) were placed between December 2016 and April 2019 in our hospital. Recurrent biliary obstruction (RBO), prognosis, and adverse events were analyzed according to Tokyo criteria 2014.

Results: The subjects were 31 cases with first metal stent placement (19 men, average age 69.4 years), primary diseases were 10 cases of cholangiocarcinoma, 8 cases of gallbladder cancer, 2 cases of hepatocellular carcinoma, 11 cases of metastatic tumor. The subjects include many cases in advanced status of the cancer, 37% of cases with performance status (PS) 3 or higher, and 70% of cases with Bismuth classification 3 or higher. Single SFCSEMS was placed in 2 cases, two SCSEMS in 24 cases and three in 4 cases with 100% of technical success rate. The clinical success rate was 90% (27/30), and all three failure cases were PS 3 or more and Bismuth 4, all of which were considered to be in liver failure. Stent removal was attempted in all 12 cases in which RBO was occurred during the course, and all of them could be removed without any adverse events. After removal, the SFCSEMS was reinserted in 6 of 12 cases and changed into plastic stents in 5 cases, and EUS-guided hepaticogastrostomy in 1 case. Median time to RBO was 128 days, and survival was 114 days. adverse events related with the deployment procedure was only 2 cases (6.7%) in 1 case of mild pancreatitis and 1 case of cholangitis. Pancreatitis was conservatively treated and cholangitis was improved by adding another metal stent to the cause biliary branch which was obstructed by SFCSEMS.

Conclusion: The slim fully-covered SEMS with 6mm diameter is considered to be an effective method because it is easy to remove, and patency is equal to or more than that of other methods, and there are few incidents.

Disclosure: Nothing to disclose

P0967 BILATERAL METAL VERSUS PLASTIC STENTING FOR PALLIATION OF JAUNDICE IN PATIENTS WITH UNRESECTABLE CARCINOMA GALLBLADDER

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Introduction: Gall Bladder Cancer (GBC) is one of the most common biliary malignancy and frequently presents as locally advanced disease with jaundice. Most of these patients cannot undergo curative surgical resection and need palliative biliary stenting for biliary decompression. Endoscopic biliary drainage is well established modality for palliation of malignant lower end biliary obstruction, but it is technically challenging for hilar biliary strictures. Plastic stents (PSs) have been widely used, but Self Expanding Metal Stents (SEMSs) are becoming increasingly popular. However, the previously published studies have been heterogenous with regard to underlying disease pathology (GBC, cholangiocarcinoma and others), level of malignant block (varying from I-IV Bismuth classification) and type of biliary system drainage (unilateral or bilateral).

Aims & Methods: This study aimed to determine the safety and efficacy of plastic or metal stent deployment in a homogenous population of patients with type II (Bismuth classification) malignant hilar block due to unresectable gall bladder cancer.

Records of all patients with Gall Bladder cancer with hilar block who underwent endoscopic biliary drainage at our tertiary-care center between January 2013 and December 2018 were analyzed for the following outcome parameters: technical success (TS), functional success (FS), early and late complications, stent patency and survival. Patients were followed from stent insertion until death or stent occlusion.

Results: A total of 71 patients were evaluated, of whom 60 [mean age of 54.2 years (range: 34-79) years; men 26, women 34] underwent bilateral stent placement. Twenty seven patients had SEMS placed and 33 patients had plastic stents (PS) placed. TS was achieved in 33(100%) patients treated with PS and in 25(92.6%) patients palliated with SEMS. SEMS provided significantly higher success of biliary drainage as compared to plastic stents, on both intention to treat (81.4% vs 57.6%, p=0.019) and per protocol analysis (88.0% vs 57.6%, p=0.019) with a lower number of ERCP procedures (1 vs 1.58) and lower complication rates (22.2% vs 39.4%) compared with PS. SEMS remained patent for a significantly longer duration than PS [122.6 days (range 25-219) vs. 25(0-94) days, respectively, p= 0.000]. Thirty days mortality was higher (but statistically insignificant) in the PS group as compared to SEMS group [18.2% vs.7.4% days, respectively, p= 0.222]. Use of metal stents was associated with a significantly longer median survival time [126.0 days (3-266)] than in patients treated with PS [87.9 days (9-291), p= 0.000].

Conclusion: SEMS should be preferred over plastic stents for palliation of jaundice in malignant hilar block due to unresectable gall bladder cancer because of better adequacy of biliary drainage, higher stent patency and patient survival with lower complication rates and reduced number of total ERCP procedures with SEMS.

References: 1. Liberato MJ, Canena JM. Endoscopic stenting for hilar cholangiocarcinoma: efficacy of unilateral and bilateral placement of plastic and metal stents in a retrospective review of 480 patients. BMC Gastroenterol 2012; 12:103. 2. Perdue DG, Freeman ML, Lee JG, et al. Plastic versus self-expanding metallic stents for malignant hilar biliary obstruction: a prospective multicenter observational cohort study. J Clin Gastroenterol 2008; 42:1040-1046. 3. Raju RP, Jaganmohan SR, Ross WA, Davila ML, Raju GS, et al. Optimum palliation of inoperable hilar cholangiocarcinoma: comparative assessment of the efficacy of plastic and self-expanding metal stents. Dig Dis Sci 2011; 56:1557-1564. 4. Mukai T, Yasuda I, Nakashima M, Doi S, Iwashita T, Iwata K, et al. Metallic stents are more efficacious than plastic stents in unresectable malignant hilar biliary strictures: a randomized controlled trial. J Hepatobiliary Pancreat Sci 2013; 20:214-222. 5. Wagner HJ, Knyrim K, Vakil N, Klose KJ. Plastic endoprostheses versus metal stents in the palliative treatment of malignant hilar biliary obstruction. A prospective and randomized trial. Endoscopy 1993; 25:213-218. 6. Sangchan A, Kongkasame W, Pugkhem A, Mairiang P. Efficacy of metal and plastic stents in unresectable complex hilar cholangiocarcinoma: a randomized controlled trial. GastrointestEndosc 2012; 76:93-99.

Disclosure: Nothing to disclose

P0968 FEASIBILITY OF ENDOSCOPIC ULTRASOUND-GUIDED BILIARY DRAINAGE REPLACEMENT OF PERCUTANEOUS TRANSHEPATIC BILIARY DRAINAGE

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Introduction: Percutaneous transhepatic biliary drainage (PTBD) for malignant biliary obstruction is a useful alternative treatment for patients in whom endoscopic transpapillary drainage is difficult to perform. We examined the feasibility of endoscopic ultrasound-guided biliary drainage (EUS-BD) replacement of PTBD for internalization of biliary drainage.

Aims & Methods: This single-center retrospective study reviewed records of patients who had undergone EUS-BD replacement of PTBD between March 2017 to April 2019. We evaluated technical success; procedure time; clinical success, defined as subsequent removal of percutaneous catheter; adverse events; time to recurrent biliary obstruction; and reintervention.

Results: EUS-BD (EUS-hepaticogastrostomy in 9 and EUS-choledochoduodenostomy in 2) was performed in 11 patients (9 males, mean age 82 years) to replace PTBD. The median period from PTBD placement to EUS-BD was 8 (range, 3-34) days. Technical success was achieved in all cases. The mean procedure time was 44.0 ± 17.1 min. There were two early adverse events, bile peritonitis in one and acute cholangitis in one. Both conditions were improved with only antibiotic administration. Clinical success was achieved in all cases with PTBD catheter removal after a median of 7 (range, 1-52) days. Median time to recurrent biliary obstruction was 100 (26-357) days. Reintervention was performed in 6 patients. Five patients were exchanged for the new stent endoscopically, and one was required reinsertion PTBD.

Conclusion: EUS-BD replacement of PTBD for internalization of biliary drainage is a feasible, effective and safe techniquefor patients in whom endoscopic transpapillary drainage is difficult. At the time of reintervention, reinsertion PTBD is not required in most cases and an endoscopic approach is possible.

Disclosure: Nothing to disclose

P0969 THE USEFULNESS OF NON-FLARED SHORT FULLY COVERED METALLIC STENT FOR REFRACTORY BENIGN PANCREATIC STRICTURES IN ADVANCED CHRONIC PANCREATITIS

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Introduction: Fully covered self-expandable metallic stent (FCSEMS) have been used recently to treat refractory benign pancreatic stricture in advanced chronic pancreatitis. However, stent migration and stent-induced ductal change are main limitations. The aim of this study was to evaluate the usefulness of non-flared short FCSEMS that was designed to minimize ductal injury and migration for refractory pancreatic stricture in advanced chronic pancreatitis.

Aims & Methods: Total 25 consecutive patients with symptomatic benign pancreatic duct strictures that was unresolved with plastic stents were prospectively enrolled between August 2012 and July 2018. A short (3 or 5 cm) FCSEMS having long lasso (7 cm) used in this study has non-flared convex ends to minimize tissue hyperplasia and smaller center portion to prevent migration. The FCSEMS placement (intraductal or transpapillary) was performed across the stricture and removal was performed after 3 months.

Results: The technical and clinical success rates of FCSEMS placement (14 intraductal and 11 transpapillary stenting) were 100% (25/25), respectively. Stent migration was observed in 1 patients (4.0%) but improved stricture and not needed for additional intervention. Intended stent removal was

successful in 24 patients (100%) (median duration of stenting, 109 days; interquartile range, 91–126). Follow-up ERCP showed resolution of duct strictures in all patients. Stent-induced ductal change was not observed in all patients. Stricture recurrence was observed in 8.0% (2/25) during 665 days of median duration of follow-up (interquartile range, 437–1244).

Conclusion: Non-flared short FCSEMS may be potentially effective option for refractory pancreatic stricture in advanced chronic pancreatitis with minimizing stent-induced ductal injury and stent migration.

Disclosure: Nothing to disclose

P0970 INTRADUCTAL PLACEMENT OF NON-FLARED FULLY COVERED METALLIC STENT FOR REFRACTORY ANASTOMOTIC BILIARY STRICTURES AFTER LIVING DONOR LIVER TRANSPLANTATION: LONG-TERM RESULTS OF PROSPECTIVE MULTICENTER TRIAL

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Introduction: Fully covered self-expandable metallic stent (FCSEMS) may be an effective modality for managing anastomotic biliary stricture (ABS) after liver transplantation. However, stent migration and stent-induced ductal injury are main limitations. The objective of this study was to evaluate the usefulness of an unflared, intraductal FCSEMS that was designed to minimize migration and ductal injury for refractory ABS after living donor liver transplantation (LDLT).

Aims & Methods: A total of 32 consecutive patients with symptomatic ABS after LDLT unresolved by plastic stents with or without balloon dilation at four tertiary medical centers were prospectively enrolled in this study. A short (3 or 5 cm) FCSEMS having long lasso (10 cm) used in this study had unflared convex ends to minimize tissue hyperplasia and smaller center portion to prevent migration. The FCSEMS was placed above the papilla in all patients and removed at 3-4 months after stenting.

Results: Technical and clinical success rates of intraductal placement with FCSEMS were 100% (32/32) and 81.2% (26/32), respectively. Early stent migration was observed in 5 (15.6%) patients. However, 3 patients with early stent migration had stricture resolution without needing additional intervention. Intended stent removal was successful in 27 (100%) patients (median, 101 days; range, 23–118 days). No stent-induced ductal change was observed in all patients. Stricture recurrence was observed in 11.5% (3/26) of patients during 639 days of median duration of follow-up (range, 366–2079 days).

Conclusion: Intraductal placement of an unflared short FCSEMS may be a promising option for refractory ABS after LDLT with minimal stent-induced ductal injury and stent migration.

Disclosure: Nothing to disclose

P0971 INTRADUCTAL PLASTIC STENT PLACEMENT IS AN EFFECTIVE THERAPY FOR UNRESECTABLE MALIGNANT BILIARY OBSTRUCTION

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Introduction: Recent reports have described the efficacy of plastic stent (PS) placement inside the bile duct for malignant biliary strictures. However, the superiority of intraductal PS placement (IS) over PS placement across the sphincter (conventional PS placement [CS]) and uncovered metallic stent placement above the sphincter of Oddi (MS) is unclear.

Aims & Methods: The aim of this study was to evaluate the efficacy of IS, and compare its efficacy with the efficacies of CS and MS for malignant biliary strictures. This retrospective study included 40 patients (43 procedures) with an unresectable malignant hilar or middle bile duct obstruction, who underwent IS between January 2008 and December 2018 at our institution. The indication for IS was a distance of at least 3 cm between the lower end of the stricture and the sphincter. We compared the efficacy of IS with the efficacies of CS (34 patients [46 procedures]) and MS (21 patients [21 procedures]). Among the 40 patients who underwent IS, the origins of the malignant biliary stricture were gallbladder cancers in 10 patients, intrahepatic cholangiocarcinomas in 11patients, bile duct cancers in 6 patients, pancreatic cancers in 3 patients, and others in 10 patiets. We evaluated complications associated with stent placement, the Time to recurrent Biliary Obstruction (TRBO), and stent removability at occlusion. We modified a 7-Fr Flexima biliary stent (Boston Scientific Co., Boston, MA) and attached a nylon thread (size 2/0) to the distal end for removal. If insertion was difficult due to winding or narrowing of the intrahepatic bile duct (ex. B3 and B6), we placed a Flexima nasobiliary drainage tube(7.5Fr), cut to the appropriate length, as an internal stent. Most stent placements were performed after preoperative nasobiliary drainage.

Results: The overall technical success rates in the IS, CS, and MS groups were all 100%. The TRBO was greater in the IS group than in the CS group (117 days vs. 45 days, P < 0.001, log-rank test); however, the TRBO was not significantly different between the IS and MS groups (117 days vs. 139days, P = 0.57). The predictive factors of longer TRBO in plastic stents were IS (vs CS), usage of anti-cancer drugs, and multiple stents replacement in univariate analysis and was IS in multivariate analysis (P< 0.001, Cox's propotional hazards model).

In the IS group, there were no early complications associated with stent placement; however, delayed complications were observed in 4 patients from this group (3 had cholecystitis and 1 had stent migration to the hepatic side). Additionally, in the IS group, 19 patients developed stent dysfunction. The causes of dysfunction were sludge or food deposition in 14 patients, reflux cholangitis in 1 patient, bending of the stent in 1 patient, tumor overgrowth in 1 patient, dislocation to the duodenal side in 1 patient, and migration to the hepatic side in 1 patient. In 14 patients from the IS group, stent replacement was attempted and was performed successfully. There were no complications associated with stent removal.

Conclusion: The TRBO is longer with IS than with CS for malignant biliary obstruction. Additionally, the TRBO tends to be shorter with IS than with MS; however, the difference might not be significant. Additionally, complications are relatively minor with IS, and the stent can be removed if dysfunction occurs. Therefore, IS is an effective option for unresectable malignant hilar and middle bile duct obstructions, and it is as effective as MS.

Disclosure: Nothing to disclose

P0972 INNOVATION OF EUS-GUIDED TRANSMURAL DRAINAGE USING A NOVEL SELF-EXPENDING METAL STENT

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Introduction: Endoscopic ultrasonography (EUS)-guided transmural drainage has been accepted as a modality of choice for pancreatic fluid collections and gallbladder (GB) drainage. Double pigtail plastic stents, conventional tubular-shaped self-expanding metal stents (SEMS), and recently introduced lumen apposing metal stents (LAMS) are commonly used for this procedure.

However, each type of stent has its own disadvantages; plastic stent is prone to occlusion due to its small diameter, fully covered SEMS has a higher risk of migration, and LAMS has been reported to cause serious

adverse events such as bleeding and buried LAMS syndrome. There are still unmet needs in dedicated stents for transluminal drainage despite the ongoing developments.

Aims & Methods: This animal study aims to evaluate a newly designed fully covered metal stent with dual coiled ends for the transluminal drainage. We performed the EUS-guided GB drainage with a newly developed metal stent in 8 mini pigs with surgically induced GB distension. This stent is a SEMS with coiled ends, which is made of nitinol wire and fully covered with silicone. The diameter of the stent is 8mm and the length is 6cm. Both pigtail ends are coiled 360 degrees in order to minimize the risk of bidirectional migrations. EUS-guided GB drainage was performed as follows; First, GB was punctured with a 19-gauge needle under direct sonographic visualization from the stomach. A guidewire was inserted through the access needle and coiled inside the GB. Further puncture with a cystotome and tract dilatation with a balloon catheter was done, followed by the deployment of the stent with an 8Fr delivering catheter under the guidance of fluoroscopy, EUS and endoscopy. After the EUS-guided cholecysto-gastrostomy was completed, pigs were raised and monitored for certain periods before the removal of a stent; 28 days in 2 pigs, 35 days in 2 pigs, 42 days in 2 pigs, and 49 days in 2 pigs. The primary outcome was technical success rate and the secondary outcomes were adverse events, stent dysfunction, stent removability, and the successful fistula formation.

Results: The stent was placed successfully between the gallbladder and the stomach without any adverse event in all cases. Neither stent migration nor dysfunction was observed during the study period and all the stents were removed easily as scheduled. Successful cholecysto-gastric fistula formation was confirmed at endoscopic and histologic level in all cases.

Conclusion: EUS-guided transmural drainage and fistula formation using a new fully covered metal stent with dual coiled ends was technically feasible without any adverse event in this animal study. We expect this newly developed stent to be useful in EUS-guided transluminal drainage. Further clinical studies on the application of this stent in real practice are needed to evaluate the efficacy and safety.

Disclosure: Dr. Lee is the inventor of the newly developed metal stent used for the study. The stents were provided free of charge and financial support was provided for the study by S&G Biotech Inc.

P0973 THROUGH-THE-SCOPE ESOPHAGEAL STENT FOR THE RELIEF OF MALIGNANT DYSPHAGIA: PRELIMINARY RESULTS OF A MULTICENTRIC STUDY (WITH VIDEO)

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Introduction: Esophageal cancer is the sixth most common cancer worldwide and in presence of non-surgical candidate presenting dysphagia, the placement of a self-expandable metal stent (SEMS) uncovered, partially covered (PCSEMS) or fully-covered (FCSEMS) nowadays represent a safe and effective palliative treatment for the relief of dysphagia. Esophageal stent are placed over-the-wire (OTW), under X-ray control, with or without endoscopic assistance during the stent release. Actually, there are no data in literature about the use of the new through-the-scope (TTS) esophageal stent placed for malignant dysphagia.

Aims & Methods: The aim of our study is to evaluate the clinical efficacy of the new TTS esophageal stent in this group of patients.35 patients (10F and 25M - mean age: 76±9.1ys) with malignant dysphagia unfit for surgery undergone TTS esophageal stent placement (Taewoong Medical Co.) were retrospectively evaluated. 27 patients presented adenocarcinoma, 6 were squamous neoplasia, 1 neuroendocrine tumor and 1 ab-extrinsic compression by breast cancer limphoadenopathy. Length of stenosis was of 5.6±2.8 cm. 28 stenosis were located at the III distal esophagus, 6 in the middle

and 1 in the proximal. 13 stent were of 18mm diameter, 18 of 20mm diameter and 4 of 22 mm. We replaced 10 SEMS, 11 PCSEMS and 14 FCSEMS. All of the stents were placed for palliation.

Results: All of the 35 of the patients had completely relief od dysphagia, starting liquid and solid oral intake 24h after the procedure. No adverse events were observed during the stent placement. In one case (2.8%) the guide-wire was not used. In 12 patients a submucosal marking of the distal part of the stenosis was used (34.2%). 5 distal migration were observed (14.7%): 1 PCSEMS after three months of chemotherapy (CT) and 4 FCSEMS (28.5% of all FCSEMS), of which 1 after 45 days of CT and 3 at 1, 2 and 5 days after placement. No technical difficulties were encountered by the endoscopists during the stent placement.

Conclusion: The efficacy of the new TTS esophageal stent, in the relief of malignant dysphagia, is comparable to the standard OTW esophageal stent but adverse events seems to be reduced. Migration rate was higher for the FCSEMS. TTS esophageal stent allows to reduce procedure's time and the technique seems more simple if compared to the OTW. An antimigration system may diminish the migration rate of the FCSEMS.

Disclosure: Nothing to disclose

P0974 EQUIVALENCE IN LONG-TERM ONCOLOGICAL OUTCOMES OF COLONIC STENTING AS BRIDGE TO SURGERY IN COMPARISON WITH SURGERY ALONE IN STAGE II AND III LEFT-SIDED OBSTRUCTIVE COLORECTAL CANCER

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Introduction: Endoscopic stenting with self-expanding metallic stent is considered as one of an effective treatment for intestinal decompression in obstructive colorectal cancer. However, many physicians remain hesitant to perform colonic stenting as bridge to surgery (BTS) in a curative setting, since it has been suggested to adversely affect oncological outcomes of colorectal cancer patients. The aim of this study is to verify the equivalence of colonic stenting to surgery alone for stage II and III left-sided obstructive colorectal cancer in long-term oncological outcomes.

Aims & Methods: This study was conducted as a retrospective chart review at a single institute in Japan. The data of patients who had operable left side obstructive colorectal cancer at first diagnosis were collected retrospectively from the clinical records of the University of Tokyo Hospital between 2007 and 2017. We defined obstructive colorectal cancer as the malignant stricture caused by colorectal adenocarcinoma that a colonoscope cannot pass and requires fasting or food restriction allowing only liquid food. We compared the patients who received colonic stenting before surgery (Stent group) and who received surgery alone without decompression treatment (Surgery alone group). Patient characteristics, pathological findings, duration of fasting, and duration of recurrent-free survival and overall survival were obtained from electric medical record.

Results: We identified 364 obstructive colorectal cancer patients during this period, of which 114 patients were classified as stage II or III. Among them, 23 patients received stent placement for decompression and 91 patients were received surgery alone. There was no difference between the 2 groups regarding gender, age and location of primary tumor. There were more cases of stage II in the Stent group than in the Surgery alone group (65.2 % vs 41.8%, P = 0.04). In pathological findings, although there was no statistical difference in the depth of tumor, the Surgery alone group had more patients with local lymph node metastasis (49.5 vs 34.8 %, P = 0.04) and neural invasion (72.7 vs 42.9 %, P = 0.04). Stent placement was clinically successful in all cases except one, and no perforation were observed. Duration of fasting was shorter in stent group (23.6 vs 28.8 days P = 0.03). Regarding the long-term oncological outcomes, no statistically significant difference was observed in recurrent-free survival or overall survival. In multivariate analysis of recurrence, local lymph node metastasis and neural invasion were risk factors, but stent placement was not identified as a risk factor.

Conclusion: Stent placement without perforation as a bridge to surgery for obstructive colorectal cancer patients does not adversely affect long-term oncological outcomes.

Disclosure: Nothing to disclose

P0975 RIGHT-SIDED COLONIC STENTING IN PALLIATIVE COLON CANCER: MORE CHALLENGING BUT LOWER LATE COMPLICATION RATE AND AT LEAST EQUIVALENT SURVIVAL

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Introduction: Stent insertion for malignant colonic obstruction is established as a palliative measure as well as a bridge to surgery. UK guidelines on colorectal cancer (NICE CG131) specifically does not recommend placement of a stent in right-sided malignant large bowel obstruction.

Aims & Methods: Patients referred for colonic stenting in our centre over a 10-year period up until 2019 were included. Technical and clinical outcomes, and subsequent progress, including late complications, surgery, re-stenting, oncological therapies, and death were recorded. To assess the durability of stent benefit, we measured time to re-intervention (re-stenting, surgery, or death without re-intervention), surgery-free survival (to surgery, or death without surgery), and overall survival (to death, irrespective of any intervention).

Results: 135 stent procedures were undertaken for malignant large bowel obstruction – of these 105 cases were index procedures with palliative intent, comprising 80 left-sided tumours and 25 right-sided obstructing tumours proximal to the splenic flexure. The median age was 74 years (range 27-94), and 56% were male. Technical and clinical success rates were respectively 90% / 86% for left-sided stents, and 72% / 68% for right-sided stent procedures (p=0.04 / p=0.07). There was evidence of improving outcomes with time with technical success in 2009-2014 and 2014-2019 being 81% and 96% for left-sided, and similarly improving from 60% to 79% for right-sided stents (p>0.05). Reasons for clinical failure in left and right-sided stents were inadequate bowel preparation (0% v 12%), inability to cross stricture with wire (7.5% v 16%), and failure to relieve obstruction after satisfactory luminal deployment of stent (5% v 4%). There were no complications during the stent procedures, but later complications requiring surgical intervention were 3 perforations in left-sided stent cases (day 1, day 27, day 101); 1 patient with an extrinsic cancer had early stent migration on day 4; 1 patient developed an abdominal wall abscess on day 47; 1 stent occlusion was operated on day 90. Stent migration was identified in a further 6 left-sided stent patients (day 27 palliated, day 123 and day 274 both re-stented; a further 3 patients, all undergoing chemotherapy and >6 months post stent, were noted on follow-up CT to have incidental stent migration, but no intervention was required). Stent occlusion in a further 7 cases required re-stenting at a median of 228 days (177 to 498 days). One right-sided patient re-obstructed on day 536 and had surgery but no other interventions occurred in this group. Comparing left and right-sided stents, overall complication rates in the 12 months after stenting were 25% / v 0% (p=0.02), duration of stent benefit was 177 v 320 days (p=0.07), surgery-free survival 223 v 320 days (p=0.12) and overall survival 306 v 320 days (p=0.29). Patients who had a failed palliative stent procedure had a median survival of only 75 days (p=0.002), which was not related to any complications.

Conclusion: Outcome and survival after right-sided colonic stenting appears at least comparable to left-sided stenting – although technical success was statistically lower, there was a lower complication rate in the 12 months after stent insertion with no re-interventions, compared to 1 in 5 in the left-sided group. The survival of right-sided stent patients was not inferior to left-sided stent patients. We believe right-sided stenting should be a management option for patients presenting with proximal large bowel obstruction and palliative cancer.

References: nice.org.uk/guidance/cg131

Disclosure: Nothing to disclose

P0976 FACTOR ASSOCIATED TECHNICAL AND CLINICAL FAILURE OF SELF EXPANDABLE METAL STENT IN MALIGNANT COLORECTAL OBSTRUCTION

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Introduction: Self-expanding metal stents (SEMSs) can be used as a palliative treatment or to decompress colon prior to definitive surgery. The purpose of this study was to investigate the factor associated clinical and technical Failure of SEMS used as palliation and bridge to surgery for malignant large bowel obstruction.

Aims & Methods: We retrospectively reviewed the records of patients with malignant colorectal obstruction who tried SEMS insertion in our hospital between January 2008 and December 2017. We analyzed demographic, clinical characteristics. Technical failure was defined as failure to deploy the stent across the colon stenosis site. Clinical failure was defined as the absence of resolution of obstructive symptoms and passage of gas and stool within 7 days despite achievement of technical success.

Results: SEMS were tried in total 466 patients. The indication of SEMS was as a bridge to surgery in 225 (48.3%) patients and as palliation in 241 (51.7%) patients. 83 (17.8%) patients were seen in right colon obstruction. 383 (82.2%) patients were seen in left colon obstruction. Technical failures were found in 50 patients (10.7%). After SEMS insertion, clinical failure was found in 23 of 416 patients (5.5%).

On univariate analysis, the rate of technical failure was high in patients with peritoneal carcinomatosis, abdominal pain (Visual Analogue Scale(VAS) ≥5), abdominal tenderness, C-reactive protein (>4.4mg/dl), fever, palliative treatment, metastasis. Multivariate analysis revealed that peritoneal carcinomatosis(odds ratio: 2.43, 95% CI: 1.22-4.83, p=0.012), abdominal pain (Visual Analogue Scale >5) (odds ratio: 3.40, 95% CI: 1.08-10.549, p=0.036) were a significant risk factor for technical failure.

On univariate analysis, the rate of clinical failure was high in patients with peritoneal carcinomatosis and elevated White Blood Cell(WBC) count(>10800/$\mu\ell$). Multivariate analysis revealed that peritoneal carcinomatosis (odds ratio: 3.14, 95% CI: 1.30-7.61, p=0.011) and elevated WBC count (odds ratio: 2.55, 95% CI: 1.03-6.33, p=0.043) were a significant risk factor for clinical failure.

Stent complication (58/466, 12.4%)	Treatment for stent complication
Perforation (15/58, 25.9%)	operation :13
	supportive care due to poor general condition: 1
	Operation refuse: 1
Migration (26/58, 44.8%)	2nd stent insertion: 11
	operation :13
	observation: 2
Re-stenosis (17/58, 29.3%)	operation: 13
	2nd stent insertion: 3
	Treatment refuse: 1

[Stent complication and treatment of complication]

Conclusion: Before trying SEMS insertion for malignant colorectal obstruction, endoscopist must consider patient condition. Patient with peritoneal carcinomatosis, abdominal pain (VAS≥5), elevated WBC count is negatively impacted outcomes of SEMS placement.

Disclosure: Nothing to disclose

P0977 ANALYSIS OF THE RISK FACTORS COLONIC PERFORATIONS IN PATIENTS AFTER STENTING FOR MALIGNANT COLORECTAL OBSTRUCTION

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Introduction: SEMS implantation is an effective method of decompression for patients with malignant colorectal obstruction. However, the use of colonic stenting is limited due to relatively high rate of complications. The most serious complication is perforation, requiring emergency surgery and associated with high mortality and risk of cancer cell dissemination. According to publications, rate of perforations is 2-10%, but we have very limited and unsystematic data about risk factor of perforations.
Aims & Methods: The aim of our research work was to analyze the factors influencing the occurrence of various types of perforation after colorectal stenting. We retrospectively carefully studied cases of 197 patients with malignant colorectal obstruction who received endoscopic SEMS insertion from December 2012 to April 2019. We divided perforations into 2 types: 1) perforation of the tumor and / or colonic wall with a stent and perforation of the proximal colon segments due to dilatation or ischemic lesion.
Results: The technical and clinical success rates were 98.0% and 92.3%. After successful procedure, in 11 (5.6%) patients perforation was recognized on 1-20 days. One patient has silent perforation (intraoperative finding), in 1 case - autopsy finding. Severe obstructive symptoms (11-15 points on the Colon Obstruction Score (odd ratio 7.2432; 95% confidence interval, 1.040-28.787) and 0-1 on the CROSS scale odd ratio, (odd ratio 4.439; 95% confidence interval, 0.48-0.59) were perforation-related factors for the entire sample of cases. Additionally, stage T4b was risk factor of perforation in first subgroup odd ratio (odd ratio 7.87; 95% confidence interval, 2.040-12.508), and cecum dilatation on X ray more 10 cm was significantly associated with occurrence of perforation in second subgroup (odd ratio 2.602; 95% confidence interval, 1.279 - 5.634).
Conclusion: Severity of obstructive symptoms was significantly associated with occurrence of perforation. In order to reduce perforation rate, clinicians should pay more attention when performing SEMS placement and monitoring patients with these risk factors.
Disclosure: Nothing to disclose

P0978 ADDITIONAL SURGERY AFTER CHEMOTHERAPY FOLLOWING ENDOSCOPIC COLONIC STENTING IN THE MANAGEMENT OF OBSTRUCTIVE COLORECTAL CANCER WITH DISTANT METASTASIS

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Introduction: Endoscopic stenting with a self-expandable metallic stent (SEMS) in patients with acute large-bowel obstruction due to CRC has been established as a palliative therapy or a bridge to surgery with more favorable rates of permanent stoma, primary anastomosis, and overall complications. In the previous study, we demonstrated that when technical and clinical successes are achieved by careful SEMS placement, chemotherapy under long-term SEMS is a feasible therapeutic option for patients with obstructive CRC. However, the outcome of additional surgery after chemotherapy under long-term SEMS placement has not been investigated.
Aims & Methods: The aim of this study was to evaluate outcome of additional surgery after chemotherapy following endoscopic colonic stenting by comparing that of chemotherapy following stenting without additional surgery and that of chemotherapy following surgery.

In total, 68 patients with stage IV CRC who visited the Aomori Prefectural Central Hospital for obstructive symptoms between January 2012 and March 2018 were evaluated. In this retrospective study, the patients were classified into an SC (stenting before chemotherapy) group (n = 36), comprising those who underwent chemotherapy following endoscopic colonic stent placement, and an OC (operation before chemotherapy) group (n = 32), comprising those who underwent chemotherapy following surgery. In the SC group, for comparison, the patients were further classified into those who did (n = 20) and did not (n = 16) undergo additional surgery. Patients' characteristics including age, gender, tumor location, performance status, obstructive symptom and prognostic nutritional index (PNI), adverse events and overall survival were evaluated.
Results: *Patients characteristics in the SC and OC groups*
There were no significant between-group differences in age, tumor location, performance status, obstructive symptom and PNI. Male to female ratio was significantly lower in the OC group (16/16) than in the SC group (28/8, p=0.017).
Patient characteristics in the SC group for those who did and did not undergo additional surgery
There were no significant between-group differences in male to female ratio, performance status, frequency of tumor locations, and response grades to chemotherapy. Patient age was significantly lower in patients who underwent additional surgery (62.9) than in those who did not (70.6, p< 0.01).
Adverse effects in the SC group
The frequency of procedure-related adverse events occurring after 30 post-stenting days included perforation (3.1%) at 149 days post-stenting, dislodgement and migration (21.9%) at 84 days post-stenting, and re-obstruction (12.5%) at 98 days post-stenting.
Overall survival
There was no significant difference in overall survival between the SC and OC groups (p = 0.371). In the SC group, patients who underwent additional surgery had an improved survival compared with those who did not (p < 0.001) and those in the OC group (p = 0.027). Furthermore, in the SC group receiving additional surgery, 8 patients with PNI increase before and after stenting had an improved survival compared with 12 patients without PNI increase (p < 0.001).
Conclusion: In the SC group, additional surgery was found to significantly improve overall survival which can be predicted by PNI evaluated before and after stenting. We conclude that chemotherapy under long-term SEMS with additional surgery is a feasible therapeutic option for patients with obstructive CRC.
Disclosure: Nothing to disclose

P0979 THE ROLE OF EUS-GUIDED GASTROENTEROSTOMY IN THE TREATMENT OF MALIGNANT GASTRIC OUTLET OBSTRUCTION

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Introduction: In patients with malignant gastric outlet obstruction (mGOO) and an expected survival of at least six weeks, surgical gastrojejunostomy (sGJJ) seems favoured over duodenal stenting. (SUSTENT-study; Jeurnink et al, 2010). There is accumulating evidence that EUS-guided gastroenterostomy (EUS-GE) could be an effective and safe alternative treatment of mGOO. It is minimally invasive with fast relief of complaints, like duodenal stenting, but it also has the potential of low reintervention rates and long-lasting patency, like sGJJ. However, the exact role of EUS-GE in the management of mGOO remains unclear and evidence about its long-term durability is limited. We therefore aimed to evaluate the long-term patency of EUS-GE.

Aims & Methods: We performed an international, multicentre retrospective analysis of EUS-GE cases that were performed between 2015 and 2019 in six centres from four European countries. All cases concerned EUS-guided placements of a Hot AXIOS Stent (Hot AXIOS™ Stent and Electrocautery-Enhanced Delivery System, Boston Scientific Corporation, USA), as palliative treatment for mGOO, regardless of the cancer etiology. Data on patient and procedural characteristics were recorded. Endpoints were:

1. Technical success (defined as a successful placement of the Hot AXIOS stent between the stomach and an intestinal or duodenal loop),

2. Clinical success (defined as the ability to tolerate a liquid diet without vomiting after a technical successful placement of the Hot AXIOS stent),

3. Long-term patency (defined as the time to recurrence after a technical and clinical successful treatment), and 4) adverse events.

Results: In total 41 patients (51% female, mean age 69.5 years (range 40-90)) were included in this study. Most patients were unable to tolerate oral intake, with 21/41 (51.2%) having a GOOSS-score of 0. Etiology of mGOO included pancreatic cancer (39%), gastric cancer (15%), duodenal cancer (7%), periampullary cancer (7%), gallbladder cancer (5%), biliary tract cancer (7%), and extrinsic compression by metastases (17%). Ascites was present in 14/41 (37%) and peritoneal carcinomatosis in 13/41 (36.1%) patients.

The Hot AXIOS stent was placed using the direct technique in 32/41 (78%) patients. Balloon assistance was used in the remaining 22%. A 15 mm diameter stent was placed in 28/41 (70%) and 20 mm in the remaining 30%. Additional balloon dilation of the stent was performed in 9 (26.5%) patients.

Technical success was achieved in 35/41 (85%) patients. Stent maldeployment/misplacement was the sole reason for technical failure (n=6). Clinical success was achieved in 30/35 (86%) of the technical successful cases. In 2/30 clinical successful cases, recurrent obstructive symptoms occurred after 33 and 283 days of follow-up. Procedural adverse events occurred in 8 (19.5%) patients which concerned misplacement in seven (four resulting in a perforation), and one punction of the colon. Postprocedural adverse events occurred in 14 (35%) patients, of which 5 were fatal.

Conclusion: The long-term patency of EUS-GE seems good once it is performed successfully and relief of symptoms has been achieved, with recurrent symptoms in only 6.7% of cases. This long-term durability makes EUS-GE a possible treatment option for mGOO. The high number of fatal complications due to misplacement of the Hot AXIOS stent might be a concern.

References: Jeurnink SM, Steyerberg EW, van Hooft JE, van Eijck CH, Schwartz MP, Vleggaar FP, Kuipers EJ, Siersema PD; Dutch SUSTENT Study Group. Surgical gastrojejunostomy or endoscopic stent placement for the palliation of malignant gastric outlet obstruction (SUSTENT study): a multicenter randomized trial. Gastrointest Endosc. 2010;71(3):490-9

Disclosure: Moons: Consultant for Boston Scientific; Perez-Miranda: Consultant & speaker for Boston Scientific, MITech, speaker for Olympus & Taewoong; Poley: Consultant for Boston Scientific, Cook and Pentax; Will: Consultant for Boston Scientific; Masaryk: Consultant for Boston Scientific; Vleggaar: Consultant for Boston Scientific

P0980 KISSING SUTURING EFFECTIVE METHOD FOR LARGE GASTROINTESTINAL WALL DEFECT CLOSURE

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Introduction: Endoscopic full-thickness resection (EFTR) has been established as a minimally invasive surgical method for en bloc resection. However, it remains a challenge to safely and efficiently close large defects left after the procedure[1]. Successful closure of the wall defect is the key procedure for EFTR technique.

Aims & Methods: Our aim was to demonstrate an easy, safe and feasible technique which uses a combination of clips and nylon loops to close large defects using a single-channel endoscope, called the "Kissing Suturing" method.

We retrospectively studied 35 patients (defect size up to 2 cm in diameter) were treated at our hospital with the 'Kissing Suturing' method for large defect closure resulting from EFTR procedure. After EFTR procedure, a nylon loop of a detachable snare was fixed in the tip of the transparent cap. Then, placed the loop in the defect area and used two clips to anchor it to the two edges of the defect. Tightening the loop produce two smaller defects which could then be closed with clips or following placing additional loops.

Results: A total of 35 patients (20 male, 15 female) with an average of 57.8 years old (range, 27-82) were treated with 'Kissing Suturing' method for large defect closure resulting from EFTR. The mean tumor size was 3.56 cm (range, 2-7 cm). A successful complete resection rate by EFTR was accomplished in 35/35 (100%). The mean defect size was 3.56 cm (range, 2-7 cm). Complete closure of all post-EFTR defects was succeeded in all patients (success rate 100%) with the mean time was 77.62 minute (range, 13-211 minute). There was no major complication such as peritonitis, delayed bleeding or perforation in all patients.

Conclusion: This study provides evidence that the use of clips and nylon loops with single-channel endoscope namely "Kissing Suturing" method for large defect closure seems to be safe, easy and feasible.

References: 1. Shi D, Li R, Chen W, et al. Application of novel endoloops to close the defects resulted from endoscopic full-thickness resection with single-channel gastroscope: a multicenter study. Surg Endosc. 2017; 31:837-842.

Disclosure: Nothing to disclose

P0981 COLONIC STENT PLACEMENT FOR MALIGNANT OBSTRUCTION: A SINGLE CENTRE UK EXPERIENCE

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Introduction: Colorectal cancer is the 4th most common cancer in the UK with an incidence of 41700 new cases every year.

Colonic Stenting for malignant obstruction has been used for palliation and as a bridge to elective surgery. The 2014 ESGE guidelines cautioned use in the latter group due to the risk of upstaging disease. More recent ACPGBI position statements suggest lower morbidity in the stent group compared with primary resection and survival equivalence.

Aims & Methods: To review the use of colonic stenting in malignant obstruction at a busy district general hospital against current clinical guidelines.

A 5 year retrospective review of patients in whom colonic stenting for malignant obstruction was attempted (Jan2014-Jan2019). Data were retrieved from endoscopy database, radiology reports and discharge summaries.

Results: A total of 36 patients (M:F 1:1) were identified. Mean age was 69 (SD 16, Range 32-97).

The 36 patients can be separated into 25% (9/36) with known colorectal cancer who eventually required a stent due to obstructive symptoms and 75% (27/36) who presented acutely with obstruction with a previously undiagnosed colorectal cancer.

47% (17/36) of patients were stented with a view to subsequent surgery. 53% (19/36) were stented for palliative treatment only.

Known cancer patients average diagnosis to stent time and admission to stent times were 243 and 2 days respectively.

Acute first presentation average diagnosis to stent time and admission to stent times were 6.23 and 2.53 days respectively.

Stents were placed in the sigmoid colon in 44% (16/36), descending colon in 17% (6/36) and splenic flexure in 17% (6/36).

All stents were performed by one of three experienced consultant endoscopists, in a symptomatic cohort.

They all had a contrast CT scans confirming the diagnosis and level of obstruction prior to the procedure.

No stricture dilatations were performed.

Uncovered Cook Evolution stents were used in all cases, from 6-10cm in length.

No patient in the cohort had extra colonic obstruction.

83% of patients had a phosphate enema, 6 patients who had no prep, with most reporting a good or satisfactory preparation on endoscopy report.

Only 9 of the 17 patients who were stented with a view to surgery proceeded to surgery. In the remaining 8 out of 17 a decision was made not to have surgery or no information was available. None of the proximal lesions which were stented had a subsequent resection.

Repeat CT imaging was performed on average 97.8 days after stent insertion.

The average time to elective surgery from stent insertion was 27.33 days (13-39 days).

35/36 stents attempted were successful on first attempt with remaining case succeeded on second attempt.

Stent complications were: 1 stent related perforation which occurred 4 days post insertion for a palliative indication and a partial stent obstruction managed conservatively.

47% (17/36) of patients died with an average stent to death time of 209 days. 11 of these had been stented with palliative intent whilst 6 had been stented with a view to subsequent surgery.

Conclusion: 1. Colonic Stenting for malignant obstruction has a high success rate, and a low morbidity and mortality rate.

2. It can provide long-term relief of obstruction in palliative patients, or provide a bridge to elective surgery.

3. The use of stenting as a bridge to surgery in potentially curable patients remains controversial but appears to be a reasonable and safe option in experienced hands.

Disclosure: Nothing to disclose

P0982 LAMS IN AFFERENT LIMB SYNDROME MANAGMENT

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Introduction: Afferent limb syndrome (ALS) or Afferent loop syndrome is a late postoperative complication of duodenopancreatectomy defined as the dilatation of the afferent limb with accumulation of biliopancreatic fluid due to the mechanical obstruction of the afferent limb usually by cancer recurrence . ALS can cause abdominal pain pancreatitis and reflux cholangitis. Standard treatment is surgery , but in patient in bad shape surgery is an invasive treatment carrying its own morbidity and mortality.

We present here an endoscopic technic for ALS managment.

Aims & Methods: We present here five cases of ALS treated by endoscopic entero-anastomosis by Lumen apposing metal stents (LAMS).The aim of the technique was to obtain an internal drainage of the afferent limb through the stomach or jejunum by creating an endoscopic anastomosis. The gastroenterostomy or enteroenterostomy was created under endoscopic ultrasound (EUS) and fluoroscopic guidance.

Results: All procedures were successful with no related complications, two patients had a complete regression of their symptoms, one experienced cholangitis recurrence after 3months, two patients died after some weeks due to their malignancies.

Conclusion: EUS-guided entero-enterostomy by LAMS offers a convenient and safe palliative solution for patients presenting ALS due to progressive malignancy after duodenopancreatectomy.

Disclosure: Nothing to disclose

Surgery II
09:00-17:00 / Poster Exhibition - Hall 7

P0983 LAPAROSCOPIC SURGERY FOR ACHALASIA: OUTCOMES OF 572 CONSECUTIVE CASES IN JAPAN

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Introduction: Laparoscopic Heller-myotomy with Dor-fundoplication (LHD) is the most common surgical treatment for achalasia. Recent development of surgical equipment allows less invasive procedures such as reduced port surgery (RPS) and needlescopic surgery (NS), providing a better cosmetic results. All these techniques are available in our tertiary referral hospital in Japan. The aim of this study is to explore the outcomes of LHD including RPS and NS based on a large cohort of 572 patients diagnosed with achalasia.

Aims & Methods: All patients diagnosed with achalasia are entered into a prospectively maintained institutional database. After Institutional Review Board approval, we queried this database to identify patients who underwent LDH between August 1994 and May 2018. Of these, 572 patients who were followed at our clinic at least 3 months after surgery were included. The mean age was 45.6 years and 279 patients were women. The following characteristics were explored in this study: surgical procedure, operative time, blood loss, number of intraoperative complications, length of postoperative hospital stay, prevalence of postoperative reflux esophagitis, prevalence of esophageal stenosis requiring endoscopic balloon dilation, and degree of patients' satisfaction for LHD scored from 1 (disappointed) to 5 (excellent) based on postoperative interview.

Results: Based on Japan Esophageal Society classification of esophagogram, 453 patients had straight esophageal type, 76 patients had sigmoid type, 26 had advanced sigmoid type, and data unavailable in 17 patients. The average maximum esophageal transverse diameter was 5.1 ± 1.6 (range, 10 to 12.5) cm grade I in 74, grade II in 327, grade III in 149, and data unavailable in 22 of them. 50 patients (9%) underwent RPS, and NS was performed in 42 (7%) patients. The average operative time was 174.8 ± 46.2 (range, 67-447) min and median blood loss was 0 ml. Intraoperative complications were observed in 98 patients (17%), which included mucosal injury on the esophagus and/or stomach in 84, the vagus nerve injury in six, piriform fossa injury in two, small intestine injury in one, and splenic injury in one patient, respectively. None but one patient (0.1%) with splenic injury required open conversion. Duration of postoperative hospital stay was 5.3 ± 3.0 (range, 3-35) days, postoperative reflux esophagitis was noted in 70 patients (12%), and endoscopic esophageal dilation was required in 7 patients (1%) due to outflow obstruction. Four patients (0.7%) underwent reoperation at 7 to 63 (mean 30 month) months after the primary surgery for postoperative stenosis, dislocation of the wrap, and delayed perforation of the small intestine. Satisfaction score for symptomatic relief was 4.7 ± 0.6.

Conclusion: The rate of intraoperative complications of LHD for esophageal achalasia was relatively high, though most of them did not require open conversion. LHD had reasonable perioperative outcomes with excellent symptomatic relief.

Disclosure: Nothing to disclose

P0984 LONG-TERM QUALITY OF LIFE AFTER TOTAL GASTRECTOMY VERSUS IVOR LEWIS ESOPHAGECTOMY

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Introduction: Surgical treatment for gastroesophageal junction (GEJ) cancers is challenging since both a total gastrectomy and an esophagectomy can be performed. The preferred treatment is unknown given the scarce evidence regarding their effects on surgical morbidity, pathology, long-term survival and health-related quality of life (HR-QoL). The aim of this study was to investigate the difference in long-term health-related quality of life in patients undergoing total gastrectomy versus Ivor Lewis esophagectomy in a tertiary referral center.

Aims & Methods: From 2014 to 2018, patients with a follow-up of at least one year after either a total gastrectomy or an Ivor Lewis esophagectomy for GEJ or cardia carcinoma completed the EORTC QLQ-C30 and EORTC QLQ-OG25 questionnaires. Problems with eating, reflux and nausea and vomiting were chosen as the primary HR-QoL endpoints. The secondary endpoints were the remaining HR-QoL domains, postoperative complications and pathology results.

Results: 101 patients with a mean age of 63 years were included, 30 after gastrectomy and 71 after Ivor Lewis esophagectomy. The response rate was 80.2%. Median follow-up was two years (range 12-84 months). Pa-

tients after total gastrectomy reported significantly more problems with eating (p=0.028, 95% CI 0.595-10.137). Reflux and nausea and vomiting were not significantly different between the two groups. Of the remaining HR-QoL domains odynophagia was significantly worse in the total gastrectomy group (p=0.014, 95% CI 1.010-8.611). After Ivor Lewis esophagectomy patients reported significantly more insomnia, choking when swallowing and coughing (p=0.021, 95% CI -11.922 - -0.981; p=0.001, 95% CI -9.437 - -2.466; p=0.000, 95% CI -18.525 - -7.643). No significant difference was found in postoperative complications or Clavien-Dindo grade between the two groups. Significantly more lymph nodes were resected in esophagectomy group (p=0.008), however, no significant difference in number of positive lymph nodes or radicality of surgery was found.

Conclusion: In light of the scarce evidence about the difference in long-term HR-QoL in patients with GEJ or cardia carcinoma undergoing gastrectomy or esophagectomy, the results of our study contribute to the promotion of knowledge on this topic. After a follow-up of more than one year problems with eating and odynophagia were more common in the gastrectomy group and insomnia, choking when swallowing and coughing in the esophagectomy group. No significant difference was found in reflux, nausea and vomiting, postoperative complications or radicality of surgery. Based on this study it is difficult to determine which procedure for GEJ cancer is preferred.

Disclosure: Nothing to disclose

P0985 C-REACTIVE PROTEIN AS A PREDICTOR FOR ANASTOMOTIC LEAKAGE AFTER ESOPHAGEAL SURGERY

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Introduction: Anastomotic leakage following an esophageal resection for esophageal cancer is a severe complication, leading to more post-operative morbidity or even death. CRP is commonly used by surgeons to raise suspicion of anastomotic leakage and other infectious complications, but optimal cut-off values and diagnostic accuracy are undetermined.

Aims & Methods: The aim of this prospective observational cohort study was to determine the accuracy and optimal cut-off values of CRP to predict anastomotic leakage, and to determine if there is an association between the level of CRP and the severity of anastomotic leakage. Consecutive patients with an esophageal carcinoma scheduled for an esophagectomy with gastric tube reconstruction between April 2016 and October 2018 in the Amsterdam UMC, location AMC, The Netherlands were included. CRP was measured routinely on post-operative day (POD) 3, 5 and 7. Anastomotic leakage was assessed and severity was scored according to the ECCG classification. Anastomotic leakage was confirmed if a defect or leakage of oral contrast was seen on a CT-scan or by endoscopy or if saliva was draining form the neck incision. The diagnostic accuracy of CRP was assessed by receiver operator curve (ROC) analysis. Youden's index was adopted to determine the cut-off value in ROC analysis with highest sensitivity and specificity for predicting anastomotic leakage.

Results: 200 patients were included in this study. A cervical anastomosis was created in 25 patients, of which 7 (28.0%) developed anastomotic leakage. An intrathoracic anastomosis was created in 175 patients of which 17 (9.7%) patients developed anastomotic leakage. Median CRP levels in patients with and without anastomotic leakage were 99 and 188 mg/L on day 3, 62 and 154 mg/L on day 5, and 45 and 163 mg/L on day 7, respectively (p< 0.001 for all days). POD 5 showed the highest area under the ROC to predict anastomotic leakage with a cut-off value of 119.5 mg/L. Severity of anastomotic leakage and level of CRP did not significantly correlate with each other on postoperative day 3, 5 and 7 (p=0.204, p=0.092 and p=0.161 respectively). The optimal cut-off value for CRP to predict anastomotic leakage or any complication is shown per day in table 1 with the corresponding area under the ROC, sensitivity, specificity, positive predicting value and negative prediction value.

Conclusion: CRP on POD 5 has the highest diagnostic accuracy to predict anastomotic leakage, using a cut-off value of 119.5 mg/L, resulting in a negative predicting value of 96% and specificity of 92%. CRP is therefore a feasible marker to predict anastomotic leakage. However, larger studies should be conducted to confirm this finding, also taking other postoperative days into account.

	Cut-off value CRP (mg/L)[a]	AUCROC	P-value[1]	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Diagnostic values for prediction of any postoperative complication							
CRP POD-3	99.65	0.657	**0.000**	75	53	72	56
CRP POD-5	119.50	0.688	**0.000**	34	93	88	48
CRP POD-7	71.90	0.719	**0.000**	62	73	81	51
Diagnostic values for prediction of anastomotic leakage							
CRP POD-3	141.40	0.695	**0.004**	71	61	19	94
CRP POD-5	119.50	0.801	**0.000**	71	82	30	96
CRP POD-7	127.85	0.756	**0.001**	69	79	30	95

[a] Youden-index, [p1] Comparison between AUCROC and reference line, CRP = C-reactive protein, POD = postoperative day, NVW = negative predicting value, PVW = positive predicting value

[Table 1. Diagnostic values for CRP to detect postoperative complications]

Disclosure: Nothing to disclose

P0986 FACTORS ASSOCIATED WITH DELAYED GASTRIC EMPTYING IN PATIENTS UNDERWENT DISTAL GASTRECTOMY FOR GASTRIC CANCER: ARE THERE ANY PREDISPOSING GASTRIC MUCOSAL FACTORS?

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Introduction: Postoperative delayed gastric emptying is one of the most common problem in the early postoperative period after distal gastrectomy and may have effects on the early recovery after surgery.

Aims & Methods: We evaluated several clinicopathological features associated with delayed gastric emptying and the primary aim of this study was to investigate whether the preoperative endoscopic findings could be associated with postoperative delayed gastric emptying.

A total of 39 patients underwent distal gastrectomy for gastric cancer at Seoul Medical Center between August 2016 and December 2018 were collected and reviewed retrospectively. All patients underwent an esophagogastroduodenoscopy for preoperative evaluation and the results were reviewed by a single qualified gastroenterologist. The patients underwent either open or laparoscopic distal gastrectomy along with D2 lymphadenectomy by a single surgeon performed all surgical procedures. And the reconstructive procedure was selected based on the tumor location and surgeon's preference among four types of reconstruction methods. And all patients also underwent a gastric emptying SPECT/CT in the early postoperative period for evaluation of early alimentary limb leakage and remnant gastric motility. The relationship between delayed gastric emptying and clinicopathological factors was statistically analyzed.

Results: Among 39 patients, 26 (66.7%) patients showed delayed gastric emptying. An average T1/2 emptying time was 244min. Reflux esophagitis was endoscopically detected in 36 patients (92.3%). 35 patients (89.7%) had an atrophic gastritis and 13 patients (33.3%) infected with Helicobacter pylori. And Helicobacter pylori infection was associated with delayed gastric emptying (*p*=0.013). Reconstructive procedure was also associated with delayed gastric emptying (*p*=0.011). Billroth I reconstruction showed no stasis in comparison to the other reconstruction methods.

Conclusion: Helicobacter pylori infection and the type of reconstruction following distal gastrectomy seem to be associated with delayed gastric emptying after distal gastrectomy.

Disclosure: Nothing to disclose

P0987 THE INCIDENCE AND RISK FACTORS OF PANCREATITIS AFTER DUODENECTOMY IN FAMILIAL ADENOMATOUS POLYPOSIS

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Introduction: Duodenectomy is recommended in patients with Familial Adenomatous Polyposis (FAP) with Spigelman stage IV duodenal polyposis to prevent cancer. Pancreticoduodenectomy (PD) (both pylorus-sparing and classic), pancreas-sparing duodenectomy (PSD) and segmental duodenal resections are all surgical options. PD consists of removal of the head of the pancreas, common bile duct, and gallbladder along with the duodenum. The anastomosis in PD includes a hepaticojejunostomy and pancreaticojejunostomy. A PSD preserves the pancreas and includes anastomoses of the jejunum to the biliary-and-pancreatic-duct complex.

Aims & Methods: We aim to evaluate the incidence and risk factors for new onset pancreatitis in FAP patients after foregut surgery. We identified consecutive FAP patients following duodenal resection (PD, PSD, segmental duodenectomy) at Cleveland Clinic, between 05/1992 and 01/2018 from the David G. Jagelman Inherited Colon Cancer Registries. A history of pancreatitis preceding the surgery or those without follow-up data were excluded. Medical records were used to determine demographics and risk factors for pancreatitis. Pancreatitis was defined as 2 out of 3: i) typical symptoms ii) lipase three times the upper limit of normal or iii) radiography consistent with pancreatitis.

Results: 77 FAP patients (51.9% male) with duodenal resection were identified. 24 underwent PD, 10 segmental duodenectomy, and 43 PSD [Table 1]. 10/77 patients (13%) developed new onset, post-surgical pancreatitis. 7/10 who developed post-surgical pancreatitis had undergone PSD and the remainder PD [Table 2]. 2/10 developed pancreatitis perioperatively within 30 days and 8 developed pancreatitis >30 days after surgery (range: 2-19 years after surgery). 9/10 required hospitalization for pancreatitis (median BISAP score 0, indicating likelihood of mortality at < 1%). 1 death from pancreatitis occurred perioperatively (BISAP score 3). Of the 8 with non-perioperative pancreatitis, 5 developed acute recurrent pancreatitis (4 of whom underwent PSD) prior to endoscopic intervention. 6/8 required endoscopic retrograde cholangiopancreatography (ERCP) with balloon dilation for stenosis at the pancreaticojejunal (PJ) anastomosis (range: 1-2 ERCPs for successful treatment). ERCP was successful at dilating the stenosis in 5 of 6 cases. No patients had family history of pancreatitis or significant alcohol intake (>2 drinks/day males, >1 drink/day females). 4/10 had history of cholecystectomy, 1 remotely for gallstones and 3 during PD.

Conclusion: FAP patients may develop pancreatitis after duodenectomy. It usually occurs years after surgery and commonly due to stenosis at the PJ anastomosis which can lead to acute recurrent pancreatitis. Evaluation of the PJ anastomosis should be considered for patients that develop pancreatitis after duodenectomy to evaluate for stenosis.

Disclosure: Nothing to disclose

P0988 THE YIELD, EFFECTIVENESS AND SAFETY OF GASTROSCOPY IN MANAGEMENT OF EARLY POST-BARIATRIC SURGERY COMPLAINTS

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Introduction: Obesity is a worldwide epidemic affecting over 600 million individuals. There are several medical treatments for obesity, however, their efficacy are limited and most patients regain weight after losing it. Still standard bariatric surgery is the most effective method for sustained weight loss with a potential for resolution of over-weight associated comorbidities. Gastrointestinal symptoms are common in the early post-bariatric surgical period making gastroscopy is the main investigative tool.

Aims & Methods: The aim of our study was to assess the yield, effectiveness and safety of gastroscopy within 3-months post-bariatric surgery performed for investigating gastrointestinal symptoms. We performed a single retrospective study in EMMS Nazareth Hospital from 2010 to 2018. All patients who underwent gastric-bypass (either Roux-en-Y(R-en-Y) or Mini-gastric bypass (MGB)) and who had early gastrointestinal symptoms were included in the study.

Results: Four-hundred and twenty-eight (428) patients were included in the study. Among them, 154 patients (36%) underwent R-en-Y surgery and 274 patients (64%) underwent Mini-gastric bypass (MGB). Baseline characteristics were similar in the two groups. The mean age (years), male gender and the BMI were among the R-en-Y group compared to the MGB group were 42.3±10.8 vs. 42.8±11.2, 54.3% vs. 53.8% and 41.7±4.7 vs. 42.3±3.7, respectively (P=NS).

Overall, 39 (9.1%) patients from the all study cohort underwent gastroscopy due to upper gastrointestinal tract complaints during the first 3 months after surgery. Eighteen (11.6%) patients in the R-en-Y group, and 21 (7.6%) patients among the MGB group, P< 0.005.

The endoscopic findings showed normal surgical anatomy in 14 (35.8%) subjects; five patients (27.8%) in the R-en-Y group as compared to 9 patients (42.8%) among the MGB (P < 0.005). Erosive esophagitis with suspected bile reflux was documented in only one patient (5.5%) among the R-en-Y group as compared to 3 patients (14.2%) in the MGB group (P< 0.005). Notably, the upper gastrointestinal tract symptoms related gastroesophageal reflux disease (GERD) improved only in one patient (the only patient after R-en-Y), and persisted among all three patients after MGB, despite high dose proton pump inhibitors (PPI) for at least 6 months of follow-up.

Anastomotic stricture, marginal ulcer, functional obstruction due to non-absorbable sutures and gastro-gastric fistula were observed in 2,3,1,0 patients (11.1%, 16.7%, 5.5%, 0% respectively) among the R-en-Y patients and 2,2,1,1 patient (9.5%,9.5%,4.7%, 4.7% respectively) among the MGB group.

A single session of balloon dilation of the anastomotic stricture was successfully performed in all 4 patients (2 in each group) with symptomatic and endoscopic improvement; moreover, removal of surgical suture was successfully performed using endoscopic scissors in 2 patients (one in each group) also with complete resolution of patient's symptoms.

There were no procedural or sedation related complications reported during or after the gastroscopy among all patients who underwent gastroscopy.

Conclusion: Gastrointestinal symptoms in the early post-bariatric surgery are common with most endoscopic examination revealing normal surgical anatomy. Although gastroscopy is mostly normal in this setting in most patients, it is safe and potentially effective in treating these uncommon complications.

Disclosure: Nothing to disclose

P0989 ENDOSCOPIC "SUCTION CHAMBER" TO TREAT COMPLEX DUODENAL LEAKS AFTER UPPER GASTRO-INTESTINAL SURGERY: A SINGLE CENTER EXPERIENCE

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Introduction: Leaks from duodenal stump after upper gastrointestinal surgery are difficult to manage and usually require re-do surgery, since conservative treatments often fail.

Vacuum-assisted drainage has been already used in the endoscopic managementof colorectal, esophageal anastomotic leaks and duodenal perforations [1]. However, it has never been reported to treat leaks from duodenal stump.

The use of negative pressure decreases the intraluminal pressure involved in the leak formation, induce the collapse of the fistula wall associated with granulation tissue formation and draw fluids and secretions away, decreasing bacterial load.

Aims & Methods: Here we report our single-center experience on the endotherapy of duodenal stump leaks after upper gastrointestinal surgery using an innovative approach. Between January 2016 and December 2018, 5 consecutive patients (M:F 3:2, mean age: 43 y.o.) were referred to our unit for complex dehiscence of the duodenal stump. Previous upper-gastrointestinal surgery included 3 subtotal gastrectomy with Roux-en-Y reconstruction(two for gastric cancer, one for stab wounds); 1 subtotal gastrectomy with Braun reconstruction (gastric cancer after liver transplantation); 1 gastric bypass (for severe obesity).

All these patients underwent a re-do surgery that failed to repair the intestinal leak.

On the basis of our expertise in the treatment of post-surgical adverse events [2-3], the rationale to treat these patients was to create a "suction chamber" to the enteral lumen: a fully-covered self-expandable enteral metal stentwas inserted with the distal crown into the peritoneum through the duodenal leak.

Subsequently, the common bile duct and the main pancreatic duct were endoscopically drained inserting a biliary and a pancreatic stent through the meshes of the enteral stent. An aspirative large naso-duodenal tube, with the tip about 1-2 cm out of the enteral stent's distal crown was placed (creating the so called "suction chamber"). If present, the surgical drainage was pulled out about 3 cm away from the leak to favorite the peritoneal-enteral pressure gradient than the peritoneal-atmospheric one.

Results: Technical and clinical success rate were achieved in all the patients (5/5, 100%).

The mean duration of aspirative patency was 36 (23-103) days with a mean duration of hospital stay of 92 (47-273) days. An abdominal CT scan check was generally performed 2 days after the procedure (to verify the reduction of the intraperitoneal fluid collections) and 30 days after the procedure to decide to stop the aspiration through the naso-peritoneal tube. Abdominal drains were removed 15 (4-26) days after the procedure, after an additional CT scan check. Stent removal was scheduled at 6 months in all the patients. Mean follow-up was 26 (13-35) months: no mortality neither long-term adverse events related to the endoscopic procedures were reported.

Conclusion: Endotherapy of duodenal stump leak is feasible and effective in tertiary referral endoscopy centers with expertise in the management of post-surgical adverse events. Our "suction chamber" method offers the possibility to treat complex dehiscence especially if re-do surgery failed.

References: 1. Kuehn F, Loske G, Schiffmann L, Gock M, Klar E. Endoscopic vacuum therapy for various defects of the upper gastrointestinal tract. Surg Endosc. 2017; 31: 3449-3458. 2. Mutignani M, Dioscoridi L, Dokas S, Aseni P, Carnevali P, Forti E, Manta R, Sica M, Tringali A, Pugliese F. Endoscopic multiple metal stenting for the treatment of enteral leaks near the biliary orifice: a novel effective rescue procedure. World J Gastrointest Endosc. 2016; 8: 533-540. 3. Mutignani M, Dioscoridi L, Forti E, Pugliese F, Fontana P, Tringali A. "Yo-yo" stents to treat pancreatic leaks and fistulas after duodenopancreatectomy: a new effective endoscopic therapy. Dig Liver Dis. 2017; 62: 2648-2657.

Disclosure: Nothing to disclose

P0990 HEPATICO-JEJUNOSTOMY'S ANASTOMOTIC STRICTURE TREATED BY ENTERAL-ENTERAL ENDOSCOPIC BYPASS GUIDED ERC: A TERTIARY REFERRAL SINGLE CENTER EXPERIENCE

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Introduction: Since re-do surgery and interventional radiology are considered the first-line treatment for bilio-digestive anastomotic stricture, endoscopic treatment has been utilized as a minimally invasive alternative for management of these adverse event, with two critical issues:

1. Ability to reach the biliary anastomosis;

2. Perform an effective therapeutic procedure. Duodenoscope, gastroscope and pediatric colonoscope have all been used, with poor rate of biliary anastomosis achievement.

Enteroscopes (short, long, single- or double-balloon) [1] have also been utilized, with an overall technical success rate of about 76%. Finally, high success rate (around 90%) have also been described for the EUS-guided approach, which has a high morbidity (18%-50%) and mortality (1.5%) [2].

Aims & Methods: We proposed a totally endoscopic approach to improve the endotherapy of bilio-digestive anastomotic stricture.

From January 2014 to April 2019, 33 consecutive patients (mean age: 60 y.o.; M/F 20/13) affected by bilio-digestive anastomotic stricture treated by endoscopic enteral-enteral bypass (EEEB) and subsequent endoscopic retrograde cholangiography (ERC) were included in the present study. To reach the anastomotic site, an EEEB between the duodenal or gastric wall and the biliary jejunal loop using luminal apposing or biflanged metal stents under both fluoroscopic and endoscopic ultrasound's guidance was performed. This allowed the establishment of a short-way for therapeutic ERC procedures using large operative channel's endoscopes.

Results: EEEB was successful in 31 patients and therapeutical ERC was performed in all the 31 cases using multiple or single large-bore fully-covered self-expandable metal stenting (SEMS). We registered a 100% clinical success with a mean number of ERC sessions of 3. During a mean follow-up of 23 months (range: 1,5 - 59 months), two anastomotic stricture recurrences (6,4%) occurred, successfully re-treated through the EEEB. One case of post-ERC bleeding due to portal hypertension occurred and was treated conservatively. No long-term adverse events were observed.

If we briefly compare EEEB-guided ERC with other techniques, the radiological/percutaneous approach allows placement of SEMSs but not their removal, while enteroscopy does not permit use of large-bore SEMSs. In addition, selective cannulation of the bile duct with cholangiography is of paramount importance to characterized complex stenosis(es) and to drive subsequent endoscopic management. This can be only obtained by using the EEEB-guided ERC. Moreover, the EEEB allowed us to perform repeated treatments in patients with complex clinical situation or re-treat those with recurrence.

Conclusion: EEEB is safe, feasible, and allows a successful long-term treatment of different biliary adverse events in a tertiary referral centers with high-level experience in both ERCP and EUS.

In the setting of bilio-digestive anastomotic strictures, EEEB-guided ERC permits to use endoscopes with large operative channel to treat the stenosis(es) with large-bore SEMS, to manage case of complex strictures and multiple-ducts biliary anastomosis, to guarantee a long-lasting gradual dilation and to re-treat the patients in case of recurrence.

References: 1. Itokawa F, Itoi T, Ishii K, et al. Single- and double-ballon enteroscopy-assisted endoscopic retrograde cholangiopancreatography in patients with Roux-en-Y plus hepaticojejunostomy anastomosis and Whipple resection. Dig Endosc 2014; 26: 136-143. 2. Giovannini M, Bories E, Napoleon B, et al. 855 multicentric randomized phase II study: percutaneous biliary drainage vs EUS guided biliary drainage: results of the intermediate analysis. Gastrointest Endosc 2015; 81: AB174.

Disclosure: Nothing to disclose

P0991 PLAVAC - RETROSPECTIVE STUDY ON THE EVALUATION OF A "PLATZBAUCH" (ACUTE FASICAL DEHISCENCE) AND V.A.C. THERAPY

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Introduction: Acute fascial dehiscence (FD) is a feared complication after laparotomy. The incidence of FD is about 3.5%, 14 - 67 % of Patients (Pat) with FD died. Known causes for FD include: wound infection, premature mobilization, increased intraabdominal pressure. However, all studies in this field are outdated. Also, we do not know the context between Vakuum Assisted Closure (VAC)-Therapy and FD. In this paper, we aim to update the database about FD and to investigate a possible therapeutic effect of VAC Therapy on FD.

Aims & Methods: We analyzed all patients who were diagnosed with FD within the first 30 days after a laparotomy between July 2007 and August 2016, retrospectively. We analyzed 180 patients with a FD. We excluded 67 patients with a laparotomy previously within one year.

Results: 113 patient (73,5% male) occurred a FD on the 10th [2;30]day after laparotomy. The main reason for FD was a wound infection (38,9%) or a

high intraabdominal pressure because of an intestinal paralysis, ileus or ascites (20,3%). A lot of pat with a FD were operated in the primary operation with an emergency indication (38,9%). They got mostly a median laparotomy (77,9%) and were closed by continuous fascia suturing (61,1%). The Pat stayed extended 33 [9;120] days at hospital. 18 patients (15,9%) died during hospitalization. 20 patients (17,7%) had a second FD. We saw that Pat with a VAC-Therapy after first FD had a significant higher risk to get a second FD (p=0,041).

Conclusion: FD is serious complication and we show that VAC-Therapy has a negative influence to get a second FD, but it is to discus whether the VAC-Therapy is the problem or the associated wound infections. It hasto be investigated in future prospectiv studies.

Disclosure: Nothing to disclose

P0992 ENDOSCOPIC SUTURING IS FEASIBLE FOR TREATMENT OF LOW COLORECTAL ANASTOMOTIC LEAK - EXPERIMENTAL STUDY

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Introduction: Anastomotic leak after low anterior resection represents dreaded complication, which is associated with a significant mortality and affects both oncological and functional outcomes. OverStitch™ (Apollo Endosurgery) is an endoscopic suturing system now widely available for a variety of endoscopic procedures allowing to place full thickness sutures.

Aims & Methods: The aim of our study was to assess the feasibility of endoscopic repair of anastomotic leak on animal model. Secondary aim was to evaluate whether this technique prevents intraabdominal sepsis.

Model of low colorectal anastomotic leak was introduced in 28 male pigs. Laparoscopic low anterior resection was performed and the anastomosis created with 28 mm circular stapler after removing half of the staples.

Fourteen pigs had an endoscopic anastomotic repair with OverStitch™ 2 days later. A double-channel endoscope was introduced and defect closed with 2/0 prolene and secured with original knotless fixation. Three-grade scale (I - closed completely, II - closed with visible gaps, III - closure not possible) was used to assess the completion of closure. The signs of intraabdominal septic complications - IASC and anastomotic healing including burst test were assessed after animals being sacrificed on 9th postoperative day. Fourteen animals with no treatment were included in control group. Chi square test was used to compare both groups.

The protocol was approved by local ethical committee in accordance with the European Convention on Animal Protection. The study was supported by AZV 16-31806A, MO 1012.

Results: Endoscopic closure was technically possible in all 14 cases (gr. I - 11, gr. II - 3 and gr. III - 0) with mean procedure time of 31 (19-70) min. Two animals from suture group died due to peritonitis on 8th and 9th postoperative day. Overall IASC rate was however significantly lower compared to the control - 5/14 vs. 11/14 (p= 0,022). The autopsy confirmed healed anastomosis with no visible defect in 10/14 cases after endoscopic suturing and in 2/14 within control group (p=0,0023). The burst test performed in 10 healed OverStitch cases confirmed sufficient closure with mean pressure of 200 (80-300) mmHg.

Conclusion: OverStitch™ endoscopic suturing is technically feasible for repair of low colorectal anastomotic leak. This technique reduced the rate of intraabdominal septic complications.

Disclosure: Nothing to disclose

P0993 LONG TERM PERSISTENCE OF ANORECTAL DYSFUNCTION FOLLOWING SPHINCTER PRESERVING SURGERY FOR RECTAL CANCER: CORRELATION WITH BASELINE PHYSIOLOGY TESTING AND BIOFEEDBACK THERAPY

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Introduction: Rectal cancer is commonly treated by chemotherapy and radiation therapy, followed by anal sphincter-preserving surgery where possible, with a temporary protecting ileostomy. Low anterior resection syndrome (LARS) is a constellation of symptoms, commonly developing following stoma reversal, which includes faecal urgency, incontinence and difficulty emptying, severely affecting quality of life of cancer survivors. Scant data exists on the natural history of LARS, and specifically on the role of anorectal physiology testing and sphincter-strengthening oriented biofeedback therapy (BF) in predicting long term symptoms.

Aims & Methods: To evaluate long term outcomes of sphincter-preserving surgery and it's correlation to baseline anorectal physiology testing and BF. 75 consecutive patients (49 males, age 61 +-12 yrs) undergoing sphincter-preserving surgery were studied. 43 (57%) patients participated in long term follow up (median 4 years, range 1-11). Severity indexes and quality of life measures at long term follow up were recorded and analyzed in correlation to baseline clinical characteristics, anorectal physiological studies and BF treatment.

Results: : Baseline characteristics of the cohort are described in Table 1. On long term follow up, mean LARS score was 34 (SD 11), with 33 patients (86%) displaying severe LARS (scores>30). Mean faecal incontinence severity index was 30 (SD 19) and mean bowel frequency/day was 7 (SD 4). Mean FI-QOL was 2.2 (SD 0.9) and SF-36 total mean was 51 (SD 22).

Sixty-six (88%) patients underwent anorectal manometry (ARM), 30% of them before stoma closure. Anal resting and squeeze pressures were low in 67% and 23% of patients, respectively. Balloon expulsion time was abnormal in 42% of patients. 23 (30%) patients underwent BF treatment (mean of 4 meetings, range 1-16), 32% of them before stoma closure. Lower resting pressure showed a trend towards predicting higher LARS scores at follow up (p=0.055). BF therapy before or after stoma closure and absence of post-surgical complications were associated with higher (less) bodily pain scores on follow up SF36 (77 vs 48, respectively, p=0.006), but did not predict symptom severity scores.

Tumor distance from anal verge - mean, cm (SD)	6 (3)
Tumor Stage (T)	
0 or 1 n(%)	23(33%)
2- n(%)	25(33%)
3- n(%)	24(32%)
4- n(%)	1(1%)
Type of surgery	
Low anterior resection- n(%)	42(56%)
Colo-anal anastomosis- n(%)	33(44%)
Post-surgery complication (including pelvic abscess, anorectal fistula and strictures)- n(%)	22(32%)
Anorectal manometry (n=66)	
Anal resting pressure- mmHg; mean(SD)	57(34)
Anal squeezing pressure - mmHg; mean(SD)	152(72)
Anal relaxation on push maneuver - %- mean(SD)	16(23)
Recto-anal inhibitory reflex - absent- n(%)	32(51%)
First rectal sensation thresholds- mean, ml (SD)	42(23)
Defaecation urge sensation thresholds- mean, ml (SD)	62(29)
Maximal tolerated volume- mean, ml (SD)	83(32)

[Table 1. Baseline characteristics of patients undergoing sphincter-sparing surgery (n=75).]

Conclusion: Severe symptoms and impaired quality of life persist at a median of 4 years following sphincter preserving surgery. ARM might help predict symptom severity, and BF might slightly mitigate symptoms' impact

on quality of life. Nevertheless, improvement of current treatment options, including utilization of a more comprehensive anorectal BF protocol and/or sacral neuromodulation, is critically needed in this group of patients.
Disclosure: Nothing to disclose

P0994 AN INTERNATIONAL STUDY ON THE USE OF PER-ORAL ENDOSCOPIC MYOTOMY (POEM) IN THE MANAGEMENT OF ZENKER'S DIVERTICULUM (ZD)

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Introduction: Treatment options for Zenker's diverticulum (ZD) include open surgery, rigid endoscopy and flexible endoscopy. Clinical success is achieved in 80-90% of cases after endoscopic septotomy, however, adverse events (AEs) occur in 14% and, importantly, symptom recurrence in up to a third of patients. Recurrence is thought to be due to incomplete septotomy. A new technique using POEM for direct visualization/complete dissection of the septum has been described; however, outcomes of POEM for ZD (Z-POEM) are not known.

Aims & Methods: To study the technical feasibility, safety, and efficacy of Z-POEM in the management of ZD. This is a retrospective international study involving 10 centers (2 Asia, 2 Europe, 1 Mexico, 5 USA). Consecutive patients who underwent Z-POEM for ZD were included. Technical success is defined as successful completion of the Z-POEM. Clinical success is defined as complete/near complete resolution of dysphagia (Dakkak/Bennett score of 0 or 1) without the need for repeat endoscopic/surgical interventions. AEs were categorized/ rated per the ASGE lexicon.

Results: A total of 75 patients (73yr, F 33) were included with an average Charleson Comorbidity Index of 4. Eleven patients had prior treatment for ZD, which included open surgery in 5, dilation in 1, and flexible endoscopy in 5. The mean size of ZD was 31.29±1.63mm (10-89mm). Most common indications for Z-POEM were dysphagia (46%) and regurgitation (29%). General anesthesia was used for all cases. The technical success rate was 97.3% (73/75). Types of septotomy device used: hybrid knife (n=44), Triangle tip knife (n=12), standard Stag-beetle knife (n=7), IT-2 knife (n=7), Hook knife (n=2), IT-nano (n=1), both hybrid and Stag-beetle knife (n=2). The 2 technical failures were due to inability to locate the septum and failed tunnel creation (Table. 1).

AEs occurred in 6.7% (5/75): 1 bleed (mild) conservatively managed and 4 perforations (1 severe, 3 moderate). One severe perforation was a small contained perforation requiring ICU monitoring which subsequently self-resolved. Of the 3 moderate perforations, 2 were treated using cyanoacrylate glue and 1 was closed using clips. The mean procedure time was 52.4±2.9 min and mean length of hospital stay was 1.8±0.2d. Clinical success was achieved in 92% (69/75) with a decrease in mean dysphagia score from 1.87 to 0.25 (p< 0.0001). The median length of follow-up was 291.5 days (IQR=103.5-436). At 12-month follow-up, 1 patients reported symptom recurrence.

Conclusion: Endoscopic management of ZD using the POEM technique is novel and feasible with promising efficacy and safety results. Long-term follow-up is needed to ensure durability of response. In addition, comparative studies with other treatment modalities are warranted.
Disclosure: Nothing to disclose

	N=75
Clinical Success %(n)	92% (69)
Technical Success %(n)	97.3% (73)
Mean POEM procedure time (min) (mean, SD)	52.4, 2.9
Repeat Intervention	
Surgical intervention (n)	0
Endoscopic intervention (n)	1
Post-procedure F/U (median, IQR)	291.5 (IQR 103.5-436)
Days of hospitalization (mean, SD)	1.8, 0.2
Pre-procedure dysphagia score (mean, SD)	1.96, 0.68
Post-procedure dysphagia score (mean, SD)	0.25, 0.52

[Technical and clinical outcomes of Z-POEM]

P0995 WITHDRAWN

P0996 ENDOSCOPIC SUTURING FOR GASTROINTESTINAL APPLICATIONS: A MULTICENTER EUROPEAN REGISTRY

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Introduction: Endoscopic suturing is an alternative to surgical treatment for a broad spectrum of care, ranging from closure of mucosal or full thickness gastrointestinal tract defects to stent fixation to primary sleeve gastroplasty. A growing number of academic referral centers and community hospitals worldwide are performing endoscopic suturing procedures using the OverStitch Endoscopic Suturing System (Apollo Endosurgery Inc. Austin, Texas).

Aims & Methods: The aim of this registry is to collect demographic, procedural characteristics and follow-up outcomes of endoscopic suturing from multiple participating centers.

A retrospective analysis of a prospectively collected series of any patient who underwent an endoscopic suturing procedure using the OverStitch device for a gastrointestinal application from 6 European centers from January 2018 to April 2019 was performed.

This registry includes five main groups:
1. Closure of full thickness defects (post-operative leaks/anastomosis dehiscence, fistula closure, perforation)
2. Closure of mucosal defects (mucosal excision defects (EMR, ESD), enterotomies (e.g. EFTR), POEM/STER mucosal entry sites, ulcers)
3. Fixation of endoprosthetics
4. Gastrointestinal Bleeding
5. Other (GERD Cardioplasty, revision bariatric procedure, any other application of the endoscopic suturing device not listed above)

The data have been entered into a secure database by an identifier known only to the physician or his/her designee(s). All information in the database is de-identified prior to entry.

Results: To date, 67 patients (all Caucasian, male: 37; median age: 60.8 years) have been entered into the registry. Six European centers contributed to this first collection with a varying number of procedures from each center (max: 29; min: 1). The distribution of cases for each group is shown in Table 1.

Regardless of the procedure type, there were no cases of failure to introduce the device and advance it to the target area. Furthemore, suturing was technically achieved as intended in all 67 cases. In the group of closure of mucosal defects, follow-up has been reported for 7 patients (range: 90 days-1 year) with a 100% success rate. A mean of 1.9 running sutures were used. Patients who underwent fistula closure had a follow-up range of 30 to >90 days with a success rate of 77.8% (2 patients required repeated suturing; 2 patients have no follow-up data). All cases of perforation were successfully closed initially with a continued success rate of 92.9% in follow-up (range 30-90 days). Closure of post-op leaks performed in 7 patients, with a continued success rate of 80% in those with reported follow-up of 90 days or more (in 1 patient with a follow-up of 30 days the leak wasn't resolved; 2 patients have no follow-up data). Thirteen stents (located in the esophagus, stomach and duodenum) were fixed by suturing with success in 84.6% (11 of 13) cases (follow-up range 30 to 90 days; no follow-up data for 6 patients).

Conclusion: This data demonstrates safety and feasibility of endoscopic suturing for several GI indications. In our opinion, this European registry is a valuable tool to pool outcomes of endoscopic suturing cases and to address future research directions.

Disclosure: Nothing to disclose

GROUPS	PATIENTS
Closure Mucosal Defect	11 (16,4%)
GI Full Thickness Fistula	11 (16,4%)
GI Full Thickness Perforation	17 (25,3%)
GI Full Thickness Post-op Leak	7 (10,4%)
Fixation of Endoprosthetics	19 (28,3%)
Gastrointestinal Bleeding	0
Other	2 (3%)

[Table 1]

P0997 TREATMENT OF REFRACTORY HEPATIC ENCEPHALOPATHY DUE TO SPLENORENAL SHUNT IN LIVER CIRRHOSIS: OCCLUSION OR DIVERSION?

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Introduction: Hepatic encephalopathy (HE) encompasses a spectrum of neuropsychiatric abnormalities observed in patients with liver dysfunction, after the exclusion of other brain diseases. Significant portal-systemic shunts are closely linked to the development of portosystemic encephalopathy. An effective approach for treating this type HE is the occlusion of the large shunts. However, the shunts that exist in cirrhosis patients are a physiologic phenomenon that has evolved to compensate for the presence of portal hypertension.

As a result, occluding the shunt is likely to increase portal pressure and the risk of hemorrhage. It is therefore important to consider whether occlusion is the optimal treatment for portosystemic encephalopathy in cirrhosis patients.

Aims & Methods: To compare the efficacy of two methods of interventional therapy for the treatment of refractory hepatic encephalopathy (HE) due to a splenorenal shunt. Fifteen cirrhotic patients with refractory hepatic encephalopathy due to splenorenal shunt were studied. Either occlusion or diversion of the splenorenal shunt was undertaken to treat HE. The shunt was occluded by coils and tissue glue in the occlusion group. Selected embolization of the spleen vein was performed between the shunt and superior mesenteric vein in the diversion group.

Results: Occlusion was performed in 8 patients(occlusion group) and splenic vein embolization in 7 patients(diversion). Complete resolution of HE occurred in all 15 patients without recurrences during the follow-up. Improvement of Child-Pugh score was found in both methods. A weak trend toward a smaller increase in portal pressure change was observed in the diversion method.

Conclusion: Hepatic encephalopathy can be effectively treated with both diversion and occlusion interventional methods. The splenorenal shunt was reserved to relieve the portal pressure change by the diversion method, comparing to the occlusion method.

References: 1.Naeshiro, N., et al., Percutaneous transvenous embolization for portosystemic shunts associated with encephalopathy: Long-term outcomes in 14 patients. Hepatol Res, 2014. 44(7): p. 740-9. 2.Franzoni, L.C., et al., Embolization of splenorenal shunt associated to portal vein thrombosis and hepatic encephalopathy. World J. Gastroenterol., 2014. 20(42): p. 15910-5. 3.Inoue, M., et al., Splenic Vein Embolization Using Coil Anchors and Prophylactic Occlusion of a Hepatofugal Collateral for Hepatic Encephalopathy due to Splenorenal Shunt: Technical Note and Literature Review. Case Rep Radiol, 2013. 2013: p. 160653. 4.Zamora, C., et al., Portosplenic blood flow separation in a patient with portosystemic encephalopathy and a spontaneous splenorenal shunt. J Vasc Interv Radiol, 2004. 15(8): p. 875-9.

Disclosure: Nothing to disclose

P0998 EFFECTIVENESS OF ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) IN EARLY GASTROINTESTINAL NEOPLASIA THERAPY

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Introduction: Endoscopic submucosal dissection (ESD) is the therapeutic endoscopic method that allows en-bloc and radical (R0) resection of early gastrointestinal neoplasia. ESD is still a technically demanding method, which needs special training and has some risk of complications.

Aims & Methods: The main aim is to evaluate effectiveness of ESD and hybrid technique ESD / EMR (endoscopic mucosal resection) in the treatment of early gastrointestinal neoplasia in one tertiary endoscopic centre. Data from a retrospective registry of patients who underwent ESD and hybrid ESD/EMR from February 2015 to March 2019 were evaluated. Therapeutic results and performance related complications were analysed.

Results: A total of 43 ESD and ESD/EMR were analysed in 40 patients (mean age 64.5 years, 27 males). The lesion distribution was as follows: rectum (n = 30), sigmoid colon (n = 2), transverse colon (n = 1), oesophagus (n = 4) and stomach (n = 6). The mean lesion size was 30.9 mm (range 5-70 mm). En-bloc resection was achieved in 39 of 43 lesions (90.7%) and R0 resection was achieved in 35 of 39 en bloc resection (89.7%). 20 lesions (46.5%) were assessed as sessile polyps (type 0-Is according to Paris classification). The classic ESD technique was used in 32 lesions (74.4%; R0 resection in 28 lesions), hybrid technique (ESD/EMR) in 11 lesions (25.6%; R0 resection in 7 lesions). Perforation was observed in 16 cases (37.2%). However, all perforations were closed with an endoscopic method using hemoclips, in one case OVESCO clip was successfully applied. Only one delayed bleeding after ESD was observed, successfully resolved endoscopically. Surgical treatment was not necessary in any of these complications. The average inpatient time was 4.7 days (2-11 days). 24 patients (55.8%) were treated with antibiotics (Cephalosporins). Histological findings were as follows: 6 cancers (14.0%) with invasion to the upper third of submucosa (sm1), 4 intramucosal carcinomas (9.3%), 1 neuroendocrine tumours (2.3%), 1 gastrointestinal stromal tumour (2.3%), 12 adenomas with high grade dysplasia (27.9 %) and 13 adenomas with low grade dysplasia (30.2%). One patient underwent surgical resection for invasive T2 carcinoma. Follow up endoscopy was performed in 29 of 43 lesions (67.4%), all with negative findings.

Conclusion: Our analyses demonstrate that ESD and hybrid technique ESD/EMR are effective and safe therapeutic methods for radical resection (R0) of early gastrointestinal neoplasia. Periprocedural complications can be treated conservatively.

Disclosure: Nothing to disclose

P0999 PERORAL ENDOSCOPIC MYOTOMY AFTER OPERATIVE INTERVENTIONS ON THE GASTROESOPHAGEAL JUNCTION

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Introduction: Peroral endoscopic myotomy (POEM) may be a challenge in patients with previous interventions on the esophageal-gastric junction. The degree of fibrosis in submucosal space plays a key role in the feasibility and safety of tunnel technique.
Aims & Methods: To evaluate the safety of peroral endoscopic myotomy in patients previously operated on the esophageal-gastric junction.
Between July 2014 and May 2018, 123 patients underwent POEM in the Moscow Clinical Scientific Center, including 46 (37%) patients previously operated on the esophageal-gastric junction. The group of operated patients involved 41 (89%) patients after pneumatic balloon dilation, 3 (6.5%) patients after Heller myotomy, 1 (2%) patient after previous esophagogastroplication, 1 (2%) after POEM.
Results: The POEM procedure was successfully completed all patients. The mean operative was comparable in both groups: 106 min (55-195 min) in previously operated patients and 103 min (45-180 min) in naïve patients. F0 degree was detected in 14 (30%) cases, F1 in 29 (63%), maximal fibrosis (F2) in 3 (6.5%) patients who had previously undergone pneumatic balloon dilation. In patients after Heller's myotomy and esophagogastroplication, the degree of fibrosis reached F1, despite the expected more pronounced fibrosis. In the group of primary patients F0, the degree was detected in 27 (35%) observations, F1 - 46 (60%), severe fibrosis (F2) was detected in 4 (5%). There were no intraoperative complications affecting the tactics of surgical intervention in one observation. There were no major bleeding episodes requiring blood transfusion in either group. In one case in the group of previously operated patients, a mucosal defect was detected after the formation of the tunnel. The lesion was clipped.
The technical success of the surgical intervention was up to 100%. There were no intraoperative complications. X-ray examination on the 1st day after intervention with a water-soluble contrast showed appropriate evacuation and no leakage. Patients were discharged the 2nd day after surgery.
Conclusion: The history of failed previous surgical interventions is not a contraindication to the POEM procedure and does not significantly affect the course of surgical intervention.
Disclosure: Nothing to disclose

IBD II

09:00-17:00 / Poster Exhibition - Hall 7

P1000 *HELICOBACTER PYLORI* INFECTION PROTECTS AGAINST CHRONIC COLITIS BY REGULATING COLONIC EPITHELIAL BARRIER FUNCTIONS

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Introduction: Large epidemiological studies and meta-analyses have demonstrated an inverse association between Helicobacter pylori (H.pylori) infection and the risk of developing inflammatory bowel diseases (IBD). However, the mechanisms by which H.pylori infection protects against IBD are still unclear. Our previous published study has found that H.pylori infection can affect the Th17/Treg balance in colon. Here, we explored the possible protective effects and mechanisms of gastric H. pylori colonization on a chronic colitis model, with focus on whether H. pylori exerted its effects through regulating the barrier function of the colonic epithelial cells (CECs).
Aims & Methods: The aims of our study is to confirm that H.pylori infection exerts its protective effect on chronic colitis in mice by regulating the colonic epithelial barrier function. Chronic colitis model was induced by DSS treatment. To evaluate the severity of colitis, the body weight, rectal bleeding and stool consistency were observed to generate a disease activity index score (DAI). All mice were sacrificed at 45 days. H&E staining was performed for pathological scoring of both colitis. The colonic permeability

of mice was measured by fluorescein-isothiocyanate-dextran (FITC-Dextran) method. Immunohistochemical staining for BrdU was performed to evaluate the proliferative activity of colonic epithelial cells. The expression of apoptosis associated proteins (Cleaved-caspase-3, Bcl-2 and Bax) and necroptosis associated proteins (p-MLKL, RIPK1 and RIPK3) were determined by western blotting. Western blotting was also used to detect the expression of tight junction proteins (Occludin and Claudin3).
Results: H.pylori+DSS group exhibited significantly less weight loss and DAI score, and increased survival rate during the experiment when compared with DSS group ($P<0.05$). In accordance with the clinical data, the colon length in H.pylori+DSS group was longer than the DSS group (6.98±0.73cm vs. 8.09±0.45cm, $P<0.05$). H.pylori+DSS group had a significant decreased microscopic histological score compared to DSS group (7.17±0.75 vs. 4.5±0.97, $P<0.05$), suggesting that H.pylori infection might ameliorate the severity of chronic colitis in mouse model.
The intestinal permeability improved in H.pylori infected group compared with DSS-induced mice (1141±55.57 pg/ml vs 913.9±32.44 pg/ml, $P<0.05$). CECs proliferation determined by BrdU staining demonstrated that the proliferative activity was increased in H.pylori infected group (38.00±7.975 vs 135.3±13.56, $P<0.05$). The expressions of tight junction protein (Occludin and Claudin3) were enhanced in H.pylori infected group (0.15±0.08 vs 0.85±0.49, $P<0.05$ and 0.11±0.06 vs 0.67±0.13, $P<0.05$). The expression of cleaved-caspase 3 and the ratio of Bcl-2/Bax decreased significantly in H.pylori+DSS group (0.60±0.42 vs 0.38±0.28, $P<0.05$; 0.09±0.08 vs 1.43±0.65, $P<0.05$), suggesting that H.pylori infection might ameliorate the apoptosis of CECs.
Notably, Compared with DSS group, H.pylori infection inhibited the necroptosis associated proteins including RIPK1(0.76±0.12 vs 0.16±0.04, $P<0.05$), RIPK3 (0.94±0.19 vs 0.24±0.08, $P<0.05$) and p-MLKL (0.90±0.19 vs 0.06±0.02, $P<0.05$), suggesting that necroptosis inhibition might be involved in the protective effects against colonic inflammation.
Conclusion: H.pylori infection can attenuate the intestinal inflammation in DSS-induced mice, which may be due to improving intestinal mucosal barrier function by enhancing the expression of tight junction protein and inhibiting the apoptosis and necroptosis of colonic epithelial cells.
Disclosure: All authors have declared no conflicts of interest.

P1001 COMMENSAL FUNGI AND THEIR CELL-WALL β-GLUCANS DIRECT DIFFERENTIAL RESPONSES IN HUMAN INTESTINAL EPITHELIAL CELLS, SUGGESTING A MECHANISM FOR MUCOSAL TOLERANCE

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Introduction: Intestinal epithelial cells (IECs) are the first to encounter luminal antigens and play an active role in intestinal immune responses. Antibodies directed against fungal cell-wall glycans are associated with Crohn's disease (CD) and may represent loss of tolerance towards intestinal microorganisms. We previously reported that the receptor Dectin-1 and its major signaling mediator Syk are expressed in normal ileal and colonic IECs. Furthermore, the fungal cell-wall glycans β-glucans induced IL-8 and CCL2 secretion by IEC lines in a Dectin-1 and Syk dependent manner.
Aims & Methods: To address the mechanism of IECs response to fungi and fungal glycans.
Mucosal samples were obtained from healthy individuals and fungal recognizing C-type lectin receptors (CLRs) expression was assessed by immunofluorescence (IF). Mucosal explants and IEC lines (HT-29 and SW480) were stimulated with *Candida albicans* and *Saccharomyces cerevisiae* and the β-glucans zymosan and curdlan. Signaling was assessed by Western blot and IF. Chemokine secretion was assessed by ELISA.
Results: The CLRs Dectin-1, Dectin-2, DC-SIGN and Mincle were identified in ileal and colonic human mucosal samples as well as in IEC lines. Stimulation of mucosal explants and IEC lines with commensal fungal particles of live, heat-killed (HK)- or UV-inactivated wild-type *C. albicans*, as well as

HK- *S. cerevisia*e and β-glucans resulted in Syk phosphorylation. However, in IEC lines, β-glucans, but not fungal particles, induced phosphorylation of the MAP kinases JNK and p38 and the transcription factors c-JUN and NFκB p65.

Furthermore, only β-glucan stimulation induced the secretion of the pro-inflammatory chemokines Gro-α, GM-CSF, IL-8 and CCL2 (e.g. 13.5±0.4 vs. 0.35±0.005 ng/ml GRO-α in zymosan-treated vs. control HT-29 cells, respectively, p≤ 0.0001). β-glucan induced chemokine secretion was sensitive to Syk (R406) and JNK (SP600125) inhibitors (e.g. 79% and 57% inhibition of zymosan induced IL-8 secretion in SW480 cells, respectively) as well as to NFκB-p65 inhibition by BAY 11-7082 (e.g. up to 90% inhibition, p≤ 0.01, of curdlan induced IL-8 and Gro-α secretion from SW480 cells). Notably, β-glucan induced NFκB p65 phosphorylation was insensitive to Syk inhibition.

Finally, co-stimulation of IEC lines with β-glucans and HK *C. albicans* yielded a decrease in all tested chemokine secretion compared to stimulation with β-glucans alone (e.g. 27% inhibition, p≤0.01, of zymosan induced GRO-α secretion in HT-29 cells and 30% and 32% inhibition, p≤ 0.01, of curdlan and zymosan induced IL-8 and GRO-α secretion respectively, in SW480 cells).

Conclusion: CLRs expressed by IECs allow recognition of luminal fungi and their cell-wall glycans such as β-glucans. Epithelial response to β-glucans includes Syk-dependent activation of JNK, p38 and c-JUN, as well as a Syk-independent activation of NFκB p65. While Syk is activated, the lack of JNK, p38, c-JUN and NFκB p65 activation and chemokine secretion upon epithelial recognition of commensal fungi may reflect regulatory signals, resulting from CLRs response to other glycans expressed by intact fungi that contribute to mucosal tolerance. This is supported by the inhibitory effect of *C. albicans* on β-glucan-induced chemokine secretion. Skewed epithelial response to commensal fungi may impair homeostasis, lead to loss of tolerance and contribute to the pathogenesis of CD.

Disclosure: Nothing to disclose

P1002 TOOLS FOR PROTEASES/ANTI PROTEASES PROFILING IN THE GUT

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Introduction: Proteolytic activity in the intestine is detected both in the lumen and in tissues in physiological conditions. It is increased in both compartments in pathological situations such as Inflammatory Bowel Disease (IBD) and Irritable Bowel Syndrome (IBS). The increased activity can be due to an overexpression of proteases, to a decreased expression of natural endogenous protease inhibitors, or both.

Aims & Methods: Our objective was to identify the disease-associated proteases and their inhibitors that are present in the intestine. We therefore developed a number of tools for that aim. First, we developed fluorescent enzymatic assays and a range of substrates to detect proteolytic activity in human tissues and feces. Next, we revealed localization of enzymatic activity by *in situ* zymography from frozen tissue sections. We used serine protease-targeted activity-based probes (ABP) coupled with mass spectrometry analysis to identify active forms of proteases present within the gut tissues of healthy individuals, patients with gastrointestinal disorders as well as in naïve mice or in mouse models of gut inflammation. Expression levels of proteases and their related inhibitors were analysed by qPCR, immunostaining and western-blots using mouse and patient's tissues as well as 3D organoids cultures.

Results: We have identified different proteases such as a previously uncovered form of epithelial elastase, chymotrypsin as well as PRSS-1, 2 and 3 in gut tissues. Importantly, *in situ* zymography revealed that most of the proteolytic activity localised in the intestine originated from the epithelium. Some proteases and inhibitors had differential expression in IBD and IBS. Expression of proteases and inhibitors in epithelium were confirmed in patients' organoids culture.

Conclusion: Epithelial proteases and protease inhibitors appear as major actors of mucosal homeostasis. Their functional study highlights new possible therapeutic intervention for intestinal pathologies.
Disclosure: Nothing to disclose

P1003 PHARMACOKINETICS AND EXPOSURE-RESPONSE RELATIONSHIPS OF USTEKINUMAB IN PATIENTS WITH ULCERATIVE COLITIS: RESULTS FROM THE UNIFI INDUCTION AND MAINTENANCE STUDIES

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Introduction: Serum concentrations of monoclonal antibody-based biologics have been shown to correlate with their efficacy. PK, exposure-response (ER), and immunogenicity of ustekinumab (UST) were evaluated in UNIFI induction and maintenance studies in UC. Induction results were presented previously[1].

Aims & Methods: PK, immunogenicity, efficacy & safety data were obtained from two Phase 3, double-blind, PBO-controlled trials in adult patients (pts) with moderate-severe UC. These included 1 induction study which enrolled 961 pts (UNIFI). Patients enrolled in the induction study received a single IV infusion at Week 0 of PBO, UST 130 mg, or weight-range-based doses approximating 6 mg/kg UST (~ 6 mg/kg: 260 mg for pts ≤55 kg, 390 mg for pts >55 kg & ≤85 kg, & 520 mg for pts >85 kg). Responders to a single IV infusion of UST comprised the primary study population for the maintenance study (n=523) & were randomly assigned to receive SC UST 90 mg q12w, UST 90 mg q8w, or PBO. Blood samples were collected to measure serum UST concentration and antibodies to ustekinumab. Key efficacy outcomes were based on the Mayo score and inflammatory biomarkers (C-reactive protein [CRP] and fecal calprotectin [fCal]). Relationships between serum UST concentrations & efficacy, and the incidence of selected safety events of infections, serious infection & serious adverse events (SAE) were evaluated.

Results: Serum UST concentrations over time were dose proportional, unaffected by concomitant immunosuppressants, & similar between pts who were biologic failures & non-failures. Median peak serum UST concentrations in the induction study were 43.2 μg/mL & 127.0 μg/mL for the 130 mg & ~6 mg/kg dose groups, respectively. At induction week 8, median UST concentrations were 2.51 μg/mL & 8.59 μg/mL, respectively. Steady-state was reached by the start of the second SC maintenance dose (16 or 20 weeks from the IV induction dose for the q8w and q12w regimen respectively). Median steady-state trough serum UST concentrations over time in the UST q8w group (2.69 to 3.09 μg/mL) were 3-fold higher than in the q12w group (0.92 to 1.19 μg/mL). During induction & maintenance, serum UST concentrations were positively associated with the proportions of pts achieving response & remission, respectively (Table), and there was an inverse association between serum UST concentrations and CRP and fCal levels. No relationship was observed between serum UST concentrations & the incidence of infections, serious infections or SAEs during induction or maintenance treatment with UST. The incidence of antibodies to UST through 1 year using a drug-tolerant assay was 3.4% among those receiving UST maintenance vs. 9.1% in the PBO group; no impact of antibodies on efficacy was observed.

Conclusion: Serum UST concentrations were approximately dose-proportional. A positive E-R of serum UST with clinical efficacy measures and an inverse relationship with inflammatory markers was observed during UST IV induction & SC maintenance treatment. Adverse events including infections did not increase with increased serum UST concentrations at the doses evaluated in induction and maintenance. These findings are consistent with those in UST for Crohn's disease.

	Serum Ustekinumab Concentration (µg/mL)*/Proportion of Patients (%)			
Efficacy Outcome	1st Quartile	2nd Quartile	3rd Quartile	4th Quartile
Clinical Response at Induction Week 8	<2.2/41.2	2.2 to <3.9/47.7	3.9 to <8.8/61.1	≥8.8/74.2
Clinical Remission at Maintenance Week 44	<0.9/29.9	0.9 to <1.9/46.2	1.9 to <3.2/46.8	≥3.2/61.5

*Serum concentration quartiles based on ustekinumab concentration at Week 8 for the induction analysis, and average steady-state trough concentration for the maintenance analysis

[Table. Proportions of Patients Achieving Efficacy Endpoints by Serum Ustekinumab Concentration]

References: 1.Adedokun OJ, Xu Z, Marano C, O'Brien C, Szapary P, Zhang H, Johanns J, Leong R, Hisamatsu T, van Assche G, Danese S, Abreu MT, Sands BE, Sandborn WJ. Pharmacokinetics and Exposure-response Relationships of Intravenously Administered Ustekinumab during Induction Treatment in Patients with Ulcerative Colitis: Results from the UNIFI Induction Study. Poster presentation at: ECCO 2019; Copenhagen, Denmark.
Disclosure: Drs. , Leong, Hisamatsu, van Assche, Danese, Abreu, Sands, Sandborn are all investigators for Janssen Research & Development, LLC Drs. Adedokun, Xu, Marano, O'Brien, Szapary, Zhang, Johanns are all employees of Janssen Research & Development, LLC

P1004 COLONIC INFLAMMATION IN CROHN'S DISEASE INDUCES CHANGES IN GLUCOSE METABOLISM THROUGH MODULATION OF ENDOGENOUS INCRETIN SYSTEM

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Introduction: The role of incretin hormone, glucagon-like peptide (GLP-1), in Crohn's disease (CD) is still poorly understood. GLP-1 is secreted by intestinal L cells and decreases blood glucose levels. GLP-1 is rapidly degraded by dipeptidyl peptidase IV (DPP-IV), with a half-life of less than 2 minutes. CD patients may be at a greater risk of glucose metabolism disturbances due to overproduction of proinflammatory cytokines and excessive administration of diabetogenic drugs. We hypothesize that a possible mechanism of disturbances in glucose metabolism may be related to changes in the levels of incretin hormones due to inflammation.

Aims & Methods: The primary aim of this study was to investigate whether colitis is associated with changes in glucose metabolism. The secondary goal was to investigate potential involvement of incretin system as an underlaying factor.

To develop a chronic colonic inflammation mimicking CD in humans, mouse model of colitis induced by intracolonic administration of 2,4,6-trinitrobenzenesulfonic acid (TNBS) at dose 150 mg/kg at day 0 was used. On day 7 mice were sacrificed and macroscopic score as well as ulcer score were recorded. In all mouse experiments the expression of inflammation markers: tumor necrosis factor-α (TNF-α), IL-6 and IL-17 was determined.

The effect of colitis on glucose metabolism was studied by measurement of fasting glucose levels, as well as the GLP-1, DPP-IV, prohormone convertase 1/3 (PC 1/3) and GLP-1 receptor (GLP-1R) expression. Moreover, to translate results obtained in mice, we measured the level of GLP-1, DPP-IV and expression of PC 1/3 mRNA in serum (n=11-15) and colon samples (n=5-6) from healthy controls and CD patients.

Results: There were significant differences in macroscopic score, ulcer score in mice with colitis compared to control mice. TNF-α was significantly higher when compared to control mice, whereas IL-17 expression was decreased. No difference in expression of IL-6 was observed between groups.

Glucose levels in mice treated with TNBS were significantly higher in comparison to control group, what was associated with non-significantly lower level of GLP-1 and significantly higher level of DPP-IV in mouse serum. In mouse colon samples, GLP-1 levels were significantly lower whereas PC 1/3 expression, an enzyme involved in processing proglucagon into GLP-1 were significantly higher in mice with colitis compared to controls. No

change in DPP-IV was observed. Furthermore GLP-1R expression was non-significantly higher in mice treated with TNBS when compared to controls. In humans, GLP-1 and DPP-IV levels were significantly decreased in the serum of CD patients in comparison to healthy control subjects. Surprisingly, GLP-1 level was significantly increased in colon samples of the same cohort of CD sufferers, when compared to control samples. Furthermore, there was no significant reduction of PC 1/3 mRNA expression in CD group when compared to control group.

Conclusion: Changes in incretin hormone levels in response to colonic inflammation contributes to the impaired glucose metabolism. Our data suggest that targeting incretin system by GLP-1R agonists or DPP-IV inhibitors may become a novel therapeutic option in the treatment of CD with both anti-inflammatory and anti-diabetic effect.

Disclosure: Nothing to disclose

P1005 A SYSTEMATIC REVIEW AND NOVEL CLASSIFICATION SYSTEM TO DEFINE DEEP REMISSION

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Introduction: Current therapeutic goals for inflammatory bowel disease (IBD) focus on symptomatic response, but many patients experience disease progression. There has been a movement towards tighter control of IBD, defined as deep remission. Achieving deep remission could lead to lower rates of complications, surgical interventions, and hospital visits. No consensus definition currently exists for deep remission, although clinical, endoscopic, and biochemical remissions are all components that have been proposed in the definition. We systematically reviewed the different variations of deep remission and created a classification system to provide uniformity when discussing deep remission among clinicians.

Aims & Methods: We performed a systematic review using the search terms ("inflammatory bowel disease" OR "IBD" OR "crohn*" OR "CD" OR "ulcerative colitis" OR "UC" OR "colitis") AND ("mucosal healing" OR "deep remission" OR "complete remission" OR "full remission" OR "endoscopic remission") in Pubmed and EMBASE on October 1, 2018. 7,514 articles and abstracts were identified. Two authors independently reviewed the publications which defined deep remission. Publications which included pediatric patients or were published in foreign language were excluded. A total of 37 peer-reviewed publications that defined deep remission were included. A classification system for deep remission was created based on the variety of definitions.

Results: There were 9 different definitions of deep remission in the 37 publications, involving combinations of the following remission variables: clinical, endoscopic, biochemical, histologic, radiographic, or immunologic. The majority of definitions, 21/37 (56.7%), only included clinical and endoscopic remissions as part of deep remission. The remaining definitions for deep remission were as follows: 4/37 (10.8%) with clinical, endoscopic, and biochemical remissions; 4/37 (10.8%) with endoscopic and histological remissions; 3/37 (8.1%) with clinical, endoscopic and histologic remissions; 1/37 (2.7%) with clinical, endoscopic, histologic, and biochemical remissions; 1/37 (2.7%) with clinical and radiographic remissions; 1/37 (2.7%) with histological remission, 1/37 (2.7%) with endoscopic and biochemical remissions, and 1/37 (27%) with immunologic and histologic remissions.

Conclusion: Given there is no consensus definition for deep remission, we propose a classification system to simplify the combinations of remission variables recognized as definitions of deep remission. Our system recognizes the most common definition of deep remission, clinical and endoscopic remission, as DR-A. However, the system allows for the flexibility of alternate definitions encompassing other remission variables. This is important as clinical treatment goals transition to tighter disease control, and physicians focus on different indicators of remission such as histologic or radiographic evidence. Future studies will likely assess greater numbers of remission variables to ensure complete dormancy of underlying inflammation in IBD patients. That transition is best represented in our classification system by DR-E. Our classification system is a stepping stone towards providing clarity amongst clinicians in discussions involving deep remission.

Disclosure: Nothing to disclose

Type of Deep Remission	Definition
Deep Remission A (DR-A)	Clinical Remission + Endoscopic Remission
Deep Remission B (DR-B)	Clinical Remission + Other Remission Variable (but not Endoscopic Remission)
Deep Remission C (DR-C)	Endoscopic Remission + Other Remission Variable (but not Clinical Remission)
Deep Remission D (DR-D)	2 Remission Variables (but not Clinical nor Endoscopic Remission)
Deep Remission E (DR-E)	>2 Remission Variables (any combination)
Remission Variables	Clinical, Endoscopic, Biochemical, Histological, Radiographic, Immunologic, or other remission types

[Deep Remission Classification System]

P1006 C86/CD16 POSITIVE CELLS ACCUMULATE IN THE MUCOSA OF B3-PATIENTS AND COULD MEDIATE EMT IN CROHN'S DISEASE

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Introduction: Macrophages contribute to fibrosis through the release of different mediators and the pattern of secretion may vary according to their phenotype.

Aims & Methods: The aim of the present study is to analyze the pattern of expression of macrophages, the expression of EMT related genes and cytokines in surgical resections from Crohn's disease (CD, n=43) patients which were categorized according to Montreal classification (B2 or B3); unaffected mucosa of patients with colorectal cancer was used as control (n=20). mRNA was isolated from intestinal samples and the expression of macrophage and EMT markers and cytokines were analyzed by RT-PCR. PBMCS were isolated from healthy donors and treated during 5 days with secretomes, from control, B2 or B3 surgical resections; the mRNA expression of macrophage markers were determined by RT-PCR. Results are expressed as mean±SEM (n≥5). Statistical analysis was performed by ANOVA + Newman-Keuls test. Correlations between data were analysed using Pearson's correlation coefficient (*p < 0.05).

Results: The expression of CD16 and CD86 was significantly higher in intestinal samples from B3 CD patients (7,2 ±1,1 and 7,7±1,3, respectively) than in controls (1,4±0,2 and 2,5±0,4, respectively) or B2 CD patients (4,8±0,9 and 4,5±0,6, respectively). The mRNA expression of CD16 and CD86 were significantly higher in PBMCS treated with B3-secretomes than in those treated with B2- or control secretomes. The expression of CD16 and CD86 significantly correlated with FSP1 (r=0.74, P=0.002* and r=0.66, P=0.003*, respectively), VIMENTIN (r=0.60, P=0.02* and r=0.82, P=0.001*, respectively), SNAIL1 (r=0.61, P< 0.01* r=0.52, P=0.04*, respectively), IL4 (r=0.63, P=0.01* and r=0.60, P=0.02*, respectively) and IFNγ (r=0.56, P=0.001* and r=0.58, P=0.01*, respectively) in intestinal tissue from the fistulizing CD group.

Conclusion: A macrophage phenotype expressing CD86/CD16 may act as a source of EMT mediators in intestinal tissue from CD patients with a penetrating (B3) behavior. IL4 and IFNγ could be responsible for the increase in the number of CD86/CD16 macrophages in the B3 behavior.

Disclosure: Nothing to disclose

P1007 CORRELATION OF THE BIOLOGICAL ACTIVITY RELATED TO STEROID-REFRACTORINESS IN ULCERATIVE COLITIS BETWEEN COLONIC TISSUE AND PLASMA

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Introduction: The steroid-refractoriness is a common complication of ulcerative colitis (UC), which appears unpredictably. Several mechanism of action (MoA) has been implicated in corticosteroid (CS) failure, however, there are no conclusive studies on the molecular functions involved in it. Therefore, ourgroup used rectal biopsies from patients with active UC and different response to CS treatment to generate a predictive computational strategy based on Biology of Systems. Combining mRNA and miRNAs intestinal expression profiles with updated molecular information related to UC and CS, we were able to identify a MoA associated with steroid-refractoriness in UC[1].

Aims & Methods: In order to transfer these results to clinical practice, we tried to explore the reflection of the biological activity of the intestinal mucosa into the plasma of these patients.
RNA-seq (Illumina, USA)-assessed plasmatic miRNAs (pmiRNAs) were statistical compared between responders and non-responders CS patients. Differential pmiRNAs between both groups of patients and their target proteins were identified. The resulting molecular data were compared with our previous intestinal mucosal results, following statistical approaches:
a) pmiRNAs vsbiopsy differential miRNAs (bmiRNAs);
b) Target proteins of pmiRNAs vs. those of the bmiRNAs;
c) Target proteins of pmiRNAs vs.proteins encoded by mucosal mRNA differentials; and
d) Target proteins of pmiRNAs vs. key proteins linked to steroid-refractoriness MoA.

Results: Four of the pmiRNA differentially expressed (miR-194-5p, miR-145-5p, miR-216a-5p and miR-224-5p) were related to biopsies findings, either sharing the same protein target with the differential bmiRNA or linked to MoA key proteins. Interestingly, the miR-145-5p targeted directly VEGF-alpha (a down-regulated MoA-protein in responder's patients1) and CDK4, an over-expressed protein at mRNA level in non-responder's patients; while miR-224-5p targeted CXCR4 (over-expressed mRNA in non-responder group) and NCOA6 (glucocorticoid receptor co-activator). Finally, another one pmiRNA (hsa-miR-487a-3p) showed differences between patients in both tissues (intestinal mucosa and plasma), over-expressed in intestinal biopsies and suppressed in plasma of non-responder's patients

Conclusion: In conclusion, there is a biological steroid-refractoriness-MoA reflection from the intestinal mucosa to the plasma in patients with UC, which making up interesting molecules (miRNAs and proteins) as possible biomarkers or therapeutic targets to improve CS response

References: 1. Lorén V., et al. ANP32E, a Protein Involved in Steroid-Refractoriness in Ulcerative Colitis, Identified by a Systems Biology Approach. Journal of Crohn's and Colitis, 2019.

Disclosure: Nothing to disclose

P1008 EFFECTS OF USTEKINUMAB MAINTENANCE THERAPY ON ENDOSCOPIC IMPROVEMENT AND HISTOLOGIC IMPROVEMENT IN THE UNIFI PHASE 3 STUDY IN ULCERATIVE COLITIS

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Introduction: Ustekinumab is an effective therapy for moderate-to-severe ulcerative colitis (UC),[1,2] but its effects on mucosal healing (endoscopic improvement + histologic improvement) during maintenance treatment are unknown.

Aims & Methods: We evaluated the effects of maintenance ustekinumab on histologic and endoscopic activity in the UNIFI Phase 3 study of ustekinumab in moderate-to-severe UC (n=961). Subjects in response 8 weeks after receiving intravenous ustekinumab were randomized to receive maintenance treatment with subcutaneous (SC) placebo or ustekinumab 90 mg every 8 (q8w) or 12 weeks (q12w). Two colonic biopsies were collected from the distal colon at screening and Weeks 0 and 44 of maintenance. Endoscopic improvement (EI) was defined as a Mayo endoscopy subscore ≤ 1; histologic improvement (HI) comprised the following Geboes score-based criteria: absence of erosions or ulcerations, absence of crypt destruction, and < 5% of crypts with neutrophil infiltration. To encompass both macro- and microscopic scales, histo-endoscopic mucosal healing (MH) was defined as achieving both EI and HI.

Results: At maintenance Week 44, EI was achieved in 28.6%, 43.6%, and 51.1% of subjects treated with placebo, ustekinumab q12w (p=0.002 vs placebo), and ustekinumab q8w (p< 0.001), respectively. HI was achieved at Week 44 in 32.9%, 54.0%, and 59.3% of subjects treated with placebo, ustekinumab q12w, and ustekinumab q8w, respectively (p< 0.001 for both q12w and q8w). MH was achieved at Week 44 in 24.1%, 38.8%, and 45.9% of subjects treated with placebo, ustekinumab q12w (p=0.002), and ustekinumab q8w (p,0.001), respectively. HI at Week 44 (irrespective of maintenance treatment) was significantly associated with EI and MH (p< 0.001) and with both lower absolute levels and larger post-treatment changes in total Mayo score, partial Mayo score, and Mayo symptom subscores for stool frequency and rectal bleeding at Week 44. Both EI and HI following 8 weeks of ustekinumab treatment were associated with clinical remission and steroid-free clinical remission at Week 44 (p< 0.05), as well as remission through Week 44 (i.e. at both Week 8 and Week 44). For example, 26% of subjects with induction HI were in clinical remission through Week 44, versus 4% of subjects without induction HI. Induction MH was similarly associated with positive outcomes at maintenance Week 44.

Conclusion: Among subjects with moderately-to-severely active UC, those receiving SC ustekinumab maintenance had higher rates of EI, HI, and MH than those receiving placebo. Both EI and HI are associated with subsequent clinical remission and steroid-free clinical remission.

Clinical Outcomes	Histologic Improvement[a]	Without Histologic Improvement[a]	p-value[b]
Week 44	N=140	N=124	
Endoscopic Improvement	62%	47%	<0.02
Mucosal Healing	59%	43%	<0.02
Clinical Remission	54%	40%	<0.02
Steroid-free Clinical Remission	52%	39%	<0.04
Week 8 AND Week 44			
Endoscopic Improvement	31%	6%	<0.0001
Mucosal Healing	40%	0%	<0.0001
Clinical Remission	26%	4%	<0.0001

a: Values are reported as mean ± SD.
b: P-values based on t-test.

[Proportions of Pts with or without Histologic Improvement at Wk8 Who Achieved Positive Clinical Outcomes at Wk44 in UNIFI Phase 3 Maintenance Study]

References: 1.BE Sands, et al. Safety and Efficacy of Ustekinumab Induction Therapy in Patients with Moderate to Severe Ulcerative Colitis: Results from the Phase 3 UNIFI Study. Presented at ACG 2018, October 9, 2018, Philadelphia, PA
2.WJ Sandborn, et al. Efficacy and Safety of Ustekinumab as Maintenance Therapy in Ulcerative Colitis: Week 44 Results from UNIFI. Presented at ECCO 2019, March 9, 2019, Copenhagen, Denmark..
Disclosure: Drs. Li, Friedman, Marano, Zhang, and Yang are all employees of Janssen Research & Development, LLC Drs. Sandborn, Sands, Feagan, Peyrin-Biroulet,and De Hertogh are all investigators for Janssen Research & Development, LLC

P1009 IN VITRO INHIBITION OF ENDOPLASMIC RETICULUM STRESS IN PATIENTS WITH CROHN'S DISEASE

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Introduction: Endoplasmic reticulum (ER) is responsible for the synthesis and processing of secretory and membrane proteins. The stress state of the endoplasmic reticulum (ERS) occurs due to the inability of certain proteins to adopt the appropriate conformation stage, thus leaving them unfolfed within the ER. The accumulation of unfolded proteins is detrimental to the cell, which may respond by driving the proteins to degradation, pausing the transcription process or even initiating apoptosis[1]. Gene association and meta-analysis studies show that ERS possibly correlates with the pathogenesis of Crohn's disease (CD)[2].

Aims & Methods: Our aim was to investigate the occurrence of ERS in the intestinal mucosa of patients with CD, and to evaluate the effect of a chemical inhibitor on its activation and modulation of pro-inflammatory cytokines. Biopsies of intestinal mucosa were collected by colonoscopy from patients with CD (CD group) and patients who did not present inflammatory bowel diseases (control group).
Cell culture was performed to evaluate the ERS and its potential resolution with chemical inhibitor. Non-parametric tests were performed for statistical analysis, with p < 0.05. The study was approved by the Research Ethics Committee.

Results: Samples were collected from 10 patients with active CD (CDEIS≥5) and 6 control patients. After cell culture, a significant difference was observed in the activation of the main ERS pathways in the CD group. A modulation in the expression of pro-inflammatory cytokines was also observed after the treatment. Treatment with a chemical inhibitor also led to a significant decrease in the expression of the genes responsible for the activation of ERS pathways and to a decrease in the main inflammatory cytokines present in CD.

Conclusion: The activation of the main ERS pathways suggests a role in the maintenance of the inflammatory process in CD. The use of a chemical inhibitor has been shown to be effective in significantly decreasing the activation of ERS and to modulate the inflammation in CD.

References: 1) Hotamisligil G.S. (2010) Endoplasmic reticulum stress and the inflammatory basis of metabolic disease. Cell 140, 900-917 2) Hoefkens E, Nys K, John JM et al., Autophagy. 2013 Dec;9(12):2046-55.
Disclosure: Nothing to disclose

P1010 PRESENCE OF ANXIETY AND DEPRESSION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE IN ALBANIA

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Introduction: The presence of anxiety and depression is higher in patients with chronic diseases compared to the general population. A long term medical illness may become a risk factor for depression. There is important evidence that inflammatory bowel disease (IBD), which includes Crohn's disease (CD) and ulcerative colitis (UC), is associated with higher rates of

anxiety and depression compared to the general population[1]. Despite this knowledge, IBD patients are not routinely screened for depression and anxiety.

Aims & Methods: The aim of our study was to show the prevalence of anxiety and depression in IBD patients in Albania and also to evaluate its correlation with the disease severity.This is a prospective study of IBD patients, followed-up in a 2 year period, at the University Hospital Mother Theresa, in Tirana, which represents the largest in and outpatient facility in Albania. The presence of anxiety and/or depression was determined using the Hospital Anxiety and Depression Scale[2], compiled under the explanations and supervision of medical staff. Patients with known mental illness followed by Psychiatry were excluded. Patient demographics, disease characteristics and medication information were collected. Multivariable analysis was used to determine associations between patient characteristics and depression and/or anxiety. Statistical analysis was made with Chi-square (p-value, significance level: 0.05).

Results: We have followed 46 IBD patients (26 F : 20 M), on treatment with anti-TNF since July 2016. Of these, there were 9 patients (19%) with Crohn's disease and 37 patients (81%) with Ulcerative Colitis. 16 patients (34%) were under treatment with Adalimumab and 30 patients (66%) were under treatment with Infliximab.Among these 46 IBD patients, there were 18.7% with depression and 34.3% with anxiety, wih a rate of 40.6% of patients suffering from depression and/or anxiety. Females were more likely to have anxiety with a significantly rate of 63% compared to males: 27%. Ulcerative colitis patients were also more likely to have depression and/or anxiety (84.6%) than Crohn's disease patients (15.4%). Disease activity calculated by Mayo score (for UC) and CDAI score (for CD), was found to be significantly associated with depression and/or anxiety. Correlation coefficient (r) between depression and disease activity was: ‑ 0.314, while for anxiety, it was calculated: -0.298 (p values respectively: 0.03 and 0.04).

Conclusion: A significant number of patients with IBD, suffer from depression and/or anxiety and this has an important impact on their quality of life. Patients with a severe disease activity are at a higher risk for anxiety and depression and this may suggest that it can be important to start screeningall the IBD patients with this questionnaire in order to evaluate them and eventually refer them to the psychiatrists.

References: 1. Graff L. A., Walker J. R., Bernstein C. N. Depression and anxiety in iflammatory bowel disease: a review of comorbidity and management. Inflammatory Bowel Diseases. 2009;15(7):1105-1118. 2. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand 1983;67:361-370.

Disclosure: Nothing to disclose

P1011 METABONOMIC CHARACTERISATION OF AXIAL SPONDYLOARTHRITIS ASSOCIATED WITH IBD

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Introduction: Prevalence of axial spondyloarthritis in inflammatory bowel disease (axSpA-IBD) is up to 25 times higher than in the normal population, and there is some evidence to suggest that different forms run different courses. In addition, the very strong association with HLA-B*27 seen in axial spondyloarthritis not associated with IBD (axSpA-not IBD) is much weaker in axSpA-IBD. This difference leads us to conclude that environmental factors, particularly the *milieu* (microbiome, metabonome and inflammatory status) in the gut lumen may be important in defining the course of disease. Establishing axSpA- IBD from axSpA-not IBD is important for both management and prognostic reasons. Here we present initial analysis from proton high-resolution nuclear magnetic resonance (1H-NMR) spectroscopy, profiling human serum, urine and stool to test the hypothesis that metabolites differ between ax-SpA-IBD, ax-SpA-not IBD, psoriatic peripheral arthritis (PsA) and control cohorts (HC). We have used multivariate statistics analysis to find distinct metabolic signatures across the cohorts.

Aims & Methods: 1H-NMR spectra were acquired from serum, urine and stool samples of 71 patients (23 ax-SpA- not IBD, 15 ax-SpA-IBD, 16 PsA and 17 HC) in a Bruker 600 MHz NMR spectrometer, following Bruker SOP pro-

tocols. Multivariate analysis of all NMR features involved principal components analysis (PCA) and orthogonal partial least squares discriminant analysis (OPLS-DA). NMR resonances for assigned metabolites influenced by gut microbiota were compared using Mann-Whitney U test.

Results: PCA revealed clustering of the groups; OPLS-DA modeling in stool metabolites was able to distinguish between ax-SpA- not IBD and ax-SpA-IBD cohorts (Q2Y 0.468, p-values for 1,000 random permutations: pR2Y= 0.102 and pQ2Y= 0.002). In this initial analysis, there was no differentiation between cohorts in urine and serum.

Conclusion: (1)H NMR-based metabolic profiling is able to distinguish between ax-SpA- IBD and ax-SpA- not IBD in stool. Further modeling of urine and serum metabolic profiles will be undertaken to examine whether the differences in stool are reflected in other biofluids as well as deeper analysis specific metabolites.

References: Asquith, M et al. The role of the gut and microbes in the pathogenesis of spondyloarthritis. Best Pract Res Clin Rheumatol. 2014 Oct;28(5):687-702. Orchard, TR et al. The prevalence, clinical features and association of HLA-B27 in sacroiliitis associated with established Crohn's disease. Aliment Pharmacol Ther. 2009 Jan;29(2):193-7. Williams HR et al. Characterization of inflammatory bowel disease with urinary metabolic profiling. Am J Gastroenterol. 2009 Jun;104(6):1435-44. Hicks LC et al. Metabonomics and diagnostics. Methods Mol Biol. 2015;1277:233-44.

Disclosure: Nothing to disclose

P1012 THE JAK INHIBITOR-TOFACITINIB INHIBITS SIGNALING PATHWAYS *EX-VIVO* AND HAS FUNCTIONAL IMPLICATIONS IN HUMAN INTESTINAL MUCOSA

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Introduction: Tofacitinib, an orally administered pan-Janus kinase (JAK) inhibitor modulating the JAK-STAT (signal transducers and activators of transcription) signaling pathway, is used for the treatment of patients with ulcerative colitis (UC). Tofacitinib effects in the intestinal mucosa are still elusive.

Aims & Methods: To identify tofacitinib effects in human intestinal mucosa and to decipher whether discordant responses occur in the normal or inflamed mucosa of patients with UC or Crohn's disease (CD).

Human mucosal explants were obtained from patients with inflammatory bowel disease (IBD) and normal controls. Phosphorylated STAT (p-STAT) levels were assessed using Western blot and Immunofluorescence. Lamina propria lymphocytes were isolated from explants and stimulated with anti-CD3/CD28 beads in the presence or absence of tofacitinib for 3 days. Cytokine production by CD3+ T cells and cell viability were assessed by flow cytometry. T_{84} intestinal epithelial cell (IEC) lines were cultured on transwells for 12-14 days to generate epithelial barrier, measured as transepithelial electrical resistance (TEER), and stimulated with IL-13 basolaterally in the presence or absence of tofacitinib for 24h. Permeability was assessed by TEER measurements and Claudin-2 (CLDN2) gene expression, assessed using RT-PCR.

Results: Mucosal explants were obtained from 11 subjects (7 controls, 4 CD). p-STAT1 and p-STAT3 expression was located mainly in the lamina propria and was higher in explants with active inflammation compared to normal controls. A dose-dependent decrease in p-STAT1 and p-STAT3 expression in response to tofacitinib was observed compared to non-treated (NT) mucosa. Normal controls and explants obtained from areas with active inflammation responded similarly. Interestingly, significantly more potent inhibitory effect on STAT1 compared to STAT3 phosphorylation was observed (100nM tofacitinib compared to NT, $p< 0.0023$).

Moreover, upon tofacitinib treatment, CD3+ IL4+ and CD3+ IFN-γ+ cells, isolated from normal and explants with active inflammation, were decreased in a dose-dependent manner (35.5% and 37.5% without tofacitinib; 20.1% and 25% with 10nM; 11.6% and14.5% with 100nM tofacitinib, respectively). No significant effect on IL-17 production by T cells or on T cells mortality

was observed. In T_{84} cells, tofacitinib prevented IL-13-induced decrease in TEER and increase CLDN2 expression in a dose dependent-manner ($p<$ 0.001 and $p< 0.0054$, respectively; n=3).

Conclusion: Tofacitinib was a more potent inhibitor of specific p-STAT in the intestinal mucosa of both normal controls and patients with IBD. Inflamed mucosal explants from patients with CD responded to tofacitinib by inhibiting JAK-STAT signaling pathway and cytokine secretion by intestinal lymphocytes. Furthermore, tofacitinib ameliorated epithelial barrier disruption induced by IL-13. Thus, beneficial effects are expected in CD. *Ex-vivo* examination of drug effects in the intestinal mucosa may be used as a tool for evaluation of treatment effects.

Disclosure: The study is an investigator-initiated research funded by Pfizer

P1013 SELF-ASSEMBLING PEPTIDE HYDROGEL ENHANCES INTESTINAL BARRIER FUNCTION IN TOPICAL TNBS MODEL IN RATS

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Introduction: Inflammatory bowel disease (IBD) often forms intractable ulcers. Self-assembling peptide hydrogel (SAPH, PuraMatrix™, 3D Matrix Co., Ltd., Tokyo) is composed of only amino acids present in the living organisms; its forms nanofibers with a diameter of 10 nm and forms a gel when it comes in contact with blood or bodily fluids or under physiological conditions. In recent years, SAPH has also been reported to promote regeneration of damaged sites in various organs. However, the tissue repair effect of SAPH in ulcers of IBD is not reported yet. In this study, we evaluated the effect of SAPH on repairing ulcers using the rat model topical trinitrobenzene sulfonic acid (TNBS) -induced colitis.

Aims & Methods: Seven-week-old male SD rats were laparotomized under anesthesia. The proximal colon was clamped with ringed forceps. An ethanol solution (35%; 0.2 ml) containing 0.15 M TNBS was injected into the proximal colon lumen via a needle to prepare a localized ulcer model. On the second and fourth day, SAPH (n = 6) or saline (n = 5) was applied to the ulcerated area under colonoscopy. On the second, fourth and seventh days, the ulcer size was measured with an endoscope. The rats were sacrificed on the 7th day, and the ulcer area of the colon, colonic weight (g /3 cm), and histologic findings were evaluated. The tissue levels of proinflammatory cytokines (interleukin [IL]-1α, IL-6, IL-22 and tumor necrosis factor [TNF]-α) and tight junctions (cloudin [Cldn]-1, Cldn-2, occludin, cadherin-1, Zo-1, Zo-3)) in tissue were determined using real time-PCR.

Results:
(i) Endoscopic evaluation: SAPH group showed reduction in ulcer size as compared with that in the control group (P = 0.015).
(ii) Macroscopic finding evaluation: Ulcer area was significantly reduced in the SAPH group than in the control group (P = 0.024). Colonic weight also tended to decrease in the SAPH group compared to the control group.
(iii) Real time-PCR analysis: In the SAPH group, expression of several proinflammatory cytokines (IL-1α and IL-6) decreased and expression of cldn-1 increased (p < 0.05).

Conclusion: SAPH effectively suppresses colonic injury through the downregulation of pro-inflammatory cytokines and the up-regulation of cldn-1. Use of SAPH has been suggested to be a potential therapeutic strategy for refractory ulcers of the intestinal tract in IBD.

Disclosure: Nothing to disclose

P1014 GLUCOCORTICOID AUGMENTS EPITHELIAL PERMEABILITY IN CD PATIENT-DERIVED INTESTINAL ORGANOIDS

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Introduction: Intestinal barrier dysfunction has emerged as a key pathogenic factor contributing to the onset and exacerbation of Crohn's Disease (CD). Exogenous glucocorticoid (GC) is a first-line therapeutic for the treatment of moderate to severe CD. Recently, GC therapy was shown to restore intestinal permeability in CD patients. However, the underlying mechanisms remain largely unknown.

Aims & Methods: The main aim of the study was to investigate the effect of glucocorticoid prednisolone on intestinal barrier integrity and to elucidate the underlying molecular mechanisms using CD patient-derived intestinal organoids. Hollow 3D intestinal organoids were generated from stem-cell containing crypts isolated from proximal colon biopsies of remissive CD patients (SES-CD< 3, n=6, ethical approval NL31636.068.10). To mimic the inflammatory microenvironment, a mixture of cytokines containing TNF-α, IFN-Y and IL-1β (20 ng/mL each) were added to the culture medium for 24 hours, with or without prednisolone (500 ng/mL) for 12 hours. Epithelial permeability of the organoids was assessed by the flux of fluorescein isothothiocyanate-labelled dextran 4 kDa (FITC-D4) from the basal to the luminal compartment using confocal microscopy. Gene expression and localization of barrier junctions were analyzed by qRT-PCR and immunofluorescent staining. Cell signaling activities were analyzed using western blot. Data are expressed as means ± SEM. Statistical significance was evaluated using one-way ANOVA and Tukey's post-hoc test.

Results: Exposure of the cytokine mixture significantly disrupted epithelial barrier function of the intestinal organoids, as evidenced by increased luminal/basal FITC-D4 ratio as compared to the control treatment (5.051+0.376 vs 1.000+0.098, p< 0.001). This effect was partially rescued upon prednisolone supplementation (1.857+0.214 vs 5.051+0.376, p< 0.001). Compared to the control treatment group, exposure of cytokine mixture resulted in a significant reduction of E-Cadherin and an increase of Claudin-2 on both mRNA and protein levels, and led to an increased phosphorylation of MLCK. Supplementation of prednisolone ameliorated the junctional alterations and barrier dysfunction induced by the cytokine mixture (p< 0.05).

Conclusion: Using CD patient-derived intestinal organoid model, we demonstrated that glucocorticoid prednisolone has a protective effect against the cytokine-induced epithelial barrier dysfunction. Prednisolone promotes epithelial integrity through enhancing the expression of E-Cadherin and reducing the expression of Claudin-2, and inhibiting the cytokine-induced MLCK phosphorylation. Our findings provide a novel mechanism for the beneficial effect of prednisolone in the treatment of IBD.

Disclosure: Nothing to disclose

P1015 DIFFERENCES IN IMMUNE CELL POPULATION SUBSETS IN INFLAMMATORY BOWEL DISEASE PATIENTS UNDER ANTI-TNF TREATMENT AND HEALTHY CONTROLS

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Introduction: Inflammatory bowel disease (IBD) is a chronic inflammation that affect gastrointestinal tract, especially small and large bowel. The pathogenesis seems to be related to environmental factors and genetic susceptibility that put together lead to the failure of functions in several immune system process like: loss of tolerance in Treg cells, detriment of

apoptosis in Th1/Th17 cells and exacerbate of proinflammatory cytokines production of TNF-α, IFN-γ and IL-17. B cells are gaining interest in this inflammatory process considering that their depletion is not favourable for the disease course. Anti TNF-α treatment usually re-establish a fair B cell level and the monitoring of the transitional B gather the condition of a good market to follow the disease development.

Aims & Methods: The aim of this study is to reveal the existence of a specific immune system cell pattern; to discover T cell ability of cytokines production and transcription factor activation; among IBD patients in remission under infliximab (IFX) therapy.

A pilot case-control study was performed. Inclusion criteria were IBD patients in clinical remission under maintenance IFX treatment. After informed consent, blood samples were obtained in IBD patients just before IFX infusions and in healthy controls. Participants were classified in different groups: Healthy control (HC), Crohn's disease (CD) and ulcerative colitis (UC). Remission was defined as a Partial Mayo < 2 in UC and a Harvey-Bradshaw < 4 in CD. Blood samples were used to determine the immune cell status of patients and negative controls. To investigate the immune system cell distribution, peripheral mononuclear blood cells were isolated from fresh blood in order to characterize: monocyte, dendritic cells (DC), Th1, Th17, Treg and B cell. Cells were then incubated with a specific fluorescent antibodies' cocktails, then identified with flow cytometry. T cells ability to produce TNF-alpha, IL-17 and INF-gamma was tested by performing intra cellular staining, while T-bet, Fox-P3 and Ror-gamma t expression thought intra nuclear staining, data were collected with flow cytometry. Results are shown in percentages and analyzed with Prism 5.0, for parametric data.

Results: Thirty participants were consecutively included, 10 CD, 10 UC, mean age of 45, all in remission under IFX maintenance therapy and 10 HC. The surface staining demonstrated differences between the group's cell subtype. CD and UC patients showed a decrease of CD25Hi CD127- Treg subset, vs negative control, pointing out that UC patients decrease 2%, while CD only 1%. Decrease of transitional B cell subset CD38Hi CD24Hi CD19+ was observed in CD and UC patients. The cytokine production in T cell, showed a significant increase of TNF-alpha (50-60% vs 20-30% HC), especially in IL-17(5% vs 1-2% HC), while no significant different was observed in IFN-gamma production. Regarding the transcription factor expression T-bet and FoxP3 increased significantly in CD and CU vs HC, with a clear tendency of CD patients to express more FoxP3 than UC patients, while Ror-γt was more specifically expressed in UC than CD.

Conclusion: The immune system cell subset is highly modified by the IBD disease type (CD, UC) despite being in remission under anti-TNF therapy, indeed the T cell ability to cytokine production demonstrate their deregulation towards the Th1 phenotype. Transcription factors expression showed as well this unbalance leading to Ror-γt and FoxP3.

Disclosure: Nothing to disclose

P1016 A NOVEL GPR68 INHIBITOR ATTENUATES INFLAMMATION IN A MURINE COLITIS MODEL

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Introduction: Local extracellular acidification occurs at sites of inflammation and ischemia. Protons present in an acidic microenvironment may lead to activation of pH-sensing G protein-coupled receptor GPR68, also known as ovarian cancer G protein-coupled receptor 1 (OGR1). Recent studies suggest a link between IBD and this pH-sensing receptor. We previously reported that GPR68 is regulated by tumor necrosis factor (TNF) via a NF-κB dependent pathway.

Further, we demonstrated that GPR68 regulates barrier function and epithelial restoration, and that GPR68 expression is enhanced in intestinal inflammation in IBD patients. We have also shown that the genetic ablation of GPR68 ameliorates colitis in different murine models. In the current study, we investigated the effects of a novel GPR68 antagonist in a murine colitis model.

Aims & Methods: Acute colitis was induced in wild type (C57BL/6) mice by the addition of 1.5% dextran sulfate sodium salt (DSS) in the drinking water for 7 consecutive days. The small molecule GPR68 inhibitor was administered by oral gavage in a vehicle solution (methylcellulose 0.5%), twice daily (interval of 12 h). Doses used were per kilogram bodyweight per day: 25 mg, 50 mg, 100 mg (n=10 mice per group). Water or DSS control groups were gavaged with vehicle solution without inhibitor (n=10 mice per group). On day 8, mice were sacrificed and inflammatory parameters were evaluated.

Results: An amelioration of murine DSS-induced colitis in the GPR68 -inhibitor treated group compared to DSS-treated control animals was observed. Endoscopy revealed that GPR68 -inhibitor treated mice showed a lower MEICS score, indicating reduced inflammation compared to DSS control animals.

Macroscopically, the colon tissue of the inhibitor treated mice showed no thickening, vascularity was similar to water control mice and no fibrin was detected. However, inhibitor treated mice showed an elevated score in stool consistency. Further colon shortening was significantly reduced in treated mice, indicating an attenuation of colon inflammation.

Microscopically, H&E staining revealed that inhibitor treated mice exhibited markedly less infiltration and epithelial damage compared to DSS control mice. Immunohistochemistry (IHC) staining for the cellular proliferation markers Ki67 showed slightly enhanced proliferation in inhibitor treated mice compared to DSS control mice.

Moreover, decreased infiltration of T-cells was observed in treated mice compared to the DSS control group. However, a difference in body weight or health score could not be demonstrated among the groups treated with the inhibitor compared to controls, and MPO activity and neutrophil infiltration did not differ between groups.

Conclusion: .The inhibition of GPR68 has an ameliorating effect on the extent of DSS-induced colitis in wild type mice. Our data suggests that targeting proton-sensing GPR68 by a specific small molecule antagonist may be a novel therapeutic approach for the treatment of IBD.

Disclosure: Nothing to disclose

P1017 EXPRESSION PROFILING OF TRANSIENT RECEPTOR POTENTIAL CHANNELS IN PERIPHERAL BLOOD FROM INFLAMMATORY BOWEL DISEASE PATIENTS

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Introduction: Transient receptor potential (TRP) channels have been identified as cellular sensors of exogenous and endogenous environments, agents and mediators. Previous studies have focused on the expressions of these TRP channel members in colonic tissue of patients with inflammatory bowel disease (IBD), whereas no data exists regarding the expressions of these channels in peripheral blood mononuclear cells (PBMCs). We examined, for the first time, the comprehensive expression profile of TRP channels belonging to the TRPV (vanilloid) and TRPM (melastatin) channel superfamilies in PBMCs from patients with IBD.

Aims & Methods: PBMCs were obtained from 44 patients with ulcerative colitis (UC), 35 patients with Crohn's disease (CD), and 45 normal subjects. The mRNA levels of TRP channels and pro- and anti-inflammatory cytokines, TNF-alpha, IL-1 beta, IL-6 and IL-10, in the PBMCs were measured using a quantitative real-time-polymerase chain reaction, and the disease activities were compared according to laboratory parameters.

Results: Overall, the mRNAs of each of the TRP channel members were expressed at different levels in the PBMCs from patients with IBD. Compared with the levels in the PBMCs from normal controls, the expression of TRPV2 mRNA was significantly lower and that of TRPM2 mRNA was higher in PBMCs from both patients with UC and those with CD.

The expressions of TRPV3 and TRPM5 mRNAs were lower and that of TRPV4 mRNA was higher only in PBMCs from patients with CD. Comparing

the two diseases, the expressions of TRPV1 and TRPV3 mRNAs were lower and that of TRPV4 mRNA was higher in the PBMCs from patients with CD than in those from patients with UC. The expression of TRPV2 mRNA was negatively correlated with disease activity in the UC and CD groups, while the expression of TRPM4 mRNA was negatively correlated with disease activity only in the UC group.

Significant correlations between the expressions of individual TRP channel members were observed in both the UC and CD group. The expression of IL-6 mRNA, TNF-alpha and IL-1 beta mRNA, was correlated with that of TRPV1 and TRPV3 mRNA in UC and TRPM5 mRNA in both UC and CD. The expression of IL-10 mRNA was negatively correlated with that of TRPV2 and TRPM2 mRNA in UC.

Conclusion: The present results indicate, for the first time, that PBMCs from patients with IBD exhibit varying mRNA expression levels of TRP channel members, which may play an important role in the progression of IBD. In addition, the expression levels of these TRP channel members in PBMCs are promising markers for IBD. Further studies are needed to determine the clinical and pathogenic role of TRP channels in IBD.

Disclosure: Nothing to disclose

P1018 SYSTEMIC IRON DEFICIENCY IS ASSOCIATED WITH ACTIVATION OF THE HIF-1α PATHWAY IN THE INTESTINAL MUCOSA OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Many patients with Inflammatory Bowel Disease (IBD) exhibit extra-intestinal disease symptoms and anemia is the most common hematological manifestation affecting up to two thirds of the patients. IBD-associated anemia is considered to be the result of a combination of iron deficiency anemia (IDA) and anemia of chronic disease (ACD). In case of IDA, patients often require intravenous iron supplementation, as this is known to increase patients' disease outcome and quality of life.

However, in clinical practice, it is difficult to determine the responsiveness of patients to iron treatment. Iron homeostasis is intimately associated with oxygen metabolism in the intestinal mucosa, which is regulated by the hypoxia-inducible factor-1alpha (HIF-1α) pathway. Here, iron (Fe^{2+}) is a critical cofactor to the hydroxylase reaction that targets the HIF-1α protein to degradation in the presence of oxygen.

Therefore, an interplay between Fe^{2+} levels and the HIF-1α pathway regulates oxygen sensing in human epithelial cells and may be a crucial mechanism underlying IDA in IBD patients. In this study, we aimed to determine the association between serum iron status and activation of the HIF-1α pathway in mucosal biopsies of IBD patients.

Aims & Methods: Biopsies were collected from both ileum and colon and evaluated for their inflammatory status. In addition, serum laboratory parameters of iron metabolism close to biopsy dates (hemoglobin, MCV, free iron, ferritin, TYBC, transferrin, transferrin saturation) were documented. Based on serum iron status and inflammation, patients were categorized into either a group having 'normal' iron status (n=81) or a group having systemic IDA (n=29). RNA sequencing data (n=167 entries) from intestinal biopsies of 110 IBD patients were retrospectively analyzed for 18 HIF-1α pathway genes, including *HIF1A*, *HIF2A*, HIF-hydroxylases (*EGLN1*, *EGLN2*) and HIF-1α target genes (*EGLN3*, *CA9*, *PDK1*, *SLC2A1*, *MUC3*, *TFF3*, *A2BAR*, *SLC29A1*, *ADK*, *HAMP*, *SLC11A2*, *HMOX1*, *TFRC* and *TF*), some of which are involved in iron metabolism, and analyzed for differential expression with iron status.

Results: The HIF-1α pathway was activated in inflamed ileal and colonic tissue compared to adjacent non-inflamed tissue. Moreover, IBD patients with systemic IDA showed increased expression of HIF-1/2α target genes in inflamed tissue, with significantly elevated mucosal levels of ileal *SLC11A2* ($P< 0.05$) and *PDK1* ($P< 0.05$) and colonic *TFRC* ($P< 0.05$) levels. mRNA levels of *HIF1A*, *HIF2A* and the HIF-hydroxylases *EGLN1* and *EGLN2* were not different between patients with or without IDA.

Conclusion: IBD patients with systemic iron deficiency show differential expression of HIF-1α target genes *SLC11A2*, *PDK1*, *SLC2A1* and *TFRC* as compared to patients with a normal iron status. These preliminary data suggest an association of systemic iron status in IBD and activation of the HIF-

1α pathway in the intestinal mucosa. These data reveal a possible disease mechanism involved in IBD-associated anemia that can be modulated by treatment.

Disclosure: Nothing to disclose

P1019 NEXT-GENERATION SEQUENCING-BASED EVIDENCE FOR A DECREASE OF GUT MICROBIOTA BUTYRATE PRODUCTION CAPABILITY IN CROHN'S DISEASE

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Introduction: Butyrate is an essential metabolite in the human gut, as it is the preferred source of energy for colon epitheliocytes and is known for its anti-inflammatory properties. The main source of butyrate is bacterial fermentation of fiber. It is known that the microbiota of Crohn's disease (CD) patients is characterized by reduced abundance of butyrate-producing bacteria. The four major pathways involved in butyrate synthesis are acetyl-CoA, lysine, 4-aminobutyrate, and glutarate pathways.

Aims & Methods: The aim of the study was to reveal the differentially abundant genes encoding enzymes involved in butyrate synthesis pathways in the gut microbiota of CD patients compared to the control group. The study included 40 CD patients and 42 healthy controls. Total DNA was extracted from stool samples and sequenced using the NextSeq 500 platform (Illumina). Reads were mapped to the ChocoPhlAn database using the HUMAnN2 algorithm to assess the representation of microbial metabolic pathways. Relative abundances of genes were calculated as "cpm" - a number of reads mapped to a gene divided by the total number of mapped reads; $p< 0.05$ was considered as statistically significant. Butyrate levels were measured in stool samples by gas-liquid chromatography.

Results: Butyrate levels were significantly decreased in the stool samples of CD patients (1.14±1.1 μg/g) compared to the control group (1.82±1.55 μg/g). All of the pathways mentioned above include conversion of crotonyl-CoA to butyryl-CoA catalyzed by butyryl-CoA dehydrogenase (Bcd). Abundance of the Bcd gene was not significantly different between the CD and control groups. The final stage of butyrate synthesis is transformation of butyryl-CoA catalyzed by butyryl-CoA:acetate CoA-transferase (But), or alternatively by butyrate kinase (Buk); this stage is catalyzed by butyryl-CoA:acetoacetate CoA-transferase (Ato) in the lysine pathway. Abundance of the But gene also did not differ between the groups. However, abundances of phosphotransbutyrylase (Ptb) and Buk genes coding enzymes that catalyze butyryl-CoA transformation to butyrate through butyryl-phosphate were reduced in CD patients (1.9±3.2 cpm and 45.9±30.5 cpm) compared to controls (2.4±1.9 cpm and 63.3±21.1 cpm, respectively). Most butyrate-producing bacteria have only one type of enzyme - But or Ptb+Buk - for the last stage of butyrate synthesis. Thus, the microbiota of CD patients is supposed to be depleted in bacteria carrying Ptb+Buk genes. The acetyl-CoA pathway is present in the majority of butyrate producers. Relative abundance of this pathway was decreased in CD patients due to a reduced number of the hydroxybutyryl-CoA dehydrogenase gene (19.1±15.2 cpm) and the 3-hydroxybutyryl-CoA dehydratase gene (20.1±15.6 cpm) compared to the control group, where these genes were detected by 26.9±10.1 cpm and 27.6±11.1 cpm, respectively. Stool samples from CD patients were characterized by a reduced abundance of 4-aminobutyrate pathway, in particular, by depletion of 4-hydroxybutyrate dehydrogenase gene (0.1±0.2 cpm) compared to controls (0.3±0.2 cpm). Ato as a part of the lysine pathway was decreased in CD patients (2.2±1.8 cpm) in comparison to the control group (2.3±4.2 cpm). The glutarate pathway was not significantly different between the cohorts.

Conclusion: Stool samples of CD patients were characterized by reduced levels of butyrate caused by a decreased number of genes coding enzymes involved in three out of four main butyrate synthesis pathways (acetyl-CoA, 4-aminobutyrate, and lysine).

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P1020 INCREASED EXPRESSION OF EPITHELIAL-DERIVED GASDERMIN-B (GSDMB), A NOVEL MOLECULE THAT PROMOTES EPITHELIAL RESTITUTION AND REPAIR, IN PATIENTS WITH IBD

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Introduction: The resolution of inflammation at mucosal surfaces is a basic physiological process that promotes restitution of the epithelial barrier and appropriate tissue repair, in an attempt to restore normal organ function and homeostatic conditions with the interfacing microenvironment. This process is critical for patients with IBD, wherein efficient resolution of inflammation and mucosal healing is one of the most important goals to attain in order to maintain long-term remission. Gasdermin-B (GSDMB), a novel molecule belonging to the Gasdermin family of proteins, has recently gained intense interest for its potential role in the pathogenesis and progression of chronic inflammatory disorders, particularly those that affect mucosal surfaces, including asthma and IBD. Importantly, GWAS have revealed SNPs within the gene encoding *GSDMB* as being reportedly associated to both an increased susceptibility of acquiring IBD and an increase in GSDMB expression.

Aims & Methods: The aim of the present study was to examine the expression pattern and functional relevance of GSDMB in the pathogenesis of IBD. Primary intestinal biopsy and isolated intestinal epithelial specimens, as well as formalin-fixed intestinal tissues, from both IBD patients and non-inflamed controls were evaluated for mRNA and protein levels by qRT-PCR and Western blots, respectively, and cellular localization was examined by IHC/confocal microscopy. Using the human colonic epithelial cell line, HT-29, CRISPR-cas9 knockout (KO) cells lacking GSDMB were generated, and used for *in vitro* XTT and cell migration functional assays. Finally, subcellular localization of GSDMB was investigated after *in vitro* stimulation with LPS and nigericin (NG) by fluorescent imaging and subcellular fractionation/Western blot analysis.

Results: We report for the first time a dramatic increase in epithelial-specific GSDMB expression in IBD patients (both UC and CD) compared to healthy controls. HT-29 epithelial cells stimulated with LPS and NG suggests regulation that is NLRP3-dependent, with a functional decrease in *in vitro* proliferative activity and wound repair in epithelial cells lacking GSDMB.

Additionally, we report unique subcellular localization of GSDMB primarily within the cytosolic compartment, with indication of migration towards a membrane/organelle compartment after stimulation with LPS and NG in human epithelial cells.

Conclusion: Taken together, our data suggests that increased epithelial-derived GSDMB during IBD is protective in function and promotes epithelial-specific proliferation. To our knowledge, this is the first report of GSDMB's functional role in IBD, and provides the rationale for the potential therapeutic use of GSDMB to obtain optimal gut mucosal wound healing towards promotion of resolution of inflammation.

Disclosure: Nothing to disclose

P1021 PRECLINICAL INVESTIGATIONS OF IMU-838, AN ORALLY AVAILABLE SMALL MOLECULE INHIBITOR OF DIHYDROOROTATE DEHYDROGENASE FOR THE TREATMENT OF INFLAMMATORY BOWEL DISEASE

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Introduction: IMU-838 is a small molecule inhibitor of DHODH (Dihydroorotate Dehydrogenase) and currently in clinical phase 2 testing for ulcerative colitis and multiple sclerosis. Inhibition of DHODH in highly activated immune cells, such as in T cells in inflammatory bowel disease, leads to induction of metabolic stress signals with immediate onset of inhibition of cytokine release of IL-17 and IFNgamma (IFNg) and later on to induction of apoptosis in those cells driving inflammation in the bowel wall. We performed in-vitro and in-vivo experiments to further explore the impact of IMU-838 on other aspects of the immune network important in inflammatory bowel disease with particular focus on regulatory macrophages and TNFalpha (TNFa).

Aims & Methods: Efficacy of IMU-838 was tested in a 2.8% DSS induced C57BL/6 colitis mouse model in a therapeutic setting with four days of colitis induction prior to treatment start with IMU-838. The impact of IMU-838 on cytokine regulation was testes in PHA stimulated human peripheral blood mononuclear cells (PBMCs) and in a mixed lymphocyte reaction (MLR). Cytokine regulation was tested via gene expression analysis and protein secretion via ELISA technique. In the MLR assay, the impact of IMU-838 on regulatory macrophages and the synergistic effects with anti-TNFa Infliximab treatment were tested via FACS analysis. Therefore, isolated PBMCs from two healthy donors were pre-incubated for 48h and then incubated for another four days with IMU-838 in four different concentrations (30, 10, 3, 1µM) with and without anti-TNFa antibody Infliximab (10µg/ml).

Results: In a DSS induced colitis model, IMU-838 was administered in monotherapy with an oral low dose of 20mg/kg in a therapeutic setting. IMU-838 demonstrated improvement of the diarrhea score, the histology score and TNFa secretion as markers for improvement of the disease. Even though IMU-838 had no impact on TNFa secretion in PHA stimulated human PBMCs, a significant reduction of TNFa secretion in a mixed lymphocyte reaction assay (MLR) was found. Administration of IMU-838 to the MLR assay slightly enhanced the percentage of regulatory macrophages (which are known to be important for improvement in IBD under anti-TNF therapy). In MLR experiments combining IMU-838 and anti-TNF Infliximab a strong increase in regulatory macrophages and decrease in TNFa secretion was shown, thereby confirming a substantial synergism of the effects for the combining the two molecules.

Conclusion: Preclinical experiments support that IMU-838 and its mechanism of DHODH inhibition testing of IMU-838 in clinical trials for IBD patients. Beside the already known inhibition of IL-17 and IFNg cytokine secretion as well as apoptosis induction of highly activated T cells, these recent investigations of IMU838 also indicate a beneficial impact on regulatory macrophages and inhibition of. In addition, combining IMU-838 with an anti-TNFa antibody has shown a strong synergism of effects on regulatory macrophages and TNFa secretion, which seems to indicate that a combination trial in IBD patients suffering from insufficient or reduced efficacy of anti-TNFa antibodies such as infliximab should be considered.

Disclosure: All authors are employees of Immunic AG

P1022 ANTI-TNFα THERAPY INDUCES T CD8^{+} EFFECTOR MEMORY PROFILE AND REDUCES LEVELS OF ACTIVATION IN PATIENTS WITH CROHN'S DISEASE

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Introduction: The dysregulation of immune system mediated by T lymphocyte seems to be the most important factor for progression of Crohn's Disease (CD) (Marsal & Agace, 2012). CD8^{+} T cells (TCD8^{+}) are a subset of cytotoxic lymphocytes that can differentiate into both central (T_{cm}) and effector (T_{em}) memory cells. Two animal models suggested that the destruction of intestinal epithelial cells by TCD8^{+} is the event that lead to the disease activity proposing a role for this cells in CD pathogenesis (Westendorf et al., 2006; Nancey et al., 2006). In patients with CD that experienced relapsing or chronically active disease, an increase in T cell activation genes and a difference in TCD8^{+} activation status was demonstrated prior to commencing treatment (Lee et al., 2011) but there is no data about the effects of Anti-TNFα therapy in TCD8^{+} subpopulations.

We hypothesized that Anti-TNFα therapy decreased the activation levels and modulate the memory phenotype of TCD8^{+} to better control the inflammatory process.

Aims & Methods: We aimed to characterize the subpopulations of TCD8^{+} in blood and in tissue of patients with CD. The blood was collected and cells were acquired by multiparametric flow cytometry. the analysis was performed by FlowJo software. For co-expression analysis, Pestle and Spice was used. We also collected five tissue samples from patients who underwent surgery and TCD8^{+} was quantify using confocal microscopy. Statistical analysis was performed using Prism5 [GraphPad software] and Mann-Whitney tests.

Results: We enrolled 44 CD patients, which 27 patients were under Anti-TNFα therapy and 17 patients was under conventional therapy. Among the patients, there was no difference between age, gender and several laboratories parameters (like Calprotectin and CRP) that was used to better define this cohort.

We first observed that patients receiving Anti-TNFα therapy had an increase in the percentage of circulating TCD8+ when compared to patients that are under conventional therapy (p = 0.0429). When we analyzed the tissue lesion and healthy area from surgery material, TCD8+ shows no statistical difference between the two regions.

When we analyzed the expression of CD38, HLA-DR, CD73 and CD39 in TCD8+ in peripheral blood, we observed lower expression of CD38 (p = 0.0033), HLA-DR (p = 0.0002) and CD73 (p = 0.0021) in patients with Anti-TNFα therapy when compared to patients receiving conventional therapy, but no statically differences was observed in the expression of CD39 between the groups.

Next, we analyzed the expression of memory subsets. Anti-TNFα therapy decrease the pool of T_{cm} cells (p = 0.0007) and T_{cm} with coexpression of CD38 (p < 0.0001) and HLA-DR (p = 0.0457). On the other hand, T_{em} cells (p = 0.0004) and T_{emra} cells (p < 0.0001) shows an increase in patients under Anti-TNFα therapy when compared to conventional therapy. The multivariate analysis of the markers CCR7, CD45RA, CD38 and HLA-DR demonstrated that the majority of TCD8+ in patients receiving Anti-TNFα therapy lacked the expression of all markers (p = 0, 0002). Already in patients that are under conventional therapy, we observed the co-expression of CD38, HLA-DR and CCR7 in the same population (p = 0, 0002). In the functional analysis CD8 T cells do not demonstrated any difference in cytokine production between groups.

Conclusion: We conclude that Anti-TNFα therapy induces a profile of TCD8+ effector memory cells and reduces the activation levels of this cells in patients of Crohn's Disease, demonstrated the capacity for induce better immune response.

References: Marsal J, Agace WW. Targeting T-cell migration in inflammatory bowel disease. J Intern Med. 2012 Nov; 272(5):411-29. Westendorf AM, Fleissner D, Deppenmeier S, Gruber AD, Bruder D, Hansen W, Liblau R, Buer J. Autoimmune-mediated intestinal inflammation-impact and regulation of antigen-specific CD8+ T cells. Gastroenterology. 2006 Aug; 131(2):510-24. Nancey S, Holvöet S, Graber I, Joubert G, Philippe D, Martin S, Nicolas JF, Desreumaux P, Flourié B, Kaiserlian D. CD8+ cytotoxic T cells induce relapsing colitis in normal mice. Gastroenterology. 2006 Aug; 131(2):485-96. Lee JC, Lyons PA, McKinney EF, Sowerby JM, Carr EJ, Bredin F, Rickman HM, Ratlamwala H, Hatton A, Rayner TF, Parkes M, Smith KG. Gene expression profiling of CD8+ T cells predicts prognosis in patients with Crohn disease and ulcerative colitis. J Clin Invest. 2011 Oct; 121(10):4170-9.

Disclosure: Nothing to disclose

P1023 VITAMIN D DEFICIENCY IN CROHN'S DISEASE: A SINGLE-CENTER PROSPECTIVE STUDY

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Introduction: Crohn's disease (CD) is a chronic inflammatory bowel disease (IBD), involving dysbiosis of intestinal microbiota, a dysfunction of the intestinal barrier and a dysregulation of innate and adaptive immunity on a genetically predisposed ground. In recent years, the immunomodulating effects of vitamin D have gained a huge interest in its possible pathogenic influence on the pathophysiology of IBD. However, it remains unclear if this association is a result of inflammatory process, or a cause. Therefore Interest in links between vitamin D deficiency and CD has grown substantially.

Aims & Methods: The aim of the study was to assess the vitamin D status in patients with CD and in healthy controls and to determine related factors associated with vitamin D deficiency in patients with CD. We conducted a prospective study over 18 months, including patients followed for a CD and age-, sex-, and socio-economic status-matched healthy controls. Serum 25-hydroxyvitamin D (25 (OH) D) concentration was measured with radioimmunoassay. Vitamin D deficiency was defined by levels < 30 ng/ml and subdivided into: vitamin insufficiency: 10 ng/ml < 25 (OH) D < 30 ng/ml and vitamin deficiency: 25 (OH) D < 10 ng/ml.

Crohn's disease activity was evaluated by a combination of clinical, biochemical, and endoscopic assessment. Crohn's disease activity index (CDAI) was calculated for each patient.

Results: We included 77 subjects (52 patients with MC and 25 controls). The mean age was of 38 years ± 11 [20 - 64]. The average level of 25 (OH) D was comparable in both groups (8.83 + 8.89 ng/ml in patients and 10.06 + 7.42 ng/ml in controls; p= 0,554), also in patients with active disease and remission (7.47 ng/ml ± 10.72 and 10.2 ng/ml ± 6.52 respectively; p=0.273). Most patients and controls had suboptimal levels of vitamin D (98% and 96% respectively) including (75% and 67% respectively) with vitamin D deficiency, (25% and 33% respectively) with vitamin D insufficiency. Deficiency rates were higher in patients than controls but this difference was not statistically significant. In univariate analysis, lower serum 25(OH) D was associated with anemia (p=0.002), hypo-albuminemia (p=0.002), elevated *C-reactive protein (*CRP) (p=0.003), CDAI (p< 0.001), ileal location (p=0.04) and immunosuppressive therapy (p=0.01). In multivariate analysis, only CDAI was significantly associated (p=0.003) with vitamin D deficiency (OR=9.33).

Conclusion: Vitamin D deficiency is common during CD and was associated with disease activity and higher CDAI. Vitamin D status should be used as a biomarker in assessing disease activity among CD patients in addition to CDAI and CRP. Supplementation could be proposed as a therapeutic to improve outcomes of the disease.

Disclosure: Nothing to disclose

P1024 INNATE IMMUNITY PROFILE FROM THE "NORMAL" MUCOSA OF ULCERATIVE COLITIS PATIENTS

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Introduction: Innate immunity modulates the integrity of the epithelial barrier, microbial detection and autophagy which occurs during the inflammatory process presented in ulcerative colitis (UC). UC is associated with polymorphisms in the TLR2 (R753Q) and TLR4 (Asp299Gly) genes, increasing expression of TLR4 and TLR2 in the mucosa and enhances the release of proinflammatory cytokines and the activation of NFκB. However, the role of innate immunity associated with macroscopically normal mucosa in UC is not well known.

Aims & Methods: Objetive: To establish the profile of gene expression related to the innate immunity of normal macroscopic (non-inflamed) mucosa in patients with UC.

Methods:Consecutive patients of UC who underwent a colonoscopy by clinical practice in a tertiary hospital were included. The total (TMS) and partial (PMS) scores were recorded according to the Mayo index at the time of the colonoscopy. The histological activity based on the Geboes scoring system was previously determined to the PCR study to stratify the samples according to the degree of colitis (inactive colitis Geboes < 3). Colon biopsies of the inflamed (iUC) and non-inflamed (safe) (sUC) mucosa were obtained in patients with active UC, stratified as mild colitis (LsUC, TMS 1-4 / Geboes < 3) and moderate / severe colitis (MsUC, TMS 5- 12 / Geboes < 3); n = 47). Likewise, patients with quiescent UC (QUC, defined as TMS = 0 / pMS = 0 / Geboes, n = 46) and a control group (non-IBD) (C; n = 13) were included. Gene expression of innate immunity was quantified using Taqman Human Immune Assay-microfluidic cards in colonic mucosa, considering the degree of UC and the location of the samples.

Results: Biopsies from mucosa with quiescent colitis (qCU), as well as those from mucosa do not affect by inflammation, both in patients with mild colitis (LsUC) and moderate / severe colitis (MsUC), demonstrated an expression of genes related to innate immunity different from the control group without UC. 36, 55 and 3 genes were overexpressed and 7, 14 and 7 underexpressed genes were under-expressed in QUC, LsUC and MsUC, respectively, compared to non-IBD controls (p< 0.05) (Table 1).

Conclusion: The normal mucosa, by endoscopic and histologic criteria, in patients with UC presents a differential pattern of innate immunity from that observed in non-IBD subjects, suggesting the existence of a pancolonic inflammatory predisposition that can condition the clinical evolution of the disease.

Disclosure: Nothing to disclose

P<0,0001	Fold changesΔ		
Genes	QUC vs C	LsUC vs C	MsUC vs C
IL-12A	0.47	0.24	
IL-10	0.48	0.33	*1.54
IL-15	0.61	0.34	
IL-2	0.46	0.25	
IL-18			*2.05
IL-8			*4.05
CCR4	0.64	0.39	
Bcl2L1	0.72	0.48	

*[Table 1. Changes in the expression of selected genes assesed by real-time RT-PCR (Taqman Human Immune Assay). *over expressed]*

P1025 BENEFIT OF MINERALOCORTICOID RECEPTOR ANTAGONISM IN INTESTINAL INFLAMMATION AND FIBROSIS

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Introduction: Mineralocorticoid receptor (MR) is involved in inflammation and fibrosis process from extra-intestinal organs and may thus constitutes a therapeutic target in inflammatory bowel diseases (IBD). MR is highly expressed in the colon and all components of renin-angiotensin system (RAS) are expressed within the gastrointestinal tract. RAS components are increased in IBD and Ramipril, a RAS antagonist decreased matrix metalloprotease (MMP) activities in tissues from Crohn's disease fistula. Lipocalin-2 is a MR-modulated in the pro-inflammatory and pro-fibrotic processes induced by mineralocorticoids. We aimed to investigate whether MR participates to IBD-induced inflammation and fibrosis.

Aims & Methods:
In vitro study: Human colon fibroblasts CCD-18Co were incubated with 10 ng/mL of TGF-ß for 24 hours to obtain an *in vitro* model of intestinal fibrosis. Cells were also induced with primary ligand of the MR (aldosterone at 10^{-8} mol/L) or MR antagonist (spironolactone at 10^{-6} mol/L) or Lipocalin-2 (5 to 50ng/mL) for 24 hours (n=4 independents experiments). Fibrosis markers such as a- SMA, CTGF, COL1A1, COL3A1 and MMP-9 expression were analyzed by Western Blot and RT-qPCR.

In vivo study: To induce colitis, mice received 2% dextran sulfate sodium (DSS) in drinking water *ad libitum* for 7 days followed by 3 days of normal water. Pharmacological MR (spironolactone, 30mg/kg, n=10) or RAS antagonists (Ramipril, 10mg/kg, n=10) were investigated in DSS colitis (DSS, n=10). Cell specific deletion of MR in smooth muscle (SM) were studied in DSS-induced SM22-MR deleted mice (n=5) and their littermate (n=3). Body weight was daily recorded. Gene expression of IL-6, MCP-1 and TNFα were evaluated by RT-qPCR. Fecal calprotectin and colon myeloperoxidase activity (MPO) were recorded.

Results: *In vitro*, TGF-ß significantly increased α-SMA, CTGF, COL1A1 and COL3A1 mRNA levels in CCD-18 Co (p<0.01). Spironolactone inhibited α-SMA (p<0.01) while aldosterone significantly increased it in TGFb-induced intestinal myofibroblasts (p<0.01).
In vivo, DSS-induced colitis led to a significative body weight loss (p<0.001) and increased inflammatory markers such as a decreased colon length (p<0.01), a higher colon MPO activity (p< 0.01) and a higher fecal calprotectin (p< 0.01). Ramipril significantly decreased body weight loss vs DSS or spironolactone groups (p< 0.05).
Ramipril increased colon length (p<0.05) while it decreased colon MPO activity (p<0.01) and fecal calprotectin (p<0.01). Ramipril significantly decreased IL-6, TNFα, MCP-1 mRNA levels compared to DSS or DSS+spironolactone treated mice (p< 0.01). SM22 specific MR deletion protected mice from DSS colitis compared to littermate mice. SM22 MR deleted mice had a lower colonic IL-6 mRNA levels (P<0.05) and a lower colon MPO activity (P=0.056).

Conclusion: MR antagonism decreased fibrosis markers *in vitro*. Smooth cell specific MR deletion prevented colitis. Ramipril treatment inhibited DSS-induced colitis. MR and RAS may represent novel therapeutic targets in intestinal fibrosis.
Disclosure: Nothing to disclose

P1026 COLONIC MUCOSAL EOSINOPHIL HYPERPLASIA AND ACTIVATION FEATURES COLLAGENOUS COLITIS AND LYMPHOCYTIC COLITIS

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Introduction: Collagenous colitis (CC) and lymphocytic colitis (LC), the two main subtypes of Microscopic Colitis (MC), are chronic inflammatory diseases of the colon, characterized by watery diarrhoea, normal (or near normal) endoscopy with characteristic histopathological features, which define its diagnosis. CC is mainly characterized by the presence of a subepithelial collagen band (>10 micrometers) and LC mainly by the presence of ≥20 intraepithelial lymphocytes per 100 epithelial cells. The inflammatory infiltrate in the lamina *propria* has been described as increased numbers of mononuclear cells in both entities. In few studies, eosinophil infiltration has been described only in CC. However, whether eosinophils characterize one or both entities and its role in the pathophysiology of MC remains unknown.

Aims & Methods: Our aim is to quantify mucosal eosinophilic infiltration and describe its activation in CC and LC. Colonic mucosal biopsies (sigma region) were obtained from newly diagnosed patients with active CC (n=8) and LC (n=15), and from healthy volunteers (HV; n=8), as the control group. Lamina *propria* and intraepithelial eosinophils were counted per high-powered field (hpf) after eosinophil-specific major basic protein (MBP) immunohistochemical (IHC) staining. The ultrastructure of eosinophils was assessed by transmission electron microscopy.

Results: In HV samples, scattered mucosal eosinophils were found across the colonic tissue and identified by weak MBP signal, while in MC, eosinophils were identified in patchy areas and displayed a large cytoplasm and high MBP signal intensity. The number of eosinophils in the lamina *propria* was significantly higher in patients (CC: 20.1±5.50; LC: 19.9±3.30 cells/hpf) as compared with controls (HV: 1.5±0.5 cells/hpf; P< 0.05).
The number of intraepithelial eosinophils was also higher in samples from MC patients (CC: 0.43 [0.0-1.88]; LC: 0.13 [0.0-4.78] cells/hpf) than from controls (HV: 0.0 [0.0-0.17]; P< 0.05). Interestingly, IHC analysis revealed extracellular staining of MBP in lamina *propria* eosinophils from MC patients (CC: 7.7±2.1; LC: 7.6±1.3 eosinophils/hpf) while few eosinophils displayed signs of protein release in control tissues (HV: 0.6±0.2 eosinophils/hpf; P< 0.05). The analysis of mucosal ultrastructure confirmed eosinophilic activation only in samples from patients. While the control group showed intact eosinophils, CC and LC samples displayed both piecemeal degranulation and eosinophil cytolysis with associated clusters of free eosinophilic granules in the lamina *propria*.

Conclusion: Despite the histological characteristics that differentiate CC and LC, mucosal eosinophilic increase and activation are observed in both, CC and LC. Further studies are needed to identify whether eosinophils play

a specific role in the pathophysiology of MC subtypes or if its contribution to mucosal inflammation is secondary to the aetiology of these diseases.
Disclosure: Nothing to disclose

P1027 FACTORS ASSOCIATED WITH THE QUALITY OF CARE PERCEIVED BY PATIENTS IN IBD UNITS FROM SPAIN. ANALYSIS FROM THE IQCARO PROJECT

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Introduction: Measuring patient's perceived quality of care (QoC) in Inflammatory Bowel Disease (IBD) units is becoming increasingly important. The aim of the current analysis from the IQCARO project was to assess the factors associated with the QoC in IBD units from Spain, by measuring the completion of a validated predefined decalogue of QoC indicators[1].
Aims & Methods: A survey including a Decalogue of QoC indicators, previously developed by patients, IBD gastroenterologist and IBD nurses, was distributed through the webpage of the Confederation of Spanish Associations of Patients with Crohn's disease and Ulcerative Colitis (ACCU). The survey also included patient's sociodemographic and clinical characteristics. Patients could answer yes/no to every item of the decalogue, scoring 1/0 respectively. The final QoC index was obtained by calculating the mean of the total score of each indicator (higher score represents better QoC). Qualitative variables were presented as absolute frequencies and percentages and quantitative variables as mean and standard deviation or median and interquartilic range depending on the distribution of the data. In the multivariate analysis the QoC index was dichotomized (high quality/low quality) with a cut-off point of 9.5 to be used as a dependent variable in a binary logistic regression model in order to determine the factors that can influence the evaluation of QoC as high.
Results: Online-completed surveys from 605 patients were considered valid for the analysis. 451 patients (74,5%) were attended by IBD specialists, 138 (22,8%) by general gastroenterologists (GG) and 16 (2,7%) by other professionals. The population included patients from the 17 Spanish autonomous communities, and 183 sites. The mean age of the patients was 42.3 years, with a mean disease duration of 13 years. 66% were women and 60.7% had Crohn's disease. The mean QoC index was 7.8/10 being significantly higher (meaning better QoC) in patients attended by IBD specialists vs GG: 8.2 vs 6.7 respectively, p< 0.001. We found no significant differences in disease activity, number of flares, hospitalizations, emergency room visits in the last year or patients' perception of controlled disease in the last two weeks, when comparing patients attended by IBD specialist or GG. When we analyzed the QoC index score as a dichotomized variable, we found that older patients, longer disease duration, routine follow-up by an IBD specialist, and a better perception of a controlled disease were all associated with high QoC while, active disease, unscheduled visits in the last year, higher number of flares, and unemployement were correlated with low QoC. The multivariate analysis showed that employment, controlled disease, low number of unscheduled visits and being attended by an IBD specialist were all associated with a high QoC. Table 1.

	coef	OR	IC95	p
IBD specialist	1.11	3.05	(1.88;4.95)	<0.001
Employed	1.09	2.97	(1.51;5.85)	0.002
Controlled disease	1.08	2.69	(1.90;4.63)	<0.001
Number of unscheduled visits	-0.20	0.81	(0.72;0.93)	0.003
ed visits Constant	-2.89			<0.001

[Binary logistic regression analysis]

Conclusion: The perception of the QoC received by IBD patients in Spain is good particularly when they are followed-up by IBD specialists rather than GGs. Personal and disease related aspects may influence the perception of the QoC received.
References: X. Calvet et al. Journal of Crohn's and Colitis, Volume 12, Issue supplement_1, February 2018, Pages S217-S218. https://doi.org/10.1093/ecco-jcc/jjx180.359
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P1028 THE SOCIOECONOMIC IMPACT OF LIVING WITH ULCERATIVE COLITIS, A BURDEN OF ILLNESS STUDY

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Introduction: Ulcerative Colitis (UC) is a chronic inflammatory disorder affecting the mucosal surface of the rectum and colon characterised by periods of relapse and remission. The increasing incidence and prevalence of UC, morbidity associated with its chronic, relapsing and remitting nature and the increasing earlier use of biological therapies, has important implications to the health economy. The lack of current data on direct and indirect medical cost of treatment and societal cost justified the urgent need to conduct a study to quantify the current economic landscape related to UC. The living with Ulcerative Colitis, identifying the socioeconomic burden in Europe (LUCID) study was a descriptive, retrospective, cross-sectional, European (France, Germany, Italy, Spain, United Kingdom, Denmark, Norway, Poland, Romania and Turkey), multi-site, bottom-up, prevalence-based Burden of Illness research study carried out by HCD Economics and the University of Chester in partnership with Crohn's and Colitis UK.
Aims & Methods: The primary objective of the LUCID study was to quantify the existing UC-related costs for each country and by disease severity. The study population was recruited through gastroenterologists (surveyed between Aug 2018- February 2019) and included adult patients diagnosed with UC by endoscopy and histology, at least 24 months prior the index date (date of clinical consultation). The study cohort population consisted of two arms; Arm 1: Patients with moderate or severe UC status at initiation of documentation period (12 months prior the index date) and, Arm 2: Patients with moderate or severe UC that achieved mild UC or remission at initiation of documentation period. Physician completed questionnaires (CRF) captured clinical information, direct medical costs and some direct non-medical costs. Each patient was invited to complete a corresponding public patient involvement and engagement (PPIE) form which captured further direct non-medical costs and indirect costs. Due to the descriptive nature of this study a formal calculation of sample size and statistical power was not applicable. Per-patient costs were calculated by multiplying the quantities of the resource use collected with the national unit price and then extrapolated to population level to calculate the total societal economic burden. Total costs were only calculated for patients with completed PPIE forms due to the need to add non-direct medical and indirect costs to the direct medical costs.
Results: Completed physician-reported forms (CRF) and PPIE forms were assessed for 1,658 patients. Of these, 1001 (60.7%) and 648 (29.3%) patients were in arm 1 and arm 2 respectively, with 9 patients unable to be assigned to either arm. Total average EU cost per patient in the last 12 months was €8,833.94 in arm 1 and €6,512.74 in patients in arm 2 with direct medical costs per patient amounting to €4381.70 in arm 1 and €3078.48 in arm 2.

Direct non-medical costs per patient were €1353.93 for arm 1 and €1128.37 for arm 2. Societal costs per patient amounted to €3098.31 of the total cost for arm 1 and €2305.89 for arm 2.

Conclusion: These preliminary results suggest that non-medical costs and indirect costs make up substantial proportions of the overall cost implying that the cost of treatment constitutes only a part of the overall burden of UC. Further analysis is planned to identify the drivers of costs in each arm in order to make comparisons between them.

Disclosure: The LUCID study was funded internationally by Pfizer and Eli Lilly and in the UK by Celgene. The study was governed by an expert reference group consisting of the authors.

P1029 INCIDENCE OF COLLAGENOUS COLITIS AND LYMPHOCYTIC COLITIS IN TERRASSA, SPAIN, 2015-2018: A CONTINUOUS EPIDEMIOLOGIC STUDY

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Introduction: The incidence of microscopic colitis (MC) has increased in several geographical areas but long-term epidemiologic data are scarce.

Aims & Methods: We report an incidence study of collagenous colitis (CC) and lymphocytic colitis (LC) during 2015-2018, as a follow-up of our previous studies 1993-2008.

Population-based study of residents of the catchment area of the hospital, with a new diagnosis of MC between 2015 and 2018. All patients with non-bloody watery chronic diarrhea referred for a diagnostic colonoscopy were included. Multiple biopsy specimen samples were obtained when the macroscopic appearance of the colonic mucosa was normal to rule out MC. Diagnosis of both CC and LC was based on accepted standard criteria. Patients were identified by diagnosis register of the Department of Pathology. Age- and gender-specific crude incidence rates based on the year of diagnosis were calculated. An exact rate ratio test was used to compare the incidence rates for the two time periods.

Results: Collagenous colitis was diagnosed in 20 patients (16 females) and LC in 27 patients (22 females). The mean annual incidence (per 100,000 inhabitants) was MC 9 (95% confidence interval: 6.6-12), CC 3.85 (2.2-5.5), and LC 5.2 (3.2-7.2). Age-specific incidence showed a peak in females older than 60 years. Female:male ratio was 14:1 in subjects < 60 years, and 3:1 in those ≥60 years. A comparison of current study period with 1993-2008 showed unchanged mean incidence of CC, but a significant increase in women with LC (Rate ratio=2.7; 95% CI, 1.5-5; p=0.001).

Conclusion: After a rise during early 2000s, annual incidence of CC has been stable during the last 10 years around 4/100,000 inhabitants. However, the incidence of LC, which was stable in the period 1993-2008, has significantly increased in women during the last decade.

Disclosure: Nothing to disclose

P1030 ANXIETY AND DEPRESSION IN INFLAMMATORY BOWEL DISEASE PATIENTS - APPLICATION OF HOSPITAL ANXIETY AND DEPRESSION SCALE

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Introduction: Inflammatory bowel diseases (IBD) are chronic and debilitating conditions, that can contribute to the development of anxiety and depression symptoms.

Aims & Methods: We aimed to assess the prevalence of these symptoms in a population of IBD patients, using Hospital Anxiety and Depression Scale (HADS), and identify predictors of these symptoms.

Unicentric, transversal cohort study, including adult outpatients with IBD. Excluded patients with psychiatric disease, severe comorbidity or malig-

nancy and those who refused to participate in the study. Assessed several clinical and analytical parameters and determined the anxiety (HADS-A) and depression (HADS-D) sub scores, which were considered positive if ≥8points.

Results: Included 99 patients, 65.7% with Crohn's Disease (CD). HADS-A≥8 in 64.6% and HADS-D≥8 in 96.0%.

HADS-A score ≥8 associated with female gender (64.1% vs 40.0%,p=0.021), presence of extraintestinal manifestations (EIMs) (91.3% vs 8.7%,p=0.002) and longer disease duration (8.2±6.7 years vs 5.2±4.1 years, p=0.017). When assessing only CD patients, HADS-A score ≥8 associated with higher consumption of benzodiazepines (29.3% vs 8.3%,p=0.048), EIMs (88.9% vs 11.1%,p=0.008) and longer disease duration (8.9±6.4 years vs 4.4±4.3 years, p=0.001).

HADS-D score ≥8 associated with intravenous biologic therapy (100.0% vs 0.0%, p=0.001), EIMs (86.9% vs 13.0%, p=0.038) and ferritin and C Reactive Protein levels (113±137 vs 44±34 ng/mL, p=0.007 and 5.6±5.6 vs 2.9±0.0mg/dL, p< 0.001). In patients with CD, HADS-D ≥8 associated with intravenous biologic therapy (100.0% vs 0.0%, p=0.019), EIMs (88.9% vs 11.1%,p=0.019) and calprotectin levels (366±337 vs 93±16ug/g, p< 0.001). In patients with ulcerative colitis no predictors of HADS-A or HADS-D scores ≥8 were found.

Conclusion: In patients with IBD, anxiety symptoms are present in nearly 2/3 of patients and depression symptoms in over 90%. Anxiety symptoms are more frequent in women and patients with long standing disease, while depressive symptoms associate with disease inflammatory activity. Presence of EIMs associated with both types of symptoms.

Disclosure: Nothing to disclose

P1031 LESS INPATIENT COMPLICATIONS AND ECONOMIC BURDEN IN FEMALE PATIENTS ADMITTED WITH ULCERATIVE COLITIS

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Introduction: Gender in ulcerative colitis (UC) is a well-studied topic with contradicting results with a slight male predominance seen in large population based studies in Olmsted County, Minnesota, while other studies have shown a slight female predominance. Yet, the relationship between UC and gender is not well-understood. Hence, it is unclear what is responsible for differences in gender.

Aims & Methods: The aim of this study is to assess the inpatient prevalence and inpatients outcomes of UC by gender.

Case-control study using the NIS 2016, the largest public inpatient database in the US. All patients with ICD9-10CM codes for UC were included. None were excluded. Female patients were identified within the database using the female gender indicator.

The primary outcome was determining the odds of UC in female patients compared to males. Secondary outcomes included determining inpatient morbidity, mortality, resource utilization, colectomy rates, hospital length of stay (LOS), and inflation-adjusted total hospital costs and charges.

Propensity score matching was used to create a matching population for Charlson Comorbidity Index and age. Multivariate regression analyses were used to adjust for income in patient zip code, hospital region, location, size and teaching status.

Results: A total of 38, 950 patients with UC were identified and propensity matched for selected covariates. The mean patient age was 45, and 47.2% were female. For the primary outcome, females had decreased adjusted odds (aOR: 0.92, p< 0.01) of being admitted for UC. For secondary outcomes, female patients displayed lower adjusted odds of multi-organ failure, being placed on TPN, and undergoing colectomy. Females also had lower adjusted mean hospital costs, charges, and length of stay (LOS). All adjusted odds and means are displayed in Table 1.

Conclusion: Females have lower inpatient prevalence of UC, complications, and economic burden compared to males. This reinforces the slight male predominance that was seen in the older Olmstead County population-based studies. One can speculate that the difference in complications, costs, charges, and LOS indicate that females have less severe disease course at hospital admission. Numerous studies have examined the association of gender with disease severity and outcomes, and there continues to be conflicting data.

Thus, future studies are needed to determine what contributes to the variation in disease prevalence and course by gender, and possibly better tailor treatment regimens by gender.

Disclosure: Nothing to disclose

Variable	Adjusted OR	95%CI	p-value
Ulcerative Colitis	0.92	0.86 - 0.98	0.01
Mortality	1.03	0.48 - 2.23	0.94
Shock	0.86	0.54 - 1.37	0.53
ICU	0.78	0.48 - 1.26	0.30
TPN	0.69	0.51 - 0.93	0.01
Multi-organ failure	0.66	0.55 - 0.80	<0.01
Colectomy	0.74	0.56 - 0.99	0.04
Variable	Adjusted Means	95%CI	p-value
Additional Adjusted Costs	-$1,677	-2508,846	<0.01
Additional Adjusted Charges	-$5,615	-9300,1929	<0.01
Additional Adjusted Length of Stay (days)	-0.5	-0.80,0.21	<0.01

[Adjusted odds ratios and means for selected variables in female patients with UC compared to males.]

P1032 USE OF TARGETED BACTERIOPHAGE COCKTAIL FOR THE TREATMENT OF INFLAMMATORY BOWEL DISEASE

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Introduction: An abnormal intestinal microbiota (dysbiosis) is associated with the inflammatory bowel disease (IBD) phenotype and is considered to be a causal or synergistic factor, together with genetic and environmental elements, in perpetuating chronic inflammation. Recent studies demonstrated that a specific *Klebsiella pneumoniae* strain (KP2H7) isolated from the oral cavity of IBD patients causes strong TH1 immune stimulation in germ free wild type mice and colitis in germ free mono-colonized colitis-prone mice [Atarashi et al. Science, 2017]. The present study aims to validate the KP2H7 bacteria as a disease-associated target in IBD patients and to initiate development of a bacteriophage-based therapy that targets this specific bacterial strain by demonstrating ability of a rationally designed phage cocktail to significantly reduce the KP2H7 load in colonized animals.

Aims & Methods: 300 stool samples from patients including IBD patients from France and Israel were assessed for the presence of KP2H7 strains by applying metagenomic analyses and KP2H7 isolation methods combined with strain specific qPCR, respectively. To examine the prevalence of KP2H7 in the IBD population in the United States (US), the metagenomic data released by the Human Microbiome Project group (HMP Part 2) were re-analyzed to determine its association with IBD.

In parallel, "phage hunting" techniques were applied to isolate tens of natural phage that target the KP2H7 strains from environmental and clinical samples. By combining phage with complementary characteristics (such as differences in their bacterial hosts and recognition of different bacterial surface receptors), phage cocktails were designed and tested for their ability to significantly reduce KP2H7 bacterial burden in mice that were colonized with this bacteria by oral gavage.

Results: A KP2H7 prevalence of about 30% was consistently observed in IBD patients across three different geographical locations (Table 1). In the subset of patients for whom deep metadata was also available, a trend in KP2H7 abundance was observed in correlation with disease severity (flare vs remission).

The phage cocktail targeting KP2H7 strains demonstrated significant reduction of bacterial burden in the stool and intestinal mucosa (5 log reduction after 3 administrations of a 5 phage cocktail) when orally administered to mice that were previously colonized with these bacteria.

Conclusion: The KP2H7 prevalence data collected from IBD patients offer support for the potential association of KP2H7 and similar strains with IBD, and have demonstrated the existence of a significant target population for phage therapy targeting these bacteria. The efficient eradication of KP2H7 strains by a specifically tailored phage cocktail administered orally to colo-

nized mice suggests that IBD patients carrying these strains may benefit from phage therapy. Since this new treatment modality addresses potential microbiome drivers of IBD and not just disease symptoms, it should be further evaluated as a potential disease-modifying therapy.

Country	Ulcerative Colitis n/N (%)	Crohn's Disease n/N (%)	IBD n/N(%)
Israel	19/52 (37)	17/57 (30)	36/109 (33)
United States	9/30 (30)	23/50 (46)	31/80 (39)
France	11/46 (24)	15/43 (35)	26/89 (29)

[Prevalence of KP2H7 strains in patients with IBD]

References: Atarashi K, Suda W, Luo C, et al. Ectopic colonization of oral bacteria in the intestine drives TH1 cell induction and inflammation. Science 2017 358; (6361): 359-365

Disclosure: All authors are employees of BiomX Ltd.

P1033 STIGMATISATION AND RESILIENCE IN INFLAMMATORY BOWEL DISEASE: RESULTS FROM AN ITALIAN, SINGLE-CENTRE, LONGITUDINAL STUDY

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Introduction: Inflammatory bowel disease (IBD) encompasses two main life-long chronic immune-mediated disorders, namely Crohn's disease (CD) and ulcerative colitis (UC). Symptoms range from abdominal pain and diarrhoea, to fever, weight loss, and malnutrition requiring hospitalisation. IBD has a negative impact on quality of life, including private and social life. IBD is also susceptible to stigmatisation, mainly because of its symptoms, the old assumption of being a psychosomatic disorder, and because it may deeply affect sexual function. Patients affected by chronic disorders may have an impaired resilience, that is defined as the capacity of thrive in face of adversity, adapting body, mind and spirits to life circumstances, including health issues. No study has ever assessed resilience in IBD patients.

Aims & Methods: Aim of this study was to investigate resilience and perceived stigmatisation in an Italian adult cohort of IBD patients. Starting January 2019, consecutive IBD patients were prospectively enrolled, and were regularly followed up at the IBD tertiary medical centre in Pavia. A definite diagnosis of CD and UC was established for a duration of at least three months prior to enrolment. Over, the same period, a cohort of blood donors from the same geographic area was enrolled as healthy controls (HC) to evaluate the average level of resilience in the Italian population. Demographic and relevant clinical data were recorded at the time of the physician evaluation, and every patient was asked to fill in the perceived stigma scale (PSS) and the 25-item Connor-Davidson resilience scale (CD-RISC25). PSS included sub-scores for significant others (friends, family members, spouse or partner) and for health care providers. Disease activity was assessed through Harvey-Bradshaw Index (HBI) for CD and partial Mayo Score for UC. The study is still ongoing and patients are being recruited.

Results: A total of 101 IBD patients were enrolled (mean age 46.37±16.5 yrs, F:M=0.8:1), including 46 CD and 55 UC. 249 HC were enrolled (mean age 42.16±12.28 yrs, F:M=1:1.5) as controls for resilience only. The mean PSS score for significant others was 0.62±0.48, and no difference was seen between CD and UC patients. Patients with an active disease had a mean PSS of 1.27 compared to those with inactive disease (0.8, p=0.05). No difference was seen between males and females (1.02 vs 0.82; p=0.22). Mean CD-RISC25 was significantly lower in IBD patients compared to HC (62.93

vs 69.45; p=0.0003). Also, females IBD patients had a lower mean CD-RISCS25 compared to males (59.43 vs 65.63, p=0.06). Mean CD-RISC25 was also lower in patients with active disease compared to inactive disease (48.5 vs 67.52; p=0.02).

Conclusion: This is the first study showing a low resilience in IBD patients, especially in those in the active phase. Also, patients with active IBD are more likely to suffer from social stigmatisation that may negatively impact on quality of life. These results should not be overinterpreted, as the study is still underway. More studies are needed in order to evaluate possible targeted interventions for this population.

References: 1. Di Sabatino A, Lenti MV, Giuffrida P, Vanoli A, Corazza GR. New insights into immune mechanisms underlying autoimmune diseases of the gastrointestinal tract. Autoimmun Rev 2015;14:1161-9. 2. Aaa Kaplan GG. The global burden of IBD: from 2015 to 2025. Nat Rev Gastroenterol Hepatol 2015;12:720-7. 3. Taft TH, Keefer L, Leonhard C, Nealon-Woods M. Impact of perceived stigma on inflammatory bowel disease patient outcomes. Inflamm Bowel Dis 2009;15:1224-32. 4. Looper KJ, Kirmayer LJ. Perceived stigma in functional somatic syndromes and comparable medical conditions. J Psychosom Res 2004;57:373-8. 5. Fife BL, Wright ER. The dimensionality of stigma: a comparison of its impact on the self of persons with HIV/AIDS and cancer. J Health Soc Behav 2000;41:50-67. 6. Taft TH, Keefer L. A systematic review of disease-related stigmatization in patients living with inflammatory bowel disease. Clin Exp Gastroenterol 2016;9:49-58. 7. Connor KM, Davidson JR. Development of a new resilience scale: the Connor-Davidson Resilience Scale (CD-RISC). Depress Anxiety 2003;18:76-82.

Disclosure: Nothing to disclose

P1034 FECAL MICROBIOTA COMPOSITION OF ULCERATIVE COLITIS PATENTS AFTER RESTORATIVE PROCTOCOLECTOMY WITH ILEAL POUCH-ANAL ANASTOMISIS- COMPARATIVE, PROSPECTIVE STUDY FROM HUNGARY

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Introduction: The exact etiology of ulcerative colitis (UC) is unknown, however, according to the present view, the disease is the result of a chronic inflammatory reaction resulting from abnormal immune response of normal gut flora in genetically susceptible individuals.

Aims & Methods: The aim of our study was to determine the composition of the intestinal microbiome in UC patients after restorative proctocolectomy with ileal pouch-anal anastomosis, compared with UC patients with varying extention, FAP (familial adenomatous polyposis) patients after colectomy and IPAA surgery and healthy controls.Active and inactive UC patients who underwent on restorative proctocolectomy and IPAA formation were enrolled in the study.

To compare, active and inactive UC patients with different extent were enrolled, as well. The same number of healthy subjects was aimed to enroll as control group. Clinical data of patients, blood and fecal samples were collected. Fecal microbiota structure was determined by sequencing the V4 hypervariable region of the 16S rRNA gene. Fecal community structure was determined at genus level.

Results: Overall, 63 patients were enrolled: 25 UC patients with pouch, 17 UC patients, 8 FAP patients with pouch and 13 healthy control. Only 6 of UC patients with pouch received maintenance therapy (5-ASA, corticosteroids), on the contrary, only one UC patient was without medication. Significant bacterial abundance differences were observed among the examined groups.

Compared to the control, both UC groups had higher *Streptococcaceae, Pasteurellaceae,* and lower *Desulfovibrionaceae* abundance. Higher bacterial abundance of *Bacteroidaceae, Erysipelotrichaceae, Clostridiaceae, Peptostreptococcaceae,* and lower *Ruminococcaceae, Rikenellaceae, Porphyromonadaceae* were found in the UC patients with pouch group compared

to UC patients and controls. There was a significant difference between the groups regarding to the abundance of *Prevotellaceae* and *Enterobacteriaceae.* Fecal microbiome determination of FAP patients are in progress.

Conclusion: Changes in bacterial abundance had been observed in UC patients with and without pouch compared to healthy controls. These changes may be a part of the pathomechanism , but the consequence of intestinal inflammation in UC, as well.

Disclosure: Nothing to disclose

P1035 THE HIDDEN BURDEN OF FAECAL INCONTINENCE IN ACTIVE AND QUIESCENT ULCERATIVE COLITIS: AN UNDERESTIMATED PROBLEM?

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Introduction: Despite advances in Ulcerative Colitis (UC) therapies, many patients suffer refractory defaecatory symptoms in the absence of active inflammation. For this group, treatment remains challenging, with a paucity of research and limited therapeutic options. In this prospective, ongoing study, we aim to determine the prevalence of faecal incontinence (FI) in patients with quiescent UC.

Aims & Methods: In a cross-sectional study, consecutive patients with UC attending Inflammatory Bowel Disease (IBD) clinics were invited to participate. Patients completed a series of validated questionnaires; including an IBD-specific FI questionnaire (ICIQ-IBD questionnaire), Hospital Anxiety and Depression Scale (HADS), the Rome IV diagnostic questionnaire, and the IBD-control questionnaire. Participants were requested to return a Faecal Calprotectin (FCP) within 2 weeks of completing questionnaires. Quiescent UC was defined as IBD-control 8 score ≥13 and IBD-control-VAS ≥85, and/or FCP levels ≤250 (where available, FCP data were used in preference to IBD-control to classify UC activity). Data were compared between active and quiescent groups using chi-square and non-parametric tests.

Results: Overall, n=97 UC patients (n=50 males, mean age 48 (range 18-82) participated. ICIQ-IBD data revealed that most patients experience FI (84/97 (87%) during 'relapses'. Interestingly, 58/97 (60%) reported FI when in 'remission', and this group had higher median HADS depression (P=0.0002), poorer QoL scores (P< 0.0001), and trend towards higher HADS anxiety (P=0.09) scores, compared to those without FI. Disease activity data (IBD-control and/or FCP) were available for all patients, and based on these 61/97 (63%) had quiescent UC. The prevalence of FI based on ICIQ-IBD did not differ between those with active (22/36, 61%) and quiescent UC (36/61, 59%), P=NS. In those with FI on ICIQ-IBD, median IBD-FI symptom scores, IBD-FI QoL scores and HADS (anxiety: P=0.47, depression: P=0.18) did not differ between disease activity groups. However, within the quiescent group, patients that met the more stringent Rome IV criteria for FI (n=13) had higher median IBD-FI symptom scores (P=0.007) and HADS-depression scores (P=0.05),a trend to worse IBD-FI QoL (P=0.07), but similar HADS-anxiety (P=0.68).

Conclusion: This study is one of the first to identify that regardless of disease activity, FI affects most patients with UC, detrimentally impacting patients' psychological wellbeing, impairing their QoL, and should therefore routinely be screened for in clinics. There is an urgent need for further research in the often neglected area of FI and quiescent disease.

Disclosure: Nothing to disclose

P1036 EARLY ENVIRONMENTAL AND LIFESTYLE FACTORS ARE ASSOCIATED WITH ETIOLOGY AND DISEASE COURSE OF INFLAMMATORY BOWEL DISEASE: AN INTERIM REPORT

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Introduction: Inflammatory Bowel Disease (IBD), consisting of Crohn's disease (CD) and ulcerative colitis (UC) are chronic inflammatory diseases of the gastro-intestinal tract. The etiology of IBD is complex with an interplay between genomic susceptibility, diet, microbiome and environmental factors. Once disease develops, its course remains highly variable and unpredictable due to yet unknown disease modifiers. The role of environmental factors in etiology and disease course remain inconclusive, while the identification of modifiable risk factors is crucial for potential personalized preventative and disease modifying strategies. We executed a large population-based study evaluating known and possibly involved environmental factors in the etiology of and disease course in IBD.

Aims & Methods: All IBD patients of the 1000IBD cohort at the University Medical Center Groningen (UMCG), the Netherlands, were asked to fill the validated Groningen IBD Environmental Questionnaire (GIEQ). Overall, 848 environmental factors were, grouped in 15 categories.
To study etiology, patients were group-matched, based on age at diagnosis and sex, in a 1:2 ratio to participants of the population-based LifeLines cohort study, who completed a comparable questionnaire. To study disease course, data collected by the GIEQ was linked corresponding clinical data from the 1000IBD cohort. Disease complications were defined as the need for biological therapy or surgery. Logistic regression was applied to estimate the multivariable-adjusted effect of lifestyle factors on IBD (odds ratio; OR) and 95% confidence intervals. Case-control comparisons were corrected for their differences in age, sex and history of smoking for etiology, as well as disease duration for disease course. A p< 0.05 was considered as nominal and Bonferroni adjusted p-value as statistically significant. A large number of environmental factors were examined, the interim results are reported.

Results: 728 patients of the 1000IBD cohort completed the GIEQ. There were no differences in baseline characteristics between participants and the remaining cohort (P>0.2). Several environmental factors were associated with statistically significant increased risk of IBD, such as the presence of more than three stressful life-events prior to diagnosis CD (OR 2.9, 95%CI 1.9-4.5) and UC (2.6,1.7-4.0); and prenatal smoke exposure for CD (1.9,1.4-2.6) and UC (1.6,1.2-2.2), but showed no effect on disease course. While living environment for the first 5 years of life showed a nominal risk increasing trend for CD and UC, an urban living environment was associated with higher odds of surgery later on (2.3,1.2-4.7). Having pets during the first year of life showed a striking protective effect for both disease (CD and UC; cat 0.4,0.4-0.5, dog 0.4,0.4-0.6), while having a pet during disease was associated with increased risk of both the need for biologicals as well as surgery in UC (2.6,1.1-6.1;4.2,1.9-9.2, respectively).

Conclusion: Stress and prenatal smoke exposure were associated with significantly higher odds of developing IBD. Childhood pets were associated with less odds of IBD, whereas current pets might negatively influence disease course in established UC. Larger studies are needed to validate these findings and further evaluate the role of modifiable environmental factors and their interactions in preventive strategies and personalized treatment.

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P1037 MYCOBACTERIUM AVIUM *SUBSPECIES* PARATUBERCULOSIS SEROPOSITIVITY IS ASSOCIATED WITH A MORE COMPLICATED DISEASE COURSE IN BOTH CROHN'S DISEASE AND ULCERATIVE COLITIS AND MIGHT BE LINKED TO IMMUNOMODULATING GENES

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Introduction: The role of *Mycobacterium Avium* subspecies *Paratuberculosis* (MAP) in Crohn's disease (CD) is controversial. Due to many similarities between CD and Johne's disease, a chronic enteritis in dairy cattle caused by MAP, its role in CD etiology has been studied repeatedly. CD patients seem more prone to MAP infection compared to healthy controls. However, whether MAP acts as a causative agent of CD, an inflammatory trigger or as a secondary invader remains elusive. Over 200 genetic risk loci have been identified in inflammatory bowel diseases, but genetic determinants of MAP infection are poorly studied. Moreover, whether MAP exposure affects CD disease course remains elusive. In this study, we explore genetic determinants of MAP infection and the association of MAP infection with the course of IBD.

Aims & Methods: Detailed clinical characteristics, serum and DNA were obtained from in total 847 patients with IBD included in the prospective 1000IBD cohort. In addition, serum samples from 53 healthy controls were collected. MAP serology was determined in all available serum samples. Two conjugates (Protein A-HRP: detects IgA, IgE, IgG1,2,4 and IgM, and Protein G-HRP: detects IgG1-4) were used to measure antibody response to four different MAP antigens (Protoplasmic MAP antigen and three recombinant MAP antigens). Cut-off values according to Bernstein et al. were used to determine seropositivity with a 95% specificity. Logistic regression models, adjusted for age, sex, disease duration, history of smoking and batch effects, were used to explore the association between MAP and IBD disease course. All patients were genotyped with the Illumina Global Screening Array, and genetic data were imputed to the Haplotype Reference Consortium reference panel. A genome-wide association study (GWAS) for presence of MAP seropositivity was performed.

Results: Patients with IBD had similar rates of MAP seropositivity as compared to controls (*P*>0.2) and baseline characteristics were comparable between seropositive and seronegative patients. Disease location, behavior and extent, classified using the Montreal classification, were not associated with MAP seropositivity (*P*>0.1). Multivariate analyses identified MAP seropositivity for conjugate A as risk factor of a more complicated disease course in patients with CD (biological use [OR 2.19; (95% CI 1.01-4.75]) and in patients with UC (surgery [OR 2.01 95% CI 1.01-3.99]). Using GWAS, a total of 50 genetic loci were associated with MAP seropositivity at a suggestive genome-wide significance threshold (P< 5x10^{-5}). One of these loci (rs7901290 [*P*=8E-7; OR=1.86) harbors the *CAMK1D* gene, which is involved the regulation of granulocytes. Another associated locus (rs1001792 [*P*=4E-7; OR=1.92]) harbors the *TNFRSF10B* gene, which has been associated with and apoptosis induction.

Conclusion: Patients with IBD had similar rates of MAP seropositivity compared to healthy controls. MAP seropositivity showed no association with IBD disease location, specifically not with ileal Crohn's disease. However, seropositivity for MAP conjugate A, representative for mucosal and acute phase immunoglobulins, was identified as a risk factor of a more complicated disease course in both CD and UC. GWAS analyses show suggestive associations between MAP seropositivity and immunomodulating genes. Future studies in independent cohorts using Ig isotype specific tests are needed to validate these findings and to explore the interaction between genetic susceptibility, MAP exposure and IBD.

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P1038 IBD PREVALENCE IN LOTHIAN, SCOTLAND, DERIVED BY CAPTURE-RECAPTURE METHODOLOGY

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Introduction: Inflammatory bowel disease (IBD) prevalence is estimated to be rising but no detailed, recent United Kingdom (UK) data are available. The last reported prevalence rate in the UK was 0.40% in 2003.[1]

Aims & Methods: We aimed to establish the current and projected future prevalence in Lothian, Scotland.

We conducted an extensive all-age multiparameter search strategy using inpatient IBD international classification of disease (ICD-10) coding (K50/51)(1997-2018), IBD pathology coding (1990-2018), primary and secondary care prescribing data (2009-18) and a paediatric registry (1997-2018) to identify "possible" IBD cases to 31/08/18.

A team of IBD physicians manually confirmed all diagnoses through electronic health record (EHR) review as per Lennard-Jones/Porto criteria. Prevalence and incidence calculations were performed using mid-year population estimates or projections from National Records Scotland.[2]

Trends in incidence, prevalence and mortality over time were reported as annual percentage change, calculated by exponentiating the beta-coefficient of Poisson regression and subtracting 1. Poisson modelling was also used to calculate significance in these trends over time. Autoregressive integrated moving average (ARIMA) regression was applied to forecast prevalence to from 31/08/18 to 01/08/28.

Results: In total, 24,601 possible IBD cases were identified and then manually reviewed, revealing 10,499 true positives. The optimum search strategy was pathology plus mesalazine prescription and ICD-10 K50/51 coding that identified 95% true positives with 6% false negatives.

The point prevalence for all IBD in Lothian on 31/08/18 was 784/100,000 (ulcerative colitis (UC) 432/100,000, Crohn's disease (CD) 284/100,000, and IBD unclassified (IBDU) 68/100,000) (Table 1).

Year	Population of Lothian Healthboard	UC (prevalence/ 100,000)	CD (prevalence/ 100,000)	IBDU (prevalence/ 100,000)	All (prevalence/ 100,000)
2008	808,940	315	216	36	567
2009	816,510	334	224	38	596
2010	825,520	349	232	41	621
2011	836,610	359	242	43	644
2012	843,740	375	249	47	671
2013	849,720	386	258	51	694
2014	858,120	398	265	56	719
2015	867,800	411	270	59	739
2016	880,000	418	274	62	753
2017	889,450	427	278	66	772
2018	897,210	432	284	68	784

[Standardised prevalence per 100,000 population for Lothian on 31st August between 2008-18]

There was no significant change in incidence between 2008-2018 (annual percentage change 14.4%; 95% CI -0.9, +32.1%, P= 0.66), nor IBD prevalent cohort mortality (annual average percentage change 10.5%, 95% CI -18.8, +50.0, P= 0.52).

However prevalence increased by 4.3% per year over the same period (95% CI +3.7, +4.9%, P< 0.0001) (Table 1). ARIMA modelling projected a point prevalence on 01/08/28 of 1.02% (95% CI 0.97-1.07%) that will affect an estimated 1.53% (95% CI 1.37-1.69%) of those over 80 years of age.

Conclusion: We report a rigorously validated IBD cohort with all-age point prevalence on 31/08/18 of 1 in 125, one of the highest worldwide. Incidence has consistently exceeded mortality in our cohort for the past 10 years, exemplifying the effects of compound prevalence.

We project prevalence will rise to 1 in 98 by mid 2028, with the majority of IBD patients over 50years of age. This has significant current and future implications for IBD service delivery.

References: 1. Stone MA, Mayberry JF, Baker R. Prevalence and management of inflammatory bowel disease: a cross-sectional study from central England. European Journal of Gastroenterology & Hepatology 2003;15:1275-80. 2. www.nrscotland.gov.uk/statistics-and-data/statistics/statistics-by-theme/population/population-estimates/mid-year-population-estimates

Disclosure: Nothing to disclose

P1039 HIV POSITIVE PATIENTS ARE AT A GREATER RISK FOR DEVELOPMENT OF INFLAMMATORY BOWEL DISEASE

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Introduction: Overlap and intersection exists between inflammatory bowel disease (IBD) and HIV with regards to mucosal barrier and immune cells. HIV is felt to potentially attenuate inflammation in IBD, however, very limited data exists on the development of IBD in HIV+ patients. This is of importance as treatments for IBD are being studied for HIV and treatments for HIV therapies are being studied for IBD.

Aims & Methods: Using Explorys (1999-2019), a HIPAA-enabled web platform that includes clinical and lab data from over 63 million unique individuals, we aimed to quantify the risk for new-onset IBD among patients who had a diagnosis of HIV versus the general population. IBD was diagnosed based on a combination of ICD-9 codes and at least one prescription for an IBD specific medication (5-ASA, immunomodulator, biologic). Relative risks (RR) with 95% Confidence Intervals (CI) are reported.

Results: A total of 357,950 patients tested positive for HIV, of which 10,570 developed new-onset IBD after their HIV diagnosis (3,043/100,000 persons). The risk of developing IBD among HIV positive patients was 5-fold higher than the general population (RR 5.26, 95% CI 4.81, 5.74, p< 0.001). The majority of patients developing new-onset IBD were not on anti-retroviral therapy for their HIV (89% vs. 11%, p< 0.001) and a higher proportion of new-onset IBD cases in the HIV positive patients were Crohn's disease as compared to the new-onset IBD cases in the general population (65% vs. 42%, p< 0.001).

	De-novo IBD in HIV+	IBD Group without HIV+	P
Subtypes, n [%]			
Crohn's Disease	6,840 [65]	152,580 [42]	< 0.0001
Ulcerative Colitis	3,000 [28]	128,560 [35]	< 0.0001
Indeterminate Colitis	730 [7]	85,480 [23]	< 0.0001
IBD-Associated Outcomes, n [%]			
Colectomy	1,180 [11]	44,720 [12]	0.0018
Proctolectomy	30 [0]	3,840 [1]	< 0.0001
Ileostomy	3,490 [33]	18,780 [5]	< 0.0001
Fistulectomy	50 [0]	2,220 [1]	< 0.0001
All-Cause Mortality, n [%]	570 [5]	21,040 [6]	< 0.0001

[HIV+ Patients and De-Novo IBD]

Conclusion: We observed that HIV positive patients are at a greater risk for development of IBD as compared to the general population. The majority of new IBD diagnoses among HIV positive patients are Crohn's disease and are often not receiving anti-retroviral therapy. Further research is needed to confirm these observations and to understand how antiretroviral therapy influences the risk for development of IBD.

Disclosure: Nothing to disclose

P1040 THE IMPACT OF EATING HABITS ON THE OCCURRENCE OF ULCERATIVE COLITIS

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Introduction: Ulcerative colitis is a chronic state, and its etiology is not currently evident. Inflammatory bowel diseases originate at the interface of inherited predisposition, impact of certain environment factors and intestinal microflora changes. Impact of nutrition factors on emergence of risk of ulcerative colitis has been discussed for many years, which was confirmed by the increased incidence of inflammatory bowel diseases in developed countries compared to developing countries. Changes in general nutrition approaches in the last years have caused the prevalence of bowel diseases to increase. It should be noted that there is an increased incidence of inflammatory bowel diseases in the countries with previously lower incidence, which is associated with the changes in the lifestyle of modern society.

Aims & Methods: Aim of this study was: to estimate the impact of nutrition factors on the risk of development of ulcerative colitis based on the analysis of food consumed; to evaluate the significance of consumption of certain nutrients in development of ulcerative colitis among Western Siberian population. We conducted a survey of 81 patients suffering from ulcerative colitis and 39 healthy respondents. We studied the profile of eating habits of patients with ulcerative colitis (prior to being diagnosed) compared to habits of healthy respondents. The study of nutritional patterns of patients with ulcerative colitis and healthy respondents was conducted using the standardized WHO CINDI questionnaire. The survey includes 12 questions regarding the frequency and amount of consumption of certain foods. Particular attention was paid to the consumption of milk and dairy products, meat, fruits, vegetables, carbohydrate foods and sugar. Respondents were offered to choose out of possible options.

Results: The diet of patients with ulcerative colitis is characterized by rare consumption and small portions of fresh and cooked vegetables and fruits prior to the first symptoms of the disease (U=1094,5; Z=-2,7; p=0,01). Patients with ulcerative colitis consumed more sugar with tea and/or coffee compared to healthy respondents prior to the first symptoms of the disease (U=1214,0; Z=-2,0; p=0,04). Patients with ulcerative colitis poorly tolerated milk and dairy products prior to the first symptoms of the disease (2I=9,72, p< 0,01). There were no statistically significant differences detected between patients with ulcerative colitis and healthy respondents and their consumption of meat (U=1330,0; Z=-1,4; p=0,16*)*, spicy, fried, salty smoked food (U=1530,0; Z=0,3; p=0,78), and frequency of visits to fast food outlets (U=040; Z=-1,0; p=0,33*)*.

Conclusion: Our study confirms the possible effect of a lack of dietary fiber and excessive sugar intake on the emergence of ulcerative colitis.

Disclosure: Nothing to disclose

P1041 FUNCTIONAL RARE VARIANTS INFLUENCE THE CLINICAL RESPONSE TO ANTI-TNF THERAPY IN CROHN'S DISEASE

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Introduction: Loss-of-function (LoF) variants are one of the most interesting forms of rare functional genetic variations as they impair the function of a gene and are more likely to lead to extreme phenotypes

Aims & Methods: Our aim was to know the impact of functional rare variants in clinical response to anti-TNF therapy in Crohn's disease (CD). CD anti-TNF naïve patients starting anti-TNF treatment due to active disease (CDAI>150) were included. The whole genome was sequenced using the Illumina Hiseq4000 platform. Clinical response was defined as a CDAI score < 150 at week 14 of anti-TNF treatment. Low-frequency variants were annotated and classified according to their damaging potential. The whole genome of CD patients was screened to identify homozygous LoF variants. The TNF signaling pathway was tested for overabundance of damaging variants using the SKAT-O method. Functional implication of the associated rare variation was evaluated using cell-type epigenetic enrichment analyses

Results: A total of 41 CD patients were included. From them, 54% were male, 75% had ileal or ileocolonic involvement, 12% had structuring and 26.8% fistulising behavior, 20% had perianal disease, 41.5% had previous surgery, 80% of them were under concomitant immunomodulators; 61% were treated with infliximab and 39% with adalimumab. At week 14, 61 % had remission and 24% were primary non-responders. A total of 3,250 functional rare variants (2,682 damaging and 568 LoF variants) associated with response to anti-TNF therapy were identified. The strongest damaging impact was detected in 10 LoF SNPs (table 1). Two homozygous LoF mutations were found in *HLA-B* and *HLA-DRB1* genes associated with lack of response and remission, respectively. Genome-wide LoF variants were enriched in epigenetic marks specific for the gastrointestinal tissue (colon, *P*=4.11e-4; duodenum, *P*=0.011). The burden of damaging variation in the TNF signaling pathway was associated with response to anti-TNF drugs (*P*=0.018); damaging variants were enriched in epigenetic marks from CD8+ (P=6.01e-4) and CD4+ (P=0.032) T cells

Conclusion: Functional rare variants are involved in the response to anti-TNF therapy in CD. Cell-type enrichment analysis suggests that the gut mucosa and CD8+ T cells are the main mediators of this response. These findings provide new insights into the underlying heterogeneity of CD, revealing the basis of TNF-dependent biological mechanisms

Men (%)	22 (53.7)
Location (%) Ileal Colonic Ileocolonic	 14 (34) 6 (14.6) 17 (41.5)
Behavior (%) Inflammatory Stricturing Fistulizing	 21 (51.2) 5 (12) 11 (26.8)
Perianal disease (%)	8 (19.5)
Extraintestinal manifestations (%)	14 (34)
Previous surgery (%)	17 (41.5)
Smoking habit (%)	16 (39)
Steroids	7 (17)
Immunomodulators (%) Thiopurines Methotrexate	 30 (73) 3 (7.3)
Anti-TNF type (%) Adalimumab Infliximab	 16 (39) 25 (61)

[Table 1. Characteristics of the study population]

P1042 USE OF TPMT GENOTYPING FOR EVALUATION OF THIOPURINES TOXICITY RISK IN LATE-ONSET IBD PATIENTS

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Introduction: Thiopurines are the most widely used immunosuppressants in inflammatory bowel disease (IBD), but in elderly IBD patients they are associated with an increased risk of adverse effects (AE) [Calafat M. et al, 2018]. Elderly patients with IBD are more vulnerable due to a higher rate of comorbidities, polypharmacy and changes in pharmacokinetics, and therefore have an increased risk for treatment related complication [Broekman M., 2017]. Starting thiopurines over 60 years of age should be followed by a closer monitoring. Thiopurine S-methyltransferase(TPMT) deficiency leads to an accumulation of higher levels of cytotoxic thiopurine nucleotides in patients carrying defective *TPMT*alleles and can prospectively identify patients at higher risk for thiopurines toxicity [Robert D. Nerenz, 2018].

Aims & Methods: To evaluate a role of TPMT genotyping in late-onset IBD patients as part oftherapeutic drug monitoring. DNA samples of 127 IBD patients over 40 years old (median age 53 years; Q1-Q3=47,0-62,0) were obtained from the Genome Database of the Latvian Population. *TPMT*genotyping with a real-time polymerase chain reaction (PCR) (TaqMan Drug Metabolism Genotyping Assays) was performed for detection of rs1800462, rs1800460, and rs1142345 single nucleotide polymorphisms (SNPs). The three common non-functional *TPMT*alleles (*TPMT*2, *3B*, and **3C*) were determined in 57,5% women and 42,5% men. Data were collected about demographics, medication intolerance, allergies and comorbidities. Data were analysed in SPSS®23.

Results: Our study includes 77% (n=98) of patients with ulcerative colitis, mean age 55±11 years and 23% (n=29) of patients with Crohn's disease, mean age 57±13 years, p=0,4. 92,1% were wild-type homozygous *TPMT*1/*1* genotype, 7,9 % (n=10) were heterozygous. In total four patients had history of azathioprine (AZA) adverse events: gastrointestinal intolerance (n=2), hepatotoxicity (n=1), myalgia (n=1). In total 20,5% (n=26) of patients marked allergies on different medication groups as antibiotics, analgesics, etc.The most frequent polymorphism was *TPMT*1/*3A* genotype in 6,3%. No patients were homozygous for any mutation. 7,9% (n=10) of

patients with *TPMT*1/*1* genotype takes AZA in standard dosage 2-2,5 mg/kg without any adverse drug effects. In total 75,6% (n=96) of patients had comorbidities as cardiovascular diseases (arterial hypertension, stenocardia, chronic heart failure) and endocrine diseases (diabetes mellitus, thyroid disorders, adiposity).

Conclusion: We have identified *TPMT*1/3A*as the most prevalent polymorphisms in late-onset IBD patients. TPMT genotyping is an effective method of thiopurines toxicity risk evaluation in late-onset IBD patients. Our data shows that AZA still remains effective treatment in late-onset IBD patients, however detection of TPMT status should be used as a part of therapeutic drug monitoring.

Disclosure: Nothing to disclose

P1043 PREDICTED EFFICACY OF A PHARMACOGENETIC PASSPORT FOR INFLAMMATORY BOWEL DISEASE

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Introduction: The therapeutic armamentarium for Inflammatory Bowel Disease (IBD) is rapidly expanding, but inter-individual variability in response remains high, partly driven by genetic variation. Several gene-drug interactions predictive of therapeutic outcomes or adverse drug responses have been identified: genetic variants in *thiopurine-S methyltransferase (TPMT)* and *nudix hydrolase 15 (NUDT15)* are predictive of thiopurine-induced myelosuppression (TIM), the *HLA-DQA1-HLA-DRB1* haplotype is predictive of thiopurine-induced pancreatitis (TIP), and recently the *HLA-DQA1*05* haplotype has been identified as a genetic determinant of immunogenicity of TNFα-antagonists. Pre-treatment pharmacogenetic testing allows personalised therapies and optimisation of therapeutic outcomes, but its uptake into clinical practice and guidelines has been slow. The aim of this study was to explore the predicted clinical effectivity of an IBD specific pharmacogenetic passport, including multiple pharmacogenetic predictors.

Aims & Methods: Detailed clinical characteristics were obtained from patients treated with azathioprine and/ or a TNFα-antagonist in an IBD specialised tertiary hospital. The presence of thiopurine toxicity and/or immunogenicity of TNFα-antagonists was retrospectively evaluated using stringent criteria (1,2). All patients were genotyped with the Illumina Global Screening Array. Genetic data underwent stringent quality control and were imputed to the Haplotype Reference Consortium panel. An in-house developed computational pipeline translated genetic data into an IBD pharmacogenetic passport with predicted risks for thiopurine toxicity and TNFα-antagonist immunogenicity for each patient. Using proposed pharmacogenetic-guided treatment guidelines, clinical effectivity estimates were calculated to show the predicted implications of pharmacogenetic pre-treatment testing in the context of IBD management.

Results: Among 817 IBD patients that were exposed to thiopurines and/or TNF-α antagonists, 165 adverse drug responses were identified. An IBD pharmacogenetic passport would have predicted 59 (36%) of these adverse drug responses. For every 50 patients genotyped for *NUDT15* and *TPMT* variants prior to start of thiopurine therapy, one case of TIM would have been prevented. When including genotyping of the *HLA-DQA1-HLA-DRB1* haplotype to predict TIP, only 41 patients need to be genotyped to prevent one case of either TIM or TIP. For every 26 patients with an IBD pharmacogenetic passport, predicting all three gene-drug interactions, 10 patients would receive a positive test result. If these 10 patients subsequently receive pharmacogenetic-guided alternative treatment strategies, one case of either thiopurine toxicity or immunogenicity of TNFα-antagonists will be prevented, which results in a number needed to genotype of 26.

Conclusion: This is the first study that assesses the predicted clinical effectivity of pre-treatment pharmacogenetic testing for multiple gene-drug interactions in a large IBD cohort. Based on our findings, an IBD pharmacogenetic passport will lead to a significant reduction in potentially life-threatening thiopurine toxicity and increased TNFα-antagonist therapy response rates, and should be implemented into clinical guidelines for IBD treatment.

References: 1. Walker GJ, Harrison JW, Heap GA, Voskuil MD, Andersen V, Anderson CA, et al. Association of Genetic Variants in NUDT15 With Thiopurine-Induced Myelosuppression in Patients With Inflammatory Bowel Dis-

ease. JAMA. 2019 Feb 26;321(8):773-85. 2. Heap GA, Weedon MN, Bewshea CM, Singh A, Chen M, Satchwell JB, et al. HLA-DQA1-HLA-DRB1 variants confer susceptibility to pancreatitis induced by thiopurine immunosuppressants. Nat Genet. 2014 Oct;46(10):1131-4.

Disclosure: Nothing to disclose

P1044 GENETIC PREDISPOSITION TO COLON CANCER IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Colonic localization of inflammatory bowel diseases (IBD), ulcerative colitis (UC) and Crohn's disease (CD), represents an important risk factor in the development of colorectal cancer (CRC). The risk of CRC increases 8-10 years after the diagnosis of IBD and strong evidences suggest that CRC occurs in the inflamed epithelium, according to the sequence dysplasia-carcinoma. To date, more than 200 genetic loci have been associated to IBD although none to the development of IBD related cancer.

Aims & Methods: The aim of this study is to clarify the role of some oncogenes and protoncogenes in the molecular mechanism that leads IBD patients to CRC. On the basis of available literature we profiled a panel of 40 genes (39 geness potentially involved in cancer predisposition and the most important gene associated to IBD, NOD2). A germline variant identification analysis pipeline was performed on the DNA of individuals with CRC diagnosis and IBD history.

Data about patients' features, disease history, disease pattern, family history, and drugs were recorded. We ranked all identified germline mutations by pathogenicity and summarized the allelic frequencies of pathogenic or likely pathogenic variants.

Results: We identified 25 IBD patients all consecutively enrolled in a single referral center. The mean age at diagnosis of IBD was of 43 yrs (range 20-72), and a mean age at diagnosis of cancer of 54 yrs (range 36-76). Independently to the disease phenotype status, 8 pts (32%) resulted carriers of at least one major NOD2 susceptibility variants. Multigene panel testing identified 23 mutations in 18 IBD patients (72%): 4 in APC, 3 in MLH1, BRCA1 and CHEK2, 2 in MYH and PDGFRA, 1 in MSH2, MSH3, EPCAM, POLD1, POLE, CDKN2A. Only in two cases (8%) the family history suggested a Lynch syndrome.

Conclusion: This study demonstrates that a high rate of pathogenic varints in CRC/IBD patients, above all in APC and mismatch repair genes. The identification of this variantsmove attention from duration of disease to genetic predisposition as risk factor to develop a CRC. Identification of carriers should make possible stratify patients who need an intensive surveillance regimen or an early indication to prophylactic colectomy.

Disclosure: Nothing to disclose

P1045 PLCG2 GENE ROLE IN INFLAMMATORY BOWEL DISEASE

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Introduction: We believe that multi-generation IBD families have a monogenetic mechanism of inheritance.

Aims & Methods: To identify gene variance associated with IBD inheritance we performed whole exome sequencing (WES) in all our IBD families receiving care at Johns Hopkins IBD Center. We included 37 (35) families with IBD in our study, 17 of which were families of Ashkenazi Jewish ancestry. One hundred fifteen members were sequenced. Affected individuals diagnosed with either Crohn's disease or Ulcerative colitis underwent deep exome sequencing (1-4 individuals/family) performed by our department in collaboration with the genetic department and pediatric gastroenterology. Using PhenoDB analysis we performed individual and merge analysis to identified candidate gene for autosomal dominant or recessive inheritance.

Results: After we have filtered out all the non-frameshift variants and those variants with allele frequency incidence of more than 1% we detected: 0-66 variants per family with autosomal recessive compound heterozygous inheritance potential, 0-39 variants per family with autosomal recessive homozygous potential and 6-454 variants per family with autosomal dominant potential. We then performed merged analysis of all the families included in the study and we identified 35 autosomal dominant variants but none autosomal recessive variants. These 35 gene variants were selected if they met the following criteria: present in 3 or more IBD families, express loss of function, present in GWAS studies, have a high genetic score, have an OMIM phenotype.

Out of the 35 gene selected PCGL2 gene variant was noted in seven families: three families from IBD adult cohort, four families from very early onset IBD. All three adult families exhibit genetic anticipation.

Conclusion: PLCG2 have been found in other autoimmune diseases characterized by antibody deficiency, in immune dysregulation syndrome and familial cold autoinflammatory syndrome 3. Understanding the PLCGL2 role in IBD inheritance associated with genetic anticipation has implications for genetic counseling for children and grandchildren of IBD patients developing novel therapy.

Disclosure: Nothing to disclose

P1046 ARE CUT-OFF RANGES OF INFLIXIMAB SERUM LEVELS IN CROHN'S DISEASE ALWAYS THE SAME IN CLINICAL PRACTICE?

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Introduction: It has been seen that 30-40% of patients treated with Infliximab (IFX) who achieve an initial response to induction therapy lose this response over time with maintenance treatment. Therapeutic drug monitoring (TDM) could be used to optimize management in such situations. However, IFX serum levels are not well defined. The aim of the study was to find our cut-off range of Infliximab serum levels in Crohn's disease (CD) patients in remission in clinical practice.

Aims & Methods: An observational retrospective study was developed from 1st February, 2016, to 30th November, 2017, in our hospital. Patients with established CD who had been on maintenance dosing schedule of IFX were included.

IFX and antibody to IFX levels were measured before each infusion at least twice and after 6 months of treatment in all patients. All the tests were performed using enzyme linked immunosorbent assay (ELISA) with Progenika kits (PROMONITOR®). Clinical remission was defined using Harvey Bradshaw Index (HBI≤4). The interpretation of data was by cluster analysis (Silhouette measure of cohesion and separation: cluster quality >0.5**).

Results: 105 CD patients were included in the study, 57.1% men, with a mean age of 39 (DE±12.9). The median (range) time of the disease was 11 years (7-15). The median (range) time of follow-up was 32 months (22-38). Montreal phenotypes were: 76% A2, 35.2% L2 and 53.3% B1. Perianal disease was present in 51.4%. 265 IFX levels were measured during the follow-up.

Patients who achieved remission had IFX serum levels between 4.26 - 8.26 ug/ml versus 0.06 - 1.43 ug/ml in patients who did not achieve remission (silhouette 0,72) the first time; and 2.84 - 7.75 ug/ml versus 0.05 - 2.69 ug/ml in patients who achieved remission versus those who did not achieve remission respectively the second time (silhouette 0,78) (Fig 1-2). 4,26- 7,75 ug/ml were the best cut-off range for remission (Table 1).

Time 1	Time 2	Most Restrictive interval	
0.06-1.43	0.05-2-69	0.06-1.43	No Remission
1.43-4.26	2.69-2.84	1.43-4.26	Uncertainly zone
4.26-8.26	2.84-7.75	4.26-7.75	Remission

[Crohn's Disease]

We found that perianal disease does not have any influence on IFX serum levels for achieved remission.

Conclusion: In our practice the best value to predict remission status in patients undergoing IFX TDM was 4 - 8 ug/ml, which was higher than in other studies.

References: **Kaufman, L., Rousseeuw, P. J. (1990). Finding groups in data. An introduction to cluster analysis. New York: John Wiley & Sons. doi: https://doi.org/10.1002/9780470316801.

Disclosure: Nothing to disclose

P1047 EARLY MONITORING OF RESPONSE (MORE) TO GOLIMUMAB THERAPY BASED ON FECAL CALPROTECTIN AND TROUGH SERUM LEVELS IN PATIENTS WITH ULCERATIVE COLITIS: A MULTICENTER PROSPECTIVE OBSERVATIONAL STUDY

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Introduction: Study objective: In order to evaluate early prediction markers for the therapy response of golimumab (GLM) in ulcerative colitis, we aimed to assess the association of an detectable GLM trough serum level together with a reduction in fecal calprotectin level in week 6 (W6) with a clinical response in week 26 (W26) in patients with moderate-severe ulcerative colitis.

Aims & Methods: The study was designed as a prospective, single-arm, multicenter, observational study with no interim analyses in Germany between October 2014 and December 2017. Patients aged ≥ 18 years, with diagnosed moderate-severe active ulcerative colitis and starting GLM treatment were offered participation in this ethics approved study at ten registered IBD centers. These sites were recruited by the IBD study platform "German Inflammatory Bowel Disease Study Group" (GISG). After screening, for each eligible patient enrolled, the study duration was 26 weeks with six visits at weeks 0 (baseline), 2, 6, 14, 22 and 26.

The primary outcome was clinical response measured by Partial Mayo Scoring Index (PMS). Clinical response was defined by a Partial Mayo Score ≤ 1 or a reduction in the PMS by two points. Calprotectin level for response in was defined as reduction of ≥50 % in comparison to baseline. Detectable GLM trough level was defined as ≥2.5 μg/ml.

The sample size was calculated for 61 patients (including 3 % drop-outs). Analysis of the primary outcome was done according to the Intention-To-Treat (ITT) method. Missing (outcome) data were imputed as follows: between W0 - W6 classified as therapy failure; between W6 - W26 as Last Observation Carry Forward (LOCF) Effect estimates were reported as relative risks with corresponding 95 % confidence intervals (CI).

Results: 61 patients were enrolled, two patients were excluded due to screening failures. During the course of the study 28 patients discontinued their participation (47,5%) due to 1. withdrawal of GLM therapy (n = 21; 35,6%), 2. withdrawal of consent (n=7; 11,9%).

In the ITT cohort, gender distribution was almost equal (female 52.5%; male 47.5%), the median age was 40.1 (Interquartile Range: 22.1), the mean duration of ulcerative colitis was 8.7 years (95% CI, 6.5 - 10.9). Patients had moderate disease according to PMS with a mean scoring point of 5.6 (95% CI, 5.2 - 6.1). 54.2 % of the enrolled patients were anti-TNF naïve, 8.5 % had experienced a primary and 37.3 % a secondary loss of TNF-alpha therapy prior to the start of GLM therapy.

We showed that patients with an early detectable positive GLM trough level in W6 and a change in calprotectin at the same time had a 1.54 fold increase chance (RR: 0.65, 95% CI: 0.44-0.95; n=45) to achieve a clinical remission at w26 in comparison to patients who had no early detectable positive GLM trough level and no change in calprotectin in w6. On the other hand we analyzed that patients without early detectable GLM trough level and no change in calprotectin in w6 had a 3.46 fold higher risk (RR 3.46; 95%: CI 0.56-22.45; p=0.1; n=45) for not achieving response in w26.

Conclusion: In this prospective multicenter study we were able to show the impact of fecal calprotectin and serum golimumab level at week 6 to predict the therapeutic response at week 26. Further studies are needed to confirm the statistical significance our primary result.

Disclosure: UH:Lecture and consulting fees: AbbVie, MSD, Ferring, Falk Foundation, Takeda, Mundipharma, Hospira, Vifor Pharma

P1048 INFLIXIMAB LEVELS & ANTIBODIES IN IBD- RELATED PERIPHERAL ARTHRALGIA

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Introduction: Extra-intestinal manifestations (EIM) are common in inflammatory bowel diseases (IBD) and may affect up to 50% of the patients during the course of the disease. Peripheral arthralgia (PA) is by far the most common EIM. To date, TNF-alpha inhibitors are the most established treatment for EIMs in IBD. Infliximab (IFX) trough levels (TL) and anti-IFX antibodies (ATI) are correlated with multiple outcomes in IBD such as clinical response and remission, mucosal healing, fistular healing and more. To date, a correlation between IFX TL\ATI and PA has not been evaluated.

Aims & Methods: This retrospective study included IBD patients followed by gastroenterology departments of Sheba Medical Center and Saint Etienne Medical Center. Patients with active peripheral arthralgia at onset of IFX treatment were included. IFX TL and ATI were evaluated at week 6, 14 and 26 and correlated with PA persistence.

Results: Forty nine patients (42 CD, 7 UC) with IBD associated arthralgia were included. The overall prevalence of arthralgia was 59.2% (29/49), 44.9% (22/49) and 53.1% (26/49) after 6, 14 and 26 weeks respectively. At 14 and 26 weeks of treatment, arthralgia was less prevalent in clinical responsive patients than in patients who didn't respond to IFX (8.8% vs 66.7%, p=0.004 and 35% vs 70.6%, p=0.031, respectively). IFX TL were not associated with PA at week 14 (median, 4.5 vs 3.15 ug/ml, p=0.26) and at week 26 (median, 3.9 vs 3.6 ug/ml, mean, p=0.84) however detectable ATI were significantly more prevalent in patients with PA than in patients without PA at week 26 (46.2% vs 13.6%, p=0.015).

Conclusion: In patients with IBD-related PA, IFX ATI are associated with an increased risk of persistence of arthralgia. No direct correlation was demonstrated between IFX TL and persistence of arthralgia.

Disclosure: Bella Ungar received consultation fees from Janssen and Abbvie.Shomron Ben-Horin received consulting and advisory board feesand/or research support from AbbVie, MSD, Janssen, Takeda andCellTrion. Uri Kopylov received speaker and advisory fees fromAbbvie, Jannsen, MSD, Takeda and Medtronic, and research sup-port from Jannsen, Medtronic and Takeda. Rami Eliakim receivedconsultant and speaker fees from Jans-sen, Abbvie, Takeda andMedtronic. None of the other authors have any conflicts to declare

P1049 DOES FIBROBLAST GROWTH FACTOR 19 (FGF19) LEVEL CORRELATE WITH INFLAMMATORY BOWEL DISEASE ACTIVITY?

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Introduction: Fibroblast growth factor 19 (FGF19) is the ileal hormone providing feedback inhibition of bile acid (BA) synthesis in the liver which may serve as a surrogate marker to assess BA malabsorption. FGF19 is a key target of the farnesoid X receptor (FXR). The FXR activation inhibits intestinal inflammation. While disturbances in BA metabolism and enterohepatic circulation have been well documented in Crohn's disease (CD), still little is known about the role of these mechanisms in the pathogenesis of ulcerative colitis (UC).

Aims & Methods: To evaluate serum FGF19 level and its correlation with inflammatory bowel disease (IBD) activity in patients with UC and CD. Fasting serum FGF19 level was measured using ELISA test in 62 IBD patients (33 M, 29 F, mean age 40.0 ± 15.8) and 19 healthy control subjects (8 M, 11 F, mean age: 39.9 ± 13.0). The IBD patients were divided into 4 subgroups according to the disease form and activity: non active UC (n=15), active UC (n=16), non-active CD (n=15) and active CD (n=16). The clinical disease activity in UC patients was assessed by Rachmilewitz index, and in CD by CDAI. The endoscopic disease activity was evaluated using the Mayo Endoscopic Score in UC and SES-CD in CD. Moreover, abdominal pain intensity using visual analog scale (VAS), as well as serum CRP and fecal calprotectin levels were measured. Non-parametric statistics were used and results are expressed as median and the lower and upper quartiles [25Q-75Q].

Results: Median serum FGF19 level was lower in active UC (114.3 pg/ml) than in non-active UC (175.3 pg/ml) (p=0.093). Median FGF19 level in the healthy controls amounted to 151.6 pg/ml, but there were no statistically significant differences between the patients with active and non-active UC compared to the controls. Despite the fluctuations of FGF19 level dependent on the disease activity, in the majority of UC patients it was still within the normal range. In patients with active CD, serum FGF19 level was significantly lower than that in the controls (56.5 vs 151.6 pg/ml, p=0.043). The lower serum FGF19 level was found in 38% of patients with active CD, and 13% of patients with non-active CD. An inverse correlation was observed between serum FGF19 and number of stools per 24 hours and Bristol Stool Form Scale score, as well as clinical disease activity in CD. No correlation between FGF19 level and endoscopic disease activity was revealed in either form of IBD. In patients with UC the inverse correlations between FGF19 level and abdominal pain intensity (R= -0.48, p=0.007), as well as inflammatory markers including fecal calprotectin level (R= -0.38, p=0.036) and serum CRP level (R= -0.36, p=0.045) were found.

Conclusion: The ELISA test for FGF19 constitutes a useful tool to evaluate BA malabsorption in the course of IBD. Serum FGF19 level, although remaining within the normal range in the majority of IBD patients, shows fluctuation dependent on the disease activity, which indicates the association between the regulatory mechanisms of BA enterohepatic circulation and IBD activity. The inverse correlations between FGF19 level and abdominal pain and inflammatory markers may imply its potential analgesic and anti-inflammatory effects - direct or due to the FXR-FGF19 axis activation. The dynamic of FGF19 level fluctuation dependent on the IBD phase suggests new therapeutic aims associated with FXR activation, which constitutes a key element of the gut-liver axis.

Disclosure: Nothing to disclose

P1050 OUTCOME OF IMMEDIATE INFLIXIMAB OPTIMISATION BASED ON RAPID ASSESSMENT OF SERUM DRUG AND FECAL CALPROTECTIN CONCENTRATIONS IN INFLAMMATORY BOWEL DISEASES PATIENTS

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Introduction: Recent studies have demonstrated that proactive therapeutic drug monitoring (TDM) with drug titration to a target trough concentration is associated with better clinical outcomes. Moreover, dose intensification strategy based on the parallel assessment of clinical symptoms, serum and fecal biomarkers and serum infliximab (IFX) concentration may further increase therapeutic response.

Aims & Methods: The aim of this study is to evaluate the outcome of IFX optimisation based on proactive drug monitoring in combination with the assessment of clinical activity and biomarkers using rapid assays.

This is a prospective study of consecutive Crohn's disease (CD) and ulcerative colitis (UC) patients on IFX maintenance therapy. Blood and fecal samples were obtained from the patients at the day when subsequent IFX infusion was scheduled. C-reactive protein (CRP) and hematocrit levels were measured. Serum IFX and fecal calprotectin (FC) concentrations were benchmarked with rapid, lateral flow-based assays. Clinical activity indices were calculated. On the basis of all data, patients were assigned to 4 groups: no intervention (NI), dose increased (DI), stopping (ST) or switch. After optimisation, patients are followed for 6 months with determining all the above mentioned parameters retrospectively at every 2 months.

Results: Twenty-six CD and 21 UC patients were enrolled. On the basis of the rapid tests, DI was performed in 14 CD and 11 UC patients, NI in 8 CD and 7 UC patients, and ST in 4 CD and 2 UC patients. One UC patients was switched from IFX to adalimumab. In DI CD group, serum level of IFX increased, CDAI decreased significantly compared to the baseline. Level of CRP and FC did not change significantly at month 2, but CRP decreased significantly at month 4.

Twelve CD patients stayed in remission in the DI group; two relapses were observed, one patient was switched to ustekinumab and one patient received corticosteroid. In DI UC group IFX level increased significantly, CRP, pMayo and FC decreased compared to baseline.

Seven patients in NI CD group and 3 patients in the NI UC group remained in remission till the end of the follow up. None of the examined parameters, except for serum IFX level at month 4 changed significantly.

One patient in the ST group required reintroduction of therapy with adalimumab at month 2. Serum IFX concentration and FC level measured with the rapid, lateral flow-based assay and ELISA kits are correlated (r=0.69, p=0.0012).

Conclusion: Change in therapy was performed in 32 cases on the bases of benchmarked concentrations of serum IFX and FC levels. Our results suggest benefit of using rapid tests in daily practice. Results of rapid, lateral flow-based assays and ELISA kits are correlated.

Disclosure: Nothing to disclose

P1051 INDIVIDUAL PATIENT-LEVEL AUTOMATIC DETECTION OF MUCOSAL INFLAMMATION ON VIDEO CAPSULE ENDOSCOPY IMAGES IN CROHN'S DISEASE

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Introduction: Capsule endoscopy (CE) is a well- established modality for diagnosis and monitoring of Crohn's disease (CD) .Some of the drawbacks of CE technology include interobserver variability and prolonged reading time. Deep learning technology is being extensively explored in several fields of medicine and has a potential to provide efficient and automated image processing.

The aim of our study was to evaluate a the patient level performance of deep learning model for detection of small bowel ulcers on capsule endoscopy images.

Aims & Methods: We retrospectively collected capsule endoscopy images of patients with established Crohn's disease and normal subjects. Each image was labeled by an expert gastroenterologist as either normal mucosa or containing mucosal ulcers. A Convolutional Neural Network (Xception) was trained to classify images into either normal mucosa or with mucosal ulcers.

We compared the results of the networks for randomly split images and for individual patients.

First we trained the network on five-folds randomly split images (each fold with 80% training images and 20% images testing). Than we conducted three experiments in which images from n-1 patients were used to train a network and images from a different individual patient were used to test the network. Areas under the curves (AUC) and accuracies were computed for each individual network.

Results: Overall, the dataset included 4,255 capsule endoscopy images from 15 patients (11 with and 4 without CD, respectively); 2,272 images contained ulcerated mucosa and 1,983 normal images.

For randomly split images the performance of CNN was excellent with AUC ranging between 0.97 and 0.99 and accuracies ranging from 96.7% to 97.8%.

For individual patient-level (patients 1,2 and 3) experiments, the AUCs were also excellent (0.97, 0.99 and 0.99, respectively). Variability was seen in the accuracies for different patients (73.2%, 88.2% and 95.6%, respectively).

Conclusion: Deep learning technology provides accurate automated detection of mucosal ulcers on capsule endoscopy images for both pooled and individual patient images. To simulate real life results, individual patient-level experiments must be conducted. This technology may be applicable for real-life processing of CE imaging in suspected and established Crohn's disease.

Disclosure: Shomron Ben-Horin received consulting and advisory board feesand/or research support from AbbVie, MSD, Janssen, Takeda and CellTrion. Uri Kopylov received speaker and advisory fees fromAbbvie, Jannsen, MSD, Takeda and Medtronic, and research sup-port from Jannsen, Medtronic and Takeda. Rami Eliakim receivedconsultant and speaker fees from Janssen, Abbvie, Takeda andMedtronic. None of the other authors have any conflicts to declare.

P1052 PULMONARY FUNCTION TESTS IN ASYMPTOMATIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE: PRELIMINARY RESULTS OF A SINGLE CENTER COHORT STUDY

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Introduction: Pulmonary dysfunction is frequently underestimated in inflammatory bowel disease (IBD) patients. The aim of this study was to investigate pulmonary function in IBD patients and identify possible risk factors for pulmonary dysfunction.

Aims & Methods: Consecutive informed and consented IBD patients < 60 years old followed up in our centre underwent pulmonary function tests (PFTs) during their regular follow up visit. Measurements conducted were forced vital capacity (FVC), forced expiratory volume in one sec (FEV1) and maximal mid-expiratory flow (MMEF 75/25). Exclusion criteria were an acute or chronic respiratory disease as well as the presence of an established pulmonary extra-intestinal manifestation.

Results: 135 IBD patients have been enrolled so far (males: 55.6%, Crohn's disease: 63.7%, mean age at IBD diagnosis: 34.2 years [SD±11.9], median [IQR] duration of IBD: 7.5 months [0.1-34.3], extraintestinal manifestations: 36.3%). Thirty-eight patients (28.1%) had never smoked with the rest being either active (36.3%) or ex- (33.3%) smokers. Thirty-four patients (25.2%), including 7/38 (35.3%) non-smokers, revealed abnormal PFTs (males: 22/34, Crohn's disease: 25/34); 12 (35.3 %) exhibited a restrictive pattern, 12 (35.3 %) an obstructive pattern and 10 (29.4%) small airway disease. Interestingly, appendectomy was more commonly reported in non-smokers with abnormal PFTs compared to those without (p=0.002). IBD was active at baseline in 4/34 and extraintestinal manifestations were present in 15/34 patients. Anti-TNFalpha agents were administered in 17/34 (50%) patients. Six patients were under combination therapy with an IMS. There was no association of abnormal PFTs with gender, disease sort or location or behavior or activity, tonsillectomy, IBD therapy either as mono-therapy or as combination therapy and the presence of anemia.

Conclusion: More than one fourth of our IBD patients in total and of non-smokers in particular demonstrate abnormal PFTs measured in a random outpatient visit without any symptoms, signs or history of respiratory disease. Appendectomy was associated with LFTs abnormality in non-smokers perhaps revealing an immunologic defect influencing the development of obscure primary or secondary pulmonopathy on the background of IBD. These results should of course be interpreted with caution for the time being, while awaiting those of a larger cohort.

Disclosure: Nothing to disclose.

P1053 DIAGNOSTIC ACCURACY OF FECAL LACTOFERRIN AND CALPROTECTIN COMPARED TO THE RILEY SCORE AND NANCY INDEX FOR THE DETERMINATION OF HISTOLOGICAL INFLAMMATORY ACTIVITY IN PATIENTS WITH ULCERATIVE COLITIS

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Introduction: This study aims to investigate the performance of Lactoferrin and Calprotectin compared to the Riley Score and especially to the Nany index assessing the histological inflammatory activity in a cohort of patients with ulcerative colitis (UC).

Aims & Methods: Secondary analysis of clinical data from UC patients who were treated in the Department of Internal and Integrative Medicine at the Kliniken Essen-Mitte, Germany. Patients were included in the present study, if colonoscopy-results, biopsies and data of the fecal biomarkers Lactoferrin and Calprotectin were available. A total of 3 biopsies were taken each in the sigma and rectum and the Riley Score and Nancy index were calculated by an experienced pathologist blinded to the results of the fecal biomarkers. The histologic scores were correlated to Lactoferrin (LF) and Calprotectin (Cal) levels in stool harvested within 7 days before the endoscopic intervention. Comparisons were done for differences between biomarker levels and the grades of the Nancy index. Sensitivity, specificity, negative predictive value and positive predictive value as well as optimized cut-offs were calculated. Remission was defined as Nancy Index ≤ 1.

Results: 228 patients (60.1 % female, mean age 45.26 years) with diagnosed UC were included in the analysis. The Riley score and Nancy index correlated significantly with LF (r_s (228) = 0.43; p < .001/ r_s (228) = 0.43; p < .001) and Cal (r_s (228) = 0.40; p < .001/ r_s (228) = 0.38; p < .001). Median levels of LF and Cal differed significantly between the grades 0-4 of the Nancy index (both p < .001). Subsequent post-hoc tests showed that LF differed between the grades 0 and 3 (z = -6.15, p < .001), 0 and 4 (z = -4.82, p < .001), 1 and 3 (z = -3.31, p = .009), 1 and 4 (z = -2.83, p = .046), 2 and 3 (z = -3.66, p = .003) and 2 and 4 (z = -2.88, p = .040) and Calprotectin between the grades 0 and 2 (z = -3.90, p = .001), 0 and 3 (z = -5.69, p < .001), 0 and 4 (z = -4.46, p < .001), 1 and 3 (z = -3.77, p = .002) and 1 and 4 (z = -3.27, p = .011). Moreover the median levels of LF and Cal differed significantly between patients in remission (Nancy Index ≤ 1) and patients with disease activity (Nancy Index ≥ 2), both p < .001. Optimized cut-off-values and the diagnostic accuracy of LF and Cal for the differentiation between active and inactive disease using the Nancy Index as reference standard are < 5.85 for LF and < 34.28 for Cal resulting in a diagnostic accuracy of .73 for LF and .76 for Cal with a sensitivity of 76.4 for LF, 64.6 for Cal and a specitifity of 64.3 for LF and 78.6 for Cal. Table 1 shows the sensitivity, specificity, positive predictive value and negative predictive value of LF and CAL.

Conclusion: The fecal biomarkers Lactoferrin and Calprotectin correlated significantly with the Riley and Nancy index. LF and CalP differed significantly between the grades of the Nancy index. The results support the utility of fecal biomarkers for detecting active histologic inflammation in patients with ulcerative colitis.

	Cut off	SE (%)	SP (%)	PPV (%)	NPV (%)
Lactoferrin	≤ 7.25 µg/g	103/144 (71.5)	55/84 (65.5)	103/132 (78.0)	55/96 (57.3)
Calprotectin	< 50 µg/g	82/144 (56.9)	68/84 (81.0)	82/98 (83.7)	86/130 (52.3)

[Table 1. Sensitivity, Specificity, positive predictive value and negative predictive value of Lactoferrin and Calprotectin using manufactures' cut-offs]

P1054 RED BLOOD CELL DISTRIBUTION WIDTH AND ITS DERIVATIVES AS POTENTIAL MARKERS IN THE COURSE OF ULCERATIVE COLITIS - AN OBSERVATION OF PATIENTS TREATED WITH INFLIXIMAB

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Introduction: Red blood cell distribution width (RDW) is associated with various medical conditions. Its elevated level was found to be the predictor of poor outcome in cancer, liver cirrhosis and cardiovascular diseases. RDW was also suggested as a marker of inflammation in the course of inflammatory bowel disease (IBD).

Nevertheless, it seems that a potential role of its derivatives (red blood cell distribution width-to-platelet ratio (RPR) and red blood cell distribution width-to-lymphocyte ratio (RLR)) in this field of gastroenterology has not been explored so far.

Aims & Methods: The aim of our study was to find out if there are deviations in RDW and its derivatives levels - RPR and RLR - in the course of infliximab (IFX) induction regimen in ulcerative colitis (UC) patients. We also looked for relationship between mentioned parameters, platelet indices and C-reactive protein (CRP). One hundred and twelve participants were qualified to the survey: 56 patients with active UC and 56 persons in control group. UC patients were treated with IFX (3 doses of standard induction therapy). RDW, RPR and RLR values were obtained in the blood of UC patients at 0, 2, and 6 weeks of induction regimen and in follow-up six weeks later. Results were compared with control group.

Results: RDW value in UC patients prior to the first dose of IFX was above normal range; it was also higher in comparison to control group (p< 0.001) and normalized in follow-up (p<0.01). Baseline RLR level in study group compared to controls was higher (p<0.001) and decreased after finished IFX induction regimen (p>0.05); Baseline RPR value did not differ significantly; in follow up its level increased (p<0.001). We noticed several correlations in UC patients.

Prior to the treatment with IFX, RPR correlated positively with mean platelet volume (MPV) (p<0.01) and platelet distribution width (PDW) (p<0.001); negative correlation was observed between RPR and plateletcrit (PCT) (p<0.001). In follow up RPR correlated negatively with PCT (p<0.001) and CRP (p<0.001); positive correlation was noticed between RPR and PDW (p=0.001).

Conclusion: Performed study revealed that RDW, RPR and RLR values are affected by IFX therapy in UC patients ad should be considered as potential laboratory markers in the course of IBD.

References: 1. Öztürk ZA, Dag MS, Kuyumcu ME, et al. Could platelet indices be new biomarkers for inflammatory bowel diseases? Eur Rev Med Pharmacol Sci. 2013; 17: 334-41. 2. Goyal H, Hu ZD. Prognostic value of red blood cell distribution width in hepatocellular carcinoma. Ann Transl Med. 2017; 5: 271.

Disclosure: Nothing to disclose

P1055 HEMATOLOGICAL MARKERS IN THE EVALUATION OF INFLAMMATION IN CROHN'S DISEASE PATIENTS

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Introduction: Recently, neutrophil-to-platelet ratio (NLR), platelet-to-lymphocyte ratio (PLR) and mean platelet volume-to platelet ratio (MPR) have been proposed as potential markers in various medical disorders, e. g. cancer, cardiovascular diseases, liver cirrhosis. However, the above-mentioned indices have not been explored in inflammatory bowel disease patients so far.

Aims & Methods: Our goal in this survey was to assess NLR, PLR, MPR and their relationships with platelet indices and C-reactive protein (CRP) in Crohn's disease (CD) patients treated with infliximab (IFX). We included 80 participants to the study: 40 patients with active CD and 40 persons in control group. CD patients were treated with IFX (five doses of standard

therapy). NLR, PLR, MPR and their relatioships with CRP, mean platelet volume (MPV), plateletcrit (PCT) and platelet distribution width (PDW) were assessed in blood of CD patients at 0, 2, 6, 14 and 22 weeks. Results were compared with controls.

Results: Baseline values of NLR and PLR among CD patients were higher in comparison to controls (p< 0.001); MPR level was lower (p< 0.01). In CD group, after five doses of IFX, a decrease in NLR (p< 0.001) and PLR values (p=0.001) together with increase of MPR level (p< 0,001) were noticed. We also observed significant correlations in CD patients, present simultaneously prior to the biological treatment and after five doses of IFX. NLR correlated positively with PLR and CRP (p< 0.01). There was a negative correlation between PLR and MPR (p< 0.01), together with positive association between PLR and PCT (p< 0.001). Finally, MPR correlated positively with MPV (p< 0.01) and negatively with PCT (p=0.001). In addition, CRP correlated negatively with MPR at baseline (p< 0.001) and positively with CRP (p=0.004) after five doses of IFX.

Conclusion: CD, IFX therapy, NLR, PLR and MPR are closely related to each other. Analyzed hematological indices might be potential tools in the monitoring of CD patients.

References: 1. Iida H, Kaibori M, Matsui K i wsp. Ratio of mean platelet volume to platelet count is a potential surrogate marker predicting liver cirrhosis. World J Hepatol. 2018; 10: 82-7. 2. Zhao Z, Liu J, Wang J i wsp. Platelet-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR) are associated with chronic hepatitis B virus (HBV) infection. Int Immunopharmacol. 2017; 51: 1-8. 3. Voudoukis E, Karmiris K, Koutroubakis IE. Multipotent role of platelets in inflammatory bowel diseases: a clinical approach. World J Gastroenterol. 2014; 20: 3180-90.

Disclosure: Nothing to disclose

P1056 NEUTROPHIL-TO-PLATELET RATIO, PLATELET-TO-LYMPHOCYTE RATIO AND MEAN PLATELET VOLUME-TO PLATELET RATIO AS POTENTIAL HEMATOLOGICAL INDICES IN THE EVALUATION OF INFLAMMATION IN ULCERATIVE COLITIS PATIENTS

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Introduction: There is a growing body of evidence that new routinely obtained noninvasive blood indices could become markers of inflammation in inflammatory bowel disease patients. Nevertheless, the number of observations devoted to this field of gastroenterology is still very small.

Aims & Methods: We aimed in our survey to look for relationships between hematological parameters in ulcerative colitis (UC) patients treated with infliximab (IFX). One hundred and twelve participants were enrolled to the study: 56 patients with active UC and 56 persons in control group. UC patients were treated with IFX (3 doses of standard induction therapy). Neutrophil-to-platelet ratio (NLR), platelet-to-lymphocyte ratio (PLR), mean platelet volume-to platelet ratio (MPR) and their correlations with red blood cell and platelet indices were measured in the blood of UC patients at 0, 2, and 6 weeks of induction regimen and in follow-up six weeks later. Results were compared with control group.

Results: NLR and PLR levels in UC patients prior to the first dose of IFX were higher in comparison to controls; MPR value was lower (p< 0.001). NLR value decreased after finished IFX induction therapy (p< 0.001). PLR level became lower too, however not significantly. MPR value became higher (p< 0.001). Several correlations were noticed in UC patients. PLR correlated positively with mean platelet volume (MPV) and red blood cell distribution width (RDW) before the introduction of IFX (p< 0.01); there were also positive correlations between MPR and both - platelet distribution width (PDW) and plateletcrit (PCT) (p< 0.001). In follow-up after finished induction regimen PLR correlated positively with NLR and PCT (p< 0.001); negative correlations were noticed between PLR and both MPR and PDW (p< 0.01).

Conclusion: Deviations in white blood cell, red blood cell and platelet indices seem to be closely related to each other in UC patients and affected by IFX therapy. NLR, PLR and MPR are potential diagnostic tools in the monitoring of UC patients.

References: 1. Ghoshal K, Bhattacharyya M. Overview of platelet physiology: its hemostatic and nonhemostatic role in disease pathogenesis. Scientific World Journal. 2014; 2014: 781857. 2. Iida H, Kaibori M, Matsui K i wsp.

Ratio of mean platelet volume to platelet count is a potential surrogate marker predicting liver cirrhosis. World J Hepatol. 2018; 10: 82-7. 3. Zhao Z, Liu J, Wang J i wsp. Platelet-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR) are associated with chronic hepatitis B virus (HBV) infection. Int Immunopharmacol. 2017; 51: 1-8.

Disclosure: Nothing to disclose

P1057 THE ROLE OF ONCOSTATIN M IN DIAGNOSIS, PROGNOSIS AND THERAPY RESPONSE OF IBD

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Introduction: Oncostatin M (OSM) has been implicated in the pathogenesis of inflammatory bowel disease (IBD), wherein its increased mucosal expression drives intestinal stromal cell inflammation and predicts non-responsiveness to anti-TNF therapy[1]. In this study we aimed to further unravel the potential of OSM as a diagnostic, prognostic and/or therapeutic biomarker.

Aims & Methods: We collected serum and mucosal biopsies from Crohn's disease (CD) and ulcerative colitis (UC) patients: (1) treatment-naïve newly diagnosed patients; (2) patients initiating anti-TNF or (3) vedolizumab therapy; (4) post-operative CD patients six months after ileocolonic resection with ileocolonic anastomosis; (5) multiple-affected IBD families including unaffected first-degree relatives (FDRs). For each group, matched samples from non-IBD controls were included as comparison. Serum OSM protein levels were measured using the Proseek Multiplex Inflammation panel (OLINK), and mucosal *OSM* expression using RNA-sequencing or microarray technology. An overview of the studied samples and the corresponding applied definitions and technologies can be found in Table 1. Wilcoxon tests (R 3.5.1) were applied to assess statistical significance, defined as a p value < 0.05.

Results: In newly diagnosed CD and UC patients, we observed increased colonic *OSM* expression (fold change (FC)=60.2, p=3.7E-09) and serological protein levels (FC=4.9, p=1.3E-11) compared to non-IBD controls, with the strongest upregulation in extensive UC and fistulizing CD. Moreover, elevated mucosal *OSM* (but not serum OSM) at diagnosis was associated with the need for biological therapy within one year after diagnosis (poor- vs. good-prognosis: FC=5.0, p=1.5E-03). Prior to both anti-TNF and vedolizumab therapy, colonic *OSM* was upregulated in future non-remitters (FC=2.5, p=5.0E-02; FC=2.3, p=1.0E-02 respectively). In contrast, baseline serum OSM could not identify future anti-TNF or vedolizumab non-remitters (FC=1.0, p=3.0E-01; FC=0.9, p=4.1E-01 respectively). In CD patients with post-operative recurrence (POR) higher serum OSM levels were found at month 6, as compared to patients without POR and to controls (FC=2.6, p=1.9E-02; FC=2.9, p=4.5E-03). Furthermore, mucosal *OSM* in POR CD patients did not differ from CD patients without POR (FC=1.2, 1.4E-01), but was significantly upregulated as compared to controls (FC=1.5, p=5.0E-03). In multiple-affected IBD families increased serum levels were observed in FDRs as compared to matched control families (FC=1.7, p=4.0E-04), and levels were similar to those of IBD patients.

Conclusion: Colonic *OSM* levels are increased in CD and UC patients at the time of diagnosis, and higher levels correlate with poor prognosis. In addition, upregulation of colonic *OSM* is associated with future anti-TNF/vedolizumab non-remitters. Therefore, *OSM* at the mucosal site is a surrogate marker of biological treatment-refractoriness in IBD.

References: 1. West NR et al. Nat Med. 2017

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COHORT	SUBGROUPS	PROTEOMICS SAMPLES	TRANSCRIPTOMICS SAMPLES (RNAseq*/microarray**)
1.Treatment-naïve newly diagnosed IBD patients (= within 6 months after diagnosis, naïve for biologicals/immunosuppressives, no IBD related surgery)	Crohn's disease (CD)	30	16 colonic samples*
	Ulcerative colitis (UC)	16	11 colonic samples*
	Non-IBD controls	40	29 colonic samples*
1.Treatment-naïve newly diagnosed IBD patients (= within 6 months after diagnosis, naïve for biologicals/immunosuppressives, no IBD related surgery)	Poor-prognosis (=the need for biological therapy within one year after diagnosis)	28	15 colonic samples*
	Good-prognosis	18	12 colonic samples*
2. Anti-TNF cohort	Remission (=the complete absence of ulcerations (CD) or a Mayo endoscopic sub-score 0 - 1 (UC))	91	12 colonic samples*
	No remission	95	21 colonic samples*
3. Vedolizumab cohort	Remission (=the complete absence of ulcerations (CD) or a Mayo endoscopic sub-score 0 - 1 (UC))	105	24 colonic samples*
	No remission	82	25 colonic samples*
4. Post-operative CD patients undergoing ileocecal resection with ileocolonic anastomosis	No post-operative recurrence (=Rutgeerts i0/i1 at month 6)	36	8 ileal samples**
	Post-operative recurrence (=Rutgeerts ≥ i2b at month 6)	17	24 ileal samples**
	Non-IBD controls	40	12 ileal samples**
5. Multiple-affected IBD families (=min. 3 first-degree relatives with IBD)	IBD	47	/
	Unaffected first-degree relatives (FDRs)	33	
	Non-IBD control families	39	

[P1057 Table 1: Overview of the studied samples and corresponding applied definitions and technologies]

P1058 PROSPECTIVE, RANDOMIZED CLINICAL TRIAL COMPARING THE EFFICACY OF TWO VACCINES AGAINST HEPATITIS B VIRUS (HBV) IN INFLAMMATORY BOWEL DISEASE (IBD) PATIENTS

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Introduction:
Aims & Methods: To compare the success rate between two HBV vaccines in IBD patients: the traditional (Engerix®) and a new vaccine with an adjuvant (Fendrix®). Secondary aim was to identify predictor factors of response to the vaccine.

IBD patients with negative HBV serology and without previous vaccination were included in this multicenter study (EUDRA-CT number: 2010-023947-14), and randomized 1:1 to receive double doses of Engerix® or Fendrix® or at months 0, 1, 2 and 6. Anti-HBs concentration was measured 2 months after the 3rd and 4th doses. Response to vaccination was defined as anti-HBs ≥100 UI/L.

Results: 173 from 180 included patients were randomized and received the first vaccine dose. 98% received the first 3 doses of vaccine and 97% completed the vaccination schedule. During vaccination, 24% of patients were under immunomodulators (IMM), 15% under anti-TNF and 24% under combo therapy (IMM and anti-TNF). 54% of patients received Engerix® and 46% Fendrix®; the main characteristics of patients (age, gender, type of IBD, treatment and proportion of drop-outs) were similar between the 2 groups.

Variables	Odds ratio	95% confidence interval
Age (>60 years vs. £60 years of age)	0.17	0.06-0.49
Fendrix (single dose) over Engerix (double dose)	1.8	0.8-4.1
IBD treatments		
Steroids vs. no treatment	0.03	0.004-0.3
Immunomodulators in monotherapy vs. no treatment	0.1	0.02-0.58
Anti-TNF in monotherapy vs. no treatment	0.05	0.01-0.3
Combo therapy vs. no treatment	0.02	0.004-0.1

[Table 1. Multivariate analysis of predictive factors associated with response (anti-HBs≥100 IU/L after 4 doses) to hepatitis B virus vaccine in infl]

Overall, in the per-protocol (PP) analysis, 45% of patients had response (pre-defined as anti-HBs³100 IU/L) after the first 3 doses (168 patients received 3 doses), and 71% after the completion of the vaccination schedule (159 completed the vaccination). 47% of patients that did not respond after the 3rd dose, responded to the 4th vaccine administration (p<0.0001). In the PP analysis, the response rate after the 4th dose was 75% (95%CI, 57-78%) with Fendrix® vs. 68% (64-85%) with Engerix® (p=0.3); however, considering anti-HBs≥10 IU/L (the standard threshold to define response), there was a trend towards higher success rate with Fendrix® than with Engerix® (88% vs. 77%, p=0.07). The response rate after 4 doses was significantly lower in patients under IMM, anti-TNF agents and combo therapy compared with no treatment: 77%, 63%, 45% and 96%, respectively (p<0.01 for each comparison).

In the multivariate analysis, older age, the treatment with steroids alone, IMM, anti-TNF agents and combo therapy were associated with lower probability of response to the vaccination. The type of vaccine -Engerix® or Fendrix®- was not associated with the response to the vaccination (table 1).

The proportion of adverse events probably related to the vaccine was significantly higher in patients receiving Fendrix® vs. Engerix® (17% vs. 4%), being local pain the most frequent one; all of them were mild.

Conclusion: We could not demonstrate a statistically significant higher response rate of Fendrix® (single dose) over Engerix® (double dose) in IBD patients. A 4-dose vaccine schedule significantly increases (over 40%) the response compared with a 3-dose regimen. Older age and IMM and anti-TNF treatment impaired the success rate of the vaccine. Both vaccines are safe in IBD patients.

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P1059 COMPLIANCE WITH INTERNATIONAL GUIDELINES ON VACCINATION AND MALIGNANCY PREVENTION AMONG PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: IBD patients receiving immunosuppressive therapy are at increased risk of developing opportunistic infections and certain types of malignancy, often associated with the type of immunosuppressive therapy. International guidelines have been published, involving vaccination protocols and malignancy screening with cervical smear, mammography and skin examination, yet adherence from patients remains low.

Aims & Methods: To determine self-reported compliance with influenza virus and pneumococcal vaccination guidelines, as well as malignancy screening with cervical smear, mammography and skin examination, among Greek patients with inflammatory bowel disease.

Method: In collaboration with the Hellenic Society of Crohn's Disease's and Ulcerative Colitis' Patients, a questionnaire was posted on the Society's website, inviting IBD patients only on immunosuppressive therapy to fill it in. The questionnaire included demographic data, disease characteristics as well as influenza and pneumococcal vaccination queries, skin examination (all patients), cervical smear and mammography screening rates (female patients).

Results: A total of 176 patients completed the questionnaire [CD=134 (76.14%) UC=42 (23.86%), male=57 (32.38%) female=119 (67.6%)]. Among them, 51(28.9%) patients were treated with one immunomodulator (MTX-AZA), 73 (41.4%) with anti-TNF, 19 (10.7%) with Vedolizumab, 3 (1.7%) with Ustekinumab whereas 30 (17%) patients were treated with combination therapy. According to the results, 97 patients (55.1%) received the influenza virus vaccine, 81 patients (46%) received the 13-strain PPV, whereas 14 patients (8%) weren't sure if they received the vaccine or not. Fifty nine patients (33.5%) received the 23-strain PPV and 25 patients (14.2%) weren't sure if they received the vaccine or not. Thirty nine patients (22.2%) underwent skin examination whereas 26 patients (14.8%) weren't aware of it. Twenty four patients (18.9%) had never undergone cervical smear testing and 57 (46.7%) had never performed a mammography. There was no statistically significant difference between vaccination and screening compliance rates of patients receiving monotherapy and combination therapy.

Conclusion: There appears to be a significant proportion of patients receiving immunosuppression therapy (>50%) that does not comply with the international guidelines on vaccination and malignancy prevention (it cannot be clarified whether this is a problem of lack of education or simply non-compliance), putting themselves at risk . Even high-risk patients (combination immunotherapy) do not seem to have better compliance rates.

Disclosure: Nothing to disclose

P1060 THE HISTOLOGICAL HEALING IN ULCERATIVE COLITIS PATIENTS CAN BE BEST PREDICTED BY THE COMBINATION OF FAECAL CALPROTECTIN AND ENDOSCOPIC HEALING ASSESSED BY ADVANCED OPTICAL ENHANCEMENT TECHNIQUES

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Introduction: Endoscopic mucosal healing (MH) is an important target of therapy and prognostic factor in Ulcerative Colitis (UC) patients. Considerable interest has been generated by reports that 18-24% of patients with endoscopic healing at white light endoscopy (WLE) are found to still have active inflammation from the histological results. Faecal Calprotectin (FC) is a widely used surrogate marker of MH. Recently, we have published and validated endoscopic MH using high definition (HD) electronic chromoendoscopy which provides fine details of mucosal and vascular patterns.[1,2]

Aims & Methods: In this study, we aim to investigate MH using Fecal Calprotectin (FCP) multiple endoscopic and histological scoring systems assessed with advanced endoscopic platforms widely available, We prospectively obtained clinical data, endoscopic scores {Mayo Endoscopic Score (MES), Ulcerative Colitis Endoscopic Index of Severity (UCEIS) PICaSSO score (Paddington International virtual ChromoendoScopy ScOre)}[1] FCP for 51 UC patients (mean age 45y, 51% male) undergoing colonoscopy for colitis assessment or surveillance using high definition iscan optical enhancement (iscan-OE) Pentax, NBI near focus (NBI-NF) Olympus or Blue Light Imaging (BLI) Fujinon . Histologic activity was scored by Robarts Histological Index (RHI) and Nancy Index (NI). Receiver Operating Characteristics (ROC) curves were plotted to determine operating characteristics of FCP alone or in combination with endoscopic scores to predict histologic healing using modelling algorithms.

Results: 24 (47.1%) patients had endoscopic remission defined as MES= 0 or UCEIS (≤1) using HD-WLE. The mean (SD) of FCP was 505.5 (741.0) µg/g and 23 (45.1%) patients had FCP≤100 µg/g. 24 (47.1%) were in histologic remission, defined as RHI ≤ 6; and 21 (41.2%) patients were in histologic remission defined as NI ≤1.

ROC curves showed that the optimum cut-off of FC alone to predict histological healing with RHI was 163 µg/g with an accuracy of 82.4% (95%CI 69.-91.6) and Area Under ROC curve (AUROC) of 83.6% (95%CI 71.8-95.5). Using NI, the best threshold was 112 µg/g with accuracy of 82.4% (95%CI 69.1-91.6) and AUROC of 85.7% (95%CI 75.4-96.0).

When FC (≤100 µg/g) and PICaSSO were combined to predict histological healing, measured with RHI, the optimum cut-off was PICaSSO=3 with accuracy of 90.2% (95%CI 78.6-96.7) and AUROC of 95.5% (95%CI 90.4-100). Combining FC with PICaSSO with the formula "FC+1.5*Picasso" the accuracy and AUROC to predict histological healing with NI at the threshold of PICaSSO=5 were 92.1% (95%CI 81.1-97.8) and 96.5% (95%CI 91.8-100), respectively.

The accuracy of predicting histological healing with RHI for the combination of UCEIS & FC (≤100µg/g) was 90.2% (95%CI 78.6-96.7) and AUROC 94.4% (95%CI 88.1-100) at the cut-off of PICaSSO=4. However, with NI, the best cut-off was PICaSSO=3, with accuracy of 92.9% (95%CI 77.5-98.0) and AUROC 92.2% (95%CI 84.7-99.7).

PICaSSO alone was able to predict histological healing at the cut-off of PICaSSO=3, with accuracy of 92.2% (95%CI 81.1-97.8) and AUROC of 95.1% (95%CI 89.1-100) with RHI. However, with NI accuracy was 90.2% (95%CI 78.6-96.7) and AUROC was 95.5% (95%CI 90.1-100) at the same cut-off.

Conclusion: The combination of advanced optical enhancement endoscopic scores such as PICaSSO with FC could help to identify UC patients with histologic healing (RHI or NI) with higher accuracy than FC alone. Using new advanced endoscopic technologies now widely available, endoscopic scoring and histologic scoring no longer have large discrepancies as reported before.[1,2]

References: 1. Iacucci M, Daperno M, Lazarev M, et al. Development and reliability of the new endoscopic virtual chromoendoscopy score: the PICaSSO (Paddington International Virtual ChromoendoScopy ScOre) in ulcerative colitis. Gastrointest Endosc 2017; 86(6): 1118-27.e5. 2. Trivedi PJ, Kiesslich R, Hodson J, et al. The Paddington International Virtual Chro-

moendoscopy Score in ulcerative colitis exhibits very good inter-rater agreement after computerized module training: a multicenter study across academic and community practice (with video). Gastrointest Endosc 2018; 88(1): 95-106.e2.
Disclosure: Nothing to disclose

P1061 METABOLIC BONE ASSESSMENT IN PATIENTS WITH CROHN'S DISEASE

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Introduction: Osteoporosis and osteopenia are frequently reported in Crohn's disease, and their prevalence varies between 15 and 30%.The aim of our study was to evaluate the prevalence of bone loss in patients with Crohn's disease and to determine its predictive factors.

Aims & Methods: We conducted a retrospective study including patients with Crohn's disease followed from 2010 to 2016. The measurement of bone mineral density (BMD) was realized by dual energy x ray absorptiometry (DXA) .BMD was evaluated by calculating bone mass expressed in g / cm2 and T-score expressed as standard deviation scores (SDS).

Results: Sixty patients were colllected.The average age was 35.7 years (19 t-70) . The sex ratio M / F was 1.41 (35 men and 25 women). Twenty two patients were smokers (36.6%), the average number of pack years was 13.3 PY. The average body mass index (BMI) was 22.7 Kg / m² (12.3 kg / m² - 30.84 kg / m². Denutrition (BMI < 18,5 kg / m²) was present in 13.33% of patients. The mean number of relapses was 2.57 (1-8). According to the Montreal classification 33.33% (20/60) were ranked L1, 13.3% (8/60) ranked L2, 50% (30/60) ranked L3, and 3.33% (2/60) classified L4. Corticotherapy was noted in 73.3% of patients, the average number of courses was 1.44 (1-5) and the average cumulative dose was 3.75 g. The average duration of the evaluation of the disease was 84 months. Twenty four patients (40%) underwent intestinal resection. Biologically, 53% of patients had an inflammatory syndrome.

BMD was normal in 24 patients (40%) and low in 36 patients (60%). Osteopenia was reported in 28 cases (46.66%) and osteoporosis in 8 cases (13.33%).

The risk factors for bone loss were an age greater than 45 years (p = 0.04), a number of corticosteroid courses > 3 (p = 0.02) and a duration of disease progression> 4 years (p = 0.045).

However, the bone loss was not related to the gender, the location of the Crohn's disease, or the history of intestinal resection.

Conclusion: Bone loss is common in people with Crohn's disease, hence the need for early detection to initiate specific treatment especially when Corticosteroid therapy is used.
Disclosure: Nothing to disclose

P1062 WHAT ARE THE PREDICTORS OF AN ADEQUATE BOWEL PREPARATION IN INFLAMMATORY BOWEL DISEASE?

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Introduction: The effectiveness of colonoscopy is dependent on the quality of bowel preparation. There are multiple modifiable and nonmodifiable factors that affect the quality of bowel preparation. One recent systematic review and meta-analysis was conducted and showed that age, male sex, inpatient status, diabetes mellitus, hypertension, cirrhosis, opioid use, constipation, stroke, and tricyclic antidepressant (TCA) use were associated with inadequate bowel preparation.

However, information regarding risk factors for inadequate bowel preparation in inflammatory bowel disease (IBD) is scarce. In this population an adequate bowel preparation is particularly important for the evaluation of the endoscopic activity and for the screening of pre-malignant lesions through chromoendoscopy.

Aims & Methods: The aim of this study was to assess the quality of bowel preparation and the predictive factors for an inadequate bowel preparation in patients with IBD. A retrospective single-center analysis of patients with IBD who underwent colonoscopy between July 2017 and December 2018 was performed. Incomplete colonoscopy or colonoscopies performed in an emergency setting were excluded. Clinical and endoscopic activity in Crohn's Disease was assessed using the Harvey-Bradshow Index (HBI) and the Simplified Endoscopic Score- Crohn's Disease and Rutgeerts, respectively. Clinical and endoscopic activity in Ulcerative Colitis was assessed using the Mayo score.

Results: 255 patients were evaluated, 51.4% male (n=131), with a mean age of 46 ± 15.1 years-old. The median American Society of Anesthesiologists (ASA) score was 1 (IQR: 1-2) and the median duration of IBD was 9.1 ± 7.7 years. Crohn's Disease was more prevalent 58% (n=148), and most of the patients were in clinical remission 68.2% (n=174) or under some medication 86.2% (n=220). Polyethylene glycol (PEG) was the main bowel preparation 40.8% (n=104) and 85.9% (n=219) had a previous nurse consultation. Bowel preparation was inadequate in 13.3% (n=34) of patients. In the univariate analysis, patients with poor bowel preparation had a higher proportion of a previous stroke (8.8% vs. 0.9%, p=0.002), higher opioid use (8.8% vs. 0%, p < 0.01), and had less frequently a nurse consultation (73.5% vs. 87.8%, p=0.03). The bowel preparation was not associated with age, male sex, body mass index, active smoking, abdominal surgical history, diabetes mellitus, ASA score, disease duration, IBD type, IBD treatment, clinical and endoscopic activity, and type of bowel preparation. In the multivariate analysis, only a previous nurse consultation showed to be associated with an adequate bowel preparation (p=0.02).

Conclusion: The quality measure of bowel preparation (≥ 90%) was not reached in this study. In this study, only a previous nurse consultation was shown to be associated with an adequate bowel preparation.

Disclosure: Nothing to disclose

P1063 LONG-TERM HEALTH STATE OF CHILDREN BORN FROM IBD MOTHERS EXPOSED TO ANTI-TNF TREATMENT DURING PREGNANCY

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Introduction: Infliximab (IFX), adalimumab (ADL) and golimumab (GLM) are anti-TNF inhibitors of IgG1 class which do not cross the placenta until the 3nd trimester of the pregnancy; therefore, they are considered a safe treatment for the foetus during the 1st and 2nd trimester of the pregnancy. Infants born from IBD mothers exposed to anti-TNFs during this period of pregnancy did not exhibit higher rates of congenital abnormalities, early life infections, or any adverse events to early vaccinations. However, at usual dosing regimens blood levels of IFX are higher in pregnant compared to non-pregnant IBD female patients. Furthermore, IFX levels may be detected in the newborn's circulation despite cessation of IFX scheduled treatment in the mother before the 22nd week.

Aims & Methods: We aimed to assess the short and long-term effects of IFX, ADL and GLM on the maturation of the immune system, response to vaccinations and development of serious illnesses in offsprings of IBD females exposed to these anti-TNFs until the 26th week of pregnancy. Prospective, single center study. Data on somatic and mental development, serious illnesses, adverse events to vaccinations and general health state of children were recorded. The source of information was information from mothers, the child's health-book (a full record of child's somatic and mental development, vaccinations and any illness necessitating a visit to the family paediatrician or a hospital) and direct or phone contacts to the family paediatricians.

Results: Data were collected for 19 children (11 female) born from 14 mothers [7 with CD (3 after right hemicolectomy), 7 with UC (4 extensive, 3 left-sided disease)] on monotherapy with IFX (10), ADL (3), GLM (1) at conventional doses from the beginning of the pregnancy until between the 19th and 26th gestational week. Three women had conceived by in vitro fertiliza-

tion, and 4 women had >1 pregnancy. Two women reported a prior spontaneous abortion. All infants were born full-term with normal somatometric data. At birth, low levels of IFX were measured in 3 children (1, 1.5 and 2 μg/ml, respectively), whose mothers had stopped treatment at 24th, 26th and 19th gestational week, respectively. Levels of ADL and BLM were undetectable. All mothers resumed anti-TNF treatment after 1-3 months postpartum. 18/20 children received regular vaccinations uneventfully but 2/20 have not yet completed all vaccinations. 4/20 children were not breast-fed but only 1/4 for fear of anti-TNF treatment. 11/20 children are aged 3-10 years. None of these has developed any serious autoimmune, allergic, or malignant disease, and have responded satisfactorily to vaccinations and have normal rates of somatometric development.

Conclusion: In this small, single-centre, prospective study, treatment with IgG1-anti-TNF agents until the 26th gestational week does not seem to be related with later development, response to vaccinations, or any later adverse life events.

Disclosure: Nothing to disclose

P1064 ASSOCIATION BETWEEN SERUM AND TISSUE PROTEIN PROFILES IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: THE ASCERTAIN STUDY

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Introduction: Molecular markers to facilitate personalized treatment of inflammatory bowel disease (IBD) are needed. Intestinal tissue might be the optimal matrix for biomarker discovery as the affected intestine contains high concentrations of inflammatory proteins. However, the use of tissue is limited due to the invasive nature of biopsy procurement. Therefore, matched validation of candidate markers in serum is an attractive approach.

Aims & Methods: The objectives of this study were to (i) investigate the correlation between the proteomic profile of intestinal biopsies and serum of patients with active IBD and (ii) to identify proteins that discriminate IBD from non-IBD and Crohn's disease (CD) from ulcerative colitis (UC). In this prospective multicentre cross-sectional study, consecutive IBD patients and controls were included between April 2017 and May 2018. Patients with IBD had active endoscopic disease defined by the presence of ≥1 ulcer (≥0.5 cm in size) in CD or an endoscopic Mayo score ≥1 in UC. Non-IBD controls were matched in age and had a normal colonoscopy. In all patients, five biopsies were procured. In CD patients, biopsies were taken from the edge of the most prominent ulcer. In UC, biopsies were taken from inflamed mucosa between 20-25 cm from the anal verge or the nearest inflamed region. In non-IBD controls, biopsies were taken between 20-25 cm from the anal verge. A predefined set of 92 inflammatory proteins was measured in both intestinal biopsies and serum using a proximity extension assay (OLINK, Uppsala, Sweden). Adjustments for multiplicity were performed using the Benjamini-Hochberg approach. Statistical significance was set at an adjusted P value < 0.05.

Results: In total, 41 patients with CD, 39 with UC and 10 controls were included. Forty-three (47.8%) patients were male and the mean (SD) age was 39.6 years (13.3). Median [IQR] CRP and faecal calprotectin values in IBD patients were 8.1 [4.2 - 22.3] (mg/L) and 452.5 [303.4 - 736.5] (μg/g), respectively. Median SES-CD score [IQR] was 8 [5 - 13] in CD. In the UC group, 20 (51.3%), 16 (41%) and 3 (7.7%) patients had an endoscopic Mayo score of 3, 2 and 1, respectively. A significant positive correlation was observed between tissue and serum in IBD patients for IL17A ($r = 0.44$), TGF-alpha ($r = 0.42$) and IL6 ($r = 0.39$). In serum, 29 proteins could discriminate IBD from controls (adjusted $P < 0.05$) of which IL17A was most discriminative. No differences in protein abundance were observed between UC and CD in serum. In tissue, none of the proteins differed between IBD and controls after adjustment for multiple testing.

When comparing intestinal tissue between UC and CD, significantly higher concentrations of five distinct proteins were observed in UC (IL-17A, IL13, CCL4, LIF and CCL3) while the CCL25 level was higher in CD than in UC (adjusted $P < 0.05$).

Conclusion: Of 92 inflammatory proteins, only IL17A, TGF-alpha and IL6 showed moderate positive correlation between tissue and serum. Twenty-nine serum proteins could discriminate between IBD and non-IBD. Six tissue proteins differentiated CD from UC. The most consistently implicated protein was IL17A. Overall, a poor correlation between tissue and serum proteomic profiles in IBD was found. Ongoing research will focus at the intestinal tissue transcriptome compared to circulating proteins.

Disclosure: TS, MK and MD: no conflicts of interest. GN: has served as speaker and/or advisor for Takeda, Abbvie, MSD, Janssen, Octal pharma, Amgen, Pfizer, Ferring, Falk Pharma. KG: served as speaker and/or advisor for Amgen, AbbVie, Biogen, Boehringer Ingelheim, Ferring, Hospira, Immunic AG, Janssen, MSD, Pfizer, Samsung Bioepis, Sandoz, Takeda, Tigenix and Tillotts. ML: Speaker and/or principal investigator for Abbvie, Celgene, Covidien, Dr. Falk, Ferring Pharmaceuticals, Gilead, GlaxoSmith-Kline, Janssen-Cilag, Merck Sharp & Dohme, Pfizer, Protagonist therapeutics, Receptos, Takeda, Tillotts, Tramedico. Research grants from AbbVie, Merck Sharp & Dohme, Achmea healthcare and ZonMW. MEW: Speaker fees from Takeda, Tillotts, research grants from Glaxo Smith Kline. DD: reports speaker and consultant fees from MSD, Abbvie, Takeda, Pfizer, Janssen, Krka, Dr. Falk Pharma, Ferring. GRD: has served as advisor for Abbvie, Ablynx, Allergan, Amakem, Amgen, AM Pharma, Avaxia, Biogen, Bristol Meiers Squibb, Boerhinger Ingelheim, Celgene/Receptos, Celltrion, Cosmo, Covidien/Medtronics, Ferring, DrFALK Pharma, Eli Lilly, Engene, Galapagos, Genentech/Roche, Gilead, Glaxo Smith Kline, Immunic, Johnson and Johnson, Lycera, Medimetrics, Millenium/Takeda, Mitsubishi Pharma, Merck Sharp Dome, Mundipharma, Nextbiotics, Novonordisk, Otsuka, Pfizer/Hospira, Prometheus laboratories/Nestle, Protagonist, Robarts Clinical Trials, Salix, Samsung Bioepis, Sandoz, Setpoint, Shire, Teva, Tigenix, Tillotts, Topivert, Versant and Vifor. Received speaker fees from Abbvie, Biogen, Ferring, Johnson and Johnson, Merck Sharp Dome, Mundipharma, Norgine, Pfizer, Samsung Bioepis, Shire, Millenium/Takeda, Tillotts and Vifor. Received research grants from Abbvie, Johnson and Johnson, MSD, Medtronics, DrFALK Pharma, Glaxo Smith Kline, Takeda, Samsung, Pfizer, Prometheus, Robarts Clinical Trials.

P1065 HISTOLOGICAL ACTIVITY AS A PREDICTIVE MARKER OF CLINICAL RELAPSE AT 1 YEAR IN ULCERATIVE COLITIS: A PROSPECTIVE MONOCENTRIC STUDY

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Introduction: The possible role of histological activity in clinical management of Ulcerative Colitis (UC) is undefined.

Aims & Methods: In a prospective study, we aimed to assess the role of histological activity as a predictive marker of clinical relapse in a cohort of UC patients (pts) undergoing colonoscopy and followed up for 1 year (yr). Secondary aim was to assess in the same cohort of UC pts, the correlation between clinical, endoscopic and histological scores of activity.From Feb. 2016 to Feb. 2017, consecutive UC pts with clinical indication for colonoscopy were prospectively enrolled. Inclusion criteria:
1) Diagnosis of UC;
2) Age>18 and ≤80yrs;
3) Regular follow up;
4) Indication for colonoscopy;
5) Compliance to clinical follow up at 1 yr.
During colonoscopy ≥2 biopsies were taken from≥1 macroscopically involved area and possibly, from ≥1 uninvolved area. All colonoscopies were performed by the same IBD-dedicated gastroenterologist. The day of colonoscopy clinical activity was assessed by the Mayo partial score (activity≥3)(1), endoscopic activity by the Mayo endoscopic score (activity≥2)(1). Histological activity was assessed by the same IBD-dedicated pathologist using the Geboes Simplified Score (GSS) for UC (activity≥3.1)(2). Scores were blindly assessed by the 3 investigators. Data were expressed as mean

[range].Spearman's correlation coefficients were used to investigate the association between different scores of activity. Cox proportional hazards regression model was used for both univariate and multivariate analyses to identify the predictors of clinical relapse at 1 year (Odds Ratio, OR [95% CI]).

Results: The study cohort included 77 UC pts with clinical, endoscopic and histological assessment at baseline, clinically followed up for 1 year. Clinical characteristics of the 77 UC pts: 43 M (55.8%); age 51 [24-80] yrs; UC duration 14.7 [1-48 yrs]. UC extent included (%): pancolitis in 33 (42.8%), left sided in 24 (31.2%), proctitis in 20 (26%) pts. The day of colonoscopy UC was clinically active in 15 (19.4%), inactive in 62 (80.6%) pts. Endoscopic activity was observed in 39 (50.6%) pts and histological activity (GSS≥ 3.1) in 37 (48%) pts; 5 of these 37 pts were in endoscopic remission. Moderate correlations were observed between clinical and endoscopic scores (r=0.439; p< 0.0001), clinical and histological scores (r=0.32; p=0.0045), endoscopic and histological scores (r=0.653; p< 0.0001). During the clinical follow at 1 yr, clinical relapse of UC occurred in 24 (31%) pts while 53 (69%) pts maintained clinical remission. At baseline 11 out of 24 (46%) UC pts were clinically active, 15 out of 24 (63%) pts showed endoscopic activity, and 16 out of 24 (67%) pts histological activity. Among the 5 pts showing endoscopic remission and histological activity at baseline, 1 pt developed clinical relapse within 1 yr. Univariate analysis identified clinical activity (OR 4.82 [2.15-10.82]; p< 0.001) and histological activity (OR 2.599 [1.11-6.08]; p< 0.027) as predictive factors for clinical relapse at 1 yr. The multivariate model retained only histological activity as predictive marker of clinical relapse (OR 2.44 [1.04-5.75]; p< 0.041). We estimated that, after controlling for age and gender, pts with histological activity (GSS≥3.1) have 2.44 fold risk of clinical relapse at 1 yr compared to pts with histological remission (GSS< 3.1).

Conclusion: Histological activity provided independent information for clinical relapse in a cohort of UC patients prospectively followed up for 1 year. Histological activity had a moderate correlation with the endoscopic and clinical activities.

References: 1.Schroeder KW. NEJM 1987;317:1625 2.Jauregui-Amezaga A. JCC 2017;11:305

Disclosure: Nothing to disclose

P1066 DURABILITY OF THE ANTI-HBS TITERS AFTER VACCINATION AGAINST HEPATITIS B VIRUS (HBV) IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE (IBD)

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Introduction: Among immunocompromised patients who respond to the HBV vaccine, clinically significant HBV infection has been documented in those who do not maintain anti-HBs concentrations > 10 IU/l.

Aims & Methods:
1) To understand the kinetics of the anti-HBs titers over time in IBD patients who have initially responded to the vaccination.
2) To identify predictive factors of negativization of anti-HBs titers over time.
This multicenter study included IBD patients vaccinated in the COMVI-B trial (EUDRA-CT number: 2010-023947-14), where patients with negative HBV serology and without previous vaccination against HBV were randomized 1:1 to receive Fendrix® or double doses of Engerix® at months 0, 1, 2 and 6. Patients with anti-HBs > 10 IU/L 2 months after the 4th dose were followed-up. Anti-HBs titers were then measured at 6 and 12 months. When anti-HBs titers were < 10 IU/L during the follow-up, they were considered negatives. Long-term maintenance of positive anti-HBs titers was

estimated using Kaplan-Meier curves. Cox-regression analysis was performed to identify potential predictive factors for losing anti-HBs protective titers during follow-up.

Results: A total of 131 patients had anti-HBs ≥10 UI/L after completing vaccination; from them, 117 patients (90%) accepted to be included in the follow-up study. From those, 55% were male, 54% had ulcerative colitis and 90% had anti-HBs ≥100 IU/L after vaccination. With respect to IBD treatments, 2.6% received solely steroids during follow-up, 29% immunomodulators in monotherapy, 15.4 anti-TNF in monotherapy and 19% combo therapy (immunomodulators plus anti-TNF agents). Fifty percent of patients received each of the vaccines (Engerix® or Fendrix®). There were no differences in the main characteristics (age, anti-HBs concentration after complete vaccination or IBD treatment) between the study groups (Engerix® or Fendrix®) but the proportion of patients exposed to anti-TNF was superior among patients vaccinated with Fendrix® (43 vs. 25%, p< 0.04). The cumulative incidence of negativization of the anti-HBs titers was 13% after 6 months and 20% after 12 months of follow-up. In the multivariate analysis, to have had anti-HBs ≥100 IU/L (vs. < 100 UI/L) after the vaccination was the only factor that was associated with a higher probability of maintaining anti-HBs titers during the follow-up (HR=9.8, 95%CI=4-23, p< 0.0001). The type of vaccine administered, patient's age or immunosuppressive treatment during follow-up were not associated with the risk of negativization of anti-HBs titers.

Conclusion: A high proportion of IBD patients with protective anti-HBs titers after vaccination loose them over time (20% of patients after 1 year). The risk of loosing protective anti-HBs titers is dramatically increased in patients achieving anti-HBs below 100 IU/L after the vaccination. Thus, anti-HBs >100 IU/L should be the threshold to consider HBV vaccination success in IBD patients. Once the patient has responded to the vaccine, patient's age or immunosuppressive treatment during follow-up seems to have no impact on the maintenance of anti-HBs titers.

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P1067 PATIENT-REPORTED OUTCOMES MEASURED WITH IBD DISK IN INFLAMMATORY BOWEL DISEASE

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Introduction: Inflammatory bowel disease (IBD) is a chronic destructive disorder deteriorating the functional status of the affected patients.

Aims & Methods: The aim of our study was to test a new tool for measuring patient-reported outcomes, the IBD Disk invented to assess disability in patients with IBD under biological treatment. Patients attending the outpatient clinic were administered the self-completion 10-item visual scale of IBD Disk. Features of interest included abdominal pain, body image, education and work, emotions, energy, interpersonal interactions, joint pain, regulating defecation, sexual functions, and sleeping. Disease activity scores (CDAI or Mayo) were assessed by the treating physician.

Results: In total, 90 patients with IBD were evaluated (75 and 15 cases of Crohn's disease [CD] and ulcerative colitis [UC], respectively). The IBD Disk total score in CD was higher for active disease (score of 49.5 ± 27.7 compared to 25.5 ± 19.5 for inactive disease, *p* = 0.013) and for female gender (32.6 ± 23.8 vs 24.0 ± 19.9 for men; *p* = 0.08). There was a significant, positive correlation of moderate strength between IBD Disk total score and disease activity (rho = 0.521; *p* = 0.023), while the score showed no association with age, disease duration, concomitant disease and previous surgeries. Interestingly, patients with inactive disease (n = 54) had severe (>50) or marked (31-50) disability (13% and 9.3%, respectively). The highest scores were achieved in the subgroups evaluating energy, body image, and emotions (4.5±2.8, 3.6±3.1 and 3.3±3.0, respectively).

Conclusion: IBD Disk was easy to administer in everyday practice while the application of the score allowed the rapid and representative assessment of patients' health-related quality of life.

Disclosure: Nothing to disclose

P1068 SERUM CALPROTECTIN ACCURATELY SEPARATES INFLAMMATORY BOWEL DISEASE AND IRRITABLE BOWEL SYNDROME

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Introduction: Even though it is known that fecal calprotectin levels correlate with inflammatory activity in inflammatory bowel disease (IBD) patients, some limitations were described, including fecal collection, sample delivery and processing (Meuwis 2013), high within-day variability (Lassan 2014) and the subsequent uncertainties on the optimal time for sampling (Calafat 2015). Recently, some authors proposed that serum calprotectin may be useful in disease activity evaluation in rheumatologic patients (Hammer 2010). Accordingly, we measured serum calprotectin levels in IBD patients in comparison with both patients with irritable bowel syndrome (IBS) and healthy volunteers, in order to test whether this blood biomarker could separate organic from functional disorders.

Aims & Methods: We enrolled 21 Crohn's disease (CD), 14 ulcerative colitis (UC) and 22 IBS patients as well as 20 healthy volunteers, comparable for age and gender (30 Females, age 35±6 yrs). We selected 18 patients in remission (10 CD and 8 UC), 7 mildly active (4 CD and 3 UC), 9 moderately active (7 CD and 2 UC) and 1 severely active (UC), according to Harvey-Bradshaw index for CD and partial Mayo score for RCU. Serum calprotectin was determined for each patient, after an overnight fast (Calprest, Eurospital, Italy). Fecal calprotectin was also measured, by means of ELISA test.

Results: As expected, after a logarithmic transformation, in IBD patients serum calprotectin levels were significantly higher than in IBS patients (1,37 mg/ml; 95% confidence interval (IC) 0,86-2,1 mg/ml in IBS vs 4,54 mg/ml 95%IC 2,09-7,1 mg/ml in IBD; p< 0,001) and healthy volunteers (1,15 mg/ml; 95% IC 0,87-1,5 mg/ml in healthy volunteers vs 4,54 mg/ml 95%IC 2,09-7,1 mg/ml in IBD; p< 0,001). Building a ROC curve, we could identify 2,42 mg/ml as the threshold level to distinguish IBS from IBD (area under the ROC curve 0,8; P< 0,001) with 67% sensitivity and 88% specificity. There was no correlation between fecal and serum calprotectin nor in the whole sample, nor in the different groups. We found no significant difference between serum calprotectin level among UC and CD patients.

Conclusion: The results of our study suggest that serum calprotectin could be a promising biomarker providing an accurate separation between IBD patients and IBS or healthy patients. The lack of correlation between fecal and serum calprotectin levels suggests that in the future this new biomarker could improve the accuracy of IBD diagnosis: in patients with abdominal symptoms of unknown origin, the combination of fecal and serum calprotectin could be helpful in identify those patients who need invasive procedures.

Moreover, in IBD serum calprotectin seems not to be influenced by the site of the disease involvement, suggesting its potential role in monitoring IBD patients.

Disclosure: Nothing to disclose

P1069 FAECAL CALPROTECTIN LEVELS IN LYMPHOCYTIC AND COLLAGENOUS COLITIS

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Introduction: Microscopic colitis (MC) is comprised of lymphocytic (LC) and collagenous (CC) subtypes, and its diagnosis is dependent on clinical symptoms of chronic watery diarrhea in addition to well-defined histological criteria [1]. Faecal calprotectin (FC) is known to be a useful non-invasive biomarker in the investigation of inflammatory bowel disease [2] but there are few published data describing FC in MC.
Previous small studies have shown that FC is elevated in 73% MC [1] and that in active CC the median FC is 48-80 µg/g [3, 2], but to the best of our knowledge no previous studies have assessed FC in LC and CC comparatively.
Aims & Methods: The two main objectives of our study were to establish whether faecal calprotectin levels are elevated in microscopic colitis and if there is a difference between faecal calprotectin levels in microscopic and lymphocytic colitis.
Electronic patient records were reviewed from our hospital to obtain FC levels measured at the time of diagnosis, for all patients with a histological diagnosis of MC between 01/01/2014 and 06/10/2017. Median and range FC levels were calculated for CC and LC as well as MC overall. The Mann-Whitney U-test was used to ascertain whether there was a difference between FC level in CC and LC, with a $p < 0.05$ considered to be statistically significant. FC level of > 16 µg/g was considered to be elevated.
Results: 70 patients had a histological diagnosis of MC between 01/01/2014 and 06/10/2017; 25/70 (36%) had FC checked at diagnosis. The average age was 60 years for LC (range 29-88 years, 4 male: 11 female), and 75 years for CC (range 50-89 years, 1 male : 9 female). 20 of these 25 patients with MC (80%) had an elevated FC, while 5 (20%) patients had a faecal calprotectin level of < 16. Table 1 shows median and range FC in LC and CC independently, and also in LC and CC combined (microscopic colitis overall).

	LC	CC	Microscopic colitis overall (LC and CC combined)
Number of patients	40	30	70
Number of patients with FC tested	15	10	25
Median FC (µg/g)	63	324	148
Range FC (µg/g)	<16 to 476	86 to >1800	<16 to >1800

[Table 1]

The Median FC in Microscopic colitis overall was elevated at 148 µg/g. The Median FC was 324 µg/g for CC and 63 µg/g for LC, which showed statistical significance using Mann-Whitney U-test ($p = 0.01078$)
Conclusion: This has been the first study to compare faecal calprotectin values in Collagenous and Lymphocytic colitis. This showed a statistically significant difference towards higher levels of FC in collagenous colitis. The main reasons for the higher calprotectin level in CC are unclear, but as faecal calprotectin is a predominantly a marker of neutrophils [4] and as damage to the surface epithelium has been shown to be more common and pronounced in collagenous colitis compared to lymphocytes [5], this could be a possible explanation.
In addition, FC was elevated in 80% of patients with MC suggesting a correlation between calprotectin levels and microscopic colitis. However, it is noteworthy that the 20% of patients in our cohort had undetectable calprotectin indicating that faecal calprotectin alone is insufficient to exclude microscopic colitis and should be used in conjunction with lower GI endoscopy and colonic biopsies, in particular in cases with a high index of clinical suspicion of microscopic colitis.
References: [1] Stoicescu A, Becheanu G, et al, Microscopic Colitis - A Missed Diagnosis in Diarrhea-Predominant Irritable Bowel Syndrome, Maedica Buchar,2012;Jan;7(1):3-9 [2]Von Arnim U, Wex T, et al, Fecal calprotectin: a marker for clinical differentiation of microscopic colitis and irritable bowel syndrome, Clin Exp Gastroenterol;2016;9:97-103 [3] Wildt S, Nordgaard-Lassen et al, Metabolic and inflammatory faecal markers in collagenous colitis, European Journal of Gastroenterology & Hepatology;July 2007;19;7;567-574 [4]Alibrahim B, Aljasser M, et al, Fecal Calprotectin Use in Inflammatory Bowel Disease and Beyond: A Mini-Review, Canadian Journal of Gastroenterology and Hepatology;2015;29;3;157-163 [5] Miehlke S, Verhaegh B, et al, Microscopic colitis:pathophysiology and clincal management, Lancet Gastroenterol Hepatol;2019;4305-14
Disclosure: Nothing to disclose

P1070 INCIDENTAL DIAGNOSIS OF INFLAMMATORY BOWEL DISEASE FROM THE ENGLISH BOWEL CANCER SCREENING PROGRAMME -FOLLOW UP OF THE FIRST REPORTED COHORT

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Introduction: The UK Bowel Cancer Screening Programme (BCSP) was launched in 2006 to cover the population of England and Wales. It screens individuals aged 60-69 years with a Faecal Occult Blood test (FOBt) followed by a screening colonoscopy if FOBt positive. We report 7-year follow up of our cohort of patients with an incidental ("asymptomatic") diagnosis of IBD first reported in 2011.
Aims & Methods: We report 7-year follow up of our cohort of patients with an incidental ("asymptomatic") diagnosis of IBD first reported in 2011. A retrospective review of BCSP outcomes was conducted at our centre from its launch in 2008 until 2011. Screening data included the number of patients invited, number screened (FOBt outcome "normal" or "abnormal") and number of colonoscopies performed. Of 136,811 patients invited, 67,485 were screened (uptake of 49. 33% ; FOBt positivity 2. 02%). Colonoscopy was performed in 1401 patients (female 523), polyps detected in 630 (41. 37%), cancer in 134 (8. 80%) and 469 (30. 79%) had a normal exam. Of 16 patients diagnosed with IBD and confirmed at histology, clinical data including demographics, disease characteristics, treatment and outcomes were recorded and follow-up data is presented until 31 May 2018.
Results: Of 16 patients, 2 died from metastatic prostate cancer and postoperative complications following colectomy. One patient was lost to follow up.
11/13 patients had UC (E1=3, E2=5, E3=3) and 3 patients had Crohn's disease(A3L2B1).
At last follow up, 2 patients with E1 UC progressed to E2 and E3 disease respectively. CD phenotype did not change.
9 of 11 patients with UC were in clinical remission and 2 patients had active disease (pMayo 3 and 4 respectively) and received anti-TNF therapy. All 3 patients with CD remained in clinical remission. Of 11 UC patients, 8 continued 5 ASA therapy , 1 received Vedolizumab (following antibody mediated loss of response to anti-TNF), 1 patient received anti-TNF with Methotrexate and another is on no treatment and in clinical remission. In the CD cohort (n=3), 2 patients were on Adalimumab monotherapy, and 1 on 6-Mercaptopurine.
Conclusion: An incidental diagnosis of IBD is not an uncommon. With the advent of endoscopic bowel cancer screening this number is set to increase. Incidental IBD appears to follow an indolent course over age 60 with a stable disease phenotype This subset of patients may present an important model for study of early disease providing novel insights into disease pathogenesis and evolving treatment paradigms.
Disclosure: Nothing to disclose

P1071 A RETROSPECTIVE REAL WORLD ANALYSIS OF 6-THIOGUANINE NUCLEOTIDE (6-TGN) MONITORING FOR AZATHIOPRINE DOSING IN INFLAMMATORY BOWEL DISEASE

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Introduction: Thiopurines (TPs) are frequently used as monotherapy to maintain remission in patients with inflammatory bowel disease (IBD). The red-cell 6-Thioguanine Nucleotide (6-TGN) biomarker is commonly measured to guide dosing. While there is scanty prospective data to support 6-TGN-directed therapy, efficacy is inferred from observed rates of remission in patients with higher levels, but the link between TP dose and TGN level is not clear [1,2].

Aims & Methods: The aim of our study was to determine the value of 6-TGN measurements in predicting treatment escalation in patients with IBD on azathioprine monotherapy at 12 months post treatment initiation, in whom the dose was not modified during the aforementioned period.

We carried out a retrospective review of all IBD patients initiated on azathioprine monotherapy between December 2010 and July 2018, at a single specialist centre in the UK. Electronic patient records were used to collect: sampling date, Sex, Age, 6-TGN result (between 2-6 months post treatment initiation), MMP, MMP:TGN Ratio, Azathioprine dose (Mg), Weight (Kg), Azathioprine dose per kilo (Mg/Kg), disease, previous medications, adverse events, and treatment escalation. Treatment escalation was defined as the addition of a steroid, 5-ASA, biologic, or surgery within 12 months of azathioprine treatment initiation.

A series of hierarchical regression experiments was carried out based on a probabilistic prediction framework, described in detail elsewhere [3,4]. In effect, variables were added in sequence to determine whether they improve the out-of-sample probabilistic prediction error (i.e. brier score) of a linear regression model with a logit-link function. 95% confidence intervals for each of the aforementioned performance metrics were calculated using a Jackknife estimator of variance algorithm. Statistical significance assessed using the Wilcoxon signed-rank test, with the significance threshold set at 5%. All predictive modelling was performed using the *R (v 3.2.0)* statistical software suite and the *mlr (v 2.7)* machine learning library. **Results:** 298 individuals were identified that met the inclusion criteria (139F; mean age 36.1±14.0y; 152 UC; 146 CD). Median azathioprine dose was 125mg (Range: 25 - 250), and median weight-adjusted dose was 1.83 mg/kg (Range: 0.3 - 3.2). Median TGN response was 313.5 (Range: 5 - 1,705). Using demographic data (i.e. sex, age, weight, diagnosis, and previous medications) as a baseline model, the resulting Brier score was 0.183 (S.E. 0.039).

Conclusion: This study is one of the largest retrospective studies [1] examining the efficacy of TGN monitoring in azathioprine monotherapy. The results suggest that metabolite data, including both TGN and MMP, does not appear to contain any additional information about the probability of requiring treatment escalation at 12 months above that of demographic information. Given the contradictory evidence in the literature, definitively recommending a 6-TGN-based dose-optimisation strategy would require prospective study.

References: [1] Moreau, AC, et al. Inflammatory bowel diseases 2014, 20(3), 464-471. [2] Chapdelaine Aet al. Clinical rheumatology, 36(6), 1341-1348. [3] Mateen BA, et al. Clinical rehabilitation. 2018 Oct;32(10):1396-405. [4] Gressmann F, et al. Probabilistic supervised learning. arXiv preprint arXiv:1801.00753. 2018 Jan 2.

Disclosure: Nothing to disclose

P1072 DIAGNOSIS OF IRON DEFICIENCY IN INFLAMMATORY BOWEL DISEASE: ARE FERRITIN AND CRP SUFFICIENT?

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Introduction: Iron deficiency and iron deficiency anemia are the most common extra-intestinal manifestations of chronic inflammatory bowel disease (IBD), significantly impairing patient's quality of life. Since the diagnostic value of ferritin as an acute phase protein (aPP) in IBD is therefore limited[1], the simultaneous determination of the C-reactive protein (CRP) is recommended for interpretation in the context of inflammation[2]. Since the CRP and ferritin have distinctly different half-lives, the WHO recommends α_1-acid glycoprotein (AGP) as a second biomarker[3].

Aims & Methods: The aim of our study was therefore for the first time to interpret the inflammatory increase of ferritin in IBD patients by CRP and AGP, individually and in combination.

By 03/2019, 118 IBD patients (45.48 ± 15.25 years, 47.46% f.) (38 with Crohn's disease, 47 with ulcerative colitis, 33 controls) were enrolled. In addition to the Hb value, ferritin (cut-off 30 µg/mL), CRP (cut-off 5 mg/L) and AGP (cut-off> 0.65 g/L) were determined in all patients.

Results: When CRP alone was used, 29.76% (25/84) had an inflammatory increase in ferritin, and 82.14% (69/84; $p < 0.05$) when using AGP or both. Increased AGP levels were more common in patients with ulcerative colitis (60 vs. 11.11%) than in patients with Crohn's disease (57.63 vs. 32.20%) compared to elevated CRP levels. Serum ferritin levels correlate with CRP (0.420 p = 0.002), but not with (0.022, p = 0.876).

There was no specific correlation between CRP and AGP (0.098, p = 0.487). The assumption that most patients with high CRP levels also have high AGP concentrations and vice versa was confirmed by our data only in 55% of cases.

There were 11 patients with complete iron deficiency when CRP alone was used, 18 patients with functional iron deficiency, one with chronic anemia (ACI) and one with mixed-type anemia. Functional iron deficiency was found in 28 patients using CRP and/or AGP (+ 55%, p < 0.05) and 5 patients had ACI (according to (4)).

Conclusion: Our data underline the problem of determining ferritin also with the aid of CRP in the diagnosis of iron deficiency in IBD. We were able to demonstrate that the determination of CRP and/or AGP significantly improves the diagnostic accuracy of serum ferritin levels in IBD patients.

References: (1) Dignass A et al. Int J Chronic Dis 2018 (2) Dignass A et al. J Crohns Colitis 2015 (3) Thurnham D et al. Am J Clin Nutr 2010 (4) Weiss G, Goodnough L New Engl J Med 2005

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P1073 REDEFINING AND VALIDATING ENDOSCOPIC AND HISTOLOGICAL HEALING BY USING VIRTUAL ELECTRONIC CHROMOENDOSCOPY IN ULCERATIVE COLITIS

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Introduction: Ulcerative colitis patients with endoscopic mucosal healing by white light endoscopy may still have histologic inflammation. Electronic chromoendoscopy (PICaSSO-Paddington International Virtual ChromoendoScopy ScOre)[1] may better predict mucosal healing. We investigated the

relationship between mucosal healing (MH) defined by PICaSSO, and histological index (RHI). We specifically explored the magnitude of difference between endoscopy and histology defined mucosal healing using refined endoscopic assessments.

Aims & Methods: A prospective study enrolling 82 UC patients (M 66%) was conducted. Mayo subscore (MES), PICaSSO mucosal and vascular endoscopic score were recorded. High definition electronic virtual chromoendoscopy was used in all patients. Histological score (Robarts histopathology index-RHI) was used to score histological inflammation. Receiver operating characteristic (ROC) curves were plotted to determine the best cut-off threshold for PICaSSO scores that predicted histological healing according to the RHI. We then validated the PICaSSO score against histology (RHI) in an independent cohort of 70 UC patients (M 52%); and sensitivity, specificity, and accuracy were calculated.

Results: A PICaSSO of ≤4 predicted histological healing at RHI ≤6, with accuracy of 92.8% (95% CI: 84.8, 97.3). The accuracy of MES in predicting histological healing with RHI was inferior at 84.2% (95% CI: 74.4, 91.2). The corresponding AUROCs were 98.9% (95% CI: 97.6, 100) and 92.0% (95% CI: 85.9, 98.6) respectively.

In the validation cohort, PICaSSO £ 4 predicted histological healing at RHI £6 with sensitivity 96.6% (95%CI 82.2-99.9), specificity 68.3% (95%CI 51.9-81.9) and accuracy 80.0% (95%CI 68.7-88.6). PICaSSO £3 predicted histological healing by RHI with sensitivity 96.6% (95%CI 82.2-99.9), specificity 92.7% (95%CI 80.1-98.5) and accuracy 94.3%.

Conclusion: The histological healing by RHI is accurately predicted by PICaSSO at threshold values of ≤3 in a validation cohort of UC patients. Advanced electronic endoscopic techniques are able to predict histologically proven MH with high accuracy. Large prospective studies are necessary to ascertain whether, with new endoscopic technologies such as readily available VCE, histology can still provide additional information about course of UC.

References: 1. Iacucci M, Daperno M, Lazarev M, et al. Development and reliability of the new endoscopic virtual chromoendoscopy score: the PICaSSO (Paddington International Virtual ChromoendoScopy ScOre) in ulcerative colitis. Gastrointest Endosc 2017;86:1118-1127.e5.

Disclosure: Nothing to disclose

P1074 THE REAL WORLD USE OF FECAL CALPROTECTIN HOME TESTING IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE UNDER MAINTENANCE TREATMENT WITH ADALIMUMAB

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Introduction: Fecal calprotectin (FC) has been suggested as an important biomarker for the management of patients with inflammatory bowel disease (IBD). It is an indirect index of disease activity and plays a crucial role in the treat-to-target strategy. Consecutive measurements of FC in patients in clinical remission can predict a disease relapse and lead to an early treatment optimization. We aimed to present our real world experience using the FC home testing in the management of IBD patients under maintenance treatment with adalimumab.

Aims & Methods: Consecutive IBD patients under maintenance treatment with adalimumab were studied retrospectively based on prospectively recorded data in a registry. The study period was from 10/2016 until 3/2019. Inclusion criteria was at least one available FC measurement (ELISA, Bühlmann fCAL Home test). During this period patients' compliance in the FC home test as well as all the treatment modifications including adalimumab intensification, change of biologic agent or IBD related surgical intervention were assessed.

Results: From a total of 72 IBD patients under maintenance treatment with adalimumab, 63 (87.5%) who had good compliance performing the home FC test [median number of measurements 3 (1-10)] and complete follow-up data were included in the study. Patient characteristics are presented in Table 1. In 21 of them (33.3%) treatment modification (10 adalimumab intensification, 1 de-escalation , 8 change to other biologic agent, 2 surgeries) has become necessary during the study period based on the evaluation of consecutive values of FC (mean FC value 718 µg/g ±314, 45% of pts had values>1000 µg/g), mostly after endoscopic confirmation of disease flare (18/21). The rest 42 patients who remained on stable treatment had mean FC levels 272 µg/g ±236, (57.1% of them had values< 250 µg/g) sig-

nificantly lower than the first group *p*< 0.0001. Twenty three out of these 42 patients underwent a colonoscopy and mucosal healing was confirmed in 7/23 (30.4%) while FC was< 50 µg/g in 9/23 (39.1%).

Conclusion: The IBD patients' compliance rate of performing the FC home test is high (87.5%). Moreover, our results confirm the important role of consecutive FC measurements at home, in combination with the endoscopic evaluation for the optimization of treatment in IBD patients receiving maintenance treatment with adalimumab.

Disclosure: Nothing to disclose

Mean age (years ± SD)	42.3± 14.9
Men (%)	37 (59%)
Disease duration (years, mean ± SD)	13.4 ± 9.5
Diagnosis	
Crohn's disease (%)	56 (89%)
Ulcerative colitis (%)	7 (11%)
Current smokers	21 (33%)
Disease location	
Ileum (L1)	24
Colon (L3)	7
Ileum+colon (L3)	25
Perianal disease (p)	14
Proctitis (E1)	0
Left sided colitis (E2)	4
Extensive colitis (E3)	3
Extraintestinal manifestations	32 (51%)
Median duration of adalimumab use in months (IQR)	32 (20-62)
Combination treatment with immunomodulators	13 (21%)
Experienced in biologic agents	28 (44%)
IBD related surgery	16 (25%)

[Table1 Demographic and clinical characteristics of the IBD patients (N=63)]

P1075 PREDICTIVE ENDOSCOPIC FACTORS OF CLINICAL SEVERITY IN ULCERATIVE COLITIS (UC) USING ULCERATIVE COLITIS ENDOSCOPIC INDEX SCORE (UCEIS)

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Introduction: Digestive Endoscopy, besides the diagnosis and surveillance of ulcerative colitis (UC), is also interesting to establish the severity of the disease by using the UCEIS score which assess vascular pattern, bleeding, and ulcers.

Aims & Methods: The purpose of our work is to demonstrate the items of the score that are most associated to the severity of the flare-ups. This is a retrospective study conducted from January2013 to January2018 including 480 patients with UC. The endoscopic severity was assessed by UCEIS score and the clinical activity by the Modified Truelove & Witts score.The statistical study was performed using SPSS20.0. A logistic regression analysis was performed as multivariate analysis. The binary dependent variable is the severe flare-up and the independent variables were the 3 items of UCEIS score. Statistical significance was established at *p* values of less than 0.05

Results: The clinical assessment revealed that the flare-ups were mild in 22.08%, moderate in 48.05% and severe in 28.57%. The study of the 3 items of UCEIS score revealed a patchy obliteration vascular pattern in 66.23%, obliterated in 27.27%, and normal in 6.49%, bleeding was absent

in 46.8%, mucosal in 42.9%, luminal mild in 37.7% and luminal severe in 1.3%, ulcers were absent in 18.2%, < 5mm in 37.7%, > 5mm in 19.5% and deep in 24.7%. Thus, the UCEIS score was as followed 6.5% were in remission, 33.8% were in mild, 49.4% were moderate, 3.9% were severe. The multivariate logistic regression analysis revealed that vascular pattern and the presence of ulcers were significantly associated and predictive of severe flare-ups (p=0,038, 0,049 respectively).

Conclusion: By studying and analyzing the UCEIS score, vascular pattern and the presence of erosions/ulcers are the items associated and predicting the clinical severity of the flare-ups.

Disclosure: Nothing to disclose

P1076 EVALUATION OF PAIRED AND SEPARATED ENDOSCOPIC READS AT BASELINE AND WEEK 14 IN THE EXPLORATORY BERGAMOT INDUCTION COHORT

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Introduction: Treatment guidelines recommend that Crohn's disease evaluation and treatment decisions should include endoscopic evaluation in conjunction with clinical and laboratory assessment (1,2). Previous work found that an adjudicated central read model (CRM) for evaluating Simple Endoscopic Score for Crohn's Disease (SES-CD) that included a local reader and at least 1 central reader reduced placebo rates, variability and increased treatment response rates versus single reader models (3). This study explored the impact on scoring by blinded reading of paired endoscopic reads versus unpaired reads scored by the CRM model.

Aims & Methods: To compare the total SES-CD as evaluated by paired readings of the week 0 and week 14 endoscopies (i.e. simultaneous assessment of pre- and post-induction treatment endoscopic videos) by the same central reader versus scores based on unpaired readings by the CRM. Patients in this analysis (n = 63) were a random subset from the exploratory BERGAMOT induction cohort, who were randomised 2:2:1 to receive subcutaneous etrolizumab 105 mg every 4 weeks (with placebo at week 2; n = 24); etrolizumab 210 mg at weeks 0, 2, 4, 8, and 12 (n = 24); or placebo (n = 15). Three central readers performed the paired endoscopy readings. The unpaired reads were evaluated using the CRM and included a predefined sliding threshold to trigger adjudication of discordant scores by a second central reader as reported previously. All readers were blinded to treatment arm, timing of the endoscopy, and the other reader's assessments.

Results: In the overall population, 48% had ileo-colonic disease, 30% had colonic disease and 22% had disease restricted to the ileum. Prior treatment for Crohn's disease included anti-TNFs (73%), oral corticosteroids (49%), or non-biologic immunosuppressants (27%). In general, the mean baseline and week 14 SES-CD evaluated by the paired read model were higher than those assigned by the CRM. Differences between models in assigning categorical thresholds were more varied (Table). The placebo rates of ≥50% SES-CD decrease from baseline, SES-CD ≤ 4, and SES-CD ≤ 2 were similarly low (0%-6.7%) with either the unpaired CRM or the paired endoscopy model. More patients achieved ≥50% SES-CD decrease from baseline with etrolizumab treatment using the CRM compared to the paired read model (21% vs 13%, respectively).

	Placebo n = 15		Etrolizumab 105 mg n = 24		Etrolizumab 210 mg n = 24		Etrolizumab 105 mg and 210 mg n = 48	
	Paired	CRM	Paired	CRM	Paired	CRM	Paired	CRM
≥50% decrease from baseline at week 14	0	0	3 (13%)	5 (21%)	3 (13%)	5 (21%)	6 (13%)	10 (21%)

[Table. SES-CD ≥ 50% decrease from baseline at week 14 by paired and unpaired (CRM) endoscopic read models.]

Conclusion: Based on data generated by experienced central readers in a small subset of patients, both paired and unpaired central reading of CD endoscopic videos resulted in very low placebo response rates. However, unpaired central reading resulted in increased treatment response rates compared to a paired read paradigm.

References: 1. Van Assche G, et al. J Crohns Colitis 2010;4(1):7-27. 2. Lichtenstein GR, et al.Am J Gastroenterol 2018;113(4):481-517. 3. Reinisch W et al. Presented at 13th Congress of ECCO; Feb 14-17, 2018; Vienna, Austria. P132.

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P1077 STATUS OF SERUM VITAMIN B$_{12}$ IN PATIENTS WITH CROHN'S DISEASE

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Introduction: Vitamin B12 is an essential vitamin for hematopoiesis. Its absorption mainly occurs at the terminal ileum.Crohn's disease (CD) primarily involves the intestinal tract and can affect vitamin absorption. This study was designed to assess the prevalence of vitamin B$_{12}$ deficiency in patients with CD, and to identify the risk factors associated with abnormal serum vitamin B$_{12}$ levels.

Aims & Methods: Aim of the work: Evaluate plasma vitamin B12 level in patients with Crohn's and identify risk factors for any vitamin B12 deficiency. It was a descriptive and cross-sectional study successively enrolling over a period of 3 months (from May 2015 to November 2015) all patients with Crohn's disease. Standard blood tests together with determination of serum vitamin B12 concentration were performed at baseline.

Results: In multivariate analysis, a terminal ileum resection segment length >50 cm and both penetrating and stricturing behavior were the independent predictive factor for vitamin B12 deficiency in these patients. Eighty-eight patients were included with a median age of 42.45 ± 13.81 years and a sex ratio of 0.87. Crohn's disease was located at the ileum in 30% of patients, the ileum and right colon in 40% of cases. CD was inflammatory in 41% of cases,stenosing in 35% of casees, penetrating in 6% of cases and both stenosing and penetrating in 18% of cases.Fourty nine percent of patients were treated by azathioprin, 7% by anti TNF α and 13% by combotherapy.

The rate of intestinal resection was 42%. Ileal resection was noted in 37% of cases with an average resection length of 35.73 ±20.79 cm [4-115 cm]. Nine patients had an extended resection (>50 cm). Vitamin B12 levels were normal (≥ 200 ng/L) in 69 patients (78%) and decreased (< 200 ng/l) in 19 patients (22%). Clinically, no patient with vitamin B12 deficiency showed clinical signs of vitamin B12 deficiency.

In univariate analysis, a resection segment length >50 cm (p=0.012 ; HR=9.06 ;95% CI [1.62-50.60]) and both penetrating and stricturig behavior (p=0.002 , HR= 7.59 ; 95% CI [2.15-26.79]) were significantly associated with vitamin B12 deficiency. However, vitamin B12 deficiency was inversely associated with the inflammatory behavior (p=0.002, HR=0.12, 95% CI [0.026-0.056]) and the history of corticosteroid therapy (p=0.004 , HR=0.32 ;95% CI [0,10-1,00]).

Conclusion: Vitamin B12 deficiency in Crohn's disease patients is quite common (22%). Only a terminal ileum resection segment length over 50 cm and both penetrating and stricturing behavior predispose to vitamin B12 deficiency. Annual monitoring of serum vitamin B12 or preferably holotranscobalamin II in these patients will detect deficient patients, which should be supplemented with vitamin B12.

Disclosure: Nothing to disclose

P1078 THE ROLE OF SMALL BOWEL CAPSULE ENDOSCOPY IN DIAGNOSIS AND MONITORING OF CROHN'S DISEASES VERSUS RADIOLOGICAL INVESTIGATIONS: A DISTRICT HOSPITAL EXPERIENCE

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Introduction: A single gold standard for the diagnosis of CD is not available. In clinical practice, It is diagnosed by clinical evaluation and a combination of endoscopic, histological, radiological and biochemical investigations. Studies have explored the role of small bowel capsule endoscopy (SBCE) in diagnosing Crohn's disease, . We collected the data retrospectively of patients at Royal Wolverhampton NHS Trust to analyze local data of Crohn's patients and the sensitivity of SBCE versus radiology to diagnose small bowel Crohn's.

Aims & Methods: We carried this study retrospectively based on data over 3 years period (2014-2017) of patients enrolled at The Royal Wolverhampton NHS Trust. Retrospective data was collected from SBCE data base, which included 90 cases. Cases were identified further who had been diagnosed with small bowel Crohn's disease either based on the results, or who had capsule for prognostic values/monitoring of established Crohn's disease. Further stratification gave us cohort of 90 patients who had both SBCE and some form of radiological investigation done for same symptoms, namely: Computed tomography (CT) Scan, CT Enterography (CTE), CT Colonography (CTC), Magnetic Resonance Enterography (MRE). Data was tabulated, and analysis was done using SPSS v20.

Results: Total 59 patients were included in the study. 38 (64.4%) were female and 21 (35.6%) were males. Age range was from 18 to 79 years with a median age of 45 years. 36 (61%) were diagnosed as new diagnosis of Crohn's disease while 23 (39%) had established diagnosis but underwent investigations based of ongoing symptoms. Except for 4 patients, rest had colonoscopy as initial investigations. Out of these 4, two were diagnosed many years ago and report couldn't be chased, while other two had new diagnosis of Crohn's, but refused colonoscopy. Frequency of radiological investigations done was follows; CT 15 (25.4%), CTC 5 (8.5%), CTE 2 (3.4%), MRE 37 (62.7%). Decision about different investigations was dictated by urgency of situation. CTC was done as initial test in patients who described mainly large bowel symptoms. Out of 59 patients, 17 (28.8%) had evidence of small bowel inflammation on both SBCE and radiology. In 2 (3.4%), diagnosis of Crohn's was made on radiology while SBCE was non-diagnostic (1 established Crohn's patient, 1 new diagnosis of Crohn's). In 40 (67.8%) patients, SBCE was diagnostic while radiology was non-diagnostic. SBCE had sensitivity of 96.61% while radiology had sensitivity of 32.20% in our study population.

Conclusion: SBCE and radiology are complementary methods for diagnosing small bowel Crohn's disease. In our study, SBCE has shown better sensitivity in diagnosing small bowel Crohn's disease as compared to radiology.

References: 1. Gomollón F, Dignass A, Annese V, Tilg H, Van Assche G, Lindsay JO, Peyrin-Biroulet L, Cullen GJ, Daperno M, Kucharzik T, Rieder F. 3rd European evidence-based consensus on the diagnosis and management of Crohn's disease 2016: part 1: diagnosis and medical management. Journal of Crohn's and Colitis. 2016 Sep 22;11(1):3-25. 2. Albert JG, Martiny F, Krummenerl A, Stock K, Lesske J, Göbel CM, Lotterer E, Nietsch HH, Behrmann C, Fleig WE. Diagnosis of small bowel Crohn's disease: a prospective comparison of capsule endoscopy with magnetic resonance imaging and fluoroscopic enteroclysis. Gut. 2005 Dec 1;54(12):1721-7. 3. Dionisio PM, Gurudu SR, Leighton JA, et al. Capsule endoscopy has a significantly higher diagnostic yield in patients with suspected and established small-bowel Crohn's disease: a meta-analysis. Am J Gastroenterol 2010;105:1240-8; quiz 1249.

Disclosure: Nothing to disclose

P1079 SPECIALIST PHARMACIST LED IMMUNOMODULATOR SERVICE REVIEW - 1 YEAR OUTCOME IN A UK DISTRICT HOSPITAL

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Introduction: Immunomodulators are widely used to achieve and maintain remission for Inflammatory bowel disease (IBD) patients [1] however these medications require regular close monitoring in order to optimise patient care. With a constant stretch on NHS resources it can be challenging to have a robust system in place to facilitate this. The introduction of an IBD specialist pharmacist clinic has the potential to improve patient outcome and disease stability. This study aims to review the impact this clinic has had on a district general hospital following its initiation in 2017.

Aims & Methods: Data was retrieved from the pharmacy patient record for the immunomodulator clinic for 2017, exclusion criteria were those with autoimmune hepatitis. General demographics including age and gender, number of referrals, cause of referrals, wait time, drug treatment, number of phone calls and patient outcomes at one year were all recorded. The 1 year outcomes were divided into four categories: stable/shared care with the general practitioner, escalation of therapy, de-escalation or discontinuation (this category comprised of adverse medications side-effects, patient movement out of area and dis-engagement from NHS services).

Results: For the year 2017, 68 referrals were made to the immunomodulator clinic. 40 (59%) had Crohns disease, 22 (32%) had Ulcerative Colitis (UC) and 6 (9%) had IBD-unspecified. Mean waiting time from point of referral was 26.1 days. Patients who needed escalated therapy had associated longer mean wait time of 30.29 days. Those with stable or de-escalated disease at one year had a mean wait time of 21.9 days.

The most common drug was azathioprine 48 patients (70.5%) of which 4 were also receiving combination therapy with allopurinol; Methotrexate 13 patients (19.2%) and mercaptopurine 7 (10.3%) of which 1 patient was also being treated with allopurinol.

At one year 30 patients achieved stabilisation of disease (35%), 9 needed escalation of treatment (13%), 6 had their treatment de-escalated (9%) and the remaining 23 were discontinued from the clinic (35%). Discontinuation was mainly due to side-effects (15/23 patients) or disengagement from NHS services (4 patients). All patients on combined therapy with allopurinol (5 patients) had stable disease at one year. The drug treatment with the lowest proportion of patients needing escalation of therapy was methotrexate with 7.7%, mercaptopurine required 14.2% to be escalated and azathioprine required 14.6%

On average 7.1 calls were made to patients in one year, ranging from 0-20 calls. Those who required escalation of therapy were called on average 3 times prior to escalation, de-escalated patients were called 5 times a year and those who had stable disease at one year needed on average 9.5 calls a year to achieve this. The small number of calls for escalation of therapy is felt to be due to the rapid escalation of management compared to the traditional clinic model.

Conclusion: The pharmacy immunomodulator clinic provides a robust and essential service to manage IBD patients who may otherwise deteriorate as well as providing a database for means of auditing. Being seen sooner in the clinic is associated with better outcomes in this study - illustrated by a higher rate of de-escalated and stabilised patients, however was not statistically significant (p value 0.55). Stability of patients is also associated with more phone calls per year to fine tune management, again reflecting the impact of a dedicated immunomodulator service on patient outcomes. Larger studies and multi-centre sites would help in sharing experiences.

References: 1 National Institute for Health and Care Excellence, Crohn's disease: management,CG152 London: National Institute for Health and Clinical Excellence;2012

Disclosure: Nothing to disclose

P1080 BENEFITS OF IMPLEMENTING A RAPID ACCESS CLINIC IN A HIGH VOLUME INFLAMMATORY BOWEL DISEASE CENTER: ACCESS, RESOURCE UTILIZATION AND OUTCOMES

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Introduction: Emergency situations in inflammatory bowel diseases (IBD) put significant burden on both the patient and healthcare system. Emergency department (ED) attendance is high among IBD patients.
Aims & Methods: We aimed to prospectively measure indicators of Quality-of-Care after the implementation of a new 'rapid access clinic' service (RAC) at the McGill University Health Centre (MUHC) tertiary care IBD center. Furthermore, to compare the resource utilization, outcomes and costs, in patients presenting via the RAC to that of the MUHC Emergency Department IBD related visits. The RAC provides patients opportunity to receive urgent evaluation by an IBD specialists, thus potentially avoiding the ED visit. The RAC service was structured by providing an emergency contactinformation to the patients, with a specific document explaining the pertinent symptoms that merit utilization of this access avenue. Each email/telephone contact was reviewed by a specialized IBD nurse or physician. Patient access, diagnostic procedures, resource utilization and outcome parameters were collected consecutive patients who contacted the RAC service between July 2017 and March 2019. For the comparative analysis data was retrieved from ED visits by patients not having access to RAC services between January 2018 and January 2019.
Results: 488 patients (41.3% men, mean age: 39 years, CD: 68.4% / UC: 31.6%) with valid medical reason for contacting the RAC clinic and 135 patients (60.7% men, mean age: 45 years, CD: 71.1% / UC: 28.9%) accessing the ED were included. 85.8% of the requests were deemed appropriate for a rapid appointment at the IBD clinic. The reason for RAC appointment was potential disease flare in 71.6% of patients. The median time to RAC visit with MD was 2 days (IQR: 0-6 days) following the first contact. Patients had a fast-track evaluation with objective laboratory (CRP (90.9%) and fecal calprotectin (73%)) and clinical assessment. Endoscopy and imaging was only performed in 17.9%, 6.7% (colonoscopy and flexible sigmoidoscopy) and 6%, 2.1% (CT and MRI). Clostridium difficile stool test and stool culture test were performed in 43.1% and 41.9. Medical therapy was changed in 54.4% of patients. ED visits within 30 days following RAC occurred in 8.8% of all patients (unplanned ED visit rate: 5.9%). Diagnostic procedures and overall resource utilization at ED visit was substantially different from the RAC visits: abdominal CT was performed in 65.7%, multiple specialists consults (gastroenterology, surgery, internal medicine). Average medical cost estimates per patient was 403.3 CAD vs 1885.5 CAD, with 64.4% of patients at ED requiring at least one day hospital admission.
Conclusion: Implementation of an IBD RAC improved patient care by facilitating easier access to IBD specific medical care as well as by avoiding unnecessary ED visits. Patients underwent fast-track evaluation with optimized utilization of diagnostic tests and lower costs compared to ED visits.
Disclosure: Nothing to disclose

P1081 ARE RANDOM BIOPSIES STILL REQUIRED DURING IBD SURVEILLANCE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Patients with colonic IBD have an increased risk for developing colorectal cancer and surveillance is recommended. There is still debate on the role of random biopsies. Studies using newer generation endoscopes and dye based chromoendoscopy have suggested that most dysplasia is endoscopically visible. A recent retrospective study found that 1 in 8 patients with dysplasia were detected by random biopsies alone(1) and a meta-analysis has shown an increased risk for developing advanced neoplasia in patients with endoscopically invisible dysplasia (2). Random biopsies however are felt to be laborious, time consuming with poor yield

and targeted biopsies alone has been advocated. The aim for this systematic review/meta-analysis was to determine what proportion of patients with dysplasia are identified by random biopsy alone and to identify if specific advanced endoscopic technologies used or the cohort's risk has an effect on this rate.
Aims & Methods: Following PRISMA guidelines, we conducted a literature search using the electronic databases MEDLINE/EMBASE. Two independent reviewers screened citations and extracted data. Data analysis was performed with STATA13. Random-effects model was used to calculate pooled proportions with 95%CI. The primary outcome was the overall pooled proportion of patients with dysplasia who were identified by random biopsy only. A subgroup analysis was performed with studies pooled according to the different endoscopic technologies used (standard definition white-light (SDWL), standard definition chromoendoscopy (SDCE), high definition white-light (HDWL), high definition chromoendoscopy (HDCE), virtual chromoendoscopy (VCE), autoflourescence and full-spectrum endoscopy) and according to the risk of cancer in the populations enrolled in the studies (high-risk defined as having either included only patients with extensive colitis, or >9% of the cohort having PSC or >20% of the cohort previously having colonic dysplasia). Heterogeneity was assessed using I^2statstic.
Results: 36 studies met our inclusion criteria. 14 RCTs, 14 prospective and 8 retrospective studies. 13.05% (95%CI 7.28-19.87%) of patients with dysplasia were identified by random biopsies alone; I^2=81.2% (p< 0.001). Subgroup analysis showed HDCE having one of the smallest proportion of patients with random biopsy only dysplasia at 4.94% (95%CI 0.00-16.10%) ($I^2$55.9% (p=0.03)) whilst SDWL had the highest pooled proportion for patients with random biopsy alone dysplasia, 20.39% (95%CI 10.70-31.79%) (I^2 =80% (p< 0.001)). The pooled proportion of patients with dysplasia identified by random biopsy alone within the high-risk group was more than double, 14.19% (95%CI 7.43-22.29%) (I^2=81% (p=< 0.001)), when compared with that of the low-risk group, 6.42 (95%CI 0.04-18.45%) (I^2=79% (p=< 0.001)).
Conclusion: This is the first meta-analysis looking at factors associated with the rate of detecting endoscopically invisible dysplasia. There was marked heterogeneity and overlapping confidence intervals reflecting the varied nature of included studies and risk groups enrolled. HDCE was associated with the least rates of endoscopically invisible dysplasia among all subgroups with at least 2 or more studies included. Random biopsies may still be required when surveillance is performed in high-risk populations. We propose that future prospective studies should undertake targeted and random biopsies along with capturing established risk factors for each individual. This will provide more robust evidence when attempting to define a subpopulation more likely to be harbouring endoscopically invisible dysplasia.
References:) Moussata D, Allez M, Cazals-Hatem D, Treton X, Laharie D, Reimund JM, et al. Are random biopsies still useful for the detection of neoplasia in patients with IBD undergoing surveillance colonoscopy with chromoendoscopy? Gut. 2018;67(4):616-24. 2) Fumery M, Dulai PS, Gupta S, Prokop LJ, Ramamoorthy S, Sandborn WJ, et al. Incidence, Risk Factors, and Outcomes of Colorectal Cancer in Patients With Ulcerative Colitis With Low-Grade Dysplasia: A Systematic Review and Meta-analysis. Clin Gastroenterol Hepatol. 2017;15(5):665-74 e5.
Disclosure: Nothing to disclose

P1082 FECAL CALPROTECTIN (FCAL) IN IBD: AN USEFUL AND NON INVASIVE PREDICTOR OF MUCOSAL HEALING AND CLINICAL RELAPSE

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Introduction: FCal emerged as useful tool for IBD management, but different assay methods, cut-offs, scenarios, patient phenotypes and populations may influence the clinical usefulness.
Aims & Methods: Two substudies were designed for for the IBD population from a Latin-American center:
1) To investigate the value of FCal in mucosal healing (MH) prediction (optimal cut-off, specificity, sensitivity, VPP, VPN) and thresholds for clinical activity and phenotypes,

2) To evaluate the ability of FCal monitoring in IBD in remission to predict relapse.

FCal was determined with Bühlmann fCAL®ELISA.

Substudy-1 (MH prediction and activity/pattern of IBD): Included 100 IBD pts: (44 UC 56 CD), who underwent routine colonoscopy (VCC) with categorization by IBSEN score (Frøslie KF, Gastroenterol 2007) "MH"(scores 0-1) and "non-MH", colleting FCal samples within previous week. Optimal FCal cut-off for "MH"prediction (opt-MH cut-off) was calculated (ROC analysis). Substudy-2 (Prediction of relapse): included 50 UC and 50 CD in clinical remission (≥3 monts), FCal: basal, ≥biannual, VCC basal/final. Analysis: Kaplan Meier survival analysis for FCal levels above and below opt-MH cut-off. Mean follow-up 23.0±11.8 monts. Global definitions of clinical activity: Partial Mayo (UC), HBI (CD), Location/Extent (Montreal).

Results:

Substudy-1: FCal levels (Mean±SD) in pts. with "MH" (25 UC, 30 CD) were significant lower vs. "Non-MH": UC (191.3±174.6 vs. 621.1±368.3, p=0.0001) and CD (237.0±196.9 vs. 618.5±319,3 p< 0.0001) Kruskal-Wallis. Opt-MH cut-off was 242µg/g, AUC 0.84 (95% CI 0.753-0.906)p=0.0001, sensitivity: 76.4%, specificity: 84.5%, PPV: 85.7%, NPV: 74.5%. By clinical criteria FCal was lower (p< 0.0001) in remission vs activity in UC (165.7±14.1 vs. 630.3±349.6) and CD (276.4±250.1 vs. 662.1±289.9), but FCal cut-off was higher (284 µg/g) than opt-MH cut-off. In endoscopically active CD pts, FCal levels in colonic CD were higher 851.9±232.0 vs. other locations 544.4±313.3 (p=0.04).

Substudy-2: Cumulative probabilities of clinical relapse at 6, 12, 18, 24 monts of pts. with FCal>242 µg/g (n 34) were 20.6%, 38.2%, 44.7%, 51.6%, and with FCal≥cut-off (n 66) rates were 1.5%, 3.1%, 5.1% and 7.9% respectively, HR: 14.22 (95% CI 6.18 to 32.72), p< 0.0001, sensitivity: 85%, specificity 82.7%, VPP: 67.7%, VPN: 93.9%. Globally, relapsed 15 (30%) of UC and 12 (24%) of CD (NS). Clinical relapses with FCal>242 were 67.7% vs. 6.1% (≤ than cut-off), endoscopic relapses (available in 91 pts.) with FCal >242: 75% vs. 6.8% (≤ than cut-off), both p< 0.00001

Conclusion:

1) Fcal was a good predictor of MH in UC and CD according opt-MH cut-off (242 µg/g), Sensitivity: 76.4%, Specificity: 84.5%, PPV: 85.7%, PNV: 74.5%.

2) FCal values were significantly lower in remission vs. activity, in UC and CD, but in endoscopically active colonic CD, FCal was higher vs. other locations,

3) FCal showed to be an effective tool to predict relapse for levels above opt-MH cut-off.

Disclosure: Nothing to disclose

P1083 ANXIOUS, DEPRESSED, PHYSICIAN-CRITICAL BUT LOTS OF COMPLAINTS – PERSONALITY CHARACTERISTICS OF CAM USERS IN PATIENTS WITH IBD

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Introduction: Many patients ask to combine complementary and alternative medicine (CAM) with guideline-based state of the art therapy in inflammatory bowel disease (IBD). In line with this, the new German S3 Guideline for the treatment of Ulcerative Colitis (UC) published in 2018 gives an update of how to use or not to use CAM in UC. In our study, we investigated the use of CAM in a cohort of IBD patients and various personality characteristics of patients to describe differences between CAM-users and non-users.

Aims & Methods: 291 German IBD patients filled in an anonymous questionnaire including 88 questions on the underlying IBD itself, on disease activity (HBI in CD and pMS in UC), QoL (SIBDQ), on CAM and CAMs used. Psychological tests (Hospital Anxiety and Depression Scale (HADS), State-Trait-Anxiety Inventory (STAI), Social Support Questionnaire (F-SozU), Complaints-list (BL-R'), NEO-Five-Factor Inventory (NEO-FFI)) were used to record differences in personal attributes between CAM-users and non-users.

Results: 138 (47.2%) male and 151 (52.8%) female patients, 183 (62.9%) with Crohn's Disease (CD) and 108 (37.1%) with UC completed the questionnaires. HBI in CD was 5.4 (± 4.6) and pMS was 2.29 (±2.4) in UC. 127 (43.6%) patients admitted intended use of CAM in the past or the present. Phytotherapies (117(92.1%)) were most frequently used, followed by probiotics (82(68.3%)), relaxation techniques (76(64.4%)) and homeopathy (59(52.2%)). We were able to identify significant differences between CAM

users and non-users with regard to depression and anxiety levels, number of complaints, patient type and personality. CAM users have significantly higher values on the depression scale (HADS, p=0.027), more disease complaints (p=0.040) and more often very severe anxiety symptoms (p=0.009). CAM users personality is characterized by higher values in openness to experiences (p=0.011), tolerance (p=0.037) and conscientiousness (p=0.038) according to NEO-FFI. In addition, CAM users reported significantly higher rates of a physician-critical patient type (p< 0.001). We could not detect any significant differences between CAM users and CAM non-users in quality of life, values of STAI anxiety scales, social support, and personality traits extraversion and neuroticism according to NEO-FFI.

Conclusion: German IBD patients widely use CAM. CAM is mainly used by patients who have higher levels of depression, more disease complaints and very severe anxiety symptoms. Since CAM users are primarily physician-critical patient types, attending IBD physicians should identify and approach such patients as early as possible, ask them about the use of CAM, and provide them with their best advice on CAM. By incorporating evidence-based CAM into conventional therapies, physicians could probably benefit from a better collaboration with physician-critical patient types.

Disclosure: Nothing to disclose

P1084 WHICH ULTRASOUND CHANGE OCCURS MOST QUICKLY IN RESPONSE TO TREATMENT IN CROHN'S DISEASE: REDUCTION IN BOWEL WALL THICKNESS OR MURAL PERFUSION?

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Introduction: Objective markers of disease activity are of paramount importance for evaluation of treatment response in Crohn's disease. Intestinal Ultrasonography (IUS) is long acknowledged for this indication, with recognized limitations, and Contrast Enhanced IUS (CEUS) shows promising results in showing blood flow response. However, the optimal timing for reduction in mural perfusion is as yet unknown.

Aims & Methods: We aim to investigate reduction in wall thickness and mural perfusion in inflamed bowel treated with Corticosteroids, Biologics or a combination of both. This observational study includes patients with known CD experiencing a flare with the need of medical treatment escalation or initiation. Patients were examined with CEUS if greyscale IUS showed bowel wall thickness (BWT) > 3 mm, as part of standard of care. Follow-up varied with treatment choice: at week (W) 1 and W4 for steroids, W4 and W12 for biologics and W1, W4 and W12 for combination, using W1 as baseline for start of biologics. CEUS was performed using the microbubble contrast agent, perflutren lipid microspheres, 0.3 ml followed by saline flush. The US machine and all parameters were constant during and between scans. Time intensity curve analysis was performed and Peak enhancement (PE), area under the curve (AUC) and Wash-in Slope (WiS) were analyzed. Blood samples and fecal calprotectin were collected at baseline, W4 and W12 for the steroid group, and baseline and W12 for the biologic group. As part of standard of care, most patients underwent endoscopy at baseline and at follow-up after W12. W12 Response to treatment was evaluated with combination endoscopy (SES-CD < 3 OR reduction from baseline > 50 % OR Rutgeerts i0-i1) and laboratory markers (CRP < 8 AND Calpro < 250).

Results: 46 treatment patients include steroids n=14, biologics n=25, and combination n=7. Mean age 35.1 years [range 19.7-77.1], 45.7 % females, BMI 25.1 [16.9-51.3]. No difference between groups although a trend to larger BWT with increasing treatment intensification 7.3 mm [3.5-11.0], 8.3 mm [4.0-13.5] and 9.8 mm [7.0-12.0] respectively, p = 0.14. Responders experienced a greater reduction in BWT after 4W of any treatment -2.2 mm (95% CI -3.1 to -1.4) vs. non-responders -0.9 mm (-1.8 to 0.1) respectively, p=0.049. Moreover 6 patients (13 %) achieved transmural healing (BWT ≤ 3 mm) within W4. Also patients responding to biologics alone reduced BWT by -2.2 mm (-3.2 to -1.3) vs. non-responders -0.3 mm (-2.1 to 1.4) at W12, p=0.037. CEUS analyzes showed a trend towards response at W4 for steroid responders, however only for diminishment of WiS -7.00 dB/s (-11.5

to -2.5) vs. -4.00 dB/s (-4.5 to -3.5), p=0.09. Same trend towards response was found in the biological group at W4 -3.3 dB/s (-5.3 to -1.4) vs. 0.4 dB/s (-5.5 to 6.3) for non-responders, p=0.09. At W12 all three parameters were significantly different for responders vs non-responders, WiS p=0.011, PE p=0.026, AUC p=0.029.

Conclusion: At 4 weeks, IUS can already show reduction in bowel wall thickness, and for some even transmural healing, predicting week 12 responders to steroid and/or biological therapy. CEUS shows significant perfusion reduction at 3 months confirming endoscopic and/or biochemical response in those with successful biologic therapy. Our study did not achieve enough power to show reduction in perfusion already after 4 weeks.

Disclosure: Lantheus Medical Imaging: contrast agent support

P1085 INTRINSIC BRAIN ABNORMALITIES IN UC PATIENTS AND EFFECT OF ANXIETY AND DEPRESSION

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Introduction: We have discovered that patients who suffered from ulcerative colitis (UC) may also accompany with anxiety and depression, which affect the quality life. According to previous researches, anxiety and depression are usually along with brain functional changes. In order to observe the relationship between brain functional changes and anxiety, depression especially in UC patients, a functional magnetic resonance imaging (f-MRI) technology was applied to conduct the study. The purpose of this study was to investigate the spontaneous brain activities and influence factors in UC patients compared with healthy people.

Aims & Methods: 27 patients diagnosed as UC were recruited from jinling hospital, 17 of them and 17 matched healthy controls with similar gander, age and years of education were underwent a functional magnetic resonance imaging (f-MRI) 3.0T scan. Regional homogeneity (ReHo) was used to measure the synchronism of regional brain activities. T test, Chi-square test, pearson correlation were used to analyse the data.

Results: On one hand, a significant decreased ReHo values in Parietal_Inf_L (except supramarginal gyrus and angular convolution) and Parietal_Sup_L were found in UC patients compared with healthy controls. Moreover, there were significant negative correlations between ReHo values and SAS scores (Pearson correlation, p=0.019, < 0.05, r=-0.3997), however no statistical significance was found between ReHo values and SDS scores (Pearson correlation, p=0.086, >0.05). On the other hand, there is statistical significance in SAS (42.72±12.543) and SDS (38.75 (33.75-53.13)) scores between UC patients and healthy controls.

Moreover, years of education revealed statistical significance in SAS scores (c2=9.047, p=0.009< 0.05) between UC patients and healthy controls. No statistical significance was found in SDS scores between several factors in UC patients and healthy people.

Conclusion: Abnormal brain functional changes exist in UC patients and they are more likely to be anxious and depressed than healthy people. These findings provide evidence that the disorder in brain-gut axis (BGA) may exist in UC patients.

Disclosure: Nothing to disclose

P1086 THE CORRELATION BETWEEN CHEST X-RAY AND CHEST CT FOR THE DETECTION OF LATENT TUBERCULOSIS DURING INFLAMMATORY BOWEL DISEASE

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Introduction: Over the last decade, Anti-Tumor Necrosis Factor (anti-TNF) agents have shown great effectiveness in the treatment of inflammatory bowel disease (IBD). Nevertheless, their use exposes the patient to an increased risk of opportunistic infections, particularly tuberculosis. For this reason, the pre-therapeutic check-up is important in order to detect latent tuberculosis.

Aims & Methods: The aim of our study was to evaluate the correlation between chest X-ray and chest CT for detection infection.

This is a descriptive retrospective study done in the Hepato-Gastroenterology unit of our university hospital, over a period of 4 years from September 2015 to December 2018 and collected all patients with IBD requiring an anti-TNF treatment. All patients had chest x-rays and chest CT scans.

Results: Sixty-seven patients were included in our study. The average age of our patients was 35.37 years. There were 22 women (32.85%) and 45 men (67.15%) with a sex ratio M/F: 2. 86. 56% of patients were followed for Crohn's disease, 11.9% for Ulcerative Colitis and 1.49% for indeterminate colitis. Respiratory symptoms were found in only 3 patients (4.47%). Chest X-ray revealed lesions in favour of latent tuberculosis in 2.9% of cases (n=2), including interstitial syndrome. Thoracic CT scan revealed lesions in favour of tuberculosis in 13.43% of cases (n=9), including micronodules in 55.55% of cases and a focal of alveolar condensation in 44.44% of cases. The Quantiferon assay was also performed in patients with positive CT; it was positive in 88.88% of cases (n=8). The diagnosis of pulmonary tuberculosis was confirmed in 9 patients. The correlation between chest CT and chest radiography was calculated using the Pearson score which showed a low correlation (r=0.048). In addition, the correlation between thoracic CT and Quantiferon, calculated using the Pearson score, was higher with a statistically significant p (p< 0.001).

Conclusion: In our series of sixty-seven patients candidate for an anti-TNF treatment, the correlation between chest X-ray and chest CT for the detection of latent tuberculosis during inflammatory bowel disease was very low (r=0.048). CT Scan should be concurred reference diagnostic tool to detect attaint tuberculosis. However, the correlation between chest CT and Quantiferon must be well studied with a larger sample.

Disclosure: Nothing to disclose

P1087 USING MAGNETIC RESONANCE ENTEROGRAPHY GLOBAL SCORES (MEGS) TO ASSESS RESPONSE TO USTEKINUMAB IN CROHN'S DISEASE

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Introduction: Magnetic resonance enterography (MRE) is a key modality in diagnosing and monitoring Crohn's disease (CD). MEGS, a quantitative MRI index of inflammatory burden in CD, has been previously validated against Harvey Bradshaw Index (HBI), C-reactive protein (CRP) and faecal calprotectin (FC)[1]. It has also been shown to reflect clinical response to anti-TNF therapy and clinical classification of disease activity[2].

Aims & Methods: To evaluate the utility of MEGS in assessing radiological response to ustekinumab, a monoclonal antibody targeting IL12/23. Patients established on ustekinumab, with a baseline and follow up MRE (at least three months after ustekinumab induction), were retrospectively reviewed. Clinical data, including HBI, CRP and FC, were collected to establish disease activity at baseline and at the first follow up MRE. Two consultant gastrointestinal radiologists, without clinical data, analysed images to calculate MEGS. Statistical analysis was performed using GraphPad Prism version 8.0.

Results: Sixteen patients (median age 37, 50% male) with moderate to severe CD at baseline, according to a Physician Global Assessment (PGA), were identified. Median time to first follow up MRE was 10 months (range 5-18). 3/16 were responders according to PGA, and although MEGS decreased in each case (44, 16.3 and 8.5 to 38, 15.5 and 5.5 respectively), this did not reach statistical significance. 13/16 were non-responders and pre-induction median MEGS increased (21 (range 2-79.5) vs. 26 (5.5-85.5), p< 0.002), reflecting increasing symptom burden and biochemical parameters despite therapy. The overall interobserver agreement between reporting radiologists was good with a mean difference between the two observers' MEGS of -3.95 (Bland Altman Limit of Detection (-16.48 to 8.57)).

Conclusion: Quantitative MRI scores for Crohn's disease activity are increasingly being used in clinical practice, and our study demonstrates good interobserver agreement. Whilst our data is suggestive of a correlation between change in MEGS and PGA in this complex, prior biologic refractory patient population, larger protocolised studies are needed.

References: 1. Makanyanga JC, Pendsé D, Dikaios N, Bloom S, McCartney S, Helbren E, et al. Evaluation of Crohn's disease activity: initial validation of a magnetic resonance enterography global score (MEGS) against faecal

calprotectin. Eur Radiol. 2014 Feb;24(2):277-87. 2. Prezzi D, Bhatnagar G, Vega R, Makanyanga J, Halligan S, Taylor SA. Monitoring Crohn's disease during anti-TNF-α therapy: validation of the magnetic resonance enterography global score (MEGS) against a combined clinical reference standard. Eur Radiol. 2016 Jul;26(7):2107-17.
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P1088 EVOLUTION OF ENDOSCOPIC LESIONS IN PATIENTS ADMITTED FOR ACUTE SEVERE ULCERATIVE COLITIS RESPONDING TO INFLIXIMAB OR CYCLOSPORINE: SUB-STUDY FROM THE CYSIF TRIAL

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Introduction: Endoscopic remission has become a major goal of treatment in patients with ulcerative colitis. Few endoscopic data are available in patients with steroid-refractory acute severe ulcerative colitis (ASUC) requiring a second-line medical therapy. The aim of the present study was to describe the evolution of endoscopic lesions in patients with ASUC responding to infliximab (IFX) or cyclosporine (Cys).
Aims & Methods: All patients enrolled into the CYSIF trial (1), that was an open-label comparison between IFX and Cys in patients admitted for a steroid-refractory ASUC, were eligible for inclusion in the present endoscopic sub-study. Only patients who achieved clinical remission at day 98 were included in this sub-study. Flexible sigmoidoscopies were planned during the study at baseline, day 7, 42 and 98. They were locally read and the presence of pre-specified endoscopic lesions was recorded per segment. Mayo endoscopic subscore (MES) was reported; UCEIS and its components, vascular pattern (VP), bleeding (B) and ulceration/ erosion (U), were post-hoc calculated from endoscopic reports. Endoscopic remission (ER) was defined as MES or UCEIS at 0. Remission for each UCEIS component was defined by VP, B or U at 0. Remission rates were compared

between VP, B and U components in the whole cohort at each time-point through paired chi-square test. Using the same method, ER rates and remission of each UCEIS component were compared between rectum and sigmoid segments. ER rates and remission rates of each UCEIS component were compared between patients treated with IFX and those receiving Cys through chi-square test or Fisher exact test when necessary. According to the numerous tests performed, significance was achieved for a p-value less than 0.01.
Results: From the 115 patients included in the trial, 63 have been included in the present endoscopic sub-study (32 IFX and 31 Cys). Mean±SD of UCEIS and MES was respectively 7.0±1.2 and 3.0±0.2 at baseline, 5.3±1.7 and 2.9±0.5 at day 7, 2.3±2.1 and 1.6±1.2 at day 42 (n=62), 1.1±1.3 (n=58) and 0.9±1.0 (n-59) at day 98. When comparing to ER rates on VP at day 7 (3%), at day 42 (29%), at day 98 (50%) in the whole cohort, ER rates on B and on U were higher at day 7 (21% and 8%, p=0.001 and p=0.38), at day 42 (63%, p< 0.001 for both) and at day 98 (76% and 83%, p< 0.001 for both). There was no observed difference in ER rates between sigmoid and rectum whatever the assessment used. ER rate at day 98 was significantly higher in patients treated with IFX than in those treated with Cys (66% vs. 24%; p=0.002), whereas no difference was observed at baseline, day 7 or day 42. This observed difference at day 98 was related mainly to the VP component.
Conclusion: In this prospective cohort of steroid-refractory ASUC patients who achieved clinical remission at day 98, UCEIS endoscopic remission started with absence bleeding, followed by ulceration/erosion and then by restoration of the vascular pattern. Endoscopic remission was similar in rectum and sigmoid. IFX provided a significantly higher rate of endoscopic remission than Cys at day 98.
References: 1. Laharie D et al. Ciclosporin versus infliximab in patients with severe ulcerative colitis refractory to intravenous steroids: a parallel, open-label randomised controlled trial. Lancet 2012; 380:1909-15.
Disclosure: D Laharie declares conselling, boards, transports or fees from Abbvie, Biogaran, Biogen, Ferring, HAC-pharma, Janssen, MSD, Novartis, Pfizer, Prometheus, Roche, Takeda, Theradiag, Tillots

P1089 EARLY IMPROVEMENT AFTER INTRAVENOUS USTEKINUMAB INDUCTION IN PATIENTS WITH ULCERATIVE COLITIS: RESULTS FROM THE UNIFI INDUCTION TRIAL

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Introduction: The UNIFI induction study evaluated the efficacy and safety of ustekinumab (UST) in patients with moderately to severely active ulcerative colitis (UC) after a single intravenous infusion. In this analysis, we evaluated the rapidity of the onset of the treatment effect.
Aims & Methods: Eligible patients were randomly assigned to placebo (PBO) or UST 130 mg or ~6 mg/kg. Patients recorded stool frequency and categorized rectal bleeding daily for the 7 days before each visit. Partial Mayo scores were calculated at baseline and Week 2 using the average of the stool frequency and rectal bleeding scores from the most recent consecutive 3-day period before the visit and the physician's global assessment score recorded at the visit. C-reactive protein (CRP) and fecal biomarkers were measured at baseline and Day 14.
Results: At baseline, the mean 3-day average daily stool frequency was 7.0 in the PBO group, 6.9 in the UST 130-mg group, and 7.0 in the UST ~6-mg/kg group. Patients receiving UST showed greater reductions in the daily number of stools compared with PBO as soon as the first assessment time point at Day 7. Mean changes from baseline in daily stool frequency were -0.7 for PBO, -1.0 for UST 130-mg (p=0.098), and -1.2 for UST ~6-mg/kg group (p=0.018) by Day 7, respectively, and -0.9, -1.6 (p< 0.001), and -1.9 (p< 0.001) by Day 13, respectively. The percentage of patients with no blood in their stool at baseline and Day 14 were 13.5% and 26.0%, respectively, in the PBO group, 10.9% and 32.5% in the UST 130-mg group, and 12.1% and 37.3% in the UST ~6-mg/kg group. Patients receiving UST showed

significantly greater improvement from baseline to Day 14 in partial Mayo score and CRP (Table, p<0.001 for all comparisons of UST vs PBO). Differences between the UST and PBO treatment groups in mean changes from baseline to Day 14 in fecal calprotectin did not reach significance (PBO -33.96 mg/kg, UST 130 mg 79.12 mg/kg [p=0.875], UST ~6 mg/kg -412.68 mg/kg [p=0.152]). However, patients receiving UST showed significantly greater improvement in fecal calprotectin at Week 4 (mean changes from baseline: PBO -226.78 mg/kg, UST 130 mg -881.22 mg/kg [p=0.013], UST ~6 mg/kg -802.75 mg/kg [p< 0.001]). Similar results were observed for fecal lactoferrin.

Conclusion: The effect of UST began rapidly after induction, with symptomatic improvement and reduction of systemic inflammation seen as early as the first assessments at Days 7 and 14, respectively.

	PBO IV	UST IV 130 mg	UST IV ~6 mg/kg
Primary efficacy analysis set	319	320	322
Partial Mayo score, mean (SD)			
Baseline	6.2 (1.46)	6.2 (1.42)	6.2 (1.33)
Change from baseline to Week 2	-1.0 (1.63)	-1.5 (1.74)	-1.6 (1.69)
Nominal p-value		<0.001	<0.001
C-reactive protein, mean (SD) mg/L			
Baseline	9.8 (16.65)	9.6 (17.07)	12.1 (19.34)
Change from baseline to Week 2	-0.7 (16.20)	-4.1 (13.41)	-4.2 (12.53)
Nominal p-value		<0.001	<0.001

[Table: Partial Mayo scores and C-reactive protein levels at baseline and changes from baseline to Week 2]

P1090 PSORIASIS UNDER TNF-A INHIBITORS IN INFLAMMATORY BOWEL DISEASE PATIENTS: A 19-YEAR EXPERIENCE OF A TERTIARY CENTRE

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Introduction: Inflammatory bowel disease (IBD) and Psoriasis are chronic inflammatory conditions with an organotropic preference, where the influence of innate and adaptative immunity seems to play a crucial role. This shared pathologic process explains the use of similar therapeutic strategies like corticosteroids, immunomodulators and monoclonal antibodies. Psoriasis can be associated to IBD as an independent entity, as an extraintestinal manifestation of IBD, or even as a paradoxical event of anti-tumor necrosis factor (TNF) therapy. Their co-occurrence adds complexity to the challenge of patient management.

Aims & Methods: Our main goal was to review our experience of patients treated with TNFa inhibitors regarding the occurrence of dermatological lesions, namely, psoriasis. We retrospectively analyzed data regarding a cohort of patients with the diagnosis of IBD and submitted to anti-TNF therapy, from January 2000 until the end of January 2019. We included patients observed by the dermatology department due to suspicious lesions during treatment with anti-TNF therapy. Data was retrieved from clinical registries.

Results: 422 patients were analyzed. Suspicious dermatological lesions were found in 111 patients (24%) and a diagnosis of psoriasis was made in 34 (8%). The prevalence was higher in the females (26 vs 8). Among patients with Psoriasis, the predominant IBD type was CD (only 1 patient with UC). The majority of the former presented ileocolonic disease(46%), a non-stricturing non-penetrating behavior(49%) and were diagnosed between 16-40 years old(79%). Psoriatic lesions were found mainly in scalp(n=13), trunk(n=10) and palmoplantar regions(n=7). 35% of the patients were diagnosed while being treated with combined therapy with

immunosuppressive drugs (4 with methotrexate and 8 with azathioprine). 41% of patients were treated with two or more biologic drugs. The diagnosis of psoriasis preceded the use of anti-TNF therapy in 7 patients. 27 patients were on treatment with TNFa inhibitors at the time of psoriasis diagnosis. The mean time from anti-TNF exposure until development of psoriasis was 28 months with a mean follow up time of 7 years. Psoriatic lesions were controlled in 4 patients by switching infliximab to adalimumab. The discontinuation of anti-TNF therapy due to psoriasis occurred in 12% (n=4/34) of patients. 50% swapped to ustekinumab or vedolizumab with good skin disease control.

Conclusion: In our cohort there was an incidence of psoriasis in IBD patients treated with anti-TNF of 8%, resulting in alterations in the management of IBD therapy. The majority of our patients improved their skin condition with anti-TNF switch, despite lack of studies regarding this. The incidence of this lesions on IBD patients treated anti-TNF therapy(6-11%) is consistent with that found in other diseases like rheumatoid arthritis. Psoriatic lesions were more frequently identified in patients with CD than in UC patients, with gender being identified as a risk factor. The paradoxically occurrence of psoriatic skin lesions, is an emergent issue in the context of anti-TNF drugs use. Effective drugs on psoriasis and IBD, targeting different pathways than anti-TNF, are changing the reality allowing further control over both diseases. Nowadays a good control of intestinal and skin inflammation can be achieved without compromising the outcomes expected for each. A multidisciplinary approach is of utmost importance in managing IBD treatment and potential complications.

Disclosure: Nothing to disclose

P1091 CLINICAL EFFECTIVENESS OF FIRST-LINE ANTI-TNF THERAPIES AND SECOND-LINE ANTI-TNF THERAPY POST-VEDOLIZUMAB DISCONTINUATION IN PATIENTS WITH ULCERATIVE COLITIS OR CROHN'S DISEASE

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Introduction: Real-world data is needed to understand outcomes in patients with ulcerative colitis (UC) or Crohn's disease (CD) who discontinue first-line (1L; biologic-naive) vedolizumab (VDZ) treatment (Tx) and go on to receive subsequent anti-tumour necrosis factors (anti-TNF) Tx.

Aims & Methods: The objective was to compare the clinical effectiveness of second-line (2L) anti-TNF Tx post 1L VDZ and 1L anti-TNF use in patients with UC or CD. This was a real-world, multi-country, retrospective chart review study in adult (≥18 years old) UC and CD patients treated with 1L anti-TNF or 2L anti-TNF after discontinuation of 1L VDZ for any reason (received May 2014 to March 2018). Patients were included from sites across Canada, Greece and the United States. Anti-TNF therapies included: adalimumab, infliximab, golimumab and certolizumab pegol. The index date was defined as date of 1L Tx initiation. Clinical effectiveness data were collected from 1L or 2L Tx initiation to earliest of death, chart abstraction date or 6 months post-1L Tx discontinuation (Canada only). Cumulative rates of Tx persistence, clinical response, and clinical remission were estimated using the Kaplan-Meier method for UC and CD (separately and combined) over 6 months. Cumulative rates of clinical response and clinical remission were assessed using pre-defined hierarchical algorithms of standard disease measures as reported in the medical records. P-values were generated using the log-rank test.

Results: This analysis included 579 anti-TNF patients (1L: 497 [UC: 224; CD: 273]; 2L: 82 [UC: 58; CD: 24]) from 36 sites. The proportion of patients in each cohort were: adalimumab (1L: 41.4%; 2L:19.5%), infliximab (1L: 52.7%; 2L: 79.3%), golimumab (1L: 4.8%; 2L: 1.2%) and certolizumab pegol (1L: 0.8%; 2L: 0.0%). Mean (SD) age at index date: 1L, 39.6 (15.2); 2L, 49.4 (18.6) years, male: 1L, 49.9%; 2L, 61.0%, median (range: min-max) disease duration: 1L, 2.0 (< 0.1 - 49.0); 2L, 3.7 (0.1 - 54.0) years. At 6 months, cumulative rates of Tx persistence (1L: 83.9%; 2L: 83.6%), clinical

response (1L: 49.5%; 2L: 65.6%) and clinical remission (1L: 29.5%; 2L: 31.4%), were similar between 1L and 2L patients (Table 1). Results were similar when data were stratified by UC and CD, albeit sample sizes were small (Table 1).

Conclusion: Cumulative rates of Tx persistence, clinical response and clinical remission observed in the first 6 months of Tx were comparable between 1L anti-TNF patients and those who switched to a 2L anti-TNF following the discontinuation of 1L VDZ. This suggests that 1L VDZ may not impact the effectiveness of subsequent anti-TNF Tx in real-world clinical practice. As 2L sample size was limited, these hypothesis-generating data warrant further study.

	Overall		Ulcerative Colitis		Crohn's Disease	
Outcomes	First-Line N=497	Second-Line N=82	First-Line N=224	Second-Line N=58	First-Line N=273	Second-Line N=24
Treatment Persistence: 3 months, % [N at risk]	91.7 [451]	95.1 [64] P=0.45	87.4 [195]	94.3 [47] P=0.18	95.2 [256]	96.4 [17] P=0.81
Treatment Persistence: 6 months, % [N at risk]	83.9 [411]	83.6 [36] P=0.87	76.6 [170]	79.5 [26] P=0.50	90.0 [241]	92.2 [10] P=0.82
Clinical Response: 3 months, % [N at risk]	33.9 [269]	43.6 [23] P=0.25	38.4 [109]	44.8 [16] P=0.54	30.1 [160]	41.3 [7] P=0.52
Clinical Response: 6 months, % [N at risk]	49.5 [186]	65.6 [9] P=0.09	57.1 [61]	61.1 [6] P=0.58	43.5 [125]	74.8 [3] P=0.13
Clinical Remission: 3 months, % [N at risk]	17.5 [310]	22.6 [30] P=0.44	9.7 [136]	11.0 [24] P=0.92	22.9 [174]	49.2 [6]* P=0.02
Clinical Remission: 6 months, % [N at risk]	29.5 [240]	31.4 [13] P=0.56	19.6 [104]	14.7 [12] P=0.69	36.2 [136]	74.6 [1]* P<0.01

Cumulative data were generated from Kaplan-Meier analyses and p-values are from the log-rank test. *Significant difference (P<0.05) between first and second-line. N at risk: Number of patients still on treatment at timepoint and clinical outcome can still be assessed. Rates of clinical response and clinical remission were assessed using pre-defined hierarchical algorithms of: CD: Crohn's disease activity index → Harvey Bradshaw index→ medical record documentation of complete or partial response → Physician global assessment. UC: Mayo Overall Score → Mayo Partial score → medical record documentation of complete or partial response → Physician global assessment.

[Clinical Effectiveness of First-Line Anti-TNF and Second-Line Anti-TNF (Post-Vedolizumab) Therapies in Ulcerative Colitis and Crohn's Disease Patients]

P1092 SAFETY, TOLERABILITY, AND PHARMACOKINETICS OF PTG-200, AN ORAL GI-RESTRICTED PEPTIDE ANTAGONIST OF IL-23 RECEPTOR, IN NORMAL HEALTHY VOLUNTEERS

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Introduction: The regulatory approval of ustekinumab (targeting IL-12/IL-23 in Crohn's Disease) and clinical data for several anti-IL-23 monoclonal antibodies support targeting the IL-23 pathway for treatment of inflammatory bowel disease (IBD). PTG-200 (also known as JNJ-67864238) is an oral peptide, that acts locally in intestinal tissues to block IL-23 signaling by selectively binding the IL-23 receptor (IL-23R). *In vitro* studies confirmed PTG-200 is a potent, selective, and competitive IL-23R inhibitor. The GI-restricted nature of PTG-200 is demonstrated by marked drug concentrations in GI tissues and feces, and limited systemic blood exposure in animal models. PTG-200 therapeutic potential was established in a rat model of TNBS-induced colitis, where the threshold concentration of PTG-200 in colonic tissue and luminal feces for efficacy and pharmacodynamics was determined.

Aims & Methods: The objectives of this first-in-human (FIH) Phase 1 study were to assess safety, tolerability, and pharmacokinetics (PK) including food effect and fecal exposure of orally administered PTG-200. This FIH Phase 1 study was a single-center, randomized, double-blind, placebo-controlled trial comprising single ascending and 14-day multiple ascending dose (SAD and MAD) oral administration in 82 male normal human volunteers. Doses ranged from 150 mg to 900 mg once daily (QD, fasted or fed) or twice daily (BID, fed). Subjects were monitored for safety and tolerability. PK in plasma, urine and feces was evaluated, including plasma PK profile following a high-fat meal.

Results: Oral administration of PTG-200 was well-tolerated. There were no serious adverse events, dose-limiting toxicities, or clinically significant adverse events. PTG-200 plasma exposure was low (Table 1), below that expected to result in systemic biological activity. Following single-dose oral administration under fasted conditions, peak plasma concentration (Cmax) exhibited a dose-related increase with a median Tmax at 2.0 h. Administration of a high-fat meal prolonged the median Tmax to 4.0 h and had a modest effect on Cmax and estimated overall exposure. Repeat dosing led to dose-related increase in plasma exposure. Consistent with a terminal half-life of ~1.5 h in plasma, PTG-200 showed no evidence of accumulation except in the 900 mg BID group (2.75-fold). PTG-200 was detected in urine only at 900 mg BID. Fecal concentrations in several cohorts met or exceeded the targeted preclinical threshold concentration which was established using the rat TNBS-induced colitis model.

Cohort	Dose and Frequency	Feeding Status	Day	Cmax (ng/mL)	AUC0-last (ng*hr/mL)
4	150 mg, QD	Fed	Day 1	0.33 ± 0.26	0.89 ± 0.81
4	150 mg, QD	Fed	Day 14	0.39 ± 0.12	0.97 ± 0.57
5a	300 mg, QD	Fed	Day 1	0.61 ± 0.60	1.79 ± 1.23
5a	300 mg, QD	Fed	Day 14	0.56 ± 0.26	1.69 ± 0.81
5b	150 mg, BID	Fed	Day 1	0.23 ± 0.08	0.80 ± 0.30
5b	150 mg, BID	Fed	Day 14	0.23 ± 0.07	0.62 ± 0.25
6	900 mg, QD	Fed	Day 1	1.16 ±0.85	3.92 ± 3.00
6	900 mg, QD	Fed	Day 14	1.11 ±0.72	3.11 ± 1.59
7	900 mg, BID	Fed	Day 1	0.48 ±0.25	2.52 ± 1.92
7	900 mg, BID	Fed	Day 14	1.06 ±0.70	5.15 ± 3.09

[Table 1. Plasma PK (Cmax and AUC0-last) of PTG-200 in MAD. Cmax and AUC0-last are presented as mean ± standard deviation.]

Conclusion: Orally administered PTG-200 was well-tolerated in this FIH study. PK was consistent with the GI-restricted design of PTG-200. These safety and PK characteristics, combined with fulfillment of preclinical fecal drug threshold concentrations, support further clinical development of PTG-200 for the treatment of IBD. A Phase 2 study in patients with moderate-to-severe Crohn's disease has been planned.

Disclosure: Nothing to disclose

P1093 THE EFFECTS OF CANNABIS EXTRACTS ON INFLAMMATORY BOWEL DISEASE (IBD) EXPLANT BIOPSIES

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Introduction: Cannabis treatment improves chemical induced Colitis in mice as well as clinical disease burden in human measured by the Lichtiger score. The mechanism by which cannabis affected Disease score is unknown. In IBD the inflamed microenvironment damages the epithelial barrier. Following damage, a process of barrier restitution begins, which depends on epithelial cell proliferation.

Aims & Methods:
Aim: To analyze the effect of cannabis on cultured colon biopsies from IBD patients and on human colon epithelial cell line exposed to soluble IBD microenvironment.

Methods: Biopsies (3-5,~10mg/biopsy) were collected during endoscopy from inflamed and uninflamed colon areas of IBD patients, cultured for 5-6hr with medium, cannabis-extract (C2F,50/100µg/ml) or methanol (C2F-solvent) and analyzed using immunohistochemistry and manually cell count or QuPath digital software for:

1) Epithelial and stromal cell proliferation and apoptosis (Ki67 and cleaved-caspase-3 expression, respectively) 2) Epithelial-cell-number/crypt-diameter. The secretomes of the cultured biopsies were analyzed for MMP9/2 activity (impair epithelial permeability, by Zymogram test) or added to colon epithelial cells (CC841) for 48hr. Following culture CCD841 cells were analyzed for viability (by Alamar-blue), cell-number and death (automatic cell-counter and trypan blue) and PCNA expression (proliferation marker, western-blot).

Results: Cannabis extract increased epithelial cell proliferation in all biopsies (p< 0.05, 12-31%), seen in both digital and manual cell-count. In correspondence with this, cannabis (100µg/ml) increased the number of epithelial cells in crypt circumference in all biopsies (~ 32%, p< 0.05). Similarly, secretomes collected from C2F treated inflamed biopsies increased CCD841 proliferation (45%↑ cell-number and 41-380%↑ PCNA expression) compared to inflamed secretomes. Whereas, secretomes collected from untreated inflamed biopsies reduced CCD841 cell number (22%) and viability (16%) compared to secretomes of uninflamed areas (p< 0.05). Exposure of CCD841 directly to C2F (100µg/ml) reduced their viability (80%↓, p< 0.05). Cannabis extract also increased Ki-67 expression in the stromal cells of the inflammatory tissue (in 5/6 experiments), yet, had no effect on epithelial and stromal cell-apoptosis. While as the cannabis (50µg/ml) reduced MMP9/2 activity in the uninflamed secretomes in 4/5 patients, it increased the MMP9 level in the inflamed secretomes (5/6 patients).

Conclusion: Cannabis facilitates colon epithelial proliferation in ex-vivo and in-vitro human models and thus may facilitate mucosal healing. However, it had a complex and area dependent effect on the MMPs activity, reflecting the complexity of cannabis anti-inflammatory effect.

Disclosure: Nothing to disclose

P1094 ASSESSMENT OF BUDESONIDE MMX® EFFECTIVENESS FOR ACTIVE, MILD-TO-MODERATE ULCERATIVE COLITIS IN THE POLISH SUB-GROUP OF THE PROSPECTIVE MULTI-CENTER OBSERVATIONAL STUDY CORE PRACTICE

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Introduction: Budesonide MMX® is approved for induction of remission in mild-to-moderate active ulcerative colitis (UC) in adults, where 5-ASA is not sufficient. There is lack of data on its effectiveness and safety in clinical reality.

Aims & Methods: This was the Polish sub-group of multi-center prospective observational study CORE Practice. The proportion of patients with clinical benefit, clinical remission, symptoms resolution, endoscopic healing, endoscopic remission, fecal calprotectin normalization, change in quality of life, treatment satisfaction, change in economic parameters as well as tolerability, treated with Budesonide MMX® for mild-to-moderate UC in a real-life setting were evaluated. Patients were prescribed Budesonide MMX® 9mg in accordance with the terms of the SmPC, within a 5 days' time window before the enrolment. The primary endpoint was the clinical improvement of Budesonide MMX® defined as the percentage of patients achieving ≥3-point decrease in the UCDAI score at the end of induction treatment.

Results: The data from the Polish sub-group cohort of 181 patients with mild-to-moderate UC were analyzed. Clinical improvement ≥ 3-point in UCDAI at the end of treatment induction was achieved in 72,2% patients. Clinical remission defined as UCDAI clinical subscore ≤ 1-point was observed in 61,4% of patients at the end of induction treatment. Symptoms resolution at the end of treatment, defined as rectal bleeding = 0 and stool frequency ≤1 was observed in 72.2% patients. Full symptoms resolution (rectal bleeding = 0 and stool frequency = 0) at the end of the Budesonide

MMX® treatment was achieved in 52,3% of patients. The significant improvement of quality of life was observed according to the SIBD-Q (p <0.001), compared with baseline, achieving increase in mean SIBD-Q total score from 40 to 56 points. The highest treatment satisfaction level (VAS score 10) was observed in 40.2% of patients. One patient discontinued Budesonide MMX® due to an adverse event that was related to the study drug, what counts for less than 1% of patients.

Conclusion: The data from the Polish sub-group of the real-life study CORE Practice confirms the clinical efficacy of Budesonide MMX® 9 mg in the majority of patients with active mild to moderate UC. Budesonide MMX® was safe, well tolerated and showed benefitable effect on patient's quality of live.

Disclosure: G.Rydzewska has declared paid and unpaid consultancies and honoraria for lectures during last few years from Ferring; K. Paridaens - nothing to disclose, S.Danese - has served as a speaker, consultant and advisory board member for Schering-Plough, Abbott (AbbVie) Laboratories, Merck and Co, UCB Pharma, Ferring, Cellerix, Millenium Takeda, Nycomed, Pharmacosmos, Actelion, α Wasserman, Genentech, Grunenthal, Pfizer, Astra Zeneca, Novo Nordisk, Cosmo Pharmaceuticals, Vifor, and Johnson and Johnson.M. Jesionowski - nothing to disclose,

P1095 PERFUSE: A FRENCH PROSPECTIVE/RETROSPECTIVE NON-INTERVENTIONAL COHORT STUDY OF INFLIXIMAB-NAIVE AND TRANSITIONED PATIENTS RECEIVING INFLIXIMAB BIOSIMILAR SB2; 1ST INTERIM ANALYSIS

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Introduction: SB2 is approved in the EU as an infliximab (IFX) biosimilar, having demonstrated bioequivalence and similar efficacy, safety and immunogenicity as the reference. There is limited real-world evidence published on persistence or immunogenicity of SB2, either in IFX-naive patients or in those transitioning from originator or another IFX biosimilar. PERFUSE is an ongoing non-interventional study intending to enrol over 1,000 patients receiving SB2 as routine therapy.

Aims & Methods: To describe clinical characteristics, immunogenicity and treatment persistence over 12 months in patients initiating SB2 in routine clinical practice at 8 specialist gastroenterology sites across France.

Eligible adult patients have a diagnosis of Crohn's Disease (CD) or Ulcerative colitis (UC) and initiated SB2 in routine clinical practice after September 2017, either as their first IFX or transitioning from treatment with IFX originator or another IFX biosimilar. Data are captured prospectively and/or retrospectively from patient records obtained during routine clinic visits for up to 12 months (M12) following initiation. Outcome measures include persistence on SB2, clinical characteristics at baseline (time of initiation of SB2), disease scores (Harvey-Bradshaw Index (HBI), Simple Clinical Colitis Activity Index (SCCAI)), trough levels (TL) and anti-infliximab antibodies (ADA).

Results: This interim analysis (IA) includes 575 IBD patients (446 with CD, 129 with UC); 273 patients with CD and 78 with UC reached M12 by data extraction date, with persistence on SB2 being 95.6% (95% CI 92.4, 97.7) and 93.6% (95% CI 85.7, 97.9) in CD and UC respectively. In the 522 patients with prior IFX, no clinically relevant difference in disease score from baseline to M12 was observed; mean individual change was -0.34 (95% CI -0.72, 0.04) and -0.22 (95% CI -0.89, 0.44) in CD and UC respectively. Baseline ADA assay was performed on 241 (50.6%) patients, showing mean total ADA concentration below 1µg/mL, with no increase over the observation period.

Conclusion: This IA indicates that patients with IBD can be successfully transitioned from originator or biosimilar IFX to SB2, with no loss of disease control and without immunogenicity concerns. Over 90% of patients initiated de novo or transitioned from originator or another IFX biosimilar continued SB2 treatment at M12 post-initiation.

		CD			UC		
		n	Mean (SD)	Q1, Q3	n	Mean (SD)	Q1, Q3
Age, years		446	38.32 (12.95)	28 - 46.75	129	39.32 (12.69)	29-49
Women n (%)			173 (38.8)	-		58 (45)	-
Duration of disease, years			13.8 (9.2)	6 - 19		9.5 (7.7)	4 - 14
Prior IFX treatment	Naïive (n) (%)	446	37 (8.3)	-	129	16 (12.4)	-
	Originator (n) (%)		316 (70.9)	-		79 (61.2)	-
	Biosimilar (n) (%)		93 (20.9)	-		34 (26.4)	-
Mean SB2 dose (mg/kg)	At initiation	369	7.2 (2.5)	5-10	107	7.1 (2.4)	5-10
	At M12	273	7.7 (2.5)	5-10	78	7.6 (2.5)	5-10
Patients remaining on SB2 at M12 (n) (%)		273	261 (95.6)	92.4- 97.7*	78	73 (93.6)	85.7-97.9*
Patients with prior IFX originator/ biosimilar exposure only:							
IFX TL (μg/mL)	Baseline	199	5.7 (4.5)	2.4-8.2	63	6.6 (5)	2.4 - 10.4
	M12	45	5.9 (4.7)	2.5-8.7	9	8.6 (6.6)	1.6-15.5
Total ADA (μg/mL)	Baseline	179	0.8 (4.5)	0.0-8.23	62	0.8 (5.2)	0.01-0.01
	M6	94	0.55 (4.2)	0.0-0.01	26	0.01 (0.02)	0.0-0.01
	M12	47	0.001 (0.001)	0.0-0.01	1	0	0.0-0.0
		n	Mean (SD)	95% CI	n	Mean (SD)	95% CI
HBI	Baseline	272	2.3 (3)	2.0, 2.7	-	-	-
	M12	222	2.2 (2.4)	1.9, 2.5	-	-	-
	Individual change: M12-baseline	187	-0.34 (2.7)	-0.72, 0.04	-	-	-
SCCAI	Baseline	-	-	-	81	1.4 (2.0)	0.9, 1.8
	M12	-	-	-	60	1.03 (1.9)	0.54, 1.53
	Individual change: M12-baseline	-	-	-	58	-0.22 (2.5)	-0.89, 0.44

[Table 1: Baseline characteristics, SB2 persistence, TDM and disease scores Data extract date: 19 March 2019; *95% confidence interval]

P1096 TUBERCULOSIS INFECTION UNDER ANTI-TNF - SHOULD WE BE LOOKING FOR IT?

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Introduction: Anti-tumor necrosis factor (TNF) therapy revolutionized the treatment of inflammatory bowel disease. However, a major concern is the increased risk of developing tuberculosis (TB), which requires diagnosis and treatment of latent TB infection (LTBI) before initiation of anti-TNF agents. Currently, no recommendations exist regarding the need to regularly re-test patients for latent TB during treatment.
Aims & Methods: We aimed to assess the incidence and to identify risk factors for newly acquired TB infection in patients under anti-TNF.
Adult patients under anti-TNF for over 12 months were retrospectively assessed. Patients with a negative pre-treatment interferon-gamma releasing assay (IGRA) that repeated IGRA during anti-TNF treatment were reviewed. Patients with a pre-treatment positive IGRA were excluded.

Results: Out of 244 patients under anti-TNF (124 infliximab, 120 adalimumab), 87 patients were included. Patients had a mean age of 40±14 years, 64.4% were females, 93.1% were under infliximab and 64.4% had Crohn's disease. Positive repeat IGRA was identified in 9 patients (10.3% of our sample, 3.7% of all patients under anti-TNF in our center), of which 3 had active tuberculosis and 6 had LTBI.
When comparing patients with and without positive repeat IGRA, no differences were found regarding age (39.6 years vs 36.7 years, p=0.991) or gender (10.7% females vs 9.7% males, p=0.999). Patients with repeat positive IGRA more frequently had close contact with patients with TB (22.2% vs 0.0%, p= 0.010), however no differences were found regarding travels to TB-endemic areas (11.1% vs 7.7%, p=0.548), professional risk for TB infection (11.1% vs 9.0%, p=0.999), concomitant treatment with immunosuppressants (77.7% vs 71.8%, p=0.999), use of systemic steroids during anti-TNF treatment (33.3% vs 35,9%, p=0,999), diabetes mellitus (11.1% vs 5.1%, p=0.429) or active smoking (22.2% vs 20.5%, p=0.999). Also, no differences were found regarding the duration of treatment at the time of repeat IGRA (30.2±26.7 months vs 42.5±30.1 months, p=0.640).
Conclusion: In patients under anti-TNF, at least 3.7% of patients have a positive repeat IGRA after starting treatment. In our sample, only close contact with patients with TB was associated with a positive repeat IGRA. Therefore, considering that infection during treatment is present in a non-negligible percentage of patients, and most of the classical risk factors can not be used to identify at-risk patients, physicians may consider routine repeat IGRA in patients under anti-TNF.
Disclosure: Nothing to disclose

P1097 CORTICOSTEROID SPARING EFFECTS OF USTEKINUMAB THERAPY IN ULCERATIVE COLITIS PATIENTS: RESULTS FROM THE UNIFI PROGRAM

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Introduction: Ustekinumab (UST), an IL12/23 blocker approved for Crohn's disease, was effective in Phase 3 induction and maintenance studies of patients with moderate-severe ulcerative colitis (UC). Since discontinuation of corticosteroids (CS) is an important goal of therapy in UC, this analysis aims to further describe the CS sparing effects of ustekinumab treatment through Week 44 of the UNIFI trial.
Aims & Methods: Responders to UST IV induction entered maintenance and were randomized to UST 90mg SC (q12wks or q8wks), or PBO. During the induction and maintenance studies, oral CS were not to be initiated or increased beyond baseline. At Week 0 of the maintenance study, a scheduled taper was recommended for all patients receiving CS. CS-free Clinical Response (CSR) and remission (CSRem) rates (at Week 44, and for >90 days prior to Week 44) were calculated for the overall population and for the subset of patients on CS at maintenance baseline. Among the subset of patients on CS at maintenance baseline, the mean prednisone-equivalent (P.Eq) CS dose (mg/day) through Week 44 were calculated as were the rates of subjects who were CS-free at Week 44 and for >90 days prior to Week 44
Results: Overall 50.6% (265/523) of patients in the primary analysis population were receiving CS at maintenance baseline. The proportions of patients who were receiving concomitant CS at maintenance baseline were 52.3%, 47.7%, and 52.3% in the UST q8w, UST q12w and PBO groups, respectively. As detailed in Table 1, in the overall population, CSR and CSRem rates were significantly higher for patients who continued on UST therapy during maintenance compared with placebo. Among the patients who achieved CSR or CSRem at Week 44, the majority achieved these endpoints

and eliminated CS use at or up to 90 days prior to Week 44. Similar results were observed in the subset of patients on concomitant CS at maintenance BL. In this group, the mean daily P.Eq CS dose at maintenance BL was approximately 15.0 mg/day for all treatment groups. Mean decrease in average daily P.Eq dose at Wk 44 was more pronounced and the proportion of patients who were CS-free was greater in the UST maintenance arms.

Conclusion: UST maintenance therapy, with both q8w and q12w dosing regimens, is effective in reducing and eliminating the use of CS in patients with UC; the majority of patients (>90%) who achieved clinical response or clinical remission were able to eliminate corticosteroids.

Overall Population	PBO Maintenance	UST q12w	UST q8w
Number of patients	n=175	n=172	n=176
CR[a] at wk 44 (n,%)	84 (48.0%)	123 (71.5%)*	135 (76.7%)*
CSR at wk 44 (n, %)	80, 45.7%	120, 69.8%*	132, 75%*
CRem[b] at wk 44 (n,%)	43, 24.6%	68, 39.5%**	75, 42.6%*
CSRem at wk 44 (n, %)	41, 23.4%	65, 37.8%**	74, 42%*
CSRem >90 days prior to wk 44 (n, %)	39, 22.3%	64, 37.2%**	74, 42% **
Patients on CS at maintenance BL			
Number of patients	n=91	n=82	n=92
CR[a] at wk 44 (n, %)	38, 41.8%	56, 68.3% **	63,68.5% **
CSR at wk 44 (n, %)	34, 37.4%	53,64.6% **	60,65.2% **
CRem[b] at wk 44 (n, %)	19, 20.9%	28, 34.1%*	37, 40.2% **
CSRem at wk 44 (n, %)	17, 18.7%	25, 30.5%**	36, 39.1% *
CSRem >90 days prior to wk 44 (n, %)	16, 17.6%	24, 29.3%**	36, 39.1% **
Mean decrease in the average daily P.Eq CS dose (mg/day)	-6.7	-11	-11.5
CS-free at wk 44	43, 47.3%	56, 68.3%*	73, 79.3%**
CS-free >90 days prior to wk 44 (n, %)	40, 44%	55, 67.1%*	71, 77.2%**

a. decrease from induction baseline in the Mayo score ≥ 30% & ≥ 3 points with either a decrease in rectal bleeding subscore (RBS) ≥ 1 or a RBS of 0 or 1
b. global definition: MAYO score ≤ 2 points with no individual subscore >1
*p<0.05
**p<0.001
CR: clinical response; CRem: clinical Remission; CSR: CS-free Response; CSRem: CS-free remission

[Table 1]

Disclosure: Drs. Danese, Sands, Peyrin-Biroulet, Rowbotham, Leong, Arasaradnam, van Assche, Sandborn, Panaccione are all investigators for Janssen Research & Development, LLC Drs. Marano, O'Brien, and Zhang are all employees of Janssen Research & Development, LLC Oortwijn is an employee of Janssen Biologics BV

P1098 COMBINED THERAPY WITH MESENCHYMAL STROMAL CELLS AND VEDOLIZUMAB CONTRIBUTES TO DEEP REMISSION IN ULCERATIVE COLITIS

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Introduction: One of the new promising methods of treatment of patients with ulcerative colitis (UC) is biological therapy using bone marrow mesenchymal stromal cells (MSC). In some cases, simultaneously with MSC, patients receive concomitant anticytokine therapy. Currently, a new strategy for UC therapy is to achieve a deep remission of the disease. To compare the level of immunobiological and histological markers of inflammation—C-reactive protein (CRP), the Geboes Score (GS) and faecal calprotectin (FCP) – in patients with UC receiving cell therapy MSC, anti-integrin therapy with vedolizumab (VDB), and combined therapy of bone marrow MSC and VDB.

Aims & Methods: To compare the effectiveness of combined therapy of mesenchymal stromal cells and vedolizumab with monotherapy MSC and VDB. 45 patients with total ulcerative colitis of moderate severity were di-

vided into groups depending on the therapy. The first group of patients with UC aged from 19 to 51 years (Me-29) (n=15) received anti-inflammatory therapy with the use of the culture of 2 million MSC/kg according to the scheme the second group of patients with UC (n=15) aged 23 to 50 years (Me-38) received VDB in accordance with the recommended scheme, the third group of patients with UC (n=15) aged 24 to 56 years (Me-31) received the MSC+VDB. The level of CRP, PCF and is was assessed 26 weeks after initiation of therapy. The baseline CRP was 24.6±1.8; 25.5±2.0 and 24.8±2.1 mg/l, respectively. Baseline GS in the groups of patients was 4.6±0.4; 4.35±0.25 and 4.5±0.3 points, respectively. The initial level of the FCP made 1090±88.8; 1000±83.9 and 1010±120.5 μg/g, respectively.

Results: After 26 weeks from the start of therapy in the first group of patients, the level of CPP was 7.8±2.1 mg/l, in the second group 7.4±1.3 mg/l, in the third group 7.5±1.0 mg/l (p>0.05). After 26 weeks from the start of therapy in the first group of patients, the level of FCP was 98.8±9.3 μg/g, in the second group 90.6±7.5 μg/g, in the third group 82.8±6.3 μg/g (p <0.05 compared with the 1-st and 3-d groups). After 26 weeks from the start of therapy in the first group of patients with GS was 0.7±0.1 points, in the second group 0.65±0.1 points, in the third-0.35±0.06 points (p<0.001 compared with the 1-st and 3-d groups).

Conclusion: Combined mesenchymal stromal cells and anti-integrin therapy with vedolizumab contributes to a more pronounced reduction in the degree of inflammation of the intestinal mucosa.

Disclosure: Nothing to disclose

P1099 HIGH INCIDENCE OF HYPERGLYCAEMIA IN STEROID TREATED HOSPITALISED INFLAMMATORY BOWEL DISEASE (IBD) PATIENTS AND ITS RISK FACTORS IDENTIFIED BY MACHINE LEARNING METHODS

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Introduction: Glucocorticoids (GC) have been first line treatment for hospitalised inflammatory bowel disease (IBD) patients for over 60 years, despite the introduction of biologic therapy. The use of steroids in IBD inpatients is common and remains prominent in international guidelines. IBD patients often have systemic inflammation complicated by malnutrition leading to metabolic stress. The frequency and specific risk factors for hyperglycaemia in hospitalised IBD patients receiving GC are unknown

Aims & Methods: 100 consecutive IBD inpatients receiving intravenous hydrocortisone (IVH) for acute flares had capillary blood glucose (CBG) monitoring automatically triggered by the electronic prescription. CBG, biomarkers, IBD severity scores (Harvey Bradshaw, partial Mayo) and weight loss were prospectively recorded. Undiagnosed Diabetes Mellitus (DM) was defined as baseline HbA1c >48 mmol/mol. Machine learning (random forest regressor, RFR) was applied to the data to evaluate risk factors of hyperglycaemia.

Results: 55% of hospitalised IVH treated IBD patients had a CBG meeting the WHO criteria of DM (>11mmol/L), while 21% and 7% had a CBG >14mmol/l and >20mmol/l, respectively. Only 7 patients had pre-existing DM, which was confirmed by admission HbA1c. RFR indicated disease severity score, duration of IVH, HbA1c and electrolyte imbalances (which affected 64%) were best predictors of hyperglycaemia.

50% were started on or switched biological therapy during hospitalisation. 59% were discharged on prednisolone, 14% on budesonide and 28% on no GC. 47 patients had HbA1c checked at 3 month follow-up of which 4 were in the diabetic range. 1 had known DM with elevated CBG during admission treated with insulin titration, 2 had elevated CBG as inpatients with no prior DM and were discharged on anti-diabetic medications (1 gliclazide, 1 insulin) and 1 was on long-term steroids for asthma who did not have CBG >11.0mmol/L as an inpatient. 4 patients discharged on gliclazide for steroid induced DM had documented repeat HbA1c recorded, which were all in the normal range.

Conclusion: Our data demonstrates that hyperglycaemia is common in IVH treated inpatients, therefore CBG monitoring should be routine practice. Predictive modelling (RFR) identifies more severe disease activity, duration

of IVH treatment and HbA1c as risk factors for hyperglycaemia. The importance of IVH duration suggests hyperglycaemia risk may be physician-modifiable.

Alternative treatment strategies such as earlier introduction of biologics (which were used in half of the cohort), rapid steroid taper and nutritional therapies could be used to minimise medication associated metabolic instability in high risk patients. Limited follow-up HbA1c data suggests oral hypoglycaemic medication may be effective to mitigate further hyperglycaemia.

Disclosure: Nothing to disclose

	Crohn's	Ulcerative Colitis	IBD-U	Combined
Total	56	39	7	100
Female (%)	27 (48%)	20 (54%)	4 (57%)	51 (51%)
Age (range)	41 (18-80)	45 (16-80)	47 (25-75)	43 (16-80)
Disease Duration	7 (0-52)	5 (0-18)	2 (0-11)	6 (0-52)
BMI	24 (15-36)	25 (16-40)	23 (16-28)	24 (15-40)
HBI / p.Mayo	15 (6-37)	8 (5-12)	5 (2-9)	n/a
Admission CRP	64 (0-303)	84 (0-440)	166 (24-300)	78 (0-440)
Calprotectin	2619 (7-7049)	3345 (628-7091)	2815 (218-6000)	2897 (7-7091)
Pre-existing DM	6 (11%)	1 (3%)	0	7 (7%)
Max CBG >11.0	28 (49%)	22 (59%)	5 (71%)	55 (55%)
Max CBG >14.0	14 (25%)	5 (14%)	2 (29%)	21 (21%)
Max CBG >20	6 (11%)	1 (3%)	0 (0%)	7 (7%)

[Cohort Characteristics and Frequency of Hyperglycaemia]

P1100 IMPACT OF MIRIKIZUMAB TREATMENT ON INFLAMMATORY BOWEL DISEASE QUESTIONNAIRE SCORES IN PATIENTS WITH MODERATE TO SEVERELY ACTIVE CROHN'S DISEASE

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Introduction: Mirikizumab (miri; LY3074828) is a humanized monoclonal antibody directed against the p19 subunit of IL-23, with efficacy demonstrated in psoriasis, ulcerative colitis, and Crohn's disease (CD). The effect of miri on health-related quality of life (HRQoL) as measured by the Inflammatory Bowel Disease Questionnaire (IBDQ) was examined as part of a Phase 2, multicenter, randomized, parallel-arm, double-blind placebo (PBO)-controlled trial (NCT02891226) in patients with moderate to severely active CD.

Aims & Methods: At baseline, subjects (N =191) were randomized in a 2:1:1:2 ratio across 4 treatment arms (PBO, 200, 600, and 1000 mg miri administered intravenously [IV] at Weeks 0, 4, and 8). The IBDQ, a 32-item patient-completed questionnaire that measures 4 domains (bowel and systemic symptoms, emotional and social function), was analyzed at Weeks 0, 4, and 12, with higher scores indicating a better quality of life. IBDQ score change from baseline (BL), IBDQ response, and IBDQ remission were assessed. Treatment comparisons were made using mixed effects for repeated measures analysis for continuous endpoints and logistic regression with nonresponder imputation for categorical endpoints

Results: Patients who received 600 or 1000 mg miri had greater change from BL in IBDQ scores at 4 weeks compared to PBO (PBO: 15.18±3.30; miri 200 mg: 24.16±4.83; 600 mg: 27.08±4.77; 1000 mg: 25.52±3.36; 600 and 1000 mg miri $p < 0.05$ vs PBO). At 12 weeks, all miri groups had greater change from BL in IBDQ scores compared to PBO (PBO: 16.23±3.65; 200 mg: 41.14±5.18; 600 mg: 45.50±5.22; 1000 mg: 41.22±3.64; all $p < 0.001$ vs PBO). Similarly, at Week 12 IBDQ response was achieved in 58.1%, 68.8%, and 68.8% of patients in miri 200, 600, and 1000 mg groups, compared

to 45.3% in the PBO group (600 mg $p < 0.1$, 1000 mg $p < 0.01$), and IBDQ remission was achieved in 35.5%, 53.1%, and 42.2% of patients in the miri 200, 600, and 1000 mg groups, respectively, compared to 15.6% in the PBO group (200 mg $p < 0.1$, 600 and 1000 mg $p < 0.001$).

Conclusion: Miri treatment produced statistically significant and clinically meaningful improvements in HRQoL as measured by IBDQ after 12 weeks in patients with CD, with clinically relevant changes noted as early as 4 weeks.

Disclosure: This study was funded by Eli Lilly and Company.

	Treatment Groups			
	Placebo	Mirikizumab		
Mean (SD) unless otherwise specified	(N=64)	200 mg (N=31)	600 mg (N=32)	1000 mg (N=64)
Week 0				
Age, years	39.0 (13.0)	38.1 (11.8)	40.4 (13.3)	37.7 (13.1)
Male, n (%)	28 (43.8)	17 (54.8)	14 (43.8)	34 (53.1)
Corticosteroid use, n (%)	21 (32.8%)	14 (45.2%)	7 (21.9%)	15 (23.4%)
Disease duration, years	10.2 (9.8)	8.9 (7.4)	10.8 (9.7)	8.6 (6.7)
Previous biologic use, n (%)	43 (67.2)	19 (61.3)	19 (59.4)	39 (60.9)
Disease location, n (%)				
Ileal	11 (17.2)	6 (19.4)	5 (15.6)	11 (17.2)
Colonic	25 (39.1)	14 (45.2)	10 (31.3)	26 (40.6)
Ilealcolonic	28 (43.8)	11 (35.5)	17 (53.1)	27 (42.2)
IBDQ	113.88 (37.07)	104.77 (34.31)	127.03 (35.47)	120.31 (32.40)
Week 4				
IBDQ Change from BL, LSM (SE)	15.18 (3.30)	24.16 (4.83)	27.08 (4.77)*	25.52 (3.36)*
Week 12				
IBDQ Change from BL, LSM (SE)	16.23 (3.65)	41.14 (5.18)***	45.50 (5.22)***	41.22 (3.64)***
IBDQ response[a], n (%)	29 (45.3)	18 (58.1)	22 (68.8)	44 (68.8)
% Difference vs PBO (95%CI)	---	12.8 (-8.5, 34.0)	23.4* (3.3, 43.6)	23.4** (6.8, 40.10)
IBDQ remission[b], n (%)	10 (15.6)	11 (35.5)	17 (53.1)	27 (42.2)
% Difference vs PBO (95%CI)	---	19.9* (0.8, 38.9)	37.5*** (18.1, 56.9)	26.6*** (11.5, 41.6)

[a]IBDQ response: ≥16-point improvement in IBDQ score.
[b]IBDQ remission: total IBDQ score ≥170.
BL=baseline; BMI=body mass index; CI=confidence interval; IBDQ=Inflammatory Bowel Disease Questionnaire; LSM=least squares mean; PBO=placebo; SD=standard deviation; SE=standard error; vs=versus; *$p < 0.1$ **$p < 0.01$ ***$p < 0.001$ vs PBO.

[Table 1.]

P1101 TUBERCULOSIS INFECTION IN INFLAMMATORY BOWEL DISEASE PATIENTS WHO RECEIVED BIOLOGIC AGENTS: A SINGLE CENTER EXPERIENCE OF 20 YEARS

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Introduction: TNF-alpha blockers increase the risk of tuberculosis (TB) infection. This risk is especially important in countries which have a high rate of TB infection. The incidence of TB infection in Turkey was reported as 15.2 / 100.000 in 2017 which shows that in our country we should be alert about the risk of TB infection in inflammatory bowel disease (IBD) patients who receive immunosuppressive treatment.

Aims & Methods: The aim of this retrospective study is to determine the rate of latent and active tuberculosis infection in IBD who received biologic treatment in our center.: 349 IBD patients who received TNF-alpha antagonist treatment from 1998 to 2018 were included in the study. Information about the demographic data, IBD type, previous and current treatment, latent TB screening results, duration of isoniazid (INH) prophylaxis treatment, lung imaging results, and diagnosis of active TB infection was obtained from patients' files and electronic data system of our hospital.

Results: A total of 349 patients (56.4 % male, mean age 42 ± 14 years) were included in the study, the mean disease duration was 10 ± 6 years, 76.5% had Crohn's disease. Taking into account that some of the patients had received more than one type of anti-TNF alpha agent; 77% of the patients (n = 269) received infliximab, where 48.1% (n = 168) received adalimumab, 5.7% (n = 20) received certolizumab, 5.4% (n = 19) received vedolizumab, and 1.1% (n = 4) received golimumab. Latent tuberculosis infection screening was positive in 171 (48.9%) patients (157 tuberculin test > 5 mm and 14 positive Quantiferon test), 96.4% (n = 165) of these patients had received INH treatment for latent TB. Incidence of active TB development was 1.7% (n = 6). Two of them had received INH treatment. In two latent tuberculosis screening was negative. The remaining two patients were inadequately screened: one of them had a negative tuberculin test but Quantiferon test was not obtained, the other patient had a borderline positivity of Quantiferon test. In three patients with active TB infection, pulmonary TB was accompanied by extra-pulmonary infection (Table). Two patients had TB infection after 4 years of TNF-alpha antagonist treatment, which can be the result of a new TB exposure. In 2 patients anti-TNF treatment was initiated again after then tuberculosis treatment was completed. None of these 2 patients developed tuberculosis reactivation. No association was found between the risk of developing TB and gender, age, disease type, type of TNF-alpha antagonist agent used and concomitant immunosuppressive therapy.

Treatment at the diagnosis of TB	INH treatment for latent TB infection (months)	PPD (mm)	Quantiferon test	Duration of TNF-alpha antagonist treatment before the diagnosis of TB (months)	Location of TB infection
AZA CS 5-ASA ADA	-	0	Negative	7	Lung +spleen +peritoneum
AZA ADA	9	6	Negative	48	Lung
5-ASA IFX	-	0	Negative	44	Lung
AZA IFX	-	NA	undetermined	2	Lung
AZA IFX	-	0	NA	7	Lung+lymph nodes
AZA ADA	6	9	NA	3	Lung+spleen

[Patients who had TB infection]

Abbreviations for the table : AZA: azathioprine ADA: Adalimumab CS: Corticosteroids IFX: Infliximab INH: Izoniazide NA:Not available TB: Tuberculosis

Conclusion: Active TB infection was detected in 1.7% (n = 6) of the 349 IBD patients who had biologic treatment during a period of 20 years. Two of these 6 patients have had isoniazid treatment for latent TB, in 2 of them screening for latent TB was negative. As a result although latent tuberculosis screening and treatment are recommended by guidelines, this modality may not be sufficient to eliminate the risk of TB infection in patients who receive biologics agents in countries with high incidence of TB infection.

Disclosure: Nothing to disclose

P1102 EFFICACY AND IMPROVED HEALTH-RELATED QUALITY OF LIFE AFTER 52-WEEKS OF MIRIKIZUMAB TREATMENT IN PATIENTS WITH ULCERATIVE COLITIS: AN UPDATE FROM A RANDOMISED, DOUBLE-BLIND, CONTROLLED, PHASE 2 STUDY

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Introduction: The efficacy and safety of mirikizumab (miri), an IL-23p19 antibody, has previously shown efficacy and health-related quality-of-life (HRQoL) improvement in patients with moderate-to-severe ulcerative colitis (UC) at 12 weeks in a phase 2, randomized, double-blind, placebo-controlled trial (AMAC, NCT02589665).

Aims & Methods: This analysis evaluated the effects of maintenance treatment with miri on clinical response, clinical remission, endoscopic healing, and HRQoL improvement in UC patients. Patients with moderate-to-severe UC (Mayo score 6-12; Endoscopic subscore ≥2) treated with miri during the induction period and who achieved clinical response or better at week 12 were re-randomized to miri 200 mg administered subcutaneously every 4 weeks (Q4W) (N=47) or every 12 weeks (Q12W) (N=46) through week 52. HRQoL was measured by the Inflammatory Bowel Disease Questionnaire (IBDQ) and evaluated using a mixed-model repeated-measures analysis. The percentage of patients at week 52 with clinical response,[1] clinical remission,[2] endoscopic healing,[3] IBDQ total score ≥170, and IBDQ improvement ≥16 were also assessed.

Results: At week 52, IBDQ scores significantly improved from baseline in both miri treatment groups (Table). In each treatment group, at week 52, ≥80% of patients had an improvement in IBDQ total score ≥16 points from baseline and ≥67% achieved IBDQ total score ≥170. Similarly, ≥76% of patients demonstrated a clinical response, ≥37% demonstrated clinical remission, and ≥48% demonstrated endoscopic healing at week 52.

Conclusion: Maintenance treatment with miri resulted in HRQoL improvement as well as clinical response, clinical remission, and endoscopic healing at week 52 in patients with moderate-to-severe UC. These are the first data in UC to demonstrate the longer-term effects of an IL-23p19 antibody on the HRQoL of patients with UC.

Disclosure: Study was funded by Eli Lilly and Company.

	Mirikizumab Q4W (N=47)	Mirikizumab Q12W (N=46)
Baseline IBDQ total score, LS mean (SE) observed	n=46 121 (4)[a]	n=46 127 (4)[a]
IBDQ total score change from baseline at Week 12, LS mean (SE)	n'=46 54 (4)[b]	n'=46 47 (4)[b]
IBDQ total score change from baseline at Week 52, LS mean (SE)	n'=42 58 (4)[b]	n'=43 51 (4)[b]
IBDQ total score improvement ≥16 at Week 52, n (%) NRI	n'=46 39 (85)	37 (80)
IBDQ total score ≥170 at Week 52, n (%) NRI	n'=46 31 (67)	31 (67)
Clinical response[1] at Week 52, n (%) NRI	38 (81)	35 (76)
Clinical remission[2] at Week 52, n (%) NRI	22 (47)	17 (37)
Endoscopic healing[3] at Week 52, n (%) NRI	27 (57)	22 (48)

[a]Analysis of variance model for baseline measures with treatment as the variable.
[b]p<0.001 vs baseline (Week 0), based on the MMRM model for post-baseline measures with baseline, geographical region, prior biologic therapy, treatment, time, and treatment*time as variables.
[1]Clinical response: 9-point Mayo score (comprising the subscores of rectal bleeding, stool frequency, and the endoscopic findings) decrease ≥2 points and ≥35% change from baseline, with rectal bleeding=0,1 or decrease ≥1.
[2]Clinical remission: rectal bleeding=0, stool frequency=0,1 with ≥1 point decrease from baseline, endoscopy=0,1.
[3]Endoscopic healing: Mayo endoscopic subscore=0,1.
LS=least squares; NRI=nonresponder imputation, used for missing values; n'= number of subjects in the population with baseline and post-baseline value at the specified time point; SE=standard error.

[Table 1.]

P1103 SILVER NANOPARTICLES BASED ON BLACKCURRANT EXTRACT ALLEVIATE DSS-INDUCED COLITIS IN MICE

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Introduction: Inflammatory Bowel Disease (IBD) is a chronic, severely debilitating disease which cannot be pharmacologically controlled due to ineffective activity or serious side effects of current therapies. In the search for new treatment options, we examined the anti-inflammatory potential of two preparations of silver particles in vitro in lipopolysaccharide (LPS)-stimulated RAW264.7 cells and in vivo in murine dextran sulphate sodium (DSS)-induced colitis model.

Aims & Methods: The nanoparticles were obtained with the use of blackcurrant extract exploiting the reducing and stabilizing potential of polyphenols, ascorbic acid and anthocyanins. The concentration of polyphenol compounds equaled 75 mg/dm3 and the extract showed high capacity for free radicals binding, as evidenced by 1,1-Diphenyl-2-picrylhydrazyl (DPPH) radical reduction assay. Based on UV-VIS analysis, the obtained, round nanoparticles show homogenous distribution and are well-dispersed within suspension. Two formulations were prepared, with final silver nanoparticle concentration equal to 100 and 500 mg/dm3 and the mean particle diameters of 95 nm (Ag95) and 213 nm (Ag213), respectively. Higher silver concentration was associated with larger particles.

Results: In vitro, Ag95 and Ag213 did not show any significant cytotoxicity in RAW264.7 cells up to 1 and 2.5 ppm, respectively, as evidenced in Neutral Red Uptake test. Opposite to the model drug, 10 uM budesonide, the preparations did not increase viability of LPS-stimulated cells. However, Ag95 at 1 ppm and Ag213 at 2.5 ppm were more effective in NO production inhibition, as evaluated by Griess test.

In vivo, both suspensions of silver particles showed anti-inflammatory properties in DSS-induced murine model of colitis. The studied preparations inhibited weight loss, decreased macroscopic score and colon shortening. Additionally, Ag95 and Ag213 reduced neutrophil infiltration assessed by myeloperoxidase activity assay. When tested at the same dose (0,4mg/kg, once daily, i.c.), Ag213 was more effective than Ag95. Higher dose (2 mg/kg) further improved Ag213 performance.

Conclusion: The anti-inflammatory action of silver preparations may be useful in IBD treatment. The objective is to maintain high anti-inflammatory potential, simultaneously minimizing the risk of side effects. The tested formulations Ag95 and Ag213, showing good bioavailability and activity, meet these requirements, which warrants further characterization.

Disclosure: Nothing to disclose

P1104 INCIDENCE AND INDICATORS OF SUBOPTIMAL RESPONSE TO TUMOR NECROSIS FACTOR ANTAGONIST THERAPY IN INFLAMMATORY BOWEL DISEASE IN NEWLY INDUSTRIALIZED COUNTRIES: RESULTS FROM THE EXPLORE STUDY

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Introduction: Inflammatory bowel disease (IBD) patients in Western countries frequently experience suboptimal response to anti-tumor necrosis factor (TNF) therapy. The EXPLORE study aimed to assess the incidence and indicators of suboptimal response to first-line anti-TNF agents in IBD patients in real-world practice in newly industrialized countries, where data are currently limited.

Aims & Methods: A retrospective chart review study was conducted in Asia-Pacific (APAC; South Korea, China, Taiwan, Singapore), Latin America (LatAm; Argentina, Colombia, Mexico) and Russia-Middle East (RME; Russia, Saudi Arabia, Turkey) in adult patients diagnosed with ulcerative colitis (UC) or Crohn's disease (CD), who initiated anti-TNF treatment between March 2010 and March 2015. The cumulative incidence (CI) of suboptimal response (Kaplan-Meier method) was assessed over the first 24 months of treatment, as the occurrence of a first indicator of: IBD-related hospitalization, dose escalation (increase in frequency and/or dose), discontinuation including switch to another anti-TNF, non-biologic therapy augmentation, or IBD-related surgery. Primary non-response (PNR) and secondary loss of response (SLOR) were defined as any suboptimal response indicator at < 4 and ≥4 months after anti-TNF initiation (excluding PNR patients), respectively.

	Overall		APAC		LatAm		RME	
	UC (N=570)	CD (N=1104)	UC (N=173)	CD (N=497)	UC (N=99)	CD (N=86)	UC (N=298)	CD (N=521)
Overall frequency of suboptimal response, n (%)	188 (33.0)	454 (41.1)	81 (46.8)	253 (50.9)	36 (36.4)	40 (46.5)	71 (23.8)	161 (30.9)
Cumulative incidence of suboptimal response, %								
12 months	24.4	30.0	34.4	40.4	25.9	30.7	18.2	19.9
24 months	32.9	41.2	45.1	54.1	38.2	42.5	23.8	29.5
Cumulative incidence of PNR[a], %	13.6	16.9	20.2	26.5	11.4	10.8	10.5	8.6
Cumulative incidence of SLOR[b], %								
12 months	12.6	15.8	17.8	18.9	16.4	22.4	8.5	12.4
24months	22.3	29.2	31.2	37.5	30.2	35.6	14.8	22.9
First indicator of suboptimal response[c], n (%)	UC (N=188)	CD (N=454)	UC (N=81)	CD (N=253)	UC (N=36)	CD (N=40)	UC (N=71)	CD (N=161)
Anti-TNF dose escalation	23 (12.2)	65 (14.3)	3 (3.7)	34 (13.4)	12 (33.3)	9 (22.5)	8 (11.3)	22 (13.7)
Non-biological therapy augmentation	57 (30.3)	108 (23.8)	25 (30.9)	68 (26.9)	15 (41.7)	14 (35.0)	17 (23.9)	26 (16.1)
Anti-TNF discontinuation including switch	45 (23.9)	42 (9.3)	31 (38.3)	18 (7.1)	5 (13.9)	4 (10.0)	9 (12.7)	20 (12.4)
IBD-related surgery	7 (3.7)	79 (17.4)	2 (2.5)	35 (13.8)	2 (5.6)	8 (20.0)	3 (4.2)	36 (22.4)
IBD-related hospitalizations	62 (33.0)	164 (36.1)	20 (24.7)	99 (39.1)	6 (16.7)	5 (14.6)	36 (50.7)	60 (37.3)

APAC: Asia-Pacific; CD: Crohn's Disease; IBD: Inflammatory Bowel Disease; LatAm: Latin America; RME: Russia-Middle East; TNF: tumor necrosis factor; UC: Ulcerative colitis. [a]Cumulative incidence at 4 months. [b]SLOR among patients who did not experience PNR and who are still on anti-TNF at 4 months. [c]6 UC and 4 CD patients had more than one suboptimal response indicator on the same day.

[P1104 Table 1. Cumulative Incidence and Indicators of Suboptimal Response to First-Line Anti-TNF Therapy in IBD Patients in Newly Industrialized Countries]

Results: Overall, 1674 first-line anti-TNF treated patients (570 UC; 1104 CD) were included: male, UC 56.1%, CD 61.2%; median (min-max) age (years), UC 39.0 (18-82), CD 31.0 (19-83); median (min-max) disease duration (years), UC 3.0 (0-34), CD 1.0 (0-33); median (min-max) follow-up (months), UC 45.9 (24-60), CD 46.5 (14-60). At 24 months, the CI of suboptimal response to first anti-TNF treatment was 32.9% in UC and 41.2% in CD patients (unadjusted log-rank: p< 0.01); the APAC region had the highest CI (UC 45.1%; CD 54.1%) (Table 1). The CI of PNR was 13.6% and 16.9% in UC and CD patients, respectively. The CI of SLOR was 22.3% in UC and 29.2% in CD patients at 24 months. The most frequent first suboptimal response indicator was 'IBD-related hospitalization' (UC 33.0%; CD 36.1%) followed by 'non-biologic augmentation' (UC 30.3%; CD 23.8%) (Table 1).

Conclusion: Suboptimal response to first-line anti-TNF agents is common in IBD patients in newly industrialized countries and is more frequently experienced in CD than in UC. Observed regional differences in the rates of suboptimal response, PNR and SLOR, may reflect local practice variations and restrictions in the management of anti-TNF treated patients.

Disclosure: The study was funded by Takeda Pharmaceuticals Company Ltd.

P1105 VEDOLIZUMAB INDUCES DEEP REMISSION AND IMPROVES QUALITY OF LIFE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES: THE ANCONA EXPERIENCE

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Introduction: Vedolizumab (VDZ) is an α4β7 integrin antagonist approved for the treatment of adult patients (pts) with moderate to severe ulcerative colitis (UC) and Crohn's disease (CD).

Aims & Methods: The primary outcome of the study was to evaluate the effect of VDZ on clinical response in pts with UC and CD at the 14th week. Secondary outcomes were to evaluate clinical remission, mucosal healing, deep remission, steroid-free remission and quality of life at different time points (14th week, 6, 12 and 24 months).

We retrospectively evaluated 39 pts who referred to our Inflammatory Bowel Disease Unit and received VDZ for moderate-severe UC (26 pts) and moderate-severe CD (13 pts). As concerns the UC and CD outcomes, clinical response was defined by a reduction in Mayo score ≥3 points and in Harvey-Bradshaw index (HBI) ≥3 points, clinical remission by a Mayo score ≤2 and by a HBI < 5 and endoscopic remission by endoscopic Mayo subscore ≤1 and by endoscopic SES-CD score ≤2, respectively. Steroid free-remission was evaluated in UC pts only. Deep remission was defined, in both diseases, as clinical, endoscopic and biochemical remission. Serum C-reactive protein (CRP) and faecal calprotectin (FC) were evaluated in pts at all time points. Quality of life (QoL) was evaluated by the 32-item version of Inflammatory Bowel Disease Questionnaire (IBDQ-32).

Results: UC pts: 12 out of 26 UC pts had previously failed anti-TNF therapy; clinical response at the 14th week was observed in 77% of the pts and no significant differences were found between naive and anti-TNF treated pts. Non-responder pts showed a more severe Mayo endoscopic subscore (2.8 vs 2.2; P< 0.02). Clinical remission occurred in 60%, 64%, 67% and 75% of pts at the 14th week, 6, 12 and 24 months, respectively. Steroid-free remission was 85% (17/20) at the 14th week and 75% at 24 months. Mucosal healing was above 70% at all time points. In pts who had a clinical response, FC levels decreased from 529.15 mg/kg at baseline to 103.7 mg/kg at the 14th week and was always less than 50 mg/kg after 6, 12 and 24 months. Similarly, CRP levels decreased from 1.85 mg/dl at baseline to 0.9 mg/dl at the 14th week, and were within the normal range (< 0.50 mg/dl) after 12 and 24 months. Deep remission was 35% at the 14th week and 75% at 24 months. QoL in responder pts was 131±34 at baseline, significantly increased after 14 weeks (171,9±29; P< 0.001) and remained stable over time.

CD pts: 12 out of 13 pts had previously failed anti-TNF therapy; clinical response at the 14th week was observed in 46% of the pts, whereas clinical remission rates were 100%, 80%, 100% and 100% at the 14th week, 6, 12 and 24 months, respectively. Mucosal healing was observed in 25% of pts at 12 months and in 100% of pts at 24 months, whereas deep-remission was achieved in 25% and 50% of pts at the same time points. In responder pts, FC, CRP and QoL showed a significant improvement starting from the 6th month.

Advers events were observed in 5/39 pts: psoriasis (2 pts), joint symptoms (1 pt), arterial hypertension (1 pt) and mild urticaria (1 pt); however only 1 pt with psoriasis had to discontinue the treatment.

Conclusion: VDZ was effective and safe for induction and maintenance of deep remission and of steroid-free remission in pts with UC, and significantly improved their QoL; serum CRP and FC levels correlated with clinical response. Even if data in CD pts are limited, VDZ appeared effective for induction and maintenance of clinical and endoscopic remission also in these pts, although the improvement in biochemical indices and in the QoL required at least 6 months.

Disclosure: Nothing to disclose

P1106 PERIPHERAL BLOOD METHYLATION PROFILES ARE STRONG PREDICTORS OF RESPONSE AND NON-RESPONSE TO INFLIXIMAB AND VEDOLIZUMAB IN CROHN'S DISEASE

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Introduction: Crohn's disease (CD) remains an incurable condition despite expanding therapeutic options. Treatment are randomly initiated and switched in case of insufficient response. Biomarkers that allow prediction of response offering guidance for treatment selection are lacking, leading to poor disease control and complications. Epigenetics, mainly DNA methylation patterns, have been shown to predict CD behavior and recurrence. We investigated the predictive power of peripheral blood (PB) methylation profiles in CD patients treated with infliximab (IFX) or vedolizumab (VDZ).

Aims & Methods: We identified CD patients who were distinct responders (R) and non-responders (NR) to IFX and VDZ based on clinical and endoscopic criteria who were prospectively sampled in the biobank Future-IBD at Amsterdam UMC. DNA was isolated from PB at baseline and 8 weeks into treatment. Methylation screening was performed using the Infinium® Methylation EPIC Bead Chip (850K) by Illumina (San Diego, CA). Response assessment was performed after 12-16 weeks.

Results: In this pilot study we analyzed 12 CD patients treated with IFX (6 R and 6 NR) and 12 with VDZ (5 R and 7 NR). Analysis of differentially methylated positions (DMPs) between R and NR both before and after induction treatment yielded 38 DMPs for IFX and 9 DMPs for VDZ, both at a Benjamin-Hochberg adjusted α of 0.05. For IFX, all DMPs showed a complete separation of responders and non-responders and a striking mean methylation difference of at least 10% between responders and nonresponders. Similar results, but for distinct loci, were obtained in the VDZ cohort. The largest effect size with complete separation of R and NR to VDZ showed a methylation difference of >30%.

Conclusion: DMPs associated with response/nonresponse to IFX and VDZ were mutually exclusive indicating that both marker sets are specific for each treatment. We observed large methylation differences between R and NR which is exceptional in complex diseases like CD. These observations open the road to personalized treatment selection in CD. Further validation of these markers is ongoing.

Disclosure: Nothing to disclose

P1107 COMPARING THE DESIGN OF TWO RECENT MESALAZINE TRIALS WITH RESPECT TO EMA GUIDELINE ON THE DEVELOPMENT OF NEW MEDICINAL PRODUCTS FOR THE TREATMENT OF ULCERATIVE COLITIS

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Introduction: Developing a new drug for treating ulcerative colitis (UC) is challenging. More challenging is the clinical trial design.

Aims & Methods: We highlight the phase 3 trial design of a new 5ASA drug (TP0503) and compare it to the latest EMA "guideline on the development of new medicinal products for the treatment of Ulcerative Colitis" from 2018. We also compare TP0503 to another recent mesalazine trial (SAT25). We also compare TP0503 to another recent mesalazine trial (SAT25).

Each item in the EMA guideline was compared to TP0503 protocol (Mesalazine 1600 mg vs. Mesalazine 400 mg; NCT01903252) and SAT25 (Mesalazine 1000 mg vs. Mesalazine 500 mg; NCT01745770). This comparison covers the patient selection (section 4 of EMA guideline), efficacy assessment (section 5) and study design (section 6). Safety aspects (section 7) and the risk management plan (section 8) were well-respected by both trials.

Results: As per EMA guideline, patient selection in TP0503 and SAT25 was based on symptoms, endoscopic and histologic findings. Patients with malignancy and Clostridium D. infection were excluded from TP0503. Patients with malignancy were not clearly excluded from SAT25. While both trial designs relied on endoscopic score to include or exclude patients, SAT25 used Rachmilewitz Endoscopic score (EI) which is less widely used than the Mayo Endoscopic Score (MES). SAT25 included patients with EI≥4 (mild to severe) without relying on central reading. All TP0503 patients had higher endoscopic score with MES≥2 (moderate to severe). MES was assessed by one central reader. TP0503 is one of the first trials that used central reading for inclusion and efficacy assessments.

For the efficacy assessment, TP0503 respected each item of the guideline looking at the symptomatic and endoscopic remission as a treatment goal for induction and maintenance of remission in UC. In TP0503, the primary endpoint (PEP) was a co-primary endpoint at week 8 of clinical remission and endoscopic remission as defined by MAYO≤2 without any subscore>1. SAT25 PEP, was less stringent and used clinical remission as the only PEP. SAT25 did not report a combined PEP of clinical and endoscopic remission, diverging from the EMA guideline.

For the study design, TP0503 respected each item of the guideline except for two. For ethical reasons, it was not possible to randomize UC patients to a placebo arm therefore TP0503 trial was a non-inferiority trial. Nor were they stratified according to prior treatment. While the SAT25 study group didn't include any placebo arm or stratify to prior treatment, they also, didn't perform any long term trial to evaluate the efficacy of the Mesalazine 1000 mg in maintenance.

With regards to missing data, TP0503 considered all missing data as failures, unlike the SAT25 trial where the LOCF was used to manage some missing data. Patients on topical co-medication were excluded from both trials. Looking at safety aspects, beside the exclusion of acute severe colitis and patients with pouchitis, which are not part of the mesalazine indications, TP0503 and SAT25 respected all other criteria.

Conclusion: TP0503 had more uptodate design than SAT25 with more stringent criteria. It mostly adhered to the 2018 EMA guideline even though it was designed 5 years prior.

	EMA Guidelines (2018)	TP0503 (2017)		SAT25 (2018)	
	Maximum score per guidelines	Scoring	(%)	Scoring	(%)
Patient selection	7	6.5	92.9%	6	85.7%
Assessment of efficacy	21	17	81.0%	12	57.1%
Study design	25	14.5	58.0%	10	40.0%
Safety aspects	7	6	82.7%	6	82.7%
Total	60	44	73.3%	34	56.7%

[Comparison between TP0503, SAT25 and EMA Guideline]

Disclosure: Employee of Tillotts Pharma AG

P1108 ANTI-TNF TREATMENT EFFECTIVELY REDUCED RATE OF HOSPITALIZATION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE WITH OR WITHOUT EXTRAINTESTINAL MANIFESTATIONS: REAL WORLD DATA IN GERMANY

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Introduction: Extraintestinal manifestations (EIMs) are prevalent among patients with inflammatory bowel diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC). However, the impact of EIMs on healthcare resource utilization is not well understood. Tumor necrosis factor inhibitors (TNFi) have shown to be effective in reducing risk of hospitalization and reducing EIMs in IBD patients.

Aims & Methods: This study assessed the prevalence of hospitalization in patients with IBD stratified by the presence of concomitant EIM(s) and evaluated the effect of TNFi on hospitalization in the real world. This study used the InGef database (2011-2017), containing anonymous claims from statutory health insurance in Germany. Adults with ≥2 CD or UC claims, ≥2 TNFi claims, and continuous enrollment for at least 12 months before (baseline) and 15 months after the first TNFi prescription (index date) were included. The rate of all-cause and IBD-related hospitalizations during baseline were compared to the 12-month period starting 3 months after the index date (follow-up). The first 3 months were excluded to allow time for the treatment to take effect.

Results: A total of 1,658 IBD patients who received a TNFi were identified (CD: 1,108; UC: 550). Over 50% (845/1658) had ≥1 all-cause hospitalization at baseline, and 90% (765/845) of the events were IBD-related. During baseline, over one-third of patients (35%) had at least one EIM (CD: 34%; UC: 38%). More patients with EIM(s) had at least 1 hospitalization compared to those without an EIM (all-cause: 56% vs. 48%, p< 0.01; IBD-related: 50% vs. 44%, p< 0.05), and the majority resulted from an emergency room (ER) visit (all cause: 34% vs. 28%, p< 0.01; IBD-related: 30% vs. 25%, p< 0.05). Patients with EIM(s) also had a greater mean number of hospitalizations than patients without an EIM (all-cause: 1.2 vs. 0.9, p< 0.001; IBD-related: 1.0 vs. 0.7, p< 0.01). During the TNFi therapy follow-up period, the proportion of patients with ≥1 all-cause hospitalization decreased by ≥17% in both groups, and almost all were IBD-related (EIM: Δ=17%; no EIM: Δ=18%, both p< 0.001, **Table**).

		With EIM[a] (N=581)			Without EIM[a] (N=1077)		
		Pre-Index	Post-Index	*P*-value	Pre-Index	Post-Index	*P*-value
All-cause	% with ≥1 hospitalization, n (%)	324 (55.8%)	224 (38.6%)	<0.0001	521 (48.4%)	335 (31.1%)	<0.0001
	% with ≥1 hospitalization resulting from ER, n (%)	199 (34.3%)	118 (20.3%)	<0.0001	301 (27.9%)	181 (16.8%)	<0.0001
	# hospitalizations, mean ± SD	1.2 ± 1.5	0.8 ± 1.4	<0.0001	0.85 ± 1.18	0.55 ± 1.04	<0.0001
	Length of stay, days, mean ± SD	11.7 ± 22.7	7.6 ± 19.6	<0.0001	7.6 ± 16.1	5.9 ± 19.7	<0.0001
IBD-related	% with ≥1 hospitalization, n (%)	288 (49.6%)	187 (32.2%)	<0.0001	477 (44.3%)	282 (26.2%)	<0.0001
	% with ≥1 hospitalization resulting from ER, n (%)	176 (30.3%)	99 (17.0%)	<0.0001	272 (25.3%)	147 (13.6%)	<0.0001
	# of hospitalizations, mean ± SD	1.0 ± 1.4	0.6 ± 1.2	<0.0001	0.7 ± 1.1	0.5 ± 0.9	<0.0001

EIM, extraintestinal manifestation; IBD, inflammatory bowel disease; ER, emergency room; SD, standard deviation.
[a]EIMs included bone manifestation, bronchopulmonary disease, hepatobiliary disease, mucocutaneous disease, musculoskeletal disease, ocular disease, oral disease, pancreatic disease, renal disease, or cardiovascular events.

[Hospitalization before and after initiating a TNFi therapy among patients with IBD by EIM status]

Hospitalizations resulting from an ER visit decreased during follow-up (EIM: Δ=14%; no EIM: Δ=11%, both p< 0.001), and almost all of the reduction was IBD-related (EIM: Δ=13%; no EIM: Δ=12%, both p< 0.001). The mean number of all-cause hospitalizations (EIM: Δ=0.4; no EIM: Δ=0.3, both p<0.001) and length of stay (EIM: Δ=4.1 days; no EIM: Δ=1.7 days, both p<0.001) was also reduced after TNFi use.

Conclusion: Hospitalization is highly prevalent among patients with IBD, especially among those with concomitant EIM(s) who had higher rates of hospitalization and ER visits than those without an EIM. TNFi treatment is effective in reducing all-cause and IBD-related hospitalizations, and this effect appeared to be comparable in both patients with or without a prior EIM.

P1109 COMBINED ENDOSCOPIC AND HISTOLOGICAL HEALING WITH VEDOLIZUMAB IN THERAPY-REFRACTORY CROHN'S DISEASE, DATA FROM THE LOVE-CD TRIAL

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Introduction: Efficacy of vedolizumab (VDZ) has been confirmed in Crohn's disease (CD), but there is limited data on mucosal healing, a combination of endoscopic and histological remission. In the LOVE-CD (LOw countries VEdolizumab in CD) trial we explored this novel endpoint in patients with active CD receiving VDZ for 52 weeks.

Aims & Methods: The aim of this exploratory analysis was to assess mucosal healing, the combination of endoscopic and histological healing, through week 26 in CD patients treated with VDZ. We included patients who had centrally read endoscopy at week 0 and 26 and paired biopsies at the same time points. Only patients with active histological inflammation at baseline (Robarts Histopathology Index (RHI) score > 7) were studied.

All patients had active CD (Crohn's Disease Activity Index (CDAI) > 220 and presence of mucosal ulcerations at baseline endoscopy) and were treated with VDZ 300 mg infusions at week 0, 2, 6 and every 8 weeks thereafter to week 52, with an additional infusion at week 10 in the absence of clinical response. Mucosal biopsies were collected from the edge of the most prominent ulcer in the terminal ileum and 4 colonic segments (ascending, transverse, descending colon and sigmoid and rectum), or from the most severely affected area if no ulcers were present.

If a segment was completely normal, two biopsies were taken at random per segment. Histopathology was assessed blindly using the RHI, which represents a reproducible and responsive index that incorporates four histologic descriptors (i.e. severity of chronic inflammatory infiltrate, the number of neutrophils in the lamina propria, the number of neutrophils in the epithelium and the severity of erosions or ulceration), each of which is graded from 0 to 3 (Mosli M et al. Gut. 2017;66(1):50-58). In case more than one biopsy was available per segment, the biopsy sample with the maximum RHI score was used for further analysis.

Results: Paired biopsies from the same segment were available in 65 patients, 40 of which (62%) had active histological inflammation (RHI score > 7) at baseline. Out of these patients, 35/40 (88%) failed on prior anti-TNF therapy and median disease duration was 8 (4-18) years. Fourteen out of these 40 patients (35%; 95% CI (0.21, 0.52)) achieved mucosal healing at week 26 (SES-CD < 4 and RHI ≤ 6). Endoscopic remission at week 26 was observed in 17/40 (43%) and histologic remission in 23/40 (58%).

Conclusion: Mucosal healing was achieved in 35% of CD patients with active histological inflammation at baseline after 26 weeks treatment with VDZ. These outcomes show that VDZ is able to induce both endoscopic and histological healing in therapy-refractory CD.

References: Mosli M et al. Gut. 2017;66(1):50-58

Disclosure: Nothing to disclose

P1110 COMPREHENSIVE LIFESTYLE-MODIFICATION INCLUDING MULTI-MODAL STRESS MANAGEMENT TECHNIQUES IN PATIENTS WITH ULCERATIVE COLITIS - RESULTS OF A RANDOMIZED-CONTROLLED TRIAL AND THE TRIER SOCIAL STRESS TEST

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Introduction: Psychosocial stress can have a negative impact on the course of disease in ulcerative colitis. A comprehensive lifestyle-modification program that includes stress management techniques addresses this unmet need.

Aims & Methods: In this randomized controlled trial, 97 patients with ulcerative colitis in remission and reduced quality of life were randomly assigned to a 10-week LSM program or a one day work-shop as control (Table 1). Perceived stress, anxiety, depression, and flourishing were measured before and after the intervention and after 24 and 48 weeks.

In an exploratory sub-study, 16 female patients (8 intervention and 8 controls) additionally underwent an acute psychosocial stress paradigm, the Trier Social Stress Test (TSST) which is a validated laboratory procedure to induce stress in human participants. Here, cardiovascular responses, blood parameters, and state anxiety were captured at baseline, stress, recovery 1 (+20min), and recovery 2 (+55min).

Results: Comprehensive lifestyle-modification significantly decreased patients' perceived stress compared to control (p< .001) at time point post intervention. Flourishing was significantly increased at 48 weeks (p=.006). No effects on anxiety (p = .075) or depression (p = .146) were evident (all p<0.05). TSST induced a rise of stress parameters in both groups. Significant differences were evident for pulse (Δ=6.99bpm; p=.015), adrenaline (Δ=-19.07pg/ml; p=.037) and on a ten percent level for state-anxiety (Δ=9.026; p=.066) at stress and for systolic blood pressure (Δ=-10.24mmHg; p=.05) and on a ten-percent-level for adrenocorticotropic hormone at (Δ=2.53ng/ml; p=.067) at recovery 2. Cortisol, noradrenaline, leukocytes, thrombocytes, lymphocytes, monocytes or neutrophiles showed no differences.

Conclusion: A Comprehensive lifestyle-modification program significantly decreased patients' perceived stress and increased flourishing in patients with UC. Those changes in stress perception were supported by results of the TSST under laboratory experimental conditions.

	Lifestyle-modification (n = 47)	Lifestyle-modification TSST (n = 8)	Control (n = 50)	Control TSST (n = 8)
Age years	50.28 ± 11.90 (18 - 74)	44.6 ± 14.3 (18 - 57)	45.54 ± 12.49 (19-71)	49.25 ± 4.30 (43 - 57)
Female n (%)	34 (72.3)	8 (100)	35 (70)	8 (100)
Weight	72.79 ± 14.90 (52-100)	71.13 ± 12.87 (62-97)	70.24 ± 16.86 (49.6 - 150)	61.19 ± 9.72 (51-79)
Height	171.19 ± 9.05 (152 - 196)	173.88 ± 6.11 (167-183)	173.76 ± 9.94 (156 - 197)	169.00 ± 4.00 (164-176)
Anamnestic pattern n (%)				
Proctitis	14 (29.8)	1 (12.5)	15 (30)	3 (37.5)
Left-sided colitis	17 (36.2)	4 (50)	15 (30)	2 (25)
Pancolitis	13 (27.7)	3 (37.5)	17 (34)	3 (37.5)
Missing	3 (6.4)	0 (0)	3 (6)	0 (0)
Time since diagnosis years	18.04 ± 12.00 (2 - 46)	10.50 ± 7.95 (2-24)	14.76 ± 10.99 (1 - 43)	12.63 ± 4.03 (5-17)
Smokers n (%)	2 (4.3)	1 (12.5)	3 (6)	1 (12.5)
Medication intake n (%)				
Steroids	2 (4.3)	0 (0)	0 (0)	0 (0)
Azathioprine	4 (8.5)	2 (25)	3 (6)	0 (0)
Other immunosuppressant	0 (0)	0 (0)	1 (2)	0 (0)
Mesalazine	33 (70.2)	7 (87.5)	34 (68)	7 (87.5)
Herbal medicine	7 (14.9)	0 (0)	15 (30)	1 (12.5)
Biologicals	3 (6.4)	2 (25)	3 (6)	1 (12.5)
Other	8 (17)	0 (0)	12 (24)	2 (25)

[Table 1. Sociodemographic and clinical characteristics]

P1111 ACUTE SEVERE COLITIS: SHORT AND LONG TERM IMPACT OF INFLIXIMAB

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Introduction: Acute severe colitis is a serious complication of inflammatory bowel disease. It can lead to colectomy and death. Its medical treatment has been step forward within the last decades, based on infliximab or cyclosporine as second medical therapy.

Aims & Methods: The aim of this study is to precise the impact of infliximab on the short and long term prognosis of acute severe colitis not responding to corticosteroids.

All patients admitted for acute severe colitis have been retrospectively enrolled, between the years 1994 and 2018. Standard therapy based on intravenous corticosteroids was initially led in all patients. We particularly interested in patients failed to steroids and hence treated with infliximab as second line medication, and we studied the rate of avoiding colectomy in the short and in the long term as well as the rate of clinical and endoscopic remission.

Results: 69 patients with acute severe colitis were reviewed (median age:34y. (15-64y.); 38 females and 31 males). There were 61% with ulcerative colitis, 33% with Crohn's disease and 6% with indeterminate colitis. 32,9% of patients (n=22) failed to corticosteroids. Among them, 9 patients have been treated with Infliximab infusions (5mg/Kg) . 88,8% of them avoided urgent colectomy and where discharged within 4 weeks. All pa-

tients experienced clinical remission within a median follow up of 64,96 mo [6 -234]. 4 patients have undergone a colonoscopy during follow up. Endoscopic remission was noticed in 3 patients and a mucosal healing without complete remission was reported in one patient. Nine other patients have been subsequently treated with Infliximab for active chronic disease. No adverse event was reported during follow up. Colectomy-free survival rates were better in the group of patient treated with infliximab but not significatevily (p=0.695)

Conclusion: Infliximab is an efficient treatement for corticoresistant acute severe colitis as a second line treatment and as a remission promoting factor. It diminished the urgent and distant colectomy without serious adverse effects.

Disclosure: Nothing to disclose

P1112 PEAK USTEKINUMAB CONCENTRATION AFTER INTRAVENOUS LOADING DOSE PREDICTS FAECAL CALPROTECTIN NORMALISATION IN CROHN'S DISEASE: POTENTIAL ROLE FOR THERAPEUTIC DRUG MONITORING?

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Introduction: Up to one third of patients with Crohn's disease do not respond or respond partially to the intravenous loading dose of ustekinumab. This was partially explained by low ustekinumab concentrations during maintenance phase (1). However, exposure-response relationship during induction, particularly during the first 4 weeks following intravenous loading, has not been sufficiently studied in the real-life setting yet.

Aims & Methods: We prospectively investigated the association of ustekinumab induction drug levels to calprotectin normalisation (defined as levels < 100 mg/kg) after intravenous induction in Crohn's disease in a real-life setting.

Ustekinumab drug levels (ELISA assay) at 4 prespecified time points during induction (one hour post-infusion (peak level), week 2, week 4 and week 8) were correlated to faecal calprotectin (Calprest assay) levels at weeks 8, 16 and 24 of starting ustekinumab. We recruited 52 consecutive patients who started ustekinumab due to active Crohn's disease at a tertiary referral university centre. All patients received an intravenous loading dose of ustekinumab (approximately 6 mg/kg as per label, infused over 60 min) followed by 90 mg q 8 weeks maintenance. Median disease duration at start of treatment was 15 years (IQR: 8-23), most patients (35/52 (67%)) had failed previous biological treatment (25 anti-TNF, 9 vedolizumab, 1 both). At inclusion 8/52 (15%) were on systemic steroids. Mann-Whitney U-test and ROC analysis were used to test for differences and identify optimal cut-offs of ustekinumab drug levels to predict calprotectin normalisation.

Results: Median calprotectin decreased from 134 (IQR:72-235) to 80 (IQR: 26-173) by week 8, to 65 (IQR:32-188) by week 16 and 66 (IQR: 35-203) by week 24 of start of ustekinumab. Faecal calprotectin was normal in 27/47 (57%), 23/42 (55%), 26/41 (63%) of patients at week 8, 16 and 24, respectively. Median ustekinumab drug levels were higher at all assessed time points in patients with normal calprotectin at weeks 8, 16 and 24 compared to those with increased calprotectin levels (Table 1). Ustekinumab levels of >94 (sensitivity 85%, specificity 65%, PPV 74%) 1-hour post-infusion, >25 (sensitivity 90%, specificity 56%, PPV 69%) at week 2, >20 (sensitivity 60%, specificity 100%, PPV 100%) at week 4, and >7 (sensitivity 60%, specificity 95%, PPV 94%) at week 8 were identified as optimum cut-offs for calprotectin normalisation at week 8, with similar values for weeks 16 and 24. Importantly, these cut-offs had a high negative predictive values (at 1h post-infusion: 71% and at week 2: 70%) for calprotectin normalisation at 6 months.

Conclusion: Our data indicate that induction concentrations of ustekinumab after an intravenous loading dose, as early as 1 hour after infusion, predict faecal calprotectin normalization during the first 6 months in Crohn's disease. These data indicate that therapeutic drug monitoring of ustekinumab during induction could potentially improve outcomes by identifying patients in need of early proactive dose optimisation.

Ustekinumab concentration [µg/mL], median (IQR)	Faecal calprotectin at week 8		P value	Area under the ROC curve (95% confidence interval)
	<100 mg/kg	≥100 mg/kg		
Peak (1 h after infusion)	111 (98-124)	92 (83-116)	0.033	0.73 (0.56-0.91)
Week 2	32 (28-36)	25 (21-30)	0.005	0.77 (0.61-0.92)
Week 4	20 (16-24)	12 (7-17)	<0.0001	0.82 (0.68-0.96)
Week 8	7 (4-11)	3 (2-5)	<0.0001	0.84 (0.71-0.97)

[Table 1]

References: 1. Verstockt B, Dreesen E, Noman M, Outtier A, van den Berghe N, Aerden I, et al. Ustekinumab exposure-outcome analysis in Crohn's disease only partly explains limited endoscopic remission rates. J Crohns Colitis 2019: 10.1093/ecco-jcc/jjz008. [published ahead of print]

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P1114 EFFECTIVENESS AND EVOLUTION IN THE USE OF USTEKINUMAB IN REAL-LIFE CLINICAL PRACTICE: A SINGLE CENTER EXPERIENCE WITH INTRAVENOUS INDUCTION THERAPY IN REFRACTORY CROHN'S DISEASE PATIENTS

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Introduction: Ustekinumab(UST) is a fully human monoclonal antibody against IL-12/23. It has shown efficacy in inducing and maintaining clinical remission in patients with Crohn's disease (CD). To date UST is approved in Spain only in refractory to AntiTNF CD patients, but information about clinical benefit of UST in patients previously exposed to several biologics in real-life practice is limited.

Aims & Methods: Retrospective cohort study in a tertiary hospital in which 73 CD patients received UST from April 2010 to April 2019 were evaluated. Those who received intravenous dose due to active disease (Harvey-Bradshaw index score [HBI] >4) were considered for the analysis. The maintenance schedule every 8 or 12 weeks was at physicians' discretion. The clinical benefit was defined by the HBI score and evaluated at week 8, 24 and 48.

Results: 68 patients included; median follow up was 5 months (IQR: 1-12). Characteristics of the study population are summarized in Table. All patients were exposed at least one biological treatment (98% anti-TNFα agent and 16% vedolizumab), and 69% more than two.

At week 8, 33% and 45% experienced clinical response and clinical remission, respectively. 41 patients reached 6 months of follow up: 24% and 71% achieved clinical response and clinical remission, respectively. 22 patients reached 12 months of follow up, 18% and 82% experienced clinical response and clinical remission, respectively. During follow-up, 8 patients (15%) required intensification at 90mg sc every 4 weeks (median: 12 months; IQR: 11-13). Of these, 4 had clinical benefit (50% response and 13% remission). Clinical evaluation still pending in 3 cases.

Patients who received UST after failure of only one biologic agent obtained better outcomes than those who received UST after 2 or 3 biologics, although it did not achieved statistical significance (p=0.09).

Withdrawal of UST occurred in 6 (9%) patients along the follow up, due to lack of efficacy in all cases. No adverse event recorded.

Clinical use of UST increased through time: among all patients included 18 (26%) received UST in 2017, 29 (42%) in 2018, and 21 (31%) in the first

trimester of 2019. Moreover, 5 (29%) of patients included in 2017 had previously failed 3 or 4 biologic agent, 7 (24%) in 2018 and 3 (14%) in the first trimester of 2019.

Conclusion: Our real-life clinical experience confirms favorable data of clinical efficacy and safety of UST in refractory CD patients and showed a trend towards an increasing and earlier use of UST.

Disclosure: Nothing to disclose

Median age (IQR) (years)	49 (40-54)
Median duration of the disease until beginning treatment with ustekinumab (IQR) (months)	146 (70-265)
Female gender (%)	31 (46)
Smoking status (%)	18 (26)
Extraintestinal manifestations (%)	57 (84)
Comorbidity (%)	17 (25)
Age at diagnosis: A1, A2 and A3 (%)	7, 53, 7 (10, 80, 10)
Ileal, colonic, ileocolonic, Upper gastrointestinal tract involvement (%)	20, 12, 31, 5 (29, 18, 46, 7)
Inflammatory, stenosing and fistulizing pattern (%)	40, 16, 12 (59, 23, 18)
Perianal disease (%)	30 (44)
Previous bowel surgeries (%)	40 (59)
Previous immunosuppressants (%)	61 (90)
Previous biological treatment (%)	68 (100)
1, 2, 3 or 4 previous biologics (%)	26, 27, 13, 2 (38, 40, 19, 3)
Median number of previous biological treatment (IQR)	2 (1-3)
Concomitant immunosuppressants (%)	15 (22)
Steroids during induction (%)	12 (18)

[Characteristics of the study population]

P1115 USTEKINUMAB IMPROVED WORK PRODUCTIVITY IN PATIENTS WITH MODERATE TO SEVERE ULCERATIVE COLITIS: RESULTS FROM THE PHASE 3 UNIFI INDUCTION AND MAINTENANCE STUDIES

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Introduction: We evaluated the effect of ustekinumab (UST) on work productivity and daily activity in patients with moderate-severe active ulcerative colitis (UC) in the UNIFI induction and maintenance studies.

Aims & Methods: In the induction study, patients were randomized to a single intravenous (IV) dose of placebo (PBO, n=319), UST 130 mg (n=320), or UST ~6 mg/kg (n=322). Patients who were in clinical response 8 wks after receiving UST IV induction were eligible for the maintenance study and randomized to subcutaneous (SC) PBO (n=175), UST 90 mg q12w (n=172), or UST 90 mg q8w (n=176). Work productivity was assessed using the Work Productivity and Activity Impairment Questionnaire (WPAI), a validated tool that assesses work time missed (absenteeism), reduced job effectiveness (presenteeism), overall work impairment, and daily activity impairment due to health over the previous week. The impact of UC on overall daily productivity at home, school, and work was assessed using a visual analog scale (VAS, 0 to 10, 0=no impact at all, 10=impacts very much).

Results: At induction baseline, patients had a mean percent work time missed ranging from 17.7% to 19.3%, impairment while working from 39.1% to 45.3%, overall work impairment from 43.7% to 49.1%, and activity impairment from 51.8% to 52.8%. At Wk8, patients who received UST IV had significantly greater improvement in WPAI domains and daily productivity VAS compared with PBO (Table).

In the maintenance study, UST-treated patients generally maintained or numerically improved WPAI scores, while scores for patients in the PBO group worsened. The mean changes from baseline to Wk44 in work time missed was 4.7% in the SC PBO group, -2.0% (p=0.133) in the SC UST 90-mg-q12w group, and 2.1% (p=0.172) in the SC UST 90-mg-q8w group, impairment while working was 7.4%, -1.6 (p=0.017), and -6.4% (p< 0.001),

respectively; overall work impairment was 7.7%, -2.2% (p=0.013), and -6.1% (p<0.001), respectively; and activity impairment was 9.3%, 0.8% (p=0.002), and -4.2% (p< 0.001), respectively. Mean changes from baseline to Wk44 in daily productivity VAS scores were 1.0, -0.2 (p<0.001), and -0.5 (p<0.001), respectively.

Domain	PBO IV	UST IV 130mg	UST IV ~6mg/kg
WPAI % work time missed due to health	-3.7% (30.41%)	-5.9%* (31.39%)	-9.1%** (23.84%)
WPAI % impairment while working due to health	-6.9% (21.89%)	-15.1%* (29.17%)	-20.4%† (24.11%)
WPAI % overall work impairment due to health	-8.0% (24.83%)	-17.2%** (30.36%)	-21.8† (26.26%)
WPAI % activity impairment due to health	-10.9% (28.66%)	-17.7%** (29.45%)	-20.8%† (26.27%)
Impact on daily productivity at home, school and work VAS (0-10)	-1.3 (2.95)	-2.3† (3.03)	-2.3† (2.84)

*p<0.05, **p<0.01, †p<0.001

[Mean (standard deviation) changes from baseline to Wk8 in WPAI and daily productivity VAS results during the induction study]

Conclusion: Patients who received UST IV induction reported significantly greater improvement in work productivity and daily activity compared with PBO. In patients who responded to UST IV induction, those who received UST SC maintenance through Wk44 sustained or improved the levels of work productivity and activity that were achieved during induction.
Disclosure: Drs. Naessens is an employee of Janssen Pharmaceutica, NV. Dr. Han is an employee of Janssen Global Services, LLC. Drs. Zhang, Johanns, and Marano are all employees of Janssen Research & Development. LLC. Dr. Sands is an investigator for Janssen Research & Development, LLC

P1116 MANAGEMENT AND OUTCOMES OF ANTI-DRUG ANTIBODIES TO INFLIXIMAB, A LONG-TERM OBSERVATIONAL STUDY

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Introduction: Secondary loss of response (LOR) to Infliximab (IFX) occurs in up to 40% of IBD patients. One of the causes of LOR is the development of anti-drug antibodies (ADAs) which neutralize IFX. At present, evidence regarding the optimal management of ADAs is lacking.
Aims & Methods: This is a long-term retrospective observational study of adult patients receiving IFX who developed ADAs >8mg/L over a study period of 3 years. This study reviewed the optimisation of Infliximab therapy and subsequent outcomes in patients who developed ADAs. The primary aim of this study is to identify the best practice of management of ADAs to IFX to avoid discontinuation of therapy/LOR and to identify predictors of development of ADAs. Secondary aims include review of adverse outcomes following development of ADAs.
Results: 132 patients with IBD and 1 patient with collagenous colitis are included in the study. Baseline characteristics include 54% male, mean age of 39.4, mean IFX drug trough level 4.7 mg/L, mean ADA level 103 mg/L, 25% were on a previous biologic and 26% were on combination therapy prior to the development of ADAs.
52% of patients discontinued IFX- 72% due to LOR, 16% due to clinical remission, 12% due to infusion reaction.
Both an increase in IFX and adjustments to combination therapy (increase in IFX + addition/increase in immunomodulator) were associated with lower rates of discontinuation of treatment vs no intervention (P-Value < 0.001, P-Value < 0.001 respectively). No difference was seen with adjustment of immunomodulator therapy alone (P-Value= 0.62). An increase in IFX resulted in a significant difference in ADAs and IFX trough levels pre and post intervention (P-Value < 0.001, P-Value = 0.032).
There was a significant reduction in ADAs overtime for the entire cohort (Mean of 103 mg/L vs mean of 55 mg/L on follow-up, P-Value= 0.008) and a correlation was noted with ADAs and low drug trough levels (P-Value= 0.056). No significant correlation was found between the presence of ADAs and CRP, fecal calprotectin or serum albumin. 15% were admitted

to hospital, 11% underwent surgery, 19% required steroids. 32% switched to another biologic- 63% of patients were switched to Adalimumab.
Conclusion: A high percentage of patients who develop ADAs to IFX experience LOR. A reduction in ADA levels was seen due to proactive drug monitoring. Both escalation of IFX alone and combination therapy resulted in lower rates of LOR. Our most common practice post LOR due to ADAs was to switch within drug class.
Disclosure: Nothing to disclose

P1117 THIOPURINE WITHDRAWAL DURING SUSTAINED CLINICAL REMISSION IN CROHN'S DISEASE

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Introduction: Cessation of thiopurines (TP) in patients with Crohn's disease (CD) in clinical remission (CR) is controversial.
Aims & Methods: To describe the evolution of CD patients who discontinued TP and to detect predictors of reactivation after withdrawal. An observational unicentric retrospective study was conducted including CD patients in clinical remission who discontinued TP.
Results: We included 39 patients with CD in remission (51.3% females; 26 inflammatory, 8 stricturing and 5 penetrating behaviour; 9 with terminal ileum involvement, 4 colonic, 26 ileocolonic, and 11 with perianal disease). TP were indicated to maintain remission after steroids in 27 (69.2%), to prevent postoperative recurrence in 8 (20.5%), and to induce remission as part of a combination therapy in 4 (10.3%).
Median azathioprine dose was 150 mg/day. Median duration of TP treatment was 5.3 years (p25-p75: 3.3-7.2) and of steroid-free remission 60.9 months (p25-p75: 32.4-76.6). Reasons for TP withdrawal were patient's choice/request in 10 (25.6%), physician proposal in 27 (69.2%) and drug-related adverse events in 2 (5.15%). By the time of TP discontinuation, median C reactive protein (CRP) was 2.5 mg/L (p25-p75: 1-3.8), faecal calprotectin (FC) 37 µg/g (p25-p75: 16-80) and mean Harvey-Bradshaw Index (HBI) 0.2.
Relapse was observed in 17 patients (43.6%), after a median follow-up of 47 (p25-p75: 26.2 – 81.5) months. Median time until relapse was 17 (p25-p75: 7-33.2) months. At relapse, median CRP was 6.6 (3-18) mg/L, FC 429 (340.5-479.5) µg/g and mean HBI 5.5. After relapse, 4 (21.1%) patients restarted TP; 4 (21.1%) were prescribed one single course of CE without further therapy; 2 (10.5%) one course of CE and TP reintroduction; 2 (10.5%) CE and a biological agent; 1 (5.3%) CE, a biological agent and mesalazine, 1 (5.3%) methotrexate; 1 (5.3%) low dose TP with allopurinol and CE and 1 (5.3%) underwent surgery.
During follow-up, 3 (17.6%) patients received another single course of CE, 1 (5.9%) needed surgery and 2 (11.8%) both. Mean follow-up of non-relapsing patients was 30.4 (13.9-49.2) months.TP treatment duration of shorter than 5 years before discontinuation, was associated to a higher risk for relapse (HR 3.69 p< 0.01).
Conclusion: TP withdrawal is possible in patients with CD in sustained clinical remission; however, almost half of them can relapse.
Disclosure: Nothing to disclose

P1118 IS THE SWITCH TO A SECOND THIOPURINE A SAFE STRATEGY IN ELDERLY PATIENTS WITH INFLAMMATORY BOWEL DISEASE? A MULTICENTRE COHORT STUDY OF THE ENEIDA REGISTRY

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Introduction: Thiopurines are the most commonly used immunosuppressants in inflammatory bowel disease (IBD), but their main limitation is the high rate of drug-related adverse events (AE) and treatment discontinuation. Switching to a second thiopurine may be an alternative in these cases, but series published up to now, include a limited number of patients. In a previous study, we demonstrated that starting thiopurines in elderly age is associated with a higher incidence of AE.

Aims & Methods: Our aim was to evaluate the tolerance of switch to a second thiopurine as well as the persistence of treatment and the factors associated with it. Based on the ENEIDA registry (a large, prospectively maintained database of the Spanish Working Group in IBD -GETECCU), adult IBD patients that switch to a second thiopurine due to AE were identified. Two cohorts were selected regarding the age at the beginning of thiopurine treatment: between 18-50 years, and over 60 years. The rate and concordance of AE that occurred with the second thiopurine, treatment discontinuation due to AE and the overall persistence of the second thiopurine were evaluated.

Results: Of the 17,371 patients who started a first thiopurine in these two cohorts, 3,903 patients discontinued thiopurine treatment due to AE. In 1,278 of them (32%) a switch to a second thiopurine was performed (93% to mercaptopurine, 7% to azathioprine), 1,105 patients below 50 years of age and 173 over 60 years. The AE of the first thiopurine were: digestive intolerance 60%, hepatotoxicity 13%, myelotoxicity 6%, acute pancreatitis 2%, other 19%. The rate of post-switch AEs was 58%, leading to the discontinuation due to AE of the second-thiopurine in 46% of cases. In those patients who presented post-switch AE, the most likely AE was the same that occurred with the first thiopurine, particularly digestive intolerance (61%). The cumulative probability of post-switch treatment discontinuation due to AE was 40%, 43%, 47% and 50% at 6 months, 1-3-5 years, respectively. The persistence of post-switch treatment was 44%, 40% and 34% at 1-3-5 years, respectively. The multivariate analysis showed that the only independent risk factors of treatment discontinuation due to AE were the switch over 60 years (53% vs. 45%, OR 1.5: 95% CI 1.1-2.1), having developed digestive intolerance (48% vs. 41%, OR 1.4: 95% CI 1.1-1.8) or pancreatitis (83% vs. 45%, OR 6.8: 95% CI 2.6-18.2) with the first thiopurine.

Conclusion: In the largest series reported to date, we observed that switch to a second thiopurine is a valid strategy except in the case of pancreatitis. Close monitoring is advisable among elderly IBD patients switching to a second thiopurines because of AEs.

Disclosure: Nothing to disclose

P1119 LONG-TERM OUTCOME OF ACUTE SEVERE ULCERATIVE COLITIS RESPONDING TO INTRAVENOUS STEROIDS: A MULTICENTRE COHORT STUDY

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Introduction: Acute severe ulcerative colitis (ASUC) is a life-threatening condition that occurs in up to 25% of patients with UC. Intravenous steroids (IVS) are effective in nearly two-thirds of patients. Few data are available on long-term outcomes of patients responding to IVS. ECCO guidelines recommended maintenance therapy with thiopurine in thiopurine-naïve patients and a biological agent in patients with previous thiopurine-failure.

Aims & Methods: We performed a retrospective observational study of consecutive patients with UC, hospitalized for ASUC (as defined by Truelve and Witts' criteria), among four tertiary centres in Paris area, between January 2006 and December 2017. Patients included responded to IVS. Relapse was defined as partial Mayo Clinic score ≥ 3 and/or any subscore >1 and the initiation of second line therapy. Patients with Crohn's disease or inflammatory bowel disease unclassified, and those in whom biologics were initiated before response to IVS could be assessed were not included. Disease activity was assessed using the Lichtiger index and the partial Mayo Clinic score. Endoscopic activity was assessed using partial Mayo Clinic endoscopic subscore and UCEIS. Relapse-free and Colectomy survival was studied with Kaplan-Meier method, log-rank test and Cox regression model.

Results: 142 patients (70 (49.3%) male; median age: 33.9 [IQR 25.5-48.1] years; UC duration 1.4 [0.1-4.3] yrs; 79 (55.6%) patients with pancolitis; 100 (70.4%) with no history of immunomodulator and biological agent use) were included in this study. At inclusion, patients had a mean total Mayo Clinic score of 10.0 ± 1.0, a mean Lichtiger index of 13.1 ± 2.2, a CRP serum level of 91.9 ± 75.4 mg/L and a mean UCEIS of 4.8 ± 1.2. Deep ulcerations were observed in 24.3% of the cases. Median hospital stay was of 8 (6-10) days. Maintenance therapy included 5-ASA in 59 (41.5%) patients, immunomodulators in 54 (38.0%), anti-TNF agents in 18 (12.7%) and vedolizumab in 5 (3.5%). More patients were treated with 5-ASA in the naïve group (54.0% vs. 11.9%, p< 0.001) and with biological agents in the failure group (47.6% vs. 3.0%, p< 0.001) whereas no difference was noted for immunomodulators (40.5% vs. 43.0%, p = 0.85). After a median follow-up of 4.8 (2.6-7.3) years, 90 (63.4%) of the 142 patients relapsed and 12 (8.5%) required colectomy. The probabilities of relapse-free survival were 58.1%, 47.8%, 45.5%, 41.9% and 39.8 % at 1, 2, 3, 4 and 5 years, respectively. The multivariate analysis demonstrated that patients treated with 5-ASA (HR=1.59, 95%CI[1.01-2.49], p=0.04) were more likely to experience failure whereas patients with < 6 stools/day at day 3 (HR=0.40, 95%CI[0.21-0.77], p=0.006) and partial Mayo Clinic score < 2 at day 5 (HR=0.48, 95%CI[0.30-0.77], p=0.003) were less likely to experience failure. There was no difference in failure-free survival between the naïve and failure group. The probabilities of colectomy-free survival were 95.8%, 95.0%, 93.2% and 92.1% at 90.9% at 1, 2, 3, 4 and 5 years, respectively. The multivariate analysis demonstrated that patients with Lichtiger index > 12 (HR=10.1, 95%CI[1.30-78.55], p=0.03) were more likely to experience colectomy.

Conclusion: In patients with ASUC responding to IVS, there was a high failure rate of the initial maintenance therapy with only 40% of patients still in clinical remission at 5 years. Conversely, the colectomy rate was less than 10% at 5 years. Improvement in maintenance therapy after ASUC responding to IVS is needed.

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P1120 TRANSLATIONAL STUDIES IN NONHUMAN PRIMATES AND HUMAN VOLUNTEERS SUPPORT THE PHASE 2 PROGRAM FOR RAVAGALIMAB IN MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS

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Introduction: Inhibition of cellular activation of lymphocytes, macrophages, and dendritic cells via interference between cluster of differentiation 40 (CD40) and its ligand (CD40L) represents an attractive target in inflammatory bowel disease (IBD). In chronic inflammatory conditions, non-hematopoietic, tissue-resident cells, such as epithelial and endothelial cells, can also express CD40, and its stimulation contributes to tissue damage. Preclinical studies with anti-mouse CD40 antagonist and agonist monoclonal antibodies (mAbs) have demonstrated that CD40 signaling is required to induce and maintain intestinal inflammation in mouse models of IBD. We developed a humanized anti-CD40 mAb antagonist, ravagalimab, as a potential therapeutic in IBD.
Aims & Methods: To test the ability of ravagalimab to block the development of T cell-dependent responses, we immunized cynomolgus monkeys with keyhole limpet hemocyanin (KLH) and assessed suppression of anti-KLH immunoglobulins M and G (IgM and IgG). In addition, healthy volunteers received single or multiple doses of ravagalimab and the functional effect of CD40 receptor blockade on CD40L-mediated induction of p38 phosphorylation was analyzed ex vivo in B cells.
Results: Ravagalimab exhibited exclusive antagonist activity in vitro. It exhibited immunosuppressive pharmacology when evaluated for T-cell-dependent antibody response in cynomolgus monkeys, completely inhibiting formation of KLH-specific IgM and IgG when compared with vehicle-treated animals. CD40 receptor occupancy on B cells from healthy subjects increased rapidly following intravenous administration of ravagalimab, reaching maximum occupancy of >90% within 1 to 3 days. This maximum receptor occupancy was maintained for up to 4 weeks (in a dose-dependent manner) after the last dose of ravagalimab. During maximum receptor occupancy, ravagalimab was able to fully inhibit CD40L-mediated induction of p38 phosphorylation in B cells from healthy subjects. Importantly, when full receptor occupancy was lost, CD40L-mediated induction of p38 phosphorylation was completely restored, indicating that the inhibition is reversible. Based on these translational studies, a clinical study to evaluate efficacy, safety, and pharmacokinetics of ravagalimab as a treatment for patients with moderately to severely active ulcerative colitis (UC) is presently conducted as a multicenter proof-of-concept study (clinicaltrials.gov, NCT03695185). The primary endpoint is the proportion of patients with endoscopic improvement (Mayo endoscopic subscore of 0 or 1) at week 8 as assessed by central endoscopy reading.
Conclusion: Translational evidence from an animal model and human cell assays strongly supports testing of the anti-CD40 antagonist mAb ravagalimab in a phase 2a study in patients with UC.
Disclosure: Stefan Schreiber has received consulting fees and/or lectured for AbbVie, Amgen, Biogen, Bristol-Myers Squibb, Boehringer, Celltrion, Janssen, Merck, Pfizer, Roche, and Takeda. Stephen H. Clarke, Bradford L. McRae, Robert G. Caldwell, Ahmed Nader, Gabriela Alperovich, and Andreas Lazar are full-time employees of AbbVie and may own stock or stock options.

P1121 IMPACT OF BIOLOGIC TREATMENT OF CROHN'S DISEASE ON HEALTHCARE RESOURCE UTILIZATION IN US PATIENTS

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Introduction: This study compared healthcare resource utilization (HCRU) among Crohn's Disease (CD) patients currently prescribed biologics and CD patients not currently prescribed biologics.

Aims & Methods: Adult (18+ years) patients with ≥1 CD diagnosis code (ICD-9: 555.x; ICD-10:K50.x) from January 1, 2017 to December 31, 2017 were included in this retrospective analysis of medical and pharmacy claims data from the IBM Marketscan Commercial, Medicaid, and Medicare-Supplemental Claims database. Patients with an Ulcerative Colitis diagnosis were excluded from this study. Subgroups analyses were conducted to compare CD patients prescribed biologics and CD patients not prescribed biologics during 2017. A two-sample t-test was conducted to compare continuous variables and chi-squared tests were used to compare categorical variables.
Results: A total of 49,292 CD were included in this analysis; 16,613 (33.7%) were prescribed a biologic and 32,679 (66.3%) were not prescribed a biologic. Biologic users were more likely to be male (46.7% vs. 41.0%; p<0.001) and younger (mean age: 40.51 vs. 46.79 years; p<0.001) when compared to patients not prescribed a biologic. Biologic users were more likely to be prescribed immunomodulators (21.9% vs/ 13.3%; p<0.001) and corticosteroids (40.8% vs. 34.3%; p<0.001), while patients not receiving biologics were more likely to be prescribed 5-ASAs (29.9% vs. 16.5%; p<0.001). Biologic users were also more likely to have gastroenterologist visits (75.1% vs. 52.2%; p<0.001). Patients not prescribed biologics were more likely to have ER visits (38.8% vs. 32.0%; p<0.001) and inpatient hospital visits (20.6% vs. 17.3%; p<0.001).
Conclusion: Medication use was higher among CD biologic users, however CD patients not prescribed biologics had higher HCRU.
Disclosure: Nothing to disclose

P1122 OLAMKICEPT (SGP130FC) DEMONSTRATES TARGET ENGAGEMENT AND INTERLEUKIN-6 PATHWAY INHIBITION ASSOCIATED WITH CLINICAL EFFECTIVENESS IN AN OPEN LABEL TRIAL (FUTURE) IN ACTIVE IBD

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Introduction: Interleukin-6 (IL-6) is a master regulator of inflammatory responses. Immediate IL-6-mediated effects are attributed to classic signalling, following binding of IL-6 to a membrane bound IL-6 receptor complex. In contrast, chronic inflammation is mediated by trans-signalling, in which a complex of circulating soluble IL-6R isoforms (sIL-6R) together with IL-6 can engage virtually every body cell by binding to the ubiquitous gp130 co-receptor. The fusion protein olamkicept (sgp130Fc, FE 999301, TJ301, ola) is a cytokine trap that selectively neutralises IL-6/sIL-6R complexes and hence intercepts trans-signalling(1). In clinical Phase I, ola showed target engagement and excellent tolerability without systemic immune suppression in >50 healthy and patient volunteers. Here, we report the first administration of ola to patients with active IBD in an open label study (FUTURE).
Aims & Methods: FUTURE was a Phase 2a open label study, in which 20 adult patients with active IBD were included (baseline endoscopies) and 16 patients (UC=9, CD=7) were dosed with ola (600 mg iv q 2 weeks for up to 12 weeks plus 42-day safety follow-up). Patients had moderately to severely active UC (Mayo score max. 11 and endoscopic sub-score ≥2) or ileocolonic CD (CDAI 220-500, SES-CD>7), immunologically active inflammation (CRP >5 mg/L), had failed conventional therapies, and had received no more than 2 prior biologics (limited to anti-TNFs and/or vedolizumab). Primary endpoint was the proportion of patients with reduced mucosal expression of a predefined 6-gene score measured by RNA sequencing. Objective assessments included centrally read endoscopies, histology and

various explorative molecular parameters and inflammatory biomarkers. The trial was sponsored and conducted by the University Medical Center Schleswig Holstein under prior approval of the medical faculty's ethics committee and the Paul-Ehrlich Institute (EUDRA-CT 2016-000205-36). Ola was provided by Ferring Pharmaceuticals A/S.

Results: Ola was well tolerated. AEs were unspecific in nature and showed no signs of immune suppression. There were no life-threatening or potentially ola-related SAEs. Activity scores were in the moderate-severe range (Mayo 10, CDAI 330) with high inflammation markers [median CRP/FCP 29.6/1,795] (UC) and 16.4/2,098 (CD)] and with median disease duration of 5.3 (UC) and 6.9 (CD) years. Pharmacokinetic studies showed stable and sustained exposure in plasma concentrations. Target engagement of olamkicept was confirmed by whole-blood STAT3 phosphorylation assays in all patients. Overall, 55% of patients with UC responded (5/9) and 22% (2/9) reached remission (Mayo), and 28% (2/7) CD patients responded with 14% (1/7) reaching remission. All patients in clinical remission also showed endoscopic healing. The primary endpoint was achieved in 12,5% (n=2/16) patients and was highly predictive of later clinical endoscopic and histologic remission. Blood transcriptome analysis showed early molecular anti-inflammatory signature (as early as 4 h after treatment) in all patients, irrespective of treatment outcome.

Conclusion: TThe first human efficacy data with ola indicate anti-inflammatory efficacy of IL-6 trans-signalling inhibition in patients with IBD. This preliminary signal appears to be stronger in UC than in CD. A larger, placebo-controlled, multinational Phase II study examining olamkicept (TJ301) in moderately to severely active UC is currently conducted in China and other East Asian countries (NCT03235752).

References: Jostock T, Müllberg J, Özbek S, Atreya R, Blinn G, Voltz N, Fischer M, et al. Soluble gp130 is the natural inhibitor of soluble interleukin-6 receptor transsignaling responses. European Journal of Biochemistry 2001;268:160-167.

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P1123 EFFICACY, SAFETY AND COST-EFFICIENCY OF ADALIMUMAB 80 MG EVERY OTHER WEEK IN PREVIOUSLY INTENSIFIED PATIENTS ON ADALIMUMAB 40 MG EVERY WEEK

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Introduction: Dose escalation is often recommended for loss of response in patients with inflammatory bowel disease (IBD) under maintenance treatment with anti-TNF, but this strategy considerably increases the costs. A new presentation of adalimumab (ADA) 80 mg has been approved with a similar price per unit in our hospital as the ADA 40 mg presentation.

Aims & Methods: The aim of this study was to evaluate the efficacy, safety and cost-efficiency of ADA 80 mg every other week (eow) in IBD patients under intensified treatment with ADA 40 mg every week.

Material and methods: A prospective and observational study was performed. Inclusion criteria were all IBD patients under intensified maintenance therapy with ADA 40 mg every week. Patients were informed about the reasons (cost and convenience) for switching to ADA 80 mg eow and asked for their consent. Follow-up time was 6 months. The Harvey Bradshaw index (HBI ≤4) and the Mayo partial index (Mayo partial index ≤2) were used to evaluate clinical remission in Crohn's disease (CD) and ulcerative colitis (UC) patients, respectively. Adverse events were monitored. Faecal calprotectin (FC) and C reactive protein (CRP) were evaluated at baseline (week 0, before first dose of subcutaneous injection of ADA 80mg) and at months 1, 2 and 6. Biological remission was defined as clinical remission, together with FC < 250 µg/g and CRP < 5 mg/dL. Trough drug concentrations and drug antibodies were measured at baseline and

at months 1, 2 and 6 by ELISA (Promonitor). Trough levels < 5 mg/L were considered as infratherapeutic. A descriptive analysis was performed and data are shown as percentage, median and range. Cost-efficacy analysis was also performed.

Results: Sixteen patients were included (15 CD and one extensive UC, median age 40 years, 56.3% male, 37.5% non-smokers and 31.3% ex-smokers). In CD, 46.7% had ileal disease, 13.3% colonic disease and 40% ileocolonic disease. 46.7% CD patients presented fistulising behaviour. At baseline, 86.7% of patients were in clinical remission and 92.3% were in clinical remission after 1 month. Median FC concentration and CRP concentration from baseline to month 6 are shown in Table 1.

	At month 0	At month 1	At month 2	At month 6
Median fecal calprotectin (µg /g) (range)	317 (6-1900)	223 (10-3754)	92 (32-4527)	82 (7-3772)
Median C reactive protein (mg/dL) (range)	0.14 (0-19)	0.44 (0.01-2.94)	0.41 (0.01-6.95)	0.16 (0.01-1.08)

[Median faecal calprotectin and C reactive protein in IBD patients under maintenance treatment con adalimumab 80 mg every other week]

60%, 53,3% and 68,8% of patients were in biological remission at month 0, 1 and 2, respectively. No adverse events were registered. No significant differences in trough levels concentrations were observed from baseline to month 2, but 7% of patients had trough levels < 5 mg/L. At month 6, three patients withdrew ADA 80mg treatment because of relapse, none of them were in biological remission at inclusion. The remaining patients maintained clinical remission; 61.5% of them were in biological remission. After six months, including only patients in remission that completed the treatment, a total of 114,000 € were saved with the new schedule of treatment.

Conclusion: Changing to a single dose ADA 80 mg eow is an effective, safe and efficient strategy in IBD patients under intensified maintenance therapy with ADA 40 mg every week.

Disclosure: Nothing to disclose

P1124 SPERMIDINE TREATMENT AMELIORATES EXPERIMENTAL COLITIS in vivo

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Introduction: Genetic variants within the gene locus encoding protein tyrosine phosphatase non-receptor type 2 (PTPN2) are associated with an increased risk for inflammatory bowel disease (IBD). In the intestine of IBD patients, cellular levels of the natural polyamine spermidine are reduced. We have already demonstrated, that spermidine activates PTPN2 and thereby supresses pro-inflammatory effects *in vitro* and *in vivo*. These effects are even further enhanced in immune cells derived from PTPN2 variant IBD patients, however the molecular mechanisms underlying the anti-inflammatory properties of spermidine remain poorly defined.

Aims & Methods: The aim of this study was to investigate the effect and molecular mechanisms of spermidine treatment in a T-cell mediated mouse colitis.

To induce intestinal inflammation, Rag2^{-/-} immunodeficient mice were injected intraperitoneally with wild-type (WT) or PTPN2-deficient (KO) naïve T-cells. Spermidine (3mM) was administered in the drinking water throughout the experiment. Colitis severity was evaluated by using mouse endoscopy, histological analysis of the colon, and myeloperoxidase activity. To assess T-cell subsets, flow cytometry was performed on lamina propria lymphocytes (LPL).

Results: Spermidine treatment significantly ameliorated colitis symptoms, as observed by decreased weight loss (p< 0.001), reduction of endoscopic colitis scores (p< 0.001), absence of colon shortening (p< 0.01) and lower signs of inflammation in histological assessment of the terminal colon (p< 0.001) in mice receiving WT T-cells and KO T-cells. In addition, myeloperoxidase activity, a measurement of infiltrating myeloid cells was signifi-

cantly reduced (p< 0.001) in mice receiving spermidine when compared to untreated mice. Furthermore, administration of spermidine resulted in a significant reduction of CD4^{+} T-cell numbers (p< 0.01) in LPL of mice receiving WT T-cells, but not in mice receiving KO T-cells. Interestingly upon spermidine treatment, relative abundance of neither IFN-γ[+] T helper (Th) 1 cells, IL-17^{+} Th17 cells nor IL-17^{+}IFN-γ[+] Th1/17 was affected in mice receiving WT T-cells or KO T-cells.

Conclusion: Our results demonstrate that spermidine treatment significantly ameliorates T-cell induced colitis. Interestingly, the mode of action of spermidine is not dependent on presence of PTPN2 in T-cells, which implicates that spermidine treatment might have a local effect on the mucosa and or other stromal cells. Nevertheless, our findings indicate that spermidine administration might be a promising novel therapeutic strategy for IBD treatment.

Disclosure: Nothing to disclose

P1125 IDENTIFICATION OF BIOMARKERS AND MECHANISTIC INSIGHT FOR UPADACITINIB IN CROHN'S DISEASE: SERUM INFLAMMATORY MEDIATOR ANALYSIS FROM THE PHASE 2B CELEST STUDY

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Introduction: The CELEST study (NCT02365649) evaluated the selective Janus kinase-1 (JAK-1) inhibitor upadacitinib (UPA) in patients with moderately to severely active Crohn's disease (CD). Improvements in clinical and endoscopic outcomes and a safety profile consistent with that reported in rheumatoid arthritis trials were observed.[1,2] Here we report pharmacodynamic profiling of serum inflammatory mediators in CELEST patients with the aim of understanding UPA mechanism of action in CD and linking biomarkers to intestinal inflammation, abdominal pain (AP), and stool frequency (SF).

Aims & Methods: CELEST was a Phase 2, multicenter, randomized, double-blind, placebo (PBO)-controlled study designed to evaluate the efficacy and safety of multiple dosing regimens of UPA versus PBO in adult patients with an inadequate response or intolerance to immunomodulators and/or TNF inhibitors.[1,2] Serum samples from the baseline (BL) visit and the end of the induction period (Wk 16) were analyzed by the OLINK® inflammation panel (92 proteins) and by Singulex immunoassay for interleukin-17A (IL-17A), IL-17C, IL-17F, IL-22, and IL-23p19. Protein level changes (BL-Wk 16) were analyzed by an ANCOVA model where the BL protein level was adjusted as a covariate and the treatment effect was considered significant when a false discovery rate < 0.10 was observed after multiplicity adjustment on F-test p-values. Spearman rank correlation coefficients (r_s) were used to determine relationships between BL levels or BL-Wk 16 level changes of serum biomarkers (also including serum C-reactive protein and fecal calprotectin) and improvements in Simple Endoscopic Score for CD (SES-CD), AP, and SF.

Results: Paired BL and Wk 16 serum samples were available from 104 patients (UPA 3 mg twice daily [BID], n=18; 6 mg BID, n=19; 12 mg BID, n=13; 24 mg BID, n=18; 24 mg once daily, n=18; and PBO, n=18). UPA treatment significantly reduced expression of serum pro-inflammatory mediators (Table) that are associated with immune cell migration, type I/II interferon (IFN) responses, T cell activation, T helper cell-1 (Th1) responses, and CD8+ T cell responses. Additionally, numerical changes for modulation of mediators of macrophage and dendritic cell activity, hematopoiesis, and neuroprotection were observed. UPA treatment did not significantly modulate expression of IL-23/Th17-related serum cytokines in CD. Correlations were observed for BL-Wk 16 changes in serum proteins and SES-CD, AP, or SF. Importantly, oncostatin-M reductions correlated with SES-CD (r_s=0.35, p=0.02) and with SF improvement (r_s=0.33, p=0.04), suggesting similar drivers of these aspects of disease. AP improvement correlated with reductions in CSF-1 (r_s=0.37, p=0.01), TNFRSF9 (r_s=0.34, p=0.03), IL-12B (r_s=0.31, p=0.07), CXCL9 (r_s=0.31, p=0.07), and CD8A (r_s=0.31, p=0.09), which are all associated with the Th1/CD8/IFN-γ pathway.

Conclusion: This analysis of inflammatory mediators in serum of CD patients from CELEST identifies potential pharmacodynamic biomarkers and mechanistic insights for the JAK-1 inhibitor, UPA. These data suggest that

UPA has a differentiated mechanism from therapies targeting IL-12/23 p40 and IL-23 p19. Correlations between biomarker changes and changes in signs, symptoms, and intestinal inflammation of CD suggest that UPA may drive improvement of these aspects of CD through distinct mechanisms.

Biomarker	p-value
TNFRSF9	0.01
CXCL10	0.01
CCL19	0.01
PD-L1	0.03
CXCL9	0.03
CXCL11	0.03
TNFB	0.04
CD5	0.08
IL-18	0.08
CCL23	0.08
SLAMF1	0.09

[Biomarkers displaying BL-Wk 16 changes (all reductions) meeting the statistical cut-off with calculated FDR adjusted p-values]

References: 1. Sandborn WJ et al. DDW 2017 [Abstract #874h]. 2. Panés J et al. ECCO 2018 [Abstract #P273]. 3. Olink proteomics website, https://www.olink.com/products/inflammation-2/, accessed Mar 28, 2019.

P1126 PREGNANCY OUTCOMES IN WOMEN EXPOSED TO GOLIMUMAB - UPDATE

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Introduction: Rheumatologic disorders and inflammatory bowel disease (IBD) can affect women of childbearing potential. Golimumab (GLM) is approved for rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), non-radiographic axial spondyloarthritis (nr-axial SpA), polyarticular juvenile idiopathic arthritis (pJIA) and ulcerative colitis (UC). To characterize pregnancy outcomes in patients treated with GLM, data obtained from maternal exposure to GLM are presented.

Aims & Methods: This dataset includes individual patient cases reported to the manufacturer through 06 April 2018. Cases retrieved included prospectively reported (ie, pregnancy outcome not known when first reported) and retrospectively reported (ie, pregnancy outcome known when first reported) maternal exposures to GLM during pregnancy or within 2 months prior to conception, and a reported pregnancy outcome. Cases originated from various sources, including spontaneous reporting, clinical studies, and registries.

Results: Two hundred nine pregnancy cases with reported outcomes (113 rheumatological, 37 UC, and 59 others) were identified. Of these 209 cases, 128 were prospective and 81 were retrospective. Overall, 9 congenital anomalies were reported (1 in UC). A total of 50 spontaneous abortions were noted (23.9%). Of these, 22.0% (11/50) received GLM in combination with MTX. Detailed outcomes are provided in Table 1.

Conclusion: The rates of congenital malformations and spontaneous abortions were consistent with published background rates for the general population. Limitations of this analysis included the lack of a direct com-

parison group, the variable amount of data available in the reports, and the possible bias towards reporting more negative outcomes in retrospective cases.

Pregnancy Outcome

	Count (%)	Rheum	UC	Other	Congenital Anomaly	MTX(a)
Prospective cases						
Live birth(b)	90 (70.3)	45 (66.2)	17 (73.9)	28 (75.7)	1 (25)	10 (45.4)
Spontaneous abortion	23 (18.0)	16 (23.5)	3 (13.0)	4 (10.8)	0	8 (36.4)
Elective/Induced abortion(c)	13 (10.2)	6 (8.8)	2 (8.7)	5 (13.5)	3 (75)	3 (13.6)
Ectopic pregnancy	2 (1.6)	1 (1.5)	1 (4.3)	0	0	1 (4.5)
Total	**128**	**68**	**23**	**37**	**4**	**22**
Retrospective cases						
Live birth(d,e)	49 (60.5)	26 (57.8)	8 (57.1)	15 (68.2)	5 (100)	3 (37.5)
Spontaneous abortion	27 (33.3)	16 (35.6)	5 (35.7)	6 (27.3)	0	3 (37.5)
Elective/Induced abortion	4 (4.9)	2 (4.4)	1 (7.1)	1 (4.5)	0	1 (12.5)
Ruptured ectopic	1 (1.2)	1 (2.2)	0	0	0	1 (12.5)
Total	**81**	**45**	**14**	**22**	**5**	**8**
Grand total	**209**	**113**	**37**	**59**	**9**	**30**

Rheum=RA, AS, PsA (a) Patient received MTX at the time of conception/during pregnancy. (b) The count includes 6 cases with pregnancy outcome live birth with AEs: Low birth weight baby (3), Premature baby (2); Feeding disorder neonatal, Jaundice and Respiratory distress (reported once each) and 1 case with congenital anomaly Foetal macrosomia. (c) The count includes 3 cases with congenital anomalies: Anencephaly, Down syndrome and Turner's syndrome. (d) The count includes 6 cases with pregnancy outcome live birth with AEs: Premature baby (2); Bradycardia foetal, Colitis ulcerative, Fungal infection, Gastric disorder, Low birth weight baby, Milk allergy, Rash generalised and Sepsis. (e) The count includes 5 cases with congenital anomalies: Atrial septal defect, Cataract congenital, Congenital anomaly, Ellis-van Creveld syndrome, Galactosaemia and Heart disease congenital.

[Table 1: Summary of Pregnancy Outcomes in Patients Treated With GLM]

Disclosure: Authors are employees of Janssen Research & Development or Janssen Biologics BV

P1127 TREATMENT OUTCOMES FOLLOWING ADMINISTRATION OF VEDOLIZUMAB IN PATIENTS WITH MODERATE TO SEVERE ULCERATIVE COLITIS

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Introduction: The anti-integrin monoclonal antibody vedolizumab (VDZ) has been approved for the treatment of moderate to severe ulcerative colitis (UC). There is a need for evaluating the clinical efficacy of VDZ in real-world clinical settings. In addition, the effect of VDZ on the endoscopic activity of UC and its ability to induce mucosal healing are still being explored.

Aims & Methods: We aimed to report the clinical and endoscopic response to VDZ in a large cohort of Greek patients with UC who were refractory to previous therapies. Patients were recruited from 11 tertiary Greek IBD centers. VDZ was administered according to standard induction and maintenance protocols. Short-term response was evaluated at week 12 and defined according to the Gemini 1 criteria (reduction in the Mayo Clinic score

of at least 3 points and a decrease of at least 30% from baseline, with a decrease of at least 1 point on the rectal bleeding subscale or an absolute rectal bleeding score of 0 or 1). Long-term efficacy was evaluated at week 54. Persistence of treatment at week 54 was considered as an indicator of clinical efficacy. The Gemini 1 Criteria for remission at 54 weeks (full Mayo score of 2 or lower and no subscore higher than 1) were also independently applied. Mucosal healing was defined as endoscopy Mayo score of 0.

Results: In total, 97 patients with UC [males=57, mean age: 45, (range: 17-79 years)] have been included in the study. Three patients had proctitis (E1), 37 left-sided colitis (E2), and 57 extensive disease (E3). Twenty-three patients (23.7%) had at least one active extraintestinal manifestation at VDZ commencement. There were 53 anti-TNF naive patients. We present herein data from the 78 patients who have completed at least one-year from initiation of VDZ treatment.

Short-term response data: At wks 12-14, 17/78 patients (21.8%) exhibited no response, while 61/78 (78.2%) fulfilled criteria for clinical response. Twenty-two patients (28.2%) were on concomitant treatment with corticosteroids and 13 (16.7%) with azathioprine/6-mercaptopurine. A colonoscopy at 12-14 wks was performed in 48 patients; 27% had complete mucosal healing (endo Mayo score=0), whereas an additional 48% had partial endoscopic response (decrease in endoscopic Mayo Score). We observed statistically significant improvement in patient-reported outcomes (PRO) from week 0 to week 12 of treatment with VDZ. In particular, PRO-UC1/rectal bleeding decreased from 1.22 ± 0.98 to 0.32 ± 0.65, ($P< 0.0001$) and PRO-UC2/number of bowel movements from 2.69 ±1.12 to 1.51 ± 0.78, ($P< 0.0001$), whereas SIBDQ score increased from 43 ± 13 to 55 ± 10, ($P< 0.0001$).

Long-term response data: At week 54, 52/78 patients were still on VDZ therapy (drug persistence: 68%). Less than 10% of patients were receiving concomitant steroids and 15% azathioprine/6-mercaptopurine. Of the patients who had a colonoscopy at week 52 (n=30), 30% demonstrated complete mucosal healing and another 43% had a partial endoscopic response. At wk 54, PRO-UC1/rectal bleeding decreased from 1.34 ± 1.03 to 0.31 ± 0.6, ($P<0.0001$) and PRO-UC2/number of bowel movements from 1.82 ± 1.12 to 0.67 ± 0.88, ($P<0.0001$), whereas SIBDQ score increased from 41 ± 16 to 50 ± 13, p=056).

Conclusion: In this national multicenter study, VDZ demonstrated high response rates both in the short- and long-term evaluations. Satisfactory outcomes were obtained at the clinical and endoscopic measurements combined with improved quality of life. Our study adds to other published data on real-world evidence and supports the notion that VDZ is a reliable therapeutic option for patients with UC.

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P1128 WITHDRAWN

P1129 WITHDRAWN

P1130 LONG-TERM SAFETY AND EFFICACY OF RISANKIZUMAB TREATMENT IN PATIENTS WITH CROHN'S DISEASE: 3-YEAR INTERIM RESULTS FROM THE ONGOING PHASE 2 OPEN-LABEL EXTENSION STUDY

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Introduction: Efficacy and safety of the IL-23 inhibitor risankizumab (RZB) have been previously assessed in pts with moderate-to-severe Crohn's disease (CD) following induction and maintenance treatments.[1,2] Pts who

responded to RZB in the Phase 2 induction and maintenance study[2,3] could enroll in an open-label extension (OLE).[4] Interim safety and efficacy of RZB maintenance treatment, up to 3 yrs, are reported from this ongoing OLE.

Aims & Methods: Pts who achieved clinical response (decrease from BL in CD Activity Index [CDAI] ≥100) without remission (CDAI < 150) after Period 2 (Wk 26) or clinical response and/or remission after Period 3 (Wk 52) of the preceding study[1] were enrolled to receive open-label 180 mg s.c. RZB every 8 wks for up to 206 wks.[4] Pts who lost clinical response or remission after completing the preceding study were re-induced with open-label 600 mg i.v. RZB at Wks 0, 4, 8. Pts receiving re-induction treatment could only receive subsequent 180 mg s.c. RZB every 8 wks if they regained response or remission following re-induction treatment. Ileocolonoscopy with central reading was performed yearly. Treatment-emergent adverse events (AEs) were collected throughout the study up to 20 wks after the last dose of study drug or the data cut-off date of Feb 04, 2019. Efficacy data (clinical remission [CR] and endoscopic remission [ER] [CD Endoscopic Index of Severity (CDEIS) ≤4 or CDEIS ≤2 for pts with isolated ileitis at baseline]) are reported to Wk 104 in the OLE, when all pts enrolled in the OLE had the opportunity to reach the visit date before the interim cut-off date. Non-responder imputation (NRI) was used for binary endpoints.

Results: A total of 65 adults with CD were enrolled, including four pts who were re-induced. Median age was 34 yrs (range 19-67 yrs) and median disease duration was 10 yrs (range 2-38 yrs). Sixty pts (92.3%) were previously exposed to TNF antagonists; 13 pts (20%) and 21 pts (32.3%) were receiving corticosteroids only and immunomodulators only, respectively, and 9 (11.8%) pts were receiving both, prior to BL of the preceding study. At the data cut-off date, mean (SD) exposure to RZB was 866.8 (316.6) days, and 18 (27.7%) pts had prematurely discontinued from the study. At Wk 0 of the current study, 47/65 (72.3%) pts were in CR and 27/63 (42.9%) pts had ER based on the observed data. Both CR and ER were sustained up to Wk 104 (Table). After a median follow-up of 31 months, AEs were reported for 58/65 (89.2%) pts; 22 (33.8%) experienced serious AEs. The most common AEs were nasopharyngitis (29.2%), gastroenteritis (20.0%), fatigue, abdominal pain, and worsening CD (18.5% each), and arthralgia (15.4%). Serious infections were reported in six pts: anal or subcutaneous abscess (1 pt each), *Campylobacter* infection (1 pt), viral gastroenteritis (2 pts), and peritonitis (2 pts). No events of tuberculosis were reported, and no malignancies or deaths occurred.

Conclusion: In this 3-yr interim analysis, both clinical and endoscopic remissions were sustained in pts with CD receiving long-term open-label RZB treatment. The safety profile of RZB remains consistent with previous results.[2] No new safety signals were identified.

	Clinical remission n/N (%)	Endoscopic remission[a] n/N (%)
Week 0[b]	47/65 (72.3)	27/65 (41.5)
Week 8	48/65 (73.9)	–
Week 16	46/65 (70.8)	–
Week 48	46/65 (70.8)	35/65 (53.9)
Week 104	41/65 (63.1)	28/65 (43.1)

All patients in the OLE had the opportunity to reach the Week 104 visit before the cut-off date. [a]Data are from central reading. [b]Visits in OLE.

[Clinical remission and endoscopic remission by visit in patients receiving open-label 180 mg s.c. RZB maintenance treatment (NRI analysis)]

References: 1. Feagan BG et al. Lancet 2017;389:1699-1709. 2. Feagan BG et al. Gastroenterology 2017;152:S1310. 3. Feagan BG et al. Lancet Gastroenterol Hepatol 2018;3:671-680. 4. Ferrante M et al. 2018, UEG Journal 2018;6(Supplement 1) [OP307].

P1131 SUPERIOR OUTCOME WITH EARLY BIOLOGIC-COMBINATION TREATMENT IN CROHN'S DISEASE: DATA FROM AN INTERNATIONAL INCEPTION COHORT

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Introduction: Crohn's disease (CD) is a complex disorder characterized by intestinal inflammation leading to progressive bowel damage. Treatment goals have evolved over preceding years from clinical remission to prevention of structural bowel damage. It is unknown which treatment options/sequences lead to the most optimal outcome in patients with newly diagnosed CD.

Aims & Methods: The aim of this study was to compare different treatment strategies and associated outcomes in early CD. We performed a retrospective study including adult patients with newly diagnosed CD at the Academic Medical Center of Amsterdam (The Netherlands) (September 2013-September 2018) or at the Imelda hospital in Bonheiden, Belgium (January 2009-January 2019). Based on first-line treatment choice, patients were assigned to one of the five pre-defined management groups. Primary outcome was time to treatment failure, defined as a switch to another treatment, escalating CD treatment, need for endoscopic balloon dilation or surgery, CD-associated hospitalization or a new perianal fistula. Kaplan-Meier survival analysis was used to estimate the median treatment survival per group.

Results: One hundred and forty-nine patients were included: treatment with corticosteroids only as first treatment (group 1) was started in 24 patients, immunomodulators (azathioprine, 6-mercaptopurine or methotrexate; group 2) in 70 patients, biological therapy (infliximab, adalimumab or vedolizumab; group 3) in 22 patients, biological therapy in combination with an immunomodulator (group 4) in 21 patients and 12 patients underwent early surgery (group 5).

Baseline characteristics (CRP, CD Endoscopic Index of Severity, Simple Endoscopic Score for CD, smoking status) were similar between treatment groups. Group 5 had significantly more patients with stricturing (Montreal B2) and penetrating (Montreal B3) disease subtypes (Table 1).

Log-rank test revealed significantly longer median treatment survivals in group 5 (215 days; 95% CI 25, 405), group 4 (863 days) and group 3 (321 days; 95% CI 184, 457) compared to median treatment survival in group 2 (119 days; 95% confidence interval (CI) 85, 152) (p≤0.01).

Median treatment survival in group 4 (863 days) was significantly longer compared to group 1 (195 days; 95% CI 139, 251) (p< 0.01) (Table 1).

	Group 1. (n=24)	Group 2. (n=70)	Group 3. (n=22)	Group 4. (n=21)	Group 5. (n=12)	Significance
Baseline (at diagnosis)						
Age (years, mean, [SD])	39 [19]	35 [16]	28 [12]	37 [16]	39 [16]	p=0.15
Active smoker (%)*	35 (n=20)	47 (n=53)	47 (n=15)	36 (n=14)	27 (n=11)	p=0.85
CRP (mg/L, mean, [SD])*	22 [28] (n=15)	29 [33] (n=38)	21 [21] (n=12)	23 [16] (n=10)	65 [79] (n=7)	p=0.51
CDEIS (mean, [SD])*	17 [5] (n=2)	9 [4] (n=14)	13 [4] (n=6)	10 [5] (n=5)	8 [5] (n=6)	p=0.06
SES-CD (mean, [SD])*	18 [14] (n=3)	13 [5] (n=16)	18 [6] (n=6)	13 [8] (n=6)	10 [6] (n=6)	p=0.27
Montreal L1 (%)	38	51	41	43	33	p=0.63
Montreal L2 (%)	16	6	18	24	0	p=0.07
Montreal L3 (%)	46	43	41	33	67	p=0.46
Montreal B1 (%)	54	61	68	71	8	p<0.01
Montreal B2 (%)	8	14	9	24	67	p<0.01
Montreal B3 (%)	8	9	5	5	50	p<0.01
Outcome						
Treatment survival (days, median, [95% CI])	195 [139, 251]	119 [85, 152]	321 [184, 457]	863 days **	215 [25, 405]	p<0.01

[Table 1. *% based on available data indicated by n=(x) **Median survival not reached after median follow-up 751 days; hence 95%-CI cannot be calculate]

Conclusion: These real-world data show superiority of biological treatment, combination therapy and early surgery in newly diagnosed CD patients.

Disclosure: Nothing to disclose

P1132 UTILITY OF VEDOLIZUMAB DRUG LEVEL MONITORING IN IBD PATIENTS - REAL LIFE EXPERIENCE: PILOT STUDY

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Introduction: Therapeutic drug monitoring has become an accepted tool in the therapy management in Inflammatory Bowel Disease (IBD). The assessment of trough levels and neutralising anti-drug antibodies are widely used to optimise the therapeutic management, and its usefulness has been more studied in anti-TNF therapies especially in situations of treatment failure. However, there is not enough data published on the usefulness of the measurement of vedolizumab (VDZ) levels in IBD patients, with no established cut-off points. The objective of our study was to evaluate the correlation between VDZ level at induction and maintenance treatment with the clinical response in patients with IBD.

Aims & Methods: This is a retrospective observational, single center study. We included adult patients with UC and EC treated with VDZ between January and December 2018, VDZ serum levels were prospectively collected before induction at 6, 14 and 24 weeks. Clinical and biochemical response was collected at 14 and 24 weeks. Data was analyzed by classification tree model to establish variables related with remission.

Results: 12 patients were included, 58.3% with UC and 41.7% with CD. 69.2% were women with a mean age of 41 ± 12 and a mean disease duration of 11.5 ± 8.15 years. 91.7% were treated with anti-TNF therapy previously. The median VDZ level was 33.4 mg/ml (26,7 -39,1), 10,3 mg/ml (7,26-12,8), 11,2ug/ml (8,47-14,45) at baseline, week 14 and week 24 respectively.

Clinical remission was achieved in 33.3% (4/12) at week 14, and 41.6% (5/12) at week 24. 33.3% (4/12) in patients who had VDZ level at week 6 between 35 - 47,4 ug/ml.

The only variable that was correlated with the remission at weeks 14 and 24 in the tree model CRT was the VDZ level at week 6 (induction therapy) (Table 1).

Clinical remission Week 14 and 24	VDZ level week 6 (ug/ml)	Prediction certainty (%)
Yes	35 - 47.4	100
No	<35 // >47,4	100

[Table 1]

Conclusion: In our cohort, the only variable that was correlated with the remission at weeks 14 and 24 was the VDZ level at week 6. VDZ level at week 14 and 24 were not correlated with clinical remission.

Disclosure: Nothing to disclose

P1133 RETROSPECTIVE STUDY OF THE EFFECTIVENESS AND SAFETY OF USTEKINUMAB IN REFRACTORY CROHN'S DISEASE

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Introduction: Ustekinumab (UST) is in Belgium increasingly used in moderate to severe Crohn's disease (CD). The goal of the current study was to describe the real-life experience with UST in our tertiary center.

Aims & Methods: A retrospective monocentric study was performed in patients with CD who were started on UST between December 2017 and December 2018. All patients received an initial intravenous dose of 6 mg/kg followed by subcutaneous UST (90 mg, q8). The clinical, biological, endoscopic and radiological response were assessed after the induction (week 4-8) and during the maintenance phase. The clinical, endoscopic and radiological response was based on the physicians' assessment. A biological response was defined as a decrease of ≥50% in C-reactive protein (CRP) and/or fecal calprotectin (FC), remission as a normalization of the parameters.

Results: A total of 51 patients were included, of which the majority was refractory to TNF inhibitors and/or vedolizumab (table 1). The median duration of follow-up was 45 weeks (IQR 24-69). UST was discontinued in 11 patients (21.6%) after a median of 26 weeks (IQR 10-34). Reasons for discontinuation were a loss of response, including 2 patients who were in need of surgery (n=5), primary non response (n=4), malignancy (n=1) and patient's wish (n=1).

The clinical response at short term (4-8 weeks after the initial IV induction), could be assessed in 43 patients: 27/43 patients (62.8%) had a response and 4 patients (9.3%) were in clinical remission. In 12 patients (27.9%) no response was seen. During the maintenance phase patients were assessed at a median of 26 weeks (IQR 23-39). A clinical response in the maintenance period was seen in 25/51 patients (49%) and an additional 12 patients (23.5%) reached remission.

A biological response was achieved in 8/37 patients (21.6%) and biological remission in 16/37 patients (43.2%), the remaining patients (35.1%) showed no response. Endoscopy was performed in 20 patients and an endoscopic response was confirmed in 10/20 patients (50%), remission in 2 patients (10%). The other 8 patients (40%) had no endoscopic response. Radiological evaluation was performed in 21 patients of which 12 showed no response (57.1%), 7/21 (33.3%) had a response and 2 (9.5%) were in radiological remission.

Ten patients (19.6%) were hospitalized for IBD-related complications, most of them for surgery (9/10). Other AEs occurred in 11 patients, most often arthralgia. One patient developed a flare of an underlying spondyloarthropathy and UST was discontinued. A paradoxical worsening of psoriasis was observed in one patient.

Conclusion: In this population of refractory CD patients, UST was efficacious to induce and maintain clinical remission. Endoscopic and radiological response in these preliminary analyses were modest.

Disclosure: Nothing to disclose

Age (years), median [IQR]	41.7 [32.4-53]
Gender (female/male), n [%]	29 [56.9]/22 [43.1]
Age at diagnosis (years), median [IQR]	24.5 [18-34.8]
Duration of disease (years), median [IQR]	12 [8-21]
History of resection, n [%]	29 [58]
Extra-intestinal manifestations, n [%]	19 [37.3]
Immunosuppressant at baseline, n [%]	11 [19.6]
Azathioprine	5 [9.8]
Methotrexate	4 [7.8]
Purinethol	1 [2]
Corticosteroids at baseline, n [%]	24 [47.1]
Previous biologicals, n [%]	
0	3 [5.9]
1	14 [27.5]
2	17 [33.3]
≥ 3	17 [33.3]

[Patient characteristics]

P1134 EFFICACY OF USTEKINUMAB INTENSIFICATION AND RE-INDUCTION IN CROHN'S DISEASE PATIENTS WITH INSUFFICIENT OR LOSS OF RESPONSE

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Introduction: Ustekinumab (UST) has proven to be an efficient maintenance therapy for moderate to severe Crohn's disease (CD). However, a significant percentage of patients treated with subcutaneous maintenance UST experience a secondary loss of response (LOR) or partial response. We evaluated the clinical, biological and endoscopic response to UST optimization including IV re-induction (intravenous UST at a dose of 6 mg/kg) and/or shortening of the dosage interval (mainly every 4 weeks) in this context.

Aims & Methods: A retrospective, single-center study was performed including patients with CD who were treated with maintenance UST and received either IV re-induction and/or shortening of the dosage interval for a partial response or LOR. The clinical and endoscopic response was based on the physician's assessment. A biological response was defined as a decrease of ≥50% in C-reactive protein (CRP) and/or fecal calprotectin (FC); remission as a normalization of these parameters.

Results: Eighteen out of the 51 (35.3%) UST-treated CD patients needed optimization of UST: 2 patients only received IV re-induction, 9 patients only shortening of the dosage interval and 7 patients received both IV re-induction and intensification.

The median time to optimization was 34.5 weeks (IQR 20.3-42.3). Response to dose optimization was assessed at a median of 15.5 weeks (IQR 6.8-19.3).

One of the 2 patients who underwent re-induction alone experienced a good clinical and endoscopic response; the other patient had no clinical, biological nor endoscopic response and UST was discontinued.

A combined re-induction and shortening of the dosage interval was performed in 7 patients. Of these, 6 experienced a clinical response and 1 patient had no response. Biological remission was confirmed in 3/6 patients, whereas the other 3/6 had no biological response. Endoscopic response was observed in 1/3 patients. Despite optimization, UST was ended in one patient due to a persistent LOR.

Nine patients underwent intensification alone, which was successful in inducing a clinical response in 3/9 (33.3%) and a clinical remission in 4/9 (44.4%). Two patients (22.2%) had no clinical response. Biological remission was observed in 4/7 patients (57.1%) and 3/7 patients had no biological response (42.9%). Endoscopic evaluation in 4 patients showed a response in 2/4 and no response in the other 2. In 2/9 patients (22.2%) UST was stopped; one due to LOR and the other patient due to an adverse event (flare of underlying spondyloarthropathy).

Other adverse events (AEs) were seen in 2 patients: 1 patient had arthralgia and 1 patient developed a rash, both AEs were mild and UST could be continued.

Conclusion: About a third of patients treated with maintenance UST underwent optimization. Of these 18 patients, 10 (55.6%) regained a good clinical response and 4 (22.2%) were in clinical remission. UST could be continued in the majority of patients.

Disclosure: Nothing to disclose

P1135 THERAPEUTIC DRUG MONITORING SUPPORTS CLINICAL DECISION MAKING WHEN EMPLOYED BEFORE AND AFTER BIOSIMILAR INFLIXIMAB SWITCHING

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Introduction: Therapeutic drug and anti-drug antibody monitoring (TDM) of infliximab (IFX) is used with increasing regularity as a tool to optimize outcomes in inflammatory bowel disease (IBD). Trough levels (TL) of 2-8 mcg/ml are recommended during maintenance IFX treatment. The introduction of biosimilar infliximab (BI) in 2015 lead to widespread switching of patients from originator infliximab (OI) to BI. The value of TDM when switching to BI has not been defined. This study aimed to assess the impact of TDM testing before and after a managed switch to BI.

Aims & Methods: Individuals with IBD treated with OI and demonstrating a satisfactory response to treatment, were entered in to BI switch programme in Dec 2016. Pre-switch information was provided to patients, virtual or face to face clinical assessment was undertaken and it was recommended that all patients had pre-switch TDM performed. After switching patients returned to routine clinical care. Further TDM was performed at clinician discretion with recommendation to follow published TDM testing guidance (1). Virtual review of all patients was undertaken 2 years post-switch. Demographics, pre and post switch TDM data, OI and BI dosing regimens and other IBD related medications were recorded along with clinical outcome data. Comparative analysis of pre-switch and most contemporary TDM results was performed.

Results: 76 individuals considered to be clinically responding to OI were entered in to the BI switch programme. 70/76 (92%) had TDM at < 3 months pre-switch. OI was discontinued prior to switch in 2 patients. 74 people were switched from OI to BI. 52/74 (70%) were on 5mg/kg 8 weekly OI pre-switch, 38 (51%) were on immunomodulators.

Of 69/74 with pre-switch TDM, 32/69 (46%) had subtherapeutic TLs (< 2mcg/ml). Median pre-switch TL was 2.2 mcg/ml (IQR 1.1-3.4 mcg/ml). Pre-switch TL review lead to 37/74 (50%) receiving an increased dose of BI at switch. In total 47/74 had ≥1 dose escalation at the time of or subsequent to switch.

58/74 (78%) had TDM testing in the 2 years after switch (median no. tests 2; range 1 - 5) at which point 54/74 (73%) remained on BI with sustained clinical response. 49 out of 54 still on BI had both pre and post switch TDM with results demonstrating a statistically significant increase in mean TLs (2.1 vs 6.3 mcg/ml; p< 0.001); only 6% had persisting sub-therapeutic TLs.

Conclusion: High rates of sustained clinical response were observed to occur following a BI switch supported by the use of pre and post switch TDM. TDM dose escalation resulted in a statistically significant increase in TLs, this may account for the rates of continued clinical response.

References: 1. Papamichael K. Frontline Gastroenterol. 2016 Oct;7(4):289-300

Disclosure: Nothing to disclose

P1136 CORRELATION OF VEDOLIZUMAB TROUGH LEVELS WITH CLINICAL AND BIOCHEMICAL MARKERS IN INFLAMMATORY BOWEL DISEASE

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Introduction: The clinical utility of vedolizumab (VDZ) trough levels (VTLs) is not well established.

Aims & Methods: The aim of this study was to determine if there is a correlation between VTLs and clinical and biochemical outcomes. We performed a prospective, cross-sectional study to examine the association between VTLs and clinical and biochemical outcomes. VTLs immediately prior to VDZ infusion were collected simultaneously with CRP and Harvey Bradshaw index (HBI)/Simple Clinical Colitis Activity index (SCCAI) (for Crohn's disease, CD, and ulcerative colitis, UC, respectively). Biochemical remission was defined as CRP ≤ 5 mg/L and clinical remission was defined as HBI ≤ 4 or SCCAI ≤ 2. Combined remission was defined as those meeting criteria for both clinical and biochemical remission. Fishers exact and Mann-Whitney U tests were used to compare groups and ROC analysis to identify a therapeutic threshold.

Results: 45 samples with matched clinical and biochemical data were collected for 43 patients (24 UC, 15 CD and 4 inflammatory bowel disease-unclassified). Approximately equal numbers of patients had 4-weekly VDZ infusions (n=21) compared to 8-weekly (n=22). 25 out of 43 patients (58%) were on concomitant immunomodulation. The median trough level was 18.3 µg/mL (range < 2 - 44.7 µg/mL) and anti-VDZ antibodies were not detected in any patient. No significant difference could be detected between median VTLs for active disease vs combined remission (24.1 µg/mL vs 16.4 µg/mL, p=0.84).

In the UC subgroup, there was a difference in median VTLs between those in biochemical remission compared to those with active disease (24.5 µg/mL vs 7.3 µg/mL, p=0.088). ROC analysis did not identify an optimal therapeutic threshold to achieve combined remission [AUC (95% CI) 0.52 (0.32-0.72)]. However, in the UC cohort a potential therapeutic threshold was identified [AUC (95% CI) 0.76 (0.41-1.0)]. A VTL of 10.7 µg/mL differentiated those with a normal CRP from those with a raised CRP. A comparison (using Fisher's exact test) of the highest vs lowest VTL quartiles did not show a significant difference in the proportion of patients who were in remission vs active disease.

Conclusion: A correlation between VTLs and clinical and biochemical markers of disease activity was not shown. However, in the UC cohort a level of 10.7 µg/mL differentiated those in biochemical remission from those with active disease. This is a preliminary, small sample size study and analysis of VTLs for our entire VDZ cohort is being conducted.

Disclosure: Nothing to disclose

P1137 EFFECT OF VEDOLIZUMAB DOSE INTENSIFICATION ON SERUM DRUG CONCENTRATIONS AND REGAIN OF RESPONSE IN INFLAMMATORY BOWEL DISEASE PATIENTS WITH SECONDARY LOSS OF RESPONSE

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Introduction: Vedolizumab (VDZ) is an approved biological treatment for moderate to severe Crohn's disease (CD) and ulcerative colitis (UC). Patients who lose response on VDZ 300 mg every 8 weeks (Q8W) during maintenance therapy may benefit from dose intensification to VDZ 300 mg every 4 weeks (Q4W). Our aim was to assess the effect of VDZ dose intensification on serum trough levels (TL) and regain of response.

Aims & Methods: We performed a multicenter prospective study from June 2017 through December 2018 including patients with loss of response to VDZ Q8W during maintenance therapy, defined as a total Mayo score >6 for UC, and a HBI score >4 with evidence of inflammation (C-reactive protein (CRP) > 5mg/L, faecal calprotectin >250 mg/kg or confirmation on endoscopic or radiological imaging) for CD. Blood samples (TL and CRP) and clinical variables (partial Mayo and HBI score) were collected at T0 (last infusion of Q8W interval and start of Q4W dosing), T1 (week 4 after dose escalation) and T2 (week 8 after dose escalation). Biological response (CRP ≤5mg/L or decrease of >50% in patients with a CRP >5 mg/L at baseline) and clinical response (decrease of partial Mayo ≥2 points for UC or decrease of HBI ≥3 points for CD) were assessed at T1 and T2. VDZ TL were measured using the vedolizumab ELISA from apDia. Non-parametric and correlation analyses were performed comparing T0, T1 and T2.

Results: A total of 62 patients (34 UC and 28 CD) were included with 28% on concomitant corticosteroids, 11% on azathioprine or 6-MP and 2% on methotrexate. After dose escalation, median (IQR) TL increased from 8.8 (5.1-13.5) µg/ml (T0) to 19 (11.9-22.9) µg/ml (T1) and 23.1 (15.5-28.4) µg/ml (T2) (all p< .0001) with a similar evolution in UC and CD (Table).

UC (n=34)	T0	T1	T2
Median (IQR) TL (µg/ml)	8.1 (4.8-11.6)	17.4 (10.8-21.6)	21.3 (14.3-25)
Median (IQR) CRP (mg/l)	5.8 (1.4-9)	5.7 (1.7-15.4)	3.9 (1.9-11)
Median (IQR) partial Mayo	5 (5-6)	3 (3-5)	3 (1-5)
CD (n=28)	**T0**	**T1**	**T2**
Median (IQR) TL (µg/ml)	9.1 (5.2-16.6)	21.2 (12.4-28.1)	23.6 (19.7-31.7)
Median (IQR) CRP (mg/l)	7.2 (2.8-14.2)	6.4 (2.9-15.1)	4.9 (2.7-9.4)
Median (IQR) HBI	8 (5-13)	4 (1-6)	3 (1-4)

[Table]

In UC patients, partial Mayo score significantly decreased from T0 to T1 (p=0.002) with a trend for further decrease from T1 to T2 (p=0.08). In CD patients, HBI score significantly decreased from T0 to T1 (p=0.002) with a trend for further decrease from T1 to T2 (p=0.07). The decrease in CRP from 6.4 (1.9-12.6) mg/L at T0 to 5.8 (2.1-15.2) mg/L at T1 and 4.4 (2.7-10) mg/L at T2 was not significant (all p>.05) and similar in UC and CD (Table). Also for patients with a CRP at baseline of >5 mg/L, the decrease in CRP from 11.6 (7.2-18.9) mg/L at T0 to 10.1 (5.2-16.7) mg/L at T1 and 8.8 (4.1 - 15.3) mg/L at T2 was not significant (all p>.05) and similar in UC and CD. Biological and clinical response was achieved in 30% and 51% at T1 and 44% and 59% at T2, respectively. The median increase in TL between T0 and T2 was similar between biological responders and non-responders (12.3 (8.3-14.8) vs. 12.4 (7.6-16.1), p=0.78) and clinical responders and

non-responders (14 (10.3-17.4) vs. 12.2 (6.9-14.6), p=0.12). No correlation was found between increase in TL between T0 and T2 and change in CRP, partial Mayo or HBI scores.

Conclusion: Dose escalation of VDZ 300 mg from Q8W to Q4W in UC and CD patients with loss of response results in higher TL at 4 and 8 weeks. Regain of biological and clinical response was observed in 44% and 59% of patients respectively but was not associated with an increase in TL.

Disclosure: Takeda research grant

Other Lower GI Disorders II

09:00-17:00 / Poster Exhibition - Hall 7

P1138 ELECTRICAL CONDUCTIVITY IN *BIFIDOBACTERIUM ANIMALIS SUBSPECIES LACTIS BB-12*

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Introduction: BB-12 is technologically well suited, expressing fermentation activity, high aerotolerance, good stability and a high acid and bile tolerance[1,2]. Because of high redox potential in the colon flora ecosystem, BB-12 is highly resistant bacteria in distress condition. The BB-12 cell envelope is an electrical and physical barrier that can be overcome by pathways that consist of redox proteins.Bacterial cellular electron transfer systems (CET) are defined microbial bioelectrochemical processes in which electrons are transferred from the cytosol to the membrane of the cell[3].Although the strength of BB-12 in the event of stress has been shown previously[2], CET features of BB-12 are not completely identified. Here we first describe that the probiotic bacteria *Bifidobacterium animalis subsp. Lactis BB-12* strain features of CET under the various atmosphere.

Aims & Methods: Mean gut bifidobacterial count of 5 billions (5x109) cfu of Bifidobacterium animalis subsp. Lactis-BB12 (Chr Hansen) were used for the experiment in Yildiz Technical University, Davutpaşa Campus, Science and Arts Faculty, Physics Department. This Bifidobacterium dissolved in 5 millilitres of distilled water and prepared sample

Results: Charge transport behavior and the effect of the RH level on it in the BB-12 film have been investigated by means of I-V measurements. Within water moisture environment, electrical conductivity of the BB-12 increased more than six decades while under N_2 environment conductivity returns to the initial current value(Figure-1). This behaviour in conductivity modulation was reversible at least in the three cycles

Conclusion: This experimental findings showed us that there was no structural transformation under relative humidity. On the other side, increase in the conductivity was interpreted by the increase in the population of charge carries, supplied by the interaction BB-12 with the water moisture, monitored by amine and carboxyl group through FTIR and Zeta potential measurements.The type of surface charge of *Bifidobacterium animalis subsp. lactis BB-12* was found to be negative by zeta potential measurements, claiming that electrons were the charge carriers. Overall, obtained result in this study indicated that *Bifidobacterium animalis subsp. lactis BB-12* has a great potential for humidity sensing device at room temperature

References: 1. Bozkurt, H.S., E. MM Quigley, B. Kara. Bifidobacterium animalis subspecies lactis engineered to produce mycosporin-like amino acids in colorectal cancer prevention. SOM 2019; Vol. 7: 1-5. 2. Ruiz, L., P. R. Madiedo, M. Gueimonde, C. G. de los Reyes-Gavilán.How do bifidobacteria counteract environmental challenges? Mechanisms involved and physiological consequences. Genes Nutr. 2011; 6: 307-318. 3. Light, S. H., L. Su, R. Rivera-Lugo, J. A. Cornejo, A. Louie. A flavin-based extracellular electron transfer mechanism in diverse Gram-positive bacteria. 2018 Nature;562:140-144

Disclosure: Nothing to disclose

P1139 HEAT-TREATED LACTOBACILLI IMPACT MURINE MICROBIOTA COMPOSITION AND PREVENT PATHOGEN-INDUCED INFLAMATION

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Introduction: Probiotics are live microorganisms that, when administered in adequate amounts, confer a health benefit on the host. These benefits can include impacts on digestive health, the host immune system, and the gut-brain axis. Increasing evidence supports a relationship between the gut microbiota, inflammation, host response and health [1-3]. More recently, a number of studies have investigated the potential of heat-treated microorganisms to confer a benefit on humans or animals; these have often been referred to as 'pharmabiotics' [2,4,5].

The therapeutic application of heat-treated microorganisms could be considered to have a number of advantages over living organisms, such as longer shelf life, no cold chain requirements, ease of storage and transport and therefore also potential applications in less developed regions, no risk of infection in vulnerable individuals, no translocation of bacterial-virulence or antibiotic-resistance cassettes if the genetic material has been destroyed by the inactivation step, and no loss of activity when used in conjunction with antibiotics or anti-fungal agents [4-6].

Aims & Methods: We have demonstrated that supplementing the diet with heat-treated *Lactobacillus* LB is capable of subtly modifying both the microbiota and behavior in healthy male mice [6]. In this study we set out to elucidate the role of heat-treated *Lactobacillus* LB in female mice, particularly focusing on the impact on the development of colitis following *Citrobacter* infection. Female mice [N=48] were divided into two groups, one fed standard chow, and one fed chow with a *Lactobacillus* LB preparation (5%). The *Lactobacillus* LB preparation consists of a heat-treated fermentate generated by two *Lactobacillus* strains, *L. fermentum* and *L. delbrueckii*. After four weeks we implemented a *Citrobacter rodentium* infection strategy that is used as a model for several important human intestinal disorders, including Crohn's Disease, Ulcerative Colitis and colon tumorigenesis [7]. Infection with *C. rodentium* results in the colonisation of the large intestine and subsequent mild inflammation that is maintained after the pathogen has been cleared [8]. This allows us to study the effect of the *Lactobacillus* LB preparation on both infection and inflammation. Throughout the experiment samples were collected for 16S rRNA analysis of microbiota, virome analysis, SCFA, and inflammation markers.

Results: Diet supplementation with the *Lactobacillus* LB preparation caused subtle but significant changes in the murine microbiota, with less abundant taxa being most affected. Prolonged consumption had no adverse effect on murine health. The *Lactobacillus* LB preparation did not provide protection against *Citrobacter* infection. However, a reduction of the length of small intestine which occurred in the control-fed *Citrobacter* infected animals was prevented by the supplemented diet. An increase of colon crypt length in control-fed *Citrobacter* infected animals was also prevented. Overall, our results suggest that the *Lactobacillus* LB preparation diet has a reproducible effect on microbiota composition and diversity, as well as limiting the effect of *Citrobacter* induced inflammation in animals.

Conclusion: This study provides evidence for the effect of heat-treated bacteria (and their metabolites) on the murine microbiota, on infection-induced inflammation and on the behaviour of healthy mice. Preparations containing heat-treated microorganisms, or pharmabiotics, can be safe and effective interventions to impact on the microbiome and on host health.

References: [1] Dinan TG & Cryan JF. The Microbiome-Gut-Brain Axis in Health and Disease. Gastroenterol Clin North Am 2017;46(1):77-89. [2] Giron F & Quigley EMM. Pharmabiotic Manipulation of the Microbiota in Gastrointestinal Disorders: A Clinical Perspective. J Neurogastroenterol Motil 2018;24(3):355-366 [3] Pedersen HK, et al. Human gut microbes impact host serum metabolome and insulin sensitivity. Nature 2016;535(7612):376-81. [4] Taverniti V & Guglielmetti S. The immunomodulatory properties of probiotic microorganisms beyond their viability (ghost probiotics: proposal of paraprobiotic concept). Genes Nutr 2011;6(3):261-74. [5] de Almada CN, et al. Paraprobiotics: Evidences on their ability to modify biological responses, inactivation methods and perspectives on their application in foods. Trends Food Sci Technol 2016;58:96-114. [6] Warda AK, et al. Heat-killed lactobacilli alter both microbiota composition and behaviour. Behav Brain Res 2018;362:213-23. [7] Collins JW, et al. Citrobacter rodentium: infection, inflammation and the microbiota. Nat Rev Microbiol 2014;12(9):612-23. [8]

Wiles S, et al. Organ specificity, colonization and clearance dynamics in vivo following oral challenges with the murine pathogen Citrobacter rodentium. Cell Microbiol 2004;6(10):963-72.

Disclosure: This study was funded by Adare Pharmaceuticals, who produced the Lactobacillus LB preparation. Adare had no part in the conduct of the experiments or in the interpretation of the data.

P1140 CHARACTERIZATION OF THE MUCOSAL MICROBIOME IN FAMILIAL ADENOMATOUS POLYPOSIS PATIENTS WITH INTACT COLON OR SUBJECTED TO POUCH SURGERY

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Introduction: Surgical treatment represents the gold standard for Familial Adenomatous Polyposis (FAP) patients with profuse disease. Most FAP patients undergo proctocolectomy with j-pouch, and pouchitis is emerging as a recurrent post-surgical complication. Alterations in the intestinal microbial community play a pivotal role in intestinal inflammation and have been found in UC patients with pouchitis. However, the impact of intestinal dysbiosis on pouchitis onset in FAP patients remains poorly characterized.

Aims & Methods: In this pilot study, we aimed to characterize the mucosal microbiome structure in FAP patients and to establish whether intestinal dysbiosis may contribute to the development of pouchitis in these patients. Sixteen patients with a clinical and genetic diagnosis of FAP (age > 18 years) were enrolled. Microbiome analysis was performed by 16S rRNA gene sequencing using an Illumina platform on DNA samples extracted from intestinal biopsies.Microbiome characterization was available for fifteen out of sixteen FAP patients. Active pouchitis was defined as a Pouchitis Disease Activity Index (PDAI) ≥ 7. We first analyzed differences in taxon relative abundance among patients with intact colon (n=6) or those who underwent hemicolectomy with ileocolic anastomosis (n=1) (Group 1; n=7) and patients who underwent proctocolectomy with ileal-pouch-anal-anastomosis (IPAA) (n=6) or those who underwent colectomy with ileo-rectal-anastomosis (IRA) (n=2) (Group 2; n=8). Moreover, among patients belonging to the Group 2 we analyzed differences between patients with healthy pouch (Group 2A; n=5) and patients with pouchitis (Group 2B; n=3).

Results: According to the PDAI score 3 out of 8 patients within the Group 2 received a diagnosis of chronic and active pouchitis. Microbiome sequencing demonstrated a reduction in the relative abundance of Actinobacteria (4.39% *vs.* 0.52%) and Bacteroidetes (28.95% *vs.* 10.11%) phyla (Families: Coriobacteriaceae and Bacteroidaceae, respectively) associated with increased levels of Proteobacteria (34.05% *vs.* 59.32%) phylum (Family: Pseudomonadaceae) in patients within the Group 2 compared with Group 1. Among patients belonging to the Group 2, patients with pouchitis (Group 2B) showed decreased abundance of Bacteroidetes (15.95% *vs.* 0.36%) and Firmicutes (31.58% *vs.* 8.83%) phyla and had a microbiota almost entirely represented by Proteobacteria (46.08% *vs.* 81.39%) (mainly Oxalobacteriaceae and Pseudomonadaceae families) compared with healthy pouch patients (Group 2A).

Conclusion: Our findings suggest that alterations in the mucosal microbiota could be involved in the development of pouchitis in FAP patients subjected to proctocolectomy with j-pouch and that gut microbiota characterization in these patients may help clinicians determining the efficacy of antibiotic therapies. Further studies are warranted on larger series to confirm these data.

Disclosure: Nothing to disclose

P1141 THE STUDY ON THE CHANGES AND ROLES OF INTESTINAL BACTERIA MICROBIOTA IN CORONARY HEART DISEASE COMPLICATED WITH NONALCOHOLIC FATTY LIVER DISEASE

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Introduction: Previous study reported that patients who suffered coronary heart disease (CHD) complicated with non-alcoholic fatty liver disease (NAFLD) had worse cardiac function and clinical outcomes than patients with CHD only. Notably, the mechanism was still unclear. Previous study focused on the role of metabolism in CHD patients complicated with NAFLD (CHD-NAFLD) and evidence showed that the microbiota was an important factor in metabolism. Therefore, this study aimed to investigate the characteristics and effects of intestinal bacteria microbiota in CHD-NAFLD patients.

Aims & Methods: People were recruited and divided into three groups, including CHD patients (without NAFLD), CHD-NAFLD patients and healthy controls (HCs). Each group contained 24 people. Fecal samples and clinical information from three groups were carefully collected. The Illumina sequencing of 16S rRNA gene V3-4 region amplicons sequencing was applied to profile the overall structure of the fecal bacterial microbiota. Based on the Operational Taxonomic Units (OTUs), the characteristics of the bacterial microbiota of the sample and the correlation with clinical indexes were analyzed.

Results: In analysis of clinical information, CHD patients showed an increase in uric acid and triglycerides compared with HCs. The CHD-NAFLD patients showed a further increase in BMI, uric acid and triglyceride. In investigation of bacterial profile, we firstly compared the overall CHD patients (including CHD-NAFLD patients and CHD patients) with HCs. As a result, there was a significant reduction in the abundance of *Parabacteroides* and *Collinsella*. We further analyzed the difference of bacterial composition in between CHD-NAFLD and CHD patients. The intestinal bacterial microbiota in CHD-NAFLD patients showed an increase in the abundance of *Copococcus* and *Veillonella*, and a reduction in the abundance of *Parabacteroides*, *Bacteroides_fragilis*, *Bifidobacterium_longum_subsp_infantis*, *Ruminococcus_gnavus* and *Bacteroides_dorei*. Among them, the abundance of *Ruminococcus_gnavus* and *Bacteroides_dorei* was significantly lower than that in CHD patients. Additionally, spearman's correlation was performed to clarify the correlation between bacterial microbiota and clinical indexes. BMI was positively correlated with the abundance of *Copococcus* and negatively correlated with the abundance of *Bifidobacterium_longum_subsp_infantis*. The abundance of *Veillonella* was positively correlated with LDL-C and AST. The abundance of *Bacteroides_dorei* was negatively correlated with ALT, AST and LDL-C. These data indicated that the abundance of intestinal bacterial microbiota was closely related to the changes in clinical indexes.

Conclusion: Changes of intestinal bacterial microbiota in CHD-NAFLD patients may be important factors affecting the degree of metabolic disorder, which may be one of the important reasons for the worse clinical outcome and disease progression in CHD-NAFLD patients than in CHD patients.

Disclosure: Nothing to disclose

P1142 THE STUDY ON THE CHANGES AND ROLES OF INTESTINAL FUNGAL MICROBIOTA IN CORONARY HEART DISEASE COMPLICATED WITH NONALCOHOLIC FATTY LIVER DISEASE

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Introduction: Patients who suffered coronary heart disease (CHD) complicated with non-alcoholic fatty liver disease (NAFLD) were reported to have worse cardiac function and clinical outcomes than patients with CHD only. However, it was not clear about the mechanism. Previous study focused

on the role of metabolism in CHD patients complicated with NAFLD (CHD-NAFLD). Lots of evidence showed that the metabolism could be regulated by the microbiota. The research on gut microbiota mainly focused on bacteria, and there were few studies related to fungi. Therefore, this study aimed to investigate the characteristics and effects of intestinal fungal microbiota in CHD-NAFLD patients.

Aims & Methods: People were recruited and divided into three groups, including CHD patients (without NAFLD), CHD-NAFLD patients, and healthy controls (HCs). Each group contained 24 people. Fecal samples and clinical information were carefully collected. The microbial genome DNA was extracted and the internal transcribed spacer (ITS) 3-4 rDNA was amplified. Illumina sequencing platform was used for high-throughput sequencing analysis. Based on the Operational Taxonomic Units (OTUs), the characteristics of the fungal microbiota of the sample and the correlation with clinical indexes were analyzed.

Results: In analysis of clinical information in recruited subjects, CHD patients showed an increase in uric acid and triglycerides compared with HCs. The CHD-NAFLD patients showed a further increase in BMI, uric acid and triglyceride. In investigation of fungal profile, we firstly compared the overall CHD patients (including CHD-NAFLD patients and CHD patients) with HCs and found the significant reduction in the abundance of *Exophiala_attenuata* and *Malassezia_restricta*. We further analyzed the difference of fungal composition in between CHD-NAFLD and CHD patients. The intestinal fungal microbiota in CHD-NAFLD patients showed an increase in the abundance of *Preussia*, *Xylodon* and *Cladorrhinum*, and a reduction in the abundance of *Candida_glabrata* and *Ganoderma*. Among them, the abundance of *Ganoderma* was significantly lower than that in CHD patients. Additionally, we used spearman's correlation to clarify the correlation between fungal microbiota and clinical indexes. The ejection fraction was negatively correlated to the abundance of *Xylodon*. Uric acid was positively correlated with the abundance of *Cladorrhin um* and *Preussia*. These data indicated that the abundance of intestinal fungal microbiota was closely related to the changes in clinical indexes.

Conclusion: Therefore, these changes of intestinal fungal microbiota in CHD-NAFLD patients may be important factors affecting the degree of metabolic disorder. But there are few reports on these fungi. More studies are needed to confirm the effects of these fungi on human.

Disclosure: Nothing to disclose

P1143 THE EFFECT OF BILE ACIDS AS A MAJOR REGULATOR OF INTESTINAL MICROBIOTA, ESPECIALLY ON DIFFERENT PARTS OF THE MICE COLON

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Introduction: Bile acids are the end products of hepatic cholesterol metabolism, assembled in the liver and they are the major regulators of intestinal microbiota. Human bile acids are mainly occupied by cholic acid(CA), chenodeoxycholic acid(CDCA), deoxycholic acid(DCA) and lithocholic acid(LCA). Since most of the bile acids secreted into the intestine are reused through the enterohepatic circulation, continuous oral administration of certain bile acids result in an increased composition ratio in the bile acid pool.[1] Each of bile acids have a varying degree of hydrophobicity and pH, so the influence on microbiotas also varies.[2,3] Rodent cecum is largely developed and there is a large amout of mictobiotas in it, so food is known to be kneaded and digested here. That is why many animal experimental studies use and analyze the strain of rodent cecum as an alternative of human. However, since cecum is not developed in humans, it is necessary to confirm that the same results are obtained in the cecum and the rest of colon of rodents.

Aims & Methods: We examined the effect of each bile acids on various microbiotas in vitro and tried to find out whether similar changes occurred in the intestines by artificially increasing the fraction of specific bile acids, especially on different parts of colon.

1. We analyzed the effects of each bile acids on the various microbiotas using the disk diffusion method commonly used for microbial susceptibility test.

2. The 6 weeks-old-male C57BL/6 mices were treated with five bile acids(CA, CDCA, DCA, LCA, UDCA (ursodeoxycholic acid) and vehicle). In six groups each bile acids were delivered at a dose of 15 mg/kg/day via the transgastric rout. Fecal samples were collected every week and also the feces directly from the colon were collected on the day of the sacrifice and were separated from the cecal feces. The bacterial population was analyzed by real-time PCR and general population of bactreias were measured by universal bacterial primer.

Results: As a result of the test for susceptibility to bile acids, the inhibitory effect on the micrbiotas of each bile acid was various, and the microbiotas found in the bile or intestinal tract were less inhibited overall than the strains found in other organs. Most of the repressed strains were inhibited by DCA and CDCA, but were also affected by other bile acids and were not consistent.

When the remainder of the rest of colon and the cecum were analyzed separately, it was reported that the total number of strains were increased in the CA and LCA administration groups in the colon except the cecum, but it was reported to be reversed in the cecum. In rest of colon, Firmicutes, a phylum known to be associated with obesity, were found to be lower than Phylum Bacterioidetes, but higher in cecum.

The results of the microbial susceptibility test for a major strains of mice were somewhat in agreement with the number of microbiotas in rest of colon, but not in the cecum.

Conclusion: Bile acids have a remarkable inhibitory effect on intestinal micrbiotas, which varies according to the type of strain and bile acid. The effect of bile acids on microbiotas in the intestinal tract is similar to that of microbial susceptibility tests and this result was significant in the colon except the cecum. The artificial control of bile acid composition can read to change the environment of bowel microbiotas. Examinations of animal models to replace human beings may be more meaningful in colon except cecum.

References: 1. Qi Y, Jiang C et al. Bile acid signaling in lipid metabolism: metabolomic and lipidomic analysis of lipid and bile acid markers linked to anti-obesity and anti-diabetes in mice. Biochim Biophys Acta 2015;1851:19. 2. Sandhya Bansal et. al. Bile Acid Amphiphiles with Tunable Head Groups as Highly Selective Antitubercular Agents. Med. Chem. Commun., 2014;5:1761 3. Begley M et. al. Gahan CG, Hill C. The interaction between bacteria and bile. FEMS Microbiol Rev 2005;29:625.

Disclosure: Nothing to disclose

P1144 DIFFERENT INTESTINAL BACTERIOCIN PRODUCTION IN COLORECTAL NEOPLASIA IN MALES AND FEMALES

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Introduction: Colorectal carcinoma (CRC) is the third most frequently diagnosed malignancy in males and the second most common malignancy in females. There were 1,006.000 new CRC diagnoses in males and 794.900 in females in 2018 worldwide. Bacteriocins are small proteins, which are produced by the *Enterobacteriaceae* bacteria, especially by *Escherichia coli*. Bacteriocins are divided into more groups, colicins and microcins are the most important ones. Colicins and microcins do possess not only antibacterial, proapoptotic and probiotic properties, but some of them have shown significant biological activity against different cancer cells *in vitro* and *in vivo* conditions. In general, colorectal neoplasia are more frequent in males.

Aims & Methods: The aim of this prospective study was to evaluate natural colicin and microcin production by large intestinal mucosal bacteria at each stage of colorectal neoplasia in males and females.

A total of 63 patients with colorectal neoplasia and 20 controls were enrolled into the study. Three groups of patients with colorectal neoplasia were included: individuals with non-advanced colorectal adenoma, non-a-A (11 men, 10 women, mean age 63±10), patients with advanced

colorectal adenoma, a-A (13 men, 7 women, mean age 65±9) and subjects with CRC (12 men, 10 women, mean age 70±10). Advanced colorectal adenoma fulfilled the following criteria: an adenoma with low grade dysplasia larger than 10 mm and/or containing high grade dysplasia being of any size and/or adenoma of any size with villous component. Control group consisted from 7 men and 13 women (mean age 57±14) with normal findings on screening colonoscopy and with negative history of colorectal neoplasia. We used the original methodology reported by our group. After appropriate microbiological culture bacteriocin production by each strain was investigated by PCR methods.

Results: A total of 239 mucosal biopsies were taken (52 controls, 63 non-a-A, 60 a-A, 64 CRC) and samples were further investigated. A total of 522 *Escherichia coli* and related strains were investigated for bacteriocin production.

There was a significantly higher colicin production in each group of colorectal neoplasia compared to controls, p< 0.01.

There was a significantly higher microcin production in each group of colorectal neoplasia compared to controls, p< 0.05.

Colicin production in men increased dramatically at the stage of CRC and differed significantly compared to production of colicins in females at the stage of CRC, p< 0.001.

There was a later onset of increased production of microcins observed during the adenoma-carcinoma sequence in men compared to women: statistically higher production of microcins was observed in females compared to males at the stage of a-A, p=0.001. Subsequently, microcin production decreased in females and increased in males at the stage of CRC, when males produced microcins significantly more frequently compared to females, p=0.023.

Conclusion: Strains isolated from the large bowel mucosa in patients with colorectal neoplasia produce bacteriocins more frequently compared to those with normal findings on colonoscopy.

Fundamental differences in colicin and microcin production have been confirmed between males and females.

References: Kohoutova et al. Escherichia coli strains of phylogenetic group B2 and D and bacteriocin production are associated with advanced colorectal neoplasia. BMC Infect Dis 2014; 14: 733. Kohoutova et al. Bacteriocin Production by Mucosal Bacteria in Current and Previous Colorectal Neoplasia. Gastroenterology 2018; 154(6), Supplement 1: Page S-413.

Disclosure: Nothing to disclose

P1145 GROWTH INHIBITION OF CLOSTRIDIUM DIFFICILE BY THE INTESTINAL ISOLATES FROM HUMAN FECES: INVESTIGATION OF KEY MICROBIOTA IN FMT (FECAL MICROBIOTA TRANSPLANTATION)

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Introduction: *Clostridium difficile* is gram-positive, anaerobic, and a spore forming, a common bacterium of the human intestine. Over the past decades, the incidence and severity of *C. difficile* infection (CDI) have increased.

Despite the clinical trial, treatment of patients with refractory CDI and those with multiple CDI recurrences is limited, and there is an ongoing for continued research to improve the outcomes these patients

Fecal Microbiota Transplantation (FMT) as an alternative treatment has been shown to be an effective treatment for recurrent and refractory CDI. However, its mechanism and a key bacteria were still unknown. In this study, we investigated the intestinal isolates to inhibit the growth of *C. difficile.*

Aims & Methods: Intestinal bacteria strains were isolated from fecal sample and identified by the 16S rRNA gene analysis. Each isolate and *C. difficile* was sub-cultivated in the broth media at 37 °C under anaerobic conditions. *C. difficile* culture was spreading on the agar plates and sterilized disc laid on the plate. Then, impregnated on the disc with the culture supernatant which removed bacteria. The plate was observed after 48hr incubation in anaerobic environment.

Results: More than forty genera including *Enterococcus, Clostridium, Bacillus, Lactobacillus, Bifidobacterium, Eubacterium* were isolated from human fecal sample. Among them, 5 strains of *Lactobacillus* and 4 strains of *Bifi-*

dobacterium were shown to suppress *C. difficile* growth. These belonged to *B. longum, B. pseudocatenulatum, B. adolescentis, B. dentium, L. ruminis, L. rhamnosus, L. sakei, L. salivarius,* and *L. gasseri.* Also, we confirmed *Coprococcus* and *Ruminococcus* species can inhibit *C. difficile* growth.

Conclusion: We found some of *Bifidobacterium* species and *Lactobacillus* species from human feces could partially suppress against *C. difficile* colonization. These results suggested a potential that some of *Bifidobacterium* species and *Lactobacillus* species could be helpful in preventing CDI. Therefore, these bacteria will be anticipated to play a crucial role in FMT for CDI treatment in the future.

Disclosure: Nothing to disclose

P1146 INTERNALLY APPLIED ULTRAVIOLET LIGHT AS A NOVEL APPROACH FOR EFFECTIVE AND SAFE ANTI-MICROBIAL TREATMENT

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Introduction: With emergence of microbial resistance and superbugs, there is a crucial need for safe, highly effective antimicrobial treatments with broad applicability to invasive pathogenic bacteria and fungi. Ultraviolet-C light (200-280 nm) is germicidal but associated with neoplastic transformation in humans. Ultraviolet-A (UVA, 320-400 nm) phototherapy reduces (epi)dermal inflammation without significant adverse effects but has not been evaluated in internal viscera. We aimed to assess the *in-vitro* bactericidal efficacy and *in-vivo* safety of intracolonic UVA using a novel light delivery system.

Aims & Methods: Customized optical rods (D=4mm, L=40mm) were designed to homogenously side-emit UVA. A mercury vapor lamp served as light source (Asahi Max-303), and UV bandwidth/irradiance peaks were assessed (Ocean Optics; Extech). UVA intensities used in this study were less than natural sunlight. (Table 1) *In-vitro* tests were performed using microbial liquid cultures of various enteric pathogens. Cultures exposed to UVA at 20-min intervals were compared to unexposed control cultures and transferred to solid medium plates for CFU counts. *In-vivo* testing of UVA effects on normal colon were performed using BALB/cJ mice (n=10, male=5). Under anesthesia, 5 mice underwent colonic UVA exposure (2,000 µW/cm²) for 30 minutes via an optic rod introduced anally up to the splenic flexure as compared to 5 mice treated with the same technique with an unlit optic rod. Rigid endoscopy (Olympus A37027A) was used to evaluate the mucosa before and serially after UVA exposure. Endoscopic videos were blindly interpreted by two gastroenterologists with expertise in animal model endoscopies. Full thickness microscopic assessments were performed by a blinded pathologist on Swiss-roll preparations of the whole colon.

Results: Exposure to UVA was associated with a significant reduction in concentrations of various microbes, including *Clostridioides difficile* and *Candida albicans* (Table 1). The germicidal effects increased with greater time of exposure. Proteus mirabilis and Pseudomonas aeruginosa did not reveal any growth after 20 and 40 minutes of exposure, respectively. During *in-vivo* tests no perforation or fatalities were seen after light exposure. No evidence of erythema, mucosal friability or bleeding was observed during endoscopies. No chronic inflammation or dysplasia was seen on examined full-thickness colonic specimens exposed to UVA.

Conclusion: UVA light exposure exhibits significant *in-vitro* bactericidal effects in array of clinically important bacteria, including *C. difficile.* UVA is also effective against *C. albicans* which may prevent fungal bloom following antibacterial treatment. In this first study of intracolonic UVA application, UVA exposure is not associated with endoscopic or histologic injury. UVA therapy can potentially provide an effective and safe novel antimicrobial approach to the treatment of enteric infections and inflammation. Future studies are required to assess the antimicrobial and anti-inflammatory effects of UVA phototherapy on internal organs.

Microorganism	UVA Intensity ($\mu W/cm^2$)	Group	Baseline CFUx10^7/mL	20 min CFUx10^7/mL	P value	40 min CFUx10^7/mL	P value	60 min CFUx10^7/mL	P value
Clostridioides difficile	2,000	Exposed Control	0.1 0.1	0.08 0.13	0.01	0.01 0.17	0.003	0.0031 0.39	0.01
Candida albicans	1,700	Exposed Control	0.14 0.14	0.09 0.17	0.007	0.03 0.2	0.001	0.0032 0.16	0.001
Pseudomonas aeruginosa	3,500	Exposed Control	0.81 0.81	0.07 0.61	<0.001	No growth 0.93	<0.001	No growth 0.85	<0.001
Klebsiella pneumoniae	1,300	Exposed Control	5.9 5.9	6.34 7.49	0.17	3.34 10.5	<0.001	1.53 13.81	<0.001
Escherichia coli	1,300	Exposed Control	1.25 1.25	0.41 3.31	<0.001	0.21 4.2	0.001	0.03 5.52	<0.001
Enterococcus faecalis	2,400	Exposed Control	9.21 9.21	2.99 10.6	0.1	0.61 14.72	0.01	0.08 17.74	0.01
Streptococcus pyogenes	1,800	Exposed Control	1.17 1.17	0.68 0.83	0.64	0.64 1.68	0.001	0.17 1.31	0.004
Proteus mirabilis	2,400	Exposed Control	0.62 0.62	No growth 0.59	<0.001	No growth 0.49	<0.001	No growth 0.54	<0.001
Staphylococcus epidermidis	2,150	Exposed Control	0.57 0.57	0.43 0.59	0.01	0.03 0.69	<0.001	0.0001 0.7	<0.001

[Concentration of microbes in the liquid suspension before and after UVA therapy as compared to unexposed controls.]

P1147 COLORECTAL CANCER SCREENING AND CHOICE OF THE POSITIVE CUT-OFF LEVEL. ARE FRENCH DECISION MAKING CRITERIA OPTIMAL IN RELATION TO A PERSON'S EQUAL ACCESS TO COLONOSCOPY IN REGARDS TO ADVANCED NEOPLASIA RISK?

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Introduction: Many European countries use fecal immunochemical test (FIT) as a test for colorectal cancer (CRC) screening using different Cut-off levels ranging from 15-80 µHb/g [Réf-1, 2]. In France the selected level is 30µgHg/g. These levels are generally adjusted to existing capacity to provide colonoscopies for the persons with positive tests. The Netherlands and England provide colonoscopy for positive test within a fixed number of days by a gastroenterologist dedicated to the screening program. In these countries the screening capacity pool is separated from the general colonoscopy pool. In France any gastroenterologist performs a colonoscopy for a person with a positive test. There is no system of prioritization in place. In France organised CRC screening program and access to screening by FIT is advised for persons with "average CRC risk". Individuals with identified two fold risk (first degree family history, adenoma history) are excluded from screening and directly prescribed a colonoscopy. [Réf-3].

Aims & Methods: Our aim was to compare, within the French screening programme, the risk to detect advanced-adenoma (AA)/CRC in persons with different Hb cut-off levels in the previous campaign and who were currently considered negative and the AA/CRC general risk. If the risk within certain cut-off levels is twice that of general population should they not have direct access to colonoscopy as do others with comparable risk? Study included a reference group of 602 731 "average risk" inhabitants of Parisian region aged 50-74 years who did their first FIT test in 2015-2016 (1st FIT campaign: R1). Two years later (R2) we examined the probability to detect cancer by a FIT test for those who were negative within this R1. Different subgroups of Relative-Risk (RR) analysis were formed, based on the haemoglobin cut-off during the R1 campaign. We compared these subgroups with a reference group.

Results: A total of 602 731 people (55.02% women, average age: 61.3 years for women and 60.9 for men) participated in the R1. Of them 4.6 % had a positive test. In this group AA and CRC detection rate was 13.0 ‰ and

2.9 ‰ respectively. Among those who had a negative test in R1, 330,469 (57.5%) (55.7% women, average age: 63.2 years for women and 63.0 years for men) performed a second test during R2. Among them 3.3% were positive, with an increased risk of positivity (2.9 % -16.2 %) correlating to Hb level in in R1. Compared with individuals of reference group R1 4644 individuals with R1 [20-30[µgHb/g level were 3.0 times more likely to have a positive R2 test, 2.6 (CI, 2.3-3.1) times more likely to have AA and 2.6 (CI, 1.9-3.7) times more likely to have CRC. At the moment of study colonoscopy results were known for 52.4% of those who tested positive in R2. The available data show an increased risk of AA and CRC correlating with the results of the faecal haemoglobin cut-off in R1.

Conclusion: The probability of detecting colorectal cancer within the second round of FIT based screening program for those who were negatives but above 20µgHb/g level, is more than two fold if we compare with the reference group who represents the average risk population of the Parisian region. This increase of risk could not be explained just by aging of 2 years. This strongly suggests that this Hb concentration level during the first test may be an equal or more important risk factor than for instance the first degree family history. Additional studies (early second test or colonoscopy based) should be conducted to confirm this hypothesis. If this hypothesis is confirmed, the French program should lower the cut off level.

References: 1.https://ec.europa.eu/health/sites/health/files/major_chronic_diseases/docs/2017_cancerscreening_2ndreportimplementation_en.pdf
2.http://www.healthscotland.scot/media/1619/bowel-screeening-inserts_nov17_english.pdf
3.https://www.edp-biologie.fr/images/stories/news/2018/Mars/joe_20180322_0068_0013.pdf If accepted for presentation the results will be updated in september 2019
Disclosure: Nothing to disclose

P1148 PREVALENCE OF COLORECTAL CANCER IN CRYPTOGENIC PYOGENIC LIVER ABSCESS PATIENTS, DO THEY NEED ROUTINE SCREENING COLONOSCOPY? A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Patients with cryptogenic pyogenic liver abscess (PLA) do not have a definite source of infection and it could be a manifestation of compromised colonic mucosal barrier due to colorectal cancer (CRC). Association of PLA and CRC is unclear. Evidence is weak and limited to small sized studies. As a result, the need for colonoscopy in PLA patients is debatable.

Aims & Methods: We conducted a comprehensive search of multiple electronic databases and conference proceedings (from inception through January 2019) to identify studies that reported on the prevalence of CRC in PLA patients. Our goals were to evaluate the pooled rate of CRC in patients with cryptogenic PLA.

Results: 12 studies were included in the analysis. Majority of them were from East Asian countries. 18,607 patients were diagnosed with PLA in the study group and 60,130 patients were in the control group. 63% were males in the age range of 56 to 94 years. 90.5% of the lesions were left sided and 93.1% were positive for *Klebsiella pneumoniae*. A total of 18,607 PLA patients were reported, of which 17,906 patients underwent screening for CRC. A total of 713 colorectal lesions were found, of which 648 were diagnosed with CRC. 60,130 patients were used as control group, of which 509 patients were diagnosed with CRC. The pooled rate of prevalence of CRC was 7.9% (95% CI 5-12.1, I²=92.4, relative risk=6.6) in patients with PLA, as compared to 1.2% (95% CI 0.3-5.7, I²=93.4) in control, with statistical significance (p=0.001). Relative risk = 6.6.

Conclusion: Although limited by heterogeneity, our study demonstrates that patients with cryptogenic PLA are at a 7-fold risk of having CRC when compared to patients without PLA. Based on our results a screening colo-

noscopy should be considered in East Asian population with cryptogenic PLA, especially when positive for *Klebsiella pneumoniae*.
Disclosure: Nothing to disclose

P1149 A NATIONWIDE ANALYSIS OF READMISSION RATES AFTER COLORECTAL CANCER SURGERY IN THE US

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Introduction: Hospital readmission after surgery constitutes a serious burden for patients as well as health systems and payers. Data on readmission rates after colorectal cancer (CRC) surgery are scarce. We analyzed US national rates of, and factors associated with, 30-day readmission after CRC surgery.
Aims & Methods: We queried the National Readmissions Database (NRD) from 2010 to 2015 to calculate national estimates of 30-day readmission rates after CRC surgery, and the causes for readmission. Patients included had non-subepithelial CRC, were aged 18 years or more, and survived the index admission. Patients with appendiceal or anal cancer were excluded. In order to allow follow-up of 30 days, patients who were discharged in December were excluded, because patients are not tracked across years. We also analyzed potential factors associated with readmission, first using non-adjusted and ultimately multivariable-adjusted logistic regression. All results were weighted for national estimates. Joinpoint analysis was performed to test for changes in temporal trends.
Results: The US national estimate for the number of overall index cases of CRC surgery during the study period was 616,348. Among these patients, 90,555 (14.7%) were readmitted within 30 days of discharge. During our study period, the readmission rate showed a decreasing trend from 15.5% in 2010 to 13.5% in 2015 (p-trend < 0.001, Table 1). Joinpoint analysis did not show any significant change in this trend over time. The most frequent diagnoses for readmission were gastrointestinal (54.8%), infectious (10.6%), and cardio-/cerebrovascular (6.3%).
The three most common gastrointestinal diagnosis codes for readmission were postoperative, post-traumatic, other device infections (11.9%); malfunction, reaction & complication of GI device or procedure (8.7%); and intestinal obstruction (5.9%). After adjusting for covariates, rectal resection (odds ratio [OR], 1.372 [95% confidence interval {CI}, 1.324-1.422]), longer length of stay (OR with log-increase in 1, 1.395 [95% CI, 1.358-1.432]), metropolitan teaching hospital (OR vs metropolitan nonteaching, 1.109 [95% CI, 1.072-1.147]), non-routine discharge including transfer to a short term hospitals (vs routine, OR, 1.617 [95% CI, 1.336-1.957]), elective admission (OR, 1.072 [95% CI, 1.034-1.111]), open laparotomy (OR, 1.172 [95% CI, 1.134-1.212]), and higher Elixhauser comorbidity score (OR for increase in 1, 1.009 [95% CI, 1.008-1.010]) were potential risk factors for subsequent readmission.
Advanced cancer (OR, 0.304 [95% CI, 0.288-0.321]), and older age (OR for >84 y vs 18-44 y, 0.790 [95% CI, 0.727-0.858]) and female gender (OR, 0.941 [95% CI, 0.916-0.966]) were associated with decreased odds for readmission.

Year	2010 (n, %)	2011 (n, %)	2012 (n, %)	2013 (n, %)	2014 (n, %)	2015 (n, %)	Overall (n, %)
Not readmitted	89,882 (84.5%)	88,371 (84.5%)	87,968 (85.2%)	86,557 (85.8%)	86,444 (85.8%)	86,571 (86.5%)	525,793 (85.3%)
Readmitted	16,480 (15.5%)	16,274 (15.5%)	15,331 (14.8%)	14,708 (14.5%)	14,275 (14.2%)	13,486 (13.5%)	90,555 (14.7%)
Total	106,362 (100%)	104,645 (100%)	103,299 (100%)	101,265 (100%)	100,719 (100%)	100,057 (100%)	616,348 (100%)

[Table 1. 30-Day readmission rate by year, US national estimates]

Conclusion: In a US national analysis, we found that the 30-day readmission rate after CRC surgery was 14.7% in the period from 2010 to 2015, with a decreasing trend from 15.5% in 2010 to 13.5% in 2015. Some associations appear as expected, such as increased odds of readmission with rectal resection, and some appear surprising and require further study, includ-

ing the decreased odds of readmission with advanced cancer and in older patients. It remains to be determined whether any of the predictors of readmission can point to modifiable factors that can decrease readmission rates after CRC surgery.
Disclosure: Nothing to disclose

P1150 FIT POSITIVE COLONOSCOPY PERFORMANCE AT A LARGE HMO SHOWS HIGH RATES OF PERFORMANCE AND OF ADVANCED ADENOMAS

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Introduction: Annual FIT at 50-75Y is currently the national screening program for CRC in Israel. FIT is considered to be effective for CRC early diagnosis but not a CRC preventive measure compared to colonoscopy. Positive FIT indicates the need for prompt colonoscopy due to a relatively high rate of advanced neoplastic lesions in the colon, while time to colonoscopy up to 6 months has been shown as effective in advanced cancer prevention.
Aims & Methods: To review colonoscopy performance among FIT positive cases and its timing after FIT. To identify factors for lack of colonoscopy performance in FIT positive cases and to study the profile of neoplastic findings in FIT positive colonoscopies performed in a large HMO in Israel. Maccabi Health care services (MHS) is an Israeli HMO with 2 million members. All MHS members aged 50-75 during 2018 were included in the analysis. MHS database was searched for FIT and colonoscopy associated parameters. CRC registry was crossed with FIT positive cases. Time between FIT performance and colonoscopy was calculated. Colonoscopy and pathology reports were individually studied for specific endoscopic lesions and corresponding histological findings, respectively.
Results: During 2018, 523,530 members were at the age group of 50-75y. among them- 134,542 performed FIT with 6,925 having positive results. For those, colonoscopy was performed after 3, 3-6, 6-9 months from FIT testing in 4035(58%), 337(5%), 49(0.7%), respectively. A survey in a subsample of 430 cases who did not perform colonoscopy up to 9 months post FIT showed that 74% did perform a colonoscopy in a private setting, 7% were still in workup, 4% refused and 8% agreed and performed colonoscopy through the survey. In another subsample of 536 colonoscopies, polyps were reported in 164/536(31%) cases and cancer in 20/536(4%).
The records of cases with polyps were searched for endoscopic and histologic findings. Cases with adenomas- 95/536(18%) with 27 non-advanced and 68 advanced (5% and 13% of total sample; 28% and 72% of adenoma cases, respectively). Advanced polyp by histology (villous of HGD) was found in 23/68 and advanced size or number in 45/68. The rate of hyperplastic polyps was 3.5%.
Conclusion: Colonoscopy performance after FIT positive test is satisfactory and mostly performed within 3 months of FIT testing according to the quality parameters of MHS. The rate of advanced adenomas is higher in about 2 folds than in average Israeli risk population (1), thus making FIT a CRC preventive measure. Rate of cancer is 3.5 folds of the rate at average risk screening colonoscopy.
References: Strul H, Kariv R, et al. J Gastroenterol. 2006 Feb;101(2):255-62. The prevalence rate and anatomic location of colorectal adenoma and cancer detected by colonoscopy in average-risk individuals aged 40-80 years.
Disclosure: Nothing to disclose

P1151 POST-COLONOSCOPY COLORECTAL CANCER VERSUS DETECTED COLORECTAL CANCER: DOES TUMOUR MORPHOLOGY AND FAMILY HISTORY DIFFER?

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Introduction: Colonoscopy is the golden standard for detecting colorectal cancer (CRC). The prevalence of post-colonoscopy CRC (PCCRC), a CRC detected within 6-36 months after a negative colonoscopy examination, has been recognized as a quality measure. Mechanisms for PCCRC either might be missed or incompletely excised lesions or CRC developed de novo since the initial colonoscopy. Little is known about histopathological features and low-risk family history for CRC in PCCRC compared to detected CRC (dCRC).

Aims & Methods: The aim of the study was to compare PCCRC and dCRC regarding different tumour morphology parameters and family history for CRC. From The Swedish low-risk CRC study 1,535 individuals operated for CRC during the years 2004-06 were included. All had data on family history for CRC (defined as at least one first degree relative with CRC) and the tumours were thoroughly histologically reviewed. Data from the Swedish patient inward and outward as well as causes of death registers were collected. Those who had performed a colonoscopy within 0-36 months before the cancer diagnosis were included for analysis. Cancers were divided into PCCRC and dCRC, with CRC diagnosis within 6-36 and 0-6 months after the colonoscopy, respectively. Statistical analysis included Chi-2 test, Students' T-test and logistic regression.

Results: There were 476 CRCs included in the analysis. Of these, there were 29 PCCRCs and 447 dCRCs. The mean age was 66.1 years in the PCCRC group and 69.2 years in the dCRC group (p=0.07). When controlling for sex and age, there was no significant difference between the two groups in five-year mortality, 34% in PCCRC and 28% in dCRC (p=0.334). The results of the logistic regression analysis are summarized in the table.

Conclusion: In this small Swedish cohort study, low-risk family history for CRC was not a significant risk factor for PCCRC. Crohn-like peritumoral lymphocytic reaction was less frequently seen in PCCRC compared to dCRC. This might be an indication of different prognosis for PCCRCs compared to dCRCs.

Covariate	OR	p-value	95% CI
Sex (female vs male)	0.91	0.845	0.37-2.25
Age (continuous)	1.00	0.854	0.95-1.04
Localisation (right vs left)	0.77	0.565	0.31-1.89
T-stage (T3/T4 vs T1/T2)	4.11	0.067	0.91-18.66
N-stage (1, 2 or 3 vs 0)	1.58	0.311	0.65-3.85
Peritumoral lymphocytic reaction (yes vs no)	0.40	0.030	0.18-0.91
Vascular growth (yes vs no)	0.19	0.110	0.02-1.46
Medullary type (yes vs no)	2.21	0.357	0.41-11.95
Family history CRC (yes vs no)	1.20	0.755	0.38-3.75

[Multivariate logistic regression for post-colonoscopy colorectal cancer (PCCRC) versus detected colorectal cancer (dCRC)]

References: Ghazi S, Lindforss U, Lindberg G, Berg E, Lindblom A, Papadogiannakis N; Low-Risk Colorectal Cancer Study Group. Analysis of colorectal cancer morphology in relation to sex, age, location, and family history. J Gastroenterol. 2012 Jun;47(6):619-34. doi: 10.1007/s00535-011-0520-9.
Disclosure: Nothing to disclose

P1152 NON-PEDUNCULATED, SCREEN-DETECTED T1 COLORECTAL CARCINOMAS HAVE AN INCREASED RISK FOR LYMPH NODE METASTASIS AS COMPARED TO NON-SCREEN-DETECTED T1 COLORECTAL CARCINOMAS

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Introduction: Implementation of the FIT-based colorectal cancer (CRC) screening program in 2014 has led to an increased detection of T1 CRCs in the Netherlands. Current risk stratification is based on non-screen-detected T1 CRCs. However, it is unknown whether screen- and non-screen-detected T1 CRCs have a comparable risk of adverse outcomes such as lymph node metastasis (LNM) and recurrence.

Aims & Methods: In this study we compared screen-detected and non-screen-detected T1 CRCs. A multicenter retrospective observational cohort-study was performed, identifying all consecutive T1 CRCs diagnosed between 2014 and 2017 in 8 hospitals in the Netherlands. Data on whether a T1 CRC were screen-detected or non-screen-detected, together with polyp characteristics, histological risk factors, treatment approach and clinical variables such as age, gender and co-morbidities were collected. Differences in LNM were evaluated by using multivariate logistic regression analysis, adjusting for clinical variables, polyp characteristics and histological risk factors.

Results: A total of 1101 T1 CRCs (median follow-up 21.7 months (IQR 19-30)) were included in the study, of which 693 (62.9%; 34.2% female) were screen-detected and 408 (37.1%; 42.4% female) were non-screen-detected. Screen-detected T1 CRCs were smaller (mean size of 20.0 mm (SD 11.5) vs. 22.5 mm (SD 13.2), p=0.005), more frequently located in the left-sided colon (61% vs. 54%, p=0.02), and patients were younger (67.2 (IQR 63-71) vs. 69.3 (IQR 62-78) years, p< 0.001) compared to non-screen-detected patients with T1 CRC. Within the group of patients referred for surgery, screen-detected T1 CRC was associated with a higher risk of LNM than non-screen-detected T1 CRC (16.4% vs. 10.4%; adjusted OR 1.78,95% CI 0.93-3.34; p=0.08). This difference was mainly attributable to a higher LNM risk in non-pedunculated screen-detected T1 CRCs (18.8% vs. 10.5%, p=0.03), as there was no significant difference in LNM risk in pedunculated T1 CRCs (9.1% vs 8.3%). Within the group of non-pedunculated T1 CRCs (n=669 (65% of total), of which screen-detected n=427(64%)) there was no difference between screen- and non-screen-detected T1 CRCs regarding histological features such as lymphovascular invasion (14.8% vs 11.1%, p=0.35) and poor differentiation (6.3% vs. 5.3%, p=0.49). However, positive (R1) or inconclusive (Rx) resection margins were more frequently present in screen-detected patients (46.9% vs. 34.7%, p=0.002), although this feature was not independently associated with LNM in this cohort (p=0.094). While non-screen-detected patients were referred for primary oncologic surgery more often than screen-detected patients (65% vs 53%, p=0.003), there was no difference in overall surgical referral rate (56.2% vs. 62.8% p=0.10).
Interestingly, the major difference in LNM in non-pedunculated T1 CRCs was found within the primary surgery group (screen-detected 17.6% vs. non-screen-detected 6.2%, p=0.008), and not in the secondary surgery group (screen-detected 20.2% vs. non-screen-detected 21.4%, p=0.871).

Conclusion: Non-pedunculated T1 CRCs detected within the FIT-based screening program have a higher risk for synchronous lymph node metastasis compared to non-screen detected T1 CRCs. This difference is most pronounced in patients referred for primary surgery, suggesting that these

polyps may have alarming malignant features with optical diagnosis. This increased risk should be kept in mind, now that local minimally invasive treatments such as full thickness resections are becoming more widely available.

Disclosure: Nothing to disclose

P1153 OUTCOMES OF COLORECTAL CANCER SCREENING STARTING AT THE AGE OF 45 IN AVERAGE-RISK, ASYMPTOMATIC PATIENTS

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Introduction: Colorectal cancer (CRC) is the fourth most common cancer diagnosed among adults in the United States and most guidelines recommend colorectal cancer screening for average-risk individuals starting at age 50. Since 1994, there has been a 51% increase in CRC among individuals younger than 55. Updated guidelines from the American Cancer Society (ACS) in May 2018 recommend starting colorectal cancer screening for all individuals at age 45. T
hese recommendations are based on modeling studies and there are limited data on the effectiveness and outcomes of colorectal cancer screening in average risk individuals younger than 50.

Aims & Methods: The aim of this study was to compare the rates of adenomas and advanced adenomas detected in average risk patients undergoing screening colonoscopies between the ages of 45-49 versus 50-54. In this retrospective study, a total of 3,760 patients undergoing colorectal cancer screening from June 2018 to December 2018 were reviewed, with 1,447 patients excluded based on active digestive symptoms, anemia or personal history of CRC. The rates of adenomatous lesions and advanced adenomatous lesions in each cohort were compared. Advanced adenomas were defined as any adenoma ≥10 mm in size, high-grade dysplasia, villous or tubulovillous histology, and adenocarcinoma. The locations of advanced adenomas were also compared.

Results: In the 45-49 cohort, there were a total of 190 patients who underwent screening colonoscopy, of which 47.7% were women. In this cohort, 73 (38%) patients had non-advanced adenomas (adenoma size < 5 mm in 27, and 5-9 mm in 46). A total of 10 (5%) patients had advanced adenomas based on advanced histology (polyp size 5-9 mm in 3, and ≥10 mm in 1) and size (adenomas ≥10 mm in 6). One 49 year old patient had an adenocarcinoma found on screening colonoscopy.
In the 50-54 cohort, there were a total of 2,123 patients who underwent screening colonoscopy, of which 52.4% were women. In this cohort, 870 (41%) patients had non-advanced adenomas (adenoma size < 5 mm in 443, and 5-9 mm in 427). A total of 119 (5.6%) patients had advanced adenomas based on histology (polyp size < 5 mm in 2, 5-9 mm in 13, and ≥10 mm in 17) and size (adenomas ≥10 mm in 87). No patients had adenocarcinoma found on screening colonoscopy in this cohort.
The adenoma detection rate was 44.2% in the 45-49 cohort and 46.6% in the 50-54 cohort (*p*=0.53). The advanced adenoma detection rate was 5.8% in the 45-49 cohort and 5.6% in the 50-54 cohort (*p*=0.91). Advanced adenomatous lesions were most frequently found in the ascending colon for both cohorts (Table 1).

45-49 cohort		50-54 cohort	
Location	**Number**	**Location**	**Number**
Cecum	1	Cecum	20
Ascending	7	Ascending	30
Transverse	1	Transverse	20
Sigmoid	0	Sigmoid	18
Rectosigmoid	0	Rectosigmoid	6
Rectum	2	Rectum	18

[Table 1: advanced adenoma locations]

Conclusion: This study provides preliminary data on the outcomes of CRC screening starting at the age of 45 in a Southwestern population since the updated ACS screening guidelines were released in May 2018. Our results show that asymptomatic patients between the ages of 45-49 who undergo screening colonoscopy have adenomas and advanced adenomas detected

at rates similar to patients screened between the ages of 50-54. Additionally, one adenocarcinoma was discovered on screening colonoscopy in a patient before the age of 50. These findings support consideration of colorectal cancer screening at age 45.

Disclosure: Nothing to disclose

P1154 POST-COLONOSCOPY COLORECTAL CANCER RATE IS SLOWLY DECREASING: A RETROSPECTIVE POPULATION BASED COHORT STUDY OF THE ADULT SWEDISH POPULATION

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Introduction: The rate of post-colonoscopy colorectal cancer, PCCRC, a cancer detected 6-36 months after a colonoscopy in which no cancer was found, has been recognised as a key quality indicator of colonoscopy. Mechanisms for PCCRC might be either missed or incompletely excised lesions or de novo cancer developed after the index colonoscopy.

Aims & Methods: The aim was to evaluate the PCCRC rates and associated risk factors for PCCRC during a 10-year period. Data was collected from the Swedish patient registries on individuals ≥ 18 of age. All unique individuals who had undergone at least one colonoscopy during the years 2003-15 were identified. Those with a CRC diagnosis prior to inclusion in the study were excluded. The rest was individually linked to the Swedish Cancer Registry and the Swedish Cause of Death Register. CRCs within 0-6 months of a colonoscopy examination were considered as detected cancers and CRCs diagnosed within 6-36 months as PCCRCs. Colonoscopies performed 2003-12 were included in the analysis. The PCCRC rate was analysed with colonoscopies as the denominator (1). Statistical analyses employed Poisson regression analysis with cluster-robust standard errors. Covariates included were age, sex, comorbidities, procedure, location of the CRC, T-stage, time-period and the geographical location of the diagnosing hospital.

Results: There were 461,031 colonoscopies performed on 349,129 (56% on women) individuals included in the study. The mean age at the first examination was 59.4 years. Of these, there were 19,178 individuals with a CRC diagnosis 0-36 months after a colonoscopy. There were 1,329 PCCRCs, which is equal to the number of colonoscopies that failed to detect a CRC. The number of colonoscopies that detected a CRC was 18,480. The PCCRC rate for the ten-year period was 6.7%. The rate was 8.1% in 2003 and 5.9% in 2012. Gender, younger age, right-sided CRC, comorbidities, previous history of colorectal polyps as well as polypectomy during the procedure and the first time-period were associated with a significantly increased risk of PCCRC.

Main group	Covariate	RR	p-value	95% CI
Sex	Male vs female	0.87	0.007	0.79-0.96
Age group	Age 18-30 years	1.40	0.128	0.91-2.18
	Age 30-40 years	1.35	0.052	1.00-1.83
	Age 40-50 years	1.31	0.028	1.03-1.66
	Age 50-60 years	1.06	0.529	0.88-1.29
	Age 60-70 years	1.12	0.134	0.97-1.29
	Age 70-80 years	1.06	0.419	0.92-1.21
	Age > 80 years (ref)	1.00		
Comorbidity	Ulcerative colitis Yes/No (No=ref)	5.12	<0.001	4.48-5.85
	Crohns disease Yes/No	3.85	<0.001	3.01-4.92
	Prior polyp diagnosis Yes/No	1.84	<0.001	1.50-2.26
Procedure	Polypectomy Yes/No	2.01	<0.001	1.68-2.41
Location CRC	Left- vs right-sided CRC	0.56	<0.001	0.49-0.64
	Undefined vs right-sided CRC	0.62	0.014	0.42-0.91
T-stage CRC	T1/T2 vs T3/T4	1.27	<0.001	1.15-1.41
	Undefined vs T3/T4	0.66	<0.001	0.55-0.80
Time period	2008-12 vs 2003-07	0.87	0.008	0.79-0.96

[Table. Multivariate Poisson regression analysis for post-colonoscopy versus detected colorectal cancer with colonoscopy as the denominator]

In the table, the multivariate analysis for the risks of PCCRC is shown. The covariates Diabetes, Diverticulosis, Ischemic Heart Disease, COPD, Heart Failure and Geography were controlled for but results not shown.

Conclusion: The PCCRC rate is slowly decreasing in Sweden. The strongest risk factors for PCCRC were UC and Crohns' disease. Increased effort for detecting CRCs in risk groups is of concern.

References: 1. Morris EJ, Rutter MD, Finan PJ, et al. Post-colonoscopy colorectal cancer (PCCRC) rates vary considerably depending on the method used to calculate them: a retrospective observational population-based study of PCCRC in the English National Health Service. Gut 2015;64(8):1248-56. doi: 10.1136/gutjnl-2014-308362

Disclosure: Nothing to disclose

P1155 PATIENTS REFERRED WITH ANAEMIA SHOULD BE INVESTIGATED FOR CANCER REGARDLESS OF IRON STATUS

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Introduction: Patients referred under the 2-week wait (2WW) pathway for gastrointestinal cancer with iron deficiency anaemia (IDA) are investigated in our centre with colonoscopy, upper GI endoscopy and CT scanning. It is necessary to justify these investigations given the burden they place upon radiology and endoscopy services.

Aims & Methods: Our aim was to examine the predictive role of ferritin in such referrals and to assess whether this might be used to better streamline investigations.

Referrals to the upper and lower GI cancer pathway over a period of one year were screened for referrals made exclusively for IDA. Data was collected on ferritin level, age, gender, cancer detection and modality of cancer detection. Low ferritin was defined as < 15µg/L. Categorical variables were compared using a chi-squared test.

Results: 3669 referrals to the upper and lower GI cancer pathway between May 2017 and May 2018 were screened for inclusion. 377 patients were referred for IDA of which 52 (13.8%) were found to have a malignancy. This compares to a national cancer detection rate of 7.6% for all referrals to 2WW pathways.

191 patients (52.0%) had a low ferritin. There was no statistically significant difference between rate of cancer detection in the low and normal ferritin groups (10.4% vs 20.8% p=0.06). Males were more likely to have a cancer detected than females (21.8% vs 6.9%, p= 0.00003). The cancers detected included several non-GI malignancies in both low ferritin and normal ferritin groups (5/20 vs 10/30, p=0.53) (See table).

CT scanning missed the malignancy in 7 cases of colorectal cancer subsequently detected on colonoscopy. 6 cancers were detected using upper GI endoscopy and all of these had been visible on CT scanning. In addition, all of the upper GI malignancies had normal ferritin levels.

	Low Ferritin	Normal Ferritin
Colon	14	11
Pancreas	1	2
Renal	1	1
Prostate	1	2
Other	Breast (1) Adrenal (1) Bladder (1)	Lung(4) Stomach (2) Oesophagus (2) GOJ (2) Lymphoma (1) No primary (1) Cholangiocarcinoma

[Cancer detection]

Conclusion: This study demonstrated a high rate of cancer detection for anaemia referrals but there was no statistically significant correlation between ferritin level and detection of cancer. Ferritin may not be a helpful marker in screening anaemia referrals. These results challenge the use of upper GI endoscopy in the investigation of anaemia on the cancer pathway since all cancers were seen on CT.

Disclosure: Nothing to disclose

P1156 THE PREVALENCE OF SESSILE SERRATED ADENOMA/POLYP IN COLORECTUM AND ITS RELATIONSHIP TO SYNCHRONOUS COLORECTAL ADVANCED NEOPLASIA: A SYSTEMIC REVIEW AND META-ANALYSIS

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Introduction: Colorectal cancer (CRC) is the third most common tumor in men and the second in women, resulting in the fourth most common cancer-related cause of death in the world. In 2010 WHO classification system divided serrated lesions in colorectum into three types: hyperplastic polyp, traditional serrated polyp, and sessile serrated adenoma/polyp (SSA/P). Among them SSA/P is an important premalignant precursor of CRC. However, the true prevalence of SSA/P and its relationship to CRC are still unknown due to unaccepted bowel preparation, detection difficulty, and poor discrimination within endoscopists and pathologists.

Aims & Methods: The aim of this systemic review and meta-analysis is to evaluate the true prevalence of SSA/P and its relationship to synchronous colorectal advanced neoplasia.

A comprehensive, computerized research was performed on PubMed published from 1 January 2010 to 6 July 2018 to search relevant articles without language limitation. Clinical trials were included in narrative systemic review if they matched the following inclusion criteria:

(1) published as case-controlled study, cohort study or cross-sectional study;

(2) defined objectively for diagnosis of SSA/P within studies;

(3) addressed the prevalence and characteristics of SSA/P.

Within these trials if they met additional criteria involving reported outcome of risk of advanced neoplasia in relation to SSA/P they were enrolled into meta-analysis.

Results: The prevalence of all SSA/Ps in this review ranged from 0.038 to 20.23% and pooled prevalence was 2.7% (95%CI, 1.9-3.9%). In subgroup analysis the overall prevalence of SSA/P between period of 2010-2014 and period of 2015-2018 showed 2.7% (95%CI, 1.2-6.0%) and 2.8% (95%CI, 1.9-4.1%) respectively.

We calculated the pooled data on the risk of SSA/P and synchronous advanced neoplasia in patient with SSA/Ps available from 8 trials resulting in pooled OR of 3.53 (95%CI, 2.39-5.20, I^2=4%) without detection in heterogeneity test.

Conclusion: In this systemic review the prevalence of SSA/P was 2.7% (95%CI 1.9-3.9%) and was no difference between the period of 2010-2014 and 2015-2018. Besides SSA/P is associated with increasing risk of synchronous advanced neoplasia in colorectum.

Disclosure: Nothing to disclose

P1157 HIGH MEAT INTAKE AND LOW SRAGE ARE ASSOCIATED WITH COLONIC POLYPS MAINLY IN SMOKERS IN A CASE CONTROL STUDY

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Introduction: Colonic polyps, both adenomatous and hyperplastic (HP), have been shown to be associated with red and processed meat consumption and with smoking habits. Recently, we have shown that red and/or processed meat consumption and pack years are inversely associated with RAGE soluble receptor (sRAGE) for advanced glycation end products. In addition, sRAGE levels have been shown to be associated with the risk for colorectal cancer (CRC) in male smokers and in post-menopausal women. However, further evidence is lacking as for the modifying effect of smoking on the association between red and/or processed meat or sRAGE levels with different types of colonic polyps.

Aims & Methods: The aims of this study were to assess the association between red and/or processed meat or sRAGE levels and different types of colonic polyps and to test the possible effect modification of smoking habits. This was a case-control study, among consecutive subjects aged 40-70 years, undergoing colonoscopy during 2010-2015.

Cases with colorectal polyps were compared to controls with no past or present polyps. Detailed information was gathered regarding polyp histology, anatomic location and lifestyle habits including smoking. Smoking was defined as ordinal variable with three levels; never smokers, light smokers (pack years under the median of the total sample corresponding to 19.75) and heavy smokers (≥19.75).

Serum sRAGE levels were measured and red and/or processed meat consumption was calculated by food frequency questionnaire (FFQ). High red and/or processed meat consumption was defined as consumption above the sample median (>0.33 portions/week) and low sRAGE defined as levels under the sample first tertile (< 1013.42 pg/ml).

Results: A total of 789 participants were included (cases with colorectal polyps n=403, controls n=386), 743 subjects had sRAGE measurements. Among the entire sample, high red and/or processed meat consumption was significantly associated with higher odds for adenomatous polyps throughout the colon and with distal HP (OR=1.41, 95% CI 1.00-1.97, P=0.048; OR=2.04, 1.02-4.05, P=0.043, respectively), but the association with total polyps was not significant (OR= 1.36, 95%CI 0.99-1.88, P=0.057).

However, stratification by pack years, revealed a significant association of red and/or processed meat consumption with total polyps among heavy smokers (OR=1.96, 95% CI 1.01-3.80, P=0.048). Moreover, low sRAGE levels were significantly associated with higher odds for HP, specifically with proximal HP (OR=2.03, 95% CI 1.06-3.89, P=0.032; OR=2.96, 1.20-7.33, P=0.019, respectively).

Conclusion: High red and/or processed meat consumption is associated with adenomatous polyps throughout the colon, with distal HP and among smokers also with total polyps. Low serum sRAGE is associated with HP, especially proximal. These results may aid in designing prevention recommendations for colonic neoplasia as well as open a new frontier in understanding CRC pathogenesis.

Disclosure: Nothing to disclose

P1158 FAECAL DNA TEST IN COMBINATION WITH FAECAL IMMUNOCHEMICAL TEST FOR HAEMOGLOBIN IS USEFUL FOR DETECTION OF COLORECTAL ADVANCED ADENOMA

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Introduction: The main approach to colorectal cancer screening worldwide is the faecal immunochemical test for haemoglobin (FIT). Although the sensitivity of the FIT for the diagnosis of colorectal neoplasia is about 90% for colorectal cancer, it falls to about 30% for the detection of advanced adenoma. To avoid this disadvantage, more sensitive methods are required.

Aims & Methods: As TWIST1 methylation is specific to colorectal neoplasia, detection of TWIST1 methylation from faeces samples might be useful for colorectal neoplasia screening. However, because the content of human DNA in faeces is very small, it is very difficult to detect TWIST1 methylation by conventional bisulphite-based methylation assays. Therefore, we developed a new methylation assay without bisulphite treatment and evaluated its sensitivity and specificity in combination with and without FIT for detection of colorectal neoplasia from faeces samples. DNA was treated with three methylation-sensitive restriction enzymes and an exonuclease, followed by measurement of TWIST1 methylation level by droplet digital PCR. The FIT and faecal DNA test were performed on 71 control individuals and 372 patients with colorectal neoplasia including 40 with non-advanced adenoma, 127 with advanced adenoma, and 205 with colorectal cancer.

Results: Sensitivity of the FIT was 7.5% for non-advanced adenoma, 32.3% for advanced adenoma, and 93.7% for colorectal cancer, and specificity was 87.3%. Sensitivity of the faecal DNA test was 27.5% for non-advanced adenoma, 47.2% for advanced adenoma, and 44.3% for colorectal cancer, and specificity was 91.5%. Sensitivity of the FIT and faecal DNA test combined was 35.0% for non-advanced adenoma, 68.5% for advanced adenoma, and 95.6% for colorectal cancer, and specificity was 80.3%.

Conclusion: Combination of the faecal DNA test with FIT may provide an alternative screening strategy for colorectal neoplasia, especially for potentially precancerous lesions.

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P1159 GENETIC RISK SCORE TO IDENTIFY INDIVIDUALS WITH AN INCREASED RISK OF COLORECTAL ADENOMAS

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Introduction: Common low-penetrance genetic variants (SNPs) has been consistently associated with colorectal cancer (CRC) risk, but the risk conferred by each of these variants is usually modest. The relevance of these SNPs in the development of colorectal adenomas has been scarcely evaluated.

Aims & Methods: To evaluate the potential of a genetic risk score (GRS) to identify individuals with an increased risk of colorectal adenomas.

Patients were selected from the Spanish colorectal cancer screening registries in Aragon and The Canary Islands. Patients with hereditary nonpolyposis CRC, familial adenomatous polyposis, history of CRC or inflammatory bowel disease were excluded. We included 858 patients with no precancerous colorectal lesions and 642 with adenomas. Genomic DNA from participants was genotyped by the MassArray™(Sequenom) platform for a panel of 99 SNPs previously associated with CRC risk. We derived a GRS based on the 11 SNPs significantly associated with adenoma development in our study. The number of risk alleles was coded as 0, 1 or 2 for each SNP assuming a log-additive genetic effect. To test the relevance of our score, we estimated the impact of having each additional risk allele by computing the odds ratio (OR) and the associated 95% confidence interval (95%CI). In addition, the predictive value for colorectal adenoma risk was calculated as the area under the ROC curve (AUC). PredictABEL R package was used to compute the genetic risk score.

Results: Five SNPs were identified using a multivariate logistic model that included the 11 SNPs that were associated with colorectal adenomas in our study: rs10505477, rs11255841, rs13181, rs4779584 and rs8180040. We observed that the risk of developing adenomas increased with the number of risk alleles (per-allele OR=1.209, 95%CI 1.122 to 1.302 *p< 0.001*). Five risk alleles were considered as reference since it was the median number in patients without adenomas. See Table 1.

Nº of risk alleles	Patients n (%)	Without lesions n (%)	With adenomas n (%)	OR (95% CI)	p-value
≤2	30 (2.1)	19 (2.3)	11 (1.8)	0.894 (0.401-1.993)	0.783
3	112 (7.8)	73 (8.8)	39 (6.4)	0.844 (0.536-1.331)	0.466
4	225 (15.6)	142 (17.1)	83 (13.5)	0.968 (0.679-1.380)	0.858
5	366 (25.4)	229 (27.6)	137 (223)	1 (reference)	
6	364 (25.8)	199 (24.0)	165 (26.9)	1.431(1.054-1.941)	0.021
7	228 (15.8)	118 (14.2)	110 (17.9)	1.621 (1.147-2.292)	0.006
≥8	117 (8.1)	49 (5.9)	68 (11.1)	2.500(1.616-3.869)	0.000
Total	1442 (100.0)	829 (100.0)	613 (100.0)	1.209 (1.122-1.302) per allele	p trend <0.001

[Risk of colorectal adenomas associated with increasing number of risk alleles in five selected SNPs in study population]

Individuals with ≥8 risk alleles had a 2.5-fold increase in adenoma risk compared with those with 5 risk alleles. The GRS adjusted by sex and age showed a discriminating power of 66% (AUC = 0.657, 95%CI 0.628 to 0.685).

Conclusion: An increased GRS based on CRC-associated SNPs was associated with increased prevalence of colorectal adenomas.

These findings may help to identify better a subgroup of patients with increased risk of adenomas who would benefit from stricter cancer screening programs.

Disclosure: Nothing to disclose

P1160 ROLE OF INTERLEUKIN 10 GENETIC POLYMORPHISMS IN MEXICAN PATIENTS WITH RECTAL CANCER

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Introduction: Chronic inflammation is a well-established risk factor for colorectal cancer. Interleukin-10 (IL-10) is a cytokine whose main biological function is to limit inflammatory responses and is crucial to maintain immune homeostasis of the gastrointestinal tract. Some single nucleotide polymorphisms (SNPs) of IL-10 have been associated with cancer risk.

Aims & Methods: To evaluate the role of SNPs rs1800896, rs1800872 and rs1800871 of IL-10 in Mexican mestizo patients with rectal cancer.

A prospective study was conducted in which 53 patients with rectal cancer and 52 healthy controls were included. Information was collected focused on the demographic, clinical, biochemical characteristics; CT, MRI and histopathological reports of each patient, by reviewing the clinical files. SNPs rs1800896, rs1800872 and rs1800871 of IL-10 were genotyped by RT-PCR with Ab3130 kit.

Results: We identified that the AA genotype of rs1800872 behaved as a protective factor for invasion of regional nodes [OR0.14 (IC95% 0.02-0.80) p=< 0.04], presence of distant metastasis [OR0.30 (IC95% 0.10-0.83) p=< 0.01] and for the development of a late stage of the disease (CS III-IV) [OR0.14 (IC95% 0.02-0.79) p =< 0.04]. The CC genotype of rs1800871 was a protective factor for the presence of distant metastasis [OR0.33 (IC95% 0.12-0.94) p=< 0.03], whereas its CT heterozygous form was at risk for greater local infiltration (T3-T4) [OR1.11 (IC95% 1.01-1.22) p=< 0.001].

The genotypic GG frequency of rs1800896 was a risk factor for non-response to neoadjuvant therapy [OR4.0 (IC95% 2.82-5.65) p=0.005], whereas the AG genotype represented a protective factor for non-response to neoadjuvant therapy [OR0.25 (IC95% 0.17-0.35) p=< 0.005]. The allelic frequency A [OR0.22 (IC95% 0.08-0.58) p=0.001] and the AA genotype [OR0.20 (IC95% 0.06-0.64) p=0.003] of rs1800872 were protective factors for non-response to therapy neoadjuvant, while the allelic frequency C [OR4.42 (IC95% 1.70-11.44) p=0.001] and the CC genotype [OR6.77 (IC95% 2.86-17.90) p=< 0.001] of the same polymorphic site were found as risk for the no response to neoadjuvance. As for the rs1800871, the allelic frequency C [OR0.27 (IC95% 0.11-0.69) p=0.004] and the CC genotype [OR0.20 (IC95% 0.06-0.60) p=0.004], were protective for the non-response to neoadjuvant, whereas the allelic frequency T [OR3.6 (IC95% 1.44-8.99) p=0.004] and TT genotype [OR6.0 (IC95% 2.10-17.12) p=< 0.001] resulted in risk for non-response to neoadjuvant therapy.

Of the patients included who underwent surgical procedures, we found a protective factor for post-surgical complications at the allelic frequency A [OR0.34 (IC95% 0.12-0.97) p=< 0.04] and the AA genotype [OR0.18 (IC95% 0.04-0.75) p=0.01] of the rs1800872, while its allelic frequency C [OR2.86 (IC95% 1.02-8.04) p=0.04] behaved as a risk for postoperative complications. rs1800871 is also involved in post-surgical complications, its allelic frequency C [OR0.30 (IC95% 0.10-0.86) p=0.02] and homozygous CC genotype [OR0.18 (IC95% 0.04-0.75) p=0.01] were protective factors for the development of post-surgical complications, however, its allelic frequency T [OR3.26 (IC95% 1.15-9.18) p=0.02] and TT genotype [OR6.0 (IC95% 2.10-17.12) p=< 0.001] represented a risk factor for postoperative complications.

Conclusion: IL-10 SNPs could impact in different aspects in evolution of rectal cancer, particularly in tumor infiltration, progression, treatment response and post-surgical outcomes. This is the first study worldwide that associate IL-10 SNPs with neoadjuvant response and post-surgical outcomes exclusively in rectal cancer patients.

References: Oncol Lett. 2019; 17(2):2365-2369. J Cancer Res Ther. 2017; 13(2):252-256. Cancer Lett. 2015; 367(2):103-7.
Disclosure: Nothing to disclose

P1161 ANALYSIS OF THE DISTRIBUTION AND PHENOTYPE OF MACROPHAGES INFILTRATING INTO TUMOR TISSUES IN EARLY-STAGE COLORECTAL NEOPLASIA

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Introduction: Inflammatory cells such as neutrophils and macrophages are infiltrated in the tumor microenvironment (TME). The macrophages found in the TME are often referred to as tumor-associated macrophages (TAMs), which are classified into two types: M1 and M2. M1 macrophages exhibit high bactericidal and tumoricidal capacity. In contrast, M2 macrophages promote tissue repair, regulate immune function, and are involved in tumor progression. It has been reported that TAMs often have a M2 phenotype form and are associated with a poor prognosis in some cancers, such as melanoma. In contrast, some reports show a positive correlation of high number of macrophages with better prognosis in colorectal cancer (CRC) patients. The role of TAMs in progression of CRC is still controversial. Although most studies report an association between TAMs and an advanced CRC, there is no report on the detail about association between TAMs and early-stage colorectal neoplasia. The aim of this study is to elucidate the distribution and function of TAMs in early-stage colorectal neoplasia.

Aims & Methods: The subjects were 40 patients of early-stage colorectal neoplasia (20 submucosal invasive cancer and 20 dysplasia, including 10 low and 10 high-grade dysplasia) treated at our hospital from 2011 to 2018. The phenotype and distribution of macrophages were assessed by double immunofluorescent staining of CD68 as a marker for total macrophages and CD163 as a marker for M2 macrophages. M1 macrophages were defined as CD68 positive and CD163 negative. The number and phenotype of macrophages were evaluated as the most representative area at each part, including center, lateral periphery, and deepest part of the tumor (invasive edge), in addition to the non-neoplastic mucosa adjacent to the tumor. Five representative high-power fields (1 HPF = 0.0988 mm2) for each part were chosen and analyzed.

Results: When comparing dysplasia and submucosal invasive cancer, the number of total macrophages in submucosal invasive cancer was significantly higher than that in dysplasia at each part, and the number of total macrophages at the deepest part of the tumor was higher as compared to that at the other parts in both dysplasia and submucosal invasive cancer. With regard to the phenotype of macrophages, in dysplasia, most macrophages were of M1 type with only a few of M2 type at each part and the number of M1 macrophages at the deepest part of the tumor was significantly higher as compared to that at the other parts. In contrast, in submucosal invasive cancer, the number of both M1 and M2 macrophages at the deepest part of the tumor was significantly higher as compared to that at the other parts. Additionally, the number of M1 and M2 macrophages at the deepest part of tumor in submucosal invasive cancer was significantly higher as compared to that in dysplasia. Especially, the difference in the number of M2 macrophages between dysplasia and submucosal invasive cancer was remarkable at the deepest part of the tumor.

Conclusion: In submucosal invasive CRC, the number of macrophages, especially M2 macrophages was significantly higher at the deepest part of tumor. These findings suggested that macrophages differentiate into M2 macrophages by interaction with tumor cells and hence promote the progression of CRC.

Disclosure: Nothing to disclose

P1162 A PROSPECTIVE COHORT STUDY ON THE BENEFIT OF PREOPERATIVE ULTRATHIN COLONOSCOPY FOR COLORECTAL CANCER PATIENTS WITH STENOSIS

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Introduction: Preoperative colonoscopy for colorectal cancer (CRC) with stenosis is often insufficient because of poor preparation or incomplete colonoscopy. There is no large cohort study to clarify the usefulness of ultrathin colonoscopy for CRC with stenosis, although data after colon stent placement using a small diameter scope have been reported.[1]
Aims & Methods: This prospective cohort study aimed to evaluate the ability of an ultrathin colonoscope (UTC) to pass through stenosis and to detect synchronous neoplasms proximal to the stenosis. If the passage of a standard colonoscope (PCF-H290ZI: outer diameter 11.7 mm) was not feasible because of the stenosis, UTC (PCF-PQ260L: outer diameter 9.2 mm) was used. A total of 100 patients in whom UTC was used were prospectively registered from September 2017 at the Shizuoka Cancer Center (UMIN000028505). Patients with stent placement, who had undergone neoadjuvant chemotherapy, and who needed right hemicolectomy were excluded.
After colonoscopy, data on the tumor location, possibility of cecal insertion, grade of bowel preparation (according to the Boston Bowel Preparation Scale), presence of synchronous neoplasms, and day of surgery were recorded. Primary endpoints were the pass-through and cecal insertion rates. The detected synchronous neoplasms (adenomas and cancers) and their pathological findings after resection were also examined.
Results: Of 650 patients with advanced stage CRC who underwent preoperative colonoscopy during the recruitment period, 193 could not undergo complete colonoscopy using a standard colonoscope. After the exclusion of 93 patients, including 15 with stent placement, 21 who had undergone neoadjuvant chemotherapy, 21 indicated for right-hemicolectomy, and 40 others, a total of 100 patients who underwent ultrathin colonoscopy were enrolled in this study until February 2019 and analyzed.
The mean age of the 100 patients was 65.6 ± 10.8 years, and 59% of the patients were male. The pass-through and cecal insertion rates were 67% (67/100) and 58% (58/100), respectively. Synchronous lesions located proximal to the stenosis were detected in 65.5% (38/58) of the complete colonoscopies, with a total of 76 lesions, including 18 advanced neoplasms with three advanced stage CRCs. The bowel preparation score in the complete colonoscopy was 6.4 ± 2.6. The number of median waiting days for surgery was significantly longer in the pass-through of the UTC group (14 days vs. 10 days, $P = 0.022$). Two patients (6.1%) in the non-pass-through group required abdominal decompression by transanal ileus tube insertion before surgery.
Conclusion: Ultrathin colonoscopy for CRC with stenosis improved insertability compared to that in standard colonoscopy. Moreover, preoperative ultrathin colonoscopy for patients with stenosis has the potential to change the treatment strategy by predicting the risk of intestinal obstruction and detecting synchronous neoplasms.
References: 1. Kim JS, Lee KM, Kim SW, et al. Preoperative colonoscopy through the colonic stent in patients with colorectal cancer obstruction. World J Gastroenterol. 2014; 20: 10570-6.
Disclosure: Nothing to disclose

P1163 QUALITY OF ONLINE MEDICAL INFORMATION ON COLORECTAL CANCER SCREENING

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Introduction: Colorectal cancer (CRC) screening improves CRC mortality. The uptake of CRC screening is influenced by patient motivation which in turn is influenced by online health information. The Internet is a widely-used resource by patients to support healthcare decisions.
However, online content is not subjected to peer review and may be of variable quality.

Aims & Methods: The aim of the study is to determine whether the quality of online information on CRC screening varies according to the source of information. As many patients will not search beyond the first page of 10 hits[1], we also assessed whether higher quality hits are found in the first page of searches.
Google search was performed to identify English websites providing online information on CRC screening. The following keywords were searched: "colorectal cancer screening", "colon cancer screening", "rectal cancer screening", "colonoscopy", "FIT/FOBT", "CT colonography", "stool DNA", "colon polyp screening", "flat polyp screening", "nonpolypoid colorectal neoplasm screening". The first 2 pages for each keyword search were compiled. Scientific papers, advertisements, newspaper articles, publicly modifiable pages, videos, sites requiring subscription and duplicate websites were excluded. Websites were classified as professional society, hospital, government agency or patient advocate group. The quality of online information was assessed by the primary author using the DISCERN instrument, a validated 16-point questionnaire (total score 16-80) that evaluates the quality of written information[2]. DISCERN scores were graded as excellent (68-80), good (55-67), fair (42-54), poor (29-41) or very poor (16-28). The proportion of websites with excellent or good grading in each category was compared. Standard tests of statistical significance were used.
Results: The search identified 191 websites of which 40 were eligible for inclusion. Sixteen (40.0%) were written by professional societies, 15 (37.5%) by hospitals, 4 (10.0%) by government agencies and 5 (12.5%) by patient advocate groups. The overall median DISCERN score was 44.5 [23.0-67.0]). The median DISCERN scores were 51.5 [30.0-67.0] vs 36.0 [23.0-67.0] vs 44.5 [41.0-52.0] vs 42.0 [40.0-45.0] respectively. None of the websites had an excellent DISCERN score. The proportion of websites with at least excellent or good grading was significantly higher in websites from professional societies compared to hospitals, government agencies and patient advocate groups (25.0% vs 13.3% vs 0.0% vs 0.0%, p=0.005) (Table 1).
Twenty five websites appeared on the first page of search results and 15 appeared on the second page. The median DISCERN scores were 46.0 [28.0-67.0] vs 43.0 [23.0-55.0] respectively. There was no significant difference in the quality of online information between websites appearing on the first and second page of search (20.0% vs 6.7%, p=0.515).
Conclusion: The quality of online information on CRC screening is highly variable. Professional societies provide higher quality of information than other sources but their websites might not be found in the first page of searches. While patients should be directed to online sources that provide high quality information, there remains an unmet need to improve the quality of online information on CRC screening.

Grading based on DISCERN score	Professional societies (n=16)	Hospitals (n=15)	Government agencies (n=4)	Patient advocate groups (n=5)
Excellent or good	4 (25.0%)	2 (13.3%)	0 (0.0%)	0 (0.0%)
Fair, poor or very poor	12 (75.0%)	13 (86.7%)	100 (100.0%)	100 (100.0%)

[Table 1. Sources of online medical information and quality of information]

References: [1] Van Deursen AJ, Van Dijk JA. Using the Internet: Skill related problems in users' online behavior. Interacting with computers. 2009 Jun 30;21(5-6):393-402. [2] Batchelor JM, Ohya Y. Use of the DISCERN instrument by patients and health professionals to assess information resources on treatments for asthma and atopic dermatitis. Allergology International. 2009;58(1):141-5.
Disclosure: Nothing to disclose

P1164 CLINICOPATHOLOGICAL FEATURES AND THERAPEUTIC STRATEGY FOR LEFT-SIDED SESSILE SERRATED ADENOMA/POLYPS

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Introduction: Although sessile serrated adenoma/polyps (SSA/Ps) are considered premalignant lesions and their clinicopathological features have been previously reported, the differences based on lesion location (left- and right-sided) have not been clarified.

Aims & Methods: This study aimed to investigate the clinicopathological features and therapeutic strategy for left-sided SSA/P. In this study, 666 consecutive patients with lesions diagnosed as SSA/P by experienced endoscopists after endoscopic examinations (white light, narrow-band imaging, and pit pattern) and resected endoscopically in Hiroshima Asa Citizens Hospital between August 2010 and March 2017 were enrolled. The pathological diagnosis of each SSA/P was evaluated by two pathologists on the basis of the following Japanese Society for Cancer of the Colon and Rectum criteria: (1) crypt dilation, (2) irregularly branching crypts, and (3) horizontally arranged basal crypts (inverted T- and/or L-shaped crypts). When at least two of the three criteria were met in ≥10% of the lesion area, the serrated lesion was diagnosed as SSA/P. Resected lesions were classified into four groups (left-sided SSA/P: 173, left-sided HP: 94, right-sided SSA/P: 340, and right sided HP: 59). Evaluated endoscopic and pathological findings of left-sided SSA/P were compared with those of left-sided HP and right-sided SSA/P. SSA/P with cytological dysplasia (SSA/P-CD) was defined as a SSA/P with conventional adenoma-like dysplasia, and serrated dysplasia (SSA/P-SD) was defined as a SSA/P showing proliferation of atypical cells that are more cuboidal in shape and have eosinophilic cytoplasm, enlarged round nuclei with open vesicular prominent chromatin, and prominent nucleoli in addition to increased mitoses.

Results: The proportion of lesions with size ≥10 mm, mucus cap, varicose microvascular vessel, and type II open pit was significantly higher in the left-sided SSA/P group than in the left-sided HP group (35% vs 6%, 35% vs 10%, 48% vs 22%, and 53% vs 18%, respectively; p< 0.01). The proportion of females and lesions with size ≥10 mm, flat morphology (0-IIa), mucus cap, and type II open pit was significantly lower in the left-sided SSA/P group than in the right-sided SSA/P group (23% vs 39%, 35% vs 53%, 25% vs 50%, 35% vs 70%, and 53% vs 77%, respectively; p< 0.01). Although there was no significant difference in crypt dilation and irregularly branching crypts in the left- and right-sided SSA/Ps, the proportion of horizontallyarranged basal crypts was significantly lower in the left-sided SSA/P group than in the right-sided SSA/P group (62% vs 84%; p< 0.01). Twenty-seven cases (5%) of SSA/P-CD and 43 cases (8%) of SSA/P-SD were included in this study. The independent endoscopic finding of SSA/P-CD was an adenomatous pit pattern accompanied by type II/open II pit pattern in the multivariate analysis. No significant endoscopic findings of SSA/P-SD, except for lesion size, were found in either the left- or right-sided SSA/Ps. The proportion of right-sided SSA/P-SD increased with larger lesion size (< 5 mm: 0%, 5-9 mm: 8%, ≥10 mm: 15%), while that of left-sided SSA/P-SD was low, regardless of lesion size (< 5 mm: 6%, 5-9 mm: 4%, and ≥10 mm: 3%).

Conclusion: The endoscopic and pathological features of left-sided SSA/P are different from those of right-sided SSA/P. Lesions with an adenomatous pit pattern accompanied by type II/open II pit pattern should be treated, but the lesion size of left-sided SSA/P is not an important indication of resection unlike that of right-sided SSA/P.

Disclosure: Nothing to disclose

P1165 THE CLINICAL IMPACT OF MRI FOR DETECTING EXTRA-PERITONEAL FINDINGS IN COLORECTAL CANCER PATIENTS CONSIDERED FOR CRS/HIPEC

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Introduction: Part of the clinical value of MRI is not only to describe the peritoneal disease load but could also be to detect extra-peritoneal metastases that contraindicate cytoreductive surgery and hyperthermic chemotherapy. The purpose of this study is to evaluate whether an preoperative wholebody MRI for assessing peritoneal disease also has led to additional extra-peritoneal findings not described with earlier imaging.

Aims & Methods: Between February 2016 and October 2017, patients with colorectal peritoneal metastases considered for CRS/HIPEC who underwent a dedicated peritoneal MRI for preoperative staging were included. The MRI was performed additionally to standard diagnostic work-up of a preoperative CT chest/abdomen. The MRI protocol consisted of diffusion weighted, T2 weighted and contrast enhanced imaging of the chest, abdomen, and pelvis. The peritoneal MRI images were evaluated by one of two radiologists with experience with diffusion-weighted imaging and whole-body MRI and all extra-peritoneal findings were scored. The reference standard was histology. The results of the MRI were compared with all other, already available, clinical and imaging data to determine whether findings of the MRI were new.

Results: Of the 86 candidates with a peritoneal MRI, CRS/HIPEC was attempted for 55 patients and was successfully in 52. All patients had undergone CT chest/abdomen imaging prior to the MRI scan and 9 patients a PET/CT was performed. The mean days between CT and MRI imaging was 28.5 (standard deviation: ±30.9). Five patients had liver metastases and four patients had lung metastases detected with regular diagnostic work up (CT/CTPET). MRI detected in 3/86 patients new liver metastases and in 2/86 patients new lung metastases. Of the 5 (5.8%) patients with one or more additional extra-peritoneal findings, 4 were deemed ineligible for CRS/HIPEC at an MDT meeting and 1 at surgical exploration (laparotomy) for histology.

Conclusion: For patients considered for CRS/HIPEC, additional peritoneal MRI including diffusion-weighted body imaging can detect additional malignant extra-peritoneal lesions such as liver and lung metastases. Peroperative imaging with peritoneal MRI can not only contribute to staging of the peritoneal disease load but can also detect contra-indications that were not seen on prior imaging and thereby prevent a potentially futile CRS/HIPEC effort.

Disclosure: Nothing to disclose

P1166 MR IMAGING TO PREDICT COMPLETE CYTOREDUCTION AND SURVIVAL IN COLORECTAL PERITONEAL METASTASES IN PATIENTS CONSIDERED FOR CRS/HIPEC

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Introduction: Selecting colorectal cancer patients with peritoneal metastases for CRS-HIPEC remains a big diagnostic problem. In order to prevent under or overtreatment an invasive surgical staging system, the Peritoneal Cancer Index (PCI), was introduced. In order to avoid these invasive staging surgeries this study assesses the performance of the PCI determined with preoperative peritoneal MRI (MRI PCI) to predict successful cytoreductive surgery (CRS), disease free survival and overall survival in HIPEC candidates. Can MRI replace surgical staging?

Aims & Methods: Between February 2016 and October 2017, 86 patients with colorectal peritoneal metastases considered for CRS/HIPEC who underwent a dedicated peritoneal MRI for preoperative staging were included. The MRI protocol consisted of diffusion weighted, T2 weighted and contrast enhanced imaging of the thorax, abdomen, and pelvis. Peritoneal MR images were evaluated by two readers, independently and retrospectively, to determine the Peritoneal Cancer Index (MRI-PCI). Relevant patient characteristics were obtained from patient files. Receiver characteristic operator (ROC) analysis was used to determine the performance of the MRI-PCI to predict successful CRS/HIPEC and Cox regression analysis to determine to prognostic value of MRI for disease free survival and overall survival.

Results: CRS/HIPEC was attempted for 55 patients and was successfully in 52. The median follow-up from MRI was 18.30 months (1st-3rd Quartile: 12.73-24.33). The mean (standard deviation) MRI-PCI of reader 1 and 2 were 11.8 (8.46) and 10.5 (8.59), respectively. An area under the curve was found of 0.83 (95% confidence interval: 0.74-0.93) for reader 1 and 0.86 (95% confidence interval: 0.77-0.94) for reader 2 to predict a complete resection. For the patients who received successful CRS/HIPEC and complete resection, the MRI-PCI showed prognostic value for disease free survival for both readers (p< 0.05). The MRI-PCI of reader 1 showed a prognostic value for overall survival (p=0.01), independently of whether complete resection was achieved, while reader 2 was borderline significant (p=0.05) in this patient cohort.

Conclusion: MRI can predict whether successful CRS/HIPEC can be achieved and shows prognostic value for disease free and overall survival. This means that MRI is an accurate tool for selecting CRC patients which may benefit from CRS-HIPEC. Surgical staging should be reserved for borderline cases after MR imaging.

Disclosure: Nothing to disclose

P1167 RISK OF METACHRONOUS NEOPLASIA ON SURVEILLANCE COLONOSCOPY IN YOUNG AND OLD AGE GROUPS AFTER POLYPECTOMY

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Introduction: Few reports exist that address the appropriate colonoscopy surveillance interval for individuals < 50 years old. We compared the risk of metachronous neoplasia among young (< 50 years), adult (50-74 years) and old (≥ 75y) age groups.

Aims & Methods: This is a single center retrospective cohort study. Subjects were eligible if they underwent their first colonoscopy with polypectomy between 2005 and 2014 and had at least one surveillance colonoscopy after 3-5 years. Exclusion criteria included known genetic syndromes, inflammatory bowel disease, previous colectomy, incomplete procedures and the occurrence of cancer or multiple polyps at baseline. Patients were stratified at baseline according to adenoma characteristics into low-risk adenoma (LRA) and advanced adenoma groups. The primary outcomes were the occurrence of overall and high-risk neoplasia at surveillance colonoscopy in each age-group.

Results: At baseline (N=495), young patients were more likely to have smoking exposure and to report a family history of CRC whereas aspirin use and diabetes were more frequent in the adult and old age-groups. In the baseline LRA- group (N= 201), the 5-year risk of metachronous high-risk neoplasia was 12.5%, 15.2% and 22.5% (P= 0.426) in the young, adult and old age-groups, respectively. In the baseline advanced adenoma group (N= 294), the 3-year risk of metachronous high-risk neoplasia was 13.3%, 14.8% and 25.3% (P = 0.041), respectively. All interval cancer in this group - 3 cases, developed in the old age-group (3.8%, P = 0.027). In multivariate analysis, after adjusting for baseline risk factors, the only risk factor for metachronous high-risk neoplasia was old age-group (old vs. young age groups: OR 2.191, CI 1.099-4.373; P= 0.026; old vs. adult age groups: OR 1.876, CI 1.087-3.238; P= 0.024).

Conclusion: Considering the comparable risk of metachronous high-risk neoplasia in young and adult patients, surveillance recommendations after polypectomy should not differ. Since this risk is higher in the old age-group, a more frequent surveillance is warranted and should be counter-balanced with the higher complication risk and comorbidities.

Disclosure: Nothing to disclose

P1168 IS THE ADENOMA DETECTION RATE AN IMPORTANT INDICATOR IN THE DETECTION OF OTHER NON-NEOPLASTIC FINDINGS?

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Introduction: Colonoscopy enables screening and prevention of colorectal cancer (CRC) by removing adenomatous polyps. Adenoma detection rate (ADR) is the proportion of screening colonoscopy patients who are found to have at least one adenoma. ADR should be used as a measure of adequate inspection at screening or diagnostic colonoscopy in patients aged 50 years or more. ADR has been inversely associated with the risk of CRC and death. However little is known about the correlation of the adenoma detection rate and the detection of other non-neoplasic findings.

Aims & Methods: The aim of this study was to evaluate if ADR is associated with a higher detection of non-neoplasic findings. We retrospectively analyzed patients undergoing colonoscopy by three endoscopists at our center (A, B, C). Patients with an incomplete colonoscopy were excluded as well as colonoscopies performed in the setting of overt gastrointestinal bleeding, inflammatory bowel disease or polypectomy/mucosectomy. Angiodysplasia, diverticula, nonspecific inflammation, erosions or ulcers or subepithelial lesions were considered non-neoplastic findings.

Results: A total of 229 colonoscopies were analyzed. The mean age was 64 ± 13.1 years-old. 54.6% were male (n=125). The median ASA score was 2 (IQR: 1 - 3). The mean indication was post-polypectomy surveillance 25.8% (n=59), followed by CRC surveillance 27.1% (n=62) and screening for CRC 20.5% (n=47). The indication for colonoscopy was significantly different between groups (p=0.04): CRC surveillance was higher in endoscopist B (31.9%, n=23) and C (36.5%, n=23), and post-polypectomy surveillance was higher in endoscopist A (35.1%, n=33). An excellent bowel cleansing was higher in colonoscopies performed by endoscopist A (A: 59.6% vs. B: 48.6% vs. C: 19%, p< 0.01). The global ADR was 36.2% (n=83) and was not significantly different between endoscopists (A: 42.6% vs. B: 36.1% vs. C: 27%, p=0.14). The ADR was not associated with higher detection rate of non-neoplasic findings (31.3% vs 30.1%, p=0.88), even when concerning each endoscopist (A: 27.5% vs 33.3%, p=0.65; B: 38.5% vs 23.9%, p=0.28 e C: 29.4% vs 32.6%, p=0.81).

Conclusion: In our study, ADR was not associated with a better detection of other non-neoplastic findings in the total sample and by endoscopist.

Disclosure: Nothing to disclose

P1169 FAECAL BACTERIAL SIGNATURE TESTING FOR COLORECTAL CANCER SCREENING IN POSITIVE FAECAL IMMUNOCHEMICAL TEST POPULATION

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Introduction: Colorectal cancer (CRC) is the third most common cancer in men and the second in women worldwide, and a leading cause of mortality. Guidelines recommend routine screening for CRC in asymptomatic adults starting at age 50. The most extensively used non-invasive test for CRC screening is the faecal immunochemical test (FIT). Although its overall sensitivity for CRC is around 61-91% and for advanced adenomas (AA) between 27-67%, these figures still imply a high false-positive rate and a low positive predictive value (PPV).

Aims & Methods: The aim of this work was to develop a new non-invasive CRC screening tool based on faecal bacterial markers capable of decreasing FIT false-positive rate in FIT-positive population. Analysis of the relative abundance of eight CRC-associated bacterial markers (B10, B46, B48, *G. morbillorum*, *P. stomatis*, *B. fragilis*, *B. thetaiotaomicron*, *R. intestinalis*) and four associated to IBD (*F. prausnitzii*, *F. prausnitzii* phylogroups I and II, *E. coli*) was performed.

The bacterial signature (*RAID-CRC Screen*) was defined in a proof-of-concept with 172 individuals and the obtained results were validated in an external cohort of 327 subjects. All study participants had joined the national CRC-screening program.

Results: In the proof-of-concept study, regardless of the colonoscopy result, the most prevalent bacteria were butyrate producers (B10, B46, B48, *F. prausnitzii*, and *R. intestinalis*), with abundance values of 19%, 16%, 18%, 16%, and 12%, respectively. *P. stomatis* and *B. fragilis* were significantly more abundant in CRC than in individuals with normal colonoscopy (p=0.002 and p=0.017, respectively).

The development of *RAID-CRC Screen* algorithm was focused on the reduction of false positive results for Advanced Neoplasia (AN; CRC+AA) among the FIT-positive subjects, while maintaining 100% sensitivity for CRC. The combination of *F. prausnitzii*, B46, B48, *G. morbillorum*, *B. fragilis*, and the total bacterial load led to the achievement of an algorithm with sensitivity of 95%, specificity of 26%, PPV of 50%, and a negative predictive value of 86%, for AN. These results lead to a decrease in the false positive rate up to 30%.

In the clinical validation of *RAID-CRC Screen* a sensitivity of 84% and specificity of 16% were obtained for the detection of AN. While with FIT 20 µg/g there were 184 false-positive results, *RAID-CRC Screen* reduced this value to 154, implying a reduction of the false-positive rate of 16%, which confirms the robustness of the defined bacterial signature.

Conclusion: *RAID-CRC Screen* test would allow reducing up to 20% of the colonoscopies that are performed unnecessarily in FIT-positive participants of CRC-screening programs. Thus, it becomes a good complement to be implemented in a CRC screening scenario.

	Characteristics	CRC	Advanced adenoma	Non-advanced adenoma	Normal colonoscopy
Proof-of-concept	n (%)	11 (6.3)	67 (39.0)	38 (22.1)	56 (32.6)
	Age (mean, range)	61 (50-69)	61 (50-69)	60 (50-69)	59 (49-69)
	Sex, female (%)	6 (54.5)	19 (28.3)	15 (39.5)	37 (66.1)
Clinical validation	n (%)	19 (5.8)	124 (37.9)	85 (26.0)	99 (30.3)
	Age (mean, range)	61 (54-69)	61 (50-73)	61 (50-70)	58 (49-69)
	Sex, female (%)	6 (31.6)	52 (41.9)	42 (49.4)	53 (53.5)

[Table 1. Characteristics of patients included in the proof-of-concept and clinical validation studies, classified according to their diagnosis.]

P1170 FABP4 PROMOTES INVASION AND METASTASIS OF COLON CANCER BY REGULATING FATTY ACID TRANSPORT

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Introduction: Colon cancer is a common malignant tumor and it is estimated that about 1,200,000 new cases are reported every year. Recent studies have shown that FABP4 can participate in tumor invasion and metastasis.

Aims & Methods: In order to explore the effects and mechanism of Fatty acid-binding protein 4 (FABP4) on proliferation, migration, invasion and energy metabolism of colon cancer cells.We measured the distribution of fat, the content of triglyceride and the level of FABP4 mRNA in colon cancer and adjacent normal tissues. At the meantime, the adipose tissue extract was co-cultured with human colon cancer cell line HCT-8 and the cells were divided into three groups: Control, Co-culture, Co-culture + inhibitor group. And we detected the proliferation, migration and invasion of HCT-8 cells. Then we analyzed the content of ATP, LDH, glycerol and fatty acid by specific kits. In addition, we used FABP4 overexpressed adenovirus to infect HCT-8 cells, and then detect cell proliferation, migration and invasion. Meanwhile, we measured the levels of intracellular metastasis related protein MMP-2, MMP-9 and energy-related protein p-Akt.

Results: The content of fat in colon cancer tissues was significantly higher than that in adjacent normal tissues and the level of FABP4 mRNA in colon cancer tissues was significantly higher than that in adjacent normal tissues. Besides, the adipose tissue could promote the migration and invasion of human colon cancer cells in vitro. Moreover, the content of intracellular ATP and LDH, glycerol and fatty acid in culture supernate were decreased significantly after co-culture and FABP4 overexpression could promote migration and invasion of cancer cells and the levels of intracellular MMP-2, MMP-9, p-Akt were increased.

Conclusion: FABP4 may promote the transfer of fat from adjacent normal tissues to cancer tissue and co-culture with adipose tissue promoted the migration and invasion of colon cancer cells and cellular energy metabolism. Overexpression of FABP4 could promote migration and invasion and increased the levels of MMP-2, MMP-9 and p-Akt protein. This may provide a new idea for the diagnosis and treatment of colon cancer.

Disclosure: Nothing to disclose

P1171 A PATIENT SELF-MADE ONE STEP QUICK FAECAL TEST REDUCES UNNECESSARY COLONOSCOPIES AND PRIORITIZES HIGH RISK SYMPTOMATIC PATIENTS

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Introduction: Gastrointestinal symptoms are a common reason for patients to consult primary care physicians. Most of these patients have no relevant pathology, but in an effort not to miss colorectal cancer (CRC), precancerous lesions or inflammatory bowel disease (IBD) many of them undergo colonoscopy. Faecal biomarkers have been proposed as useful diagnostic tools in this setting. Quick faecal tests, which can be performed by patients and give immediate results, may be a useful strategy to determine which patients need rapid investigation and also the ones who have low risk of significant pathology.

Aims & Methods: To evaluate the diagnostic accuracy of a one-step combo card test for the simultaneous semi-qualitative detection of human haemoglobin (hHb), human transferrin (hTf), human calprotectin (hCp) and human lactoferrin (hLf) in stool samples of symptomatic patients.

Methods: Symptomatic patients referred for colonoscopy, who returned stool samples and completed colonic examinations, were prospectively recruited. Certest FOB+Transferrin+Calprotectin+Lactoferrirn® (Certest Biotec S.L, Zaragoza, Spain), a coloured chromatographic inmmunoassay for the simultaneous semi-qualitative detection of hHb, hTf, hCp and hLf, was performed. Cut-off values of the test are 5.1 µg/gr for hHb, 0.4 µg/gr for hTf, 50 µg/gr for hCp and 10 µg/gr for hLf.

CRC, advanced adenoma (>10mm, >3 adenomas, villous component, high grade dysplasia), IBD, angiodisplasia and microscopic colitis were considered as relevant pathology.

Positive and negative predictive values (PPV, NPV), sensitivity and specificity for each marker and for the different combinations were calculated.

Results: 482 patients (251 - 52.1% female, median age 63 years, IQR: 51.5-74.5) were included. The most frequent indications for colonoscopy were recent history of rectal bleeding (128/482, 26.6%), chronic diarrhea (99/482 -20.5%), abdominal pain (85/482 - 17.6%), and anemia/iron deficiency (79/482 - 16.4%). Colonoscopies were mainly requested by primary care level (315/482 - 65.4%), and by Gastroenterology outpatient's clinics (117/482 - 24.3%).

Relevant pathology was found in 115/482 (23.9%) patients. CRC was diagnosed in 24/482 (5%) patients. IBD was detected in 14/482 (2.9%) patients. Diagnostic accuracy of hHb, hTf, hCp and hLf for relevant colonic pathology are summarized in Table 1.

162/482 (33.6%) patients had negative results of all 4 biomarkers. 151/162 colonoscopies of this group have no relevant pathology (NPV 93.2%). This 11 patients with pathology were 9 advanced adenomas and two microscopic colitis, so no case of CRC or IBD would have been potentially missed (NPV 100%). 29/482 (6%) patients had all 4 biomarkers positive, 13/29 (44.8%) were diagnosed with CRC and 7/29 (24.1%) with IBD (PPV 68.9% for CRC + IBD).

Test	Negative test	Positive test	PPV	NPV	Sensitivity	Specificity
hHb	362	120	57.5%	87.3%	60%	86.1%
hCp	183	299	33.1%	91.2%	86.1%	45.5%
hTf	380	102	47%	82.4%	41.7%	85.3%
hLf	417	65	53.8%	80.8%	30%	91.8%

[Table 1.]

Conclusion: This semi-quantitative rapid self-made faecal combo test may be a useful and quick diagnostic tool to avoid unnecessary colonoscopies and to prioritize high risk symptomatic patients.

Disclosure: Nothing to disclose

P1172 MANAGEMENT OF RECTAL NEOPLASTIC LESIONS BY ENDOSCOPIC SUBMUCOSAL DISSECTION AND TRANSANAL ENDOSCOPIC MICROSURGERY IN THE NATIONAL CANCER INSTITUTE IN SLOVAKIA

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Introduction: Colorectal carcinoma is the most common type of cancer in Slovakia. Recognition and successful removal of the early forms of colorectal carcinoma reduces morbidity and mortality caused by this disease. When removing early neoplastic lesions in the rectum "en bloc", we have a choice between endoscopic submucosal dissection (ESD) and transanal endoscopic microsurgery (TEM).
Aims & Methods: The aim of this study was to compare the outcomes of endoscopic submucosal dissection (ESD) and transanal endoscopic microsurgery (TEM) in a cohort of patients with neoplastic rectal lesions in our hospital (National Cancer Institute in Slovakia).We retrospectively analyzed the cohort of 100 patients consecutively treated for neoplastic colorectal lesion by ESD (60 patients) or TEM (40 patients) in the National Oncology Institute in Slovakia.
We collected clinical, endoscopic and histological data including the diameter of removed lesions, duration of the procedures, histopathological types of lesions, the rates of "en bloc" and R0 resections, the rates of acute and late complications, the length of hospital stay and the rate of recurrence.
Results: The average diameter of lesions removed by ESD were significantly greater when compared to TEM (45,6 mm vs. 34,9 mm; p< 0,01). We observed higher rates of "en bloc" resections (95 % vs. 75%; p< 0,01) and R0 resections 93,3 % vs. 67,5%; p< 0,001) in the ESD group. The average length of hospital stay was significantly shorter in ESD group. (5,6 vs. 8,8 days; p< 0,0001). The average duration of procedure was significantly shorter in the TEM group (151,1 vs. 77,7 min; p< 0,001).
Conclusion: ESD and TEM have both proven to be effective and safe for treating neoplastic lesions of rectum. In our hospital, ESD was more effective in achieving "en bloc" resection, R0 resection and was also associated with shorter hospital stay. However, in our conditions, the average duration of ESD was longer than TEM.
Disclosure: Nothing to disclose

P1173 WITHDRAWN

P1174 WITHDRAWN

P1175 LOW RISK SUPERFICIALLY INVASIVE CARCINOMA IN LARGE LATERALLY SPREADING COLONIC LESIONS REMOVED BY PIECEMEAL EMR HAS A LIMITED RISK OF RESIDUAL DISEASE

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Introduction: Endoscopic mucosal resection (EMR) is established as a safe, effective, efficient and definitive first line therapy for the management of large (>20mm) laterally spreading colonic lesions (LSL). 4 % of referred LSL contain covert submucosal invasive carcinoma (SMIC), which is only detected after EMR. Although enbloc resection is ideal, when this has not occurred, at present, there are no established guidelines on the optimal management for these patients. Surgery is usually advised but such patients are often elderly with multiple co-morbidities and surgery is more expensive, resource intensive and morbid.
Aims & Methods: To determine outcomes in patients with covert SMIC within a large prospective multicentre cohort.
Patients within the Australian colonic endoscopic resection (ACE) cohort were prospectively followed, and cases with SMIC were identified. Overt SMIC cases, where EMR was not attempted due to clear malignancy, were excluded, and only those in whom EMR was completed and cancer was subsequently diagnosed (covert) were included. Surgical and histologic outcomes were recorded and presence of residual local malignancy (defined as either lymph node involvement or residual carcinoma in the resection specimen) was determined.
Results: From a prospective cohort of 3372 cases of LSL, 225 cases of SMIC were identified. 74 overt SMIC cases were excluded. Of 151 covert SMIC cases, complete outcomes were available in 124. 95 patients proceeded to surgical resection (77%), while 29 were managed conservatively (23%). Patients managed conservatively were older (p=0.001) and had higher ASA scores (p=0.001). Based on the EMR histology, 57 (46%) had Kikuchi SM1 disease and 67 (54%) had Kikuchi SM2 or 3 disease. Overall, residual local malignancy was detected in 32 of 95 cases (34%). Of 56 with SM1 disease, 37 (66%) proceeded to surgical resection. Within this group residual luminal cancer was detected in 6 cases (16%) and nodal disease in 2 (5%), in both cases the tumour was poorly differentiated. Of 19 SM1 cases managed conservatively (due to advanced age in 3, co-morbidities in 7 and patient preference in 9), follow up colonoscopy was performed in 14 (74%). Recurrence was detected in 1 case, who subsequently underwent successful surgical resection. Over a median follow-up of 36 months (range 5-95 months) 1 death occurred due to cardiac disease, and the other 18 remain alive and disease free. On multivariate analysis with stepwise backward regression, independent risk factors associated with subsequent residual surgical disease., were presence of SM2 or 3 invasion (odds ratio 3.4 (95% CI 1.3-9.3), p=0.015), and presence of submucosal fibrosis (SMF) (odds ratio 2.5 (95% CI 1.1-6.1), p=0.041).
Conclusion: The majority of patients with covert SMIC proceeding to surgical resection have no residual local disease. This risk is increased with deeper submucosal invasion at initial EMR histology (SM2 or SM3) and presence of submucosal fibrosis. In patients with disease confined to SM1 where no SMF is present, the need for surgery needs to be balanced against the patient's age and co-morbidities. Further data are needed to more precisely inform this decision process.
Disclosure: Nothing to disclose

P1176 INCIDENCE OF METACHRONOUS ADVANCED NEOPLASIA AFTER SUBMUCOSAL INVASIVE COLORECTAL CANCER RESECTION

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Introduction: Surveillance colonoscopy is strongly recommended after surgical resection (SR) of colorectal cancer (CRC) or endoscopic resection (ER) of adenoma because of their risk of metachronous colorectal neoplasia. However, there is little evidence about metachronous lesions following resection of submucosal invasive CRC (SM-CRC), for which both surgical and endoscopic resection can be chosen.

Aims & Methods: The aim of the present study was to clarify the incidence of metachronous advanced neoplasia (AN) after SM-CRC resection. This retrospective observational study reviewed consecutive patients who underwent surgical or endoscopic resection of SM-CRC at the National Cancer Center Hospital East, Kashiwa, Japan, between January 2005 and December 2013. We included patients who underwent:

(i) histopathologically-proven complete resection of SM-CRC by SR or ER as the first-line treatment;

(ii) resection of all other colorectal neoplasia; and,

(iii) one or more surveillance total colonoscopies after resection of SM-CRC.

The overall and cumulative incidence of metachronous AN detected at surveillance colonoscopies were calculated using the Kaplan-Meier method and compared by the log-rank test. The Cox proportional hazards model was used to analyze risk factors of incidence of metachronous AN.

Results: A total of 343 patients were eligible for inclusion. The median age was 65 years (range, 33-87), and 219 (63.9%) were male. The location of SM-CRC was right-sided colon in 100 (29.2%), left-sided colon in 131 (38.2%), and rectum in 112 (32.7%). 93 (27.1%) underwent only ER (ER group), and 250 (72.9%) underwent ER followed by SR or only SR for SM-CRC (SR group). The median follow-up period was 61.7 months (range, 12.6-151.6), and the median number of surveillance colonoscopies was 3 (range, 1-12). The median follow-up period of the SR group was 61.9 months, whereas that of the ER group was 60.5 months. The median number of surveillance colonoscopies of the SR group was 2, whereas that of the ER group was 4.

The overall incidence rate of metachronous AN was 8.5% (29/343 patients; 95% confidence interval [CI], 5.7-11.9). The overall cumulative incidence rates at 3 and 5 years were 4.8% and 6.0%, respectively. The cumulative incidence rate was significantly higher in the ER group than in the SR group (P < .001); in the colon group than in the rectal group (P = .021); and in the group with synchronous AN than in the group without synchronous AN (P < .001). The multivariate analysis identified ER (hazard ratio [HR], 2.90; 95% CI, 1.26-6.68) and synchronous AN (HR, 4.37; 95% CI, 1.96-9.73) as significant risk factors for metachronous AN.

Conclusion: ER and Synchronous AN were significantly associated with incidence of metachronous AN after SM-CRC resection. Intensive surveillance colonoscopy should be considered after ER of SM-CRC and patients with synchronous AN.

Disclosure: Nothing to disclose

P1177 A LONG WAY FROM HOME: LIGHTS AND SHADOWS OF THE COLON-RECTUM LEARNING CURVE IN ESD EN BLOC RESECTION

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Introduction: In the last decade ESD has shown very promising results, but the technique is still burdened by complications, depending mostly on endoscopist experience. Organizational options such as preventive hospitalization seem to play a role too, but no clear guidelines are available on this issue. In Eastern Countries, an endocopist is considered an expert with more than 80 ESD performed in the stomach (in general, gastric lesions are easier to remove with this technique). In Western Countries, a low incidence of gastric lesions makes ESD very difficult to be learned by professionals, and, actually, the learning curve of this procedure is longer and performed mostly in the colon-rectum tract.

Aims & Methods: Aims are: 1.to estimate the number of ESD procedures to be performed by a single operator to learn proficiently the technique in a Western country; 2.to establish if the patient has to be hospitalized when performing ESD compared to other resection techniques and which are main complications. From 2012 to 2019 in a urban hospital, all mucosectomies >2 cm of a single operator were collected to draw the ESD learning curve. The cumulative summation analysis (CUSOM) was calculated to establish ESD learning curve for *en bloc* resection parameter.

Information was collected on preventive hospitalization, complications (perforation; acute and delayed bleeding), hospital length of stay, neoplasm relapse at follow-up. The results were compared with EMR and EFTR (performed using the Full Thickness Resection Device (FTRD®). Statistical analyses: chi squared and t Student tests were performed for comparison, setting statistical significance p < 0.05.

Results: 311 procedures were collected (128 ESD, 152 EMR and 31 EFTR). 81.6% were hospitalized with a mean length of stay of 2.7±2.04 days (range 1-13). 54.8% were females (M:F=171/311) with a mean age 66.4±11 yrs. 160 patients made a regular follow-up (mean follow-up 18.6±15.6 months). The CUSOM curve for *en bloc* parameter after 128 ESD showed a decrement of the curve without reaching the inferior limit (-1.23), we estimated that further 10 consecutive ESD procedures are needed to complete the curve (138 in all). ESD sites: rectum (59), colon sx (31), colon dx (22), stomach/esophagus/duodenum (16). EMR sites: rectum (17), colon sx (25), colon dx (90), stomach/esophagus/duodenum (20). EFTR sites: rectum (4), colon sx (7), colon dx (16), stomach/esophagus/duodenum (4). No significant differences were found in hospital length of stay (EMR 2.74-ESD 2.85-EFTR 2.23 p=ns). Perforation was significantly higher in ESD technique (ESD 26/128 20.3% vs EMR 5/152 3.2% vs EFTR 0/31 0%, p< 0.05). The mean recovery stay was longer in patients with perforation 3.5 days±2.9 Vs no perforation 2.5±1.8 (p=ns), no perforation underwent surgery. No differences were observed for acute or delayed bleeding according to the endoscopic technique (acute: ESD 3/128 2.3%; EMR 4/152 2.6%; EFTR 2/31 6.4%, p=ns; delayed: ESD 8/128 7.8%; EMR 7/152 4.9%; EFTR 1/31 3.4%, p=ns). All the delayed bleedings happened after patients discharge. During the follow-up were observed 20 neoplasms relapse (20/160 pts in regular follow up -12.5%): 12 (15.6%) in EMR; 8 (10.4%) in ESD, 0(0%) in EFTR. Relapses were associated with margins R1+ in *en bloc* resections in 23.1% of cases (p< 0.05). Margins R0 showed 2.8 % relapses.

Conclusion: In our experience, to become expert in ESD in the colon nearly 140 procedures need to be performed. Patients need to be hospitalized only if a perforation occurs during the procedure. Delayed bleeding is rare and in our casuistry it happened always after discharge.

Disclosure: Nothing to disclose

P1178 IMPACT OF OBESITY IN COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION

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Introduction: The difficulty in insertion of colonoscope, the poor maneuverability, or the abundant fat tissue in submucosal layer sometimes occur during colorectal endoscopic submucosal dissection (ESD) in patients with obesity. However, association between obesity and colorectal endoscopic submucosal dissection (ESD) has not been investigated. In this study, we evaluated the clinical impact of obesity in patient who underwent colorectal ESD.

Aims & Methods: We retrospectively reviewed 543 patients who underwent colorectal ESD at Omori Red Cross Hospital from April 2012 to February 2019. Patients that we could not confirmed BMI records, we discontinued the ESD, or had recurrent lesions were excluded. The remaining 536 patients (599 lesions) were divided two groups based upon body mass index (BMI, kg/m^2): obesity group (BMI$\geqq$25) and non-obesity group (BMI<25).

Results: 120 patients (132 lesions) were in obesity group and 416 patients (467 lesions) were in non-obesity group. There is no significant difference between both groups in mean age (67.8±9.9 vs. 68.5±12.4), lesion diameter (27.1±14.5mm vs. 26.4±13.1mm), location (C/A/T/D/S/R= 18/34/31/12/18/19 vs. 66/108/101/36/68/88) and macroscopic type (I/IIa/IIc/combined/SMT= 21/107/0/3/1 vs. 78/371/5/7/6). In short term clinical outcomes, there is no significant difference in procedure time (47.2±43.7min vs. 42.0±34.7min), en bloc resection rate, curable resection rate, and pathological diagnosis. While the amount of sedative (flunitrazepam) per body weight was significantly lower in obesity group (1.62×10^{-2}±0.85×10^{-2}mg/kg vs. 1.92×10^{-2}±0.95×10^{-2}mg/kg), cases in which reduction of percutaneous arterial oxygen saturation occurred were significantly more in obesity group (46.7% vs. 29.8%). The procedure time by trainee (less than 100 cases of colorectal ESD experience) was significantly longer in obesity group (58.8±48.1min vs. 48.1±31.3min).

Conclusion: This study showed colorectal ESD could be performed safely and effectively in obese patients. However, ESD in patients with obesity requires attention to changes especially in respiratory condition.

Disclosure: Nothing to disclose

P1179 RISK OF LYMPH NODE METASTASIS IN PT1SM2 COLORECTAL CARCINOMA: RESULTS OF BICENTRIC STUDY

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Introduction: Lymph node risk assessment has become a major issue to recommended additional surgery with lymph node dissection after endoscopic resection (ER) of a superficial colorectal cancer. This risk is based on histological criteria (depth invasion, differenciation, lymphovascular invasion, budding, positive margins) and their presence is an indication for additional surgery at this time. The challenge is to determine if there are any subgroups for which surgery could be avoided.

Aims & Methods:

Aims: Evaluate the relapse-free survival rate in all patients and in specific subgroups, measure the lymph node and/or metastatic risk of colorectal adenocarcinoma pT1sm2 and evaluate the morbidity rate of endoscopic resections for tumor pT1sm2.

Methods: Patients with endoscopic or surgical resection of colorectal adenocarcinoma pT1sm2 between 2012 and 2018 at Institut Paoli Calmettes (Marseille, France) and Edouard Herriot hospital (Lyon, France) were retrospectively included. We evaluated two predefinied groups of patients . First group was "supposedly good prognosis" patients (SGP) including ER alone with no pejorative histological criteria, patients with ER and additional surgery with favorable histology (pT0N0) or primary surgery with adenocarcinoma pT1sm2 and no pejorative criteria. The second group was "supposedly effective endoscopic resection"(SEER) including ER alone with no pejorative criteria, ER with additional surgery, histologically pT0N0 and negative deep margins. At last we studied patients treated by ER alone. For each group, free-recurrence survival rate (FRS) at 12 and 24 month and complete remission (CR) rate (defined as absence of local or metastatic recurrence in the first 12 months, excluded local recurrence treated by endoscopy) were assessed. The rate of histological lymph node invasion, adverse events of endoscopic and surgical treatment were recorded.

Results: 74 patients were included (38 women and 36 men) with a median age of 68 years (51-88). The mean hospitalization lenght was 2 days (1-7) and the median follow-up was 16 months (0-81). 33 tumors were located in the descending colon, 18 in the ascending colon, 4 in the transverse colon and 18 in the rectum. All tumors were well differentiated, 49 % had budding , 2,7% vascular invasion, 5,6% lymphatic invasion and 40% had positive deep margins. 68 patients had ER : 22 patients alone and 46 had additional surgical treatment with lymph node staging. 6 patients were operated without previous endoscopic resection. During the follow-up, 4 patients died. No deaths were related to cancer. There were 4 local recurrences and 3 were treated by a new ER and 1 by endocavitary radiation therapy. In the general population, the FRS rate was 98% at 12 months and 97% at 24 months. CR rate at 12 months was 98%. In the "SGP" group, the FRS rate was 100% and 97% at 12 and 24 months respectively. The CR rate at 12 months was 100%. In the SEER group, the FRS rate at 12 months was 100% and 94% at 2 years and the CR rate 100%. In the "endoscopic resection alone" group alone: 8 patients had no pejorative criteria, 14 had at least 1 and the FRS rate was 100% and 90% respectively. The lymph node invasion rate was 6.4% with a mean number of lymph nodes examined of 15 (7-30). The complication rate for endoscopic resections was 11% (all treated by endoscopy) and 9,5% for surgical complications.

Conclusion: Endoscopic resection of pT1sm2 adenocarcinoma without histological pejorative criteria might be a good candidate to avoid additional surgery. However a longer follow-up and more patients are needed to confirm this approach.

Disclosure: Nothing to disclose

P1180 RISK OF CANCER BETWEEN FAMILY MEMBERS OF PATIENTS WITH PROBABLE LYNCH SYNDROME

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Introduction: Lynch syndrome (LS) is one of the most frequent causes of hereditary colorectal cancer (CRC). However, there is a group of patients who develop CRC or tumors of the LS domain in which microsatellite instability and / or loss of expression of DNA repair genes are observed in the tumor, but without evidence of pathogenic mutation. This group of patients is known as Lynch-like syndrome (LLS) and they represent approximately 30% of all patients with unstable tumors. There is no consensus about follow-up and management of relatives of LLS patients.

Aims & Methods: Our aim is to compare risk of cancer in first-degree relatives (FDR) in a large cohort of LLS and LS patients. Patients who met criteria for LLS diagnosed with CRC were included, when their tumors showed immunochemical loss of MSH2, MSH6, PMS2, or loss of MLH1 with BRAF-wild type and/or no MLH1 methylation and absence of pathogenic mutation in these genes, and was compared with those with confirmed LS and CRC. Neoplasms were followed in patients diagnosed with LS and LLS and among their relatives. Based on this information, we calculated the standardized incidence ratios (SIRs) for CRC and other neoplasms associated with LS, among FDR of patients diagnosed with LLS and compared it with SIRs among FDR of patients with LS.

Results: A total of 205 families with LS and 126 families with LLS had complete pedigrees, including the ages of relatives without cancer. A total of 1896 FDRs were included: 1198 from families with LS and 698 from families with LLS. FDR of patients with LLS have a high incidence of CRC (SIR 2.11; 95% CI, 1.59-2.75), that was significantly lower than in FDR of confirmed cases of LS (SIR 4.28; 95% CI, 3.69-4.93; p< 0.001). The risk of development neoplasms associated with LS (other than CRC) was also observed increased among relatives of patients with LLS (SIR 2.04; 95% CI, 1.44-2.80), but lower than the risk presented among family members of patients with LS (SIR 5.10, IC95%: 4.35-5.94; p< 0.001).

Conclusion: Relatives of patients with LLS have a high risk of developing CRC, although this risk is lower than that of families with Lynch syndrome. FDR of patients with LLS should be managed taking into account this increased risk of CRC.
Disclosure: Nothing to disclose

P1181 WAS "LEAVE-IN-SITU STRATEGY" FOR DIMINUTIVE ADENOMAS WELL TOLERATED?

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Introduction: Colonoscopy with polypectomy of adenomas reduces the incidence and mortality of colorectal cancers (1). With recent increment of the number of screening colonoscopies, it is reported that eradication of adenomas during colonoscopy can be a big burden for endoscopists (2). On the other hand, some studies suggest the safety of following diminutive polyps up without removal might be sufficient (3,4). According to the Japanese Society of Gastroenterology guidelines (5), diminutive adenomas which has no evidence of carcinoma in their appearance are allowed to be left in situ, provided strict surveillance colonoscopies within 3 years (="leave-in-situ strategy") are conducted, which is different initiative from the European or American guidelines(6,7). However, the tolerability of the "leave-in-situ strategy" of diminutive adenomas are unknown.

Aims & Methods: The aim was to consider tolerability of the "leave-in-situ strategy" of diminutive adenomas by retrospectively assessing it's safety and compliance. Patients whose diminutive adenomas were not resected at the initial colonoscopies between April 2001 and November 2015 at a referral center were chosen as the subjects. All the subjects were asked to receive surveillance colonoscopies within 3 years. The primary outcome measure is the incidence rate of index lesions (ILs) at the surveillance colonoscopy within 3 years. The ILs were defined as follows: adenomas $\geqq 10$ mm , high grade dysplasias, villous adenomas, and invasive cancers. The secondary outcome measures included the rate of patients who received the 3-year surveillance colonoscopies and the number of the diminutive polyps which were detected at both the initial and surveillance colonoscopies.

Results: A total of 4816 patients were left untreated of diminutive adenomas (n=2502) at the initial colonoscopies. The incidence rate of index lesions at the surveillance colonoscopies was 2.3%(36/1543; 12 adenomas $\geqq 10$ mm, 22 high grade dysplasias, and 2 invasive cancers). The rate of patients who underwent 3-year surveillance colonoscopies was 32.0% (1543/4816).

Conclusion: "Leave-in-situ strategy" of diminutive adenomas can be acceptable whose rate of ILs in the surveillance colonoscopies is limited to 2.3% which is similar to those in the National Polyp Study (8). However, strict instruction to the patients is indispensable considering the low receiving rate of surveillance colonoscopies.

References: 1. Zauber AG, et al. N Engl J Med. 2012, 366: 687 696. 2. Jasper L.A., et al. Gastrointest Endosc. 2017,85(6):1169-1176. 3. Maeda Y , Kudo SE , et al. ONCOLOGY LETTERS. 2017,14:2735-2742 4. Ninomiya Y , et al. Digestive Endoscopy 2017, 29(7):773-781 5. Tanaka S, et al. J Gastroenterol 2015, 50: 252-260. 6. Cesare Hassan, et al. Endoscopy 201,45: 842-851 7. Davila RE, et al: Gastrointest Endosc 2006, 63: 546 557 8. Winawer SJ, et al. N Engl J Med. 1993, 328 ; 901-906
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P1182 HIGHLY VARIABLE FOLLOW-UP IN PATIENTS WHO REFRAIN FROM ADDITIONAL SURGERY AFTER ENDOSCOPIC RESECTION OF A HIGH-RISK T1 COLORECTAL CARCINOMA IN THE NETHERLANDS

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Introduction: The incidence of submucosal invasive (T1) colorectal cancers (CRCs) has increased with the implementation of the national screening program. In case of endoscopic resection of a T1 CRC with histological risk factors for an adverse outcome, the guidelines advise adjuvant surgical segmental resection. For various reasons (comorbidity, perceived low risk of residual cancer, risk of surgery), an additional resection may not be carried out and patients wish to have regular follow-up. A standard protocol for surveillance of these patients is unavailable.
Aims & Methods: In this national survey, an inventory has been made of the surveillance strategy for patients after endoscopic resection of a high-risk T1 CRC who refrain from additional surgery. Dutch gastroenterologists and surgeons participating in the Dutch T1 CRC Working group were asked to participate in an online survey. They were questioned on demographics, baseline staging after detection of a T1 CRC and surveillance protocols.
Results: In total, 69/130 (53%) physicians (87% gastroenterologist) participated in the survey. In case of an unexpected malignancy after polypectomy, 36/69 (52%) performed full oncological staging, the remainder only in case of high-risk features in the endoscopically removed specimen. Pathology criteria used to determine high risk status were; lymphovascular invasion (100%), resection margin not free/indeterminable (93%), poor differentiation (90%), malignancy ≤ 1 mm from resection margin (78%), tumor budding grade 2/3 (57%), and submucosal invasion depth >1000 μm (47%).
A local protocol was available in 30% of participating centers only. We recorded 61 different surveillance strategies in 63 participants, using 19 different combinations of diagnostic tests. Most common used combinations were endoscopy only (n=9); endoscopy and rectal MRI (n=8); endoscopy, rectal MRI, liver ultrasound, chest X-ray and CEA (n=7) and endoscopy, rectal MRI, abdominal CT and CEA (n=6). Endoscopy was used in all schedules, in 50 of 63 strategies (79%) at least twice in the first year. 48/63 (76%) used MRI in case of a rectal T1 CRC. 30/63 (48%) used abdominal CT and 22/63 (35%) abdominal ultrasound for surveillance, of which 6 physicians used a combination of both. 23 of 63 physicians performed chest imaging, 60% used serum CEA. Mean follow-up time was 36 months (95% CI 31.5-40.5) for endoscopy, 26 months (95% CI 20.0-31.6) for rectal MRI and 30 months (95% CI 21.7-37.7) for abdominal CT (all varying 3 - 60 months). The interval between surveillance investigations differed from 3-monthly in the first year to >1 year. Peaks were seen at 3, 6, 12, 24, 36 and 48 months for each modality. Most physicians experienced none (27/69), or 1-3 (28/69) recurrences.
Conclusion: There is a high inter-practitioner variety in the follow-up of patients with an endoscopically resected high-risk T1 CRC who refrain from adjuvant surgery. A prospective study to evaluate the efficacy and safety of strict surveillance is needed.
Disclosure: Nothing to disclose

P1183 CLINICAL AND ONCOLOGICAL OUTCOMES OF LATERAL LYMPH NODE DISSECTION USING BOTH TRANSABDOMINAL AND EXTRAPERITONEAL APPROACH

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Introduction: Total mesorectal excision (TME) with lateral pelvic lymph node dissection (LLND) is a standard procedure for lower rectal cancer in Japan. However, ME alone is the international standard surgical procedure for rectal cancer and complete LLND is difficult because of the narrow visual field in the pelvic cavity and the complicated anatomical structure.
Aims & Methods: Our LLND using a transabdominal and extraperitoneal approach provides a wider visual field through the paravesical space and enables us to perform complete lymph node dissection of these regions.

Herein we introduce our LLND procedure and report the clinical and oncological outcomes.
After ME, bilateral hypogastric nerves were separated to be preserved. Firstly, common iliac nodes were dissected; aortic bifurcation nodes and median sacral nodes were also dissected by exposing the aortic bifurcation and the pelvic surface of the sacrum through a transabdominal approach. Secondly, after external iliac nodes dissection was performed to the peripheral side by the abdominal approach as possible. Proximal internal iliac nodes were removed and superior vesical artery was separated. Subsequently, the paravesical space was opened widely via an extraperitoneal approach, the external iliac artery was exposed and the external iliac nodes were completely removed from inguinal ligament. Obturator nodes were completely dissected while preserving the obturator nerve, resecting the obturator artery and vein, and confirming lateral pelvic wall and sciatic nerve. Finally, distal internal iliac nodes from the coccygeal muscle (Alcock's canal) were completely dissected while preserving the superior vesical artery and the pelvic plexus, and transecting several inferior vesical arteries.
Results: Between 2008 and 2018, we performed ME with LLND for 239 patients with cStageI-III lower rectal cancer. The median operative time was 380 min, and the median blood loss was 620 ml. Postoperative complications developed in 124 (51.9%) patients, and the most frequent one was pelvic cavity infection (including lymphocele) in 51 (21.3%) patients. Temporary urination disorder developed in only 19 (7.9%) patients, and persistent urination disorder required intermittent urethral catheterization developed in only one woman. Lateral Lymph node metastasis was pathologically found in 57(23.8%) patients after LLND. The 5-year local-recurrence-free survival was 84.3% and the numbers of patients with local recurrence were 14 (5.9%), respectively. Overall 5-year survival rate excluding cStageIV patients was 89.1%.
Conclusion: Our LLND provides a wider visual field in the pelvic cavity by using both transabdominal and extraperitoneal approach, and results in favorable clinical and oncological outcomes.
We introduce our procedure of LLND. However LLND is invasive procedure which needs longer operative time and greater blood loss. So we show laparoscopic LLND as our new procedure securing equivalent range of lymph node dissection.
Disclosure: Nothing to disclose

P1184 FACTORS INFLUENCING INTERRUPTION OF COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION FOR DETERMINING THERAPEUTIC STRATEGIES

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Introduction: Although the colorectal endoscopic submucosal dissection (ESD) procedure is standardized worldwide, the difficulty of the procedure is well known. However, there have been no studies on the causes of treatment interruption.
Aims & Methods: The present study aimed to evaluate the factors involved in interruption of colorectal ESD. We retrospectively analyzed 1116 consecutive superficial colorectal neoplasms of 1012 patients who were treated with ESD between August 2008 and September 2018. The clinical and pathological characteristics and treatment outcomes were analyzed.
Results: Interrupted ESD was reported for 16 lesions (1.4%) of the total study population. Univariate analysis of clinical characteristics indicated that age, 0-I macroscopic-type tumor, and tumor location on the left side colon were risk factors for interruption. Multivariate analysis revealed that 0-I macroscopic-type tumor was the sole preoperative independent risk factor for interruption. Univariate analysis revealed that the presence of muscle-retracting sign (MRS), deep submucosal tumor invasion, and intermediate invasive growth pattern represented the etiology of interruption.
Multivariate analysis indicated MRS to be the sole independent cause of interruption. Additionally, the resectability and curability of 0-I type tumors were significantly inferior to those of predominantly lateral spreading tumors. Observations of 0-I macroscopic-type tumors, MRS, and submucosal deep invasion were significantly more frequent in interrupted

cases. Conventional endoscopic images without magnification endoscopy were more associated with interruption than irregular surface or Vi pit pattern in cases with 0-I type tumors.

Conclusion: Endoscopic submucosal dissection of 0-I type tumors is highly disruptive, and undiagnosable submucosal infiltration can reduce the curability.

Disclosure: Nothing to disclose

P1185 ARTIFICIAL INTELLIGENCE PREDICTS THE LYMPH NODE METASTASIS OF T2 COLORECTAL CANCER - PROPOSAL OF A NOVEL INDICATION FOR FULL-THICKNESS ENDOSCOPIC RESECTION

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Introduction: Although all T2 colorectal cancers (CRCs) undergo surgical colectomy with lymph node dissection, they actually show approximately 30% of lymph node metastasis (LNM)-positivity. Thus, the remaining 70% patients have an option of receiving local resection such as full-thickness endoscopic resection. However, accurate pre-operative prediction of LNM of T2 CRCs has been considered impossible. The aim is to investigate whether artificial intelligence (AI) can predict LNM-positivity of T2 CRCs.

Aims & Methods: A total of 511 consecutive patients with T2 CRCs that were surgically resected in 2001-2016 were retrospectively analysed. We divided patients at a ratio of 3:1: data from 383 patients were used for machine learning for the AI model, and the remaining 128 patients were included for model validation. The AI model analyzed 37 clinicopathological factors and then predicted LNM-positivity or LNM-negativity on support vector machine which is a representative machine learning method. Operative specimens were used as the gold standard for the presence of LNM. The AI model was validated by calculating the sensitivity, specificity, and accuracy for predicting LNM.

Results: The rate of LNM-positivity in validation dataset was 28% (36/128). The AI model showed a sensitivity of 100% (95% CI, 86%-100%), specificity of 20% (12%-29%) and accuracy of 42% (34%-51%), respectively.

Conclusion: The AI model accurately predicts 20% of the LNM-negative T2 CRCs. Such patients can be good candidates for the local resection without lymph node dissection such as full-thickness endoscopic resection.

Disclosure: Nothing to disclose

P1186 AUTONOMIC RESPONSE TO DISTINCT MENTAL AND PHYSICAL STRESSORS IS IMPAIRED IN PATIENTS WITH IRRITABLE BOWEL SYNDROME

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Introduction: Irritable bowel syndrome is the most common functional gastrointestinal disorder (FGID). The pathophysiological mechanisms of FGID are complex. Accumulating evidence indicates that autonomic dysregulation contributes to FGID. The symptoms of IBS are often triggered by stress, however, the mechanisms of autonomic dysregulation in IBS, especially in response to stress are incompletely understood.

Aims & Methods: The aim of this study was to assess potential changes of vagal and sympathetic regulation in patients suffering from IBS in response to distinct types of stressors (active mental stress vs. passive physical stress).

Methods: Studied population included 12 patients diagnosed with IBS and 12 sex- and age-matched healthy controls. All patients were diagnosed according to ROME IV criteria for functional gastrointestinal disorders. Blood

pressure (BP) and heart rate were continuously recorded using Finometer MIDI (FMS, Netherlands) at rest and during two distinct stressors - mental arithmetic test and cold pressor test (cooling of forearm in 1-3°C water bath for 5 min). Evaluated parameters:

1. baroreflex sensitivity (BRS, calculated from spontaneous heart rate variability and BP variability) reflecting reflex of vagally-mediated heart rate regulation in response to changes of BP,
2. spectral power in low-frequency band of systolic BP variability (LF-SBP) reflecting sympathetic alpha-adrenergic stimulation of vascular smooth muscles,
3. systolic and diastolic BP, and;
4. mean heart rate.

Results: BRS (reflecting vagal reflex function) in patients with IBS was substantially reduced compared to controls at rest and in response to both mental arithmetic test and to cold pressor test (p<0.01 for all comparisons). In contrast, LF-SBP (reflecting sympathetic function) was normal at baseline, but significantly increased in IBS compared to controls during cold pressor test (p<0.05). No differences were found in systolic and diastolic BP and heart rate.

Conclusion: Our data show impaired dynamic sympatho-vagal balance in patients with irritable bowel syndrome at rest and in response to different types of stressors. The vagal function was reduced both at baseline and during stress, while exaggerated sympathetic response is evoked predominantly by stress. These findings support the hypothesis of altered autonomic regulation during stress as a potential mechanism worsening the symptoms of IBS.

We suggest that comprehensive evaluation of stress response using non-invasive analysis of distinct autonomic effectors could help to better understand the role of autonomic dysregulation in functional gastrointestinal disorders.

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Disclosure: Nothing to disclose

P1187 EXPRESSION OF TOLL-LIKE RECEPTORS IN IRRITABLE BOWEL SYNDROME

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Introduction: Our aim was to investigate the underlying etiological mechanisms in the development of irritable bowel syndrome (IBS). Recent studies implicate the involvement of innate immune system dysfunction and low-grade inflammation in the pathogenesis of IBS. Toll-like receptors (TLRs) are a family of transmembrane innate immune receptors that recognize various bacterial and viral cell components and regulate immune response. TLR-signaling alterations have been suggested as an underlining factor in the manifestation of the syndrome.

Aims & Methods: A total of 44 IBS patients and 25 healthy controls were included in the study population. All participants underwent colonoscopy and right-sided colonic biopsies were obtained from 31 patients. TLR expression was measured with real-time quantitative Reverse Transcription PCR (RT-qPCR).

Total RNA was isolated and was reversed transcribed to cDNA and quantification of TLR2 and TLR4 mRNA levels was achieved by RQ-PCR. Quality of life questionnaires, Rome III criteria and stool pattern questionnaires were completed by all participants.

Results: There were no significant differences between healthy controls (HC) and IBS patients regarding age, body mass index and gender. IBS patients were subdivided in constipation group (23%), diarrhoea (57%) and mixed type (13%). TLR2 and TLR4 mRNA expression were increased in IBS patients compared to controls though there was no statistical significance. IBS-D patients had elevated TLR4 expression (p=0.008) compared to HC and IBS-C patients had decreased TLR4 (p=0.027). Furthermore, IBS-D patients presented with increased TLR2 and TLR4 mRNA expression compared to IBS-C patients (p=0.018 and p=0.005).

Conclusion: Expression of TLR2 and TLR4 was investigated in IBS patients and HC. Increased levels of TLRs were documented in the IBS group although there was no significant difference to the HC group. TLR4 was overexpressed in IBS-D patients and on the contrary IBS-C patients presented with decreased expression of TLR4. TLR2 and TLR4 were increased significantly in IBS-D patients compared with IBS-C subgroup.

Disclosure: Nothing to disclose

P1188 COLONIC EOSINOPHILIA IS ASSOCIATED WITH CURRENT BUT NOT INCIDENT DEPRESSION INDEPENDENT OF IBS STATUS

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Introduction: There are multiple reports of persons with depression have displayed elevated levels of pro-inflammatory cytokines compared to healthy controls, but the origin of the inflammation is not determined. Eosinophils are normal in the GI tract (except in the esophagus). We have found subtle increased duodenal eosinophilia is linked to mood changes in dyspepsia, and have identified increased colonic eosinophils in a subset with IBS diarrhea.

Aims & Methods: Given the abundance of mucosal associated lymphoid tissue present in the gut and evidence of gut-brain axis communication, we hypothesised that there may be a direct association between colonic eosinophilia and depression. The random population based colonoscopy study (PopCol) was performed 2002-2006 and included colonoscopies with biopsies on 745 individuals from the general population (Kjellström et al Eur J Gastro Hep 2014). Eosinophils (per 5 high power fields) have been counted in 161 out of the 745 individuals. Current depressive symptoms were reported on HADS at a baseline visit before the colonoscopy, 6 individuals (4 %) had a HADs depression score of 11 and above. Incident depression was defined as a Stockholm County registry recording of health care visit with an ICD-10 code F32 or F33 during 2006-2015 in individuals with HADS score below 11 at the baseline investigation. The cross sectional association between eosinophil counts and depressive symptoms were calculated using linear regression bootstrapped with 2000 replications. The association between baseline eosinophil counts and incident depression (17 cases, 138) was calculated using logistic regression.

Results: There was an association between eosinophil counts in transverse (beta: 0.23, p=0.028) and sigmoid colon (beta: 0.28, p=0.001), but not terminal ileum (beta: -0.08, p=.44), caecum (beta: 0.06, p=0.49) and rectum (beta: 0.16, p=0.27), and HADs depression scores, independent of smoking, age and gender. No association was found between eosinophil counts and incident depression (p's>0.13). Adjusting for IBS status (32.9 % had IBS) did not change the results.

Conclusion: The present result supports a direct association between colonic eosinophilia and depressive symptom severity in a general population. Future studies are needed to elucidate if this is a causal association.

Disclosure: Nothing to disclose

P1189 PHENOTYPICAL CHANGES IN ENTERIC GLIAL CELLS AND THEIR ASSOCIATIONS WITH THE NEURONAL PROCESS ELONGATION STIMULATED BY NEUROMODULATORS FOR ENTERIC NERVOUS SYSTEM

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Introduction: Enteric glial cells (EGCs) present at the submucosal plexus and myenteric plexus change own phenotype by themselves and bring by-directional and functional roles with adjacent neurons. Such phenomena occur under the stress circumstances in accordance with chemical mediators closely related to the pathogenesis of irritable bowel syndrome. However, direct mechanism(s) of these glial changes remains to be elucidated especially for effects of neuromodulators. Although some reports suggest

the significance of neuronal process elongation in visceral hypersensitivity, effects by above neuromodulators and associations between the neuronal process elongation and glial efficacy are also unknown.

Aims & Methods: For screening of phenotypical changes in EGCs and neurons, we investigated the cellular proliferation and morphology of EGCs and neurons such as cytoplasmic shape, process elongation, and connections after stimulation with chemical mediators including expressions of nerve growth factor (NGF), and GAP43 in EGCs. We also evaluated phenotypical changes in neurons after stimulation with the conditioned medium of EGCs. EGC (CRL-2690 purchased from ATCC) and PC12 (CRL-1721.1) were used for the consequent experiments after reaching to sub-confluent condition. Morphological changes of these cells were evaluated by immunofluorescence with F-actin (a cytoskeletal marker) and S100β (a marker of glial cell) or PGP9.5 (a marker of neuron) antibody after stimulation with each mediator (NGF: 50 ng/ml, corticosterone: 1 μM, 5-HT: 1 μM, ATP: 1 μM, and tryptase: 1 μM) for 24 hours. We evaluated expressions of NGF in the EGCs after stimulation with tryptase. To evaluate interaction between EGC and neuron, we collected the condition medium of EGCs after stimulation with tryptase for 6 hours, and evaluated morphological changes of PC12 by immunofluorescence with F-actin or GAP43 and PGP9.5 after incubation with the condition medium for 24 hours. We measured cell number for cellular proliferative evaluation.

Results: In a screening of each mediator affecting phenotypical change of EGCs, NGF (2-fold) and tryptase (1.8-fold) significantly induced cell proliferation of EGCs. In glial morphology, NGF did not affect cell body of EGC from the basal culture condition (a star-shaped form). However, NGF markedly induced irregularly branched processes with dense connecting with adjacent EGCs. On the contrary, corticosterone and 5-HT significantly changed cell body of EGC from star-shaped form to fibrous or spindle form (thin cytoplasm) with long-branched processes with freely connecting with other EGCs. Tryptase slightly extended cytoplasm of EGCs, and ATP induced long-branched processes with dense and free connecting with adjacent EGCs as well as corticosterone and 5-HT. On the other hand, NGF and corticosterone increased neuronal proliferation. In neuronal morphology, these mediators extended cytoplasm of neurons and increased intracellular F-actin and extracellular spicule formation in parallel with process elongation. However, 5-HT, ATP, and tryptase did not affect neurons including proliferation and morphology. Expression of NGF was increased in EGCs stimulated with tryptase but not corticosterone. Conditioned medium of EGCs stimulated with tryptase caused neuronal process elongation similar to the effect of NGF stimulation, and increased GAP43 proteins.

Conclusion: These neuromodulators induced phenotypical changes in EGCs more prominently than neurons. Phenotypical changes in EGCs may result in neuronal process elongation mediated by NGF.

Disclosure: Nothing to disclose

P1190 IMPACT OF MUCOSAL GLIAL CELLS AND SUBMUCOSAL GLIAL CELLS ON ENHANCEMENT OF NEURONAL NETWORK MEDIATED BY NERVE GROWTH FACTOR IN A RAT MODEL OF VISCERAL HYPERSENSITIVITY

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Introduction: Neuronal elongation toward the epiderm is caused by an imbalance of nerve attractive factors such as nerve growth factor (NGF) and nerve repulsive factors such as semaphorin 3A (Sema3A). The phenomenon is partly responsible for itch sensitization (so called somatic hypersensitivity) in patients with atopic dermatitis. Previously, we reported that hyperplasia of myenteric glial cells contribute to hypercontraction in an irritable bowel syndrome (IBS) model. In addition, abnormalities of enteric neuron and glial cells observed in the colonic mucosa are reported to contribute to the pathogenesis of IBS. However, it is unknown how glial cells and nerve elongation factors change and associate with the neuronal network formation both in the mucosa and submucosa layer of IBS.

Aims & Methods: We evaluated the changes in the neuronal network separately in the mucosa and submucosa and the dynamics of glial cells and neuronal elongation factors in an IBS model. We used Wistar Kyoto rats (WKY) which are genetically instable to anxiety, and prepared an IBS models after intracolonic injections of acetic acid (2 mL, 0.6%) to these rats. Distal colonic segments were obtained from control (Wistar rats), WKY, and IBS models, and each layer (mucosa, submucosa, and muscle) were sepa-

rately striped from the whole colonic tissues. Between the mucosal and submucosal layers, we compared mRNA expression of NGF and Sema3A by real-time RT-PCR. To evaluate the morphological changes of glial cells and neuronal network formation, whole mount submucosal plexus tissues were prepared for immunohistochemistry with glial fibrillary acid protein and PGP9.5 (pan-neuronal marker) antibodies. To evaluate the neuronal outgrowth in the mucosa, frozen colonic tissues were prepared for immunohistochemistry with GAP43 antibody. We also evaluated the localization of NGF and Sema3A in the mucosa and submucosa layer.

Results: mRNA expressions of NGF (2.3-fold) and Sema3A (3.1-fold) were significantly increased in the submucosal layer in the WKY group compared to the control, while there were no change in the mucosa between both groups. In the IBS group, mRNA expression of NGF initially begun to increase in the submucosal layer, and its increase was subsequently observed in the mucosa. Sema3A mRNA expression was increased in the submucosal layer, but decreased in the mucosal layer. Submucosal glia exhibited hyperplasia of their processes that apparently overlapped with the neurons and changes in bulbous swelling of terminals in the IBS group. Neuronal network was dramatically enhanced in the submucosal layer of the IBS group, whose change gradually appeared from the outer submucosal plexus toward the inner submucosal plexus. As well as submucosal plexus, nerve fiber outgrowth (GAP43 positive neuron) was increased in the mucosal layer. NGF was localized in the both submucosal and mucosal glial cells but not mast cells in this model.

Conclusion: Enteric glial cells are associated with enhanced neuronal network both in the mucosa and submucosa mediated by the coordination of NGF and Sema3A in the IBS model. These findings may underlie in the pathogenesis of visceral hypersensitivity in IBS.

Disclosure: Nothing to disclose

P1191 GASTROINTESTINAL SYMPTOMS IN A POPULATION AFFECTED BY INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME (IC/BPS): FROM IRRITABLE BOWEL SYNDROME (IBS) TO NARCOTIC BOWEL SYNDROME (NBS) AND THERAPEUTIC RELEVANCE OF BODY MASS INDEX (BMI) CONTROL

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Introduction: Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS) is a debilitating chronic, inflammatory disorder of the bladder characterized by variable degree of pain, frequency and urinary urgency, with a negative impact on the Quality of Life (QoL). BPS patients are often affected by gastrointestinal symptoms such as abdominal pain, dyspeptic symptoms, constipation and diarrhea, often consistent with a diagnosis of IBS. Severe chronic abdominal pain is sometimes treated with opioids. Furthermore, patients introduce many dietetic restrictions in order to improve their symptoms.

Aims & Methods: This study aimed to evaluate the effects of chronic opioid treatment on abdominal pain, gastrointestinal symptoms and QoL. It also aimed to better understand how a weight control strategy can influence IBS/BPS patients' psychological state. A two-year study was conducted in the Multicentric Interstitial Cystitis Referral Center of the Catholic University in Rome, in a population of 44 female, aged 25-78, affected by IC/BPS according to the "European Society for the Study of Interstitial Cystitis (ESSIC)" criteria. Patients were categorized into groups according to opioid use and BMI: 17 "opioid users (at least 1 month)" and 27 "non-opioid users (in the last month)"; normal BMI group (BMI: 19-24.9) including 20 patients, underweight group (BMI < 18.9) including 8 patients and overweight group (BMI >25) including 16 patients. All subjects were asked to fill our Psycho-Gastroenterological Questionnaire (PGQ), which includes Visual Analogue Scale (EQ-VAS), Bristol Stool Chart (BSC), Gastrointestinal Symptoms Rating Scale (GSRS), State-Trait Anxiety Inventory (STAI Y-1, STAI Y-2), Psychological General Well-Being Index (PGWBI), Hospital Anxiety and Depression Scale (HADS), General Self-Efficacy Scale (GSE), Connor-Davidson Resilience Scale (CD-RISC). Differences between groups were evaluated by Student's t test and considered significant for p< 0.05.

Results: Compared to opioid users, non-opioid users had a higher EQ-VAS score (46.7±14.9 vs 29.7±21.6, p=0,004), a lower grade of stypsis on BSC (3.4±1.7 vs 1.6±0.9, p=0,0002), and a lower GSRS score (14.2±6.5 vs

19.9±6.1, p=0,006). Within the GSRS, "abdominal pain" (1.1±0.8 vs 1.9±0.8, p=0,002), "heartburn" (0.9±0.7 vs 1.7±1.0, p=0,003), "acid regurgitation" (0.7±0.7 vs 1.2±1.0, p=0,05), "nausea and vomiting" (0.7±0.9 vs 1.4±0.9, p=0,01), "hard stools" (1.2±1.0 vs 1.8±0.9, p=0,05), and "feeling of incomplete evacuation" (0.7±0.8 vs 1.8±1.1, p=0,0004) were significantly lower among non-opioid users. On the other hand, there were no differences between groups in the other scores. Compared to pathologic BMI group (underweight plus overweight patients), normal BMI group has a higher EQ-VAS score (44.3±21.0 vs 36.7±18.3) and a lower GSRS score (15.9±7.0 vs 16.8±6.9), but these differences were not statistically significant. On the other hand, all psychometric scores are significantly better among normal BMI group: STAI Y-1 (48.6±11.5 vs 55.6±12.5, p=0.06), STAI Y-2 (42.1±11.3 vs 51.7±10.3, p=0.005), PGWBI (61.0±20.5 vs 47.3±17.2, p=0.02), HADS-A (7.1±4.4 vs 11.0±5.1, p=0.01), HADS-D (5.8±3.6 vs 9.4±3.3, p=0.001), CD-RISC (70.2±16.9 vs 56.6±12.3, p=0.003).

Conclusion: Our study demonstrates that chronic opioid treatment increases abdominal pain and worsens gastrointestinal symptoms and QoL in subjects with IC/BPS+IBS, configuring a condition of NBS. On the other hand, weight control can strongly improve patients' QoL. Further studies in larger samples are required to establish the influence of potential confounders.

References: Gillenwater J, Wein AJ. Summary of National Institute of Arthritis, Diabetes, Digestive and Kidney Diseases workshop on Interstitial Cystitis. J Urol 1998; 140: 203-6.

Disclosure: Nothing to disclose

P1192 METABOLOMICS REVEALS PERTURBATION OF TRYPTOPHAN-KYNURENINE AXIS IN PATIENTS WITH FUNCTIONAL GASTROINTESTINAL DISORDERS AFTER A SINGLE ORAL DOSE OF FRUCTOSE

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Introduction: Fructose intolerance is common in patients with Functional Gastrointestinal Disorders (FGID) and is typically attributed to intestinal malabsorption. However, fructose is also known to invoke systemic metabolic changes, including modulation of the tryptophan (TRP)-kynurenine (KYN) pathways. This modulation has been associated with low-grade inflammation and cognitive changes, both of which are reported to be common in FGID and may be effected by either host or microbiome pathways (1-3).

Aims & Methods: Plasma TRP, KYN and further systemic metabolites were quantified in FGID patients after fructose ingestion and related to measures of fructose intolerance and malabsorption.Thirty-one male and female FGID patients, defined by Rome III criteria, were prospectively enrolled into a double-blind, randomised, crossover study (4). Blood, breath samples and symptom ratings were collected at 0, 0.5, 1 and 2h post-ingestion of 35g fructose or the blinded nocebos, 3.9mL cyclamate/saccharine sweetener or water. Plasma TRP and KYN were quantified via liquid chromatography mass spectrometry, while other systemic metabolites were profiled via gas chromatography time-of-flight mass spectrometry.

Results: The KYN/TRP ratio (KTR) increased from 0h to 2h after fructose ingestion (p< 0.001) in all FGID patients, and the change in KTR was significantly higher following fructose than water (p< 0.01) and cyclamate/saccharine (p< 0.01). Twelve other metabolites were significantly different (Variable importance in projection>1, p< 0.005) between fructose and water interventions, including long-chain fatty acids (myristic acid, oleic acid, palmitic acid, palmitoleic acid, stearic acid) and pro-inflammatory mediators (linoleic acid, arachidonic acid). Breath hydrogen and methane concentrations and symptoms did not correlate significantly with the changes in KTR.

Conclusion: Ingestion of fructose resulted in acute changes in the tryptophan-kynurenine axis and in fatty acid metabolism in patients with FGID. These changes do not appear to be specifically associated with malabsorption or intolerance of fructose and may rather be related to tryptophan metabolism and the recently highlighted link to the aryl hydrocarbon receptor and downstream effects on microbiome and host neuroimmune

function (5). Fructose stimulation may consequently be useful for further mechanistic assessment of the known immune activation and neural sensitization in FGID.

References: 1. Berstad A. et al. Scand J Gastro 2014;49:1493-1498. 2. Ledochowski M. et al. Scandi JJ Gastro 2001;36:367-371. 3. Enko D. et al. Psych Res 2018;62:595-599. 4. Wilder-Smith CH et al. Neurogastro Mot 2019;31:e13497. 5. Neavin DR et al. Int J Mol Sci 2018;19. pii: E3851. doi: 10.3390/ijms19123851.

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P1193 AN EVALUATION OF PREDICTIVE FACTORS FOR BOWEL PREPARATION BEFORE COLONOSCOPY USING THE BOSTON BOWEL PREPARATION SCALE

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Introduction: Before colonoscopy, adequate bowel preparation is mandatory to achieve high-quality observation for entire mucosa. Several previous studies have reported factors associated with inadequate bowel preparation, including an older age, obesity, and diabetes mellitus. We investigated the predictive factors for bowel preparation.

Aims & Methods: We evaluated 800 colonoscopies performed from March 2016 to Jun 2019 to analyze the degree of bowel preparation using the Boston Bowel Preparation Scale (BBPS) and assessed the predictive factors for inadequate bowel preparation. All patients received low-volume (2 L) polyethylene glycol solution with ascorbate (MoviPrep®) before colonoscopy. The potential predictive factors for inadequate bowel cleansing were older age (≥ 75), male gender, obesity (BMI ≥ 25), constipation, laxative use, a history of abdominal surgery, single- or split-dose intake preparation, diverticulosis and diabetes mellitus. Inadequate bowel preparation was defined as a BBPS ≤ 5. We excluded patients with a diagnosis or history of colonic stricture, inflammatory bowel disease or prior colectomy.

Results: The median (range) patient age was 68 (27-84), and 43% were women. The median (range) number of bowel movements per week was 5.7 (1-11). The median (range) BBPS score was 8 (3-9), and the rate of adequate bowel preparation (BBPS ≥ 6) was 94.3%. A univariate analysis of the factors associated with inadequate bowel preparation were obesity ($P = 0.007$), diabetes mellitus ($P = 0.005$) and constipation ($P = 0.0428$). A multivariate logistic regression analysis showed that obesity (OR 2.76 [95% CI 1.07-7.23], $p=0.035$) and diabetes mellitus (OR 3.65 [95% CI 1.32-9.64], $p=0.0133$) were independent factors related to inadequate bowel cleansing.

Conclusion: Using the BBPS score to evaluate colon cleansing, the predictive factors associated with inadequate bowel preparation were obesity (BMI ≥ 25) and diabetes mellitus.

Disclosure: Nothing to disclose

P1194 A NOVEL METHOD FOR CHARACTERISING POSTPRANDIAL INTESTINAL CONTRACTIONS, EFFECTS OF GLUCAGON AND RECTAL DISTENTION IN DOGS

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Introduction: Motility disturbances are frequently implicated in functional gastrointestinal disorders. Current options for assessing intestinal motility provide limited information on the propagation pattern of the intestines.

Aims & Methods: This study aimed to investigate the validity of a new method for examining and quantifying intestinal motility. Seven healthy female dogs were operated on to have a cannula placed in their duodenum. The canine intestinal motility was studied under three sets of experiments (postprandial; glucagon injection and rectal distention, RD). A solid-state 4.2 mm manometric catheter with 10 sensors spaced at 1-cm intervals was inserted into the intestinal lumen via the cannula. The luminal contractile signals were converted into electrical signals by the pressure transducer and saved for further analysis. A special software was developed to analyse the data collected. The intestinal motility was evaluated by frequencies of antegrade, retrograde and simultaneous contractions, motility index (MI), propagation pattern (percentages of antegrade, retrograde and simultaneous contractions), propagation distance and velocity of antegrade and retrograde contractions.

Results:
1. Feeding did not induce changes in the frequencies of different contractions. The frequencies of postprandial contractions (numbers per min, npm) were 8.1±1.4 npm for antegrade contractions; 3.5±1.0 npm for retrograde contractions; and 8.9±0.7 npm for simultaneous contractions. MI also remained unchanged (11.8±0.5 vs. 11.4±0.2, p = 0.19). Postprandially, the dominant propagation pattern was antegrade (45.0±8.1%), followed by simultaneous (34.5±5.2%) and retrograde (20.5±2.0%). The average distance propagated was 4.8±0.8 cm with the antegrade contractions, 4.4±0.3 cm with the simultaneous contractions and 2.3±0.2 cm with retrograde contractions. The propagation velocity of the antegrade contractions was 12.1±0.4 cm/min and 10.7±0.5 cm/min for retrograde contractions.
2. Post glucagon injection, the frequencies of antegrade contractions decreased from 7.6±1.0 to 4.3±0.6 npm (p = 0.001), the frequencies of other contractions did not change significantly. MI was reduced slightly (11.5±0.4 vs. 10.6±0.2, p = 0.013). The dominant propagation pattern became simultaneous (42.0±2.9%), followed by antegrade (34.6±2.8%) and retrograde (23.1±3.7%). The average distance propagated by antegade contractions decreased to 3.6±0.5 cm/min (p = 0.0287). The propagation velocity was not altered by glucagon injection.
3. RD did not significantly disrupt the intestinal contractile and propagation patterns.

Conclusion: Our method was able to differentiate between antegrade, retrograde and simultaneous contractile and propagation patterns. Clinically it can be used to quantify the dynamic intestinal propagation process and pinpoint whether the motility issue is due to antegrade, retrograde or simultaneous contraction. This could greatly enhance the clinical use of manometry in investigating the cause of intestinal dysmotility.

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P1195 AFFECTIVE DETERMINANTS OF SYMPTOM SEVERITY IN IBS PATIENTS

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Introduction: Irritable Bowel Syndrome (IBS) is one of the most common and challenging disorder confronting gastroenterologist. Symptoms include abdominal pain associated with altered bowel habits. The disorder is characterized by heightened anxiety and depression. Even IBS patients with no comorbidities have higher, although still subclinical levels of anxiety and depression. There are many aspects of anxiety that can possibly contribute to IBS symptom perpetuation, but perhaps the most illness specific one is visceral anxiety.

Aims & Methods: The aim of this study was to test the predictive value of trait anxiety, depression and visceral anxiety in the prediction of IBS symptom severity.
A total of 39 Rome IV-diagnosed IBS outpatients at tertiary care centre (79.4% F, M age = 49.4 years) were recruited. They completed a set of questionnaires, including State-Trait Anxiety Inventory (STAI-T), Beck Depression Inventory (BDI-II) and Visceral Anxiety Inventory (VSI). They also

kept a diary for 14 days which, among other aspects, involved completing a short symptom intensity scale. The total symptom intensity was calculated for each day and a final average of 14 days was used for each participant.

Results: Symptom severity was positively correlated with trait anxiety (r=.37*), depression (r=.35*) and visceral anxiety (r=.58**). Hierarchical regression analysis showed that in the final model only visceral anxiety was a significant predictor (β=.51**) of symptom severity and the model explained a total of 35.8% of symptom severity variance. Considering that trait anxiety significantly predicts symptom severity (β=.37*) when entered in the model alone and that adding depression (β=.17) in the second step reduces that effect to non-significant (β=.24), and finally adding visceral anxiety in the third step completely nullifies that effect (β=.08) there are indications that depression partially and visceral anxiety fully mediates the trait anxiety - symptom severity relationship.

Conclusion: The obtained results indicate that trait anxiety and depression might be related to symptom severity via visceral anxiety, which emphasizes the importance of using this simple, yet very informative measure of illness-specific anxiety in IBS patients.

Disclosure: Nothing to disclose

P1196 IS THERE A LINK BETWEEN IBS AND STUTTERING? PRELIMINARY RESULTS

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Introduction: Theories of stuttering have described the role of anxiety in several ways, from treating it as the main cause of the disorder to a mere by-product of stuttering. Most studies have detected a positive correlation between anxiety and stuttering severity, with higher levels of anxiety in the stuttering population compared to healthy persons. Irritable Bowel Syndrome (IBS) is one of the most common and challenging disorder confronting gastroenterologist. Symptoms include abdominal pain associated with altered bowel habits. The disorder is characterized by heightened anxiety and depression.

Aims & Methods: The aim of this study was to examine the prevalence of IBS in a sample of people who stutter and to explore the relationship between several anxiety measures and IBS symptom frequency among people who stutter. A total of 57 people who stutter (73.6% M, M age = 32.4 years) and were treated for stuttering at VaLMod rehabilitation centre were recruited. During their regular holistic multidimensional logopaedic treatment they completed the Rome IV diagnostic questionnaire, a short questionnaire on the frequency of 6 IBS symptoms, State-Trait Anxiety Inventory (STAI-T), Visceral Anxiety Inventory (VSI) and Anxiety Sensitivity Index ASI.

Results: Only 8 participants (4F, 4M) fit the IBS criteria (Rome IV), which is a somewhat lower prevalence rate compared to the general population. It needs to be pointed out that the sample consisted of almost three times as many men than women. If we look at women alone, the prevalence rate is around 26% which is close to prevalence in the general population. People who stutter, but do not fit the IBS criteria, have higher STAI scores (M=44.53; SD=9.34) than a normative age group of healthy persons (M=35.55; SD=9.76), which is in line with previous studies (Ezrati-Vinacour & Levin, 2004; M=46.00; SD=8.80). People who stutter and fit the IBS criteria have even higher (t=2.59; df=9.62; p< .05) STAI scores (M=53.99; SD=9.41). Their STAI score seems to be higher than the score obtained for the regular, non-stuttering IBS population, previously published in our other studies (M=46.30; SD=9.63).

People who stutter and fit the IBS criteria have higher scores in VSI scores (t=2.26; df=8.34; p< .05), ASI scores (t=2.76; df=8.34; p< .05) and the frequency of IBS symptoms (t=4.67; df=8.18; p< .01) than those who don't fit the IBS criteria. In the total sample of people who stutter, IBS symptom frequency is correlated with all three anxiety measures (STAI r=.42**; VSI r=.52**; ASI r=.67**), with VSI explaining 27.4% of symptom frequency variance.

Conclusion: It seems IBS is not more frequent in people who stutter. However, it seems that stuttering aggravates anxiety in IBS. Patients who stutter and have IBS seem to have more pronounced anxiety than people who stutter but don't have IBS and people who have IBS but don't stutter.

Disclosure: Nothing to disclose

P1197 THE ASSOCIATION BETWEEN JOINT HYPERMOBILITY SYNDROME AND ROME IV FUNCTIONAL GASTROINTESTINAL DISORDERS: A CASE-CONTROL STUDY OF PREVALENCE, QUALITY OF LIFE IMPAIRMENT, HEALTHCARE UTILISATION AND NON-GI SOMATIC SYMPTOMS

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Introduction: Individuals with joint hypermobility syndrome (JHS) are increasingly encountered within gastroenterology services and pose complex clinical challenges. Limited data suggests a high prevalence of functional gastrointestinal disorders (FGIDs) in JHS, with non-GI somatic symptoms a potentially relevant confounder. However, no study has addressed the prevalence and associations for FGIDs in subjects with JHS against age and sex-matched general population-based controls.

Aims & Methods: An Internet based cross-sectional general health survey was completed by 642 subjects with JHS - recruited with the help of the charity organization Ehlers-Danlos Support UK - and 642 age/sex-matched population controls from the UK. The mean age was 39 years (SD 13) and 96% were female. The survey enquired for FGIDs using the Rome IV diagnostic questionnaire, non-GI somatic symptoms, quality of life, and healthcare utilisation. FGID prevalence data was compared between the groups, with subsequent logistic regression models (adjusting for the number of non-GI somatic symptoms) used to determine the associations for FGIDs and healthcare utilisation in subjects with JHS compared to the general population.

Results: Nearly all subjects (98%) with JHS fulfilled symptom-based criteria for any Rome IV FGID compared with 46% of the general population. The parts of the digestive tract most commonly affected by FGIDs in JHS and control subjects were the bowel (90% vs. 39%, respectively), gastroduodenal (70% vs. 13%) and anorectal (54% vs. 10%) regions. Moreover, those with JHS were more likely than the general population to have FGIDs in ≥ 2 regions (84% vs. 16%). Subjects with JHS reported a higher number of non-GI somatic symptoms (9 vs. 4.4), poorer mental and physical quality of life scores, and greater healthcare utilisation such as physician consultations, abdominal surgeries, use of opiates (84% vs. 28%) and neuromodulators (43% vs. 20%). Following adjustments for non-GI somatic symptoms, the association of FGIDs and healthcare utilisation in subjects with JHS was reduced by up to fourfold and in some instances eliminated.

Conclusion: This large case-control study shows that individuals with JHS report a very high prevalence of Rome IV FGIDs and incur considerable health impairment and health care utilisation. These associations are drastically reduced when controlling for non-GI somatic symptoms. Hence, reducing non-GI somatic symptoms should be considered as an early therapeutic target in JHS.

Disclosure: Nothing to disclose

P1198 DIFFERENCE OF THE DEFECATION DESIRE BETWEEN CONSTIPATED PATIENTS AND NON-CONSTIPATED PATIENTS: A LARGE-SCALE INTERNET SURVEY

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Introduction: Chronic constipation (CC) is a functional bowel disorder with a high prevalence worldwide. However, treatment satisfaction and quality of life (QOL) is low, and several clinical problems remain unresolved today. Loss of defecation desire (LODD) is presumed to be one cause of impaired QOL; however, it is still unknown whether LODD is more common in patients with CC than those without. Understanding the difference of the defecation desire between constipated patients and non-constipated controls is important to help solve the clinical problems.
Aims & Methods: To compare the rate of LODD between patients who had self-recognition of constipation and actually met the Rome-IV criteria (CC arm) and age-sex-matched controls who have no symptoms of constipation and do not meet the Rome-IV criteria (non-CC arm), we performed a nationwide internet questionnaire survey in March 2019 targeting the Japanese adults (aged 20-79 years old) registered in the large-scale panel on the website owned by Rakuten Insight, Inc.
We used an original online questionnaire which collected information about sex, age, presence or absence of defecation desire, stool form, constipation score, and whether meeting the Rome-IV constipation criteria or not. Degree of defecation desire is stratified into the following four scales; 'never', 'rarely', 'usually', and 'always', then 'never' and 'rarely' are defined as LODD.
Results: A total of 20990 subjects, 9669 with self-recognition of constipation and 11321 without any symptoms of constipation, were included during the 10 days investigation period. Of the 9669, 26.8% (n=2591) met the Rome-IV criteria and were selected as CC arm. Rate of LODD in CC arm and non-CC arm was 57.4% and 8.0%, respectively (p< 0.001, OR;15.4 [13.1-18.1]). LODD was observed evenly from young to old people in CC arm.
Conclusion: This study confirmed that patients with CC are much more likely to decrease or lose defecation desire than non-constipated controls regardless of age. To improve the problematic clinical situations in this filed, physicians should pay more attention to 'defecation desire' as an indicator of treatment effect in daily clinical practice.
Disclosure: This study was supported by Mochida Pharmaceutical Co, Ltd.

P1199 THE MOST BOTHERSOME SYMPTOM IN FUNCTIONAL BOWEL DISORDERS INFLUENCES USE OF MEDICATION, QUALITY OF LIFE AND HEALTH CARE UTILIZATION

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Introduction: Functional bowel disorders (FBDs) are defined based on different combinations of abdominal pain, bloating/distension, and abnormal bowel habits, i.e. diarrhea or constipation. Which of these symptoms patients consider most bothersome varies between individuals.
Aims & Methods: We aimed to examine how the most bothersome bowel symptom differs between different FBDs and how this relates to health care utilization, quality of life, non-GI symptoms and demographic factors in the general population. A community sample of 6,300 adults 18 years and older in the US, United Kingdom (UK) and Canada (2,100 in each country) completed a secure online survey. Quota-based sampling was used to ensure equal proportion of sex and age groups across countries, and to control education distributions. The survey included the Rome IV diagnostic questionnaire for adults, the Short Form - 8 (SF-8) quality of life questionnaire, the Patient Health Questionnaire - 12 (PHQ-12) for non-GI somatic symptoms, questions on health care utilization, abdominal surgery, use of medications, and question about the most bothersome of the four symptoms defining FBD in the past three months.

Results: Data from 5,931 individuals were retained for analysis (49.2% female; mean age 47.4 (range 18-92) years) after 369 inconsistent responders were eliminated. Rome IV criteria for FBDs were fulfilled by 27.8% of subjects. The symptoms most commonly reported to be most bothersome by FBD subjects were "watery or mushy stools, or having many bowel movements in a day" (29%), and "hard stools or going several days without having a bowel movement" (25%), followed by abdominal bloating or distension (21%) and abdominal pain (17%). The most commonly reported most bothersome symptom among individuals with IBS was abdominal pain (40%), in functional constipation and in opioid-induced constipation it was hard and infrequent stools (44% and 61%), and in functional diarrhea and functional abdominal bloating/distension all patients reported that the symptom defining each disorder (loose stools and bloating/distension, respectively) was the most bothersome. For men with FBDs, loose, frequent stools were the most common most bothersome symptom (36%), whereas this was hard, infrequent stools for females (27%). FBD individuals with different most bothersome symptoms also differed regarding healthcare utilization, quality of life, and overall somatic symptom severity (Table 1): Those with abdominal pain as their most bothersome symptoms had the poorest quality of life and highest non-GI somatic symptom burden, and had the highest proportion of frequent health care users (doctor visits ≥ once a month). The abdominal pain group also had the highest proportion of subjects regularly taking medications for nausea, acid reduction, and pain (OTC), whereas regular use of constipation and diarrhea medications, respectively, was most common among individuals with those symptoms as their most bothersome bowel symptoms.
Conclusion: The most bothersome bowel symptom differs among individuals meeting Rome IV FBD criteria, and this influences health care utilization, medication preference, quality of life and overall somatic symptom severity. Targeting the most bothersome symptom when treating FBDs seems relevant to improve health care outcomes.

	Abdominal pain (n=285)	Loose, frequent stools (n=483)	Hard, infrequent stools (n=412)	Abdominal bloating / distension (n=343)	p-value
Mental QOL (SF-8)	42±12	44±12	45±12	42±13	0.004
Physical QOL (SF-8)	44±10	46±11	45±12	47±10	0.001
Non-GI Somatic symptoms (PHQ-12)	7.9±4.4	6.2±3.5	6.5±3.3	6.3±3.5	<0.0001
Doctor visits 1+ times a month (%)	19%	12%	14%	12%	0.03
Abdominal surgeries (%)	31%	29%	28%	29%	0.86

[Table 1. Different Most Bothersome Symptoms and Associated Factors]

Disclosure: Magnus Simren and Ami Sperber are members of the Board of Directors, and William Whitehead former board member, of the Rome Foundation, which sponsored the study. Olafur Palsson received research support from the Rome Foundation to carry out the study.

P1200 THE INTESTINAL GAS QUESTIONNAIRE (IGQ): PSYCHOMETRIC VALIDATION OF A NEW INSTRUMENT FOR MEASURING GAS RELATED SYMPTOMS AND THEIR IMPACT ON DAILY LIFE AMONG GENERAL POPULATION AND IBS

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Introduction: Gas-related symptoms (GRS) are common among the general population and patients with functional gastrointestinal disorders. There is no patient-reported outcome covering these symptoms and their

impact on daily life. We first performed interviews in 3 countries among IBS patients and general population (GP) (1). This resulted in a 43-item pilot questionnaire (17 symptom items with 24h recall period and 26 impact items with 7-day recall).

A psychometric validation study is reported here.

Aims & Methods: One hundred subjects (60 IBS, 40 GP) complaining of GRS had to be included in each of the 3 countries (UK, Spain, France) to ensure reliable item statistics. IBS patients fulfilled ROME IV criteria with IBS-SSS scores between 150-300. Subjects completed the IGQ, The functional Digestive Disorders Quality of Life (FDDQL) score (0-100, higher = better quality of life) and the generic EQ-5D. Among the 100 subjects, 30 were asked to repeat the IGQ after a 7-day interval on paper or electronically. After item analysis and reduction, convergent/divergent (IGQ vs FDDQL and EQ-5D) and known-group validity (IGQ vs IBS-SSS) and test-retest reliability (intraclass correlation, ICC) were checked.

Results: 305 subjects were included (UK: 105; Spain: 100; France: 100), with 186 IBS (IBS-C: 68; IBS-D: 61; IBS-M: 57), and 119 GP. Mean age was 42±14 yrs, 69% were female. Mean IBS-SSS was 252±41 among IBS. FDDQL total score was 45±13 (IBS) vs 59±19 (GP). Factorial analysis (n=304) resulted in a 6-factor structure, bloating symptom items loading on the first factor. The structure was similar among IBS and GP. Twenty-six items (10 symptom and 16 impact items) were deleted (high floor effect or inter-item correlation, cross-loading or no clear loading).

The confirmatory factorial analysis on the remaining 17 items (7 symptom and 10 impact items) among 302 subjects, with no missing data, yielded a 6-factor structure explaining 67% of the variance with respectively bloating (6 items), flatulence (3), belching (2), bad breath (2), stomach rumbling (2) and difficult gas evacuation (2). Scores from 0 to 100 (worse) were computed: for each of the 6 symptoms, a total score and a score gathering the 5 other symptoms except bloating.

Scores were worse among IBS vs GP, e.g. 75±19 vs 66±22 for total score (p< 0.001). IGQ total and bloating scores were correlated with the FDDQL global, Discomfort and Diet dimension scores (r between 0.42-0.68). Logically there was no correlation between IGQ and EQ-5D. IGQ total score got worse in parallel with IBS-SSS (r=0.24, p=0.0006): 59±34. ICC of IGQ scores was between 0.47-0.84, except for flatulence (0.27) among the 67 subjects who were considered stable at the 2nd visit after an interval of 7.3±0.9 days.

Similarly, the correlation between the completion of IGQ in paper vs electronic among these 67 stable subjects was high (ICC: 0.77 for global score).

Conclusion: The IGQ is a robust instrument for capturing and measuring gas related symptoms. The final 17-item questionnaire has good psychometric properties and is available in paper and electronic versions in 3 languages.

References: (1) Chassany O, Tugaut B, Marrel A, Guyonnet D, Arbuckle R, Duracinsky M, Whorwell PJ, Azpiroz F. The Intestinal Gas Questionnaire: development of a new instrument for measuring gas-related symptoms and their impact on daily life. Neurogastroenterol Motil. 2015 Jun;27(6):885-98.
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P1201 SACRAL NERVE STIMULATION FOR SLOW TRANSIT CONSTIPATION: A RANDOMIZED, DOUBLE BLINDED, CROSSOVER STUDY

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Introduction: Chronic idiopathic constipation has a favorable response with conservative measures in most cases, but in a small proportion of patients surgical strategies may be necessary, having inconsistent results. Sacral nerve stimulation (SNS) is a potential alternative, and as a temporary device is used previous to a definite implantation, other possible treatments are not excluded if the result is not as expected. Results in current published data vary, probably due to the design of the studies, small number of patients and the inclusion of different types of constipation.

Aims & Methods: The main objective was to evaluate the short and long-term efficacy of sacral neuromodulation (SNS) in patients with chronic slow transit constipation (CSTC). Secondary outcomes were to evaluate adverse effects of implantation of the device and to correlate the efficacy with transit time and anorectal manometry (AM) data.

Methods: a multicenter, controlled, crossover randomized, double-blind trial was designed. Patients with CSTC(< 2 bowel movements (BM)/week; refractory to maximum conservative available treatment) were included for 4 weeks of peripheral nerve evaluation (PNE), the ones with response in BM(>3times/week), decreased intake of laxatives (reduction >50 % of laxatives or enemas/week) and subjective improvement (VAS), were implanted with SNS. Patients were randomly included in a 6-week ON and OFF stimulation period separated by a 2-week washout phase. After the randomization all stimulators were left in ON. A stool diary (4 weeks), visual analog scale (VAS), Cleveland Clinic Constipation Score (CCCS), Short Form Health Survey (SF-36) and a local validated survey for constipation (CVE-20) were evaluated at 6 and 14 weeks, every 3 months during the first year and then once a year. CTT and AM were performed after 6 months and subsequently every year.

Results: 19 out of 26 patients met inclusion criteria (18 women, median age 52.74 years). 13 (68%) responded to PNE and underwent permanent SNS implantation, mean follow-up of 25.98 ± 12.65 months. When analyzing ON and OFF periods, significant improvement in successful BM (21.64 vs 15.18) p< 0,01). During the follow-up and at the end of it, 9 out of 15 variables of the stool diary improved significantly compared to baseline, as well as CCCS (27,66 vs 10,99, p < 0.001) and VAS (92,79 vs 47,71 p< 0.001). Quality of life evaluated by SF-36 improved except in social impairment and with CVE-20, specific for constipation, it improved in most aspects except in emotional aspects.

Anal pressures did not change, whereas rectal sensitivity for urgency decreased significantly. Changes in CTT (Fig 2) were also significant (171 +/-9 vs 116 +/- 23, p< 0.004). No severe adverse events were registered, only mild sacral/anal pain or in the implantation site.

Conclusion: In a selected group of patients with CSTC, SNS implantation can be an effective treatment and is associated with an improvement in CTT.

References: 1. Dinning PG et al. Treatment efficacy of sacral nerve stimulation in slow transit constipation: a two-phase, double-blind randomized controlled crossover study. Am J Gastroenterol 2015; 110: 733-40. 31 12.- Patton V et al. Sacral nerve stimulation fails to offer longterm benefit in patients with slow-transit constipation. Dis Colon Rectum 2016; 59: 878-85. 32 2. Zerbib F et al. Randomized clinical trial of sacral nerve stimulation for refractory constipation. Br J Surg 2017; 104: 205-13. 3. Mowatt G, Glazener C, Jarrett M. Sacral nerve stimulation for faecal incontinence and constipation in adults. Cochrane Database Syst Rev 2007; (3):CD004464. 4. Ganio E, Masin A, Ratto C, Altomare DF, Ripetti V, Clerico G, Lise M, Doglietto GB, Memeo V, Landolfi V, Del Genio A, Arullani A, Giardiello G, de Seta F (2001) Short-term sacral nerve stimulation for functional anorectal and urinary disturbances: results in 40 patients: evaluation of a new option for anorectal functional disorders. Dis Colon Rectum 44(9):1261-1267
Disclosure: Nothing to disclose

P1202 METAGENOMIC ANALYSIS OF INTESTINAL MICROBIOTA AND MYCOBIOTA AMONG DIARRHEA-PREDOMINANT IRRITABLE BOWEL SYNDROME PATIENTS FROM ARGENTINA

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Introduction: It has been suggested intestinal microbiota is associated with the development of diarrhea-predominant Irritable Bowel Syndrome (IBS-D). There is scarce evidence regarding this aspect among IBS-D patients from a South American population. Additionally, intestinal mycobiota has not been exhaustively studied on this patients

Aims & Methods: To describe bacterial and fungal composition of intestinal microbiota among Argentinean patients with IBS-D.

Adult patients with IBS-D (Rome III criteria) from Buenos Aires, Argentina were consecutively enrolled. One fecal sample per patient was collected for microbiota and mycobiota analyses. Patients completed the IBS Symptom Severity Scale (IBS-SSS). Demographic features were assessed as well as stool consistency via the Bristol Stool Scale. After genomic DNA extraction and purification, bacterial and fungal composition of fecal samples

were analyzed based on 16S rDNA and ITS2 sequencing respectively. Correlation between microbial and fungal abundance and the clinical features was assessed by Pearson correlation test.

Results: 71 patients fulfilling inclusion criteria were enrolled. *Firmicutes* was the predominant phyla (73.61%), followed by *Bacteroidetes* (13%). A relatively elevated proportion of *Proteobacteria* (8%) was identified. *Alistipes* was the most represented genus. When analyzing correlations between microbiota composition and different clinical features, we found a negative correlation (r= -0.5, p 0.003) between stool consistency score and butyrate-producing microorganisms, such as *Butyricicoccus* and *Lachnospiraceae* UCG010 genera. Symptom severity assessed by IBS-SSS was positively correlated with the abundance of *Victivallaceae* uncultured organisms, *Synergistes* and *Ruminococcus gnavus* groups genera (r= 0.42, 0.33 and 0.32 respectively, p 0.05). ITS2 DNA sequences analysis showed that the predominant fungal phyla was *Ascomycota* (89.12%), followed by *Basidiomycota* (2.78%); *Saccharomyces*, *Debaryomyces* and *Candida* were the dominant genera. No significant correlation between mycobiota components and clinical features was found.

Conclusion: We describe the bacterial and fungal composition of intestinal microbiota in IBS-D patients from Argentina. Although certain significant correlations were identified between microbiota composition and clinical features such as symptom severity, the clinical implications of such findings deserve further research.

Disclosure: Dr. Luis Bustos Fernandez is member of the Latin American Board of Biocodex

P1203 THE AGEING GUT: SYMPTOMS COMPATIBLE WITH FUNCTIONAL GI DISORDERS IN OLDER ADULTS IN THE GENERAL POPULATION

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Introduction: Little is known about changes in symptoms compatible with Functional GI Disorders (FGID) with increasing age at the population level, since most published studies have used clinical samples, and mostly focus on younger individuals.

Aims & Methods: A community sample of 6,300 individuals age 18 and older in the US, UK and Canada (2,100 in each country) completed a secure online survey. Quota-based sampling was used to ensure equal proportion of sex and age groups (40% aged 18-39, 40% aged 40-64, 20% aged 65+) across countries, and to control education distributions. The survey included the Rome IV Diagnostic Questionnaire, demographic questions, questionnaires measuring overall somatic symptom severity and quality of life, and questions on health care utilization, medications and surgical history.

Results: 6,300 individuals completed the survey. 374 were excluded due to inconsistent responses, leaving 5,926 (49.2% female; mean age 47.4 ±17.1 years) for our analyses; of these 4,700 were 18-64 years and 1,226 aged 65+. Symptoms compatible with at least one FGID were less prevalent in 65+ (32.9%) than in subjects aged 18-64 years (41.3%) (p<0.0001). This difference was significant in females (38.1% vs. 49.7%; p<0.0001), but not in males (29.0% vs. 32.6%; p=0.08), and in the US (31.0 vs. 42.2%; p< 0.0001) and the UK (29.4% vs. 39.3%; p<0.0001), but not in Canada (38.1% vs. 42.4%; p=0.12). For symptoms compatible with upper FGID (esophageal and gastroduodenal), lower prevalence for most disorders was noted in the 65+ group (see Table).

For lower FGID (bowel and anorectal) a different pattern was seen, with lower prevalence for irritable bowel syndrome (IBS), functional abdominal bloating/distension and proctalgia fugax in 65+, no differences in prevalence for the functional bowel disorders defined by abnormal bowel habits, i.e. functional constipation, functional diarrhea and opioid-induced constipation, whereas fecal incontinence was the only FGID that was more common in 65+ (Table). Regarding other factors, subjects aged 65+ reported less severe overall somatic symptoms, better mental, but worse

physical quality of life, had undergone abdominal surgery more frequently, consumed more acid-reducing and pain medications, but less psychotropic medications, and used health care more frequently than younger adults (p< 0.0001 for all).

Conclusion: In general, symptoms compatible with FGID decrease in older adults at the population level, with the exception of fecal incontinence which increases, and bowel habit disturbances, which remain unchanged in prevalence. This pattern needs to be taken into account when planning GI health care for a growing population of older adults.

Upper GI Disorders:	18-64 years	65+ years	p-value	Lower GI Disorders:	18-64 years	65+ years	p-value
Functional Chest Pain	1.7%	1.2%	0.25	IBS	6.5%	2.8%	**<0.0001**
Functional Heartburn	2.2%	0.2%	**<0.0001**	Functional Constipation	6.5%	5.7%	0.36
Reflux Hypersensitivity	1.7%	0.5%	**<0.0001**	Functional Diarrhea	5.6%	5.0%	0.44
Globus	1.1%	0.9%	0.75	Functional Abd. Bloating/ Distent.	3.7%	2.4%	**0.03**
Functional Dysphagia	4.8%	3.4%	**0.04**	Unspecified Functional Bowel Disorder	10.3%	8.9%	0.16
Functional Dyspepsia	10.3%	5.4%	**<0.0001**	Opioid-induced Constipation	1.5%	1.3%	0.69
Belching disorders	1.0%	0.2%	**0.008**	Fecal Incontinence	2.9%	4.8%	**0.002**
Rumination Syndrome	3.7%	2.2%	**0.008**	Levator Ani Syndrome	1.9%	1.1%	0.06
Chronic Nausea and Vomiting Syndrome	1.6%	0.3%	**<0.0001**	Proctalgia Fugax	5.8%	3.7%	**0.003**
Cyclic Vomiting Syndrome	1.4%	0.2%	**<0.0001**				
Cannabinoid Hyperemesis Syndrome	0.2%	0.1%	0.70				

[Prevalence of symptoms compatible with FGID.]

Disclosure: Magnus Simren and Ami Sperber are members of the Board of Directors, and William Whitehead former board member, of the Rome Foundation, which sponsored the study. Olafur Palsson received research support from the Rome Foundation to carry out the study.

P1204 INCIDENCE OF POST-INFECTIOUS IRRITABLE BOWEL SYNDROME AND FUNCTIONAL DYSPEPSIA AFTER A NOSOCOMIAL NOROVIRUS GASTROENTERITIS OUTBREAK

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Introduction: Bacterial and parasitic intestinal infections are well-known risk factors for development of post-infectious irritable bowel syndrome (PI-IBS), but the natural history of viral gastrointestinal infections is poorly understood. In May 2017, an outbreak of Norovirus gastroenteritis (GE) was reported at Hospital de Bellvitge, with 250 affected workers. In order to determine the incidence and risk factors of functional gastrointestinal disorders (FGID) after a Norovirus GE, we conducted this prospective cohort study with control group.

Aims & Methods: By e-mail, during the 4 weeks after the GE outbreak, we invited all hospital workers to participate, both the affected cases and those who not (controls). Questionnaires evaluating digestive symptoms using the Rome IV criteria for IBS and functional dyspepsia (FD) were sent at baseline and at 6 and 12 months. The severity of the GE episode was also assessed using the Vesikari scale.

Results: 71 cases and 84 controls answered the questionnaires. Baseline characteristics of cases and controls were similar. Prior to the infectious episode, the prevalence of IBS and FD was identical in both groups (IBS: 6% and 6% respectively; FD: 17% and 17% respectively, p = 0.9).
Excluding individuals with previous FGID, after 6 months of the GE the proportion of individuals who developed IBS or FD was higher in the case group than in the control group (IBS: 14% and 5% respectively, p=0.06; FD: 18% and 3% respectively, p=0.006). After 12 months, there were no differences in prevalence of IBS and FD between cases and controls (IBS: 5% and 4% respectively, p=0.7, FD: 9% and 6% respectively, p=0.5). Independent predictors of FGID were the GE severity assessed by Vesikari scale (OR 1.32 IC95% (1.05-1.65), p=0.017) and smoking (OR 3.9 IC95% (1.01-14.9), p=0.048).
Conclusion: Functional gastrointestinal disorders are common after Norovirus gastroenteritis but they are often transient. The risk is determined by the severity of the infectious episode.
Disclosure: Nothing to disclose

P1205 PREVALENCE AND IMPACT OF SELF-REPORTED CONSTIPATION IN THE GENERAL POPULATION

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Introduction: Chronic constipation, as defined by the Rome IV criteria, is a highly prevalent functional bowel disorder. However, as the criteria impose strict diagnostic thresholds, the prevalence of self-reported constipation is considerably higher, and there is major overlap with other bowel disorders, especially irritable bowel syndrome. We therefore conducted a pooled-analysis to evaluate the presence of self-reported constipation in the general population, its association with other bowel symptoms and its health-economic impact.
Aims & Methods: We used an internet survey (Medistrat internet panel, representative of the national adult population) to collect information on bowel symptoms' prevalence and their impact. In this analysis, we focused on patients who reported constipation symptoms over the last 12 months. First, we compared participants who experienced constipation to those who reported other bowel symptoms. Second, subjects reporting constipation were subdivided in painful constipation (PC), and those who did not experience abdominal pain (NPC).
Results: 1012 subjects (mean age 45.2±0.5 years, 62% females), of whom 217 (21%) reported constipation, completed the survey. Subjects reporting constipation experienced more other bowel symptoms than those without constipation [3(2-6) vs. 2(1-4), p< 0.0001]. The constipation group reported higher prevalence's of abdominal pain, altered stool frequency, alternating bowel habits and bloating (all p< 0.05). Further, constipated subjects reported higher symptom occurrence ≥3 days per month (65.9% vs. 52.9%; p< 0.01).
Furthermore, the days of symptom occurrence significantly differed between the constipated participants and those with other bowel movements. Those with constipation had symptoms 1-2 days/week (28.6% vs. 22.7%), while those with other bowel movements experienced symptoms >2 days/month more often (35.7% vs. 24.9%); (p=0.036). Finally, in total 44% of participants with constipation reported taking laxatives for their complaints, compared to just 8% of those whom reported other bowel symptoms (p< 0.001).

Of those with constipation, 134 patients reported NPC compared to 83 patients with PC (43±14.29 and 41±14.46 years, respectively). Women were significantly more represented in the group reporting constipation compared to those reporting other bowel symptoms (81.57% vs. 56.60%, p< 0.0001). Thirty-eight out of 83 PC patients (45.24%) fulfilled the Rome IV IBS criteria.
More patients with NPC compared to PC marked constipation as their most bothersome symptom (75% vs. 44%, p = 0.014). In addition, excessive gas was experienced more frequently in the NPC compared to the PC group (64% vs. 39%, p = 0.044). PC patients also reported more consultations with a medical doctor (40.24% vs. 14.29%, p< 0.0001), and more visits to specialists (50% vs. 10%, 95% CI 1.8-44.9), but not to general practitioners or other doctors in the past 12 months. Concerning medication, the use of anti-spasmodics was significantly higher in the PC-group compared to the NPC-group (38.24% vs. 12%, p=0.025).
Conclusion: Self-reported constipation, often associated with other bowel symptoms, is a highly prevalent condition in the general population. Especially when abdominal pain is present, this generates major healthcare costs.
Disclosure: Nothing to disclose

P1206 EXTRA-GASTROINTESTINAL SYMPTOMS CHARACTERIZE CLUSTERS OF FUNCTIONAL GASTROINTESTINAL DISORDERS THAT ARE NOT READILY DISTINGUISHED BY ROME III CRITERIA

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Introduction: Functional gastrointestinal disorders (FGID) are defined according to the Rome criteria by the grouping of non-specific GI symptoms without demonstrable underlying organic pathology. These definitions do not consider extra-GI symptoms or extra-GI pathology. The non-specific GI symptoms accompany a wide range of pathologies, including some without primary GI origin.
Aims & Methods: The aim of this large single-centre study was to characterize subgroups of FGID patients based on GI and extra-GI chronic symptom profiles using cluster analysis. Furthermore, the relationships between retrieved clusters and different Rome III groups of FGID were assessed. Successive male and female patients over 18 years of age referred to our GI practice for investigation of FGID and without evidence of organic disease were included. Patients completed a standardized, extensive GI and extra-GI symptom questionnaire focusing on their long-term symptom profiles and FGID was classified according to the Rome III criteria. The long-term symptom profile data were subjected to latent class analysis to identify unobserved clustering in the patient population and to find meaningful groups that were similar in their clinical assessment parameters. For each patient cluster, the prevalence of irritable bowel syndrome (IBS), functional dyspepsia (FD), functional bloating (FB), functional diarrhoea (FDa) and functional constipation (FCo) was determined.
Results: In 2083 patients with FGID (mean age 39.7 years, 70% females), the optimal number of clusters was 6. Face validity was apparent, with some distinctions seen between clusters in distributions of GI symptoms, but more apparent differences seen for distributions of extra-GI symptoms. GI fermentation-type symptoms were present across all 6 clusters and exclusively characterized Cluster 1 (35% of patients). The further clusters were distinguished by additional reflux-like (cluster 2: 19%), allergy-like (cluster 3: 6%), central nervous system (cluster 4: 17%), musculoskeletal (cluster 5: 10%), and generalized extra-GI (cluster 6: 14%) symptoms. Us-

	Cluster 1 GI fermentation-like (n=736)	Cluster 2 fermentation + reflux-like (n=117)	Cluster 3 fermentation + allergy-like (n=391)	Cluster 4 fermentation + central nervous system (n=348)	Cluster 5 fermentation + musculoskeletal (n=208)	Cluster 6 fermentation + generalized extra-GI (n=283)	p-values
Irritable bowel syndrome	195 (26)	35 (39)	138 (35)	126 (36)	68 (33)	110 (39)	0.001
Functional dyspepsia	605 (82)	91 (78)	373 (95)	319 (92)	182 (88)	269 (95)	<0.001
Functional bloating	67 (9)	12 (10)	7 (2)	8 (2)	9 (4)	5 (2)	<0.001
Functional diarrhoea	248 (34)	35 (30)	149 (38)	118 (34)	69 (33)	107 (38)	0.42
Functional constipation	89 (12)	16 (14)	67 (17)	75 (22)	34 (16)	63 (22)	<0.001

[P1206 Patients numbers (%) defined by Rome III subgroups in symptom clusters. There is considerable overlap between Rome groups.]

ing Rome III criteria, the prevalence of the FGID subtypes differed significantly between the 6 symptom clusters (see Table):

IBS (26-39%; p=0.001), FD (78-95%; p<0.001), FB (2-9%; p<0.001), FDa (30-38%; p=0.42) and FCo (12-22%; p<0.001). The differences in prevalence of FGID subtypes across the symptom clusters were statistically significant, but mostly not clinically relevant (see Table).

Conclusion: Patients with FGID fall into distinct subgroups based mainly on their extra-GI long-term symptoms. The Rome III definitions did not readily distinguish between subgroups of FGID across the clusters. Inclusion of extra-GI symptoms in the classification of FGIDs may be helpful in identifying subgroups with distinct underlying pathologies and thereby therapeutic possibilities.

Disclosure: Nothing to disclose

P1207 DOES INTESTINAL MICROBIOTA COMPOSITION DIFFER BETWEEN DIARRHEA-PREDOMINANT IRRITABLE BOWEL SYNDROME PATIENTS WITH OR WITHOUT AN ALTERED LACTULOSE BREATH TEST?

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Introduction: Background: It has been suggested that the intestinal microbiota is associated with the development of diarrhea-predominant Irritable Bowel Syndrome (IBS-D). A significant proportion of such patients exhibit abnormal hydrogen excretion on lactulose breath tests, which could be associated with small intestinal bacterial overgrowth (SIBO). Patients with IBS-D and an abnormal lactulose breath test may show a different intestinal microbiota profile, which could be associated with such alterations in gas excretion.

Aims & Methods: To compare the bacterial and fungal composition of intestinal microbiota of IBS-D Argentinean patients with or without SIBO. Adult patients with IBS-D (Rome III criteria) were consecutively enrolled. One fecal sample per patient was collected for microbiota and mycobiota analyses. Furthermore, patients undertook a lactulose breath test (LHBT). An increase of at least 20 ppm in hydrogen excretion before 100 minutes was considered to be a criterion for SIBO. After genomic DNA extraction and purification, bacterial and fungal composition of fecal samples were analyzed based on 16S rDNA and ITS2 sequencing respectively.

Results: 71 patients were enrolled; mean age was 43.5±14.5 years and 62% were female. 76% were SIBO positive. No significant differences were found in terms of demographic features between SIBO-positive and SIBO-negative patients. 16S rDNA alpha and beta diversity analyses showed comparable microbiota composition between SIBO positive and SIBO negative. However, Akkermansia genus and upper-related taxa were significantly more abundant (+672%, p=0.009) in SIBO negative patients. Furthermore, Turicibacter genus and upper-related taxa were also more abundant (+535%, p=0.04) in SIBO negative patients. Cloacibacillus genus was greatly increased in SIBO negative patients (+8463%, p=0.0006). On the other hand, Ruminococcaceae UCG 003 and Ruminoclostridium 9 genera were decreased in SIBO negative patients (-70% and -46.6%, p=0.003 and 0.0007, respectively). Mycobiota analyses showed no major difference.

Conclusion: Differences in terms of bacterial and fungal composition of intestinal microbiota were found between SIBO-positive and SIBO-negative IBS-D patients. Clinical implications of these findings require further investigation.

Disclosure: Dr Bustos Fernandez is memeber of thge Latin American Board of Biocodex

P1208 THE INTRA-INDIVIDUAL VARIABILITY OF FECAL CALPROTECTIN IN HEALTHY INDIVIDUALS

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Introduction: Fecal Calprotectin (FC) is a marker for intestinal inflammation, which allows the clinician to distinguish between functional and organic intestinal illnesses, as well as to evaluate the activeness of disease in chronic inflammatory bowel disease (IBD). There are singular studies that report day-to-day variability in FC concentration measured in patients with IBD. If such a variation also exists in healthy individuals has not been evaluated as of yet.

Aims & Methods: Our aim was to determine the intra-individual day-to-day variability of FC in the intestinally healthy. The results could influence the further management of patients with intestinal discomfort. To achieve this, 163 healthy volunteers without gastrointestinal symptoms, colitis related manifestations or intake of NSAID gave three stool samples of the morning bowel movement on three consecutive days. The samples were sent via mail. The FC-analysis was made by enzyme-linked immunosorbent essay (ELISA) method after Bühlmann (Rothen Medizinische Laboratorien AG Basel).

Material was financed by Netzer AG, analysis by MCL Laboratorien Niederwangen. The threshold to pathological FC- values was 50μg/g, as recommended in Switzerland. Volunteers with elevated values were investigated further, only those remained in the study who had no signs of organic gastrointestinal disease.

Results: 163 volunteers (aged 17-66y, mean 37y, median 32y, f=100), showed a range of FC-values of 3 - 2142 μg/g. The first measurement showed a range of 3 - 587 μg/g, mean value 44.5, median 20, standard deviation (sd) 75.1. The second measurement showed a range of 6 - 2142 μg/g, mean value 60.3, median 22, sd 183.4. The third measurement showed a range of 9 - 699 μg/g, mean value 41, median 18, sd 73.7. Every one of the three measurement series showed only two values >400 μg/g. Of all 163 volunteers, 114 (69.9%) showed FC- values of 50μg/g and lower in all three samples, thus having inconspicuous results throughout. 49 volunteers (30.1%) showed at least one value deemed pathologic. Of these 49, 40 (24.5%) showed both normal and elevated (>50μg/g) values and 9 (5.5%) showed elevated values throughout. By applying a cut-off of 100μg/g, 26 volunteers (15.9%) showed at least one elevated measurement and only 4 (2.5%) had values consistently over 100μg/g.

Conclusion: The presented data show a high variability of FC in a short amount of time in a third of the healthy volunteers. This suggests several measurements of FC to be adequate to reach a decision if further investigation (e.g. endoscopy) is necessary. The mean value of three measurements could show a higher correlation to actual intestinal inflammation and could help reduce unneeded interventions. Further investigations in a non-healthy population are recommended. The data also support the question, if raising the cut-off to 100μg/g would be appropriate to keep the rate of false positive results low without missing relevant disease, as several investigators have recommended already.

Disclosure: Nothing to disclose

P1209 IRRITABLE BOWEL SYNDROME AND GLUTEN CHALLENGE: RESULTS OF A RANDOMIZED SINGLE-BLIND CONTROLLED TRIAL

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Introduction: The major dilemma in medical practice is the gluten tolerance assess in IBS patients and evaluation of symptoms in different dosage of gluten challenge. For this purpose, we designed a single-blind free diet controlled gluten challenge to report a true NCGS prevalence among IBS patients

Aims & Methods: In this trial, 40 participants were asked to follow low FODMAP+ strict gluten free diet for 6 weeks. Then, all patients were randomly allocated to one of the following groups:

Group A: patients received special bread containing of 8 g/ gluten for 2 weeks. Those who had tolerance to prescribed dose received 16 g/d for more 2 weeks. Then tolerated patients took 32 g/d for further 2 weeks;
Group B: continued gluten free diet for more 6 weeks;
Group C: received regular gluten containing diet for 6 weeks.

At the end, participants were asked to fill VASs scale to evaluate the improvement of symptoms, SF-36 and Zung questionnaire.

Results: After 6 weeks of following gluten free and low FODMAP diet, all IBS symptoms, except for defecation frequency, were significantly improved. In group A: 25% tolerated up to 8 g 20% to 16 g, and 55% to 32 g gluten. At the end of the study, no significant difference was found between groups in terms of pain, bloating, satiety, impact on community function, defecation and total score. In regard to SF-36 questionnaire, significantly lowest bodily pain was found in group C (A: 3.93±1.44, B: 4.71±2.33 and C: 3.29±0.95) (p=0.02). Borderline significant difference was detected for social functioning score (p=0.049). There was significant reduction regarding nervous and anxiety score (p=0.021), calmness (p=0.047), dry and warm hands (p=0.02) and easily asleep (p=0.01) in group B compared other groups.

Conclusion: Most patients with irritable bowel syndrome have tolerance to gluten. But following gluten free diet would decrease anxiety in IBS patients.

Disclosure: Nothing to disclose

P1210 OSTEOPONTIN HAS NO ROLE AS A DIAGNOSTIC BIO-MARKER IN IRRITABLE BOWEL SYNDROME (IBS)

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Introduction: Osteopontin (also known as early T lymphocyte activation Eta-1), a cytokine which promotes Th1 immune responses. Several recent reports have suggested an important role for osteopontin in the pathogensis of inflammatory bowel diseases as well as its possible use as a bio-marker. It has been proposed that inflammation may play a role in IBS, based on several lines of evidence.

Aims & Methods: The aim of this work was to find out the diagnostic potential of osteopontin as bio-marker in irritable bowel syndrome. 40 patients, who were fulfilling Rome IV criteria for IBS, were investigated. As well as 20 healthy subjects were enrolled as controls.All subjects were subjected to:medical history taking,thorough physical examination and laboratory investigations which included:-Routine laboratory tests ,fecal calprotectin assessment and serum osteopontin assessment.Colonoscopy and histopathological examination of biopsies from the colon were done for patients only after informed consent.

	IBS Cases (n = 40)	Control (n = 20)	t	p
ESR at 1st hrs (mm/hr)				
Mean ± SD	12.13 ± 2.05	11.80 ± 2.38	0.548	0.586
Median	13.0	13.0		
ESR at 2nd hrs (mm/hr)				
Mean ± SD	24.55 ± 3.17	23.25 ± 4.38	1.315	0.194
Median	25.0	23		
CRP (mg/l)				
Mean ± SD	4.44 ± 1.53	4.13 ± 1.10	0.791	0.432
Median	4	4		
Calprotectin (mg/kg)				
Mean ± SD	28.60 ± 19.24	21.75 ± 9.08	1.872	0.066
Median	19	20		
Osteopontin (ng/mL)				
Mean ± SD	2.92 ± 0.91	2.50 ± 0.78	1.748	0.086
Median	2.80	2.25		

[Comparison between the two studied groups according to the markers of inflammation]

Results: Out of 40 patients (group I); 20 were IBS-D (diarrhea predominant), 14 IBS-C (constipation predominant) and 6 IBS-A (alternating diarrhea and constipation). Both group I and group II were matched as regard age and sex. There were no statistical significant difference between the two studied group in routine laboratory investigations. Stool analysis was normal in all subjects. No statistical significant difference between the two groups as regard the mean erythrocytes sedimentation rate (ESR) at the first and second hour [p = 0.586& 0.194 respectively]. Also no statistical significant difference between the two groups as regard the mean C-reactive protein (CRP), the mean fecal calprotectin level and the mean serum osteopontin level [p = 0.432, 0.066 &0.086 respectively]. As regard colonoscopic findings in IBS patients: Hyperemia was found in 4 patients, polyps were found in 2 patients, diverticulae, ulcers and mass were not found in any patients. Regarding histopathological findings of colonoscopic biopsies in IBS patients: Non specific colitis was found in 30 patients and 10 patients were normal. Lymphocytic colitis was not found in any of the patients group.

Conclusion: Osteopontin has no role as a diagnostic bio-marker in IBS. Further work on a larger patients sample will be required to study the probability of the use of osteopontin as non invasive bio-marker in the differentiation between functional and inflammatory gastrointestinal disorders.

References: 1. Sperber AD, Drossman DA. Review article: the functional abdominal pain syndrome.Aliment PharmacolTher 2011; 33: 514-24. 2. Nobaek S, Johansson ML, Molin G, Ahrné S, Jeppsson B. Alteration of intestinal microflora is associated with reduction in abdominal bloating and pain in patients with irritable bowel syndrome. Am J Gastroenterol 2000;95:1231-8. 3. Ortiz-Lucas M, Saz-Peiró P, Sebastián-Domingo JJ.Irritable bowel syndrome immune hypothesis. Part one: the role of lymphocytes and mast cells.Rev Esp Enferm Dig 2010;102:637-47. 4. Grover M, Herfarth H, Drossman DA. The functional-organic dichotomy: postinfectious irritable bowel syndrome and inflammatory bowel disease irritable bowel syndrome.ClinGastroenterolHepatol 2009; 7:48-53.
Disclosure: Nothing to disclose

P1211 BOTH OBJECTIVE EXPERIMENTAL AND NATURALISTIC RESPONSES DIFFERENTIATE GASTROINTESTINAL SYMPTOMATIC FROM ASYMPTOMATIC INDIVIDUALS

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Introduction: An objective method of differentiating functional gastrointestinal disease (FGID) from health remains an elusive goal although there has been some promising work using biomarkers[1]. Another potential avenue comes from work showing that FGID individuals have altered central (brain and central nervous system) processing of visceral stimuli relative to healthy controls[2]. Further, FGID individuals appear to have selective attention to gastrointestinal words[3] suggesting an attentional bias towards GI-relevant terms. Individuals meeting criteria for FGIDs have also been shown to exhibit exaggerated threat perception[4]. Previous work has taken either an experimental approach, eg fMRI studies of acute, regional brain activation in response to noxious stimuli, or an epidemiological approach based on measuring symptom experiences by questionnaires or daily diary record. How well gastrointestinal disease might be differentiated from health based on a combination of these distinct objective and subjective profiles is lacking in the literature.

Aims & Methods: This study aimed to determine whether a combination of objective responses to experimental stimuli (EEG, below) and subjective but prospectively recorded, naturalistic responses to daily events (EMA, below) can differentiate symptomatic and asymptomatic individuals. 28 GI symptomatic and 27 asymptomatic individuals were recruited from the community. Organic pathology and current mood disorders were ruled out by self-report. All subjects viewed 20 GI-illness-related words, 20 negatively-valenced words, and 20 neutral words from a validated word bank six times in a randomised order. Attention was measured through ERP peak amplitude in the Occipital region measured via an electroencephalograph (EEG) in the P100 period (75-125 milliseconds after word stimulus presentation), as this clearly corresponds to pre-attentional processing. Average level and variability in gastrointestinal and non-gastrointestinal pain

as well as mood were recorded prospectively using ecological momentary assessment[5] (EMA) via a smartphone app over a 14-day period. Total GI symptom burden was measured through the gastrointestinal symptom rating scale[6] (GSRS). Discrimination between symptomatic and asymptomatic subjects was evaluated through the area under the ROC curve (AUC).

Results: GI symptomatic subjects yielded a higher average P100 response to all stimulus categories than asymptomatic subjects (b=1.28, 95% confidence interval 0.74, 1.82, p< .001), consistent with enhanced threat perception but not limited to GI concepts. A combination of increased P100 response amplitude, higher average level and greater variance in current mood and higher average level and greater variance in GI pain and higher average level and greater variance in non-GI pain yielded strong discrimination between symptomatic and asymptomatic subjects (AUC=0.90) which increased to AUC=0.93 if total GI symptom burden is included.

Conclusion: In contrast to a large body of past work which has used an individual's recall of past symptom experience to classify individuals as diseased or healthy, this study demonstrated prospectively that FGID individuals have a distinct day-to-day experience of both GI and extra-GI pain and respond to experimentally-induced stimuli differently to asymptomatic individuals. The combination of these responses provide good differentiation of symptomatic individuals from healthy controls. The use of non-invasive, inexpensive stimuli offers a promising avenue of investigation for objective diagnostic testing.

References: 1. Jones MP, Chey WD, Singh S, et al. A biomarker panel and psychological morbidity differentiates the irritable bowel syndrome from health and provides novel pathophysiological leads. Alimentary pharmacology & therapeutics. 2014;39(4):426-437. 2. Rubio A, Pellissier S, Van Oudenhove L, et al. Brain responses to uncertainty about upcoming rectal discomfort in quiescent Crohn's disease - a fMRI study. Neurogastroenterology & Motility. 2016:n/a-n/a. 3. Gibbs-Gallagher N, Palsson OS, Levy RL, Meyer K, Drossman DA, Whitehead WE. Selective recall of gastrointestinal-sensation words: evidence for a cognitive-behavioral contribution to irritable bowel syndrome. The American journal of gastroenterology. 2001;96(4):1133-1138. 4. Crane C, Martin M. Risk Perception in Individuals With Irritable Bowel Syndrome: Perceived Susceptibility to Health and Non-Health Threats. Journal of Social and Clinical Psychology. 2004;23(2):216-239. 5. Mujagic Z, Leue C, Vork L, et al. The Experience Sampling Method--a new digital tool for momentary symptom assessment in IBS: an exploratory study. Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society. 2015;27(9):1295-1302. 6. Svedlund J, Sjodin I, Dotevall G. GSRS--a clinical rating scale for gastrointestinal symptoms in patients with irritable bowel syndrome and peptic ulcer disease. Digestive diseases and sciences. 1988;33(2):129-134

Disclosure: Nothing to disclose

P1212 THE SEVERITY OF GASTROINTESTINAL SYMPTOMS AS A PREDICTOR OF TREATMENT EFFECT IN A 12- WEEK MULTIDISCIPLINARY INTEGRATED TREATMENT APPROACH FOR FUNCTIONAL GASTROINTESTINAL DISORDERS (FGIDS)

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Introduction: Current treatment for FGIDs categorise patients based on symptoms and attempt to target potential biological disease mechanisms, yet extensive literature suggests FGIDs result from interactions between biological, psychological and social factors. Therefore, a biopsychosocial framework for treatment for FGIDs should be considered. We have previously demonstrated that an Integrated Care Clinic (ICC) approach incorporating a multidisciplinary integrated treatment program in the setting of a gastroenterology outpatient department (OPD) significantly reduces overall gastrointestinal (GI) symptom burden in FGID patients. This study aimed to identify whether the effect of the intervention is moderated by the severity of GI symptom burden at baseline, to help identify predictors that may characterise a patient's response to a multidisciplinary integrated treatment program.

Aims & Methods: This study explored total GI symptom burden at baseline as a predictor of reduction in total GI symptom burden post intervention. 51 consecutive gastroenterology outpatients recruited to the ICC were included. These patients received a team-based integrated care approach including individualised assessment and treatment sessions with a gastroenterologist, general practitioner, psychologist, dietician and exercise physiologist, as deemed necessary by the team to meet the patient's needs.

Patients were grouped into total GI symptom burden-stratified subgroups according to baseline gastrointestinal symptoms severity as measured using the validated Structured Assessment of Gastrointestinal Symptoms scale (SAGIS) which measures the intensity of 22 upper and lower gastrointestinal symptoms, 0 = no problem to 4 = very severe problem for a maximum score 88 points. Stratification groups were based on mean baseline score (M = 27): low for total SAGIS score below 27 and high for total SAGIS score above 27. Within-subject changes were compared using a paired sample t-test and change scores between GI symptom severity strata were compared using an unpaired t-test.

Results: Mean age was 41.7 (SD-14.90) years with 84% females. In total, 53% of patients had irritable bowel syndrome, 10% had functional dyspepsia, and 37% had overlap of both. The mean baseline score was 27 and the overall mean change in total GI symptom burden post intervention was 9 units; by total GI symptom burden strata the mean was 4 units for the GI symptom burden low group and 14 units for the GI symptom burden high group. Total GI symptom burden significantly decreased from baseline (*p* < 0.015 by paired t-tests within both groups).

However, the decrease was higher in the GI symptom burden high group than the GI symptom burden low group (*p* = 0.002 comparing the change scores between the two groups using an unpaired t-test). Clinically significant reductions in total SAGIS score were present in 70% of the total GI symptom burden high group compared to 33% of the total GI symptom burden low group.

Conclusion: These results indicate that total GI symptom burden independent of varying GI total symptom burden is reduced by a multidisciplinary integrated treatment approach in FGID patients However, the reductions were substantially greater in patients with more severe manifestations of FGID, and this will need to be considered in future studies on the cost-benefit analysis of multidisciplinary treatment approaches.

Disclosure: Nothing to disclose

P1213 RECRUITMENT IN FUNCTIONAL BOWEL DISORDER STUDIES: WHY IS IT SO CHALLENGING?

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Introduction: Recruitment can be a major challenge to randomized clinical trials, and failure to achieve recruitment goals can endanger the overall quality of the study and lead to costly delays and non-completion [1]. In functional bowel disorder (FBD) studies, recruitment rates are particularly low and many studies fail to recruit patients on time and within budget [2]. Several factors attribute to this failure. Although FBD is relatively common, patients are often discharged quickly and have limited chance to build a rapport with the research team. Conversely patients who are not discharged often have severe refractory symptoms, rendering them far from ideal for most trials. Patients are often reluctant to come off laxatives/anti-diarrhoeals, thus are not keen to risk being on placebo, and are less willing to undertake the trial burden compared to studies of higher mortality conditions.

Aims & Methods: Our aim was to design a study for irritable bowel syndrome with diarrhoea (IBS-D) that was both deliverable and would maximise recruitment potential. The trial RELIEVE IBS-D, is currently recruiting 430 patients in 27 sites in the UK studying the effectiveness of the intestinal adsorbent Enterosgel for the treatment of IBS-D. We developed a study that was suitable for primary and secondary care recruitment, and that included pragmatic (real life) inclusion / exclusion criteria with low screen thresholds. Patient involvement (PPI) was used in both study design and all patient-facing documentation. An open label phase was included so that all patients received the intervention, as it is known that obtaining a form of personal gain through participation is a primary factor influencing participation in clinical trials.

Rescue therapy was only restricted for baseline and a re-screening phase was introduced to compensate for the variable nature of the condition [3]. Patient burden was restricted with a reduced visit number, low questionnaire number and an online daily diary with text-based reminders and limited number of questions. Following the guidelines, participants were encouraged to adjust their daily dosage during both phases based on their symptoms to better imitate "real world conditions" [4].

Several recruitment strategies are being employed. We use primary care patient identification centres for hospital sites to reduce attrition rates [5] and we contact eligible patients through the new ContactME IBS registry that enrols patients who have expressed an interest in research participation. A number of sites are also leveraging Clinithink Inc software that allows extensive mining of hospital records for eligible patients. We have used various forms of advertising through social media to gain a good representation of the clinical profile of IBS patients in the general population.

Results: The study began in October 2018 with recruitment starting in November, as of end of March 2019, 94 patients have been consented and 41 randomised. These rates are expected to increase as the main recruitment strategies will be employed in April to coincide with IBS awareness month.

Conclusion: Although recruitment is still a challenge, careful consideration during study design and employment of a comprehensive range of recruitment strategies can go some way to mitigate any potential issues from failure to recruit.

References: 1. Anderson, DL. A Guide To Patient Recruitment. CenterWatch/Thomson Healthcare; Boston, Massachusetts, USA: 2001. 2. Walters SJ, Bonacho dos Anjos Henriques-Cadby I, Bortolami O, et al. Recruitment and retention of participants in randomised controlled trials: a review of trials funded and published by the United Kingdom Health Technology Assessment Programme. BMJ Open 2017;7:e015276. 3. Kahan, BC. Using re-randomization to increase the recruitment rate in clinical trials - an assessment of three clinical areas. Trials. 2016;17:595-604 4. European Medicines Agency. Guideline on the evaluation of medicinal products for the treatment of irritable bowel syndrome 25 September 2014 CPMP/EWP/785/97 Rev. 1 5. Dal-Ré R, Luque A, Guardiola L, Rodríguez F. Irritable bowel syndrome: attrition rates of patients identified at primary care centers during a 50-week period versus those identified in hospitals in a phase II clinical trial. Int J Clin Pharmacol Res. 2001;21(3-4):127-36.

Disclosure: CAH and EM are employees of Enteromed Ltd the sponsor of the RELIEVE IBS-D study. AK, PP, JM, PW, MD, JG, CK, and YY have no conflicts of interest to declare.

P1214 ASSOCIATION BETWEEN DIETARY INTAKE AND SYMPTOMS IN PATIENTS WITH IRRITABLE BOWEL SYNDROME

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Introduction: Irritable bowel syndrome (IBS) is one of the most common functional gastrointestinal (GI) disorders with a prevalence of 5-10%. Previous evidence shows that GI symptoms can be triggered by dietary intake, resulting in patients avoiding certain foods in order to relieve these symptoms.

Aims & Methods: We aimed to enhance our understanding of food intake as trigger for symptom generation by correlating habitual dietary intake and symptom outcomes. Two IBS cohorts were included, using the first cohort for exploratory (hypothesis-generating) and the second for confirmatory (hypothesis-testing) purposes. Patients kept 4-day food diaries of their habitual food intake and simultaneously filled out symptom questionnaires, including information about bowel habits (Bristol stool form scale), quality of life (IBS-QOL), and IBS symptom severity (IBS-SSS and GSRS-IBS). Nutrient intake was calculated using dedicated software, and additionally FODMAP intake in the exploratory cohort, and health-consciousness of the diet in the second cohort were determined. We tested linear correlations between dietary variables and symptom variables and conducted a principal component analysis (PCA) with two principal components of the dietary intake data of both cohorts. Moreover, we tested mediation in the association between total calorie intake and IBS symptom severity.

Results: The exploratory cohort (N=112, 75% female, aged 33.5±11.3 years, body mass index (BMI) 23.1±3.8 kg/m², IBS-SSS 310.5±83.7, 23% IBS-constipation (IBS-C), 44% IBS-diarrhea (IBS-D), 7% IBS-mixed (IBS-M), 26% IBS-unsubtyped (IBS-U)) and confirmatory cohort (N=76, 81% female, aged 42.2±16.4 years, BMI 24.3±3.8 kg/m², IBS-SSS 308.1±66.1, 39/16/3/42% IBS-C/D/M/U patients) demonstrated various statistically significant food-symptom correlations. Total caloric intake correlated with overall GI symptom severity (GSRS-IBS) (exploratory (e): R=-0.213 , p=0.026; confirmatory (c): R=-0.274, p=0.018), fiber intake with hard (R_e=-0.217, p_e=0.027) and loose bowel movements (BM) (R_c=0.247, p_c=0.037), and legume intake with quality of life (R_e=-0.296, p_e=0.002; R_c=-0.269, p_c=0.029). In the PCA, PC 2 was negatively correlated with the IBS-SSS score (R=-0.27, p< 0.001). PC 2 was characterized by a higher intake of calories (loading: 0.54) and legumes (loading: 0.38), but a lower intake of diet drinks (loading: -0.40), and less nighttime consumption (loading: -0.40). No significant correlations were found between FODMAP intake and IBS symptom severity, nor between the heath-consciousness of the diet and IBS symptom severity or quality of life. The negative association between total calorie intake and IBS symptom severity was mediated by not eating and not being hungry due to symptoms.

Conclusion: Based on this analysis of two IBS cohorts, we were able to demonstrate associations between dietary intake and GI symptoms as well as disease-specific quality of life. Patients with severe IBS may have reduced energy intake because of GI symptoms. Further characterization of food-symptom associations can lead to the development of personalized dietary advice in the management of IBS.

Disclosure: Nothing to disclose

P1215 EFFECT OF A MUCOPROTECTANT (XYLOGLUCAN + PEA PROTEIN AND TANNINS + XYLO-OLIGOSACCHARIDE) ON INTESTINAL PERMEABILITY AND MUCOSAL MICROINFLAMMATION IN THE JEJUNUM OF IRRITABLE BOWEL SYNDROME WITH DIARRHEA

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Introduction: Irritable Bowel Syndrome (IBS) is a disorder of brain-gut interaction characterised by chronic and recurrent abdominal pain, altered defecation and sensitivity to stress. One of the important advances in the knowledge of the origin of IBS is the common finding of a dysfunction of the intestinal barrier (permeable barrier) associated with structural and molecular alterations in the intercellular junctions and the presence of immune activation and low-grade mucosal inflammation, particularly in IBS-diarrhea (IBS-D). Mucoprotectans such as the combination of xyloglucan + pea protein and tannins + xylo-oligosaccharide (XPPTX) may be useful to control permeability changes induced by life stress.

Aims & Methods: Our hypothesis is that XPPTX, through the establishment of a mucus-associated biofilm, exerts a direct local protective effect capable of preventing the increase of intestinal permeability and the immuno-inflammatory response triggered by acute experimental stress in patients with IBS-D. Therefore, we aimed to:

- To determine the effect of the administration of XPPTX on intestinal permeability induced by acute stress in the jejunum of patients with IBS-D, and to
- Evaluate the effect of the administration of XPPTX on changes in tight junctions and intestinal microinflammation induced by acute stress in the jejunum of patients with IBS-D.

Methods: We designed a randomised, double-blinded, placebo-controlled pilot study in patients with IBS-D. In a first step, 28 healthy subjects (15 F) were included to determine control baseline small bowel permeability (SBP) using the lactulose/mannitol test for 2 h. In a second step, we evaluated SBP in 104 patients with IBS-D (70 F). Out of these, thirty three IBS-D showed values of baseline SBP over percentile 75 of healthy (188,4 mg/L of mannitol). Twenty-two were randomised to receive 7 days of oral (b.i.d.) XPPTX (n=10, 6 F) or placebo (cornstrach)(n=12, 8 F), followed by a determination of SBP after 15 min of acute experimental stress (cold pressor test) and a jejunal biopsy using Watson's capsule. Biopsies were processed for histology (H&E staining), mast cell (CD117), intraepithelial lymphocytes (CD3) & eosinophil counts (H&E), mucus evaluation (PAS-Alcian blue), and transmission electron microscopy (TEM). In addition, background stress levels (tests of Holmes-Rahe & Cohen), depression (Beck's inventory) and severity of IBS (IBS-SSS) were also evaluated.

Results: There were no differences in baseline demographics, background stress, psychological characteristics and IBS-SSS between XPPTX and placebo groups. We did not identify any difference in mucus evaluation, mast cell, lymphocytes and eosinophil counts between groups. Compared to baseline, both placebo (26.8±39.6%) and XPPTX (31.1±21.2%) reduced significantly SBP (P< 0.0001) after cold stress but without differences between them (P=0.79). Response to XPPTX was much more consistent and homogeneous than placebo. Mean (Placebo=23.1±3.3 nm; XPPTX=23.5±1.6 nm) and maximum (Placebo=28.3±5.7 nm; XPPTX=28.4±1.9 nm) intercellular space at the level of apical tight junctions was similar in both groups, though again response to XPPTX was much more consistent and homogeneous than placebo. No correlations were found between permeability and clinical and psychological parameters.

Conclusion: The mucoprotectant XPPTS significantly reduces post-stress intestinal permeability in IBS-D but is not superior to placebo in this small pilot study. Future studies with higher number of patients are needed to determine the efficacy of XPPTX in controlling SBP in IBS-D and its potential clinical benefit.

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P1216 THE EFFECT OF *LACTOBACILLUS PLANTARUM* ON SYMPTOMS AND THE MICROBIOME IN SUBJECTS WITH IRRITABLE BOWEL SYNDROME

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Introduction: Irritable bowel syndrome (IBS) is a complex condition with variable symptomatology involving a broad range of both physiologic and psychological symptoms, such as mucosal integrity and function, gut function, visceral perception and brain-gut dysregulation. Intake of a probiotic bacteria is one alternative to improve IBS.

Aims & Methods: The aim of the study was to investigate if *Lactobacillus plantarum* DSM 9843 (LP) could improve symptoms and affect the faecal microbiome in subjects with IBS.

After a 2-week run-in period, subjects with IBS according to Rome III criteria, were randomized to receive either LP or placebo capsules for 4 weeks. A total of 197 male and female patients with IBS were included at two sites in the Netherlands (PreCare Trial & Recruitment). An irritable bowel severity scoring system (IBS-SSS) form was filled in at each visit (Day -14, Day 1 and Day 28). Abdominal pain, frequency of bowel movements and stool consistency were reported daily. Faecal samples were collected before and after the intervention and the microbiome analysed with 16S rRNA gene profiling (NIZO).

Results: There was no significant difference in abdominal pain, IBS-SSS, bloating, frequency of bowel movements and stool form when comparing subjects that consumed LP or a placebo product. However, a subgroup analysis on the subjects that had IBS with predominant constipation (IBS-C, 25% of the subjects), showed that IBS-SSS was reduced significantly in the LP group compared with the placebo group (Table 1). The IBS-SSS form is validated and includes five questions: abdominal pain (severity, frequency), abdominal distension, satisfaction with bowel habits and how IBS affects and interferes with the life in general (Francis *et al.* 1997). The maximum score is 500 (100 scores/question) and a reduction with 50 scores indicates an improvement.

	LP (n=20) Mean (SE)	Placebo (n=27) Mean (SE)	P-value between treatments, t-test
Before treatment	249 (10)	260 (8)	
After 4 weeks treatment	183 (19)	251 (17)	
Change	- 66 (20)	- 9 (16)	0.027

[Table 1. Change in IBS-SSS after intake of Lactobacillus plantarum DSM 9843 or placebo. Subgroup with IBS-C.]

Analysis of the faecal microbiome showed that the family Lactobacillaceae was more abundant in the group that consumed LP than in the placebo group, reflecting the presence of the given *Lactobacillus plantarum* strain in the faeces. Furthermore, the genus *Oscillospira* was significantly higher in the LP group compared to the placebo group. A lower abundance of this genus has earlier been found in infants suffering from Crohn's disease (Kaakoush *et al.* 2012) and in patients with flatulence (Manichanh *et al.* 2014).

Conclusion: A beneficial statistically significant effect of treatment with LP as compared with placebo on symptoms associated with IBS could not be demonstrated. Subgroup analysis of subjects with IBS-C showed a beneficial effect on the total IBS-SSS score after consumption of LP. Minor changes in the microbiome were found except an increase of the given bacteria and of *Oscillospira* after intake of LP. Further studies are suggested to investigate the mechanism behind the beneficial effect on IBS symptoms shown after consumption of LP in subjects with IBS-C.

References: Francis CY, Morris J, Whorwell PJ, The irritable bowel severity scoring system: a simple method of monitoring irritable bowel syndrome and its progress. Alimentary Pharmacology& Therapeutics 1997;11:395-402. Kaakoush NO, Day AS, Huinao KD, Leach ST, Lemberg DA, Dowd SE, Mitchell HM. Microbial dysbiosis in pediatric patients with Crohn's disease. J Clin Microbiol. 2012 Oct;50(10):3258-66. Manichanh C, Eck A, Varela E, Roca J, Clemente JC, González A, Knights D, Knight R, Estrella S, Hernandez C, Guyonnet D, Accarino A, Santos J, Malagelada JR, Guarner F, Azpiroz F. Anal gas evacuation and colonic microbiota in patients with flatulence: effect of diet. Gut. 2014 Mar;63(3):401-8.

Disclosure: G Önning, N Larsson and A-K Robertson are affiliated to Probi AB, that owns the bacterial strain investigated in the study.

P1217 TRADITIONAL CHINESE MEDICINE WITH SUBTYPE MODIFICATION FOR THE TREATMENT OF CONSTIPATION PREDOMINANT IRRITABLE BOWEL SYNDROME IN A RANDOMISED, DOUBLE BLIND, PLACEBO-CONTROLLED STUDY

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Introduction: Irritable bowel syndrome (IBS) is a prevalent condition which negatively impacts quality of life and places a large burden on healthcare globally. Current pharmacological treatment has variable efficacy and often has unsatisfactory results. Traditional Chinese Medicine (TCM) is widely accepted in Asia and many seek it as alternative therapy. To date, attempts to characterize TCM efficacy universally suffer from poor scientific

method or they do not faithfully replicate authentic TCM best practice. We sought to address these deficiencies combining the best of TCM practice with western medicine in this study.

Aims & Methods: This was a randomised, double blind, placebo controlled parallel group study carried out in a single centre in Singapore. Patients who fulfilled ROME III criteria for IBS-Constipation predominant subtype (IBS-C), and the TCM syndrome of Liver Qi stagnation (LCS) were recruited. To reflect typical TCM practice, LCS diagnosis can be further "modified" into 3 subtypes based on a standardised TCM diagnostic criteria. TCM treatment consist of a standardized core herbal formula specific for treatment of LCS or a modified formula based on the LCS subtype. After a 2-week run in, subjects were randomised (1:1) to receive the prescribed TCM treatment or placebo with 10% of active core ingredients for 8-weeks. The primary endpoint was change of IBS-Symptom Severity Score (IBS-SSS) at end of treatment compared to baseline. Secondary outcomes include change in individual gastrointestinal symptoms, Bristol stool scale, bowel movement, psychological scale, quality of life and adverse events. Analysis was performed based on Intention to treat using 2-sided T test and chi-squared as appropriate. Ethics Board review was obtained. The trial was registered on Singapore and international (ClinicalTrials.gov) trial registries prior to recruitment.

Results: 59 patients were screened, 40 were randomized and 39 patients with valid data were analysed. Patient characteristics and primary outcome is shown in table 1. Patient characteristics were similar in both arms. There was a non-significant benefit in IBS-SSS in the TCM group vs the control group with adjusted difference by baseline of -28.0 (95% CI = -84.9, 28.95; p=0.325). TCM was well tolerated, there was no serious adverse events in both arms, only 2 patients from the placebo arm withdrew from the study. One due to body ache which resolved after cessation of treatment, another due to hair loss. There was no significant difference in the other secondary outcomes.

	TCM	Control	p-value
Female (%)	90	74	0.19
Mean Age (years)	43.3	42.7	0.90
Race			
Chinese (%)	95	84	0.24

	Baseline	End of Treatment Response	Change	Baseline	End of Treatment Response	Change	
IBS-SSS mean (SD)	256.2 (101.0)	205.4 (103.8)	-50.8 (49.83)	227.3 (102.6)	215.6 (118.9)	-11.7 (106.99)	0.32

[Patient Characteristics and Primary Outcome]

Conclusion: A TCM treatment regime which allowed for subtype modification reflecting typical TCM practice showed a non-significant benefit in patients with constipation predominant irritable bowel syndrome in a randomised, double blind, placebo-controlled study design. The treatment was well tolerated with minimal side effects. Larger RCTs should be conducted to further validate this.

Disclosure: Nothing to disclose

P1218 THERAPY OF IRRITABLE BOWEL SYNDROME AND OTHER FUNCTIONAL GASTROINTESTINAL DISEASES WITH STW 5 IN A SELF MEDICATION SETTING

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Introduction: Surveys on everyday life therapeutic use and patient satisfaction are important tools to gain real life evidence and understanding of patients' needs for medicinal products [1].
The herbal combination preparation STW 5 has been available in the German market for more than 58 years [2]. Its scientific evidence for treatment of functional gastrointestinal diseases like irritable bowel syndrome and functional dyspepsia includes a multitude of clinical, pharmacological and toxicological studies [3].

Aims & Methods: Up to now, few data on self-assessed usage behavior, perception of effectiveness and tolerability for STW 5 are available. Therefore, pharmacy customers with product desire or recommendation for STW 5 were asked whether they would participate in a survey on the product. Patients received a questionnaire regarding demographic data, gastrointestinal complaints, effectiveness, tolerability and satisfaction with the product. They were asked to answer it during the next few days and send it back to a contract research institute within a week.

Results: Data from 843 patients were evaluated. 29.4 % were male and 70.6 % female. The majority was in the 30-49 age range. In 384 patients, complaints were related to the upper, in 139 to the lower abdomen, in 311 patients to both regions. In 7.3 % of the 384 patients a functional dyspepsia had been diagnosed, in 16.9 % of the 139 patients an irritable bowel syndrome. Up to 64% of the patients specified a good or very good improvement of the respectively predominant symptom with treatment of STW 5. Symptom relief was perceived as fast and covered the comprehensive spectrum of complaints. Tolerability was rated good to very good in 97.4 % of all patients and did not differ between patient groups. Correspondingly 93.2 % of the users were "very satisfied" or "satisfied". 91 % of the customers would recommend STW 5 to others for treating their complaints.

Conclusion: Overall, it can be concluded that this patient survey gives a reliable picture of the behavior of users of STW 5 in a self medication setting, with high satisfaction values as well in irritable stomach as in irritable bowel syndrome and single symptoms. The favorable tolerability ratings confirm the ratings from the clinical studies on the product.

References: 1. Nieber K. and Lehmacher W. Med. Wochenschr. f. Pharmazeuten 2009 (8): 301-306 2. Storr M. et al. Pharmakon 2016, 4(4):356-364 3. Abdel-Aziz H. et al., Planta Med. 2017, 83(14/15):1130-1140

Disclosure: BV, SS and OK are employees at Steigerwald Arzneimittelwerk GmbH. JM is intern at Steigerwald Arzneimittelwerk GmbH.

P1219 NETWORK META-ANALYSIS OF THE EFFICACY AND SAFETY OF PHARMACOLOGICAL THERAPIES FOR IBS-D AND IBS-M

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Introduction: Over half of patients with irritable bowel syndrome have either diarrhoea (IBS-D) or a mixed stool pattern (IBS-M). The relative ef-

ficacy of pharmacological therapies in IBS-D and IBS-M is unclear in the absence of head-to-head trials. We conducted a network meta-analysis to resolve this uncertainty.

Aims & Methods: We searched MEDLINE, EMBASE, EMBASE Classic, the Cochrane central register of controlled trials, and clinicaltrials.gov through January 2019 to identify randomised controlled trials (RCTs) assessing the efficacy of pharmacological therapies in adults with IBS-D or IBS-M. Trials included in the analysis reported a dichotomous assessment of overall response to therapy at 8 to 12 weeks of follow-up, and data were pooled using a random effects model. Efficacy and safety of all pharmacological therapies were reported as a pooled relative risk of remaining symptomatic with 95% confidence intervals (CIs) to summarise the effect of each comparison tested. Treatments were ranked according to their P-score.

Results: We identified 21 eligible RCTs (7 alosetron, 5 ramosetron, 2 cilansetron, 1 ondansetron, 2 rifaximin, 4 eluxadoline), containing 10654 patients. With the exception of ondansetron, all drugs were superior to placebo, according to the Food and Drug Administration (FDA)-recommended endpoint of improvement in both abdominal pain and stool consistency for trials in IBS. Alosetron 1mg twice-daily ranked first for efficacy, based on this composite endpoint (RR = 0.69; 95% CI 0.60 to 0.80, P-score = 0.95), as well as for effect on global symptoms of IBS (RR = 0.62; 95% CI 0.52 to 0.75, P-score = 0.95). With respect to effect on stool consistency all drugs, including ondansetron 12mg once-daily, were superior to placebo, but alosetron 1mg twice-daily was again ranked first (RR = 0.70; 95% CI 0.60 to 0.81, P-score = 0.85). Ramosetron 2.5mcg once-daily was ranked first for effect on abdominal pain (RR = 0.74; 95% CI 0.65 to 0.85, P-score = 0.89). Total numbers of adverse events were significantly greater with alosetron 1mg twice-daily, compared with placebo. Rifaximin 550mg three times daily ranked first for safety, with ondansetron 12mg od ranked second (P-scores 0.74 and 0.68, respectively). Constipation was significantly more common with all drugs, except rifaximin 550mg three times daily and ondansetron 12mg once-daily.

Conclusion: In a network meta-analysis of randomised controlled trials of pharmacological therapies for IBS-D and IBS-M, we found all drugs to be superior to placebo, but the $5HT_3$-receptor antagonists alosetron and ramosetron appeared to be the most effective. Unfortunately, these drugs are unavailable in the UK and Europe. Ondansetron, which is available although unlicensed, ranked well across all analyses, but was only superior to placebo for its effect on stool consistency, based on the inclusion of a single small trial. Overall, improving access to $5HT_3$ receptor antagonists may be helpful for the management of IBS-D and IBS-M, and the result of further trials of ondansetron will be informative.

Disclosure: MC has received research funding from Allergan. DLE has acted as a consultant for Prometheus Laboratories. EMQ has acted as a consultant to Almirall, Synergy and Salix. PM has received honoraria from Allergan and Salix, and research funding from Allergan. LAH has acted as a consultant for, and received research funding from Takeda, USA, and has acted as a consultant for Pfizer, USA. ACF has acted as a consultant for and received researching funding from Almirall

Paediatric: Lower GI II

09:00-17:00 / Poster Exhibition - Hall 7

P1220 COST-EFFECTIVENESS OF THE USE OF HLA-DQA1-HLA-DRB1 POLYMORPHISM TO IDENTIFY PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE AT RISK FOR AZATHIOPRINE-INDUCED ACUTE PANCREATITIS

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Introduction: Thiopurines may be effective for maintaining remission in pediatric inflammatory bowel disease (IBD), but due to their low safety profile, the most recent evidence-based guidelines recommend they should be reserved as second-line therapy after 5-ASA has failed (1). One idiosyncratic adverse effect of thiopurines is acute pancreatitis and affects 2-7% of patients treated with azathioprine (AZA) (2,4). Its development

is unpredictable and usually leads to drug withdrawal. An association within the HLA-DQA1*02:01-HLA-DRB1*07:01 haplotype has been previously identified (3). The risk of pancreatitis during AZA-therapy was highly predictable and genotype-dependent: 0.5% for wild-type (A/A), 4.3% for heterozygous (A/C), and 14.6% for homozygous patients (C/C). Some authors even propose a new AZA treatment algorithm that could help to select those patients with higher risk of pancreatitis (4).

Aims & Methods: The aim of our study was to conduct a cost-effectiveness analysis of the use of HLA-DQA1-HLA-DRB1 polymorphism to identify pediatric patients with inflammatory bowel disease at risk for azathioprine-induced acute pancreatitis (A-IAP).

We perfromed a theoretical analysis of costs and benefits resulting from routinely studying the HLA-DQA1*02:01-HLA-DRB1*07:01 haplotype in those pediatric patients with IBD that are candidates for the use of azathioprine as maintenance therapy, in order to avoid using this treatment in those at risk of A-IAP. We calculated the number needed to screen (NNS), defined as the number of patients that need to be screened to prevent one adverse event, based on the available data. This was computed as the inverse of the Absolute Risk Reduction (ARR), defined as the difference in percentage outcomes between the related and un-related haplotype.

The costs of the HLA typing were based on the INNO-LiPA® test (FUJIREBIO, Spain).

The costs of acute pancreatitis cases were based on the diagnosis-related group (DRG) weights applied by the Spanish Ministry of Health. These relative weights represent the expected cost of a particular kind of patient compared to the average cost of all the acute hospitalized patients.

Results: The cost of the screening for the HLA-DQA1*02:01-HLA-DRB1*07:01 haplotype was approximately 90€ per patient. Considering the previously reported incidence of A-IAP of 0.5% in the A/A, 4.3% in the A/C and 14.6% in the C/C genotype; NNS was 5.4. NNS was rounded up to 6 patients, so the expected cost for avoiding one case of A-IAP was 540€.

The A-IAP diagnose in the DRG 32nd version (DRG 282.3) has a mean weight of 1.15. The total cost of a case of A-IAP was about 20.109 € per patient. This leads to saving up to 19.569€ for every 6 patients screened before starting the AZA treatment.

Conclusion: Based on our results, routinely performing HLA-DQA1-HLA-DRB genotyping prior to initiation of AZA could be cost-effective in order to avoid A-IAP. Furthermore, the caregivers' absenteeism costs derived from a child hospitalization were not included in this analysis and would reinforce our conclusions. However, the costs derived from the therapeutic alternative that would be considered for those who could not receive AZA should be considered. But, most importantly, and beyond the economic rationale, preventing this potentially severe adverse effect could improve the clinical outcomes of our patients and allow an individualized management. This patient-tailored approach should be the goal of clinicians, not only to optimize the use of Public Health Funds, but also to maximize our patients' quality of life.

References: 1. Turner D, Ruemmele FM, Orlanski-Meyer E, Griffiths AM, Martin de Carpi J, Bronsky J, et al. Management of paediatric ulcerative colitis, Part 1: ambulatory care- an evidence-based guideline from ECCO and ESPGHAN. 2018; 2. Ledder OD, Lemberg DA, Ooi CY, Day AS. Are thiopurines always contraindicated after thiopurine-induced pancreatitis in inflammatory bowel disease? J Pediatr Gastroenterol Nutr. 2013;57(5):583-6. 3. Heap GA, Weedon MN, Bewshea CM, Singh A, Chen M, Satchwell JB, et al. HLA-DQA1-HLA-DRB1 variants confer susceptibility to pancreatitis induced by thiopurine immunosuppressants. Nat Genet. 2014;46(10):1131-4. 4. Wilson A, Jansen LE, Rose R V., Gregor JC, Ponich T, Chande N, et al. HLA-DQA1-HLA-DRB1 polymorphism is a major predictor of azathioprine-induced pancreatitis in patients with inflammatory bowel disease. Aliment Pharmacol Ther. 2018;47(5):615-20. 5. Dan Mayer. Essential Evidence-Based Medicine, Volumen 2. Cambridge University Press, 2004: 272-274.

Disclosure: Nothing to disclose

P1221 SAFETY AND EFFECTIVENESS OF GRANULOCYTE AND MONOCYTE ADSORPTIVE APHERESIS IN PAEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A MULTICENTRE COHORT STUDY

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Introduction: The usefulness of granulocyte and monocyte adsorptive apheresis (GMA) in paediatric patients with inflammatory bowel disease (IBD) has not been evaluated in detail. We investigated the safety and effectiveness of GMA in paediatric patients with IBD who participated in the "Post-marketing surveillance study on the safety and response of GMA treatment in patients with Crohn's disease or ulcerative colitis with at least one special situation who received Adacolumn (PARTICULAR)".

Aims & Methods: The aim of this study is to investigate the safety and effectiveness of GMA in paediatric patients with IBD who participated in the PARTICULAR study. This retrospective, multicentre cohort study included patients with ulcerative colitis (UC) or Crohn's disease (CD) who had at least one special situation feature and who had received GMA therapy in medical institutions of Japan between November 2013 and March 2017. Patients with at least one special situation, including elderly patients, patients with anaemia and patients on multiple immunosuppressants were enrolled. Patients >18 years were excluded from this study. GMA was performed using Adacolumn (JIMRO, Takasaki, Japan). Each patients received up to a maximum of 11 sessions. All adverse events (AEs) were recorded during the observation time interval. In addition, feasibility problems (FPs) during the operation of the GMA column were recorded. Any AE for which the causality of GMA could not be ruled out was classified as adverse device effect (ADE). The safety of GMA was assessed in all patients. The effectiveness of GMA was assessed in patients with UC with a partial Mayo (pMayo) score of ≥3. Remission was defined as a pMayo score of ≤2, while response was defined as a decrease in the pMayo score by ≥2 points and by ≥30% decrease relative to that at baseline plus all 3 sub-scores ≤1. Patients receiving concomitant treatment with infliximab, adalimumab or calcineurin inhibitors were excluded from the effectiveness assessment.

Results: A total of 53 paediatric patients (40 UC, 13 CD; 30.2% female) from 27 institutions, with a median age of 16.0 years [range 6-12 (9 patients), 13-15 (14 patients) and 16-18 (30 patients)]; median body weight 49.6 Kg and median duration of disease 0.7 years. The incidence of AEs, ADEs and FPs were 18.9%, 5.7% and 20.8%, respectively. The ADEs included abdominal discomfort in 2 patients (3.8%) and one patient each with fever, nausea/vomiting and headache (1.9% each). The FPs included blood access failure in 10 patients (18.9%), venous pressure elevation in 4 patients (7.5%), clot formation in the apheresis lines in 2 patients (3.8%) and venous access difficulty in 1 patient (1.9%). GMA therapy was discontinued in 17 patients (32.1%) ahead of their planned treatment schedule. Among these patients, the GMA therapy was discontinued for the following reasons: (1) decision by the physician (n = 12), (2) withdrawal due to AE (n = 4) and (3) withdrawal by own will (n = 1). No patients discontinued GMA therapy due to ADE and FP. The effectiveness of GMA was assessed in 29 patients with UC. The remission and response rate of the paediatric patients with UC were 55.2% and 65.5%, respectively.

Conclusion: There were AEs and FPs in approximately 20% of paediatric patients with IBD who were treated with GMA. However, none of these discontinued GMA treatment owing to ADE or FP. Remission and response were achieved by GMA in 55% and 66% of paediatric patients with UC, respectively. These data suggest that GMA is a well-tolerated treatment alternative for paediatric patients with IBD.

Disclosure: Hiroki Tanaka has received lecture fees from JIMRO Co. Ltd., AbbVie GK, EA Pharma Co. Ltd., Mochida Pharmaceutical Co. Ltd., Kyorin Pharmaceutical Co. Ltd. and Mitsubishi Tanabe Pharma Corporation. Katsuhiro Arai has received lecture fees from Takeda Pharmaceutical Co. Ltd, AbbVie GK, Nippon Kayaku Co. Ltd, EA Pharma Co. Ltd and Kyorin Pharmaceutical Co. Ltd.; and has received research grants from Nippon Kayaku Co. Ltd. Naoki Yoshimuara has received lecture fees from JIMRO Co. Ltd., AbbVie GK, Mochida Pharmaceutical Co. Ltd. and Mitsubishi Tanabe Pharma Corporation. Satoshi Tanida has received research grant from EA Pharma Co. Ltd. Eiji Hosoi is employee of JIMRO Co. Ltd. All other authors have nothing to disclose.

P1222 EXCLUSIVE ENTERAL NUTRITION FOR INDUCTION OF REMISSION IN PAEDIATRIC CROHN'S DISEASE: COMPARISON BETWEEN A DISEASE-SPECIFIC FORMULA AND STANDARD POLYMERIC FORMULAS

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Introduction: Exclusive enteral nutrition (EEN) is effective and currently recommended as the first line of treatment to induce remission in children and adolescents with acute active Crohn's disease (CD). Standard enteral nutrition (polymeric, normocaloric with moderate fat content) can be used for primary and supportive nutritional therapy in active CD.

Aims & Methods: The main aim was to demonstrate the non-inferiority of an age-appropriate normocaloric polymeric formula (F0) versus an inflammatory bowel disease (IBD) specific normocaloric polymeric formula (F1) to induce remission in paediatric patients newly diagnosed of CD. Secondary objectives were to evaluate the nutritional status and analyze the percentage of withdrawal before 8 weeks, their causes and the need of other treatments. This observational, descriptive and retrospective study included patients under 18 diagnosed with CD from September 2008 to December 2018 in the paediatric IBD Unit of a tertiary care hospital in whom EEN was indicated to induce remission at diagnosis. Patients were divided into two groups (EEN with F0 or EEN with F1), comparing clinical, analytical and anthropometric data at diagnosis, and after 2 and 8 weeks of EEN. Clinical remission was defined as a Paediatric Crohn Disease Activity Index (PCDAI) ≤10.

Results: We included 29 patients, 9 (31%) women and 20 (69%) men with a mean age of 9.9 years (2.1-17.5) at diagnosis. Eleven patients (37.9%) received F0 and 18 (62.1%) F1. The mean duration of EEN was 56.3 days (18-78). One patient (3.5%) refused the treatment and required tube feeding and 6 (20.7%) dropped out from EEN before 8 weeks (33.3% F0 and 66.7% F1). Among 6 withdrawals, 5 (83.3%) developed a fistulizing perianal disease (40% F0 and 60% F1) and required biological therapy, and 1 (16.7%) did not respond to EEN with F1, requering corticosteroids. The PCDAI mean value was 36.4 (20-52.5) at diagnosis in the group with F0 and 31.47 (12.5-57.5) with F1. After 2 weeks, 62.5% of patients with F0 and 56.3% with F1 reached clinical remission. After 8 weeks, 90.9% of patients with F0 and 77.8% with F1 maintained clinical remission. There were no statistically significant differences between the 2 groups at both endpoints. The C-reactive protein (CRP) mean value at diagnosis, and after 2 and 8 weeks was 7.7 mg/dl (0.2-27.3), 1.7 y 1.1 mg/dl respectively in the F0 group, and 5.6 mg/dl (0.2-12.8), 1.2 y 0.9 mg/dl in the F1 group, without statistically significant differences (p=0.7; 0.93; 0.34 respectively). After 8 weeks, median CRP decreased significantly in F0 group (p=0.01) and F1 group (p< 0.0005). The mean erythrocyte sedimentation rate (ESR) at diagnosis, at 2 and 8 weeks was 39.1 mm (11-69), 26 and 17 mm respectively in the F0 group, and 42.4 mm (11-78), 23.2 and 14.6 mm in the F1 group, without statistically significant differences (p=0.65; 0.64; 0.43). Median ESR decreased significantly at week 2 with F1 (p=0.001) but not with F0 (p=0.17). However, there was a significative reduction in both of them at week 8 (p< 0.05). Weight and body mass index (BMI) improved with F0 and F1, but only the F1 group reached statistical significance (p=0.007 for weight and p=0.003 for BMI), and not the F0 group (p=0.24 and 0.37)

Conclusion: The use of F0 was not inferior to F1, without any statistically significant differences in the percentage of patients in clinical remission after 2 and 8 weeks with EEN, nor in the decrease of CRP and ESR after 8 weeks. Faster ESR reduction was found in patients treated with F1 and only these ones presented a statistically significant improvement in their nutritional status.

Disclosure: Nothing to disclose

P1223 LONGTERM CLINICAL OUTCOME AFTER THIOPURINE DISCONTINUATION IN ELDERLY IBD PATIENTS

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Introduction: Thiopurines - although still used frequently in treatment of inflammatory bowel diseases (IBD) - carry a significant malignancy risk, particularly with prolonged use and in patients over the age of 60. Mainly the risk of lymphoma, but also non-melanoma skin cancer and nodular regenerative hyperplasia of the liver are well reported. These concerns question the continuation of thiopurines in IBD patients above 60. Stopping therapy however may trigger relapses and therefore needs to be balanced against the safety risk. We assessed the longterm outcome of elderly IBD patients after discontinuation of thiopurines (TP) while in clinical remission with emphasis on relapse rates and the management thereof in these patients.
Aims & Methods: The electronic medical records from all IBD patients above the age of 60 followed at our referral center who ever received treatment with TP were reviewed. Patients who stopped TP after 60 years of age while in clinical (symptom control) and endoscopic remission (mucosal healing) were the target population. Longterm outcomes of interest included duration of thiopurine-free clinical remission, time to clinical relapse and therapies given in case of relapse. The risk for malignancies was also recorded.
Results: From the 674 identified patients who ever received TP therapy, 532 patients stopped therapy < 60 years of age (regardless of reason for withdrawal). A total of 142 patients >60 years of age on TP were identified. Of those, 91 patients (55 Crohn's disease (CD) and 36 ulcerative colitis (UC)), stopped TP at >60 years while in clinical and/or endoscopic remission and 51 stopped while not in remission. After a median follow up of 31.4 months after TP discontinuation, 63 (69.2%) patients remained in clinical and endoscopic remission and 28 (30.8%) relapsed. Remission rates and median time to relapse were similar between CD patients (40/55 or 72%; median 22 months) and UC patients (23/36 or 64%; median 20 months). However, the median duration of TP therapy in the patients with relapse was significantly shorter than in the patients who remained in remission (median duration of TP 45 months versus 102.5 months respectively; p=0.005). Of the patients who relapsed, 17 were initiated on a biological (61%) and 7 patients received a short course of steroids (25%). However, surgery was eventually needed in 36% of patients (10/28), including total colectomy with ileostomy in 2 UC patients. In the total group of 142 IBD patients on TP at>60 years, 26 malignancies (18%) developed: non-melanoma skin cancers (8), colon adenocarcinoma (5), hematologic malignancies (3), lung (2), breast (2), brain (1), endometrium (1), prostate (1), glottis (1), bladder (1) and melanoma (1). For 7 patients, the development of a malignancy was the direct reason for stopping TP.
Conclusion: In this single center retrospective cohort of elderly IBD patients in remission and on TP, discontinuation of TP resulted in sustained clinical remission in 69% of patients after a median of 20 months. Patients who flared after discontinuation of TP were mostly rescued with biological therapies although more than one third of patients necessitated surgery. A significant proportion of patients developed malignancies under TP but also after TP discontinuation, indicating that these patients necessitate a continued close follow up. Decision making in this vulnerable subgroup of patients remains difficult with a careful balance between adverse events when continuing TP and risk for major surgery when stopping TP.
Disclosure: Nothing to disclose

P1224 TOXIN PRODUCING *KLEBSIELLA OXYTOCA* IN INFANTS: COMMENSAL OR PATHOBIONT?

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Introduction: Klebsiella (K.) oxytoca is a gastrointestinal pathobiont that has the potential to produce the cytotoxin tilivalline, which causes antibiotic-associated haemorrhagic colitis. *K. oxytoca* colonizes healthy adults in up to 9%, however, there is no data on the natural occurrence and its potential to produce tilivalline in healthy children.
Aims & Methods: We investigated *K. oxytoca* colonization and its ability for toxin production in healthy infants.We collected stool samples of healthy infants at 3 different time points (week 0, 4 and 8). *K. oxytoca* colonization was determined using conventional stool culture and PCR analysis. Toxicity of isolated *K. oxytoca* strains was analysed by cell culture MTT toxin assay and *K. oxytoca* toxin PCR.
Results: Of 61 infants (25 male, 36 female, age 1 - 28 weeks) 30 (49%) tested positive for *K. oxytoca* in conventional stool culture and 44 (72%) tested positive in *K. oxytoca* PCR. Colonization increased with time: 21% / 62% (culture / PCR) at week 0, 26% / 67% at week 4, 31% / 69% at week 8. One patient tested negative for PCR but positive for conventional stool culture. 48% of *K. oxytoca* positive infants were exclusively breastfed at the time of study inclusion, compared to 82% of *K. oxytoca* negative patients (p=0.02, Fisher's exact). There were no statistical differences between positive and negative infants in regard to age, weight or sex, C-section, use of probiotics, previous antibiotic therapy or previous diseases. The cell culture MTT toxin assay confirmed toxicity of culture positive *K. oxytoca* isolates in 49%. *K. oxytoca* toxin PCR was positive in 75% of PCR isolates. Conformity of cell culture toxin assay and toxin PCR was noted in only 71% of the analyses, whereas the negative predictive value of the toxin PCR was 100%.
Conclusion: In contrast to adults, more than 70% of healthy infants were colonized with *K. oxytoca*, the majority of which possessed the ability to produce the cytotoxin tilivalline. Exclusive breastfeeding might decrease the probability of *K. oxytoca* colonization. PCR shows a higher detection rate of *K. oxytoca* compared to conventional stool culture but lacks information about the clinical significance (e.g. relative abundance) of *K. oxytoca* colonization. *K. oxytoca* toxin PCR alone can not be used to confirm actual toxin production, but with a negative predictive value of 100% can be used to rule out the potential of toxin production of the isolated strain. Pediatricians have to be aware of the high prevalence of toxin producing *K. oxytoca* in infants, especially when confronted with haemorrhagic colitis during antibiotic therapy in this age group.
Disclosure: Nothing to disclose

P1225 SHOULD HYPNOTHERAPY BE THE FIRST LINE TREATMENT OPTION FOR SCHOOL CHILDREN AND ADOLOESCENTS WITH IRRITABLE BOWEL SYNDROME?

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Introduction: Irritable Bowel Syndrome (IBS) symptoms in school children and adolescents are relatively common, often causing considerable embarrassment, social withdrawal, disruption to education and psychological distress. Pharmacological options in this group are limited due to safety concerns concerning antidepressants, making behavioural therapies such as gut-focused hypnotherapy an attractive treatment option.

Aims & Methods: Here, we evaluated outcomes from gut-focused hypnotherapy in patients with IBS ≤ 18 years of age. Consecutive young patients (≤18 years of age) with severe IBS symptoms referred to our tertiary neuro-gastroenterology unit received 12 sessions of gut-focused hypnotherapy at weekly intervals using the Manchester Protocol. All patients completed the Tellgen Absorption Scale before treatment and all completed the following measures before and after hypnotherapy; IBS symptom severity score (IBS-SSS), Hospital Anxiety and Depression scale (HADS), Non Colonic Symptom score and quality-of-life (QoL) score. Interference with education and the impact of hypnotherapy was also recorded. The primary outcome measure was response to hypnotherapy defined by a 50 point reduction in IBS-SSS. Data, expressed as mean ± standard error, were compared statistically before and after treatment using paired t-tests.

Results: 26 young patients fulfilling Rome III diagnostic criteria for IBS (median age 16 (range 8-18) years, *n*=17 (65%) female, mean duration of IBS 5.3 ± 0.9 years, IBS-D *n*=11, IBS-C *n*=6 and IBS-mixed *n*=9), completed the hypnotherapy programme. Mean baseline IBS-SSS was 321.5 ± 16.0. After hypnotherapy, *n*=23/26 (88%) responded, with an overall mean reduction in IBS-SSS of -160.9 ± 15.4 (*P*< 0.0001), and *n*=19/26 (73%) achieved the FDA recommended outcome of ≥30% reduction in abdominal pain scores. Hypnotherapy also improved; mean non-colonic symptom score by 102.1 ± 15.0 (*P*< 0.0001), mean HADS-anxiety by -3.0 ± 0.8 (*P*=0.0007), mean HADS-depression by -2.1± 0.6 (*P*=0.002), and improved mean QoL score by +89.7 ± 13.1 (*P*< 0.0001).

Conclusion: These data, which form one of the largest reported series of gut-focused hypnotherapy in children and adolescents with severe IBS, suggest that this treatment is even more effective in this group of patients than in adults. Hypnotherapy in severe childhood IBS patients may therefore have a role in preventing further suffering in adult life, reducing healthcare utilisation and related costs with wider socio-economic benefits. Furthermore, it allows many of them to return to full time education. These results, taken with previous clinical trial data, raise the possibility that early intervention with hypnotherapy for childhood IBS might reduce the subsequent burden of this problem in adults.

Disclosure: Nothing to disclose

Oesophageal, Gastric and Duodenal Disorders II

09:00-17:00 / Poster Exhibition - Hall 7

P1226 IL-7 RECEPTOR INFLUENCES ANTI-TNF RESPONSIVENESS AND T CELL GUT HOMING IN INFLAMMATORY BOWEL DISEASE

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Introduction: It remains unknown what causes inflammatory bowel disease (IBD), including signaling networks perpetuating chronic gastrointestinal inflammation in Crohn's disease (CD) and ulcerative colitis (UC), in humans.

Aims & Methods: According to an analysis of up to 500 patients with IBD and 100 controls, we report that key transcripts of the IL-7 receptor (IL-7R) pathway are accumulated in inflamed colon tissues of severe CD and UC patients not responding to either immunosuppressive/corticosteroid, anti-TNF, or anti-α4β7 therapies.

Results: High expression of both IL7R and IL-7R signaling signature in the colon before treatment is strongly associated with nonresponsiveness to anti-TNF therapy. While in mice IL-7 is known to play a role in systemic inflammation, we found that in humans IL-7 also controlled α4β7 integrin expression and imprinted gut-homing specificity on T cells. IL-7R blockade reduced human T cell homing to the gut and colonic inflammation in vivo in humanized mouse models, and altered effector T cells in colon explants from UC patients grown ex vivo. Our findings show that failure of current treatments for CD and UC is strongly associated with an overexpressed IL-7R signaling pathway. In addition, we observed a significant increase of IL-7 concentration in the serum of UC and CD patients compared to various autoimmune diseases such as multiple sclerosis or autoimmune hepatitis.

Conclusion: Thoses results point to IL-7R as a relevant therapeutic target and potential biomarker to fill an unmet need in clinical IBD detection and treatment.

Disclosure: BV and NP are shareholders of OSE Immunotherapeutics, a company owning IL-7 receptor antagonists.

P1227 AN IMMUNOSUPPRESSIVE PD-L1 POSITIVE TUMOUR MICROENVIRONMENT MARKS OESOPHAGEAL ADENOCARCINOMAS REFRACTORY TO NEO-ADJUVANT CHEMORADIOTHERAPY

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Introduction: Oesophageal adenocarcinoma is an aggressive cancer with a poor overall prognosis. For patients with a locally advanced resectable tumour and no distant metastases neo-adjuvant chemoradiotherapy (nCRT) followed by oesophageal resection is associated with better survival than surgery alone. However, a large proportion of patients still develop disease recurrence. The mechanism of poor response to nCRT is not yet understood. An effective antitumour immune response is critical for a successful tumour elimination. Therefore, an immunosuppressive tumour microenvironment may play an important role in failure of standard therapies.

Aims & Methods: The aim of this study was to characterize tumour microenvironment and immune infiltrate in oesophageal adenocarcinoma patients in relation to pathological treatment response to nCRT.

Methods: Surgical resection specimens were used from 65 patients with oesophageal adenocarcinoma treated with nCRT: 40 responders (Mandard tumour regression grade 2) and 25 non-responders (Mandard tumour regression grade 4 or 5). Tumour sections were stained with pSTAT1, CD3, CD8, FOXP3 and PD-L1 antibodies. Immunostained slides were scanned at high resolution and digital image analysis was performed using Halo software (version 2, Indica Labs, Corrales). Group differences were analysed using the chi-square test or the Mann-Whitney U test.

		Total		Responders		Non-responders		p-value
Patients		65		64		25		
Median age in years (range)		63	(44-82)	64	(44-82)	63	(46-78)	
Gender	Male	51	(79%)	31	(78%)	20	(80%)	0.811^
	Female	14	(21%)	9	(22%)	5	(20%)	
pT stage	pT1	13	(20%)	11	(27%)	2	(8%)	0.012^
	pT2	10	(15%)	9	(23%)	1	(4%)	
	pT3	40	(62%)	20	(50%)	20	(80%)	
	pT4	2	(3%)	0	(0%)	2	(8%)	
pN stage	pN0	38	(58%)	27	(68%)	11	(44%)	0.203^
	pN+	27	(42%)	13	(32%)	14	(56%)	
PDL1 expression*	Positive	18	(28%)	6	(15%)	12	(48%)	0.006^
	Negative	42	(65%)	30	(75%)	12	(48%)	
	Unknown	5	(7%)	4	(10%)	1	(4%)	
Mean CD3 density/mm2		1693		1295		2332		0.002º
Mean CD3 density/mm2		654		486		924		0.014º
Mean FOXP3 density/mm2		218		215		224		0.182º

pT stage = pathological T stage; pN stage = pathological N stage (TNM 7th edition)
*Oesophageal tumours were designated as PD-L1 positive if at least 10% of stroma cells demonstrated membranous staining
^chi-square test; ºMann-Whitney U test

[Table 1]

Results: Both responders and non-responders displayed active interferon gamma signaling in the tumour cells as judged by positive pSTAT1 staining, suggesting that tumour antigen presentation on MHC class I and tumour-specific stimulation of the immune system were common in both groups.

Surprisingly, a significantly higher amount of CD3+ (p=0.002) and CD8+ (p=0.014) tumour infiltrating lymphocytes was seen in non-responders as compared to responders. Thus, differences cannot solely be explained by induction of T-cell infiltration in responders compared to non-responders. Also, the amount of FOXP3+ regulatory T-cells was similar in both groups. Significantly more non-responders were found to have PDL-1 expression in the tumour stroma than responders (48% versus 15%, p=0.006).

Conclusion: In tissue samples of oesophageal adenocarcinoma patients treated with neo-adjuvant chemoradiotherapy, the presence of an immunosuppressive tumour microenvironment was associated with absence of treatment response, suggesting that cancer immunotherapy may be a valuable alternative treatment option for this group of patients.

Disclosure: Nothing to disclose

P1228 AUTOANTIBODIES TOWARDS ATP4A AND ATP4B SUBUNITS OF GASTRIC PROTON PUMP H+,K+-ATPASE ARE RELIABLE SEROLOGICAL PRE-ENDOSCOPIC MARKERS OF CORPUS ATROPHIC GASTRITIS

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Introduction: Corpus atrophic gastritis (CAG) is a risk factor for gastric cancer and carcinoids. Histology is the gold standard for diagnosis, non-invasive serological tests include gastrin, pepsinogens and parietal cells autoantibodies (PCA)(1,2). Autoantibodies targeting the H+/K+-ATPase are considered diagnostic markers of autoimmune atrophic gastritis, whose diagnostic utility remains to be defined(3). A high diagnostic performance of a luminescent immunoprecipitation system (LIPS) assay detecting autoantibodies to H+/K+-ATPase alpha (ATP4A) or beta (ATP4B) subunits in patients with known diagnosis of CAG has been shown(4).

Aims & Methods: To validate the diagnostic performance of ATP4A and ATP4B LIPS assays as pre-endoscopic diagnostic tools for detecting CAG in patients at clinical suspicion for this condition as compared to histology of gastric biopsies as reference test.

Prospective study on 211 consecutive patients (age 65, range 18-90 years, female 61.6%) with clinical suspicion of CAG collected between May 2017-April 2018. Inclusion criteria were: anemia (iron or cobalamin deficiency), autoimmune diseases, family history for CAG, history of long-standing non-investigated dyspepsia, chronic proton pump inhibitors. Exclusion criteria were: age< 18 years, previous diagnosis of CAG. Included patients underwent gastroscopy with standard biopsies for histopathology (updated Sydney). A serum sample for each patient was preserved at -20°C for the LIPS ATP4A and ATP4B assays, pepsinogen I, and EIA parietal cell antibodies (PCA). Serological results were compared with histology to assess the diagnostic performance of LIPS assays. For ATP4A and ATP4B LIPS assays, recombinant antigens fused to a luciferase reporter were incubated with test sera and immune complexes recovered using protein A-sepharose; after addition of the luciferase substrate light output was measured in a luminometer and converted to arbitrary units using results from a positive serum as reference (5). Pepsinogen I and EIA PCA were assessed by commercial kits.

Results: Histopathology of gastric biopsies proved presence of CAG in 115(54.5%) and absence in 96(45.5%) patients. ATP4A LIPS yielded a 76.5% sensitivity and a 86.4% specificity, ATP4B LIPS a 77.4% sensitivity and a 87.5% specificity. EIA PCA showed a 65.1% sensitivity and a 91.7% specificity, and Pepsinogen I a 71.3% sensitivity and a 92.7% specificity. The areas under the ROC curve of ATP4A (0.822) and ATP4B (0.836) were similar to that of EIA PCA (0.820, p>0.05), while that of pepsinogen I was higher (0.907, p< 0.01). Considering both LIPS assays or EIA PCA and pepsinogen I together, sensitivity increased to 83.5% or 83.3% at cost of specificity, 82.3% or 88.3%, respectively.

Regarding ATP4A LIPS, in false negative patients (23.5%) severe corpus atrophy (p< 0.001), intestinal metaplasia (p=0.001), and age< 65 years were less frequent (p=0.043) than in true positives. Regarding ATP4B LIPS,

in false negative patients (22.6%) severe corpus atrophy (p< 0.001), and intestinal metaplasia (p=0.05) were less frequent than in true positives, but age was similar.

Conclusion: The LIPS assays detecting autoantibodies against ATP4A and ATP4B subunits showed a good pre-endoscopic diagnostic performance in patients with clinical suspicion of CAG, with higher specificity but lower sensitivity than traditional EIA PCA. Sensitivity of LIPS assays and EIA PCA was increased by combining pepsinogen I. These autoantibodies seem promising serological biomarkers of CAG suggesting a close relationship between their expression and advanced oxyntic mucosa damage.

References: 1) Neumann WL, Coss E, Rugge M, Genta RM. Autoimmune atrophic gastritis--pathogenesis, pathology and management. Nat Rev Gastroenterol Hepatol 2013; 10: 529-41 2) Lahner E, Norman GL, Severi C, et al. Reassessment of Intrinsic Factor and Parietal Cell Autoantibodies in Atrophic Gastritis With Respect to Cobalamin Deficiency. Am J Gastroenterol 2009; 104: 2071-9. 3) Rusak e, Chobot A, Krzywicka et al. Anti-parietal cell antibodies – diagnostic significance. Advances in Medical Sciences 2016; 61(2):175-179. 4) Lahner E, Brigatti C, Marzinotto I, Carabotti M, Scalese G, Davidson HW, Wenzlau JM, Bosi E, Piemonti L, Annibale B, Lampasona V. Luminescent Immunoprecipitation System (LIPS) for Detection of Autoantibodies Against ATP4A and ATP4B Subunits of Gastric Proton Pump H+,K+-ATPase in Atrophic Body Gastritis Patients. Clin Transl Gastroenterol 2017; 8: e215. doi: 10.1038/ctg.2016.71. 5) Lahner E, Marzinotto I, Brigatti C, Davidson H, Wenzlau J, Piemonti L, Annibale B, Lampasona V. Measurement of Autoantibodies to Gastric H+,K+-ATPase (ATP4A/B) Using a Luciferase Immunoprecipitation System (LIPS). Methods Mol Biol 2019; 1901:113-131.

Disclosure: Nothing to disclose

P1229 NLRP3 INFLAMMASOME-DERIVED INTERLEUKIN-1β ATTENUATES STRESS-INDUCED GASTRIC INJURY VIA THE COX-2/PGE₂ AXIS

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Introduction: Activation of inflammasomes, a multiprotein complex consisting of one of NOD-like receptors (NLRs), ASC, and pro-caspase-1, resulted in cleavage of pro-caspase-1, leading to processing of pro-IL-1β into its mature form. Water immersion restraint stress (WIRS) can induce inflammatory responses and severe mucosal injury in the stomach. We recently reported that inflammasomes were activated to protect the damage during the development of WIRS-induced gastric injury (Gastroenterology 2018: S-207, 2018).

Aims & Methods:

Aims: We investigated the mechanisms by which the inflammasome protected WIRS-induced gastric damage. We also determined which inflammasome was involved in the protection of the injury.

Methods: After fasting for 24 h, male wild-type, caspase-1-knockout (KO) and NLPR3 KO mice were placed in a restraint cage and immersed in the water bath. Mice were sacrificed after WIRS, and mucosal lesions were subjected to measurements of ulcer size and assay of mRNA levels by real-time RT-PCR. Protein levels of mature IL-1β and cleaved caspase-1 in stomach were measured by Western blotting. Prostaglandin E_2 (PGE_2) production by gastric tissue was assessed by enzyme immunoassay. Some animals were given rabeprazole, a proton pump inhibitor, before administration of the stress to examine the involvement of gastric acid in the inflammasome activation.

Results: Macroscopic gastric injury developed 3 h after WIRS, while significant increases in mRNA expression of IL-1β and protein levels of mature caspase-1 and IL-1β were observed on 30 min. NLRP3 mRNA expression increased by WIRS, whereas that of other NLRs did not change during experimental period. NLRP3 KO as well as caspase-1 KO mice exhibited high sensitivity to the stress induced injury with reduced expression of mature IL-1β protein. Administration of recombinant IL-1β (rIL-1β) abolished such aggravation of the injury in these KO mice without affecting gastric mucosal pH. In wild-type mice, the levels of cyclooxygenase (COX)-2 mRNA and PGE_2 production by gastric tissue significantly increased on 30 min after WIRS. Supplementation of rIL-1β further increased COX-2 expression and PGE_2 production and inhibited the injury. Immunoneutralization of IL-1β

exerted opposite effects on the injury and COX-2/PGE$_2$ axis. Rabeprazole attenuated the stress-induced injury with the increase of gastric mucosal pH, but failed to prevent inflammasome activation.

Conclusion: These results suggest that NLRP3 inflammasome-mediated IL-1β plays a protective role in stress-induced gastric injury via activation of the COX-2/PGE$_2$ axis. Gastric acid may not be involved in the activation of the NLRP3 inflammasome in stress-induced gastric injury.

Disclosure: Nothing to disclose

P1230 REAL WORLD DATA ON EMOTIONAL STRESS, DISABILITY AND SOCIAL CARE FOR CED PATIENTS

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Introduction: Inflammatory bowel disease (IBD) often manifests itself at a young age before or in the middle of working life. There has been insufficient research into the emotional stress levels of IBD patients, how often they suffer from a recognised

Aims & Methods: The aim of this study was to assess the level of emotional stress and the degree of recognised disability in IBD patients. The aim was also to evaluate whether there was any contact with the social system. Furthermore, it was examined whether predictive parameters regarding recognised disability can be identified in IBD patients. Between 15 November and 21 December 2018, patients with IBD and non-IBD volunteers were invited to participate in an online survey developed specifically for this study (accessible via www.soscisurvey.de).

Results: 505 patients with IBD (441 women, 87.3%) and 166 non-IBD patients (control group; 109 women, 65.7%) participated in the online survey. Patients with IBD reported significantly increased levels of everyday and work-related stress within the last six months and five years (p=0.0001), respectively. IBD patients were more likely to have a recognised disability (p=0.0001). A low academic status was the strongest indicator (p=0.006). Interestingly, only 153 IBD patients (30.3%) reported that they had been in contact with social workers or other forms of social support due to their illness. A recognised disability was the strongest indicator for this (p=0.0001).

Conclusion: Our study provides real-world data on emotional stress and the disability in a large German IBDcohort. It could be shown that patients with IBD suffer more often from emotional stress and more often have a recognised disability than non-IBD patients. There were differences between Crohn's disease and Ulcerative colitis. In addition, it was found that only about 1/3 of the patients had come into contact with the social system and the corresponding support and that this patient group is therefore apparently undersupplied in this area.

Disclosure: Nothing to disclose

P1231 ON-TREATMENT IMPROVEMENT OF AN EMERGING PSYCHOSOMATIC DEPRESSIVE DISORDER AMONG SALMONELLA CARRIERS: A MULTICENTER EXPERIENCE FROM EGYPT

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Introduction: Based on our observations, as physicians in a referral hospital, we have been noticing the association between history of enteric fever and somatic disorders associated with low mood. At 2 hospitals: Al-Hussein university hospital, Cairo; National Liver Institute hospital, Menoufia; we are receiving patients from all over Egypt, including rural areas where enteric fever is endemic.

Aims & Methods:

Aim: Here we report this series for 60 Egyptian patients referred to us for evaluation of different somatic disorders.

Methods: After extensive evaluations, the patients' symptoms were proved to be functional, their typhoid carrier states were documented, they were evaluated for depression using Hamilton-D questionnaire and the severity of depression was recorded. All patients were treated by ceftriaxone, 2 gm, IV, daily for 15 days. Clinical evaluation and Hamilton score were reassessed at the end of treatment and 6 weeks thereafter. The patients did not receive any anti-depressant nor anti-anxiety treatment during their course. Typhoid carrier was defined by documenting the history of typhoid fever that was diagnosed by culturing the salmonella species not by serology, plus at least one occasion of salmonella isolates from stool culture while a febrile, plus absence of fever in the past 3 weeks. The Widal test wasn't accepted as a criterion for enrollment.

Results: Typhoid carrier status was diagnosed in 60 patients, 32 males (53%) and 28 females (47%), the median age was 47 and the age range was 19-63 years. All patients were Egyptians and were referred to us from rural/villages area. 40 patients (66%) weren't complaining of any chronic diseases while 12 (20%) had diabetes mellitus, 16 (26%) had hypertension and 4 (6%) were suffering from bronchial asthma. As regarding smoking, 24 patients were smoker (40%) while 60 % weren't smoking before. Patients showed clinically significant improvement in term of the presenting somatic complaints as well as their Hamilton-D score immediately post-treatment and consolidate for 6 weeks post-treatment completion. The changes in the presenting somatic complaints were highly statistically significant P value< 0.01. It shows that fatigue and myalgia were present in 60 (100%) patient, anorexia in 48 (80%), chronic abdominal pain in 44 (73%), change in bowel habits in 52 (86%), vomiting in 24 (40%), myalgia in 28 (46%), atypical chest pain in 16 (26%), palpitations in 36 (60%), dyspnea in 32 (53%),urinary frequency in 24 (40%), erectile dysfunction in 18 out of 32 males (50%), while menstrual disturbance was present in 12 out of 28 females (42%). At the 6th week point the figures and percentages were 4 (6%), 12 (20%), 16 (26%), 28 (46%), 24 (40%), 0 (0%), 0 (0%), 4 (6%), 8 (13%), 4 (6%), 12 (20%), 4 (6%) and un-applicable, respectively.

Conclusion: Typhoid carrier, in our study, was associated with psychosomatic depression that improved on antibiotic therapy.

Disclosure: Nothing to disclose

P1232 WITHDRAWN

P1233 PERCUTANEOUS TREATMENT OF COMPLICATED HYDATID LIVER CYSTS: ABOUT 49

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Introduction: The of the liver hydatid cyst (LHC) is a parasitic disease due to the development of the larval form of the taenia of the dog echinococcus granulosus. This pathology remains frequent and constitutes a public health problem. Infectious, biliary and thoracic complications are present in 40% of cases. Topographic diagnosis has become easy thanks to advances in medical imaging. Percutaneous treatment was validated by the WHO in 1997 for uncomplicated cysts, and its place in the treatment of complicated forms remains controversial.

Aims & Methods: The aim of this work is to evaluate, the place of percutaneous treatment in complicated liver hydatid cysts (LHC) essentially those are infected or with biliary fistula.

this is a retrospective and descriptive study included all patients with complicated(HLC), confirmation of biliary fistula (BF) was done by bilious aspect of the aspirated liquid, or on the determination of bilirubin level with a rate higher than 5 mg / l, the diagnosis of infected (HCL) was made on the purulent aspect of the liquid and the bacteriological exam . All our patients had percutaneous treatment either by suction aspiration drainage or by PAIR (puncture, aspiration, injection, reaspiration), and received albendazole. The evaluation of the efficacy was made on ultrasound criteria.

Results: Forty-nine patients followed for (HLC) complicated with biliary fistula and / or infection had received percutaneous treatment in our department, their average age was 33 years [5- 75], with no predominance of sex: 25 F and 24 H, 47% had history of (HLC) surgery, and most of them had a recurrence, and only two (4%) patients had previous PAIR . For the (HLC) treated , the average size was 9.4 cm [3.3-20]; 60% of (HLC) were type I, 38% type II and only 2% type III according to the GHARBI classification. Twenty-five patients presented with biliary fistula (51%), five had an infected (HLC) (10%), both complications were present in nineteen patients (38.7%) and the success rate in our series was of 73% :100% in infected cysts, 76% in case of biliary fistula, 68% in case of combination of the two complications.

Conclusion: Percutaneous treatment is an effective and safe method to treat complicated (HLC). Further studies are needed to confirm these results. But the best treatment of liver hydatid cyst remains the prevention.

Disclosure: Nothing to disclose

P1234 RELATIONSHIP BETWEEN PATIENT BACKGROUND AND THE CAUSATIVE BACTERIA OF CHOLANGITIS AND DRUG SENSITIVITY

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Introduction: Cholangitis increases the internal pressure of the biliary duct, resulting in bacteria in the bile flowing out from the hepatic vein into the systemic circulation, which is said to cause bacteremia. This study aimed to identify the effective initial pharmacotherapy that is suitable for individual patients by investigating the relationship between patient background and the causative bacteria of cholangitis and drug sensitivity.

Aims & Methods: The study conducted a statistical analysis on the relationship between the primary disease of cholangitis, details of biliary drainage treatment, causative bacteria, and drug sensitivity of the bacteria in 107 patients with cholangitis who were admitted to the hospital between April 2014 and October 2018, where the causative bacteria could be identified using endoscopic retrograde cholangiopancreatography in blood and bile cultures.

Results: The 107 patients were comprised of 46 men and 51 women, with a mean age of 77 years. A total of 308 strains of causative bacteria were identified from blood cultures, and 333 strains were identified from bile cultures. The primary disease was cancer such as pancreatic cancer in 80 patients and non-cancerous conditions such as choledocholithiasis in 27 patients. The biliary drainage treatment in the patients with cancer consisted of self-expandable metal (n = 49) and plastic stents (n = 31),

with significantly more self-expandable metal stents used in the cancer patients (p < 0.001). The culture results indicated that the patients with cancer tended to have a significantly higher number of strains resistant to third-generation cephalosporin antibiotics such as cefotaxime and fourth-generation cephalosporin antibiotics such as cefepime. In particular, while ESBL-producing *Escherichia coli* was not isolated from the patients without cancer, it was detected 22 times in the patients with cancer. A significantly higher number of resistant strains were found in the plastic stent group in the subgroup analysis of the patients with cancer.

Conclusion: This study found a significantly higher number of resistant strains in the patients with cancer and cholangitis, which was particularly high in the patients where drainage was performed with a plastic stent. Possible causes include the following: patients with cancer have repeated occlusion of the bile duct as the cancer progresses, the plastic stent is more prone to occlusion than the self-expandable metal stent, and the patients have a greater exposure to antibiotics due to their immunocompromised state. Broad-spectrum antibiotics, excluding cephalosporin antibiotics, are preferable as initial treatment for cholangitis caused by cancer.

Disclosure: Nothing to disclose

P1235 VARIATION IN PNEUMONIA RATES BY ENDOSCOPIC PROCEDURE AND SEDATION PERFORMED IN OUTPATIENT SETTINGS

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Introduction: Aspiration pneumonia following endoscopic procedures is associated with anesthesia assistance. We aimed to examine the type of sedation and rates of hospitalization for pneumonia following endoscopic procedures performed in the outpatient hospital setting.

Aims & Methods: The January 2015-December 2018 United States Medicare fee-for-service claims of individuals 65 and older were queried. This age groups represents about 30% of the United States population. Bronchoscopy, colonoscopy (diagnostic and screening), cystoscopy, EGD and ERCP were included. Monitored anesthesia care (MAC) and moderation sedation were identified by Healthcare Common Procedure Coding System (HCPCS) and associated modifiers. Simultaneous anesthesia care for 2-3 and 4 or more procedures was examined. Aspiration pneumonia within 7 days was identified by a hospitalization with ICD codes 5070, 5078, J690 or J698 and infectious pneumonia was identified by codes 480-486 and J12-J18. Only pneumonia recorded as present on admission was considered an event to increase specificity that the patient was admitted with this condition. Logistic regressions for pneumonia included the sedation variables, type of procedure, age, sex, race, year, comorbidities, screening vs diagnostic procedure, and procedure discontinuation.

Results: There were 9,023,288 eligible procedures (4,096,589 colonoscopy [26% screening], 3,853,942 EGD, 178,350 ERCP, 633,864 cystoscopy, and 351,527 bronchoscopy). MAC was documented for 58% of procedures (56% colonoscopy, 62% EGD, 81% ERCP, 69% cystoscopy and 43% bronchoscopy). Aspiration pneumonia was recorded in only 19 patients; older age and male sex were associated with an increased risk of aspiration pneumonia. There were only 40 admissions for infectious pneumonia; no factor was associated with infectious pneumonia.

Conclusion: In the outpatient hospital setting in the United States, pneumonia after endoscopy procedures that the hospital considered as present on admission was rare.

Disclosure: Nothing to disclose

P1236 ENDOSCOPIC FINDINGS IN SEVERE YELLOW FEVER PATIENTS PRESENTING WITH ACUTE UPPER GASTROINTESTINAL BLEEDING: A RETROSPECTIVE CASE SERIES STUDY

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Introduction: The incidence of yellow fever in Brazil has been low during the last decades, but since December 2016, an epidemic yellow fever has resurged in this country. In the severe form (15%-60%), gastrointestinal hemorrhage can be present, with a high mortality rate (20-50%). This is one of the first studies reporting the causes of gastrointestinal bleeding in patients with severe yellow fever. We aimed to describe the main endoscopic findings in patients with severe yellow fever in whom an emergency upper gastrointestinal endoscopy (UGE) was performed.

Aims & Methods: This is a retrospective case series study that included a total of 26 patients referred to a tertiary care center in Brazil for suspected severe form yellow fever diagnosis (between December 2017 and April 2018), undergoing UGE for acute upper gastrointestinal bleeding. The principal reasons of hospitalization of theses patients in our hospital were acute liver failure (88%).

Results: The mean age was 36 years (range 16 yo - 63 yo), and 84,61% were men.

The table 1 summarizes main endoscopic findings and treatments
In the esophagus, four cases of Mallory-Weiss syndrome (three with active bleeding treated endoscopically with adrenaline injection in two cases and band ligation in one case); two cases of active variceal bleeding treated with band ligation and one case of esophageal perforation (Boerhaave's syndrome) that evolved into a bilateral esophago-mediastinal fistula treated with endoscopic placement of two plastic pigtail stents and bilateral pleural drainage.

In the stomach, eight cases presented with of severe hemorrhagic pangastritis (four with diffuse oozing bleeding that did not allow adequate endoscopic hemostasis and four without active bleeding); one case with focal oozing hemorrhage of the gastric mucosa, which resolved after a second UGE with hemoclip placement; four cases with gastric ulcers (two with active bleeding treated with hemoclip); one case with a vascular Dieulafoy lesion treated with hemoclip.

In the duodenum, one case presented with hemorrhagic duodenitis with diffuse oozing bleeding that did not allow adequate endoscopic hemostasis; one case with an active duodenal ulcer treated with hemoclip; one case with bulbar telangiectasias without bleeding. In two cases the specific cause of bleeding was not determined, due to the presence of large amounts of non-aspirable blood clots in the stomach and duodenum.

Conclusion: This is one of the first series describing the endoscopic findings and experience in this subset of patients. Liver acute failure due to yellow fever is an uncommon condition for endoscopists worldwide. 88% of the patients included in this study were hospitalized due to acute liver failure.

Severe vomiting episodes before gastrointestinal bleeding explained Mallory-Weiss and Boerhaave's syndrome cases. Most cases presented diffuse hemorrhagic gastritis probably due to the severe coagulopathy that limited endoscopic therapeutic options. UEG in severe yellow fever patients is challenging and required endoscopic treatment in 32 % in this case series study.

Disclosure: Nothing to disclose

P1237 EPIDEMIOLOGY AND TIME TRENDS OF UPPER GASTROINTESTINAL BLEEDING - A POPULATION BASED COHORT STUDY OVER MORE THAN 30 YEARS

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Introduction: Gastrointestinal bleedings (GIBs) are acute events which are potentially severe but not always life threatening and often can be safely treated. There have been numerous studies reporting on the rates of GIBs associated with use of drugs but very few studies have examined the rates of upper GIBs (uGIBs) in the general population and trends over time

Aims & Methods: The aim of this study was to evaluate the incidence rates of uGIBs and the trends over time in the general population of Finland. Data from participants of prospectively conducted population-based FINRISK health examination surveys was utilized for this study. FINRISK enrolled persons aged 25-74 years, recruited by random sampling from the population register, stratified by 10-year age group, sex and study area. The total number of participants in each survey was approximately 6000-8000. The participation rate in 1972 survey was >90% with a gradually declining trend to 57% in men and 67% in women in 2012. The follow-up took place using record linkage to the country-wide electronic health registers which included hospital discharge register and causes of death register. With the help of these national registers, the coverage of the follow-up was 100% for persons living in Finland. The follow-up period was from the enrollment up to the onset of an uGIB leading to hospitalization, death due to any cause, or end of the follow-up period which was December 31st, 2016. Participants with a history of GIBs before the baseline were excluded from the analyses. Incidence rates, recurrence rates (events recorded were >30 days apart), cause-specific mortality rates and 28-day case-fatality rates for uGIBs were calculated with 95% confidence intervals (CIs). The time-trends in event rates were calculated using a log-linear poison regression model adjusting for baseline age, gender, region, and the year of enrollment. Age standardization was conducted using weights from the European standard population

Results: A total of 71,068 participants were included in the study and they experienced 1643 incident uGIBs. The median age of participants experiencing uGIBs was 48.6 years, among the ones without GIBs it was 45.4 years. The age standardized incidence rates for uGIBs in males and females were 1.59 and 0.95 per 1000 py, respectively. Among men, the incidence rates declined approximately by half by the end of the study period compared to late 1980's (ref. period), and among women a consistent decline was seen, so that at the end of the study period the rates were less than 20% of those in the late 1980's. Among incident uGIBs, the recurrence rates of uGIBs in males and females were 20.3 and 13.3 per 1000 py, respectively. There was a substantial random variation but the general trend in proportion of recurrent uGIBs was increasing. Cause-specific mortality rates from uGIBs in males and females were 0.14 and 0.07 per 1000 py, respectively. Compared to the late 1980's, mortality due to uGIBs decreased sharply in the early 1990s by 40-60% and remained stable since the late 1990s, approximately at 20% of the level in the late 1980's. The 28 day case-fatality rates in males and females were 8.2% and 6.6%, respectively. The case-fatality rate for overall uGIBs for males and females calculated for 5-year periods since 1987 showed a declining trend up to the period 2002-06. However, no further decline was seen in the last decade.

Conclusion: Overall, the age-standardized incidence rates of uGIBs are higher in males than in females. The rates of uGIBs and deaths due to uGIBs have significantly decreased since the late 1980's over the years.

P1238 EFFICACY OF PURASTAT IN UPPER AND LOWER ACUTE GASTROINTESTINAL BLEEDING: A DUAL CASE SERIES EXPERIENCE

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Introduction: Gastrointestinal (GI) bleeding is a common cause for hospitalization, resulting in significant mortality and morbidity. Innovative topical hemostatic modalities have been developed for endoscopic use. Our aim is to demostrate the efficacy, feasibility and safety of Purastat to control GI bleedings. Puramatrix is a synthetic, bioresorbable material used to produce Purastat, created to control venous/arteriolar bleedings, It's easy, quick and trasparent allowing to continue the procedure/to use other haemostatic therapies.

Aims & Methods: We report a case series of 33 patients (23 males, 10 women, median age 74 years) recovered to two endoscopy units (Garbagnate Milanese and Monza) for acute GI bleeding after failure of other hemostatic strategies (injection/clipping/thermal coagulation). 14/25 patients presented a lower GI haemorrhage from an oozing site after mucosectomy for non polypoid colon adenomas in different sites of the colon (8 pts from the right colon) 5 patients showed melena for duodenal bleeding from bulbar kissing ulcers, 4 patients with melena and anemization after duodenal mucosectomy for a laterally spreading tumor of the second part of the duodenum, 4 patients had emathemesis after Vater papilla's sphincterotomy, 1 patient showed progressive anemization for bleeding inside a pseudocyst after endoscopy ultrasound guided drainage, 1 patient presented with a massive rectal bleeding after a prostatic biopsy, 3 patients from neoplastic gastric ulcer localized in the body and in the fungus and 1 patient with a massive bleeding after gastric random sampling due to obscure underlying arteriovenous in-wall malformation.

Results: In all these patients, we tried to achieve a successfull hemostasis first of all using an adrenaline injection and subsequently with clipping and/or argon plasma coagulator application without success. Finally we used a strate of Purastat applying 3 ml of gel, with a successfull, stable hemostasis and a complete patients recovery in few days after the procedure, no pain and haemodinamical stability. No need to surgery or radiological haemostatic procedures

Conclusion: Purastat is a new, safe and feasible hemostatic device capable to control different types of GI haemorrhages even if the arteriolar massive ones.

Disclosure: Nothing to disclose

P1239 ARE THERE ANY EPIDEMIOLOGIC OR MANAGEMENT DIFFERENCES BETWEEN UPPER GASTROINTESTINAL BLEEDING NOT ASSOCIATED AND ASSOCIATED TO PORTAL HYPERTENSION? COMPARATIVE ANALYSIS IN A SOUTHERN SPANISH AREA

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Introduction: The aim is to evaluate comparatively different epidemiologic and management aspects of Upper Gastrointestinal Bleeding not associated (UGBNPH) and associated (UGBPH) to Portal Hypertension, in Puerta del Mar Hospital, Cádiz, Andalucía, Spain.

Aims & Methods: Retrospective research including every patient admitted to Gastroenterology Department of Puerta del Mar Hospital (Cádiz), between January 2016 and December 2016, because of Upper Gastrointestinal Bleeding (UGB).

We analysed different variables: relation to Portal Hypertension, age, cardiovascular risk factors such Arterial Hypertension (AHT), Diabetes Mellitus (DM) and Dyslipidemia (DLP); concomitant treatment with Proton Pump Inhibitors (PPIs), Antiplatelets, Antithrombotics, Nonsteroideal Anti-Inflammatory Drugs (NSAIDs) and Antidepressants; clinical and en-doscopic findings; red blood cells and iron requirement. We also analysed short and medium term survival rates and recurrence rate in one-year period.

Results: We included 105 patients admitted because of Upper Gastrointestinal Bleeding (71,4% not associated to Portal Hypertension; 28,6% associated to Portal Hypertension), with an average age older in the first group (UGBNPH 69,7 years old; UGBPH 59,8 years old).

We did not find significant differences by etiology when analyzing DM (29,5%). However, it was more usual the AHT (53,3% vs 36,7%) and DLP (34,7% vs 16,7%) in not associated to Portal Hypertension group.

We did not find significant differences when analyzing use of PPIs (37,1%) and Antidepressants (17,1%). Nevertheless, it did exist a higher frecuence of Antiplatelets (29,3% vs 6,7%), Antithrombotics (29,3% vs 3,3%) and NSAIDs (20% vs 0%) in patients with UGBNPH).

Clinical debut as Melena (66,7%) and Hematemesis (61,9%) was similar, with no differences depending on etiology of bleeding.

Regarding Endoscopic findings, we found more frecuently Gastric Ulcer in UGBNPH (37,3%) and Esophageal Variceal bleeding among UGBPH (70%). We did not find significant differences by etiology regarding amount of patients that required red blood cells transfusion during admission (62,9%), the number of packed blood cells used (4 as average) and iron treatment beginning (21,9%).

Short and medium-term survival rates were slightly higher in not associated to Portal Hypertension group: short-term (94,7% vs 90%) and medium-term (one year after admission) (84% vs 80%). Finally, recurrence rate in one-year period was fairly higher in associated to Portal Hypertension group (40,7% vs 14,1%), especially in women and Portal Hypertension Gastropathy bleeding.

Conclusion: Upper Gastrointestinal Bleeding not asocciated to Portal Hypertension is more frecuent that the associated one in our environment. Cardiovascular risk factors such as Arterial Hypertension, Dyslipidemia or concomitant treatments as Antiplatelets, Antithrombotics and NSAIDs are more often related to UGBNPH. The amount of patients with red blood cells transfusion requirement was similar by different etiologies. Survival rates are slightly higher in UGBNPH, while bleeding recurrence is quite more frecuent in UGBPH.

Disclosure: Nothing to disclose

P1240 NOVEL HEMOSTATIC POWDER STOPS BLEEDING IN A LIVE PORCINE MODEL OF UPPER GI BLEEDING

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Introduction: Hemostatic powders are an attractive option in upper GI bleeding. However, currently available powders are not effective in Forest Ia bleeds and are associated with unacceptably high rebleeding rates. These limitations are related to their mechanism of action which is based on provision of a mechanical bandage on, rather than delivery of any therapeutic agents to, the site of injury.

CounterFlow is a novel hemostatic powder which based on self -propelling technology can deliver thrombin against blood flow and into the site of injury.

Aims & Methods: To determine efficacy of CounerFlow hemostatic powder in stopping bleeding in a live porcine model of acute severe upper GI bleeding.

Bleeding model includes anesthetised pig, surgical laparotomy and 1cm gastrotomy, placement of gastroepliploic vascular bundle into gastric lumen, incision of artery with ERCP needle knife to create an actively spurting bleed, and delivery of powder by upper endoscopy and a 7Fr catheter using a CO2 powered hand held delivery system.

Results: A total of 8 bleeds were created in 4 different pigs. Successful hemostasis was achieved in 100% of bleeds. Average time to achieve hemostasis was 4.31 mins (range 1 -11 mins). Average mass of powder required to achieve hemostasis was 2.4g (range 1.1 - 6.7g).

Conclusion: A novel self propelling hemostatic powder has shown early promise in stopping bleeding in a live porcine model of acute severe upper GI bleeding.

References: Self-propelled particles that transport cargo through flowing blood and halt hemorrhage. Baylis JR et al. Sci Adv. 2015 Oct 2;1(9):e1500379

P1241 EFFICACY OF HEMOSTATIC POWDERS IN THE TREATMENT OF GASTROINTESTINAL BLEEDING RELATED TO NEOPLASTIC OR NON-NEOPLASTIC LESIONS

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Introduction: EndoClot System (Endoclot Plus Inc., Santa Clara, CA, USA) and Hemospray (Cook Medical, Winston-Salem, NC, USA) are two sprayable powders for induction of immediate bleeding stop recently introduced in gastrointestinal endoscopy.
Aims & Methods: Aim of the study was to evaluate the efficacy and safety of the two kinds of hemostatic powder (HP) in the management of gastrointestinal bleeding (GIB). From September 2017 to March 2019, all patients with endoscopically confirmed GIB were considered eligible for the study. Inclusion criteria were active bleeding at the time of the endoscopy and the failure (complete or partial ineffectiveness) or inapplicability of standard procedures of hemostasis (local adrenaline infiltration, argon plasma coagulation or electrohemostasis, mechanical with clips). Once identified the source of GIB, Endoclot System or Hemospray was sprayed over the lesion and the short-term efficacy was evaluated observing the bleeding lesion for several minutes. The choice of which kind of HP to be used was arbitrary or related to the availability of the product in the endoscopy room. The efficacy of HP was evaluated according to the hemostasis which was defined as follows: immediate =no bleeding after application up to end of the procedure; stable=no bleeding recurrence in the 72 hours after the procedure; definitive =no more episodes of bleeding till the discharge. We also evaluated any adverse event possibly related to the use of HPs.
Results: A total of 29 patients (19 males; median age: 72 years, range: 32-89) were included. All patients had symptoms of upper GIB but two with rectal bleeding (one following an endoscopic submucosal dissection and one due to colorectal cancer). Of 29 patients, 20 were at first episode of GIB while 9 had already been submitted to an endoscopic hemostatic procedure for GIB. All patients were found to have an active GIB due to: chemotherapy-related mucosal damage or graft versus host disease (two patients, both with extensive mucosal denudation in the esophagus); ulcer in the stomach (3 patients), in the duodenum (4 patients), and in the gastric anastomosis (4 patients); inoperable malignancy infiltrating the wall of the stomach (8 patients), duodenum (4 patients), or colon (one patient); post-endoscopy procedures (sphincterotomy in two patients and endoscopic submucosal dissection in the rectum in one patient). The use of HP achieved immediate hemostasis in 28 out of 29 patients (97%), stable hemostasis in 23 patients (79%) and definitive hemostasis in 22 patients (76%). No adverse events occurred.
Conclusion: The HPs are effective for stopping GIB related to different kinds of neoplastic and not neoplastic lesions, not responding or not amenable to be treated with standard hemostatic techniques.
Disclosure: Nothing to disclose

P1242 OUTCOME OF UPPER GI HAEMORRHAGE IN PATIENTS WITH ACUTE OR CHRONIC RENAL FAILURE AND INFLUENCE OF RENAL FAILURE ON RISK STRATIFICATION SCORING

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Introduction: Renal failure is associated with poorer outcome following upper gastrointestinal haemorrhage (UGIH) and is a parameter in some pre-endoscopy risk stratification scores which are used to identify low-risk patients who may be safely managed as outpatients. We studied the outcome of patients admitted with UGIH in relation to their renal function and risk stratification scores.
Aims & Methods: Prospectively collected data from a 1-year international multi-centre study of consecutive patients presenting with UGIH. Demographics, endoscopic findings, treatment and outcomes were recorded. eGFR was determined retrospectively from admission creatinine. If eGFR was < 60ml/minute, it was recorded whether this was acute kidney injury (AKI) or chronic kidney disease (CKD) by review of electronic patient notes. Glasgow Blatchford (GBS), admission Rockall (aRS), AIMS65 and PNED scores were determined. Need for endoscopic therapy, transfusion, surgery, rebleeding within 7days and 30-day mortality rates were recorded.
Results: The main findings are shown in table 1 and are median or percentage except where indicated.

	Normal renal function	AKI	CKD	p value
Number	1208	165	250	
Age	52	75	82	<0.0001
Female	39.7%	42%	50%	<0.05
Endoscopy findings				
Normal	12.0%	11.5%	12.4%	
Benign ulcer	17.9%	24.2%	19.2%	
Varices	5.2%	6.7%	4.4%	
Cancer	2.2%	0%	2.4%	
Not scoped	27.6%	24.2%	18.4%	NS
Endoscopic therapy	18.6%	25.9%	27.6%	<0.001
Surgery	0.6%	0%	1.2%	NS
Rebleed <7days	4.6%	8.4%	6.8%	0.06
30-day mortality:				
Bleed related	1.2%	7.2%	4%	
Non bleed related	3.1%	10.8%	13.2%	<0.0001
Transfusion	27.7%	41.6%	49.6%	<0.0001
Transfusion (average units)	3.7	4.7	4.4	<0.05
Need for treatment or Died	37.5%	57.8%	63.2%	<0.0001
Length of stay (average in days)	3.96	8.11	6.58	<0.0001

[Table 1. Results summary]

In determining low risk patients who did not require endoscopic therapy, transfusion, surgery, radiological embolisation and did not die within 30d, GBS < 1 gave highest sensitivity for those patients with normal renal function, AKI or CKD (94.8-100%). Specificity was 51.6-64.8%, although GBS < 1 only identified "low risk" patients in 1.9% and 2.0% of AKI and CKD patients compared to 30% of those with normal renal function.
In comparison, AIMS65=0 had sensitivity 70.4-80%, specificity 54.1-94.3% identifying more patients as low risk (44.2%, 22.7%, 6.4% respectively). Admission Rockall = 0 identified a similar percentage to GBS as low risk with poorer sensitivity (75-100%). PNED < 1 identified the highest number of low risk patients (52.8%,18.9% and 12.4%) but had low sensitivity (53.6-80.5%).

Conclusion: Patients admitted with UGIH and renal impairment are older and more likely to be female, than those with normal renal function. Transfusion requirements, need for endoscopic therapy, rebleed rate and mortality (bleed and non-bleed related) and are all increased in this group. GBS identifies low risk patients with AKI or CKD with high sensitivity, although few low risk patients are in this group. No other commonly used pre-endoscopy risk score is accurate in identifying low-risk patients with renal impairment.
Disclosure: Nothing to disclose

P1243 EVOLUTION OF ADMITTED PATIENTS WITH GASTROINTESTINAL BLEEDING AND ANTIPLATELET-ANTICOAGULANT THERAPY FOR CARDIOVASCULAR DISEASE

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Introduction: The evolution of admitted patients due to gastrointestinal bleeding (GB) and previously treated with new oral anticoagulants (NOAC) has not completely characterized and compared to admitted patients with GB and previous treatment with other antiplatelet (AP) or anticoagulant (AC) therapy.
Aims & Methods: Our aim was to compare re-bleeding and mortality rates between both groups. A prospective multicenter cohort study was design and patients with AP-AC treatment for cardiovascular disease and acute GB were consecutively included between January 2017 and march 2018 in Alicante, Spain. Demographic, physical, endoscopic, blood parameters, previous treatment and evolution outcomes were recorded. Descriptive and analytic analysis were performed, comparing outcomes between patients with NOACs vs patients with other AP-AC therapy. Chi-square and t-Student test were used in univariate analysis for comparative analysis, while mean +/- standard deviation (SD) or frequencies and percentages showed descriptive results. P< 0.05 was considered significant.
Results: 170 patients were included with a mean length of admission of 11.0 days (SD 9.8). 59% of patients were men and the mean age was 76.3. 50 (29.4%) had suffered a previous GB. NOACs were part of therapy in 61 (35.9%) patients, whereas the rest were being treated with other AP-AC therapy. During their stay at the hospital, a total of 24 patients rebled, 5 patients had ischemic complications and 6 patients died. Comparisons show that NOAC group had lower systolic pressure (118 vs 127; p=0.05) and a trend to higher cardiac frequency (87 vs 80 bpm; p=0.06). A lower but non-significant cypher of hemoglobin was also detected (8.9 vs 9.8 g; p=0.39).
No differences were seen in the number of transfusions and Blatchford score. The length of admission was also similar between them (mean 11.3 vs 11.0 days, p=0.87). Rebleeding (p=0.23), ischemic complications (p=0.46) and mortality (p=0.47) rates did not differ between both groups. Comparing different NOACs, no significant differences were seen in the same rates either.
Conclusion: In our prospective cohort study, no differences were detected during the admission of patients with acute bleeding concerning related complications and mortality in patients with NOACs vs patients with other AP-AC therapy.
Disclosure: Nothing to disclose

P1244 PREDICTORS OF ENDOSCOPIC INTERVENTION IN UPPER GASTROINTESTINAL BLEEDING DURING HOSPITALIZATION IN MEDICAL WARDS INPATIENTS ADMITTED FOR OTHER CAUSES

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Introduction: Upper gastrointestinal bleeding is a complication often encountered in inpatients hospitalized for another reason. Often these patients are unstable and the decision to perform upper endoscopy in these patients is not easy.
Aims & Methods: To characterize variables that may predict endoscopic intervention in inpatients admitted for non-gastrointestinal bleeding (GIB) causes who later developed inpatient upper GIB. A retrospective analysis of patients who underwent inpatient gastroscopy from 5.2014 to 12.2017 at two academic medical centers were performed. Clinical and laboratory data were collected.
Results: One-hundred and seven patients were included. Nineteen patients (17.8%) underwent endoscopic intervention (group A) and 88 patients underwent endoscopy without intervention (group B). Average age in groups A and B was 66.7±18.4 and 71.1±14.6 years (P=0.13), respectively. Predictors of endoscopic intervention were cirrhosis (31.5% vs. 3.4%, P< 0.0001), lower blood pressure (109.8/60.8 mmHg vs. 126.8/68.3 mmHg, P< 0.03) and higher heart rate before gastroscopy (97.7 vs. 87.7, P=0.03), mechanical ventilation during admission (41.7% vs. 18.7%, P=0.04), number of blood units administered (4.3 vs. 2.6 units, P=0.001), lower hemoglobin level at time of gastroscopy (8.3 mg/dl vs. 9.3 mg/dl, P=0.04), increase in urea level delta (7.1 vs. 2.55, P=0.05) and higher Glasgow Blatchford (13.9 vs. 11.2, P=0.0004), AIMS-65 (2.3 vs. 1.5, P=0.001) and Rockall (6.4 vs. 4.3, P<0.0001) scores, respectively.
Recent antiplatelets, anticoagulation use and infectious etiology didn't predict endoscopic intervention (P>0.1 and P=0.6, respectively). Proton pump inhibitors at admission and prior to endoscopy didn't decrease the need of endoscopic intervention (P=0.3). Mortality rate was similar between groups A and B (36.8% vs. 39.7%, P=0.4).
Conclusion: Several clinical and laboratory parameters were found to predict endoscopic intervention in inpatients with DE NOVO upper GIB. Further prospective studies are needed to validate our findings
Disclosure: Nothing to disclose

P1245 OVER-THE-SCOPE CLIP AS A RESCUE THERAPY FOR FIBROTIC BLEEDING ESOPHAGEAL VARICES: A SINGLE-CENTER EXPERIENCE

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Introduction: Repetitive endoscopic band ligations (EBL) are associated with fibrosis of the esophageal wall. Fibrosis of the esophageal wall impaired the band ligation of esophageal varices during endoscopy.
Sclerotherapy is the standard rescue therapy for the management of fibrotic esophageal varices; however, feasibility and safety are a concern for sclerotherapy.
Aims & Methods: Aim: We aimed to evaluate the safety and efficacy of Over-The-Scope clip in the management of actively bleeding fibrotic esophageal varices.
Methods: This was a historic cohort study. Data from patients with upper gastrointestinal bleeding from a single tertiary center were retrospectively recorded and prospectively analyzed. Patients in whom endoscopic band ligation failed to adhere to fibrotic esophageal varices were treated with the deployment of over-the-scope clips.
Results: Ninety-six patients with actively bleeding esophageal varices were included from September 2016 to January 2019. Five patients had fibrosis within the esophageal wall and active bleeding esophageal varices. Thus, the over-the-scope clip was deployed over the bleeding fibrotic varix as rescue therapy. The median age was 65 years old (range: 52 - 83); three

patients were female. The cirrhosis etiology was alcohol in one patient, and NASH in four patients. Two patients had two previous EBLs, two patients had three previous EBLs before the index bleed and one patient a single previous EBL. Four patients have a Child-Pugh B and one patient a Child-Pugh C. During follow-up esophagogastroduodenoscopy, two patients were submitted to further EBL for variceal eradication after the index over-the-scope clip therapy. Neither re-bleeding nor mortality during the index bleeding was documented. Table 1 summarizes patients data per each case.

Patient No.	Age (years)	Etiology	Child score	Previous EBL	Further EBL	Mortality
1	69	Alcohol	B	2	2	No
2	60	NASH	B	3	0	No
3	65	NASH	B	3	0	No
4	52	NASH	C	1	2	No
5	83	NASH	B	2	0	No

[Table 1. Characteristics of patients with fibrotic esophageal varices treated with Over-The-Scope Clip (OTSC).]

Conclusion: The over-the-scope clip is a safe and effective alternative in the management of fibrotic esophageal varices. The over-the-scope clip might be considered as an alternative to sclerotherapy in the management of fibrotic esophageal varices. Randomized controlled trials are required to validate these data.
Disclosure: Nothing to disclose

P1246 OUTCOMES ON THE USE OF HEMOSPRAY IN UPPER GASTROINTESTINAL BLEEDS SECONDARY TO PEPTIC ULCERS: PROSPECTIVE MULTICENTRE INTERNATIONAL HEMOSPRAY REGISTRY

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Introduction: Peptic ulcers are the commonest cause of upper Gastrointestinal (GI) bleeding (UGIB), accounting for 44% of all UGIBs. The mortality from GI bleeding remains high at 7%. Hemospray (Cook Medical, North Carolina, USA) is a novel haemostatic powder aimed to treat GI bleeding. The aim of this study is to look at outcomes in patients with GI bleeds secondary to peptic ulcers treated with hemospray in 14 centres, and examine outcomes based on baseline ulcer morphology based on the Forrest classification.
Aims & Methods: Data was prospectively collected on hemospray use in UGIBs in the UK, France, Germany and the USA (Jan'16-March'19). Hemospray was used during emergency endoscopy for UGIBs secondary to peptic ulcers (oesophageal, gastric or duodenal) at the discretion of the endoscopist as a monotherapy, dual-therapy with standard haemostatic techniques or rescue therapy once standard methods have failed. Haemostasis was defined as cessation of bleeding within 5 minutes of hemospray application. Rebleeding was defined as a sustained drop in Hb (>2g/l), haematemesis or melaena with haemodynamic instability following index endoscopy.

Results: 202 patients with UGIBs secondary to peptic ulcers were recruited (136M, 66 F, 125/202 (62%) duodenal, 47/202 (23%) gastric, 30/202 (15%) oesophageal). Immediate haemostasis was achieved in 178/202 (88%) patients. The median Blatchford score was 12 at baseline (IQR, 10-14), median rockall score was 7 (IQR, 6-8).
Immediate haeomastasis was achieved in 34/39 (87%) patients with Forrest 1a ulcers, 99/117 (85%) with forrest 1b, 25/25 (100%) with forrest 2a, 20/21 (95%) with Forrest 2b. There was 7/29 (24%) rebleeds with forrest 1a ulcers, 13/84 (15%) with forrest 1b. In the 24/196 (12%) patients who did not achieve haemostasis 18/24 (75%) were Forrest 1b ulcers.
In the total PUD cohort treated with hemospray, 26/154 (17%) had a rebleed, the median rockall score in this group was 7 (IQR,6-8). The number of rebleeds in oesophageal ulcers was 2/23 (9%), 6/38 (16%) in gastric ulcers, 18/93 (19%) in doudenal ulcers.

	Forrest 1a (n=39)	Forrest 1b (n=117)	Forrest 2a (n=25)	Forrest 2b (n=21)
Haemostasis	34/39 (87%)	99/117 (85%)	25/25 (100%)	20/21 (95%)
Median Blatchford score	13 IQR: 11-14	12 IQR:10-15	12 IQR: 11-14	13 IQR: 11-14
Median Rockall score	7 IQR: 6-8	7 IQR:6-8	7 IQR: 6-8	7 IQR: 6-8
Rockall score 7 predicted re-bleeding rate: 25-40%				
Re-bleeding	7/29 (24%)	13/84 (15%)	2/23 (9%)	4/18 (22%)
Rockall score 7 predicted mortality: 20-30%				
7-day mortality	7/34 (21%)	11/99 (11%)	1/23 (4%)	3/19 (16%)
30-day mortality	9/34 (26%)	21/99 (21%)	3/23 (13%)	5/19 (26%)

[Outcomes in different Forrest classification groups]

Conclusion: Hemospray is effective in achieving immediate haemostasis in UGIBs secondary to peptic ulcers. The baseline Blatchford score and rockall scores in our cohort are high with patients recruited from tertiary centres with a complex mix of potentially high-risk cases compared to community centres. The rebleeding and mortality rates are in keeping/ below the predicted rate based on the scores.
The best outcome with hemospray was seen in patients with forrest 2a ulcers, with 100% haemostasis, lowest number of re-bleeds and lowest overall 30-day mortality. The majority that did not achieve haemostasis were forrest 1b ulcers. Highest rebleeding rate was in doudenal ulcers. The hemospray registry will continue the expand with the recruitment of US sites.
Disclosure: Nothing to disclose

P1247 COMPARISON OF ENDOSCOPIC HEMOSTASIS AND TRANSARTERIAL EMBOLIZATION (TAE) OF HEMORRHAGIC GASTRIC ULCER AT OUR HOSPITAL

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Introduction: Endoscopic hemostasis is the first choice of treatment for hemorrhagic gastric ulcers; however, if endoscopic hemostasis fails, switch to transarterial embolization (TAE) and surgery should always be considered. It may be possible to provide prompt treatment by examining predictive factors of switch from endoscopic hemostasis to TAE. This time we retrospectively compared endoscopic hemostasis with TAE for the treatment of hemorrhagic gastric ulcer at our hospital.
Aims & Methods: This study was aimed to assess predictive factors for requirement of switch from endoscopic hemostasis to TAE. Patients with benign hemorrhagic gastric ulcer requiring endoscopic hemostasis (clip method, coagulation method, and injection of hypertonic saline epinephrine(HSE)) who visited the hospital between December 2009 and December 2018 (n= 393) were enrolled. They were classified into two groups; one group underwent only endoscopic hemostasis, while the other received endoscopic treatment and TAE. Age, medical history, medication, Glasgow-Blatchford score (GBS), number of endoscopic hemostasis, total blood transfusion volume, and blood test of hemoglobin (Hb), serum albumin (Alb), blood urea nitrogen (BUN) and PT-INR were retrospectively reviewed and statistically considered.

Results: Of the 393 patients with hemorrhagic gastric ulcer underwent endoscopic hemostasis, hemostasis was achieved with endoscopy alone in 382 cases (97.2%) and 11 cases (2.8%) were switched to the TAE. The overall mean age was 68.7 years, and there was no significant difference between the 2 groups in terms of the medical and oral history (antithrombotic drugs, gastric acid inhibitors, and NSAIDs). Eight patients (72.7%) of TAE were able to achieve complete hemostasis; however, 2 did not achieve hemostasis with TAE, and surgery was performed. One patient was unable to identify point of bleeding; however, natural hemostasis was achieved. In one case, a splenic abscess was formed after the TAE, and splenectomy was performed, suggesting a complication due to TAE. There was no intestinal necrosis or perforation after TAE. The mean GBS at the first examination was 10.0±3.3 in endoscopic hemostasis group and 12.2±3.5 in TAE group, which was significantly higher in TAE group (p=0.0382); further, number of endoscopic hemostasis was 1.1±0.3 and 2.5±1.1 (p=0.0008), and total blood transfusion volume was 3.8±3.8 units and 20.8±11.3 units (p=0.0007) respectively, which were also statistically higher in TAE group. Hb and Alb at the first visit were significantly lower in TAE group (Hb; p=0.0241, Alb; p=0.0230).

Conclusion: As predictive factors of cases switching from endoscopic hemostasis to TAE, it is suggested that GBS at the first examination, number of endoscopic hemostasis, total blood transfusion volume, blood parameters of Hb and Alb at the first examination could be useful indices.

Disclosure: Nothing to disclose

P1248 ASSESMENT OUTCOMES OF NEW THRESHOLDS OF THE GLASGOW BLATCHFORD SCORE IN MANAGING PATIENTS WITH UPPER GASTROINTESTINAL BLEEDING. THE EXPERIENCE OF A TERTIARY CENTER

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Introduction: Upper gastrointestinal bleeding(UGIB) remains a significant cause of hospital admission. In order to stratify patients according to the risk of complications and to predict the need of clinical intervention, several risk scores(RS) have been proposed and their in the early patients assesment is repeatedly recommended by international guidelines to distinguish high-risks patients, who may need clinical intervention and hospitalization, from low risk patients with a lower chance of developing complications (1). Many RS have been developed, being pre-endoscopy scores more appropriate because it seems more important to predict risk as soon as possible after the UGIB onset to help direct management, especially when the endoscopist is on-call (2). The most well established pre-endoscopic score is the Glasgow-Blatchford score(GBS). Patients with a GBS=0 have less than 1% likelihood of requiring endoscopic intervention and may safely be discharged before undergoing endoscopy, however, 90% of patients have a GBS>0 and would require inpatient management. A more recent study used a cutoff of ≤ 1 and show a 99.2% sensitivity when identifying low-risk patients, which identification would decrease the number of admitted patients admitted by half(3).

Aims & Methods: The aim of our study is to assess outcomes in patients with UGIB and GBS ≤ 1.

This was a prospective study on consecutive UGIB patients (variceal and non variceal) treated in "Virgen de las Nieves" University Hospital from 2013 to 2018. All patients underwent upper endoscopy. Information regarding clinical and biochemical data and procedures was collected. Documented clinical outcomes were in-hospital and delayed (6-months) mortality, rebleeding and delayed 6-months hemorrhagic and cardiovascular events. Descriptive and inferential statistical analysis was carried out.

Results: 632 UGIB patients were included,613 GBS>1 and 19 GBS≤1. GBS≤1 patients differed from GBS>1 in comorbidities (26.3%vs.75.4%; p<0.001), antithrombotic use (10.5%vs.38.2%; p=0.014), smoking habit (0%vs.20.8%, p=0.026), alcohol intake (5.26vs.18.99; p=0.001), melena at presentation (31.6%vs.70.1%; p< 0.001), loss of consciousness (0%vs.12.2%; p=0.027), pulse (80.26vs.90.32; p=0.003), urea (31.68vs.86.11; p<0.001), creatinine (0.79vs.1.21; p<0.001), hemoglobin (13.8vs.9.4 ;p<0.001), INR (1.01vs.1.56; p<0.001), endoscopic treatment (10.5%vs.43.9%; p=0.004), rebleeding (0%vs.17.8%; p=0.043), red cell units transfusions (0vs2.78; p<0.001), days of admission(1.37vs.8.89; p<0.001), in-hospital mortality (0%vs.10.1%;

p=0.047), delayed mortality (0%vs.11.1%; p=0.036), delayed hemorrhagic events (0%vs.19.2%; p=0.035), delayed cardiovascular events (0%vs9.5%; p=0.045). No differences were found in terms of sex, age, hematemesis, blood pressure, albumin, platelets and need for surgery or interventional radiology (0%vs4.1%; p=0.360).

Conclusion: This study showed patients with GBS≤1 are less complex and have great outcomes. This finding is similar to what has been previously described(3).

Being a referral center, our hospital takes care of a high number of patients with a special dedication to GI bleeding. This fact, as well as a 24/365 on-duty gastroenterologist determines a low threshold to perform urgent GI endoscopy.

In light of these findings we support what has been published previously, that is the safe outpatient management of patients with a GBS≤1. Delaying endoscopy in these cases would not have changed the results, with healthcare savings.

In conclusion, as international guidelines recommend, we should use a risk score to guide our performance.

References: 1. Monteiro S, Gonçalves TC, Magalhães J, et al. Upper gastrointestinal bleeding risk scores: Who, when and why? World Journal of Gastrointestinal Pathophysiology 2016;7:86-96 2. Stanley AJ, Laine L. Management of acute upper gastrointestinal bleeding. BMJ. 2019;25; 364:l536. 3. Laursen SB, Dalton HR, Murray IA, et al. Performance of new thresholds of the Glasgow Blatchford score in managing patients with upper gastrointestinal bleeding. Clin Gastroenterol Hepatol 2015;13:115-121.

Disclosure: Nothing to disclose

P1249 THE IMPACT OF ON-CALL VS. ON-DUTY ENDOSCOPIST IN MORTALITY AND CLINICAL OUTCOMES FOR PATIENTS WITH UPPER GASTROINTESTINAL BLEEDING: A PROSPECTIVE STUDY IN A TERTIARY CENTER

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Introduction: Upper gastrointestinal bleeding (UGIB) is a true emergency, associated with significant morbidity, mortality and healthcare costs. Several factors have been found to influence UGIB outcomes including the experience of the endoscopist, off-hours hospital admission, hospital volume and time to endoscopy(1). A recent meta-analysis shows that patients with UGIB who were admitted during off-hours had a significantly higher mortality and were less likely to receive endoscopy within 24 hours of admission. Indeed, there seems to be a strong correlation between timely endoscopic management and staff coverage in the hospital, particularly the availability of on-call endoscopists during off-hours(2).

Aims & Methods: The aim of our study was to compare whether there are differences in UGIB outcomes between two periods in our hospital, one with on-call endoscopist (OCE) and another with on-duty endoscopist(ODE). This was a prospective study on consecutive UGIB patients (variceal and non variceal) treated in "Virgen de las Nieves" University Hospital from 2013 to 2018 (OCE until July 2016, ODE afterwards, always a resident on-duty). Every patient underwent upper endoscopy in the first 24h. Information regarding clinical and biochemical data and procedures was collected. Documented clinical outcomes were in-hospital and delayed (6-months) mortality, rebleeding and delayed (6-months) hemorrhagic and cardiovascular events. Descriptive and inferential statistical analysis was carried out.

Results: 638 patients with a diagnosis of UGIB were included, 505 OCE and 133 ODE. Not differences were found between OCE and ODE in terms of in-hospital complications (15.8%vs.16.5%,p=0.845), number of red blood cell units transfusions (2.84vs.2.28;p=0.441),days of hospital stay (8.98vs.8.61;p=0.463), rebleeding(16.9%vs.18.9%;p=575), need for surgery or interventional radiology (4.4%vs.3%;p=0.484), acute mortality (9.7%vs.9.5%,p=0.960), delayed mortality (11.6vs.7.3%;p=0.177), delayed hemorrhagic events(18.5%vs.17.4%,p=0.855) or delayed cardiovascular events (9.1%vs.8.7%;p=0.922). Patients managed by ODE presented higher rate of mayor bleeding stigmata (64.2%vs.48.8%,p=0.005) and need for endoscopic treatment (50.4%vs.41.2%,p=0.045).

Conclusion: Our hospital is a tertiary and referal center, with an 24/365 on-duty endoscopist. In this study, we observed no differences in the main UGIB outcomes between patients management by OCE vs. ODE, compen-

sated probably by optimal timing and performance of endoscopy within 24 hours by an experienced endoscopist in the first period. This finding is in accordance with previous result from Xian Feng Xia et al. showing that in hospitals providing endoscopy outside normal hours, off-hours admission was not associated with an increased risk of mortality(2).

However, we found a higher rate of bleeding stigmata and need for endoscopy in ODE. This finding may be explained by the shortened lapse between admission and endoscopy. Longer delays might allow the physiological healing process to downstage endoscopic lesions, reducing endoscopic therapy requirements.

In conclusion, endoscopic attention during off-hours is important for the quality of care for patients with UGIB to warrant endoscopic performance within 24 hours(3) with no relevant differences between an on-call vs. on-duty endoscopist schedule.

References: 1. O'Byrne M, Smith-Windsor E, Kenyon CR, et al. Regional differences in outcomes of nonvariceal upper gastrointestinal bleeding in Saskatchewan. Can J Gastroenterol Hepatol. 2014; 28:135-9. 2. Xian Feng Xia, Philip Wai Yan Chiu, Kelvin Kam Fai Tsoi, et al. The effect of off-hours hospital admission on mortality and clinical outcomes for patients with upper gastrointestinal hemorrhage: A systematic review and meta-analysis of 20 cohorts. United European Gastroenterol J. 2018; 6: 367-381. 3. Stanley AJ, Laine L. Management of acute upper gastrointestinal bleeding. BMJ. 2019;25; 364:l536.
Disclosure: Nothing to disclose

P1250 OUTCOMES OF UPPER GASTROINTESTINAL BLEEDING SECONDARY TO NEOPLASM

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Introduction: Upper gastrointestinal bleeding (UGIB) is one of the main causes of hospital admission and urgent endoscopy in Gastroenterology departments and represents a true emergency, associated with significant morbidity, mortality and healthcare costs.

Bleeding from upper GI neoplasms (UGIN) has been reported to be responsible for 1-5% of all acute UGIB (1). Although surgical treatment has been shown to control the bleeding episode and improve survival, most patients present with advanced-stage unresectable cancer (2).

Endoscopy therapy has proven to be effective in these cases and hemostasis has been achieved in 67-100% of patients (3).

However, treatment outcomes for UGIB caused by neoplasms have been scarcely reported.
Aims & Methods: The aim of our study was to compare the outcomes of patients with UGIB secondary to neoplasms with those with UGIB secondary to other causes.

This was a prospective study on consecutive patients with UGIB (variceal and non variceal) treated in "Virgen de las Nieves" University Hospital from 2013 to 2017.

All patients underwent upper endoscopy, and information regarding clinical and biochemical data, procedures, and outcomes for 6 months after admission were collected. The clinical outcomes documented were in-hospital mortality and rebleeding. Descriptive analysis, bivariate analysis and multivariate logistic regression models were carried out.
Results: 638 patients with a diagnosis of UGIB were included, in 28 secondary to neoplasms. We included gastric neoplasm (12 patients), gastric polyps (8 patients), gastrointestinal stromal tumors (GIST)(4 patients), gastric lynphoma (3 patients) and a duodenal tumor invasion (1 patient). These patients differed from the rest in age, previous neoplasms history, heart failure, haemoglobin and platelets levels at admission, anticoagulant drugs intake and mortality within 6 months (table 1). They did not differ in comorbidities, interventions, complications, acute and rebleeding.

There were 5 patients (17,9%) who died in hospital, only one associated with the hemorrhage. Within the first 6 months, 6 patients died (21%), all of them due to disseminated cancer, not to GI bleeding.

Age (OR 1,04; 95% CI 1,01-1,07. p0,01) and previous neoplasm history (OR 20,78; 95% CI 1,63-265,44. p0,02) were independent risk factors for delayed-6months mortality.

Conclusion: In this study, we observed that UGIB due to neoplasms has a similar clinical curse in the acute episode than bleeding secondary to other causes with regards to in-hospital mortality, complications, need for interventions or rebleeding. We observed some differences in the long term outcomes such as mortality within 6 months after discharge. As expected, a previous neoplasm history is a clear predictor of mortality for these patients.

	Neoplasm	Others	p
Age	73,4	64,3	0,001
Previous neoplasm history	28,6%	12,3%	0,012
Heart failure	21,42%	9,67%	0,04
Haemoglobin	8,38	9,56	0,022
Platelets	269821	207542	0,006
Anticoagulant	32,1%	16,1%	0,026
Comorbidities (ASA>2)	64,3%	68,05%	0,67
Hospital stay (days)	12,29	8,92	0,12
Blood unit transfusion	3,29	2,69	0,38
Blood pressure	110,7	112,7	0,66
Endoscopic treatment	25%	39,7%	0,12
Rebleeding	3.7%	7,7%	0,71
Acute complications	14,28%	16,06%	0,53
Acute mortality	19,23%	9,24%	0,09
Mortality 6months	21%	10%	0,027

[Table 1]

References: 1. Schatz RA, Rochey DC. Gastrointestinal bleeding due to gastrointestinal tract malignancy: natural history, management and outcomes. Dig Dis Sci (2017) 62:491-501. 2. Kim Y, Choi J, Cho SJ et al. Outcome of endoscopic therapy for cancer bleeding in patients with unresectable gastric cancer. Journal of Gastroenterology and Hepatology (2013) 1489-1495. 3. Savides TJ, Jensen DM, Cohen J et al. Severe upper gastrointestinal tumor bleeding: endoscopic findings, treatment, and outcome. Endoscopy 1996; 28: 244-8.
Disclosure: Nothing to disclose

P1251 UPPER GASTROINTESTINAL BLEEDING IN SCOTLAND: TRENDS IN DEMOGRAPHICS AND OUTCOMES 2000-2015

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Introduction: Upper gastrointestinal bleeding (UGIB) remains a common cause of presentation and admission to hospital in the UK, with the incidence in Scotland one of the highest in the world. Over the past 15 years there have been several developments to improve management of patients with UGIB. Our aim was to investigate the number of patients presenting to Scottish hospitals with UGIB between 2000-2015 and assess the difference in demographics, aetiology of bleeding and clinical outcomes, including those for weekends and weekday presentations.
Aims & Methods: Data were collected from SMR01 hospital admissions records and GRO death certificates for the period 1st January 2000 to 31st December 2015 and analysed in the national safe haven. All outputs were disclosure-checked for confidentiality purposes. Admission and death rates were computed for each year with trends over the study period estimated using Poisson regression. Standard errors were adjusted to account for any serial dependence.
Results: A total of 129,404 patients presented to Scottish hospitals with UGIB between January 2000 and December 2015. Mean age at admission increased over this period from 59.2 years to 61.4 years (P=0.049). There was no difference in the annual number of patients over the 15-year pe-

riod. The incidence of UGIB was highest in the more deprived quintiles, although there was a reduction in incidence in the three most deprived quintiles over the study period (SIMD1; P< 0.001: SIMD2; P =0.002: SIMD3; P=0.001). There was a significant decrease in 30-day case-fatality from 10.1% in 2000 to 7.9% in 2015 (p< 0.001), which was significant across all the deprivation quintiles (P< 0.001). This reduction was seen for both variceal and non-variceal bleeding (IRR 0.967; P< 0.001 and IRR 0.980; P< 0.001 respectively) with deaths as a proportion of admissions declining fastest in the variceal compared to the non-variceal group (24.4% to 14.5%, and 9.8% to 7.8% respectively). The mean length of stay also fell from 3.9 days to 2.1 days, an average decline of 0.14 days per year (95% CI .15612 - .11723; P< 0.001). There was no difference in 30-day case-fatality between patients presenting at weekdays or weekends.

Conclusion: The number of patients presenting with UGIB to Scottish hospitals annually has remained similar over the 15-year study period. However case-fatality and length of hospital stay has fallen, despite a rise in the mean age of patients.

Disclosure: Nothing to disclose

P1252 PEPTIC ULCER BLEEDING - TIME TREND ANALYSIS OF INCIDENCE AND OUTCOME BETWEEN 2007 AND 2017

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Introduction: The aim of this study was to demonstrate differences in epidemiological, clinical, endoscopic characteristics and outcome of peptic ulcer bleeding (PUB) between 2007 i and 2017.

Aims & Methods: From January 2007 to December 2007 a total of 137 patients referred to our emergency department due to PUB, and from January 2017 to December 2017 a total of 128 patients referred to our emergency department due to PUB. They were screened and enrolled in this study.

Results: There was no statistically significant difference in PUB incidence between 2007 and 2017(38.8/100000 vs 36.3/100000). In 2017 74% patients with PUB was older than 65 years (p< 0.001). Men were the majority in both groups of patients (over 60%) and most of the patients were bleeding from stomach ulcers(more than 55%). In the year 2017 more patients were bleeding from high risk peptic ulcers(Forrest 1a, 1b, 2a i 2b)(63.3 vs 48.9%, p < 0.001). In 2017 most patients had moderately severe to severe comorbidities(50.3 vs 34.3%, p< 0.001). Initial hemostasis was performed more in 2017 than 2007(61.7 vs 40.9%, p < 0.001). There was no difference in the recurrence of bleeding(8.6 vs 6.7%), in required for surgical intervention(4.7 vs. 6.6%), 30-day mortality(7 vs. 4.4%) and need for red blood cell transfusion(55.5 vs 50.4%) between year 2017 and 2007. In 2017 significantly more patients received fresh frozen plasma transfusion(12% vs 4.4%, p < 0.05) and patients were longer hospitalized(7 vs. 6 days, p < 0.01). In the year 2017 and 2007 the majority of patients with PUB were taking agents that attenuate cytoprotective function of stomach and duodenal mucosa(51.1 vs 52.4%). In 2017 higher number of patients was taking anticoagulant and antiplatelet therapy compared to 2007(32.8 vs 13.3%, p < 0.01).

Conclusion: PUB predominantly occurs in older age groups with significant comorbidities, and it is associated with taking agents that attenuate cytoprotective function of stomach and duodenal mucosa, especially with antiplatelet and anticoagulant therapy.

References: 1. Holster IL, Kuipers EJ. Management of acute nonvariceal upper gastrointestinal bleeding: current policies and future perspectives. World J Gastroenterol. 2012 ;18:1202-7. 2. van Leerdam ME. Epidemiology of acute upper gastrointestinal bleeding.Best Pract Res Clin Gastroenterol. 2008;22:209-24. 3. Nagashima K, Tominaga K, Fukushi K, Kanamori A, Sasai T, Hiraishi H.Recent trends in the occurrence of bleeding gastric and duodenal ulcers under the Japanese evidence-based clinical practice guideline for peptic ulcer disease. JGH Open. 2018;2:255-261.

Disclosure: Nothing to disclose

P1253 RIKKUNSHITO INCREASED APPETITE THROUGH THE ACTIVATION OF VTA, REWARD CENTER IN BRAIN

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Introduction: reviously we reported that Rikkunshito (RKT), Japanese herbal medicine improved urocortin1-induced appetite loss through an increase in ghrelin< span> < /span>secretion in rats [Am J Physiol Endocrinol Metab 2011; 301: E72-82, Psychoneuroendo-crinology, 2014;50:300-10]. Recently RKT was also elucidated to improve symptoms of functional dyspepsia (FD) [Neurogastroenterol Motil 2018; 30]. In the present study, we undertook to elucidate a mechanism for orexigenic effects of RKT in the central nervous system using in-vivo experiment with rats. To study effects of RKT on the function of< span> < /span>brain, we evaluated expression of c-Fos as an indicator of activation of neurons in the nuclei of appetite control system and reward system in the brain. Then the activation of dopamine neuron was also evaluated using immunohistochemical staining of tyrosine hydroxylase (TH) which is the rate-limiting enzyme in the synthesis of dopamine and norepinephrine.

Aims & Methods: Study on appetite: As anorexic models, rats with cholecystokinin-8 (CCK) administration and restraint stress (RS) were used, because these factors were known to induce anorexia and were supposed to be involved in the pathophysiology of FD. Effects of CCK or/and restraint stress on food intake were examined with or without RKT. To elucidate the involvement of brain in the actions of RKT, RKT was given to rats 2 hrs before treatments with CCK and RS. The brains were fixed with transcardial perfusion with paraformaldehyde and glutaraldehyde, and the brains were removed and continuously fixed and cut into serial transverse sections. The sections were incubated with anti-c-Fos polyclonal antibody solution followed by incubation with anti-TH antibody and the immunohistochemical staining was performed. Numbers of c-Fos-immunoreactive (ir) neurons or TH-immunoreactive (ir) neurons were counted under bright field microscope.

Results: 1. RKT significantly (p< 0.05) restored food intake inhibited by the combination of CCK and RS. RKT increased c-Fos-ir neurons not only in the neuclei on hypothalamus but also in ventral tegmental area (VTA) [RKT(-): RKT (+) 298±34 : 631.3±30, p< 0.01] and nucleus accumbens (Nac) [RKT(-): RKT (+) 111.0±19 : 232±35, p< 0.05] in CCK and RS-treated rats. Number of neurons double-stained with anti-c-Fos antibody and anti-TH antibody was markedly increased by RKT in VTA [RKT(-): RKT (+) 13±1.7 : 74±17, p< 0.05]. GHSR1A (ghrelin receptor) antagonist, D-Lys[3]-GHRP-6 suppressed RKT-induced increase in food intake and c-Fos expression in the neurons of VTA in CCK and RS-treated rats.

Conclusion: The result suggests that RKT restores appetite through the ghrelin-dependent activation of the neurons in reward system such as VTA and Nac. The results may explain the mechanism for the effects of RKT to improve appetite in patients with anorexia due to FD and other causes.

Disclosure: Nothing to disclose

P1254 EX VIVO IMAGING OF NEURONAL ACTIVATION BY USING GCAMP6S IS SUITABLE FOR PHARMACOLOGICAL STUDIES OF ION CHANNELS MEDIATING ACTION POTENTIAL CONDUCTION IN THE AXONS OF VISCERAL NOCICEPTORS

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Introduction: The information about noxious and inflammatory stimuli in the visceral organs is transmitted to the central nervous system by the action potentials conducted in the axons of visceral pain-mediating afferent nerves (nociceptors). Although it is well established that the voltage-gated sodium channels (NaV1) are essential for the action potential conduction, it is unknown which of 9 known NaV1 subunits (NaV1.1 thorough NaV1.9) mediate the action potential conduction in the axons of visceral nociceptors. Selective inhibition of the NaV1s mediating action potential conduction in nociceptors could aid the treatment of visceral pain. Unfortunately, the electrophysiological single fiber recording is extremely time consuming for this type of studies.
Aims & Methods: To evaluate the hypothesis that ex vivo imaging of neuronal activation by the calcium indicator GCaMP6s expressed in sensory neurons is suitable for pharmacological studies of NaV1 channels mediating the action potential conduction in the axons of visceral nociceptive (capsaicin-sensitive) neurons.
Methods: The vagus nerve with the sensory jugular/nodose ganglion (JNG) was isolated from the Pirt-Cre;R26-GCaMP6s mice in which virtually all JNG neurons express GCaMP6s. The distal end of the vagus nerve was electrically stimulated by the concentric electrode and the resulting activation of JNG neurons was detected by imaging GCaMP6s with multiphotone microscopy (excitation wavelength 920nm,6-10 optical sections separated by 20μm, frame rate 0.17Hz). NaV1 inhibitors were selectively superfused (37°C) over the desheathed segment of the vagus nerve between the stimulation electrode and JNG. The putative nociceptive subset of vagal neurons was identified by the GCaMP6s response to capsaicin (1μM) applied to JNG.
Results: Vagal electrical stimulation with increasing frequency 0.5-10Hz (pulse 1ms, 100V) for 20s evoked increasing intensity of the GCaMP6s signal in JNG neurons. When normalized to the signal at 5Hz, the signal evoked by 0.5, 1, 3, 5 and 10Hz was 6±1%, 16±1%, 67±2%, 100±0% and 134±5%, respectively (N=160 capsaicin-sensitive neurons). Therefore, the stimulation with 5Hz was used. The NaV1 inhibitor tetrodotoxin (TTX, 0.1μM) applied to the vagus nerve completely abolished activation evoked by 5Hz electrical stimulation of the vagus nerve in 88% of capsaicin-sensitive neurons (N=93). This is consistent with the previous findings that TTX-sensitive NaV1s are required for action potential conduction in the vast majority of axons in the vagus nerve. The selective NaV1.7 inhibitor PF-05089771 (3μM) applied to the vagus nerve completely abolished activation evoked by 5Hz electrical stimulation of the vagus nerve in 57% of capsaicin-sensitive neurons (N=282).
Conclusion: Our data show that the activation of vagal neurons evoked by electrical stimulation of the vagus nerve and detected by calcium reporter GCaMP6s expressed in vagal neurons can be abolished in the predictable all-or-none fashion by NaV1 inhibitors applied to the vagus nerve. We conclude that ex vivo imaging of neuronal activation by the GCaMP6s expressed in sensory neurons is suitable for the pharmacological studies of the NaV1 channels mediating the action potential conduction in the axons of visceral nociceptive neurons.
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Disclosure: Nothing to disclose

P1255 THE GASTROPEPTIDE PGP REMOVES GLUTAMATE-INDUCED CHANGES OF [CA^{2+}]$_I$ AND MITOCHONDRIAL POTENTIAL IN CULTURED NEURONS AND REDUCES THEIR DEATH

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Introduction: Glutamate (Glu) is the major excitatory neurotransmitters of a brain, but an excess of Glu, results in hyperactivation and subsequent death of neurons. The tripeptide Pro-Gly-Pro (PGP) is a fragment of various regulatory oligopeptides. PGP effectively protects the gastric mucosa from stress-induced ulcers and damage caused by prolonged administration of monosodium glutamate (food supplement).
Aims & Methods: We studied the effects of PGP (10 uM), its N-acetylated and N-phosphorylated derivative (AcPGP and P-PGP) on the intracellular Ca^{2+} concentration ([Ca^{2+}]$_i$), mitochondrial potential (ΔΨm) and cell survival of primary neuroglial cultures subjected to glutamate excitotoxicity. Primary cultures were prepared from the cortex 1-2-day old Wistar rats. Single cell [Ca^{2+}]$_i$ and ΔΨm fluorescence microscopy measurements were performed employing Fura-FF and Rh123, respectively. The survival of neuroglial cultures was studied using vital fluorescent dyes Syto-13 and EthD-1. Peptides were synthesized at the IMG RAS. The experiments with animals were carried out in accordance with the declaration on the human behavior towards animals and in accordance with the Order of the Ministry of Healthcare and Social Development of Russia "On Approval of Laboratory Practices".
Results: PGP and AcPGP by itself were not neurotoxic. In contrast to them P-PGP revealed a weak neurotoxicity reducing cell survival by ~20%. Glu reduced the ratio of live/dead cells by ~45%. Addition of PGP ~30min prior to Glu application increased the proportion of live cells by ~27%. It is has been shown earlier that the acetylation of PGP makes it more resistant to prolyl peptidases preventing its hydrolysis. However PGP but not AcPGP delayed the development of the Glu-induced delayed calcium deregulation (DCD) and synchronous with DCD profound drop of ΔΨm.
Conclusion: Uncovered earlier gastroprotective effect of the peptide PGP against monosodium Glu-induced ulcer could be, at least partially, related to neuroprotection of gut innervation. We have shown that PGP (10 μM) diminish the excitotoxic effect of Glu 33 μM and promote recovery of [Ca^{2+}]$_i$ and mitochondrial potential after Glu removal from the cell culture. Acetylation or phosphorylation of the N-terminus of PGP prevented its neuroprotective effect. In our early studies it has been shown that dipeptide GP has a pronounced gastroprotective effect on the stressor model of ulcer formation. Probably the gastro-neuroprotective effect of PGP is partially mediated by its dipeptide moiety GP.
Disclosure: Nothing to disclose

P1256 EVALUATION OF GASTROINTESTINAL MOTILITY IN PATIENTS WITH MIONEUROGASTROINTESTINAL ENCEPHALOPATHY (MNGIE)

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Introduction: Myoneurogastrointestinal encephalopathy (MNGIE) is a rare mitochondrial disease caused by mutations in the thymidine-phosphorylase enzyme gene. Clinically it is characterized by severe gastrointestinal dysmotility associated with cachexia and a demyelinating sensory-motor

polyneuropathy. Given the low incidence (1-9 per million), most patients are mistakenly diagnosed of other digestive diseases. Despite the fact that gastrointestinal symptoms are progressive and invariably lead to death, there are so far no studies evaluating gastrointestinal function in these patients.

Aims & Methods: We retrospectively studied patients with biochemically and genetically confirmed MNGIE who had been referred for evaluation of gastrointestinal function to our Motility Unit between August 2008 and January 2019.

Results: In this period, 8 patients ultimately diagnosed of MNGIE (age range 16-41 years, 5 men and 3 women) were evaluated. At the time of referral, 5 of the 8 patients were misdiagnosed as Crohn's disease (n = 2), celiac disease (n = 1) and superior mesenteric artery syndrome (n = 2). All patients were severely underweight (BMI range 9 - 15.4 kg/m2) and complained of chronic digestive symptoms including abdominal pain, vomiting and diarrhea; six of them required total parenteral nutrition. All patients except one, showed radiological signs suggestive of intestinal pseudo-obstruction: air-fluid levels by plain abdominal x-ray and intestinal dilatation by CT scan in the absence of mechanical obstruction. Specific motility tests were performed depending on clinical symptoms and the patient's tolerance. Gastric emptying evaluation by scintigraphy was performed in 5 patients and detected gastroparesis in 4. Esophageal manometry was performed in 5 patients, all of which exhibited ineffective motility and a hypotensive lower esophageal sphincter. Small bowel manometry was performed in 4 patients and all showed a rare giant non-propagating contraction pattern. In 3 of them this manometric pattern helped to establish the diagnosis of MNGIE within the clinical context. Six of the 8 patients died (1 to 60 months after diagnosis, median 2 mo) due to gastrointestinal complications of the disease.

Conclusion: In patients with MNGIE severe digestive symptoms due to gastrointestinal dysmotility often lead to misdiagnosis. We have detected a specific intestinal dysmotility pattern which may help to identify patients with MNGIE.

Disclosure: Nothing to disclose

P1257 OBESITY DOES NOT IMPACT OUTCOMES OR RATES OF GASTROESOPHAGEAL REFLUX AFTER PERORAL ENDOSCOPIC MYOTOMY IN ACHALASIA

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Introduction: Outcomes of laparoscopic Heller's myotomy (LHM) in obese patients with achalasia are sub-optimal along with increased risk of gastroesophageal reflux disease (GERD). The impact of obesity on treatment success and GERD after POEM are not well known. Hence our study aims were to compare the clinical outcomes and rates of GERD after POEM in non-obese versus obese patients with achalasia.

Aims & Methods: Chart review of all achalasia patients who underwent POEM at our institution between April 2014 and June 2018 was performed. Patients with timed barium oesophagram (TBE) and high-resolution oesophageal manometry (HREM) prior to POEM along with post-POEM TBE, HREM and oesophageal pH study were included. Patients were categorized into two groups, non-obese (body mass index, BMI< 30 kg/m^{2}) and obese (BMI≥30 kg/m^{2}). Patient demographics, TBE, HREM, pH study findings and Eckardt scores were compared between the two groups.

Results: A total of 89 patients (46 non-obese; 43 obese) met the study criteria. There were no significant differences in age, gender, achalasia subtype, operative time, length of stay (LOS) and complication rates between the two groups. Treatment success (Eckardt score <3) was similar in both groups (97.7% non-obese vs 92.7% obese, p=0.35). Abnormal DeMeester scores on pH study (>14.72) were similar in non-obese and obese patients (58.7% versus 46.5%, p=0.25). Symptomatic GERD was also similar in both groups (17.8% in non-obese vs. 20% in obese, p=0.79).

Conclusion: POEM is an equally safe and effective treatment option for both non-obese and obese patients with achalasia in the short term. Interestingly, POEM does not lead to higher rates of GERD in obese compared to non-obese patients.

Disclosure: Nothing to disclose

Factor	Non-obese (n=46) (mean BMI: 25.1 ± 2.4 kg/m2)	Obese (n=43) (mean BMI: 36.2 ± 5 kg/m2)	p-value
Age at POEM (years)	58.1±16.4	56.6±13.9	0.64
Operative time (minutes)	102.5[84.0,120.0]	98.0[79.0,118.0]	0.51
Rate of complications	2.2%	4.7%	0.61
Pre-POEM Eckardt score	7.0[5.0,8.0]	6.0[5.0,8.0]	0.46
Pre-POEM Eckardt score	0.00[0.00,1.00]	1.00[0.00,2.0]	0.16
POEM success rate	97.7%	92.7%	0.35
POEM failure rate	2.3%	7.3%	0.35
Rate of symptomatic GERD	17.8%	20%	0.79
Abnormal DeMeester score on 24-hr oesophageal pH study	58.7%	46.5%	0.25

[Patient demographics, procedural details and outcomes]

P1258 EFFICACY OF GASTRIC ELECTRICAL STIMULATION IN INTRACTABLE NAUSEA AND VOMITING AT 10 YEARS: A RETROSPECTIVE COHORT STUDY

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Introduction: Gastric electrical simulation has been shown to relieve vomiting and nausea in medically refractory patients. Efficacy of gastric electrical stimulation has been reported mostly in short term studies, however no studies have evaluated its efficacy beyond 10 years after implantation.

Aims & Methods: Patients implanted at our center for medically refractory severe and chronic nausea and/or vomiting were evaluated at baseline and over 10 years after implantation using symptomatic scale and quality of life score (GIQLI score). Improvement was defined a s a reduction of more than 50% of the vomiting frequency.

Results: 50 patients were implanted from January 1998 to December 2009. The mean follow-up was 10.5 (+/- 3.7) years. Among the 50 patients, 7 were explanted due to a lack of efficacy, 2 patients died and 4 were lost to follow-up. Out of the 37 patients evaluated, 27 (73%) showed a reduction of of the frequency of vomiting episode by at least 50%. In intention to treeat analysis, 27/50 (54%) of patients reported an improvement. Beyond 10 years, an score improvement of early satiety (3.05 vs 1.76 , < 0.001), bloating (2.51 vs 1.70, p = 0.012), nausea (2.46 vs 1.35 , p=0.001), and vomiting (3.35 vs 1.49 p < 0.001) was observed. Quality of life was improved over 10 years (GIQLI score: 69.7 vs. 86.4, p = 0.005) as well as body mass index (BMI: 23.4 vs. 26.2 p = 0.048).

Conclusion: Gastric electrical simulation is safe and effective in the long term in patients with medically refractory nausea and vomiting, with an efficacy of 54% at 10 years on an intention to treat analysis.

Disclosure: Chloe Melchior has interests with MSD, Kyowa Kirin, Mayoly Spindler; Guillaume Gourcerol has interests with Allergan, Kyowa Kirin, Biocodex, Sanofi, Mayoly Spindler, Laborie. All other authors have no conflicts of interest of financial ties to disclose.

P1259 PER-ORAL ENDOSCOPIC MYOTOMY (POEM) IS A SAFE AND EFFECTIVE TREATMENT OPTION FOR MORBIDLY OBESE PATIENTS WITH ACHALASIA

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Introduction: With global epidemic of obesity, it is not uncommon to encounter morbidly obese patients with achalasia. The management of morbidly obese or class III obesity patients (BMI ≥40 kg/m^2) with achalasia is complex and the existing literature is sparse. We conducted a study to assess the outcomes of per-oral endoscopic myotomy (POEM) in morbidly obese patients with achalasia.

Aims & Methods: Medical records of all the achalasia patients who underwent POEM between April 2014 and June 2018 at our institution were reviewed. Morbidly obese patients (BMI ≥40) who underwent timed barium oesophagram (TBE) and high-resolution oesophageal manometry (HREM) prior to POEM along with 2-month post-POEM oesophageal pH study, TBE and HREM were included. Demographics, type of achalasia, prior interventions, TBE, HREM, Eckardt scores and pH study findings were analyzed. Eckardt score of ≤3 was considered as successful palliation of symptoms. Wilcoxon singed rank tests were used to assess changes in HREM and TBE findings (pre-POEM vs. 2 month post-POEM) and a p-value < 0.05 was considered statistically significant.

Results: A total of 13 patients met the study criteria. Average age at POEM was 56.1±1 years, with majority of the patients being females (69%; n=9) and Caucasians (58.3%; n=7). Mean duration of achalasia symptoms was 6 years [1.0, 8.0] and type-II achalasia was most prevalent. 23% (n=3) and 30% (n=4) patients had undergone prior treatment with botulinum toxin and pneumatic dilation respectively. Median operative time was 80 minutes [63.0,100.0] and average total myotomy length was 8.8±0.80 cm. There were no complications except for post-operative pneumonia in 1 patient. POEM was successful in 92% (12/13) of the patients. Significant improvement was noted in post-procedure Eckardt's scores, basal mean pressure and integrated relaxation pressure on two month follow up. In addition, there was significant improvement in the width of barium column at 1 minute and height at 5 minutes. A trend of improvement was noted in height of barium column at 1 minute and width at 5 minutes, but it did not reach statistical significance. In the post-POEM pH study, DeMeester scores were abnormal in 70% (7/10) of patients, however only 10% (1/10) of patients complained of gastro-oesophageal reflux (GOR) symptoms.

Conclusion: POEM is a safe and effective treatment option for morbidly obese patients with achalasia. POEM leads to significant improvement in Eckardt scores, HREM and TBE parameters at short-term follow up. Although symptomatic reflux was low, a significantly higher rate of abnormal oesophageal acid exposure was noted on objective testing.

Disclosure: Nothing to disclose

Factor	Class III obese patients (n=13)
Age at POEM (years)	56.1±13.5
Operative time (minutes)	80.0 [63.0,100.0]
Complications	7.6% (n=1) post-operative pneumonia
Pre-POEM Eckardt score	6.0[6.0,8.0]
Post-POEM Eckardt score	0.00[0.00,1.5]
POEM success rate	91.7%
POEM failure rate	8.3%
Rate of symptomatic GERD	10% (n=1)
Abnormal DeMeester score on 24-hr oesophageal pH study	70% (n=7)

[Patient demographics, procedural details and outcomes]

P1260 ENDOSCOPIC PYLOROMYOTOMY (G-POEM), EFFICACY EVALUATION AFTER ONE YEAR, IN REFRACTORY GASTROPARESIS: FRENCH MULTICENTRIC STUDY

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Introduction: Long term results of G-POEM for refractory gastroparesis are lacking. Here we report the results of the largest multicenter study with long term follow up about G-POEM for refractory gastroparesis.

Aims & Methods: Retrospective, multicentric study of all G-POEM cases, performed in seven French expert centers, for refractory gastroparesis, within at least one year of follow up

Primary Endpoint: One year clinical success defined by improvement of GCSI by at least one point.

Secondary Endpoints: complications rate, identification of predictors of clinical success, clinical success at two years.

Our inclusion criteria were, at least one year follow up, and available GCSI score prior GPOEM and 12 months after.

Exclusion criteria were missing GCSI score, technical failure, normal gastric emptying scintigraphy and loss of follow up.

Results:

Description of the population: 133 patients were analysed in 7 French expert centers and 10 diferent operators. Among them we included 92 patients for the efficacy analysis, 61% were women, the median age was 55 years old. About aetiologies : 35% diabetes, 26% post-surgery, and 33% idiopathic. The median evolution duration of the symptoms was 40 months. Twenty seven percents had already a prior interventional treatment. The median 4h% remaining in stomach before G-POEM, was 45%. The mean GCSI average before G-POEM was 3,6.

Technical success was achieved in 99,2%.

Primary Endpoint:Clinical success was achieved in 65,2% at one year , with a mean GCSI amelioration of 41%. The GCSI score decrease significantly one year after the GPOEM (p=0,0001)

Secondary Endpoints: In univarieted analysis, we identified predictives factors of success, wich are a high Satiety subscore in GCSI score (2,12 [1,31-3,44], p=0,002), an elevated pre-operative GCSI score (1,85 [1,07-3,20], p=0,027) and an advanced age (1,03 [1,00-1,06], p = 0,04). We also identified predictives factors of failure, which are a BMI >20kg/m^2 (0.62 [0.39-1.00], p=0,048) and an elevated gatric retention rate on pre-operative gastric emptying scintigraphy (0,98 [0,961,00], p=0,048).

We noticed any immediate complication, and only 6% of later complications.

At two years clinical success was maintained at 73,2% (n=41).

Conclusion: This large and multicentric study confirms the efficiency and safety of G-POEM in the treatment of refractory gastroparesis The clinical success after one year is achieved for 65% of the patients. We identified interesting predictives factors of succes. G-POEM should be the first treatment in case of refractory gastroparesis.

Disclosure: Nothing to disclose

P1261 ENDOLUMINAL FUNCTIONAL LUMEN IMAGING PROBE (ENDOFLIP) PREDICTS THE OUTCOME OF GASTRIC PER-ORAL ENDOSCOPIC PYLOROMYOTOMY (GPOEM): A MULTICENTER PROSPECTIVE STUDY

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Introduction: Gastroparesis is a complex and a disabling gastrointestinal motility disorder characterized by delayed gastric emptying without physical stomach obstruction and its management is challenging due to the limited relief that traditional treatment options provide Gastric peroral endoscopic myotomy (GPOEM) has emerged as a promising novel endoscopic technique for the management of refractory gastroparesis. Despite the promising outcomes, the main challenge remains in identifying the subset of patients with pylorospasm that will potentially benefit the most from the procedure. Endoluminal Functional Lumen Imaging Probe (EndoFLIP) is a novel device that evaluates sphincter physiologic parameters including distensibility; however, the role of EndoFLIP in G-POEM is still unknown.
Aims & Methods: Aim is to determine the association of EndoFLIP measurements with symptoms improvement following GPOEM in patients with refractor gastroparesis. In this prospective multicenter study, EndoFLIP evaluation was performed on patients who underwent G-POEM procedure for management of gastroparesis. EndoFLIP measurements, including pre- and post-G-POEM pylorus diameter (D) (mm), cross-sectional area (CSA) (mm2), pressure (P) (mmHg), compliance (C) (mm2/mmHg), and distensibility index (DI) (mm2/mmHg), were recorded at 40 ml bag volume. Delta (d) of each measurement was defined as the change of value from prior to after G-POEM. Clinical success was defined by at least one score decrease in the total Gastroparesis Cardinal Symptom Index (GCSI) scoring system with more than a 25% decrease in at least 2 of its sub-scales.
Results: A total of 36 patients (23 [63.9%] female, median age 55yr [IQR: 43.3-62.0]) at 4 tertiary centers (3 US, 1 Europe) underwent G-POEM with EndoFLIP evaluation and were followed for 6 months. Clinical success was achieved in 19 (52.8%) patients at 6 months. Comparing mean Endoflip measurements between patients with and without clinical success, pre G-POEM P was significantly lower (14.22 ± 4.54 vs 19.04 ± 7.81, p=0.35), while post G-POEM D (14.59 ± 2.54 vs 10.91 ± 4.62, p=0.007) and post G-POEM CSA (171.97 ± 56.88 vs 108.92 ± 82.53, p=0.016) were significantly higher in patients who achieved clinical success (Table. 1).

	Pre-GPOEM measurements		P-Value	Post-GPOEM measurements		P-Value
	Patients without symptom improvement	Patients with symptoms improvement		Patients without symptom improvement	Patients with symptoms improvement	
Diameter	12.08 (SD 3.81)	11.99 (SD 3.17)	0.938	10.91 (SD 4.62)	14.59 (SD 2.54)	0.007
CSA	125.22 (SD 77.38)	120.33 (SD 51.27)	0.831	108.92 (SD 82.53)	171.97 (SD 56.88)	0.016
Pressure	19.04 (SD 7.81)	14.22 (SD 4.54)	0.035	17.44 (SD 7.56)	17.44 (SD 5.22)	0.942
DI	6.57 (SD 3.63)	9.94 (SD 6.14)	0.086	7.58 (SD 8.24)	7.58 (SD 8.24)	0.362
Compliance	131.48 (SD 72.37)	198.09 (SD 121.45)	0.087	151.65 (SD 164.45)	151.65 (SD 164.45)	0.265

[Comparison of EndoFLIP measurements in patients with vs without symptoms improvement]

Logistic regression model identified pre G-POEM C (OR = 1.023, 95% CI 1.001-1.045), dD (OR = 2.156, 95% CI 1.106-4.204), and dP (OR = 1.311, 95% CI 1.001-1.716) to be independent predictors of clinical success at 6 months after G-POEM. Receiver operating characteristic (ROC) analysis revealed that dD, with an area under the curve (AUC) of 0.785 (95% CI 0.625-0.946), had the highest accuracy for prediction of clinical success, providing specificity of 77% and sensitivity of 63% at a cut-off point of 2.3 mm. On the other hand, dP with AUC of 0.737 (95% CI 0.564-0.909), and pre G-POEM C with AUC of 0.664 (95% CI 0.470-0.858) had lower predicting accuracies.
Conclusion: Increase of at least 2.3 mm in pylorus diameter post-GPOEM procedure is useful for predicting clinical success in patients with gastroparesis. EndoFLIP may have a potential role in identifying G-POEM candidates among patients with refractory gastroparesis, thus allowing better.
Disclosure: Dr. Mouen Khashab is a consultant for Medtronics, Dr. Vivek Kumbhari is a consultant for Medtronics.

P1262 COMPARISON OF PER-ORAL ENDOSCOPIC MYOTOMY (POEM) OUTCOMES BETWEEN PATIENTS WITH RECURRENT SYMPTOMS AFTER PRIOR PNEUMATIC DILATATION (PD) AND PRIOR LAPAROSCOPIC HELLER'S MYOTOMY (LHM)

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Introduction: Pneumatic dilation (PD) and laparoscopic Heller's myotomy (LHM) are established treatment options for achalasia. However, recurrence of symptoms requiring re-interventions is not uncommon during long-term follow-up. Per-oral endoscopic myotomy (POEM) is emerging as an effective treatment modality for palliation of symptoms in such patients. In this study, we compared the outcomes of POEM between patients with recurrent symptoms after prior PD and LHM
Aims & Methods: Medical records of all the achalasia patients who underwent POEM between April 2014 and June 2018 were reviewed. Patients who underwent timed barium oesophagram (TBE) and high-resolution oesophageal manometry (HROM) prior to POEM along with 2-month post-POEM oesophageal pH study, TBE and HROM were included. Patients were categorized into two groups as: failed PD (no exposure to LHM) and failed LHM (no exposure to PD). Patients in either groups might have had prior Botox injections. Patient details, TBE, HROM, pH study findings and Eckardt scores were compared between the two groups.
Analysis of covariance was performed to assess the association between prior treatment groups and 2-month outcomes while adjusting for possible confounders and a p-value < 0.05 was considered statistically significant.
Results: A total of 49 patients (failed PD=28; failed LHM=21) met the study criteria. There were no significant differences in demographics, myotomy length or complication rates between the two groups. However, patients with failed PD were more likely to be obese, with higher ASA classification and required shorter operative time. There was a significant improvement in Eckardt scores, HROM and TBE parameters at 5 minutes in both groups. POEM success rate was similar at 96.3% and 90% in failed PD and failed LHM groups respectively (p=0.57).
Patients in failed LHM group did not have a significant change in 1-minute TBE measures. On univariate analysis, patients in failed PD group had significantly higher pre-POEM LES basal pressure and lower width of barium column at 1 and 5 minutes. In addition, patients in failed PD group had significantly lower post-POEM barium height and width at 1 and 5 minutes. On adjusted analysis, change in height of barium column at 1-minute was significantly higher in patients in failed PD group. There were no differences in the pH study findings such as DeMeester scores and/or total acid exposure times between the two groups.
Conclusion: POEM is safe and equally effective treatment modality for successful palliation of symptoms in patients with recurrent symptoms after both PD and LHM. Operative time is shorter and there was greater improvement in TBE parameters in prior PD group. Post POEM GERD rates were similar in both groups. Long-term efficacy studies of POEM are needed in these patients.
Disclosure: Nothing to disclose

Factor	Failed pneumatic dilatation (PD); (n=28)	Failed laparoscopic Heller myotomy; (n=21)	p-value
Operative time (minutes)	80.5 [70.0,101.0]	110.0 [87.0,130.0]	**0.008**
Rate of complications	0 (0%)	1 (4.8%)	0.43
Pre-POEM Eckardt score	6.0[5.0,9.0]	6.0[5.0,8.0]	0.66
Post-POEM Eckardt score	1.00[0.00,2.0]	0.00[0.00,2.0]	0.77
POEM success rate	96.3%	90%	0.57
POEM failure rate	3.7%	10%	0.57
Rate of symptomatic GERD	18.5%	11.1%	0.68
Abnormal DeMeester score on 24-hr oesophageal pH study	53.8%	47.1%	0.66

[Patient demographics, procedural details and outcomes]

P1263 HIGH RESOLUTION MANOMETRY TRADITIONAL PARAMETERS ARE NOT USEFUL TO PREDICT RESPONSE TO ENDOSCOPIC TREATMENT IN PATIENTS WITH ESOPHAGO-GASTRIC JUNCTION OUTFLOW OBSTRUCTION

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Introduction: According to Chicago Classification vers. 3.0, Esophago-Gastric Junction Outflow Obstruction (EGJ-OO), is a major oesophageal motor disorder characterized by an elevated IRP (i.e. higher than 15 mmHg*s*cm with Medtronic device) and preserved peristalsis. Pathogenesis and treatment of this high-resolution manometry (HRM) diagnosis is unknown, although the majority of the experts agree on using endoscopic dilation or botox injection, particularly in patients reporting dysphagia and weight loss. To date, limited data are available to support the hypothesis that HRM may be of clinical value in identifying patients who will respond to endoscopic therapy.

Aims & Methods: We aimed to investigate whether HRM features could be useful to predict the therapeutic outcome in EGJ-OOpatients undergoing endoscopic therapy.Patients with symptoms of esophageal dysfunction (e.g. dysphagia, chest pain, and regurgitation) underwent upper endoscopy to rule out organic disease, and thereafter HRM. Symptom severity was assessed by a Likert type scale with four items, from 0 (absent symptom) to 3 (severe symptom), for each symptom. A manometric diagnosis of EGJ-OO was made according to CC ver. 3.0. and in case of drugs-unresponsive (i.e. calcium channel blockers or phosphodiesterase 5 inhibitors) symptoms after six months, an endoscopic treatment (pneumatic dilation or botox injection) was proposed to the patients. We opted for using botulinum toxin injection in elderly subjects (> 75 years) or in case of relevant co-morbidities. Clinical response was defined by a symptom score of 0 or 1 for the main symptom (i.e. the leading one requiring outpatient visit and further investigations). Only patients with a follow-up of at least 6 months were considered.

Results: Thirteen [8M, mean age 64 (50-83)] patients with EGJ-OO underwent endoscopic treatment (11 pneumatic dilation and 2 botulinum toxin injection). In the group treated by pneumatic dilation, 9/11 (82%) had a good response and 2 failed thetreatment. Among the two patients who underwent botox injection, 2/2 (100%) had a good response. The difference in efficacy of the two treatments was found to be not statistically significant by Fisher's test (p=ns) analysis. By using uni- and multivariate regression analysis, a monometric parameter predictive of response to treatment was not observed (p=ns).

Conclusion: Traditional HRM parameters are not useful to predict the response of EGJ-OO patients to endoscopic treatment. Further metrics should be developed in order to understand which patients may benefit of endoscopic treatment in case of EGJ-OO diagnosis
Disclosure: Nothing to disclose

P1264 MULTIPLE RAPID SWALLOW DISCRIMINATES FUNCTIONAL FROM ANATOMICAL ESOPHAGO-GASTRIC JUNCTION OUTFLOW OBSTRUCTION

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Introduction: According to Chicago Classification vers. 3.0, Esophago-Gastric Junction Outflow Obstruction (EGJ-OO), is a major oesophageal motor disorder characterized by an elevated IRP (i.e. higher than 15 mmHg*s*cm with Medtronic device) and preserved peristalsis. In case of EGJ-OO, an evaluation by using Computer tomography (CT) or ultrasound endoscopy (EUS) has been suggested in order to rule out presence of organic disease. Indeed, at least 50% of EGJ-OO is associated with anatomical abnormalities, including hiatal hernia, peptic stricture, previous foregut surgery or EGJ cancer.

Aims & Methods: We aimed to evaluate whether additional high-resolution manometry (HRM) tests such as multiple rapid swallow (MRS) and rapid drinking challenge (RDC) can discriminate between functional and anatomical EGJ-OO in order to further select which patients should undergo radiology or EUS. Consecutive patients referred to Digestive Physiopathology Unit of the Gastroenterology Unit of Padua University and complaining of oesophageal symptoms were enrolled. Each patient underwent to upper endoscopy and esophagogram with barium and thereafter an oesophageal HRM was performed. In case of IRP>15 mmHg*s*cm without a pattern of achalasia, a diagnosis of EGJ-OO was established. Anatomical EGJ-OO was defined by the presence of: hiatal hernia, abnormalities induced by previous foregut surgery, peptic strictures, mucosal or submucosal lesions, and eosinophilic esophagitis. Only in absence of any of these diagnoses, a functional EGJ-OO was defined. Patients assuming opioid drugs chronically were excluded from the analysis.

Results: Forty-nine patients with EGJ-OO were enrolled [24 Male, mean age 49 (10-83)]. Fourteen (29%) presented an anatomical abnormality, whereas thirty-five (71%) were has a functional EGJ-OO. Multiple Rapid Swallow test was available in thirty-seven patients and was abnormal in 8/9 of anatomical EGJ-OO and in 13/28 of functional EGJ-OO. Using Fisher's test, the difference in percentage of abnormal MRS test in the two group was statistically significant (p< 0.05). Mean DEA and peak-DCI were higher in the functional EGJ-OO as compared to the anatomical EGJ-OO (68±28 vs 108±49 and 2409±1702 vs 4763±3701, respectively). In contrast, the mean DCI was higher in functional EGJ-OOcompared to anatomical EGJ-OO(1379±1050 vs 2752±2535), but this difference was not statistically significant (p=0.07). RDC was not different between the two groups (p=ns).

Conclusion: Abnormal MRS test in patients with EGJ-OO could be a useful tool to segregate anatomical from functional EGJ-OO patients. Among the functional EGJ-OO patients, a major contractile force seems to be present, suggesting that this could be correlated with inadequate adaptation of the esophageal body motility to the appearance of a recent flow obstruction.
Disclosure: Nothing to disclose

P1265 IMPAIRED ESOPHAGOGASTRIC JUNCTION ELEVATION AS AN INDICATOR OF A FULL-THICKNESS PER-ORAL ENDOSCOPIC MYOTOMY

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Introduction: Per-oral endoscopic myotomy (POEM), a highly-effective treatment for Achalasia cardia has also been associated with increased risk for post-procedure gastroesophageal reflux (GER). One of the risk factors for post-POEM GER seems to be the dissection of both circular and longitudinal muscle fibers (full-thickness myotomy-FTM). Irrespective of whether it is intentional or accidental, selective and full-thickness dissection may coexist, making it difficult to determine whether e.g. a partial FTM has a functional consequence.

Aims & Methods: To investigate whether the disturbance of post-swallow transient proximal, "elevation" of the esophagogastric junction (EGJ), mediated by contraction of the longitudinal muscle fibers, could serve as a reliable objective indicator of a POEM with FTM. Forty-four patients with achalasia -mean age (standard deviation): 53 (15), male:female ratio 1.1:1- that underwent posterior POEM at Showa University Koto Toyosu Hospital were included. POEM reports, videos, pre- and post-POEM High Resolution Manometry (HRM-Star Medical Inc, Tokyo, Japan) images were examined and compared to determine the presence/absence of esophageal shortening/EGJ vertical elevation as well as absent, segmental or full-length FTM.

The Chicago Classification 3.0 was utilized to distinguish achalasia subtypes: type I (N=14), type II (N=23), type III (N=3) and early onset achalasia (N=4). HRM assessment was performed in a blinded fashion for presence/absence of FTM.

Results: Selective myotomy/absent FTM was documented in 27 patients (61%), segmental in 11 (25%) and full-length FTM in 6 (14%). Pre-POEM HRM was consistent with absent/minimal EGJ elevation in 13 cases (30%), all diagnosed as type I achalasia. Post-POEM HRM revealed 7 additional cases (20 in total, 45%, P=0.19) with absent/minimal EGJ elevation that received either full-length (N=5) or long-segment (N=2) FTM. The sensitivity and specificity of absent EGJ elevation for the detection of FTM post-POEM, was 87.5% and 64%, respectively. A limitation of the present study is that comparison could not be performed in the case of type I achalasia, as HRM-documented EGJ elevation was predominantly absent both pre- and post-POEM.

Conclusion: Utilizing HRM and the "elimination" of EGJ elevation as a marker, the occurence of significant FTM during POEM can be reliably documented in patients with all achalasia subtypes except type I.

Disclosure: A. Manolakis received grant from the Hellenic Society of Gastroenterology H. Inoue is an advisor for Top Corp and Olympus Corp

P1266 DUODENAL HYPERPERMEABILITY AND SYSTEMIC MARKERS OF LOW-GRADE INFLAMMATION ARE LINKED WITH GASTRIC EMPTYING AND SYMPTOMS IN FUNCTIONAL DYSPEPSIA PATIENTS WITH POSTPRANDIAL DISTRESS

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Introduction: We previously demonstrated increased duodenal mucosal permeability and low-grade inflammation with eosinophils in functional dyspepsia (FD) patients (1). However, the role of duodenal alterations in relation to gastric emptying and symptoms in functional dyspepsia (FD) patients is still unclear.

Aims & Methods: FD patients with symptoms of postprandial distress (PDS) according to Rome IV criteria were recruited. Gastric emptying for liquids and solids was determined using the calculated half emptying time of the 13C-glycin (significantly delayed > 75 min) and 14C-octanoic acid (significantly delayed > 110 min) breath tests, respectively. Duodenal biopsies were collected to measure the transepithelial electrical resistance (TEER) and paracellular passage of a fluorescein-labeled dextran (4kDa) in Ussing chambers. After the endoscopy, a naso-duodenal tube was positioned in the second part of the duodenum with aspiration of fluids before and after a liquid meal (Fortimel, 300kCal) with measurement of pH. Plasma samples were collected to measure high-sensitivity C-reactive protein (hs-CRP) and patients filled out the Patient Assessment of Gastrointestinal Disorders Symptom Severity Index (PAGI-SYM). Descriptive and correlation analyses were performed to determine markers of gastric emptying and FD symptoms.

Results: In total, 17 FD patients (15 females, median (IQR) age 28 (22-34) years) with 15 (88%) belonging to the pure PDS group and 2 (12%) the overlap group with epigastric pain syndrome (EPS). The median gastric half emptying time was 68 (41-76) min for liquids and 66 (57-80) min for solids. Significantly delayed gastric emptying was present in 4 patients (24%) for liquids and only in 1 patient (6%) for solids. Median TEER was 22.1 (19.2-27) $\Omega*cm^2$ and paracellular passage 25.2 (20-30.3) pmol. Fasting and fed pH were similar (7 (5.2-7.3) vs. 6.5 (6.2-6.8), p=0.72) and median hs-CRP was 2 (0.6-5.5) mg/L. Fasting duodenal pH correlated positively with gastric emptying for liquids (r= 0.59, p=0.02). Gastric emptying for solids was positively correlated with both duodenal paracellular passage (r=0.62, p=0.03) and plasma hs-CRP (r=0.57, p=0.03). In addition, gastric emptying for solids was negatively correlated with the intensity of bloating (r=-0.53, p=0.04).

Conclusion: Although delayed gastric emptying for solids is uncommon, duodenal alterations with increased permeability and low-grade systemic inflammation are linked with gastric emptying in FD patients with PDS-symptoms. These data provide further substance for the potential central role of the duodenum in symptom generation and gastric motor abnormalities.

References: (1) Vanheel et al., Gut 2017
Disclosure: Nothing to disclose

P1267 EVALUATION OF A PROTOCOL FOR MEASUREMENT OF DISTENSIBILITY OF THE LOWER ESOPHAGEAL SPHINCTER IN THE CLINICAL FOLLOW UP OF PATIENTS WITH ACHALASIA

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Introduction: The Endoflip™ (Crospon Ltd, Ireland) impedance planimetry system is now commonly applied to assess the distensibility of the lower esophageal sphincter (LES), which is of particular relevance in the diagnosis, treatment and follow up of patients with achalasia. A suggested procedure protocol is available (1), and a graded filling approach of the balloon up to maximum fill volume of 50 ml is recommended. The 40 ml volume is most reliable to determine the distensibility of LES (1). Limited data are available on the use and feasibility of assessment of LES distensibility in clinical follow up of patients with achalasia.

Aims & Methods: The aim of the present study was to evaluate the feasibility and the recommended protocol for LES distensibility measurements by applying the Endoflip™ system in the clinical follow up of patients with achalasia one year after per oral endoscopic myotomy (POEM).

At our department, achalasia patients are routinely having a clinical follow up one year after POEM. After acquiring the Endoflip™ system, distensibility measurement of LES with the probe EF-325 was included in this follow up and performed directly after an upper endoscopy with the patient in the supine position. The recommended protocol with graded filling of the balloon at 30, 40 and 50 ml fill volume was applied. After reaching the maximum fill volume of 50 ml, a repeated measurement at 40 ml was performed. To compare the two measurements at 40 ml fill volume, Wilcoxon signed rank test was applied. Summary values are given as median (range).

Results: During the first four months with distensibility measurements, the Endoflip™ system was applied without complications in eleven consecutive POEM controls (four females) with a median age of 54 years (26-73).

The two distensibility measurements at 40 ml performed prior to and after 50 ml fill volume differed significantly (Table).

Conclusion: Performing LES distensibility measurement is feasible in clinical follow up of patients treated for achalasia by POEM. However, LES distensibility at the recommended 40 ml balloon fill volume is significantly higher when measured after maximum fill volume. The protocol for measurements should thus be standardized with respect to whether results have been acquired prior to or after maximum balloon fill volumes to ensure reliability and validity of the results.

Balloon fill volume	30 ml	40 ml	50 ml	40 ml	p-value*
Luminal diameter (mm)	8.7 (6.1-13.0)	13.1 (10.3-19.9)	16.9 (13.8-23.8)	15.3 (12.1-20.1)	0.05
Intra balloon pressure (mm Hg)	34.4 (15.9-78.0)	31.8 (24.5-92.0)	42.4 (19.9-109.0)	30.3 (22.5-88.0)	0.11
Distensibility (mm²/mm Hg)	2.7 (0.8-7.3)	3.8 (1.5-7.9)	6.2 (2.1-12.2)	5.6 (2.1-8.9)	<0.01

[Endoflip™ measurements with different balloon fill volumes (*comparison of the two measurements with 40 ml fill volume)]

References: 1. Endoflip™ impedance planimetry system. Protocol and interpretation. Pandolfino J, Clarke J, Vela M, et al. Medtronic review 2018.
Disclosure: Nothing to disclose

P1268 IS BELCHING INCREASING AFTER BARIATRIC BY-PASS SURGERY IN THE LONG TERM PERIOD?

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Introduction: By-pass surgery is currently one of the most effective treatments available for obesity and type II diabetes. Some limited data reports increased gastric belching after sleeve gastrectomy. However, there is no data about bariatric by-pass surgery and belching.
Aims & Methods: We aimed to evaluate belching after bariatric by-pass surgery. Seventeen morbid obese patients and 12 healthy volunteers were enrolled in the study. Twelve patients had Roux-en-Y gastric bypass (RYGB) and the other 5 pts had gastric mini-bypass surgery, median 24 months (18-54 months) ago. All patients were questioned about the presence of symptoms for belching, gastroesophageal reflux disease, and dyspepsia. 24-hour pH-impedance were performed in all patients and healthy volunteers. Each of the patients underwent gastroscopy before 24-hour pH-impedance.
Results: Female dominance was observed in patients group [%76.5 (n=13) vs %41.7 (n=5)]. However, ages and gender were not statistically different in both groups (*P* > 0.05). The mean DeMeester score was significantly higher in patients (9.11 ± 19.40 vs 6.04 ± 5.60, *P* = 0.048). However, pathologic acid reflux (DeMeester score >14) rate were similar in both groups (11.8% vs %8.3). Symptom association probability positivity was detected in 11.8% of patients in the impedance study. The rate of alkaline reflux rate was higher in patients (6% vs 0%). The belching rate was 50% in patients according to questionnaire. Esophagitis was detected in 25% of patients in gastroscopy. The number of gas reflux (123.24 ± 80 vs 37.2 ± 21.5, *P* = 0.001) and Supragastric/Gastric belches was significantly higher in patients (182 ± 64/228 ± 66.69 vs 25.08 ± 15.20/12.17 ± 17.65, *P* = 0.001). Although number of supragastric belching is higher in controls. Gastric belching was higher than supragastric belching in patients.
Conclusion: Belching is increasing afterthe bariatric by-pass surgeryin the long term period. Gastric belching frequency is higher than supragastric belching in these patients.
Disclosure: Nothing to disclose

P1269 *HELICOBACTER PYLORI* ERADICATION THERAPY MAY CONTRIBUTE TO EASY DETECTION OF AUTOIMMUNE GASTRITIS WITH H. pylori INFECTION

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Introduction: Endoscopic features of autoimmune gastritis (AIG) include severe atrophy of the gastric body and lesser atrophy of the gastric antrum. Strict criteria for diagnosing AIG are important because this condition can cause anemia, gastric neoplasms, and autoimmune polyendocrine syndrome. However, diagnostic criteria for AIG have not yet been determined.
Aims & Methods: We investigated AIG at our center from 2007 to 2018. This retrospective cohort study evaluated patients' gender, medical history, history of *Helicobacter pylori* eradication, laboratory data [serum gastrin, parietal cell antibody (PCA), intrinsic factor antibody (IFA), anti-*H. pylori* antibody, and pepsinogen (PG) I and II levels], and histological diagnosis of AIG. We defined complete AIG as severe atrophy of a gastric body, as evidenced on endoscopy, predominantly of the gastric body rather than the gastric antrum, hyper serum gastrin(>200pg/ml), positive PCA or IFA, and histological diagnosis of AIG. We defined suspected AIG as patients who did not meet the criteria for complete AIG.
Results: Twenty-eight of the 87951 patients who underwent endoscopy were enrolled in this study. There were 16 cases of complete AIG and 12 cases of suspected AIG. The mean patient age was 69.1 (range, 41-87) years for complete AIG and 71.5 (range, 52-86) years for suspected AIG. Males constituted only 4 (25.0%) of all complete AIG cases. Furthermore, 4 (25%) of all complete AIG cases had history of cancer (stomach, breast, and colon). All patients exhibited severe endoscopic atrophy, predominantly of the gastric body. Mean serum gastrin levels were 2939 (range, 225-9590) in patients with complete AIG and 1026 (range, 180-2270) in patients with suspected AIG. Two (12.5%) cases were negative for PCA and positive for IFA in the complete AIG group. In the suspected AIG group, six cases were negative for both PCA and IFA; however, they still exhibited severe atrophy of the gastric body on endoscopy and elevated gastrin levels (range, 490-5410). Two cases in the complete AIG group were *H. pylori*-antibody positive (2/16); in contrast, there were five positive cases in the suspected AIG group (5/12). PG I level (range, 3.8-19.9) was low among all patients in the complete AIG group and in 4 patients with suspected AIG. In one patient with suspected AIG, we could not calculate PCA because of the anti-mitochondrial antibody and IFA negativity; however, this patient exhibited severe atrophy of the gastric body on endoscopy and was histologically diagnosed with AIG. Two cases had histories of *H. pylori* eradication and exhibited more severe atrophy of the gastric body on endoscopy after (rather than before) *H. pylori* eradication.
Conclusion: Diagnostic criteria for AIG are warranted, and further study is needed. *H. pylori* eradication therapy may contribute to easy detection of AIG with *H. pylori* infection, because this therapy reduces the influence of *H. pylori* in patients with autoimmune gastritis with *H. pylori* infection.
Disclosure: Nothing to disclose

P1270 GASTROPARESIS: OUTCOME OF FOCUS GROUPS FOR THE DEVELOPMENT OF A QUESTIONNAIRE FOR SYMPTOM ASSESSMENT IN PATIENTS SUFFERING FROM IDIOPHATIC AND DIABETES GASTROPARESIS

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Introduction: Gastroparesis (GP) is defined as "a combination of symptoms and documented delay in gastric emptying (GE) in the absence of mechanical obstruction". The main causes of GP are Idiopathic gastroparesis (IGP) and Diabetes gastroparesis (DGP). To date, no validated patient reported outcomes (PRO) for evaluation of treatment efficacy in these conditions

are available. According to FDA guideline, PRO instrument item genera-tion and selection should be derived from patient focus groups (FGs) and cognitive interviews (CIs).

Aims & Methods: Our aim was to perform FGs and cognitive interviews for the development of a new questionnaire for the assessment of symptom pattern and severity in both IGP and DGP. Patients with IGP, a negative endoscopy and a strongly delayed GE rate (T1/2 >109min, GE breath test) were invited to participate. During the FGs, symptom spectrum of gastro-paresis was discussed to determine type of symptoms, triggering by meals or factors, duration, bothersomeness, predictability and impact. A verbal descriptor for each symptom was proposed to the patients after discussion of the symptom. Threshold for selection of symptoms was 50%. From the list of emerged relevant symptoms, Subsequently, FGs for DGP patients were organized using the same framework.

Results: 14 IGP (11 Females, 43.6±3.3 years, T1/2:155.2±16.2) patients partic-ipated. All (100%) confirmed experiencing symptoms that were triggered or aggravated by ingestion of a meal. Main symptoms corresponded to postprandial fullness (PPF:100%), epigastric pain (EP:100%), early satia-tion (ES:100%), nausea (N:100%), retching (RT:71%) and vomiting (V:57%). . Other relevant symptoms were bloating (B:86%), abdominal distention (AD:71%), heartburn (H:79%) and regurgitation (RG:64%). In **diabetic gas-troparesis (n=10**, 7 Females, 45.5±3.7 years, t1/2:156.9±17.0 min) symptoms were also meal related (100%) and comprised PPF (100%), EP (100%), ES (70%) N (100%), V (70%), RT (70%), RG (50%), B (90%), AD (70%), belch-ing (70%) and H (80%). Following this, pilot instruments were developed and customized through CIs for qualitative and cognitive debriefing to es-tablish content validity.

Conclusion: This study confirm that symptoms corresponding to postpran-dial fullness, epigastric pain, early satiation, nausea, vomiting, retching regurgitation, bloating and heartburn are the key items for developing a PRO for both idiopathic and diabetic gastroparesis.

Disclosure: Nothing to disclose

P1271 DOES MEASUREMENT OF SYMPTOMS DURING A GASTRIC EMPTYING TEST IMPROVE CORRELATION BETWEEN SYMPTOMS AND EMPTYING RATE?

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Introduction: Functional dyspepsia (FD) and idiopathic gastroparesis (IGP) are characterised by upper gastrointestinal symptoms and a negative en-doscopy, and severely delayed emptying in case of gastroparesis. It is ar-gued whether distinguishing these entities is necessary as previous stud-ies showed a poor correlation between delayed gastric emptying (GE) and symptom severity.

Aims & Methods: We aim to evaluate the relationship between symptom severity and GE when simultaneously assessed. During a GE test (breath test with ^{13}C-octanoic acid labelled 250 Kcal meal), severity (0-4) of 6 symp-toms (postprandial fullness (PPF), epigastric pain (EP) and burning (EB), bloating (BL), nausea (N) and belching (B)) was assessed before and every 15 min for 4hs postprandially. The sum of individual symptom scores gen-erates the meal-related symptoms score; the sum of all symptoms gener-ates overall global meal-related symptom severity. Data were compared in patients with normal and delayed GE (cut-off $T_{1/2}$ ³ 109 min) using non-parametric statistical tests, Mann-Whitney test, 2-Way-Anova with Bonfer-roni posthoc-test correction and spearman correlation.

Results: Of 504 FD patients (70% females (F), 43.6±0.7 years, 23.3±0.2 kg/m²), 382 patients (67% F, 43.8±0.8 years, 23.3±0.2 kg/m²) had normal and 122 patients (77% F, 42.7±1.5 years, 23.2±0.6 kg/m²) had delayed GE. Global symptom severity tended to be higher in patients with delayed GE (81.9±3.4 vs. 99.5±7.1, p=0.06). Only nausea was significantly increased in patients with delayed GE (10.7±0.8 vs. 15.9±1.6, p=0.01). However, no correlations were observed between GE rate and any of the symptoms (global symptom score: r=0.06, p=0.2; nausea: r=0.08, p=0.09). In all analysis, 2-Way-Anova showed significant interactions for increasing symptoms over time, but no significant differences were observed between normal and delayed GE. Only nausea showed partially significant increase in delayed GE 90 min after the meal (p< 0.01) compared to normal GE.

Conclusion: IGP patients tend to display higher dyspeptic symptoms se-verity, but only meal-related nausea scores were significantly higher. The severity of symptoms, even when assessed during the meal, was not as-sociated to the GE rate. These findings have important implications for the value of routinely applying GE testing in clinical practice.

Disclosure: Nothing to disclose

P1272 HIGH PREVALENCE OF SMALL INTESTINAL BACTERIAL OVERGROWTH AMONG FUNCTIONAL DYSPEPSIA PATIENTS

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Introduction: Functional dyspepsia (FD) is a multifactorial disorder as its development may be based on several different pathophysiological mech-anisms. Small intestinal bacterial overgrowth (SIBO) is characterized by either increased numbers or presence of colonic type bacteria in the upper gastrointestinal tract. FD could be related to SIBO since impaired motility of the gastrointestinal tract is one of the main etiologic factors involved in both diseases pathogenesis.

Aims & Methods: Consecutive outpatients fulfilling Rome IV criteria for FD underwent upper gastrointestinal endoscopy. Severity of FD symptoms was graded by the patient assessment of upper gastrointestinal symptom severity index (PAGI-SYM) questionnaire. 2cc of duodenal juice (3rd - 4th part) was aspirated in special sterile traps. SIBO was defined as ≥10^3 CFU/ml of duodenal aspirate and/or presence of colonic type bacteria. Patients with Irritable Bowel Syndrome (IBS) and healthy controls (HC) - under-going gastroscopy due to gastroesophageal reflux disease (GERD) - com-prised positive and negative controls, respectively. Concentrations (pg/ml) of tumor necrosis factor-alpha (TNFα), interleukin (IL)-1β and IL-6 were measured in the duodenal fluid. We aimed to compare the SIBO preva-lence between FD patients, IBS patients and healthy controls.

Results: We enrolled 347 subjects (FD 227/90 IBS/30 HC) aged 53.7±14.6years. Among FD patients, 144 (63.4%) had Postprandial Distress syndrome (PDS), 64 (28.2%) Epigastric pain Syndrome (EPS) and 19 (8.4%) mixed type. SIBO was diagnosed in 44/227 FD patients, with Gram (-) bac-teria being the predominant species (24/44, 54.5%). SIBO prevalence among FD subtypes was: PDS 30/114 (26.3%); EPS 8/64 (12.5%); mixed 6/19 (31.6%). Overall, SIBO prevalence was significantly higher in FD compared to HC [44/227(19.3%) vs. 1/30(3.3%), p=0.037] and it was similar to IBS [44/227(19.3%) vs. 15/90(16.7%), p=0.63]. SIBO prevalence was lower in the EPS group as compared to the PDS and mixed symptoms groups (12.5% vs. 27.1%, p=0.11). SIBO presence correlated neither with total nor with any subscale score of the PAGI-SYM questionnaire. Mean concentration of IL-1β was similar between FD and HC subjects (5.13±17.9 vs. 6.3±14.3, p=0.65) but it was significantly lower than that of IBS individuals (402±89.6 vs. 5.13±17.9, p< 0.001 and 401.9±89.6 vs. 6.3±14.3, p< 0.001 respectively). TNFα and IL-6 concentrations did not differ between the three groups.

Conclusion: In a cohort of Greek FD patients, SIBO prevalence is similar to that of IBS subjects and higher compared to that of healthy controls.

Disclosure: Nothing to disclose

P1273 GASTRIC EMPTYING SCANS: POOR ADHERENCE TO NATIONAL GUIDELINES

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Introduction: Gastric-emptying scintigraphy (GES) is considered the gold standard for measuring gastric emptying. Performing the test correctly is critical as it ensures an accurate diagnosis which directly influences patient care from both a diagnostic and therapeutic perspective. While published protocol guidelines for GES exist, national compliance with

these guidelines has not been thoroughly studied. This study aimed to determine whether facilities that perform GES adhere to well-established national guidelines published 10 years ago.

Aims & Methods: To assess compliance with GES protocol guidelines, we developed a questionnaire that evaluated a total of 51 measures addressing the relevant procedure subcategories of the published Procedure Guideline for Adult Solid-Meal Gastric Emptying Study 3.0. Questions focused on patient preparation (16), pertinent medical history (15), precautions/contraindications (2), radiopharmaceuticals (5), image acquisition (4), processing (2), interpretation criteria (5) and reporting (2). Demographic data was also collected. The anonymous questionnaire was distributed electronically. Responses were entered into an excel table and analyzed using standard statistical methods.

Results: 109 medical institutions (MI) responded; of these, 45 (41.3%) were academic/teaching medical centers. The mean number of annual GES procedures was 165.9 (range, 12 to 450 GES/year). The validated egg meal is utilized in 58.4% of the MI and 60.0% of MI conduct a 4 hour GES. 89.2% ask if the patient has an egg allergy prior to GES, although 92.8% do not stop the test if the patient reports an egg allergy. Blood glucose levels of diabetic patients are tested in 17.5% of the MI prior to GES. Discontinuation of opioids is required in 65.0% of MI prior to GES and 50% of these MI require at least two days of discontinuation of opioids. 36.4% of MI record dose and frequency of pain medications. 29.5% of MI ask if the patient uses tobacco products. 69.5% of MI report GES results at 1, 2, and 4 hours. Metoclopramide or erythromycin is administered during the test in 2.3% of the MI. Academic/teaching medical centers had the lowest compliance rate on twelve (23.5%) of the 51 adherence measures.

Conclusion: Our results suggest that adherence to national guidelines for performing GES is low, even at academic medical centers. This suggests that a barrier exists between established clinical guidelines and institutional implementation that has a direct impact on patient care.

Disclosure: Nothing to disclose

P1274 BUDESONIDE ORODISPERSIBLE TABLETS ARE SUPERIOR TO MAINTAIN AND EVEN FURTHER IMPROVE QUALITY OF LIFE IN ADULT PATIENTS WITH EOSINOPHILIC ESOPHAGITIS: RESULTS FROM THE 48-WEEKS, DOUBLE-BLIND, PLACEBO-CONTROLLED PIVOTAL EOS-2 TRIAL

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Introduction: In the recent EOS-1 trial, a 6-week therapy with a novel budesonide orodispersible tablet (BOT), with a unique mode of delivery and esophageal targeting, given twice daily (1mg BID) led to a significant improvement in the validated disease specific overall Adult Eosinophilic Esophagitis Quality of Life (EoE-QoL-A) questionnaire and all of its subscores (1).

Aims & Methods: This maintenance study also assessed the Health related Quality of life (HRQoL) and its change from baseline over 48 weeks of treatment. In total, 204 patients being in clinico-histological remission were randomized (1:1:1) to a 48-weeks treatment with BOT 1 mg BID, BOT 0.5 mg BID or placebo.

The overall EoE-QoL-A 30 items score was assessed with a weighted average score between 0 to 4 at baseline and end of treatment (EOT) - higher scores denoted better HRQoL.

Results: For the overall EoE-QoL-A 30 items score a statistically significant increase (i.e., improvement in QoL) from Baseline to EOT was observed in both budesonide groups. In contrast, the overall EoE-QoL-A 30 items score showed a statistically significant decrease (i.e., deterioration in QoL) from Baseline to EOT in the Placebo group. The differences in the absolute changes from baseline between the budesonide groups and placebo were also clinically relevant and statistically significant (see Table).

	BOT 1mg BID (n=68)	BOT 0.5mg BID (n=68)	Placebo BID (n=68)
Baseline, Mean (SD)	3.2 (0.59) n=64	3.2 (0.56) n=64	3.0 (0.70) n=64
EOT, Mean (SD)	3.5 (0.48) n=67	3.3 (0.46) n=66	2.8 (0.75) n=65
Absolute change from DB Baseline to EOT, Mean [95% CI]	0.3 [0.14; 0.39] n=63	0.2 [0.12; 0.34] n=62	-0.2 [0.39; 0.08] n=61
Difference between absolute changes from Baseline to EOT (BUL vs. Placebo)* [95% CI]*	0.50 [0.30; 0.70] p<0.0001 (2-sided)	0.46 [0.27; 0.66] p<0.0001 (2-sided)	

*For intergroup differences (BOT 0.5mg BID or BOT 1mg BID vs Placebo) between absolute changes from Baseline to EOT a two-sided t-test was used for exploratory testing.

[Disease specific overall Adult Eosinophilic Esophagitis Quality of Life (EoE-QoL-A) 30 item questionnaire]

Conclusion: Both, BOT 1mg BID and BOT 0.5mg BID were able to maintain and even further improve patient's HRQoL compared to placebo over 48 weeks.

References: (1) Lucendo AJ, et al. Gastroenterology 2019, DOI:https://doi.org/10.1053/j. gastro.2019.03.025

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P1275 EOSINOPHILIC ESOPHAGITIS - VISUAL SCORE: A NOVEL PICTORIAL SELF-ADMINISTERED TOOL TO ASSESS QUALITY OF LIFE IN PATIENTS WITH EOSINOPHILIC ESOPHAGITIS

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Introduction: Eosinophilic Esophagitis (EoE) is a chronic disease characterised by significant impairing of quality of life (QoL). Current methods for measure QoL are almost tricky and not easy to use routinely. Starting from the validated EoE-QoL-A questionnaire (EQA), we elaborated the EoE Visual Score (EVS), an easy and quick, self-administered questionnaire for daily clinical practice.

Aims & Methods: The aim of this pilot study was to evaluate EVS and its correlation with clinical response to therapy, histological disease activity and EQA.

Thirty patients (7 Female, mean age 33-yo, range 18-75-yo) with a definite diagnosis of EoE, referred to our Unit, were included. The diagnosis was done according to the latest international criteria. Patients were enrolled at outpatient level, at first admission or follow-up, between January 2018 to February 2019. The EVS is a 10-scale, 11-item pictogram, depicting the different areas involved in the assessment of QoL in EoE patients (eating/diet impact, social impact, emotional impact, disease anxiety, choking anxiety). Patients, were clinically and histologically evaluated, before (baseline) and after medical therapy (proton pump inhibitors or topical

steroid for 8weeks). At both time points, all patients completed the EQA and EVS. Histologic activity was described as dichotomous parameter: 0 for less than 15eos/hpf and 1 for more than 15 eos/hpf. Pearson correlation coefficient and paired t test were used for the analysis.

Results: At baseline, patients were all histologically active, with a mean value of EQA and EVS of 45.07±SD32.69 and 26.37±SD20.43, respectively. After 8 weeks of medical treatment, mean value of EQA and EVS were 37.63±SD28.37 and 21.43±SD20.92, respectively. A strong significant correlation between EQA and EVS at both time points (r=0.784 p< 0.001 and r=0.816 p< 0.001, respectively) was observed. EVS had a significant mean value difference before and after treatment (p=0.032). After 8 weeks of medical treatment, 21patients (70%) achieved histological response, but no difference in EVS mean values was found between histological responders and. non-responders (p=0.222). Moreover, no significant difference for EVS mean values was observed before and after treatment in both histological non-responder (p=0.064) and responders (p=0.105).

Conclusion: The EVS is an effective and quick tool for daily clinical practice, able to depict patients QoL and to facilitate the assessment of therapeutic response. It well correlates with the already validated EQA. Nevertheless, further larger studies are required to evaluate the usefulness of EVS in clinical practice.

References: Taft TH, Kern E, Kwiatek MA, Hirano I, Gonsalves N, Keefer L. The adult eosinophilic oesophagitis quality of life questionnaire: a new measure of health-related quality of life. Aliment Pharmacol Ther. 2011 Oct;34(7):790-8. Lucendo AJ, Sánchez-Cazalilla M, Molina-Infante J, Pérez-Martínez I, Tenías JM, Barrio J, Nantes Ó, Ciriza-de-los-Ríos C, Perelló A, Arias Á. Transcultural adaptation and validation of the "Adult Eosinophilic Esophagitis Quality of Life Questionnaire" into Spanish. Rev Esp Enferm Dig. 2014 Jun;106(6):386-94.

Disclosure: Nothing to disclose

P1276 FECAL EOSINOPHIL CATIONIC PROTEIN AS POTENTIAL MARKER OF DISEASE ACTIVITY IN PATIENTS WITH EOSINOPHILIC ESOPHAGITIS

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Introduction: Eosinophilic Esophagitis (EoE) is a chronic disorder, characterized by symptoms of esophageal dysfunction and, histologically, by eosinophilic-infiltration. Endoscopic and histological examination is required both at diagnosis and follow-up, since a reliable non-invasive marker has not been identified yet. Eosinophil cationic protein (ECP) is released during eosinophils degranulation and it can be assessed in human faeces.

Aims & Methods: The aim of the study is to evaluate the potential use of ECP in EoE patients' faeces (F-ECP) as a potential marker of disease activity.

29 consecutive EoE-patients assessed at our Unit between January 2018 to January 2019 for endoscopic follow-up, were included. Faecal and histological specimen were collected on the same day. Histological activity was staged considering the number of eosinophils for high-power field (Eos/HPF). A control-group of 71 patients (mean age 52-yo, range 35-64, 38 Male), in whom EoE had been ruled out according to International criteria, was included. F-ECP was evaluated with a fluorescence-enzyme-immuno-assay (PHADIA, Thermo Fisher Scientific). Spearman's rank correlation was applied for statistical analysis and F-ECP predictive positive and negative values (PPV, NPV) were calculated.

Results: EoE-study-population consisted of 29 patients affected by EoE (mean age 32-yo, range 18-62 yo, 24 M), showing F-ECP values ranging from 0 to 172 ug/L (mean value 17,3 ug/L), compared to values ranging from 0 to 32 ug/L (mean value 8,1 ug/L) in the control-group. A statistically significant relationship between F-ECP and Eos/HPF was observed (p 2-tailed = 0.02438). PPV and NPV of F-ECP were evaluated using two cut-off values, F-ECP < 2 ug/L (as negative) and F-ECP < 8,1 ug/L (as mean value in the control group). Among the study group, 21 patients (72%) showed histo-

logical remission, but only 8 (38%) had F-ECP negative values. Setting a cut-off value of 8,1 ug/L, F-ECP NPV and PPV for histological remission were 86% and 40%, respectively, while they were 100% and 38% with cut-off value of 2 ug/L.

Conclusion: Our preliminary data show a good correlation of F-ECP values with histology activity and a clear difference in terms of levels between EoE patients and controls. However, the wide variability of ECP levels evaluated in our series requires further cases and more histologically-active patients, in order to assess its usefulness in clinical practice.

Disclosure: Nothing to disclose

P1277 PREVALENCE AND CLINICAL FEATURES OF ENDOSCOPY NEGATIVE EOSINOPHILIC ESOPHAGITIS

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Introduction: Some patients with eosinophilic esophagitis (EoE) do not have typical endoscopic findings. Therefore, multiple esophagus biopsies are recommended regardless of endoscopic findings in patients with dysphagia. This study aimed to investigate the prevalence and clinical features of endoscopy negative EoE.

Aims & Methods: We conducted two retrospective studies. In the first study, forty-seven patients with dysphagia were included. All patients underwent endoscopy and esophageal high resolution manometry (HRM) test. Multiple esophageal biopsies were taken from the middle and lower esophagus. The prevalence of EoE and the presence or absence of endoscopic findings were examined. In the second study, thirty-five patients diagnosed with EoE in the same period were included. Patients were divided into those with typical endoscopic findings and those without, differences of clinical features were examined.

Results:

Study 1: Of the 47 patients, 12 patients (26 %) were diagnosed with achalasia, 3 (6 %) with ineffective esophageal motility, 5 (11%) with esophagogastric junction (EGJ) outflow obstruction, 4 (9%) with Jackhammer esophagus, 5 (11%) with absent contractility, and 2 (4%) with distal esophageal spasm (DES). The remaining 16 patients' (34%) results were normal. As a result of biopsies, 6 patients (13%) were diagnosed with EoE (HRM results: normal in 4, DES in 1, and EGJ outflow obstruction in 1).

Study 2: Of 35 patients with EoE, 21 (60%) had white plaques, 22 (63%) had longitudinal furrows, and 11 (31%) had esophageal rings. Eight patients (23%) did not have typical endoscopic findings. We examined differences between patients with endoscopic findings and those without. Symptom severity (Frequency Scale for Symptoms of GERD: FSSG score) was 10.18 for endoscopic findings and 18.43 for negative cases, and there was a significant difference (p = 0.021 < 0.05) between the two groups. There were no significant differences without FSSG score (gender, age, height, weight, BMI, presence or absence of allergic disease, esophagus eosinophil count, proton pomp inhibitor and steroid history, blood eosinophil count, and IgE levels).

Conclusion: Thirteen percent of the patients with dysphagia were diagnosed with EoE, and 23 % of EoE patients do not have typical endoscopic findings. Patients with negative endoscopic findings had more severe symptoms than those with positive findings.

Disclosure: Nothing to disclose

P1278 APPLICATION OF CONVOLUTIONAL NEURAL NETWORKS FOR DIAGNOSIS OF EOSINOPHILIC ESOPHAGITIS BASED ON ENDOSCOPIC IMAGES

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Introduction: Eosinophilic esophagitis (EoE) is a clinicopathological disease diagnosed by symptoms related to esophageal dysfunction accompanied by esophageal eosinophilia, and its prevalence has been rapidly increasing in Western and Asian countries. Subjective symptoms associated with EoE such as dysphagia are not specific, thus endoscopic identification of suggestive EoE findings is quite important for facilitating endoscopic biopsy sampling, leading to histopathological identification of esophageal eosinophilia. However, poor inter-observer agreement regarding diagnosis among endoscopists has become an issue, especially with inexperienced practitioners. On the other hand, image recognition performed with artificial intelligence (AI) with deep learning through convolutional neural network (CNN) has dramatically improved and is increasingly applied for diagnostic imaging in a variety of medical fields, though its effectiveness for endoscopic diagnosis of EoE has not been evaluated.
Aims & Methods: We evaluated the diagnostic utility of AI for EoE with endoscopic imaging. A total of 1484 training images of 165 patients histologically proven to be in an active phase of EoE (≥15 eosinophils per high power field), including 1182 obtained with white light imaging (WLI) and 302 with narrow band imaging (NBI), as well as 2318 normal esophagus images, including 1292 obtained with WLI and 1026 with NBI, were examined retrospectively. All images were obtained from the records of Shimane University Hospital and related facilities, and used to develop deep learning through CNN to diagnose EoE. Additionally, we prepared a second set of 1156 test images from 40 patients with EoE and 96 subjects with a normal esophagus, including 336 with EoE and 820 with a normal esophagus, and used those to evaluate the diagnostic accuracy of the CNN for each image and case. When more than half of the images were diagnosed as EoE or normal, that was used as the final diagnosis for each case.
Results: The CNN required 31 seconds to analyze 1156 test images from 136 cases, and correctly diagnosed EoE in 79.8% using comprehensive diagnosis of WLI and NBI per image analysis, with an overall sensitivity of 78.6% and specificity of 80.2%. Diagnosis using only WLI tended to have a higher level of sensitivity than that with both WLI and NBI (92.8% vs. 78.6%), while accuracy and specificity were not significantly different between them. For each case, the CNN correctly diagnosed 36 of 40 EoE cases using comprehensive diagnosis of WLI and NBI, with overall sensitivity and specificity of 90.0% and 90.6%, respectively. Likewise, diagnosis with only WLI tended to have a higher sensitivity than that with both WLI and NBI (94.9% vs. 90.0%).
Conclusion: We developed a new CNN system for detecting EoE using endoscopic images, which provided accurate diagnosis based on WLI within a very short time period. Our findings indicate the usefulness of CNN when diagnosing EoE, especially for aiding inexperienced endoscopists.
Disclosure: Nothing to disclose

P1279 CHROMOENDOSCOPY WITH IODINE-POTASSIUM IODINE SOLUTION IN EOSINOPHILIC ESOPHAGITIS

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Introduction: Eosinophilic esophagitis (EoE) is an immune-mediated condition associated with chronic allergy. Endoscopic findings in EoE may include linear furrowing of the mucosa, white plaques or exudates, concentric rings, friable and diffuse luminal narrowing or strictures, but can often be normal. Biopsies are taken randomly and are often negative. The aim of the study was to evaluate whether chromoendoscopy with Iodine/Potassium iodine solution (IPIS) is useful for identification of EoE during endoscopy, target and reduce the numbers of needed biopsies.
Aims & Methods: We included 10 patients with known EoE and 10 patients with dyspepsia. All underwent gastroscopy with IPIS staining 0.5-1% of the whole esophagus. Selective biopsies were taken from the areas without uptake and areas with uptake of IPIS stain for histopathological comparison and diagnosis.
Results: Normal squamous esophageal epithelium took up IPIS and colored it dark brown, while pathologic epithelium become light yellowish due to reduced iodine uptake. In all 10 patients with EoE we observed diminished uptake of IPIS in whole length of the esophagus. 4 patients with EoE had leopard skin pattern after installation IPIS. In these patients, all biopsies from areas with low uptake, showed histologically confirmed EoE (mean 88 eosinophils per high power field (HPF)), whereas areas with more normal uptake showed significantly lower number of eosinophils (mean 18 eosinophils/HPF). In the group with dyspepsia, the uptake of IPIS was found to be normal, with even dark brown colorization of the esophageal mucosa.
Conclusion: IPIS seems be useful for identification of patients with EoE during endoscopy. Areas with uptake deficit in otherwise normal looking squamous epithelium should be biopsied. The technique allows targeted biopsies for improved identification of EoE and reduce sampling errors. Further studies in an unselected patient population must be performed to further explore this finding.
Disclosure: Nothing to disclose

P1280 EOSINOPHILIC OESOPHAGITIS: THE RISING INCIDENCE AND BURDEN OF DISEASE IN A LARGE NHS TRUST

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Introduction: Eosinophilic oesophagitis (EoE) is an immune-mediated inflammatory condition of the oesophagus that, despite an increasing awareness and incidence of the disease in the last few years, remains poorly characterised and poorly understood. The diagnosis is relatively easily made on biopsy by the presence of an eosinophilic infiltrate (>15 eos/HPF) in patients presenting with symptoms of oesophageal dysfunction and/or suggestive endoscopic features.
Despite this in many cases opportunities for diagnosis are missed and the diagnosis delayed which a potential impact on disease severity and progression. The spectrum of disease is wide and is putting an increasing burden and economic cost on specialist services managing the disease.
Aims & Methods: The aim of our study was to quantify the scale of the problem, the spectrum of disease, and the disease burden in a large NHS Trust covering a population of 600,000. We performed a retrospective search was performed of the histopathology database using the term 'eosinophilic oesophagitis' to identify positive oesophageal biopsies, cross-referencing with the endoscopic database. Demographic data was collected including indication for endoscopy, endoscopist, relevant endoscopic findings, and treatment. Patients for whom full endoscopy records were unavailable were excluded as were those with reflux related eosinophilia.
Results: 136 cases of definite EoE were identified over a four year period with a year-on-year increase in cases. 96 (70.6%) cases were male with a mean age at diagnosis 44.6 years. The vast majority of cases were identified by either nurse endoscopists (45%) or medical gastroenterologists (41%) with the nurse endoscopists with the highest proportion of biopsies taken in patients presenting with dysphagia in a normal oesophagus. The main indications for endoscopy were dysphagia (63.7%), food bolus obstruction (16.4%), known eosinophilic oesophagitis (6.6%), stricture/dilatation (5.5%) and reflux (5.5%).
The endoscopic appearance was recorded as normal in 51% of cases. In the remaining patients the most common findings were concentric rings (24%), fibrotic stricture (12%), narrowed impassable lumen (9%) and reflux oesophagitis (4%).
These findings support a spectrum of disease. Approximately 50% of patients responded to acid suppression with the rest treated with oral topical steroid and dietary manipulation. A small number of patients (11%) had strictures that required endoscopic dilatation.

Conclusion: The incidence of EoE in our population was high considering it is a relatively rare condition. There was male predominance in keeping with the known literature. Dysphagia was the most frequent indication for endoscopy and there were a few known cases of eosinophilic oesophagitis undergoing reassessment after treatment. Nurse endoscopists appeared particularly effective at appropriately biopsying and diagnosing the disorder which may represents a greater awareness of the condition and a greater adherence to current guidelines regarding biopsy. However in a significant minority of cases opportunities for diagnosis were missed and the diagnosis delayed. In 51% of cases the oesophagus looked normal which has important implication regarding biopsy. The severity of disease appears to vary widely from asymptomatic non-progressive disease to severe fibrosis and stricturing. This study has provided an insight into an increasingly important condition and provides a basis to improve case finding and prompt earlier diagnosis.
Disclosure: Nothing to disclose

P1281 THE EXPRESSION OF FREE FATTY ACID RECEPTORS 1-4 IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE – A PILOT STUDY

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Introduction: Gastroesophageal reflux disease (GERD) is one of the most common upper gastrointestinal disease with prevalence reaching 25.9% in Europe. Current therapy of GERD aims primarily at decreasing the acid secretion in the stomach and the most effective drugs are proton pump inhibitors which are the first-line treatment. Noteworthy, the Barrett's esophagus (BE) and thus esophageal adenocarcinoma (EA) may develop on a basis of GERD. The marker of such transformation is still sought after to lower the cost of potential surveillance of patients. Free fatty acid receptors (FFARs) are G protein-coupled receptors playing a role in immune responses and tumorigenesis, the two processes involved in the GERD-BE-EA transformation. The role of FFARs in GERD has not been yet investigated.
Aims & Methods: The primary aim was to compare the expression of FFARs 1-4 in esophageal mucosa between the patients with GERD and healthy controls (HC). FFAR expression was quantified using quantitative RT PCR in esophageal samples obtained from patients with GERD and healthy controls. Moreover, patients were asked to fill GERD-Health Related Quality of Life (GERD-HRQL) questionnaire. Student's t-test was chosen when comparing two means; one-way ANOVA followed by the Newman-Keuls post-hoc test was used for analyses of multiple treatment means. Pearson correlation was used to assess the correlation between the FFARs expression and GERD-HRQL results.
Results: A total of 35 patients with GERD (27 with non-erosive reflux disease (NERD) and 8 erosive reflux disease (ERD)) and 8 HC were recruited to the study. Overall, the relative expression of FFARs 1-4 were non-significantly higher in esophageal biopsies taken from patients with GERD than in HC. FFAR1 appeared to be the most profoundly expressed FFAR in esophageal mucosa of either GERD patients or HC and presented a non-significantly higher relative expression compared to three other FFARs (2938.00±726.90 for FFAR1 vs 1802.00±454.30 for FFAR2 vs 2136.00±703.00 for FFAR3 vs 64.17±9.07 for FFAR4 for GERD patients and 1846.00±707.00 for FFAR1 vs 1145.00±447.00 for FFAR2 vs 640.00±219.00 for FFAR3 vs 34.59±6.18 for FFAR4 for HC). Expression of FFAR4 was the lowest of all FFARs in all biopsies. When classifying patients with regard to endoscopic findings, all FFARs exhibited higher expression in NERD vs. ERD patients and HC. The expression of FFAR2 was non-significantly lower in patients with ERD vs HC. All other FFARs demonstrated similar expression when comparing ERD to HC. Lastly, we performed Pearson correlation test to analyze possible association between the relative expression of FFARs to GERD-HRQL score. All correlations were negative and only FFAR3 expression significantly, negatively correlated with GERD-HRQL score (r=-0.4305, p=0.025).
Conclusion: We observed an increase in relative expression of FFARs in esophageal biopsies from GERD patients compared to HC, especially in case of NERD. This trend was most profoundly visible for FFAR1 and least for FFAR4. Noteworthy, FFARs expression negatively correlated with patients' quality of life, meaning that the higher expression of these receptors may be associated with lower intensity of symptoms perceived by patients with GERD. Taken together, our results show that FFARs indeed may play a role in GERD pathophysiology.
Disclosure: Nothing to disclose

P1282 TRANSEPITHELIAL TISSUE PERMEABILITY IN ESOPHAGEAL EPITHELIUM DECREASES IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE FOLLOWING ANTI-REFLUX SURGERY

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Introduction: Gastroesophageal reflux disease (GERD) is a chronic disorder and typical symptoms recur six months after the discontinuation of medical therapy in 75-80% of patients. Anti-reflux surgery is a successful alternative in some cases and success rate is high. It is also a good model to evaluate the recovery of the epithelium with decreasing the contact time of noxious gastric refluxate including acid, pepsin, bile acids and pancreatic juice.
Aims & Methods: We aimed to evaluate the electrophysiological recovery in esophageal epithelium of the cases before and after laparoscopic anti-reflux surgery and compare with healthy controls. Esophageal biopsies from 15 patients with GERD and predominantly typical symptoms included (10 men; 43,7 ± 12,6 years). All patients were evaluated with GERD and quality of life questionnaires, high resolution esophageal manometry, 24 h impedance-pH monitoring, upper gastrointestinal endoscopy with distal esophageal biopsies. 3-4 months after laparoscopic anti-reflux surgery upper gastrointestinal endoscopy repeated in asymptomatic patients and esophageal biopsies were taken. 23 healthy controls (7 men; 41,9 ± 10,8 years) were also included. The transepithelial resistance (TEER) and tissue permeability via fluorescein diffusion within 2 hours were recorded.
Results: TEER of esophageal epithelium was significantly higher after the surgery (p=0.0002) and healthy controls (HC) (p=0.0009). There was no difference between pre-operative patients and HC in TEER. Mucosal permeability measured with fluorescein diffusion of post-operative measurements was significantly decreased than pre-op patients (p=0.038). There was no significant difference neither pre-operative nor post-operative measurements than HC *(Table)*.
Conclusion: The TEER and permeability results implicate that laparoscopic anti-reflux surgery showed an efficient recovery within esophageal epithelium in patients with GERD. One possible explanation of the higher tissue resistance following the surgery than HC might be explained with the continue "silent" reflux in HC.
Disclosure: Nothing to disclose

	TEER (Ohms)	Flourescein permeability (pmols)
Healthy controls	166.8 ± 46.2	36.9 ± 13.5
Pre-op patients	151.0 ± 51.6	48.6 ± 27.8
Post-op patients	214.8 ± 61.0*	29.5 ± 17.3**

(*; p< 0.001 vs. pre-op patients and vs. healthy controls, **; p< 0.05 vs. pre-op patients)

[Transepithelial resistance and flourescein permeability results of the groups]

P1283 ELECTROPHYSIOLOGICAL CHANGES AND MUCOSAL PERMEABILITY IN ESOPHAGEAL EPITHELIUM BEFORE AND AFTER STRETTA TREATMENT FOR GASTROESOPHAGEAL REFLUX DISEASE

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Introduction: Stretta is an option for patients with gastroesophageal reflux disease (GERD), offering an alternative to invasive surgery, endoscopic therapies or continue PPI therapy.

Aims & Methods: We aim to investigate the electrophysiological differences and diffusion characteristics as a reflection of tissue integrity within esophageal mucosa before and after stretta. Patients with predominantly typical symptoms and true nonerosive reflux disease or LA-esophagitis A were included. GERD and quality of life questionnaires, high resolution esophageal manometry, 24 h impedance-pH monitoring, upper gastrointestinal endoscopy with distal esophageal biopsies were performed in nine patients before stretta (4 men, 44.5±10.4 years). 3-4 biopsies were put into the chambers to measure the transepithelial resistance (TEER), potential difference (PD) and tissue permeability via fluorescein diffusion within 2 hours as well as evaluation of dilated intercellular spaces with light microscopy. The Stretta procedure performed under sedation with regular protocol without any complication. Three weeks of PPI therapy was given to all patients following the procedure than stopped. All patients were symptom free or have less than 50% of typical symptoms at the end of the 8 weeks of follow up. Approximately two months after stretta, upper GI endoscopy repeated, esophageal biopsies were taken. All results were compared with 23 healthy controls (7 men; 41,9 ± 10,8 years). 24 h impedance-pH monitoring was performed in eleven out of 23 HC.

Results: TEER of pre-stretta group was significantly lower than healthy controls (HC) (p=0.037). But no significance was found between pre-stretta and post stretta group (p=0.17) even though there was a great margin (124.6 ± 55.7 vs 157.2 ± 61.3). No difference was shown in post stretta group compared to HC (166.8 ± 46.2) (p=0.59). Mucosal permeability in pre-stretta group was significantly lower than post-stretta group (p=0.006) and HC (p=0.015) while there was no significance between post stretta and HC (Table).

	TEER (Ohms)	Flourescein permeability (pmols)
Pre-stretta	124.6 ± 55.7*	67.2 ± 31.5*
Post-stretta	157.2 ± 61.3	28.5 ± 18.2**
Healthy controls	166.8 ± 46.2	36.9 ± 13.5

(*; p<0.05 pre-stretta vs HC, **; p<0.05 pre-stretta vs post-stretta)

[Transepithelial resistance and flourescein permeability results of the groups]

Conclusion: Electrophysiological results indicate that epithelial permeability and possibly mucosal damage has recovered after stretta treatment within esophageal epithelium. Those changes might be explained with less reflux load at the distal esophagus. A direct effect of the procedure inside the tissue is a low possibility since application effects only a small area.
Disclosure: Nothing to disclose

P1284 PAR2, P2X2 AND P2Y2 MRNA EXPRESSION IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE AND THEIR RELATIONSHIP TO REFLUX SYMPTOMS: A PILOT STUDY

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Introduction: Current treatment of gastroesophageal reflux disease (GERD) aims primarily at decreasing the acid secretion, however there is still a group of patients not responding to conventional therapy. According to recent model of GERD pathogenesis, reflux esophagitis is an immune cell-mediated damage, rather than a caustic chemical injury. Acid exposure can increase expression of several receptors on esophageal epithelial cells. The proteinase-activated receptor-2 (PAR2) is a member of the G protein-coupled receptor family and has been involved in inflammation, visceral hyperalgesia, and in transepithelial resistance. Purinergic receptors are a family of membrane-bound receptors using ATP as transmitter. P2X and P2Y receptors play important roles in signaling visceral pain and esophageal hypersensitivity. Thus these receptors represent a potential target for future pharmacological treatment of GERD.

Aims & Methods: The aim was to assess the expression of PAR2, P2X2 and P2Y2 mRNA in esophageal mucosa in different groups of GERD patients as well as to compare with reflux symptoms and HRQL.

PAR2, P2X2 and P2Y2 mRNA expression was quantified using quantitative RT-PCR in esophageal samples obtained from patients with GERD and healthy controls. Moreover, patients completed the GERD-Health Related Quality of Life (GERD-HRQL) questionnaire. Student's t-test was chosen when comparing two means; one-way ANOVA followed by the Newman-Keuls post-hoc test was used for analyses of multiple treatment means. Using Pearson correlation test we analyzed relationship between the relative expression of receptors and GERD-HRQL score.

Results: A total of 53 patients with GERD (37 with non-erosive reflux disease (NERD) and 16 erosive reflux disease (ERD)) and 9 healthy controls were recruited to the study. Overall, the relative expression of PAR2, P2X2 and P2Y2 were non-significantly higher in esophageal biopsies taken from patients with GERD than in controls (77.60±28.50 vs 284.60±67.72; 26.81±10.27 vs 274.40±77.46; 3476.0±508.2 vs 7215.0±1338.0, accordingly). When classifying patients to non-erosive and erosive reflux disease PAR2 receptor expression was non-significantly higher in ERD compared to NERD and controls (326.10±112.30 vs 266.90±84.76 vs 77.60±28.50).

P2X2 exhibited the highest expression in NERD compared to ERD and controls (302.20±82.94 vs 40.18±17.78 vs 26.81±10.27), similarly to P2Y2 which expression was higher in NERD than in ERD and controls (7321.00±1651.00 vs 5306.0±1738.00 vs 3476.00±508.0).

GERD-HRQL scores revealed significant positive correlation to PAR2 expression (r=.03883), as well as to P2Y2 expression (NS), however were negatively correlated with P2X2 expression (r=-0.2991).

Conclusion: Higher PAR2 expression was found in erosive reflux disease and may be associated with higher intensity of symptoms perceived by patients with GERD. Relative expression of P2X2 and P2Y2 were increased particularly in NERD, where they could mediate sensitization of esophagus. Our results show that PAR2, P2X2 and P2Y2 may play a role in GERD inflammation and could be in future a therapeutic targets for reflux symptoms.
Disclosure: Nothing to disclose

P1285 THE EFFECT OF DIFFERENT PH REFLUXATE ON THE TYPE OF IMMUNE RESPONSE IN GERD PATIENTS

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Introduction: Assessment of 24-hour pH-monitoring can provide confirmatory evidence of gastroesophageal reflux disease (GERD). The primary outcome of 24-hour pH-monitoring is the distal oesophageal acid exposure time (AET) < 6%. Currently, discusses the possible impact of immune response (Th1 or Th2) in the development of the inflammatory response in the esophagus.

Aims & Methods: The aim of the study was to investigate interleukin (IL)-8 and IL-10 expression after exposure to different human refluxates (pH< 5, pH 5-7, pH>7) to peritoneal macrophages of C57/BL6 mice (n=68) with the following macrophage culturing in standard conditions (10% FBS, RPMI1640) for 36 hours. According to data of endoscopy and 24-hour pH-monitoring (normative value of AET< 6%*) we divided 68 patients with GERD to 28 (14 men, 45.74±2.23 yr) non-erosive reflux disease (NERD), 22 (15 men, 45.0±3.24 yr) erosive reflux disease ERD and 18 (13 men, 47.22±2.95 yr) Barrett's esophagus (BE). We performed 24-hour pH-monitoring on the Ohmega - Ambulatory Impedance-pH Recorder (Medi-

cal Measurements Systems (MMS), Netherlands). Macrophage culturing (RPMI1640 medium, 10% FBS) in standard conditions (37oC, 5% CO2) for 36 hours flow cytometry (Beckman Coulter, FC500). Assessment of secretory activity of peritoneal macrophages (proinflammatory cytokine IL-8 and anti-inflammatory cytokine IL-10). The statistical analysis was done using SPSS Statistics 17.0.

Results: In NERD patients median pH of refluxates was 6.18 [4.2; 7.4], in ERD – 6.71 [5.7; 8.1], in BE – 6.24 [4.6; 7.3]. Median value of the level of IL-8 after exposure refluxates with pH< 5 was 69.0 [42.1; 125.3] pg/mL, with pH 5-7 was 60.3 [15.4; 120.0] pg/mL, with pH>7 – 37.6 [8.7; 73.4] pg/mL. Median value of the level of IL-10 after exposure refluxates with pH< 5 was 4.1 [1.5; 10.2] pg/mL, with pH 5-7 was 7.8 [1.3; 33.8] pg/mL, with pH>7 – 16.8 [5.7; 61.3] ph/mL. Exposure to acid refluxates causes an increased production of Th1 proinflammatory cytokine IL-8 (r= -0.352, p= 0.026), but exposure to non acid refluxates causes an increased production of Th2 anti-inflammatory cytokine IL-10 (r= 0,697, p= 0,001). The results of 24-hour pH-monitoring demonstrated that in NERD patients median AET was 4.7 [0.3; 18.0] %, in ERD – 9.3 [0.2; 57.8] %, in BE – 14.5 [1.3; 49.9] %.

Conclusion: Exposure to acid refluxates causes an increased of Th1 immune response with increased production of Th1 cytokine (IL-8). Exposure to non acid refluxates causes an increased of Th2 immune response with increased production of Th2 cytokine (IL-10). Th1 and Th2 cytokines production demonstrates statistically significant different with acid and non acid refluxates. We observed that AET was higher in ERD and BE patients than in NERD patients. It suggests that high level AET may lead to Th1 immune response.

Disclosure: Nothing to disclose

P1286 ESOPHAGEAL INFUSION OF MENTHOL DOES NOT AFFECT ESOPHAGEAL MOTILITY BUT EVOKES HEARTBURN IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE (GERD)

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Introduction: A common food additive menthol is thought to trigger the symptoms of GERD by influencing esophageal peristalsis and the lower esophageal sphincter (LES) function. However, recent studies reported the expression of TRPM8 receptor for menthol and cold in esophageal sensory C-fiber nerves.
Aims & Methods: We evaluated the effect of esophageal infusion of menthol on esophageal motility and the sensations evoked from the esophagus. High resolution manometry (HRM) catheter with attached thin tube for menthol infusion (opening 5 cm above LES) was placed transnasally. HRM protocol which included baseline recording and 10 water (5ml) swallows was performed in supine position before and after esophageal infusion of menthol (3mM, 20 min, 8ml/min). The sensations evoked by menthol infusion were evaluated for quality and for intensity of painful component by visual analogue scale (VAS, range 1-10). In additional subjects menthol infusion was performed without HRM and only the sensations were evaluated.
Results: Menthol did not appreciably affect HRM measurements characterizing LES function and esophageal peristalsis in healthy subjects (N=12) or GERD patients (N=10). For example, in healthy subjects esophageal infusion of menthol did not change the magnitude of the inspiratory augmentation of LES (10.6+1.8 mmHg before vs. 9.1+1.6 mmHg after menthol, P=0.3), distal contractile integral (DCI, 742±137 vs. 840±124, P=0.5) nor the percentage of ineffective swallows (40±10% vs. 23±8%, P=0.13). Similarly, in GERD patients menthol did not change the inspiratory augmentation of LES (9.5+1.2 mmHg vs. 9.1+1.2 mmHg, P=0.6), DCI (287±86 vs. 314±102, P=0.7) nor ineffective swallows (75±10% vs. 71±13%, P=0.6).
In contrast, menthol had a striking effect on esophageal sensations in patients with GERD. While the esophageal infusion of menthol evoked only a cold sensation in 11 of 12 healthy subjects, it evoked heartburn in 10 of 10 patients with GERD (P< 0.01).
In healthy subjects the cold sensation was perceived only as a minor discomfort (VAS score 1.9±0.3) but in patients with GERD the menthol-induced heartburn was perceived as painful (VAS score 5.6±0.5, P< 0.01).

The intensity of menthol-induced heartburn was comparable to the intensity of heartburn evoked by a brief infusion of acid (pH=1.0, 10min) in a separate group of patients (VAS score 7.1± 0.7, N=12).
Conclusion: We conclude that esophageal infusion of menthol does not affect esophageal motility. However, the sensations evoked by menthol change dramatically from a relatively non-painful cold sensation in healthy subjects to painful heartburn in patients with GERD. Our results suggest that menthol triggers the symptoms of GERD directly by influencing esophageal nerves rather than indirectly by affecting esophageal motility. Supported by VEGA 1/0304/19.
Disclosure: Nothing to disclose

P1287 EFFICACY AND SAFETY OF TRANSORAL INCISIONLESS FUNDOPLICATION (TIF) IN REFRACTORY GASTROESOPHAGEAL REFLUX DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Refractory gastroesophageal reflux disease (GERD) is common and can affect up to 40% of patients who are on proton pump inhibitor therapy. Surgical fundoplication (Nissen fundoplication) has proven to be an effective treatment option for these patients but it remains an invasive procedure in this era of minimally invasive surgery. Several endoluminal approaches to GERD management have been developed as a potential bridge between medical management and surgical fundoplication. Transoral incisioness fundoplication (TIF) is a novel endoscopic technique which has shown some promise in early studies; however, its safety profile and efficacy remain uncertain.
Aims & Methods: We aimed to assess the efficacy and safety of TIF in refractory GERD through a systematic review and meta-analysis.We performed a thorough literature search using PubMed, EMBASE, Cochrane library, Medline, Google Scholar and Science citation index between January 2010 to January 2018. Search terms included MeSH and non-MeSH terms relating to gastroesophageal reflux disease, refractory gastroesophageal reflux disease, endoscopic techniques in gastroesophageal reflux disease and transoral incisionless fundoplication. Additional case-reports, case series, and abstracts were retrieved by searching from references of relevant studies. Primary outcomes measured were cumulative technical success rate and adverse events. Secondary outcomes measured were the improvement in Gastroesophageal Reflux Symptom Score (GERSS), DeMeester score and Reflux symptom index (RSI).
Results: Based on our search criteria, 41 studies were identified and 6 were excluded after careful review. 35 studies which included 1586 patients (49.4% males) were analyzed. The overall technical success rate of TIF was 98.4% (95% confidence interval [CI] 96 to 99, p < 0.001) and had an adverse event rate of 3.2% (95% CI 1 to 4, p < 0.001). Post TIF, there was a significant improvement in GERSS score (mean difference 17.29, 95% CI 17.26 to 18.28,p < 0.001),RSI (mean difference 14.37, 95% CI 13.39 to 15.19,p < 0.001) and DeMeester score (mean difference 9.78, 95 % CI 8.12 to 11.89, p < 0.001).
Conclusion: TIF is a technically feasible and effective endoscopic therapeutic option for refractory GERD with good clinical responses. However, more controlled trials are required in future to compare the efficacy and safety between TIF and Nissen fundoplication.
Disclosure: Nothing to disclose

P1288 COMPARISON OF THE EFFICIENCY OF TWO DIFFERENT PPI FORMULA IN TREATMENT OF ATYPICAL GERD PATIENTS, A RANDOMIZED STUDY

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Introduction: Patients with atypical gastro-esophageal reflux disease (GERD), including cough, globus, and hoarseness usually require more aggressive or double dose proton pump inhibitor (PPI) therapy than patients with typical GERD. The prospective, open-label, randomized study aims to compare the efficacy of lansoprazole, a fast orally-disintegrating PPI and dexlansoprazole, a dual delayed release PPI in patients with atypical GERD symptoms.

Aims & Methods: Patients with atypical GERD symptoms and a total Reflux Symptom Index (RSI) score ≥11 were eligible for enrollment. From Jan. 2017 to Dec. 2018, 232 subjects were randomly assigned (1:1 ratio) to receive oral lansoprazole 30 mg, once daily before breakfast or oral dexlansoprazole 60 mg, once daily before breakfast for 8 weeks. The primary endpoint is to compare the response rate after 8-week PPI therapy between the two groups.

Results: There were 101 (43.5%) with cough, 144 (62.1%) with globus, and 41 (17.7%) with hoarseness among these 232 study subjects. After 8-week PPI therapy, dexlansoprazole treated group had a significantly higher symptoms response rate than lansoprazole treated group in cough (76.5 % vs. 38.0 %) and globus (69.7 % vs. 30.8 %)(p all< 0.05 by intention to treat). Multivariate logistic regression analysis showed that use of dexlansoprazole, presence of dyslipidemia and typical GERD symptoms (acid reflux and heart burn) and absence of globus symptom were predictors for symptom response for cough; use of dexlansoprazole, no cough symptom, and presence of erosive esophagitis were predictors for symptom response for globus (p all < 0.05). No predictor for therapy response to hoarseness was noted.

Conclusion: There is a higher response rate for cough and globus symptoms in atypical GERD patients after a 8-week PPI therapy with dexlansoprazole rather than lansoprazole.

Disclosure: Nothing to disclose

P1289 EFFICACY OF DA-5204 (STILLEN 2X®) FOR PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PILOT STUDY

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Introduction: Proton pump inhibitor (PPI) alone is not satisfactory for the treatment of gastroesophageal reflux disease (GERD). Therefore, we investigated the efficacy of DA-5204 (Stillen 2X®, 90mg of Artemisia asiatica 95% ethanol extract per tablet) and PPI combination therapy on GERD in comparison to PPI alone.

Aims & Methods: This randomized, double-blind, placebo-controlled study randomly assigned 70 patients with endoscopically proven esophageal mucosal injury (Los Angeles classification A or B) into 2 groups: pantoprazole 40mg once daily with DA-5204 twice daily (DA-5204 group) or pantoprazole 40mg once daily with placebo twice daily (placebo group) for 4 weeks. The primary endpoints were endoscopically effective (normal mucosa or minimal change) or complete healing (normal mucosa) rates, and secondary endpoint was sufficient relief (≥ 50% reduction) of reflux symptoms using Gastroesophageal Reflux Disease Questionnaire (GerdQ) questionnaire.

Results: Final analyses included 29 patients with the DA-5204 group and 30 patients with the placebo group. At weeks 4, there was a significantly difference of the endoscopically effective healing rate between the two groups (DA-5204 group vs. placebo group; 93.1% vs. 56.7%; p = 0.001) as well as the complete healing rate (DA-5204 group vs. placebo group; 82.8% vs. 33.3%; p < 0.000). The rates of sufficient relief for reflux symptoms according to GerdQ tended to be higher in the DA-5204 group than in the placebo group, with no significant difference.

Conclusion: Our findings suggest that combined therapy with PPI and DA-5204 is more effective in treating GERD than PPI alone.

Disclosure: Nothing to disclose

P1290 ON-DEMAND VERSUS CONTINUOUS PROTON PUMP INHIBITOR THERAPY AS FIRST-LINE TREATMENT FOR GASTROESOPHAGEAL REFLUX DISEASE: A SINGLE-CENTER PROSPECTIVE STUDY

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Introduction: The recommended schedule of proton pump inhibitor as first-line treatment for gastroesophageal reflux disease (GERD) is 4-8 weeks of continuous medication; however, patients often do not take all prescribed medication and spontaneously resort to on-demand schedule. We compared the efficacy of esomeprazole as first-line treatment according to the pattern of medication adherence (on-demand vs. continuous).

Aims & Methods: Patients who diagnosed with GERD by GERD questionnaire (Gerd-Q) between December 2017 and May 2018 were enrolled. The patients were prescribed with daily esomeprazole 20 mg for 4 weeks. After regularly taking the medicine for at least 1 week, the patients were allowed to choose between continuous and on-demand therapy during the remaining 3 weeks depending on the degree of the subjective measure of symptoms. The number of remaining pills in the on-demand group was calculated, and Gerd-Q scores of the two groups were compared at baseline and after the 4-week study period.

Results: Out of a total of 94 patients, 62 enrolled in the on-demand group and 32 in the continuous group. In the on-demand group, the median number of remaining pills was 7.50 (range, 1-21). In the on-demand group and the continuous group, the mean Gerd-Q scores were 9.42 and 9.47 at baseline (*p*=0.850) and 7.21 and 6.91 at 4 weeks (*p*=0.149), respectively. Total and individual item scores of the Gerd-Q were significantly decreased in both groups at the end of the study period (*p*< 0.001). There were no significant differences between the two groups in terms of mean changes in the Gerd-Q score (on-demand vs. continuous groups: -2.21 vs. -2.56, *p*=0.537).

Conclusion: On-demand therapy with esomeprazole 20 mg showed comparable efficacy to continuous therapy in terms of subjective symptom management in patients with GERD.

Disclosure: Nothing to disclose

P1291 ADMINISTRATION OF A BITTER TASTANT HAS NO INFLUENCE ON THE NUMBER OF TRANSIENT LOWER OESOPHAGEAL SPHINCTER RELAXATIONS IN HEALTH

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Introduction: Dietary measures such as avoiding high fat meals, sweets, coffee, alcoholic and carbonated beverages are often advised to patients with gastro-oesophageal reflux disease (GORD) due to their 'reflux inducing' characteristics. However, the evidence for these advices is weak due to conflicting findings and the small number of patients included in the currently available clinical studies. Our group previously showed that administration of a bitter compound can alter the intragastric pressure (IGP) after a meal (1). Additionally, we demonstrated the existence of a negative correlation between IGP and the number of transient lower oesophageal sphincter relaxations (TLOSRs) (2). However, the effect of a bitter compound on TLOSRs and subsequent reflux episodes has never been investigated and it is unclear whether bitter food items should be avoided in GORD. We hypothesise that bitter administration in healthy volunteers (HV) will lead to an increase in the number of TLOSRs.

Aims & Methods: After an overnight fast, 19 female HV (36 y [21-63]) underwent a high-resolution impedance manometry (HRiM) measurement. After placement of the HRiM probe (Unisensor, Attikon, Switzerland), 10 µmol/kg (0.1 mL/kg) of a 100 mM denatonium benzoate solution or an identical volume of placebo (water) was administered directly into the stomach. The number of TLOSRs and reflux episodes were quantified 30 minutes before and two hours after consumption of a high caloric meal (mashed potatoes, apple sauce and meatloaf; 1000 kcal), using the dedi-

cated software (Solar GI, Laborie, Canada). The HV were asked to complete a questionnaire concerning the presence and intensity of different upper gastro-intestinal (GI) symptoms every 15 minutes. The study was organised in a double-blind, randomized, cross-over design with at least one week washout between both administrations. Results were analysed using a paired t-test or Wilcoxon signed rank test when appropriate.

Results: There was no significant difference in the number of TLOSRs nor the number of reflux episodes between the bitter and placebo condition (Table 1).

	Bitter	Placebo	p-value
TLOSRs	17 ± 5.5	15 ± 4.4	0.14
Reflux episodes	10 ± 6.0	10 ± 4.7	0.73

[Table 1: The number of TLOSRs and reflux episodes in the two different conditions (mean ± SD).]

Additionally, no differences were observed in the nature (gas or liquid) and extent of reflux events between the different conditions. LOS pressures dropped significantly in the first postprandial hour to start recovering slowly back to baseline values during the second postprandial hour ($p < 0.0001$), without any difference between both conditions. No difference in GI symptom occurrence was noted.

Conclusion: Administration of the bitter tastant denatonium benzoate, had no influence on the number of TLOSRs nor on the number of reflux episodes compared to placebo. Therefore, we speculate that the consumption of bitter food will not have an influence on the number of reflux episodes nor on the occurrence of GORD-related symptoms in GORD patients.

References: 1. Andrews CN, Verschueren S, Janssen P, Maes A, Deloose E, Depoortere I, et al. Su2072 The Bitter Taste Receptor Agonist Denatonium Benzoate Alters Intragastric Pressure Profiles During Nutrient Drink Test in Healthy Volunteers. Gastroenterology. 2013;144(5):S549. 2. Pauwels A, Altan E, Tack J. The gastric accommodation response to meal intake determines the occurrence of transient lower esophageal sphincter relaxations and reflux events in patients with gastro-esophageal reflux disease. Neurogastroenterol Motil. 2014;26(4):581-8.

Disclosure: Nothing to disclose

P1292 IW-3718, A NOVEL GASTRIC-RETENTIVE BILE ACID SEQUESTRANT, IMPROVES GERD SYMPTOMS IN PATIENTS WITH PERSISTENT GERD DESPITE ONGOING PPI TREATMENT – PHASE 2B STUDY RESULTS

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Introduction: Proton pump inhibitors (PPIs) are the standard therapy for gastroesophageal reflux disease (GERD). However, it is estimated that approximately 30% of patients with GERD have persistent symptoms despite taking label-dose PPIs. GERD and persistent GERD are characterized by reflux of stomach contents into the esophagus resulting in heartburn (HB) and regurgitation (RG), esophageal injury, and complications. IW-3718 is a novel gastric-retentive bile acid sequestrant in clinical development for persistent GERD. The positive impact of IW-3718 was previously reported for HB and RG, based on derived endpoints. The aim of this study was to determine the impact of IW-3718, added to label-dose PPIs, on individual GERD symptoms measured by the modified Reflux Symptom Questionnaire-electronic Diary (mRESQ-eD), a patient-reported, evidence-based clinical outcomes assessment.

Aims & Methods: This double-blind, placebo-controlled study included a screening, a 2-week pretreatment, and an 8-week treatment period. Enrolled patients were taking label-dose PPIs; had GERD, evidenced by erosive esophagitis (EE) on esophagogastroduodenoscopy (EGD) and/or abnormal acid exposure while taking PPIs (pH < 4 for ≥4.2% of a 24-hour interval; "Bravo-positive"); and had HB or RG symptoms ≥4 days per week for 8 weeks despite ongoing use of label-dose PPIs. Patients were strati-

fied by baseline (BL) EE status and randomized (1:1:1:1) to placebo (PBO) or IW-3718 (500, 1000, or 1500 mg) twice daily (BID) in addition to once-daily (QD) PPI. During the pretreatment and treatment periods patients self-reported the severity (6-point scale [0=did not have, 5=severe]) or frequency (5-point scale [0=never, 4=very often]) of 10 symptoms associated with GERD on the mRESQ-eD daily. The symptoms assessed for "severity" were HB, burning feeling behind breastbone or center of upper stomach, pain behind breastbone or center of upper stomach, difficulty swallowing, hoarseness, and cough. The symptoms assessed for "frequency" were RG (liquid or food) moving upward toward throat or mouth, acid or bitter taste, coughing, and burping. For each of the 10 symptoms, change from BL to Week 8 in the weekly average was analyzed using an analysis of covariance model with treatment group and EE status as factors and BL score as a covariate. No adjustment was made for multiplicity.

Results: The modified intent-to-treat population included 280 patients (68-71/arm). At BL, 52% had EE and 73% were Bravo-positive. Demographics were similar across groups. Changes from BL to Week 8 for each of the 10 mRESQ-eD symptom items are presented in Table 1. Greater improvements were seen for all symptom items in the 1500-mg IW-3718 group compared with PBO ($P≤0.05$), except burping frequency ($P=0.17$).

Conclusion: In addition to improving HB and RG, IW-3718 (1500 mg BID) improved other GERD-related symptoms in patients with persistent GERD who continued receiving PPIs QD.

Endpoint Statistic: Mean change from Baseline	PBO (PPI alone) BID n=69	IW-3718 500 mg BID n=71	IW-3718 1000 mg BID n=71	IW-3718 1500 mg BID n=68	P value IW-3718 1500 mg vs PBO
Heartburn severity	-1.4	-1.5	-1.7	-1.8	0.03
Burning feeling behind breastbone or center of upper stomach severity	-1.3	-1.4	-1.6	-1.8	0.01
Pain behind breastbone or center of upper stomach severity	-1.3	-1.3	-1.5	-1.7	0.03
Difficulty swallowing severity	-0.9	-0.8	-1.0	-1.2	0.03
Hoarseness severity	-0.6	-0.7	-1.0	-1.1	<0.01
Cough severity	-0.6	-0.7	-1.0	-1.2	<0.01
Regurgitation (liquid or food) moving upward toward throat or mouth frequency	-0.8	-1.0	-1.0	-1.2	<0.01
Acid or Bitter Taste Frequency	-0.9	-0.9	-1.1	-1.2	0.05
Coughing frequency	-0.6	-0.6	-0.7	-1.0	<0.01
Burping frequency	-0.8	-1.0	-0.9	-1.0	0.17

[Table 1. mRESQ-eD Symptom Items: Change From Baseline to Week 8 in Weekly Average (mITT Population)]

Disclosure: J. Hanlon, R.S. Mittleman, M. Hall, J.Z. Shao, Y. Chen, L. Lane, A.M. Gates, N. Borgstein, and M.G. Currie are current or former Ironwood employees and may own stock or stock options in Ironwood Pharmaceuticals, Inc. M.F. Vaezi, R. Fass, and N. Vakil have served on medical advisory boards as paid consultants for Ironwood Pharmaceuticals, Inc.

P1293 DIAGNOSING DYSPLASIA IN BARRETT'S OESOPHAGUS – THE SEATTLE PROTOCOL REMAINS THE DOMINANT STRATEGY IN NON EXPERT CENTRES

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Introduction: Detection of dysplasia at Barrett's surveillance depends on a number of factors including: the endoscopist's skill, use of advanced imaging (NBI, Acetic acid), adherence to Seattle protocol, and high-risk patient factors like male sex, smoking, length of Barrett's segment and

family history of oesophageal adenocarcinoma. Whether the high rates of visible dysplasia diagnosis reported from expert tertiary centres needs further study.

Aims & Methods: The aim of this pre-EQuIP study was to analyse routes to dysplasia diagnosis in a dedicated Barrett's surveillance programme, specifically looking at the grade of the endoscopist, use of image enhancement (IE), diagnosis by Seattle biopsy protocol vs. random biopsy, and the nature of dysplasia (Low grade, LGD vs. high grade, HGD). An electronic database search of over 600 Barrett's surveillance histology was carried out for the period 2015-2018 in two NHS Trusts, extracting all reported dysplasia. The endoscopy database was then interrogated for the following: patient demographics, grade of endoscopist (medical consultant gastroenterologist, non-medical endoscopist and surgical consultant), sedated vs. unsedated procedure, visible dysplasia, HD-white light vs. IE, length of Barrett's segment and Prague classification, Paris classification of any visible lesions, targeted vs. Seattle Protocol biopsies, and grade of dysplasia. All endoscopies were done with high-resolution scopes; where a visible lesion was identified, a targeted biopsy was taken.

Results: 148 patients with dysplasia were analysed, M:F ratio 4.5:1, mean age 68yrs. Barrett's length ranged from 1-14cm, with 50% endoscopists reporting the Prague classification. Surveillance was done by: consultant gastroenterologists (70pts), nurse endoscopists (55pts), consultant surgeons (15pts) and registrars (8pts). At Site A only 3.2% of endoscopists explicitly mentioned a Seattle biopsy protocol in their report. Across both sites histology showed that protocol had been followed in 56.7% of endoscopies, with 54.2% gastroenterologists, 52.6% nurse endoscopists and 73.7% surgeons taking multi-level biopsies (Seattle equivalent protocol). The distribution of dysplasia LGD:HGD:carcinoma in the Seattle group was 1:1.48:1.32 vs. random biopsy of 2.54:2.47:1. In Site A, there was a statistically significant difference between the two groups, showing that more carcinomas were picked up in the Seattle group, chi-square statistic 12.65, DF=3 p=0.0018.

Conclusion: In this real-world NHS study, we found that after 4 years of the BSG guidelines, visible dysplasia is extremely difficult to detect. The Seattle biopsy protocol was followed in only 56.7% of endoscopies and is the dominant route, indicating a need for quality improvement & training amongst medical and non-medical endoscopists, including IE surveillance and chromoendoscopy.

Disclosure: Nothing to disclose

P1294 RELATIONSHIP BETWEEN BARRETT'S ESOPHAGUS AND COLONIC DISEASES: REFERENCE TO ENDOSCOPIC SURVEILLANCE

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Introduction: Given that the risk factor of Barrett's carcinogenesis is predictable, an appropriate management and surveillance of Barrett's esophagus (BE) may be provided. There are many reports regarding positive relationship between BE and colorectal neoplasm (CNs) in Western countries, this has been suggested BE and esophageal adenocarcinoma (EAC) are related with some colonic disease. However, it is still conflicting and little is known in Asian countries whose EAC has been also increasing. The purpose of this retrospective study was to investigate the relationship between BE or EAC, and colonic diseases including CNs, colon diverticulosis and inflammatory bowel diseases (IBD).

Aims & Methods: We retrospectively reviewed the medical records of 5606 patients (male gender: 56.9%, and median age: 68.2, range 16-98 years old) received both of colonoscopy and esophagogastroduodenoscopy between January 2016 and December 2017 in 3 core hospitals, and investigated their endoscopic findings and clinical covariables were age, gender, BMI, smoking, alcohol intake drug use (aspirin/NSAIDs, anti-coagulants, proton pump inhibitors, statins, anti-diabetics). BE was defined when Barrett's mucosa with more than 1.0cm of M-extent according to the Prague C and M criteria.

Results: BE with more than 1cm in length were found in 728 out of 5606 (12.9%) patients. The Predictors for BE were male gender (63.4%, P< 0.001), age (mean 69.3 +/- 11.8 years old, P< 0.001), PPI administration (35.2% vs. 29.0%, P< 0.001), anti-diabetics administration (12.3% vs. 9.8%, P=0.041), reflux esophagitis (15.6% vs. 7.9%, P< 0.001), hiatal hernia (59.0% vs. 34.5%, P< 0.001), presence of CNs (74.0% vs. 54.0%, P< 0.001), colon diverticulosis (34.0% vs. 29.3%, P=0.011) and IBD (0.6% vs. 1.8%, P=0.020). Related CNs were adenoma and adenocarcinoma, but not hyperplastic polyp, especially located in the proximal colon. Multivariate analysis showed that colon neoplasms (t = 8.54, P< 0.001), reflux esophagitis (t = 5.27, P< 0.001), and hiatal hernia (t = 11.73, P< 0.001) were positively correlated with presence of BE.

Conclusion: Presence of CNs was strongly associated with patients with BE. Colon diverticulosis and IBD may be a positive and negative predictor for BE. Information provided from colonoscopy appear useful to establish the strategy for the surveillance of BE.

Disclosure: Nothing to disclose

P1295 THE ASIAN BARRETT'S CONSORTIUM (ABC) MULTINATIONAL SURVEY ON THE PREFERRED DIAGNOSIS AND MANAGEMENT APPROACH OF BARRETT'S OESOPHAGUS (BO) IN THE ASIA-PACIFIC

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Introduction: The ABC is an Asia-Pacific workgroup on BO, affiliated to the National Cancer Institute in the United States. At present, guidelines from major societies worldwide provide differing definitions and viewpoints, making the standardization of the diagnosis of BO challenging. As a result of studies using different methodologies, endoscopic practices and histopathological criteria used in the diagnosis of BO, there is substantial variability in the published prevalence of BO in Asia.

Aims & Methods: We aim to better understand current practices and perceptions of Asian endoscopists regarding BO. We designed an online survey of 11 key questions to understand the preferred diagnosis and management practices of Asian Endoscopists on BO.

Results: Of 985 invited respondents, 593 completed the survey (response rate of 60.2%) with 60.5% from Japan vs. 39.5% outside Japan. 90.6% were physicians, and 77.4% of respondents spend at least 20% of time performing endoscopy. Results are shown in Table 1. The preferred landmark of the oesophagogastric junction in Japan was the distal margin of palisade vessels in 59.3% of Japanese but outside Japan, the squamocolumnar junction was preferred in 59.8% (P< 0.001). Any length of columnar-lined epithelium was the preferred definition of BE in 63.5% of Japanese vs. 71% outside Japan that preferred a minimum length of 1cm (P< 0.001). 46% respondents from Japan did not use the Prague C&M criteria, whereas outside Japan, 82.5% of respondents did so to varying extents (P< 0.001). The Seattle protocol for biopsies was not a routine among 73% of Japanese respondents, whereas outside Japan there was increased adherence although only 12% routinely do so (P< 0.001). Regarding histology, in Japan, a third (32.9%) felt that no histological confirmation was required but another third (35.4%) required only columnar tissue, but outside Japan, 38% preferred only columnar tissue while 36.3% required specialized intestinal metaplasia to diagnose BO (P< 0.001). Two-yearly surveillance endoscopy for long segment BO without dysplasia was performed in 81.3% within Japan vs. 59.4% outside Japan (P< 0.001). For treatment of BO without dysplasia with Proton Pump Inhibitors (PPI) only for oesophagitis or when symptomatic, it was preferred by 80.8% in Japan vs. 69.7% outside Japan

Q1. What is your preferred endoscopic landmark of the esophagogastric junction?	Squamo-columnar Junction (Z-line): 27.9% (Japan) vs 59.8% (Outside Japan)	Proximal margin of gastric folds: 11.7% (Japan) vs 26.9% (Outside Japan)	Distal margin of palisade vessels: 59.3% (Japan) vs 10.7% (Outside Japan)	Diaphragmatic pinch: 1.1% (Japan) vs 2.6% (Outside Japan)			p<0.001
Q2. What is your preferred endoscopic definition of Barrett's esophagus?	Length of columnar lined epithelium ≥2 cm: 23.4% (Japan) vs 38.9% (Outside Japan)	Length of columnar lined epithelium ≥1 cm: 13.1% (Japan) vs 32.1% (Outside Japan)	Any length of columnar lined epithelium in the esophagus : 63.5% (Japan) vs 29.1% (Outside Japan)				p<0.001
Q3. How often do you use the Prague C & M criteria in your assessment of Barrett's esophagus?	All the time: 12% (Japan) vs 22.2% (Outside Japan)	>70% of the time: 5.3% (Japan) vs 15% (Outside Japan)	30-70% of the time: 8.6% (Japan) vs 13.7% (Outside Japan)	<30% of the time: 28.1% (Japan) vs 31.6% (Outside Japan)	Never: 46% (Japan) vs 17.5% (Outside Japan)		p<0.001
Q4. What is your preferred histologic definition of Barrett's esophagus?	Any columnar tissue: 35.4% (Japan) vs 38% (Outside Japan)	Specialized Intestinal Metaplasia: 17% (Japan) vs 36.3% (Outside Japan)	Gastric Metaplasia: 14.8% (Japan) vs 20.1% (Outside Japan)	No histological confirmation required: 32.9% (Japan) vs 5.6% (Outside Japan)			p<0.001
Q5. In your practice, how regular do you survey your long-segment Barrett's esophagus without dysplasia?	Every 2 years: 81.3% (Japan) vs 59.4% (Outside Japan)	Every 3 years: 5% (Japan) vs 18.8% (Outside Japan)	Every 5 years: 1.4% (Japan) vs 4.7% (Outside Japan)	None at all: 12.3% (Japan) vs 17.1% (Outside Japan)			p<0.001
Q6. How often do you follow the Seattle protocol (i.e. four-quadrant biopsies every 2 cm) in your biopsies of Barrett's esophagus during surveillance endoscopy?	All the time: 2.5% (Japan) vs 12% (Outside Japan)	>70% of the time: 3.6% (Japan) vs 8.5% (Outside Japan)	30-70% of the time: 3.6% (Japan) vs 16.2% (Outside Japan)	<30% of the time: 17.3% (Japan) vs 44.4% (Outside Japan)	Never: 73% (Japan) vs 18.8% (Outside Japan)		p<0.001
Q7. What is your preferred treatment of Barrett's esophagus without dysplasia?	Lifelong Proton Pump Inhibitor (PPI) : 17% (Japan) vs 22.6% (Outside Japan)	PPI only when patient has symptoms of gastroesophageal reflux or evidence of esophagitis : 80.8% (Japan) vs 69.7% (Outside Japan)	Radiofrequency Ablation: 0.8% (Japan) vs 4.3% (Outside Japan)	Anti-reflux procedure (e.g. fundoplication): 1.4% (Japan) vs 3.4% (Outside Japan)			p=0.002
Q8. For Barrett's esophagus patients whose biopsies showed indefinite for dysplasia, your preferred approach is:	Confirm with second pathologist and repeat endoscopy after a course of PPI: 33.1% (Japan) vs 58.5% (Outside Japan)	Surveillance 6 monthly: 36.5% (Japan) vs 20.5% (Outside Japan)	Surveillance yearly: 29.8% (Japan) vs 19.7% (Outside Japan)	Surveillance 3-5 yearly: 0.6%% (Japan) vs 1.3% (Outside Japan)			p<0.001
Q9. For Barrett's esophagus patients without a lesion but whose biopsies showed low grade dysplasia, your preferred approach is:	Surveillance 6 monthly: 61.3% (Japan) vs 48.3% (Outside Japan)	Surveillance yearly: 22.3% (Japan) vs 20.9% (Outside Japan)	Surveillance 3-5 yearly: 1.1% (Japan) vs 3% (Outside Japan)	Ablative therapy, e.g., radiofrequency, cryotherapy, argon plasma coagulation : 1.1% (Japan) vs 17.9% (Outside Japan)	Endoscopic mucosal resection: 2.2% (Japan) vs 6.8% (Outside Japan)	Endoscopic submucosal dissection: 12% (Japan) vs 3% (Outside Japan)	p<0.001
Q10. For Barrett's esophagus patients without a lesion but whose biopsies showed high grade dysplasia, your preferred treatment is:	Endoscopic mucosal resection: 14.2% (Japan) vs 22.6% (Outside Japan)	Endoscopic submucosal dissection: 82.5% (Japan) vs 54.7% (Outside Japan)	Ablative therapy, e.g., radiofrequency, cryotherapy, argon plasma coagulation: 2.2% (Japan) vs 17.9% (Outside Japan)	Surgery, e.g., esophagectomy: 1.1% (Japan) vs 4.7% (Outside Japan)			p<0.001

[P1295 Table 1]

(*P=0.002*). For biopsies indefinite for dysplasia, a third (33.1%) of Japanese would confirm with a second pathologist and another third (36.5%) would rescope 6 monthly but outside Japan, 58.5% of respondents would perform the former (*P< 0.001*). For low grade dysplasia without a lesion, 6 monthly surveillance was preferred in 61.3% within Japan vs 48.3% outside Japan (*P< 0.001*). For high grade dysplasia without lesion, endoscopic submucosal dissection was the preferred option for 82.5% of Japanese vs. 54.7% outside Japan (*P< 0.001*).

Conclusion: In conclusion, diagnosis and management approach of BO appear to vary widely within Asia, with stark contrast between Japanese and non-Japanese endoscopists. Lack of standardization, education and research are possible causes for the observed differences.

Disclosure: Nothing to disclose

P1296 COMPARATIVE ANALYSIS OF THE EFFICACY AND SAFETY OF STANDARD VERSUS SIMPLIFIED RADIOFREQUENCY ABLATION PROTOCOL FOR DYSPLASTIC BARRETT'S ESOPHAGUS: A DUAL-INSTITUTION STUDY

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Introduction: Radiofrequency ablation (RFA) has been validated as a safe and effective treatment modality for dysplastic Barrett's esophagus (BE). The standard protocol of RFA includes an intermediary cleaning phase between two ablation session. A simplified protocol which omits this cleaning phase is less labour intensive and has shown to be as efficacious in studies based on single ablation procedures.

Aims & Methods: The aim of this study was to compare the efficacy and safety of the standard and simplified RFA protocols used for the whole treatment pathway and including both circumferential and focal devices. We performed a retrospective analysis of prospectively collected data on patients who received RFA between 2007-2017 at two institutions within the UK. Outcomes assessed were: 1) complete remission of dysplasia (CR-D) and intestinal metaplasia (CR-IM) at 18 months, and 2) rate of esophageal stricture. Patients that received a combination of both treatment protocols were excluded.

Results: 145 patients were included in the analysis of which 73 patients received the standard protocol and 72 patients received the simplified protocol. CR-D was achieved in 94.5% and 95.8% of patients receiving either the standard or simplified protocol, respectively (p=0.71). CR-IM was achieved in 84.9% and 77.8% of patients in the standard and simplified protocol groups, respectively (p=0.27). Complications were observed in 11.4% of patients, including 13 cases oesophageal strictures, and 1 case of mild esophageal tear during sizing of RFA balloon. Esophageal strictures were significantly more common among patients who received the simplified protocol (12.5%) compared to the standard protocol (1.4%, p=0.008). The median number of esophageal dilatation required was 1 (range 1-7).

Variable	Standard protocol	Simplified protocol	All patients	P value
Number of patients	73	72	145	-
Age, mean (SD)	66.3 (9.0)	67.0 (9.7)	66.6 (9.3)	0.66
Gender (% males)	86.3	86.2	86.2	0.97
BE length, M value (median, IQR)	5.0 (5.0)	4.0 (4.0)	4.0 (4.0)	0.35
Prior-EMR, n (%)	47 (64.4)	42 (58.3)	89 (61.4)	0.45
Extent of prior-EMR (median, IQR)	2 (2)	3 (3)	3 (2)	0.12
Number of RFA (median, IQR)	3 (1)	2 (1)	2 (1)	0.17
Dysplasia Grade, n (%) - LGD - HGD - IMC	- 7 (9.6) 27 (37.0) 39 (53.4)	- 13 (18.1) 33 (45.8) 26 (36.1)	- 20 (13.8) 60 (41.4) 65 (44.8)	0.082
CR-D, % (95% CI)	94.5 (89.2-99.9)	95.8 (91.1-100)	95.2 (91.6-98.7)	0.71
CR-IM, % (95% CI)	84.9 (76.5-93.3)	77.8 (67.9-87.6)	81.4 (75.0-87.8)	0.27
Rescue EMR, % (95% CI)	9.6 (2.7-16.5)	6.9 (0.9-13.0)	8.3 (3.7-12.8)	0.56
Strictures, % (95% CI)	1.4 (0-4.1)	12.5 (4.7-20.3)	6.9 (2.7-11.1)	0.008

[Table 1. Patient baseline characteristics and comparative outcomes stratified by different RFA protocols]

Conclusion: The simplified RFA protocol is equally effective compared to the standard protocol in terms of eradication of dysplasia and IM. When deciding treatment options for patients, the advantages of the simplified protocol which includes shorter procedural time and reduced discomfort for patients will need to be balanced against the significantly higher risk of strictures.
Disclosure: Nothing to disclose

P1297 NARROW BAND IMAGING ENDOSCOPY WITH TARGETED BIOPSIES VERSUS STANDARD ENDOSCOPY WITH RANDOM BIOPSIES IN PATIENTS WITH BARRETT'S OESOPHAGUS: A META-ANALYSIS

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Introduction: Barrett's oesophagus (BO) is the only identifiable premalignant condition for oesophageal adenocarcinoma (OAC) which represents the eighth most common cancer and the sixth cause of cancer-related deaths worldwide1. Surveillance in BO aims to detect and subsequently eradicate dysplasia and early OAC. The present guidelines2 recommend surveillance endoscopy in BO to be performed with random biopsies (Seattle protocol) every 2-3 years.

However, this method has high sample errors, laborious and correctly implemented only by half of endoscopists. Image enhancing technologies such as narrow band imaging (NBI) could provide an alternative to random biopsies. NBI has the ability to enhance the features of oesophageal mucosa and submucosa potentially allowing the endoscopist to take only targeted biopsy from areas that show an abnormal mucosal pattern that could be harporing dysplasia. Although NBI-targeted biopsy has been shown to perform equally or better in several studies, random biopsies remains up-to-date the standard of care.

Aims & Methods: This metanalysis intends to critically evaluate all available literature in this field and determine based on a comparative metanalysis if NBI targeted biopsies equally performs or outperforms random biopsies method for surveillance of BO.

This metanalysis was conducted according to the Preferred Reporting Items of Systematic reviews and Meta-Analyses (PRISMA) recommendations. It has been registered in advance in PROSPERO under ID: CRD42017073281. A comprehensive search for studies utilising NBI for BO was conducted by two researchers in the Cochrane Register, MEDLINE/Pubmed, EMBASE and grey literature. Human studies that compared NBI targeted biopsies with random biopsies for BO were retrieved. Methodological quality of included studies was assessed by the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2). Data from included studies were extracted, entered and analysed using the RevMan version 5 software. Analysis was performed with random effects method and the results reported per-patient rather than per-lesion.

Results: 14 studies were initially selected for the systematic review but only 6 studies with totoal 493 patients have fulfilled our inclusion criteria for metanalysis. The overall sensitivity (Sn), specificity (Sp), negative predictive value (NPV), and positive predictive value (PPV) for NBI-targeted biopsy detecting all dysplasia is 76%(95% CI 0.61-0.91), 99%(95% CI 0.99-1.00), 97%(95% CI 0.96-0.99), and 84% (95% CI 0.69-0.99), respectively. For high-grade dysplasia, the results respectively are 83%(95% CI 0.73-0.93), 99%(95% CI 0.99-1.00), 97%(95% CI 0.93-1.00), and 92%(95% CI 0.84-1.00). For detection of intestinal metaplasia, the same parameters respectively are: 0.83 (95% CI 0.63-1.00) 0.89 (95% CI 0.81-0.97).

Conclusion: NBI-guided targeted endoscopic biopsy has high diagnostic accuracy and can replace the current standard of care of random method in expert tertiary centres. For wider adoption of this NBI method more studies with better methodology are needed in the future.

References: 1\ J. Ferlay, I. Soerjomataram, M. Ervik, R. Dikshit, S. Eser, C. Mathers, M. Rebelo,D.M. Parkin, D. Forman, F. Bray Lyon FIA for R on C. Cancer Incidence and Mortality Worldwide [Protocol]. Cochrane Database of Systematic Reviews 2014, Issue IARC CancerBase No. 11. 2\ Nicholas J. Shaheen , MD, MPH, FACG 1 , Gary W. Falk , MD, MS, FACG 2 , Prasad G. Iyer , MD, MSc, FACG 3 and Lauren Gerson , MD, MSc, FACG. ACG Clinical Guideline: Diagnosis and Management ofBarrett's Esophagus [Protocol]. Cochrane Database of Systematic Reviews 2015, Issue The American Journal of GASTROENTEROLOGY. [Other:]

Disclosure: Nothing to disclose

P1298 EFFICACY, TOLERANCE AND SAFETY OF HYBRID ARGON PLASMA COAGULATION FOR THE TREATMENT OF BARRETT'S ESOPHAGUS: A US PILOT STUDY

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Introduction: Hybrid APC is a novel technique that has been recently developed for the ablation of Barrett's Esophagus. It is based on the combination of APC and submucosal saline injection to overcome some of the disadvantages of standard APC ablation. The current literature on this method is however limited.

Aims & Methods: The aims of this US pilot study were to evaluate the efficacy, tolerance and safety of Hybrid-APC for the treatment of BE.
Patients with biopsy proven BE were eligible with both treatment-naïve and patients previously treated included. Procedures were performed by two expert endoscopists using a standardized technique. Efficacy of ablation was measured on by demonstrating either a reduction of visible BE or biopsies proving complete resolution of intestinal metaplasia (CRIM). To evaluate tolerance and safety, patients were called on post-procedure days 1 and 7.

Results: 22 patients with BE (4.5% Intramucosal CA, 31.8% High Grade Dysplasia, 18.1% LGD, 36.3% non-dysplastic, 9.1% indefinite for dysplasia) underwent 40 treatments with Hybrid APC. Average age was 67.5 years, 86% male. Mean initial Prague score was C0.73, M1.99. 50% of patients had undergone prior RFA, 22.7% prior EMR, 13.6% prior cryotherapy, and 36.3% were treatment naive. The average index treatment time was 23.9 minutes. With regards to efficacy, 17 out of 22 (73%) patients achieved CRIM. All patients had endoscopic improvement of BE disease with an average length of BE at follow-up of C0.21, M0.63. Average pain scores (0-10 scale) on follow up were 2.65 and 0.62 at day 1 and 7 respectively. There were two treatment-related strictures (9%) which required a single balloon dilation. There were no other early or late complications.

Conclusion: Based on this US pilot study, Hybrid APC appears to be promising in the treatment of Barrett's Esophagus. The ablation protocol used in this study demonstrated efficacy, tolerability and a safety profile similar to radiofrequency ablation. Given the significant price difference of Hybrid APC with other modalities for Barrett's ablation, this modality may be more cost effective.

Disclosure: None

P1299 REDUCED STRICTURE RATES WITH A NOVEL HALO 360 RADIOFREQUENCY REGIME FOR BARRETT'S DYSPLASIA

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Introduction: In the UK, radiofrequency ablation (RFA) is established as treatment of choice for flat oesophageal neoplasia or after removal of focal lesions by endoscopic mucosal resection (EMR) to eradicate Barrett's mucosa[1]. A specific complication of RFA is oesophageal stricture develop-

ment. The UK national RFA registry has quoted a 11-17% rate of strictures requiring dilatation, with higher rates in patients treated with 12J rather than 10J paired ablations using the HALO 360 Express RFA catheter (p< 0.01). Two 10J ablations, separated by a cleaning step requiring removal of the catheter, is now standard of care. The cleaning step is time-consuming and can be poorly tolerated.

Aims & Methods: In December 2017 we adapted our practice to include irrigation with 30cc normal saline between 10J ablations as a cooling phase during the HALO RFA procedure and removed the cleaning phase between ablations. We have audited patient and disease demographics and outcomes data, especially oesophageal stricture rate, for all patients who had first HALO 360 express for 12 months before and after technique modification (1/12/16-1/12/18) in our hospital. Statistical analysis of variables was calculated using fisher's exact test, Wilcoxon ranksum, and logistic regression analysis.

Results: In the capture period, 36 patients had standard treatment and 48 patients underwent the modified technique. In the latter group, a significantly longer mean Barrett's segment was observed (6.1cm vs 8.2cm; p=0.01). We observed a stricture rate of 22.2% (8/36) in the standard treatment group, and 4.2% (2/48) in the modified group (p=0.014).
Stricture rate was significantly higher (p=0.026) with increasing Prague circumferential and maximum Barrett's length (p=0.023). There was no statistical difference in stricture rate when prior EMR or degree of dysplasia was considered.
The modified treatment was the only variable independently associated with stricture formation. A logistic regression model showed 85% reduced odds of stricture using the modified treatment (p=0.036) after adjusting for age, procedure type, grade of dysplasia, prior EMR, and Prague measurements.

Conclusion: These findings suggest a benefit of our novel adaptation of HALO 360 RFA treatment in Barrett's neoplasia with the novel treat-cool-treat technique resulting in significantly lower rate of stricture development.

References: 1. https://www.bsg.org.uk/resource/bsg-guidelines-on-the-diagnosis-and-management-of-barrett-s-oesophagus.html

Disclosure: E Saffouri has received educational support or hospitality from Gilead, Ferring, Cook, and Dr Falk.

P1300 LYMPH NODE METASTASIS RISK OF SIEWERT TYPE II ADENOCARCINOMA: COMPARISON OF BARRETT'S ESOPHAGEAL ADENOCARCINOMA AND GASTRIC CARDIA ADENOCARCINOMA RESECTED BY ENDOSCOPIC SUBMUCOSAL DISSECTION AND SURGERY

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Introduction: Esophagogastric junction adenocarcinoma includes Barrett's esophageal adenocarcinoma and gastric cardia adenocarcinoma. Curative criteria for endoscopic submucosal dissection in esophagogastric junction adenocarcinoma patients are controversial. Therefore, we elucidated the clinicopathological differences between Barrett's esophageal adenocarcinoma and gastric cardia adenocarcinoma and estimated risk factors of lymph node metastasis.

Aims & Methods: Patients who underwent surgical resection or endoscopic submucosal dissection for superficial esophagogastric junction adenocarcinoma of Siewert type II were included.

Results: Sixty-nine patients (44.2%) had Barrett's esophageal adenocarcinoma, and 87 (55.8%) had gastric cardia adenocarcinoma. Barrett's esophageal adenocarcinoma patients were significantly younger (62 vs 70 years, *p< 0.01*) and had a high frequency of poorly differentiated adenocarcinoma components (30% vs 15%, *p=0.02*) and lymphatic invasion (28% vs 12%, *p=0.01*). There was lymphovascular invasion in the deep muscularis mucosa in 31.6% of patients with Barrett's esophageal adenocarcinoma. Ten cases of lymph node metastasis were identified. Lymph node metastasis was not identified in patients with standard submucosal invasion < 500 μm without risk factors [tumor size >30 mm, lymphovascular invasion, poorly differentiated components]. Frequency of tumor size >30 mm (60% vs 17.1% *p< 0.01*), undifferentiated adenocarcinoma (40% vs 2.7% *p< 0.01*), poorly differentiated component (80% vs 17.8% *p< 0.01*), and lymphovascular invasion (90% vs 20.5% *p< 0.01*) was significantly higher in Barrett's esophageal adenocarcinoma patients.

Conclusion: Standard submucosal invasion < 500 µm without lymphovascular invasion, poorly differentiated components, and tumor size >30 mm were considered candidates for curative endoscopic resection for esophagogastric junction adenocarcinoma. Furthermore, histopathological surveillance for lymphovascular invasion is important for deep muscularis mucosa invasion of Barrett's esophageal adenocarcinoma.
Disclosure: Nothing to disclose

P1301 PUBLIC PREFERENCES AND PREDICTED UPTAKE FOR ESOPHAGEAL CANCER SCREENING STRATEGIES: A DISCRETE CHOICE EXPERIMENT

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Introduction: The majority of patients with esophageal adenocarcinoma (EAC) present with advanced disease, resulting in poor survival rates. Screening for EAC and its precursor Barrett's esophagus could possibly reverse the increasing incidence of EAC. In order to realize screening, it is important to understand the factors that influence population preferences for different EAC screening strategies and using them to achieve high attendance rates for a screening program for EAC.
Aims & Methods: We aimed to determine individuals' preferences for EAC screening and to assess to what extent procedural characteristics of EAC screening tests predict willingness for screening participation.
A discrete choice experiment questionnaire was sent by postal mail to 1000 individuals aged 50 to 75 years who were randomly selected from the municipal registry. Each subject answered 12 discrete choice questions of two hypothetical screening tests that comprised five attributes: EAC-related mortality risk reduction, procedure-related pain and discomfort, screening location, test specificity, and costs. A multinomial logit model was used to estimate patient preferences for each attribute level and to calculate relative importance scores of each attribute and expected rates of uptake. Regression analyses was performed to determine if socio-demographic characteristics predicted how respondents made decisions.
Results: In total, 375 patients (37.5%) completed the questionnaire. Test specificity had the highest impact on respondents' preferences, accounting for 27.2%, followed by pain and discomfort (26.8%), and mortality reduction (24.6%). Women were twice as much likely than men to value pain and discomfort as the most important attribute category (OR 2.08; 95%CI 1.28 - 3.33; P=0.003). In contrast, men were more likely to report mortality reduction as the primary determinant (OR 1.83; 95%CI 1.08-3.11). Individuals who worry about their own risk of developing cancer consider pain and discomfort to be important (OR 2.17; 95%CI 1.25-3.75) and worry less about test specificity (OR 0.45; 95%CI 0.25-0.82). Respondents preferred a test causing no or moderate pain and they were willing to give up 29 avoided EAC-related deaths per 10,000 screened individuals if the test causes only moderate instead of heavy pain.
The average expected uptake of EAC screening was 62.8% (95%CI 61.1-64.5). However, with the most preferred screening test, the probability of screening participation increased to 88.9% (95%CI 87.1%-90.4%). Heavy pain and discomfort had the largest impact on screening uptake (-22.8%; 95%CI -26.8- -18.7). Male gender (β 2.81; P< 0.001), cancer worries (β 1.96; P=0.01), upper endoscopy (β 1.46; P=0.05) or population-based screening (β 2.47; P=0.05)experience, and upper gastrointestinal symptoms (β 1.50; P=0.05) were significantly associated with screening participation.

Attributes	Impact of attribute levels on probability of screening participation (%) (* indicates p<0.05)			
Mortality reduction (per 1000 screened individuals)	*2 per 1000* **Reference**	*3 per 1000* **+5.8%***	*4 per 1000* **+14.0%***	*5 per 1000* **+17.8%***
Pain and discomfort	*No pain* **Reference**	*Mild pain* **-1.5%**	*Moderate pain* **-2.0%**	*Heavy pain* **-22.8%***
Out-of-pocket costs (€)	*Costs: €0* **Reference**	*Costs: €25* **-6.2%***	*Costs: €50* **-10.3%***	*Costs: €75* **-16.7%***
Specificity (%)	*Specificity: 50%* **Reference**	*Specificity: 70%* **-3.2%**	*Specificity: 90%* **+12.7%***	*Specificity: 100%* **+17.1%***

[Effects of changing the screening program characteristics on the probability of participation in esophageal cancer screening.]

Conclusion: This study suggests a substantial interest in EAC screening in the general population. Based on our results, an optimal screening test should have high specificity, cause no or mild to moderate pain or discomfort and result in a decrease in EAC-related mortality. Understanding individuals' preferences for EAC screening tests helps to further design the optimal screening modality by selecting the attributes that maximize attendance and further reduce morbidity and mortality from EAC.
Disclosure: Nothing to disclose

P1302 BARRETT'S ESOPHAGUS SCREENING: ACCURACY OF EXHALED BREATH ANALYSIS USING AN ELECTRONIC NOSE DEVICE

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Introduction: The majority of patients with esophageal adenocarcinoma (EAC) present with advanced disease, resulting in poor survival rates. Timely detection of EAC and its precursor Barrett's esophagus (BE) could decrease both cancer mortality and incidence. Currently, an accurate, minimally-invasive screening method for BE for widespread use is not available.
Aims & Methods: We aimed to assess the accuracy with which an electronic nose for breath analysis could discriminate patients with BE from controls without BE.
In this multicenter, cross-sectional, proof-of-principle study, patients undergoing a clinically indicated upper endoscopy between August 2017 and March 2019 were invited to provide a 5-minute breath sample using an electronic nose immediately prior a scheduled endoscopy. Patients were subdivided in three subgroups: BE (defined as ≥1 cm of columnar mucosa with histopathologic confirmation of intestinal metaplasia without dysplasia), gastroesophageal reflux disease (GERD) (defined as GerdQ-score ≥8 or the endoscopic presence of reflux esophagitis), and controls without BE or GERD.
The Aeonose™ is an olfactory system that analyses volatile organic compounds (VOC). Three metal-oxide sensors interact with VOCs in the breath sample to create a digital breath print specific to the VOCs. Data is analyzed by an artificial neural network to identify data classifiers to extract breath-print differences between patients with BE, GERD and controls, respectively. Optimal models were cross-validated using a leave-10%-out approach. Main outcomes were sensitivity and specificity for detecting BE compared with upper endoscopy as the reference standard.
Results: Breath samples were obtained from 212 individuals. Recruitment rates were 95%. Mean age of participants was 59.6 years and 56% were male. Seventy-three patients had a diagnosis of BE with a median (IQR) length of the BE segment of 4 (3-7) cm, 68 patients were diagnosed with GERD (32.4% reflux esophagitis), and 71 control patients did not have any esophageal abnormalities except for hiatal hernia. Diagnostic accuracy was high for discrimination of BE from both GERD and controls (area under the curve [AUC] 0.80, sensitivity 85% [95%CI: 74% - 92%], specificity 66% [95%CI: 58% - 74%]). Similarly, breath prints of BE patients could be differentiated from GERD patients (AUC 0.78, sensitivity 82% [95%CI: 71% - 90%], specificity 68% [95%CI: 55% - 78%]).
In a sub-analysis of patients using proton pump inhibitors for at least 1 month prior to study enrolment (n = 157; 68 BE, 46 GERD and 43 controls), a similar diagnostic accuracy for discriminating BE from both GERD and controls was observed: BE versus both GERD and controls AUC 0.81, sensitivity 71% and specificity 80%; BE versus GERD AUC 0.86, sensitivity 93% and specificity 70%; BE versus controls AUC 0.87, sensitivity 74% and specificity 88%.
Conclusion: This portable electronic nose is able to detect the presence or absence of BE in patients with and without GERD with good diagnostic accuracy. Given the high tolerability, high acceptability and low costs, breath testing may be a promising approach to be used for non-invasive screening for BE in a primary care setting.
Disclosure: The eNose company supplied the electronic noses used in this study for free.

P1303 STUDIES TO DETERMINE RISK FACTORS FOR BARRETT'S NEOPLASIA IN WOMEN SHOULD FOCUS ON A FAMILY HISTORY OF ESOPHAGEAL CARCINOMA, ONGOING GERD SYMPTOMS AND OBESITY

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Introduction: Current guidelines do not recommend endoscopic screening for Barrett's esophagus (BE) in females, except in patients who have multiple risk factors for BE and esophageal adenocarcinoma (EAC). However, it is unclear which factors most predict BE neoplasia risk in females. Therefore, identifying how females with EAC and high-grade dysplasia (HGD) differ from males may be useful to develop screening recommendations for women.

Aims & Methods: We conducted a retrospective analysis of a prospectively maintained database comprising consecutive patients with early stage EAC (T1a and T1b) and HGD at a single, tertiary-referral center from March 2001 to July 2017. Information regarding baseline clinical characteristics, drug and risk factor exposures, clinicopathological staging of EAC/HGD and follow-up status including treatment outcome such as complete remission of dysplasia (CR-D) and complete remission of intestinal metaplasia (CR-IM) were determined. Univariate and multivariate analyses were performed to identify factors that differed significantly between female and male patients with EAC/HGD.

Results: We identified 511 patients with T1 EAC and HGD (383 and 128, respectively); 88 (17%) patients were female. Compared to male patients, female patients were more likely to have ongoing GERD symptoms and a family history of esophageal carcinoma (51% vs. 39%, p=0.045; 8.3% vs. 2.8%, p=0.033, respectively) and less likely to have ever been smokers or drinkers of alcohol (65% vs. 76%, p=0.030; 58% vs. 81%, p< 0.001, respectively) on univariate analysis. On multivariate analysis, ongoing GERD symptoms, family history of esophageal carcinoma and obesity (BMI>30) were significant independent factors. Although the maximum length of BE in females was significantly shorter than in males (4.1 cm vs. 5.0 cm, p=0.024), there were no significant differences in terms of pathological findings such as tumor depth of invasion, differentiation, lymphovascular invasion or deep margin positivity. Furthermore, there were no significant differences between the groups regarding outcomes of endoscopic therapies with CR-D, CR-IM and recurrence of dysplasia and intestinal metaplasia with a mean follow-up period of 44.3 ± 30.2 months.

Conclusion: Female patients with T1 EAC or HGD were more likely to have a family history of esophageal carcinoma, ongoing GERD symptoms and obesity compared to male patients despite similar clinical outcomes with endoscopic therapies. While guidelines recommend BE screening in male patients, female patients should be considered for screening endoscopy if they possess these risk factors.

Disclosure: Nothing to disclose

P1304 THE IMPACT OF IMAGE ENHANCED ENDOSCOPY SCREENING FOR SYNCHRONOUS ESOPHAGEAL NEOPLASM ON SURVIVALS OF HEAD AND NECK CANCER PATIENTS

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Introduction: The incidence of esophageal second primary tumor (SPT) in head and neck cancer (HNC) patients is not low. The impact of routine image-enhanced endoscopy (IEE) screening for SPT of esophagus on the prognosis of HNC patients is not elucidated.

Aims & Methods: Patients with registered malignancies of head and neck region and esophagus were recruited from a hospital-based cancer registry between July 2000 and December 2016. Magnifying endoscopy with narrow-band imaging and chromoendoscopy with Lugol's solution was performed for IEE screening. The biopsied specimen reported with revised Vienna classification category 1 and 2 was defined as group I and category 3 to 5 as group II. The outcome assessment was connected to national death registry database and Kaplan-Meier estimate and Cox regression model were used for survival analysis.

Results: Finally, 1,577 HNC and 501 esophageal cancer patients were enrolled for analysis. The 5-year overall survival (OS) rate of stage I/II HNC, stage III/IV HNC and esophageal cancer patients were 58%, 29%, and 8%, respectively (p< 0.01). The 5-year OS rate of HNC patients with negative IEE results were higher than HNC patients without IEE screening, followed by IEE screening group I and II, and esophageal cancer patients (44% vs. 39% vs. 35% vs. 11% vs. 8%, p for trend < 0.01).

Among advanced HNC patients, those who received IEE screening of esophagus had a trend of better prognosis than those without (5-year OS rate of 31% vs. 28%, p=0.17).

In multivariate analysis of OS, age [hazard ratio (HR) 1.01, p< 0.01] and cancer of oropharynx (HR 1.43, p=0.01) were associated with poor survival. Compared with stage I/II HNC who received IEE screening of esophagus, stage III/IV patients with IEE (HR 2.33, p< 0.01) and without IEE (HR 2.77, p< 0.01) screening had worse survival.

Conclusion: The application of IEE screening for esophageal SPTs is helpful in risk stratification and prognosis prediction for HNC patients. Routine IEE screening is recommended in newly-diagnosed HNC patients.

Disclosure: Nothing to disclose

P1305 SIGMOID TYPE AND AGING AS POTENTIAL RISK FACTORS FOR DEVELOPING ESOPHAGEAL SQUAMOUS CELL CARCINOMA IN ACHALASIA PATIENTS: A RETROSPECTIVE STUDY

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Introduction: Incidence of esophageal cancer has been reported to be increasing recently. Achalasia has been considered as one of the risk factors for developing esophageal squamous cell carcinoma (ESCC). Although patients with achalasia were reported to have a higher risk of developing ESCC compared to the general population, details and characteristics of achalasia patients who develop ESCC are still not clearly defined.

Aims & Methods: This study aims to evaluate the characteristics of patients with achalasia associated with developing ESCC. A retrospective analysis study between January 2010 and November 2018 has been conducted at Showa University Koto Toyosu Hospital, Tokyo, Japan. Database of patients who underwent Per-oral Endoscopic Myotomy (POEM) has been reviewed. Patients who were diagnosed with esophageal achalasia based on the Modified Chicago Classification were included in the study.

Results: A total of 19 patients (1.5%) were identified to have ESCC from 1256 achalasia patients. Eleven (57.9%) were males and 8 (42.1%) were females. Median age was 64 (IQR= 55.5-75). Based on the Modified Chicago Classification, the type of achalasia seen were as follows: Type I/II/III= 9/7/3. In terms of histopathological findings, 17 patients (89.47%) exhibited mucosal ESCC, and 2 patients (10.53%) showed SCC extending to the submucosal layer. The occurrence of ESCC in achalasia patients was noted to be more likely in the older population (median: 68 vs 46, p= <0.001) compared to achalasia patients without ESCC.

Furthermore, a higher prevalence of sigmoid type (56% vs 12%, p= < 0.001) was observed in achalasia patients with ESCC in comparison with those non-ESCC achalasia patients. There were no significant differences between the two groups in terms of gender, types of Chicago classification, and Eckardt Score. All patients underwent successful endoscopic resection without any complications.

Conclusion: Achalasia has been deemed to be a risk factor for developing ESCC which involves various mechanisms. Patients with achalasia who belong in the older population and presenting with a sigmoid type were recognized to be at a higher risk for developing ESCC and should be monitored more closely during follow-up.

P1306 ENDOCYTOSCOPIC OBSERVATION AND DEEP LEARNING ARTIFICIAL INTELLIGENCE FOR ESOPHAGEAL LESIONS

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Introduction: Endocytoscopy (ECS) is a novel endoscopic technique that allows detailed diagnostic examination of the gastrointestinal tract at the cellular level. ECS was first developed and applied for clinical use in 2003 in our own study.
Aims & Methods: In the present study, we used the ECS to observe various esophageal lesions, and evaluated the diagnostic accuracy in distinguishing neoplastic from non-neoplastic lesions using both endoscopist's and pathologist's opinion. Further, we applied deep-learning artificial intelligence (AI) to analyse ECS images of the esophagus to determine whether AI can support endoscopists for the replacement of biopsy-based histology. We examined the morphology of surface cells using vital staining with toluidine blue and compared the histological features of 272 cases, including 129 cases of esophageal squamous cell carcinoma (ESCC) and 143 non-neoplastic esophageal lesions (65 cases of radiation esophagitis, 54 case of gastro esophageal reflux disease (GERD), and 13 cases of other esophagitis, 3 cases of benign tumor and 8 cases of normal squamous epithelium). One endoscopist classified the lesions using the type classification (Type 1; surface epithelial cells have a low N/C ratio and cell density but without evident nuclear abnormality. Type 2; surface epithelial cells have a high nuclear density but no evident nuclear abnormality and clear borders between cells. Type 3; surface epithelial cells have evidently increased nuclear density and nuclear abnormality, such as irregular nuclear size and shape.). Further, we consulted one pathologist for judgement in each case as "neoplastic", "borderline", or "non-neoplastic" from the ECS cell images.
Using 4,715 ECS images (1141 malignant and 3574 non-malignant images) from 240 cases, a deep learning AI was trained. To evaluate the diagnostic accuracy of the AI, test set of 1520 ECS images, collected from 55 patients (27 ESCCs and 28 benign esophageal lesions) were examined.
Results: On the basis of *in vivo* ECS observation, the endoscopist classified 82 cases as type1, 57cases as type2, and 133 cases as type3. The sensitivity, specificity and overall accuracy of ECS for malignant lesions by the endoscopist were 96.1%, 93.0% and 94.5%, respectively, if Type 3 was considered to be malignant. The pathologist classified 130 cases as non-neoplastic, 17 cases as borderline, and 125 cases as neoplastic. With regard to the pathologist's interpretation of the ECS images, the sensitivity, specificity and overall accuracy of ECS for malignant lesions were 96.1%, 94.4% and 95.2%, respectively if borderline category is considered to be correctly diagnosed. On the basis of ECS images, neither the endoscopist nor the pathologist was able to clearly distinguish regenerative squamous epithelium and pseudo-malignant erosion in gastroesophageal reflux disease and esophagitis after radiotherapy from esophageal cancer. In such cases, biopsy histology would be necessary in addition to ECS diagnosis. The AI correctly diagnosed 25 of the 27 ESCC cases, with an overall sensitivity of 92.6%. 25 of the 28 non-cancerous lesions were diagnosed as non-malignant, with a specificity of 89.3% and an overall accuracy of 90.9%. Although this result was inferior but close to the result obtained by the endoscopist.
Conclusion: ECS diagnosis for the esophagus realize the concept of optical biopsy, and enables us to omit biopsy histology. AI may support endoscopists in diagnosing ESCC based on ECS images in the future.
Disclosure: Nothing to disclose

P1307 USEFULNESS OF ENDOSCOPIC LARYNGOPHARYNGEAL SURGERY FOR SUPERFICIAL PHARYNGEAL SQUAMOUS CELL CARCINOMA

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Introduction: Endoscopic laryngopharyngeal surgery (ELPS) for superficial pharyngeal squamous cell carcinoma (SPSCC) has been reported as a minimally invasive treatment. However, the usefulness of ELPS for SPSCC was not investigated well because a small number of patients was involved in previous studies and an indication of ELPS for SPSCC invading up to subepithelial layer was still controversial. This study aimed to reveal the effectiveness of ELPS for pharyngeal squamous cell carcinoma (SCC) invading up to epithelial and subepithelial layer with short- and mid-term outcomes.
Aims & Methods: The patients who underwent ELPS for SPSCC between April 2015 and March 2019 were included. We retrospectively analyzed a clinical course, adverse events, en bloc/R0 resection rate, recurrence, and prognosis. Tumor thickness was evaluated from the tumor surface to the base of the malignant tissue in the thickest tumor section based on general rules for clinical studies on Head and Neck Cancer 2018. After ELPS, surveillance was performed with physical examination and laryngoscope observation every three months, computed tomography at intervals of every 6 months and endoscopic observation under narrow band imaging (NBI) every year.
Results: Forty-three patients with 56 SPSCCs were included this study. Table shows outcomes of ELPS for SPSCC. The median hospitalization was 11 days (range, 7-38). Dysphagia was found in 5 cases and 3 of them required hospitalization for more than 30 days. In those 5 cases all lesions were located in the hypopharynx and the resected lesion size was 35 mm or more. There were statistically significant differences in removed lesion size between patients with dysphagia (n=5) and without dysphagia (n=46) (median; 40mm vs. 25mm, p< 0.001). No patients received additional treatment even though lymphovascular invasion was found. During the follow-up (median=24 months; range, 1-43) no local recurrence was observed but pharyngeal lymph node metastasis was found in a case who had SCC located in the hypopharynx invaded up to subepithelial layer (tumor diameter: 17mm, tumor thickness: 3500μm, ly[+], v[+]) after 16 months from ELPS. This patient received chemoradiotherapy and survived for 24 months without recurrence. Metachronous H&N and oesophageal SCC were found in three cases (7%) and six cases (14%), respectively during follow-up period. All lesions were found under endoscopic observation with NBI and those were completely removed by additional ELPS. Two patients died of oesophageal cancer recurrence.

Patient (n=43)	
Male	41 (95%)
Age; median (range)	70 (59-85)
Synchronous or metachronous squamous cell carcinoma; head and neck / oesophagus	15 (35%) / 36 (84%)

Lesions (n=56)	
Location; oropharynx / hypopharynx	5 / 51
Tumor diameter; median (range), mm	17 (3-40)
En bloc resection rate / R0 resection rate	98% / 71%
Invasion depth (epithelial / subepithelial)	16 / 40
Adverse event; post-operative bleeding / perforation / dysphagia	0 / 0 / 5

[Outcomes of ELPS for SPSCC]

Conclusion: ELPS was effective for SPSCC including tumors invaded into the subepithelium. Resection of larger lesion was a risk factor for dysphagia, which affected the prolonged hospital stay. After ELPS, surveillance with NBI endoscopy should be performed considering the high cumulative incidence of metachronous pharyngeal and oesophageal carcinoma.
Disclosure: Nothing to disclose

P1308 TREATMENT STRATEGY FOR CERVICAL ESOPHAGEAL CANCER

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Introduction: Treatment for cervical esophageal cancer (CEC) is mainly surgery and definitive chemo-radiotherapy (dCRT). However, treatment strategy for CEC recently has been changed in condideration of quality of life after treatment. We have been performing neoadjuvant chemotherapy for CEC using FP (5FU/CDDP) from 2003 and using DCF (Docetaxel/CDDP/5FU) from 2009, and have decided to perform whether operation or dCRT by response of NAC.
Aims & Methods: 59 esophageal cancer patients who underwent operation or dCRT between 2003 and 2017 were analyzed as to treatment outcome, retrospectively.
Results: There were 43 men and 16 women, with a median age 64years. The average of duration of follow-up periods were 1367±1587 days. Tumors were located at CePh in 17 patients, Ce in 26, and CeUt in 16. Clinical T stage was 1b in 2 patients, 2 in 4, 3 in 21, and 4a in 32. Clinical N stage was 0 in 20 patients, 1 in 16, 2 in 18, and 4 in 4. Clinical Stage was I in 1 patient, II in 13, III in 20, and IVa in 25. 30 patients underwent FP, and 29underwent DCF as NAC. After NAC, no patients were obtained complete response (CR), 19 exhibited a partial response (PR), 31 had a stable disease (SD), and 1 presented with progressive disease (PD). 40 patients underwent surgery, and 19 received dCRT. Of 40 patients, 35 underwent pharyngo-laryngo-esophagectomy (PLE), and 5 cervical esophagectomy. 36 patients obtained a pathologically complete response (pCR) by surgery. Of 19 patients who received dCRT, 12 patients obtained a clinical CR. Postoperative complications were developed in 10 patients and detail as follows: 4 had recurrent nerve palsy, 3 necrosis or ulcer of trachea, 2 necrosis of free jejunum, 1 osteomylitis, and 5 others. 24 patients were received adjuvant therapy. Of 24, 11 received radiotherapy, 9 chemoradiotherapy, and 4 chemotherapy. 21 patients had recurrences after surgery. Of 21, 17 had distant metastasis, 11 lymph node metastasis, and 3 local recurrence. Of 12 patients who had obtained CR by dCRT, 8 had no recurrence. The 4 remained patients and 2 patients who obtained non-CR by dCRT underwent salvage surgery (PLE). The overall survival rates at 5 years (OS) were 47%, and those of patients who underwent surgery and dCRT were 39% and 74 %, respectively (p=0.07).
Conclusion: It suggests that dCRT could become alternative therapy of surgery for cervical esophageal cancer. Surgery for non-responder for NAC and salvage surgery for patients with recurrence after clinical CR by dCRT would play an important role. It is necessary for improvement of treatment outcome to find a new treatment for recurrence after surgery, because of high incidences of recurrence.
Disclosure: Nothing to disclose

P1309 CLINICAL EFFECTIVENESS AND SAFETY OF SELF-EXPANDING METAL STENT PLACEMENT FOLLOWING PALLIATIVE CHEMOTHERAPY IN PATIENTS WITH ADVANCED ESOPHAGEAL CANCER

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Introduction: To investigate the effect of prior chemotherapy on self-expanding metal stent (SEMS)-related complications in patients with locally advanced primary esophageal cancer.
Aims & Methods: Data from patients with locally advanced primary esophageal cancer who received SEMS placement with or without prior chemotherapy were retrospectively reviewed. Patients were grouped according to prior palliative therapy: group A had received SEMS only, and group B had received palliative chemotherapy prior to SEMS placement. Patient age, stricture length, location, and dysphagia score prior to SEMS placement were evaluated. Outcomes after SEMS placement, including technical and clinical success rates, the occurrence of complications and survival, were compared.

Results: The study included 105 patients (group A, n = 41; group B, n = 64). There were no significant differences between the two groups prior to SEMS placement. SEMS placement was technically successful in all patients, with no procedure-related complications reported. Clinical success was achieved in 95.1% of patients in group A and 96.8% of patients in group B. The duration of stent patency was significantly shorter in group B (162 days; 95% CI, 126.6-198.4 versus group A (339 days; 95% CI, 258.8-419.3), p = 0.001. No significant differences were seen between the two groups regarding dysphagia score improvement (p = 0.66), complications (p = 0.094), or survival (p = 0.592).
Conclusion: Prior chemotherapy did not increase the risk of complications following SEMS placement in patients with locally advanced esophageal cancer.
Disclosure: Nothing to disclose

P1310 VALIDATION OF MAGNIFYING ENDOSCOPIC CLASSIFICATION OF THE JAPAN ESOPHAGEAL SOCIETY FOR ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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Introduction: Predicting the invasion depth of superficial esophageal squamous cell carcinoma (SESCC) is crucial for determining the precise indication for endoscopic submucosal dissection (ESD), because the rate of lymph node metastasis increases in proportion to the invasion depth of SESCC. Recently, the Japan Esophageal Society (JES) developed a simplified classification for SESCC based on the degree of microvascular irregularity observed on magnifying endoscopy (ME). The JES classification defines severely irregular microvessels as type B vessels, which corresponds to cancerous lesions. The type B vessels are subclassified into type B1, B2, and B3 vessels that are correlated to histological invasion depth of T1a-EP or T1a-LPM, T1a-MM or T1b-SM1, and T1b-SM2, respectively. According to previous studies, the diagnostic accuracy of type B2 vessel is about 60%-70%, which is considered to be relatively low and unsatisfactory.
Aims & Methods: Predicting the invasion depth of superficial esophageal squamous cell carcinoma (SESCC) is crucial for determining the precise indication for endoscopic submucosal dissection (ESD), because the rate of lymph node metastasis increases in proportion to the invasion depth of SESCC. Recently, the Japan Esophageal Society (JES) developed a simplified classification for SESCC based on the degree of microvascular irregularity observed on magnifying endoscopy (ME). Type B vessels are subclassified into type B1, B2, and B3 vessels that are correlated to histological invasion depth of T1a-EP or T1a-LPM, T1a-MM or T1b-SM1, and T1b-SM2, respectively. According to previous studies, the diagnostic accuracy of type B2 vessel is about 60%-70%, which is considered to be relatively low and unsatisfactory.
Results: Of the 50 target areas, the number of the areas showing type B1, B2, and B3 vessels were 39, 9, and 2, respectively. The number of SESCC with tumor depths T1a-EP or T1a-LPM, T1a-MM or T1b-SM1, and T1b-SM2 were 44, 4, and 2, respectively. The sensitivity/specificity/positive predictive value (PPV)/negative predictive value (NPV) of the B1, B2, and B3 vessels were 86.4%/83.3%/97.4%/45.5%; 75%/87%/33.3%/97.6%; and 100%/100%/100%/100%, respectively. The accuracy of the B1, B2, and B3 vessels were 86%, 86%, and 100%, respectively. The PPV of B2 vessels was relatively low.
We noted 3 and 6 cases in the B2-narrow and B2-broad groups, respectively. The sensitivity/specificity/PPV/NPV of the B2-narrow and B2-broad groups were 0%/16.7%/0%/50% and 100%/50%/50%/100%, respectively. The accuracy of the B2-narrow and B2-broad groups were 33.3% and 66.7%, respectively. We noted 4 and 5 cases in the B2-only and B2-mixed groups, respectively. The sensitivity/specificity/PPV/NPV of the B2-only and B2-mixed groups were 100%/83.3%/75%/100% and 0%/16.7%/0%/25%, respectively. The accuracy of the B2-only and B2-mixed groups were 88.9% and 11.1%, respectively.
Conclusion: The accuracy of type B2 vessel was 86% whereas its PPV was as low as 33.3%. Contrastingly, the accuracy of the B2-only group, a proposed subcategorization of type B2 vessels, was 86%. The B2-only group was considered to be a useful predictor of T1a-MM or T1b-SM1.
Disclosure: Nothing to disclose

P1311 UTILITY OF STENT DOUBLE PALLIATION FOR ESOPHAGEAL CANCER WITH AIRWAY INVOLVEMENT - THE EXTREMIS OF CARE

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Introduction: Primary esophageal cancer (EC) frequently presents as an advanced disease with airway involvement. Placement of combined esophageal (eS) and airway stents (aS) have been reported in small series to be effective palliation strategies.

Aims & Methods: Our aim is to present the largest cohort of EC patients who underwent double stent palliation, and to evaluate the safety and efficacy of this approach. Methods - Longitudinal cohort study of patients with primary EC undergoing 2-stage esophageal and airway stent placement at an oncology referral institute (Jan2000-Jan2019). Assessments: baseline demographics and clinical variables; baseline and week 2 dysphagia, dyspnea and performance status [PS] scores; baseline and week 8 BMI; overall survival. Statistics: Paired t-Test; Kaplan-Meier method.

Results: Seventy patients (89% men, mean age 60.20 ± 8.41) underwent double stenting. eS was placed for esophageal stenosis and dysphagia (n=41; placement of a second eS due to recurrence in 9 cases) or ERF (n=29); aS was required for ERF sealing (n=29+7 new ERF after eS) and to ensure airway patency due to malignant stenosis (n=29; placement of a second aS due to recurrence in 13 cases) or compression (n=5).

There were 13, endoscopically managed, major complications after eS (hemorrage [n=1] migration [n=5], new fistulas [n=7]. As for aS, 4 major complications were recorded (hemorrage [n=1] and 3 deaths due to respiratory infection and ultimately respiratory failure 3 to 7 days after the procedure).

Overall, patients showed significant improvement in dysphagia and dyspnea symptoms (3,21vs.1,31 e 15,56vs.10,87; p=0,00). Along with symptom outcomes, there was a PS improvement for 89,2% (n=58) of the patients. BMI at week 8 was comparable to baseline records.

Mean survival was 137.83 ± 24.14 days (95% CI: 90.51-185.15). Survival was longer for lower performance status (PS1, 249.95 days; PS2, 83.74 days; PS3, 22.43 days; PS4, 30.00 days)

Conclusion: This is the largest comprehensive assessment of double stent palliation in advanced incurable EC. For both esophageal or airway stenosis and fistula, placement of combined eS and aS was a feasible, effective, fast-acting and safe modality for symptom palliation and BMI maintenance. Patient autonomy followed symptom improvement.

Since it is impossible to provide treatment for cure in most of these cases, this endoscopic strategy, performed in differentiated units with the required technical capacity, may guarantee treatment for the relief of paliative EC.

Disclosure: Nothing to disclose

P1312 IS BIPOLAR KNIFE SAFE THAN MONOPOLAR KNIFE IN ENDOSCOPIC SUBMUCOSAL DISSECTION FOR ESOPHAGEAL NEOPLASIA

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Introduction: Endoscopic submucosal dissection (ESD) is a standard treatment for early stage esophageal neoplasia. It was reported that the bipolar knife required significantly less energy and resulted in less tissue damage, and can decrease the incidence of perforation in animal model. On the other hand, all cases had submucosal fibrosis and it was not decreased esophageal stricture under esophageal ESD using bipolar knife compared with monopolar knife in porcine model. However, little is known the efficacy and safety of bipolar knife for esophageal ESD in clinical.

Aims & Methods: In the absence of prior reports, we evaluated the efficacy and safety of bipolar knife for esophageal ESD.

This was a retrospective observational study in a single institution. Between May 2012 and July 2018, 543 consecutive patients with 918 esophageal lesions were treated with ESD. Cases using multiple device and cases for esophageal SMT were excluded. The largest lesion was the target in patients with multiple lesions. Bipolar knife were used in anterior half and monopolar knife were used in posterior half. The primary outcomes were resectability and adverse events of esophageal neoplasia such as perforation, delayed bleeding, stricture, subcutaneous emphysema, pneumothorax, and mediastinal emphysema. We compared these outcomes of cases using bipolar needle knife with monopolar needle knife. Perforation was defined as a visible hole in the esophageal wall, exposing the mediastinal space. Generalized estimating equation were used for statistical analysis, and inverse probability of treatment weighting (IPTW) with propensity scores was used to reduce selection bias between the groups.

Results: A total of 531 cases with 633 lesions were evaluated. Monopolar and bipolar group were 368 case with 440 lesions and 163 cases with 193 lesions.

No significant difference was observed between the groups, such as age, gender, comorbidities, antithrombotic use, history of previous chemoradiotherapy, CO2 use, location, macroscopic appearance, lesion size, lesion circumference, clinical invasion depth, hemostatic forceps use, prophylactic steroid use and traction method use. En bloc and complete (R0) resection rates in the monopolar and bipolar group were high and similar, (99.5% vs 100.0%, and 97.0% vs 96.9%). Perforations and postoperative bleeding also occurred similar rate (2.7% vs. 2.1%, p=0.79, and 1.4% vs 1.0%, p=1.00). The incidence of subcuteneous emphysema and pneumothorax also similar, (1.1% vs 0.5%, p=0.67, 0.0% vs 0.5%, p=0.13). However, mediastinal emphysema were observed more frequently in the bipolar group than monopolar group (19.2% vs 11.4% vs, p= 0.01). All cases could be treated with endoscopic and conservative management. The incidence of stricture was similar between the groups (8.6% vs 5.2%, p=0.15). IPTW methods showed similar results and mediastinal emphysema occurred more frequently in bipolar group (OR=6.32, 95% CI: 1.79-22.38, p=0.004). Limitations of this study were retrospective single center analysis and all cases were not evaluated mediastinal emphysema by computed tomography after ESD.

Conclusion: ESD for esophageal neoplasia using bipolar needle knife was safe and effective as well as that using monopolar knife. Mediastinal emphysema might increase than monopolar knife.

Disclosure: Nothing to disclose

P1313 ENDOSCOPIC THERAPY IS AS EFFECTIVE AS SURGICAL RESECTION FOR EARLY OESOPHAGEAL CANCER: A TERTIARY REFERRAL EXPERIENCE OF 251 CONSECUTIVE CASES

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Introduction: Endoscopic eradication therapy (EET) is considered first line for the management of early oesophageal adenocarcinoma, but the transition from surgical management with primary oesophagectomy, the historical treatment of choice for high grade dysplasia and early cancer, has been challenging. Recent National audit data from the UK (NOGCA) demonstrated access to EET was variable according to geographic region, and only 65% were offered EET as first line. This study therefore aimed to compare the short and long term outcomes of consecutive patients with early oesophageal cancer treated during a transition period from oesophagectomy to EET in a single tertiary referral centre.

Aims & Methods: A single centre contemporaneously maintained database of consecutive patients treated for High grade dysplasia (HGD) and early oesophageal adenocarcinoma at a tertiary referral centre between 2000-2018. All patients were discussed at MDT and histology confirmed by central pathology review by 2 expert GI pathologists. EET was adopted as first choice treatment in 2012. All patients underwent EMR using Duette MBM kit by 2 experienced operators (JD,SZ). Follow up was either with RFA or APC according to standard protocols. Oesophagectomy was not preceded by neoadjuvant chemotherapy although some patients underwent resection following an initial attempt at EMR. Primary outcomes were overall and disease specific survival. Secondary outcomes included hospital stay, complications and cancer recurrence.

Results: 251 patients were identified; 113 patients underwent oesophagectomy and 138 patients were treated with EMR +/- further EET (59% + RFA/APC, 25% + RFA, 9% + APC, 7% stepwise EMR). The mean age for oesophagectomy was 64.6 years vs. EET 71.6 years (p=< .0001). The mean follow up time for oesophagectomy patients was 5.6 years vs 2.4 years after EET. The proportion of T1b cancers was higher in the oesophagectomy group (HGD 25% vs 39%, T1a 17% vs 34%, T1b 43% vs 16%, p< 0.001). Poor differentiation (23% vs 5%, p< 0.001) and lymphovascular invasion (19% vs 4%, p< 0.001) were also significantly higher in the surgical group. Inpatient hospital stay was significantly higher in the oesophagectomy group (median 14 days vs 1.5 days EMR; p=< .0001). In-hospital and 30 day mortality was 0% in both groups. The surgical group was associated with more significant complications (Clavien dindo ≥ 3) 26% vs. EMR 1%, p=< .0001. Cancer recurrence occurred in 18% of patients after oesophagectomy (local 4%, systemic 9%, mixed 5%) vs. 5% following EET (all local). The time to recurrence in both groups was not statistically significant. There was no difference in overall survival between both groups (HR 0.83 95%CI 0.45-1.54). Stage matched survival in the HGD, T1a and T1b sub-groups did not significantly differ between the groups.

Conclusion: In this large consecutive series of early oesophageal adenocarcinoma patients treated during a transition period from oesophagectomy to EET, there was no difference in overall disease free survival between both modalities. Post procedure mortality was zero in both groups. Importantly EMR/EET was safe, with no patients requiring surgery or ICU admission. Oesophagectomy was associated with prolonged recovery and significant post-operative morbidity - complications were more common and severe. These data add weight to the argument that EET should be available for all patients with early OAC as the gold standard of care. After EMR, patients with adverse prognostic features may still benefit from oesophagectomy.

Disclosure: Nothing to disclose

P1314 APPLICATION OF CONVOLUTIONAL NEURAL NETWORKS TO EVALUATING THE INVASION DEPTH OF EARLY GASTRIC CANCER BASED ON ENDOSCOPIC IMAGES

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Introduction: Endoscopic diagnostic accuracy of the invasion depth of early gastric cancer is reported to range from 71% to 95% [1]. Recently, artificial intelligence (AI) has been applied to endoscopic examination and is expected to improve endoscopic diagnosis [2, 3].

Aims & Methods: The aim of this study was to evaluate the feasibility of convolutional neural networks (CNN), a type of AI, for evaluating the invasion depth of early gastric cancer based on endoscopic images. From patients who underwent treatment for early gastric cancers in our hospital between January 2012 and December 2016, we selected 100 patients with mucosal cancers that were treated with endoscopic resection (ER) (M group), 50 patients with cancers invading the submucosa that were initially treated with ER (SM-ER group), and 50 patients with cancers invading the submucosa that were treated surgically (SM-OPE group). A total of 3508 non-magnifying endoscopic images of early gastric cancers, including white-light imaging, linked color imaging, blue laser imaging-bright, and choromoendoscopic images with indigo-carmine, were included in this study. The following images were excluded: narrow-band imaging, blue laser imaging, magnifying endoscopic images, poor images because of bleeding or edema caused by scope contact, and poor images because of halation or tarnishing of the lens. Three-fold cross-validation was conducted, and the results are presented as the mean value of three tests. The patients of each group were divided into three subgroups each. A deep CNN was pre-trained and fine-tuned on a dataset of endoscopic images from two-thirds of patients in the M and SM-OPE groups, and a dataset of endoscopic images from the other one-third of patients in all three groups was evaluated by the CNN. Invasion depth was evaluated for each image and patient. Majority decision was applied to the patient evaluation and a lesion was diagnosed as a mucosal cancer when the number of images diagnosed as mucosal cancers and as cancers invading the submucosa was the same.

Results: Regarding the image evaluation, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for diagnosing mucosal cancer were 82.7%, 63.0%, 69.1%, and 78.4%, respectively. Regarding the patient evaluation, the sensitivity, specificity, PPV, and NPV for diagnosing mucosal cancer were 82.0%, 71.0%, 73.9%, and 79.8%, respectively. The diagnostic accuracy for early gastric cancer, including both mucosal cancer and cancer invading the submucosa was 72.8% and 76.5% for the image and patient evaluations, respectively.

Conclusion: The application of CNN to evaluating the invasion depth of early gastric cancer based on endoscopic images is feasible, although some devices are required to improve diagnostic accuracy.

References: 1. Matsuura N, Iishi H, Uedo N et al. Diagnosis of invasion depth of early gastric cancer by normal endoscope [in Japanese with English abstract]. Stomach and Intestine. 2015; 50: 603-615. 2. Hirasawa T, Aoyama K, Tanimoto T et al. Application of artificial intelligence using a convolutional neural network for detecting gastric cancer in endoscopic images. Gastric Cancer. 2018; 21: 653-660. 3. Kanesaka T, Lee TC, Uedo N et al. Computer-aided diagnosis for identifying and delineating early gastric cancers in magnifying narrow-band imaging. Gastrointest Endosc. 2018; 87: 1339-1344.

Disclosure: Nothing to disclose

P1315 THE OUTCOMES OF UNDERWATER EMR AND CONVENTIONAL EMR FOR SUPERFICIAL NON-AMPULLARY DUODENAL EPITHELIAL TUMOR; A PROSPECTIVE STUDY WITH A COMPARISON TO HISTORICAL CONTROLS

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Introduction: Underwater EMR (UEMR) has been reported as an alternative to EMR for superficial non-ampullary duodenal epithelial tumor (SNA-DET). However, the detailed outcomes are still unclear.
Aims & Methods: This study aimed to compare the clinical outcomes of UEMR and EMR for SNADETs smaller than 20 mm.This was a prospective observational study with a comparison to historical controls. From November 2017 to December 2018, 104 consecutive cases with SNADETs smaller than 20 mm were prospectively included (UMIN000025442). A total of 240 cases of attempted EMR were chosen as historical controls. We compared the adverse event rates, rates of conversion to ESD, en bloc resection rate and R0 resection rate. Next, multivariate analysis was constructed to identify predictors for conversion to ESD, piecemeal resection, and RX or R1 (RX/R1) resection.
Results: Concerning adverse events, there were no significant differences between the two groups (delayed bleeding: 2% for UEMR and 1% for EMR; perforation: 0% in both groups). The conversion rate to ESD in the UEMR group was significantly lower than that of the EMR group (13% vs 30%, p< 0.01). Conversely, the en bloc resection rate and R0 resection rate of the UEMR group were significantly lower than those of the EMR group (en bloc resection: 87% vs 96%, p< 0.01, R0 resection: 67% vs 80%, p=0.05). In multivariate analyses, attempted EMR, lesion size and depressed type were independent predictors of conversion to ESD. Attempted UEMR was an independent predictor of piecemeal resection and RX/R1 resection.
Conclusion: The present study revealed that UEMR was equivalent to EMR in terms of safety. UEMR reduced the number of cases requiring conversion to ESD. However, it increased the risk of piecemeal and RX/R1 resection.
Disclosure: Nothing to disclose

P1316 WHAT KIND OF EARLY GASTRIC CANCER AFTER *H. PYLORI* ERADICATION IS DIFFICULT TO DIAGNOSE?

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Introduction: Early gastric cancer (EGC) occurring after successful *Helicobacter pylori* eradication is difficult to diagnose, due to non-neoplastic epithelia covering the periphery of the surface of cancerous areas. This might lead to unclear demarcation of the cancer when observed using narrow band imaging with magnifying endoscopy (NBI-ME).
Aims & Methods: This retrospective control study aimed to clarify the histopathological characteristics of EGC that has cancerous areas covered with non-neoplastic epithelia. There were 383 cases of EGC that underwent endoscopic submucosal dissection (ESD) between November 2011 and January 2019 at Okayama Medical Center. Sixty two lesions from 55 patients who had received *H. pylori* eradication before ESD were included. The specimens resected by ESD were cut by a width of 2 mm. For each lesion, every section was evaluated histopathologically, and the percentage of sections that had non-neoplastic epithelia covering the carcinoma was calculated. Based on the percentages calculated, the lesions were classified into two groups: covered group (27 lesions, 143 sections) (50% or more) and non-covered group (35 lesions, 139 sections) (less than 50%). Baseline characteristics, endoscopic features, and histological findings were evaluated. For endoscopic features, the following were evaluated: irregular microvascular/micro-surface pattern, light blue crest, green epithelium, intraepithelial microinvasion, over flow, and demarcation line.

The lengths of non-neoplastic epithelia covering the carcinoma, percentage of sections in which non-neoplastic tubules exist among cancer tubules, and background mucosa (fundic or pyloric glands/intestinal metaplasia) were evaluated in the histopathological evaluation.
Results: No significant differences were observed for the baseline characteristics. For the endoscopic features, only the demarcation line demonstrated a significant difference; the lesions classified as covered group had a higher proportion of unclear demarcation lines (p=0.0006). For the histopathological evaluation, the average length of non-neoplastic epithelia covering the carcinoma was 1.11 mm in the covered group, which was significantly longer than 0.57 mm in the non-covered group (p=0.001). The proportion of sections in which non-neoplastic tubules exist among cancer tubules was 77.8% in the covered group; this was significantly higher than the 48.6% observed in the non-covered group (p=0.001). The proportion of background mucosa which were fundic or pyloric glands was 62.7% in the covered group; this was significantly higher than the 49% observed in the non-covered group (p=0.02).
Conclusion: EGC occurring in the area where background mucosa is a fundic or pyloric gland tends to be covered with non-neoplastic epithelia peripherally. More careful observation is required in the fundic or pyloric gland area than in the intestinal metaplasia area.
Disclosure: Nothing to disclose

P1317 YIELD OF INVESTIGATING ISOLATED HYPOFERRITINAEMIA REFERRED FROM PRIMARY CARE

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Introduction: The value of investigating isolated hypoferritinaemia is unclear. The BSG guidelines on iron deficiency anaemia (IDA) suggest consideration of endoscopic investigation in those aged >50 after discussing the risk and potential benefit
Aims & Methods: We prospectively evaluated consecutive patients seen by a consultant gastroenterologist who had been referred from primary care with isolated hypoferritinaemia. All patients were offered investigation as per IDA guidelines following clinic consultation. Data was collected from the initial consultant consultation letter and from Infoflex (endoscopy) and Sunquest ICE system (blood results, radiology and histology). Lesions judged to be sources of significant blood loss were as defined by Rockey et al[1] (carcinomas, adenomatous polyps >15mm, vascular ectasia ≥5 or >8mm, duodenal / gastric / colonic ulcers >1cm, oesophagitis [LA grade D], erosive gastritis and active colitis).
Results: Eighty-two patients (median age 67.5 {42-93}; 58 females) were seen over a 5-year period (2014-2019). Thirty patients (36%) were asymptomatic (no symptoms or lethargy only). Fifty-eight patients (71%) had bidirectional endoscopies, 15 (18%) a combination of endoscopic and radiological imaging, and 6 (7%) having imaging alone. Two patients were excluded (1 died before investigations and 1 investigated as part of BCSP). Colonic carcinoma was discovered in 1 patient (1.3%). No gastric carcinomas were found (although a gastric carcinoma was discovered 12 months following a normal examination in a patient with a partial gastrectomy for previous gastric carcinoma). Other significant findings were: colonic polyps in 2 (2.5%); coeliac disease (serology negative, Marsh 3a) in 1 (1.3%); complex renal cyst resulting in nephrectomy in 1 (1.3%); hyperplastic/regenerative gastric polyps in 2 (2.5%); and an oozing gastric polyp in 1 (1.3%). There were no significant gastric or duodenal ulcers or angiodysplasias. Investigations were normal or non-significant in 74 (93%) patients: normal 25 (31%), gastritis 24 (30%), gastric polyps 10 (13%), colonic adenomas 8 (10%), oesophagitis LA grade A-B 4 (5%), haemorrhoids 4 (5%), duodenitis 2 (2.5%), Barrett's 1 (1.3%), duodenal adenoma 1 (1.3%), gastric ulcer 1 (1.3%), oesophageal erosions 1 (1.3%). Lung carcinoma was discovered in 1 patient who had a CT for associated weight loss; and a hepatocellular carcinoma in 1 patient, identified on renal tract ultrasound.
Conclusion: Gastrointestinal malignancy is rarely found in investigation of isolated hypoferritinaemia.
References: 1. Rockey DC and Cello JP. Evaluation of the gastrointestinal tract in patients with iron deficiency anaemia. N Engl J Med 1993; 329: 1691-5
Disclosure: Nothing to disclose

P1318 SCREENING ENDOSCOPY IN PATIENTS WITH ADVANCED CHRONIC LIVER DISEASE BEYOND PORTAL HYPERTENSION: HIGHER PREVALENCE OF GASTRIC NEOPLASIA IN COMPARISON TO A HEALTHY SCREENING POPULATION

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Introduction: The Baveno VI and the expanded Baveno VI criteria were proposed to help identify patients who could safely avoid screening esophagogastroduodenoscopy (EGD) for clinically significant varices among patients with compensated advanced chronic liver disease (cACLD). Although several studies have meanwhile validated those criteria, all fail to acknowledge the possible role of the avoided EGD for the same time screening of gastric neoplasia in cACLD population. Liver diseases are associated with an increased risk of extra-hepatic malignancies. Previous epidemiological studies have suggested that patients with cirrhosis have an increased risk for gastric cancer.

Aims & Methods: We aimed to evaluate the prevalence of gastric neoplasia in patients with cACLD who underwent screening EGD in a country with intermediate gastric cancer risk and high Helicobacter pylori prevalence. This retrospective cohort study enrolled all asymptomatic cACLD patients who underwent EGD for varices screening from January 2008 to June 2018. Cases were matched with asymptomatic healthy individuals who underwent EGD for gastric cancer screening at the same time as colonoscopy performed for colorectal cancer screening. Patients with prior history of organ transplantation and/or GI bleeding were excluded.

Results: We included 1974 subjects (610 patients, 1364 controls) 46.3% male, with a median age of 58 (50-66) years. Besides a male predominance in cases (69.0% vs. 45.6%, p< 0.001), no other demographic characteristic differed between cases and controls. The leading aetiology of cACLD was alcoholic liver disease (53.3%), followed by chronic hepatitis C (16.2%). Of the 610 patients with cirrhosis, 13 (2.1%) had gastric neoplasia [gastric cancer, n=10; high-grade dysplasia (HGD), n=2; low-grade dysplasia (LGD), n=1]. Most of the lesions (61.5%) were located in the gastric body, with a median size of 18 mm (15-24). Eight patients underwent surgical resection (R0 resection rate of 100%). Complications were observed in three of these patients (anastomotic leak n=2; nosocomial pneumonia n=1), with associated decompensated liver disease, leading to death in two of them. Three patients underwent endoscopic resection [n=2 endoscopic submucosal dissection (ESD), n=1 endoscopic mucosal resection (EMR)], with an en bloc resection rate, R0 resection rate and curative resection rate of 100%, without complications. Two patients were referred for palliative care due to decompensated liver disease. Compared to controls, cirrhotic patients had a higher prevalence of gastric neoplasia (2.1% vs. 1%, p=0.044; gastric cancer 1.6% vs. 0.8%, p=0.08). The prevalence of Helicobacter pylori infection was lower in patients compared to controls (36.2% vs. 47.2%, p=0.004). In the 13 cACLD patients in whom were detected neoplastic gastric lesions, 8 were diagnosed on the initial screening endoscopy. Four of these patients would have an avoidable EGD according to the Baveno VI criteria.

Conclusion: The prevalence of gastric neoplasia is significantly increased in cACLD patients compared to healthy screening population. Despite growing evidence supporting the role of non-invasive methods to rule out varices, EGD should still be considered in these patients, at least in those from countries with intermediate gastric cancer risk. Detection at an early stage may allow adequate treatment with less invasive techniques such as ESD, avoiding the considerable morbidity and mortality associated with surgical intervention in these patients.

References: De Franchis R, Baveno VI. Faculty. Expanding consensus in portal hypertension. Report of the Baveno VI Consensus Workshop: Stratifying risk and individualizing care for portal hypertension. J Hepatol Zullo A, Romiti A, Tomao S, et al. Gastric cancer prevalence in patients with liver cirrhosis. Eur J Cancer Prev. 2003; 12(3): 179-82.

Disclosure: Nothing to disclose

P1319 NON-CARDIA EARLY GASTRIC CANCER IN CENTRAL VIETNAM: UNCOMMON BACKGROUND MUCOSA AND PRELIMINARY RESULTS OF ESD TREATMENT AFTER 5 YEARS

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Introduction: Gastric cancer (GC) is the second leading causes of malignancy-related death in Vietnam, with increasing incidence of non-cardia early gastric cancer (EGC). Data on accurate diagnosis of EGC and treatment of this disease by endoscopic submucosal dissection (ESD) in Vietnam is still very limited.

Aims & Methods: To describe the characteristics of non-cardia EGC and evaluate the effectiveness and the safety of ESD in the context of Central Vietnam.

We prospectively enrolled patients with EGC detected by magnified chromoendoscopy from December, 2013 to December, 2018 at Hue University Hospital, Vietnam. Selected cases of non-cardia EGC received standardized ESD technique and have been following up carefully as in protocol.

Results: Among 606 cases of GC, 46 cases were non-cardia EGC and underwent ESD. The depth of invasion was T1a in 33 (71.7%), T1b1 in 10 (21.7%), and T1b2 in 3 (6.6%) cases. Mild- moderate chronic atrophic gastritis background, most being C2, and the gastritis-like with little malignant appearance EGC was the predominant type (63%). Severe chronic atrophic gastritis was found in only 2.2% of cases. ESD was performed of which 97.8 % received en-bloc resection; the mean procedure time was 76 ± 22 minutes (24-155), and mean sample size was 28 ± 7 mm (16.5-60). Complications consisted of two patients with severe bleeding and one case with minor perforation, all was successfully managed endoscopically. The longest follow-up time was 5 years with no recurrence. However, there were 2 cases who developed new high-grade dysplasia lesions and both of them underwent ESD second time successfully.

Conclusion: In Central Vietnam, a significant proportion with non-cardia EGC have a background mucosa of mild chronic atrophic gastritis and the gastritis-like with little malignant appearance. ESD treatment has demonstrate early promising results in that it appears effective and relatively safe.

	Italy [1]	France [2]	South East Asia [3]	Vietnam (our data)	p
Study period	2005-2011	2010-2013	2009-2015	2013-2018	
Study method	Retrospective	Prospective	Retrospective	Prospective	
Cases' number	20	319	35	46	
ESD size (mm)	Median 29	39 ± 23	Median 20 (5-60)	28±7 (16.5-60)	0.001*
ESD time (minutes)	Median 119.1	108.2 ± 62	Median 105 (15-480)	76 ±22 (24-155)	0.006*
ESD knives	IT knife, Hook knife	Dual knife, Flush knife	IT knife, Hybrid knife	IT2 knife, Flush knife	
En-bloc resection rate	NA	91.5%	91.4%	97.8%	0.134*
R0 rate	90%	71.2%	77.1%	95.7%	0.01**
Severe bleeding	0	15 (4.7%)	1 (2.9%)	2 (4.3%)	0.72**
Perforation	3/20 (15%)	26 (8.1%)	0	1 (2.2%)	0.15*

[Comparison with the ESD data of some other areas]

References: 1.Catalano, F., et al., Endoscopic submucosal dissection in the treatment of gastric submucosal tumors: results from a retrospective cohort study. Gastric Cancer, 2013. 16(4): p. 563-70. 2. Barret, M., et al., The expansion of endoscopic submucosal dissection in France: A prospective nationwide survey. United European Gastroenterol J, 2017. 5(1): p. 45-53. 3. Najib Azmi, A., et al., Endoscopic Submucosal Dissection Outcomes for Gastroesophageal Tumors in Low Volume Units: A Multicenter Survey. Diagn Ther Endosc, 2016. 2016: p. 5670564.

Disclosure: Nothing to disclose

P1320 EFFECT OF POTASSIUM-COMPETITIVE ACID BLOCKER TO HEALING OF ARTIFICIAL ULCER AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION: PROSPECTIVE RANDOMIZED TRIAL

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Introduction: Recently, endoscopic submucosal dissection (ESD) is commonly carried out to treat early-stage gastric cancer. Patient age, lesion size, location, and histology of tumor are related to the incident rate of complications and the healing speed of artificial ulcers after ESD. Vonoprazan (VPZ) is a novel potassium-competitive acid blocker (P-CAB), which exerts faster, more potent, sustained gastric acid inhibition than proton pump inhibitors (PPIs). However, it remains unclear whether the P-CAB effectively plays for the healing of artificial ulcer after ESD.
Aims & Methods: We compared healing process of artificial ulcer after ESD between treatment of P-CAB and PPI, as a prospective study at a single center. In addition, we evaluated influence of Helicobacter pylori (H. pylori) infection status in healing speed of artificial ulcer. One hundred nineteen six patients with gastric cancers or gastric adenomas treated by ESD at Shiga University of Medical Science from September 2015 to August 2018. By the minimization method using location of tumor (upper, middle or lower of the stomach) and tumor size (less than 20 mm or more), we randomly divided kinds of acid inhibitory drugs (VPZ 20mg for 8 weeks or lansoprazole (LPZ) 30mg for 8 weeks). Artificial ulcer size was endoscopically measured at the 1st, 2nd, 4th and 8th weeks after ESD. In addition, based on H. pylori status, we finally classified into 4 groups: V+ subgroup: H. pylori-positive and VPZ, V- subgroup: H. pylori-negative and VPZ, L+ subgroup: H. pylori-positive and LPZ, and L- subgroup: H. pylori-negative and LPZ.
Results: There were no significant differences in patient characteristics, location, depth and size of tumor among 2 groups. Reduction rates of artificial ulcer of VPZ were 37.8±32.8% at the 1st week, 73.8±19.4% at the 2nd week, 94.0±6.2% at the 4th week, and 99.8±0.1% at the 8th week, respectively. Reduction rates of LPZ were 30.2±34.0% at the 1st week, 69.4±24.7% at the 2nd week, 93.4±8.1% at the 4th week, and 99.9±0.1% at the 8th week, respectively. There was no significant difference between the 2 groups.In H. pylori-negative status, reduction rates were similar for V- and L- subgroup. In H. pylori-positive status, reduction rates of V+ subgroup was relatively higher than L+ subgroup at 2nd week (75.3±16.2%, 67.5±15.8%, P=0.06).
Conclusion: P-CAB has advantage to healing of artificial ulcer after ESD due to faster, more potent, sustained gastric acid inhibition than PPIs, especially in early phase within 2 weeks after ESD. These observations suggested that VPZ has high potential to prevent adverse events including bleeding, irrespective with H. pylori-infection status.
Disclosure: Nothing to disclose

P1321 GASTRIC CANCER PATIENTS WHO UNDERWENT GASTRECTOMY ARE HIGH RISK FOR COLORECTAL NEOPLASIA: A CASE CONTROL STUDY

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Introduction: Several studies suggested that colorectal neoplasia could be prevalent in gastric cancer patients. However, most of studies included gastric cancer patients before gastrectomy. The aim of this study was to investigated whether colorectal neoplasia was more prevalent in gastric cancer patients after gastrectomy than normal population.
Aims & Methods: We reviewed medical records of consecutive gastric cancer patients who underwent screening colonoscopy in 2017. Colonoscopy was done after at least 1 year of gastrectomy. Healthy individuals who received colonoscopy during the same period were matched to gastric cancer group by age and sex, at a 2:1 manner. We compared the frequency of colorectal neoplasia, advanced neoplasia, and cancer among gastric cancer patients with that of the control group.
Results: A total of 354 (118, gastric cancer; 236, control group) were included in this study. The rate of colorectal neoplasia and advanced neoplasia were higher in the gastric cancer patients than the control group (colorec-

tal neoplasia, 49.2% vs 33.5%, *p* < 0.01; advanced neoplasia, 21.2% vs 11.0%, *p* < 0.01). The rate of colorectal cancer didn't differ between the two groups (3.4% vs 0.8%, *p* = 0.10). Age ≥ 50, male gender, and gastrectomy for gastric cancer were significant risk factors for colorectal neoplasia in multivariate analysis.

	Gastric cancer group (total 118)	Control group (total 236)	P-value
Colorectal neoplasm	58 (49.2%)	79 (33.5%)	< 0.01
Advanced colorectal neoplasm	25 (21.2%)	26 (11.0%)	< 0.01
Colorectal cancer	4 (3.4%)	2 (0.8%)	0.10

[Rate of colorectal neoplasm in gastric cancer patients who underwent gastrectomy]

Conclusion: Colorectal neoplasia and advanced neoplasia were significantly more prevalent in patients with gastric cancer who underwent gastrectomy than the control group. Gastric cancer was independent risk factor for colorectal adenoma. We recommend regular colonoscopy in gastric cancer patients after gastrectomy.
Disclosure: Nothing to disclose

P1323 FLAT ELEVATED LESIONS WHICH HAVE BEEN DIAGNOSED WITH ADENOMA JUST BY CONVENTIONAL ENDOSCOPY CAN BE DISCRIMINATED BETWEEN EARLY GASTRIC CANCER AND ADENOMA BY MAGNIFIED ENDOSCOPY WITH NBI

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Introduction: A white and flat elevated lesion is a typical endoscopic finding of gastric adenoma with an intestinal phenotype. However, histopathological studies have recently revealed that some of these lesions which have a gastric phenotype just in part are consequently diagnosed as gastric cancers, because disease progression are faster than adenoma. Thus it is crucial to distinguish between these two phenotypes.
Aims & Methods: Magnified endoscopic findings were compared between lesions with a gastric phenotype (gastric cancers) and those with an intestinal phenotype (adenomas), all of which were detected as white and flat elevated lesions by conventional endoscopy. A total of 211 gastric neoplasias were treated by endoscopic submucosal dissection (ESD) at Kochi Red Cross Hospital between October 2010 and November 2018. In these lesions, 51 lesions which showed white and flat elevated were included this study. All lesions were examined by ME-NBI before ESD and resected en an block. The central region of the lesions was immunostained by MUC5AC, MUC6, MUC2, and CD10. These lesions were divided into 2 groups, Group A and Group B, according to the result of immunostaining. Group A was the lesions which had gastric phenotype, positive for MUC5AC and / or MUC6, diagnosed of gastric cancers. Group B was the lesions which had only intestinal phenotype, positive for only MUC2 and/or CD10, diagnosed of typical gastric adenoma. Mucin expression in ≥10% and < 10% of cells was defined as positive and negative, respectively, in accordance with previous reports
1). The magnified endoscopic findings were retrospectively examined and compared between the groups: microstructure of the surface, microvascular pattern, deposition of white opaque substances (WOS), and the presence of a crypt opening (CO). Microstructure pattern was classified as having an intralobular loop (ILL) pattern, which was defined as having a papillary or granular structure containing looped vessels; a fine network pattern (FNP), which was defined as having a regular crypt opening with regular polygonal microvessels; and a mixed pattern
2). Microvascular pattern was classified according to the VS classification system reported by Yao et al.
Results: There were 21 lesions in Group A and 30 lesions in Group B. The ILL pattern was dominant in Group A (81.0%, 17/21), and the FNP was dominant in Group B (60.0%, 18/30). Only one case had vessels exhibiting an epithelial circular (VEC) pattern. The microvascular pattern was irregular in 47.6% (10/21) of cases in Group A and in only 3.3% (1/30) of cases in Group B. The proportion of lesions with WOS deposition was slightly higher in Group B (50.0%, 15/30) than in Group A (42.9%, 9/21), and the proportion of lesions with the presence of a CO was higher in Group B (86.7%, 26/30) than in Group A (19.0%, 4/21).

Conclusion: Among white and flat elevated lesions that are diagnosed with adenomas by standard endoscopic observation, those with a gastric phenotype, which are diagnosed with cancers, have characteristic magnified endoscopic findings, including an ILL pattern and an irregular microvascular pattern. These findings will be important for distinguishing between adenomas and adenocarcinomas.

References: 1) Kanemitsu T, Yao K, et al. Magnifying Endoscopic Diagnosis of Extremely Well-differentiated Pure Adenocarcinoma of the Gastric Type. Stomach and intestines 53 (1) ,43-59, 2018 2) Yokoyama.A, Inoue H, Minami H, et al. Novel narrow band imaging magnifying endoscopic classification for early gastric cancer. Digestive and liver disease 42, 704-708, 2010

Disclosure: Nothing to disclose

P1324 RASPBERRY SHAPED GASTRIC LESIONS IN *HELICOBACTER PYLORI*-NEGATIVE PATIENTS

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Introduction: A reddish semipedunculated polyp with a morphological raspberry-like appearance in *Helicobacter pylori (Hp)*-negative patients has been recognized to be hyperplastic polyp (HP) conventionally. However, part of this poly is reported as gastric adenocarcinoma of foveolar-type (GAFV) which has recently proposed as a new rare variant of gastric adenocarcinoma and has garnered much attention as one of *Hp*-negative gastric cancer [1]. In this way, this type of polyp which is newly categorized as a raspberry shaped gastric lesion (RSGL) includes various lesions. However, clinicopathological and endoscopic features and differential diagnosis of RSGLs in *Hp*-negative patients have not been elucidated.

Aims & Methods: This study aimed to clarify the clinicopathological and endoscopic features of RSGLs in *Hp*-negative patients. We collected RSGLs from endoscopic database in our hospital between April 2014 and February 2019 including 556 EGCs which underwent endoscopic resection. We classified RSGLs histopathologically, and analyzed their clinicopathological and endoscopical features.

Results: A total of 17 RSGLs (10 males, 7 females) in *Hp*-negative patients were collected (Table), and classified into 6 histological types as follows;

	GAFV	GAFG	GAFGM	HP	FGP like lesion with atypical foveolar hyperplasia	Hyperplasia of foveolar epithelium and parietal cell
Number of cases	7	2	2	4	1	1
Age	52.5	65.5	41.5	69	70	65
Gender (male/ female)	5/2	0/2	1/1	2/2	1/0	1/0
Location (U/M/L)	4/3/0	2/0/0	2/0/0	3/0/1	1/0/0	0/1/0
Location (Greter curvature/ Lesser curvature)	7/0	2/0	2/0	1/3	1/0	0/1
Tumor size(mm)	5(3-8)	8.5(5-12)	4.5(4-5)	5.5(3-9)	12	6
Macroscopic type (elevated / depressed)	7/0	2/0	2/0	4/0	1/0	1/0
Depth of invasion (M/SM)	7/0	0/2	1/1			

[Clinicopathological findings of raspberry shaped gastric lesion in Helicobacter pylori-negative patients]

1. GAFV (7cases), 2. gastric adenocarcinoma of fundic gland type (GAFG, 2cases), 3. gastric adenocarcinoma of fundic gland mucosal type (GAFGM, 2cases), 4. HP (4cases), 5. fundic gland polyp (FGP) like lesion with atypical foveolar hyperplasia (1cases), 6. Hyperplasia of foveolar epithelium and parietal cell (1cases). "FGP like lesion with atypical foveolar hyperplasia" and "hyperplasia of foveolar epithelium and parietal cell" showed parietal cell protrusions histopathologically, which considered to be associ-

ated with long-term use of proton pump inhibitors. Clinicopathologically, RSGLs were frequently found in the greater curvature of upper gastric body except for HP. All RSGLs showed strongly reddish protruded lesions macroscopically. In white-light endoscopic images, GAFV were observed as entirely reddish lesions, however, other lesions partially accompanied with whitish areas. Magnifying endoscopy with narrow-band imaging was performed in 9 cases (GAFV/ GAFG/ GAFGM/ HP/ FGP like lesion with atypical foveolar hyperplasia / hyperplasia of foveolar epithelium and parietal cell=3/2/2/1/1/1). Only 2 case of GAFGM was diagnosed as cancer with MES-DA-G [2], however, GAFV and GAFG were diagnosed as non-cancer. There were no endoscopic findings that were useful to distinguish each lesion.

Conclusion: RSGLs in *Hp*-negative patients could be classified into various types histopathologically and should be suspected as gastric cancer. Though RSGLs are characterized by the location, RSGLs may be difficult to diagnose endoscopically. Therefore, RSGLs should be diagnosed histopathologically, and further examination will be needed for precise endoscopic diagnosis of RSGLs.

References: 1. Isono Y, Baba Y, Mukai K, et al. Gastric adenocarcinoma co-existing with a reddish semipedunculated polyp arising from Helicobacter pylori-negative normal gastric mucosa: a report of two cases. Clinical journal of gastroenterology 2018; 11, 481-486. 2. Muto M, Yao K, Kaise M, et al. Magnifying endoscopy simple diagnostic algorithm for early gastric cancer (MESDA-G). Digestive endoscopy : official journal of the Japan Gastroenterological Endoscopy Society 2016; 28, 379-393.

Disclosure: Nothing to disclose

P1325 SARCOPENIA IS A RISK FACTOR FOR ASPIRATION PNEUMONIA ASSOCIATED WITH ESOPHAGEAL AND GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) IN ELDERLY PATIENTS

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Introduction: Endoscopic submucosal dissection (ESD) is a safe and effective treatment for gastric and esophageal neoplasms even in elderly patients. However, this approach involves adverse events, including perforation, bleeding, and aspiration pneumonia. Although aging is an independent risk factor to develop aspiration pneumonia, other risk factors for aspiration pneumonia among elderly patients are unclear. Here, we aimed to investigate risk factors for aspiration pneumonia among elderly patients.

Aims & Methods: This was a retrospective observational study conducted at a single center, which included 170 patients ≥80 years of age who had undergone esophageal or gastric ESD. We compared patients with sarcopenia (sarcopenia group) with patients without sarcopenia (non-sarcopenia group). The presence of sarcopenia and aspiration pneumonia were confirmed by computed tomography.

Results: The overall incidence of sarcopenia was 42.9%. In the sarcopenia group, the incidence of aspiration pneumonia was 21.9% whereas it was 9.3% in the non-sarcopenia group (p=0.0212). Body mass index was significantly lower in the sarcopenia group than in the non-sarcopenia group (20.6±2.9 vs 23.6±3.1, p< 0.001). Procedure time did not significantly differ between the two groups (72±54 minutes vs 62±44 minutes, p=0.201) nor did the proportion of abnormal respiratory function tests was not significantly different between two groups (62.1% vs 63.5%, p=0.87). On multivariate analysis, sarcopenia was an independent risk factor for the development of aspiration pneumonia (odds ratio=2.61, 95% confidence interval 1.07 to 6.37, p=0.0347).

Conclusion: Sarcopenia was a risk factor for aspiration pneumonia after esophageal or gastric ESD.

Disclosure: Nothing to disclose

P1326 ROLE OF MULTIDISCIPLINARY TEAM IN THE MANAGEMENT OF NEUROENDOCRINE NEOPLASIA: A REAL-WORLD EXPERIENCE

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Introduction: Neuroendocrine Neolpasia (NENs) are rare and heterogenous diseases, in terms of both pathological and clinical features. Their prognosis is affected by including primary tumor site, staging, and grading.Due to the complexity of NENs management, a multidisciplinary approach is widely advised for an effective care of patients with this uncommon kind of cancer. Multidisciplinary care is strongly encouraged by both Neuroendocrine Tumor Society (ENETS and NANETS). Since data on multidisciplinary management of patients with NENs in specialized centers with dedicated MDT are scanty.

Aims & Methods: Aimed to analyze modality of presentation and clinical outcome in patients with NENs managed in a center of excellence with dedicated MDT. Prospective observational study including all consecutive newly patients visited at the Sant'Andrea Hospital site of the Rome ENETS – Center of Excellence between January 2014 and June 2018. All the major clinical and pathological data were collected in an electronical anonymized database. All patients were discussed in a NEN multidisciplinary team which included clinicians involved in patients' management

Results: A total of 318 patients were evaluated. Of these, 122 patients were excluded because referred to the center for a second opinion; since these patients no data on their follow-up were available. Thus, the final analysis was performed on 196 patients, including with a median age of 59 yr (IQR 50.5 – 70.5 yr). Of these, 164 patients had GEP NENs (83.7%), and 19 patients had lung primary NEN (9.7%).At time of initial visit at the center, Ki67 value was available in 178 patients (90.8%), median value being 3% (IQR 2 – 9). Overall, 159 patients (81.1%) already had NEN diagnosis at time of referral; in these patients, median interval between initial NEN diagnosis and time of referral to the center was 4 months (IQR 2 - 12 months). The remaining 37 patients (19.9%) were newly diagnosed at the center. A total of 64 patients (32.7%) got in touch with the center by using the center's website form, whereas 132 patients (67.3%) booked the first visit by public health regional system tools. Overall, 74 patients (37.8%) were referred to the center by other hospitals. Median waiting time to obtain the first visit in the NEN-dedicated ambulatory was 7 days (IQR 7 - 10 days). After first visit, all patients were discussed at the MDT meeting. Additional cross-sectional radiological examinations or nuclear medicine diagnostic procedures were requested in 164 patients (83.7%). After these procedures, a change in disease staging was performed in 50/164 patients (30.5%). After MDT meeting discussion, pathological revision of available histological slides was advised in 53 patients (27%), whereas new bioptic sampling was advised in 30 patients (15.3%). Overall, a change in clinical management was observed in 98 patients (50%) after MDT discussion. Of these, 67 patients (68.4%) received medical treatment (somatostatin analogs 37 pts 37.8%; everolimus 15 pts , 15.3%, systemic chemotherapy 6 pts, 6.1%, peptide receptor radionuclide therapy 4 pts 4%), 9 patients (9.2%) underwent surgery, and 19 pts (19.4%) were followed up without medical or surgical intervention. The remaining 3 patients were treated by endoscopic resection (n=2) or liver radiofrequency (n=1).

Conclusion: This study reports the features of NEN pts admitted to an Italian center of Excellence, which mostly had non-functioning tumors, advanced disease and low Ki67. In those pts referred by other hospital, the median interval between initial diagnosis and taking care by the center was 4 months.

Disclosure: Nothing to disclose

P1327 ENDOSCOPIC ULTRASOUND-GUIDED ANGIOTHERAPY OF GASTRIC VARICES WITH COMBINED COILS AND GLUE INJECTION: AN EUROPEAN STUDY

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Introduction: Gastric varices (GV) represent 20% of patients with portal hypertension.
Endoscopic cyanoacrylate injection is recommended in bleeding gastric varices.
Nevertheless, it is associated with more than 25% of re-bleeding and serious adverse events, mainly glue embolization. Endoscopic ultrasound (EUS)-guided and combined coil and glue injection provide a new alternative treatment for bleeding varices.

Aims & Methods: This is a retrospective analysis of EUS-guided coil and glue injection for gastric varices bleeding from 10/2013 to 03/2019. We used linear therapeutic ultrasound endoscopes without fluoroscopic control. The procedures were performed on general anesthesia and antibioprophylaxia. We injected cyanoacrylate combined with Lipiodol after the application of one or many coils (5 x 50 mm). A control EUS was done at 4 weeks.
The primary outcomes were varices obliteration and the need of reintervention.

Results: 33 patients were treated by EUS-guided coil and glue injection, 26 (78%) for recent bleeding varices and 7 (22%) for primary prophylaxis. There was 60% of males and the mean age is 61 years (28-84). Technical success was achieved in all patients (100%). The mean number of coil was 1.2 (1-3 coils) and the mean volume of glue injected was 1.5 mL (0.5-3 mL). Complete obliteration was confirmed for the 33 patients (100%), 30 after one session (91%), 2 after 2 sessions and one after 4 sessions. Post-procedure pain occured in 3 patients (9%) during 1 to 7 days. No symptomatic embolization was observed with a mean follow-up of 436 days (21-1818).

Conclusion: EUS-guided combined coil and glue injection for gastric and ectopic varices appears to be a feasible and highly effective technique with less re-bleeding and complication than the classic endoscopic glue-only injection.

References: EUS-guided treatment of gastric fundal varices with combined injection of coils and cyanoacrylate glue. Bhat YM, Weilert F, Fredrick Rt, Kane SD, Shah JN, Hamerski CM, Binmoeller KF. Gastrointest Endosc. 2016 Jun;83(6):1164-72.

Disclosure: Nothing to disclose

P1328 SHARED ANGIOGENIC DRIVERS OF INTESTINAL VASCULAR DISORDERS

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Introduction: Neovascularisation is common to a variety of GI disorders with differing etiologies and presentations. Shared angiogenic factors modulated by disease specific elements could be a common denominator and represent novel diagnostic and therapeutic targets. As yet, assessment of angiogenic factors across common GI vascular disorders has not been reported.

Aims & Methods: To assess serum levels of angiogenic factors in intestinal vascular disorders.
Following ethical approval and informed consent, serum from patients with small bowel angiodysplasia (SBA), portal hypertensive gastropathy (PHG), gastric antral vascular ectasia (GAVE) and non-bleeding, non-anaemic controls were collected. Using ELISA, concentrations (ng/ml) of Angiopoietin 1 (Ang-1), Angiopoietin 2 (Ang-2) and Vascular Endothelial Growth Factor (VEGF) were measured. Results were expressed as a mean

and compared between groups using a T-test, p-value of < 0.05 was considered significant. The relative expression of Ang-1 and Ang-2 was calculated between groups.

Results: To date 44 samples were tested: 10 SBA, 11PHG, 8 GAVE and 15 Controls. Mean age 60 (range 20-86) years and 20 (45%) were males. Controls were significantly younger (49 vs 66yrs) p =0.0005. There was no difference in VEGF levels between the groups, 443 ng/ml, 316 ng/ml, 435 ng/ml V's 421 ng/ml (p=0.59). SBA, PHG and GAVE Ang-1 levels were similar and were significantly lower than controls: 35696 ng/ml, 23111 ng/ml, 30753 ng/ml, V's 53115 ng/ml, (p=0.0002, 95%CI 241 to 701). Ang-2 levels were higher in PHG and GAVE cases: 4298 ng/ml, 4232 ng/ml, V's 1899 ng/ml in controls (p=0.01, 95%CI 77.8 to 668) but were similar for SBA 2803 ng/ml (p=0.4).

As a result, the ratio of Ang-1/Ang-2 was found to be significantly lower in PHG 10 (p=0.002, 95%CI 8.65 to 35.50) and GAVE 10 (p=0.004, 95%CI 7.82 to 35.28) groups compared to Controls 32 respectively. While SBA Ang-1/2 ratios were similar to controls 32.

The ratio of Ang-1/Ang-2 did not differ within the control group by age, < 65 years Ang1/2 ratio 33 V's >65 years Ang-1/2 ratio 22 (p=0.4). The mean age within disease groups was similar SBA 69 (range 53-86); PHG 60 (range 38-81); GAVE 68 (range 58-85). Age is therefore unlikely to explain the discrepancy in Ang-2 levels and resultant Ang-1/Ang-2 ratios between the SBA and the other disease groups.

Conclusion: Our novel study of intestinal vascular disorders suggests a common alteration in Ang-1 levels, a vascular factor associated with vessel stabilization and maturation, across a variety of GI vascular disorders. Differences in Ang-2 profiles and resultant Ang-1/Ang-2 ratios among vascular disorders suggest disease-specific modulation and reflects the known variability in Ang-2 roles. VEGF appears not to play a significant role in the vascular conditions investigated.

Disclosure: Nothing to disclose

P1329 ACUTE NECROTIZING OESOPHAGITIS: A VIEW INTO THE DARK

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Introduction: Acute necrotizing esophagitis (ANE), also known as "black oesophagus", is a rare condition characterized by circumferential necrosis of varying lengths in the oesophagus.

The aim of this study was to determine the incidence of ANE, its clinical presentation and endoscopic appearance, risk factors and associated conditions, related complications, management, short and long-term outcomes.

Aims & Methods: The aim of this study was to determine the incidence of ANE, its clinical presentation and endoscopic appearance, risk factors and associated conditions, related complications, management, short and long-term outcomes.

Retrospective analysis of all upper endoscopies performed over an eight-year period (2011-2018) in a tertiary care hospital. We considered acute necrotizing esophagitis the endoscopic appearance of diffuse or spotty dark pigmentation oesophageal mucosa with abrupt transition to normal-appearing mucosa at gastroesophageal junction in a patient without any other cause to explain it and with no previous history of relevant oesophageal disease.

Results: Over an eight-year period, there were performed 37 403 upper endoscopies and 7103 were done in an urgent setting. Acute necrotizing esophagitis was observed in 13 patients and all underwent urgent upper endoscopy. Therefore, overall prevalence was 0.03% and in urgent setting it was 0.18%. The median age was 67 years-old (±12) and 77% (10/13) were male. The main clinical manifestation of AEN was upper gastrointestinal bleeding, which occour in 77% (10/13) of the patients. At the time of clinical manifestation 85% (11/13) of the patients had severe comorbid conditions and it was possible to identify previous hemodynamic instability in 62% (8/13).

In all cases the endoscopy was done within 12 hours of clinical manifestation. Endoscopically besides the black-appearing oesophageal mucosa, 71% (10/14) had other abnormal endoscopic findings, the most common finding was peptic ulcer disease. All patients underwent CT that ruled out AEN complications, except for one patient that had mediastinitis, which was successfully treated conservatively.

Regarding the treatment, cases were managed with supportive therapy and endovenous proton pump inhibitor. Most of the patient were also on broad-spectrum antibiotics (77%).

23% (5/13) of the patients died during the hospital stay and 40% (2/5) of them died in the first 24h after clinical manifestation of AEN. None of the deaths were related with AEN or its complications. All causes of death were related to underlying clinical condition, the most common cause of death was sepsis. All the discharged patients had no complications related with AEN and were alive in the 2 years follow-up. In all the endoscopically re-evaluated patients the condition had completly resolved.

Conclusion: AEN is an important cause of upper gastrointestinal bleeding in critically ill patients with severe co-morbidities. ANE is an important marker of severe disease and increased overall mortality. Even though AEN it is not a serious clinical condition per se, its association with high mortality will largely depend on the underlying critical illness.

Disclosure: Nothing to disclose

H. Pylori II

09:00-17:00 / Poster Exhibition - Hall 7

P1330 INDIVIDUAL CHARACTERISTICS ASSOCIATED WITH *HELICOBACTER PYLORI* INFECTION IN THE GISTAR STUDY POPULATION IN LATVIA

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Introduction: Prevalence of *H. pylori* (HP) infection is higher in developing countries comparing with developed ones and is linked to lower socio-economic status. Studies covering the association between HP and individual level characteristics other than socioeconomic factors are lacking in Europe [1]. To our knowledge, no such studies have been published for Northern and Eastern European populations, where several countries have a high prevalence of HP infection.

Aims & Methods: The aim of the current study was to identify individual characteristics associated with HP infection in a high income country with high HP prevalence (79%) and gastric cancer incidence (27/100,000) [2,3]. 1855 participants aged 40-64 years from the "*Helicobacter pylori* eradication and pepsinogen testing for prevention of gastric cancer mortality (GISTAR) study" in Latvia were included in the analysis [2]. All participants were tested for *H. pylori* IgG antibodies (Eiken Chemical, Japan). Data on sociodemographic characteristics (gender, age, income, education, employment status), diet (consumption of ≥ 400g of fruit/vegetables, ≥ 200g dairy, portions of red and white meat daily, frequency of consumption of meat products, pickled, smoked, salted, and spicy products, coffee, tea (days per week), very hot food/drinks weekly, adding salt to already salted food), exercise, smoking (current, former), alcohol consumption, binge-drinking, and medical history (self-reported history of disease, surgery, drug use) were obtained by survey and compared for participants positive (HP+) and negative for HP (HP-). A multiple logistic regression model was built adjusting for potential confounders (income, age and gender [1]). Individual characteristics with p < 0.10 in univariate analysis investigating their association with HP+ were included in the final model as follows: level of education, smoking, binge-drinking, consumption of ≥200g dairy, ≥400g of vegetables/fruit daily, very hot food/drinks, pickled products, adding salt to food, self-reported history of HP eradication, peptic ulcer, thyroid and cardiovascular disease.

Results: 1044 (56.3%) participants were HP+. In fully adjusted multiple logistic regression HP+ was positively significantly associated with consumption of dairy (OR 1.36; 95% CI 1.10, 1.67), very hot food/drinks weekly (OR 1.33; CI 1.04, 1.69), and addition of extra salt to already salted food (OR 1.29; CI 1.04, 1.60), current smoking (OR 1.43, CI 1.07, 1.91) and binge-

drinking (OR 1.34, CI 1.02, 1.75). In addition, HP+ was inversely associated with consumption of fruit/vegetables (OR 0.77; CI 0.61, 0.97), self-reported history of HP eradication (OR 0.56; CI 0.38, 0.82), peptic ulcer (OR 0.56; CI 0.38, 0.80), and cardiovascular disease (OR 0.78; CI 0.61, 0.98).

Conclusion: We found HP+ to be associated with lifestyle factors, rather than socioeconomic indicators. Lifestyle intervention and possibly *H. pylori* eradication may be especially beneficial in this subset of the population because those HP+ were also more likely to have other and multiple risk factors for the development of gastric cancer (smoking, increased salt, but decreased fruit/vegetable intake, history of peptic ulcer disease).

References: 1. Eusebi LH, Zagari R.M, Bazzoli F. Epidemiology of Helicobacter pylori Infection. Helicobacter, 2014:19:1-5. 2. Leja M, Park JY, Murillo R et al. Multicentric randomised study of Helicobacter pylori eradication and pepsinogen testing for prevention of gastric cancer mortality: the GI-STAR study. BMJ Open. 2017;7(8):e016999. 3. Statistics on Oncology. The Centre for Disease Prevention and Control of Latvia. 16.08.2018. Accessed: 10.04.2019. https://www.spkc.gov.lv/lv/statistika-un-petijumi/statistika/veselibas-aprupes-statistika1

P1331 WITHDRAWN

P1332 SPANISH SPECIALYST CARE SURVEY ON THE MANAGEMENT OF *H. PYLORI* INFECTION: PREFERENCES AND DECISIONS

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Introduction: *H. pylori* (*HP*) is the most common bacterial infection in the world. The increase in bacterial resistance to the antibiotics most used against this microorganism significantly conditions the treatment of this infection. Recently, the new recommendations of the International and National Consensus have proposed different therapeutic strategies to improve the eradication.

Aims & Methods: To evaluate the preferences and current therapeutic decisions of the Spanish Gastroenterology Specialists in the management of *HP* infection. An online survey was designed to register 21 variables regarding demographics, type of practice, continuous education received and preferences on management. Responses were anonymously codified. Responses were weighted by age, years of experience, training received in HP treatment and type of center (public, private) where work.

Results: A total of 369 gastroenterologist participated in the study giving response to the survey. The study was performed between March and May 2018. 54% were women and the average age was 39 years (±10.2). 92% of responses came from public practices and 44% from private sector, meaning that many participants worked in both. 17.6% worked in populations of more than 500,000 inhabitants, 62.1% in populations from 100,001 to 500,000 inhabitants and 20.3% in populations of less than 100,000 inhabitants. 53% have received continuous education program on *HP* infection in the last 12 months. 16% have participated in some research program about infection. 75% of the surveyed doctors said that the management of the infection is a decision of each doctor, there was no protocol in their workplace for the management of the infection. The most common first-line therapy of choice was non-bismuth quadruple concomitant therapy [57%, with clarithromycin, metronidazole, amoxicillin and a proton pump inhibitor (PPI)] followed by bismuth quadruple single capsule therapy (36%, with a PPI, tetracycline, metronidazole and bismuth), triple therapy (5%, with a PPI, clarithromycin and amoxicillin) and other (2%). Triple therapy was more used in private practice and by gastroenterologists with more than 20 years of professional experience. The factors that most influenced the decision of the choice of first-line treatment were therapeutic efficacy (53%), over prescription limitations in their sanitary environment (29%), economic burden (5%), safety (4%), lower risk of side effects (4%), patient characteristics (2.4%), possible interactions with other medications (1.6%) and treatment characteristics that may favor adherence to treatment (1.6%).

Conclusion: This survey shows how Spanish gastroenterologists have adapted rapidly to current *HP* consensus recommendations, using quadruple therapeutic strategies in first line to ensure greater efficacy of treatment against increased bacterial resistance. It draws attention to how the management of *HP* infection is a decision of each doctor, without following an established protocol in their workplace.

P1333 MODIFIED 7-DAY VERSUS STANDARD 10-DAY CONCOMITANT THERAPY FOR *HELICOBACTER PYLORI* ERADICATION: A RANDOMIZED CONTROLLED TRIAL

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Introduction: Eradication rates for H. pylori with a standard triple therapy have declined globally. A 10-day standard concomitant therapy (SCT) is associated with slightly higher eradication rates, but with more side effects, when compared to that of the triple therapy. More aggressive acid suppression may allow shortening treatment duration without compromising eradication rates.

Aims & Methods: This study aimed to compare the H. pylori eradication rates between a 7-day modified concomitant therapy (MCT) and a 10-day SCT.

This open-label, randomized study was conducted at Rajvithi Hospital, Bangkok, Thailand during November 2016-2017. Patients with active *H. pylori* infection were included (n=240) and randomized (1:1) into either 7-day MCT (omeprazole 40 mg BID, amoxicillin 1000 mg BID, clarithromycin 500 mg BID and metronidazole 400 mg TID for 7 days) or 10-day SCT (omeprazole 20 mg BID, amoxicillin 1000 mg BID, clarithromycin 500 mg BID, and metronidazole 400 mg TID for 10 days). *H. pylori* eradication was evaluated by ^{14}C-urea breath test at 4-6 weeks after the completion of treatment. Eradication rates were analyzed by per-protocol (PP) and intention-to-treat (ITT) analysis. Side effects and patient compliance were recorded.

Results: A total of 120 patients were randomized into each treatment group. There was no significant difference in baseline patient characteristics between groups. In ITT analysis, *H. pylori* eradication rates were 88.3% (106/120) and 88.3% (106/120) in the 7-day MCT and 10-day SCT groups, respectively (*p*>0.99). In PP analysis, *H. pylori* eradication rates were 94.6% (106/112) and 95.5% (106/111) in the 7-day MCT and 10-day SCT groups, respectively (*p*=0.77). Bitter taste was the most common treatment-related side effect in both groups (72.3% in the 7-day MCT vs. 66.7% in the 10-day SCT, *p*=0.36). Headache (9.8% vs 18.9%, *p*=0.05) and diarrhea (17% vs 27.9%, *p*=0.05) were less commonly reported in the 7-day MCT than in the 10-day SCT group, respectively.

Conclusion: The 7-day MCT was safe and able to achieve similar eradication rate, as compared with a 10-day SCT. Due to its better tolerability, 7-day MCT may be a practical alternative first-line treatment option for *H. pylori* eradication.

P1334 COMPARATIVE STUDY OF SEQUENTIAL VERSUS CONCOMITANT NON-BISMUTH QUADRUPLE THERAPY AS FIRST-LINE ERADICATION FOR HELICOBACTER PYLORI

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Introduction: Helicobacter pylori (Hp) is a major cause of peptic ulcer disease and gastric malignancies. Hp eradication rate has reduced, in part because of increased antibiotic therapy resistance. Recent international guidelines have shown preference towards Concomitant non-bismuth quadruple therapy as first-line empirical option, instead of sequential treatment, when choosing a non-bismuth regimen.

Aims & Methods: We aim to compare the efficacy of the sequential and concomitant non-bismuth quadruple therapy as first line empirical antibiotic regimens in terms of Hp eradication rate. We conducted a retrospective study between January/2015 and March/2019 including patients with Hp infection. Patients were treated as first-line eradication therapy with the Sequential quadruple treatment (comprising 5 days of proton-pump inhibitor and amoxicillin, followed by 5 days of proton-pump inhibitor, clarithromycin and metronidazole) or the Concomitant non-bismuth quadruple therapy (comprising 14 days of proton-pump inhibitor, amoxicillin, metronidazole and clarithromycin). Eradication of Hp was confirmed after treatment. Eradication rate was calculated for each treatment regimen.

Results: 101 patients were included (52,5% female, mean age of 55,4±13,4 years). Main indications for Hp testing were dyspepsia (33%), peptic ulcer disease (31%) and erosive gastritis/bulbitis (27%). The tests more frequently used for diagnosis of Hp infection were histology (56%) and rapid urease test (35%). 55 (54,5%) and 46 (45,5%) patients were treated with Sequential and Concomitant therapies, respectively. Hp eradication was mainly confirmed by stool antigen test (53%), histology (20%) and urea breath test (18%). Global eradication rate was 88%. Hp eradication rate achieved 89% with Sequential therapy and 87% with Concomitant treatment, with no statistical difference (p>0,05).

Conclusion: Global erradication rate with non-bismuth quadruple regimens was good (88%), with no statistical difference between Sequential and Concomitant treatments. Therefore, we suggest that both the protocols may be used in current clinical practice as first line empirical eradication treatment.

Disclosure: Nothing to disclose

P1335 THE EFFICACY AND SAFETY OF SECOND-LINE REGIMENS FOR HELICOBACTER PYLORI ERADICATION TREATMENT: A SYSTEMIC REVIEW AND NETWORK META-ANALYSIS

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Introduction: The prevalence of antibiotic resistance varies greatly among countries and increases gradually in recent years. Declined first-line *Helicobacter pylori (H. pylori)* eradication rate becomes a significant healthcare burden and challenge for prescribing adequate second-line eradication therapy. Secondary antibiotic resistance to clarithromycin, metronidazole, and levofloxacin were more than 15% after first-line treatment failure. Optimal second-line eradication regimen to achieve best eradication rate remain elusive.

Therefore, we conducted a network meta-analysis to compare the relative efficacy of second-line *H. pylori* eradication among 15 regimens since 2000 to find the favorable regimens in treatment-experienced patients.

Aims & Methods: We reviewed three major bibliographic databases, including PubMed, Embase, and Cochrane Central Register of Controlled Trials, and enrolled relevant randomized trials and cohort studiesthat evaluated second-line *H. pylori* eradication rate between January 2000 and September 2018.We performed network meta-analysis by WinBUGS and STATA software and assessed the quality of enrolled articles withRoB 2.0 tool for randomized trials and ROBINS-I tool for non-randomized studies of interventions.

The odds ratio (OR)was calculated for the comparative treatment effects between second-line therapieswhen compared to 7-days clarithromycin-based triple therapy as well as in subgroup analysis.

Results: In our study 66 trials with 10582 treatment-experienced participants were recruited in the network meta-analysis. Among all regimens, add-on therapy of probioticsafter and/or duringsecond-line antibiotic therapy(OR4.39, 95% CrI1.46-12.80), quinolone-based sequential therapy for 10-14 days (OR 3.38, 95% CrI1.29-8.65), quinolone-based quadruple therapy for 10-14 days (OR 3.32, 95% CrI1.28-8.47), add-on therapy of probiotics before and/or during second-line antibiotic therapy(OR 3.12, 95% CrI 1.01-9.32), and add-on therapy of probiotics during second-line antibiotic therapy(OR 3.03, 95% CrI 1.09 - 8.22)had greater efficacy with statistical significance. Besides regimens with longer duration tend to show higher efficacy of eradication compared with regimens with shorter duration.

Conclusion: In our meta-analysis we found add-on therapy of probiotic-sbefore/during/after second-line antibiotic therapy, quinolone-based sequentialtherapy for 10-14 days, and quinolone-based quadrupletherapy for 10-14 days are superior to the rest of regimens in treatment-experienced patients.In addition, extending the duration of regimens achieved higher efficacy of eradication rate than those with shorter duration.

Disclosure: Nothing to disclose

P1336 A REAL-LIFE STUDY ON BISMUTH QUADRUPLE AND NON-BISMUTH QUADRUPLE THERAPY (10 AND 14 DAYS) IN THE ERADICATION OF *H. PYLORI* INFECTION IN PATIENTS NAÏVE TO TREATMENT

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Introduction: International guidelines suggest bismuth quadruple (BQ) or non bismuth quadruple (i.e. concomitant) (CT) therapy as first line regimens to eradicate *H. pylori* infection. Choice should be based on knowledge of prevalence of antimicrobial resistance in a particular area, previous antimicrobial exposure, drug allergy. In areas of high clarithromycin (CLA) or dual (i.e. CLA + metronidazole) resistance BQ should be preferred because of its higher efficacy compared to CT. We hypothesized that previous exposure to CLA might be more likely associated to infection with a CLA resistant strain.

Aims & Methods: In this real life study, therefore, we evaluated the efficacy of BQ vs CLA-containing CT (10 or 14 days) in *H. pylori* infected subjects naïve to treatment. Patients who had previously been exposed to CLA were given BQ whereas those who had not were given CT. In Italy BQ is only possible through the 3-in-1pill formulation for 10 days. Two hundred and 1 patients (pts) (125F and 76M, mean age 47.3yrs) were treated with BQ (esomeprazole (ESO) 40 mg bid, 3-in-1pill formulation 3 tablets qid), 203 patients received CT (ESO 40 mg bid + CLA 500mg bid + amoxicillin 1gbid + tinidazole 500mg bid) of these 100 pts for 10 days (CT10d) (54F and 46M, mean age 46.4 yrs) and 103 (55F and 48M, mean age 48.3 yrs) pts for 14 days (CT14d). All pts received probiotics during therapy. Diagnosis of *H. pylori* infection was through [13]UBT or histology in those pts who underwent esophagogastroduodenoscopy. Assessment of eradication was through [13]CUBT at least 1 month after the end of therapy. Incidence of treatment-related adverse events (TRAEs) was evaluated by a questionnaire at the end of therapy. Compliance was considered to be good if at least 80% of medications had been taken. Intention-to-treat (ITT) and Per Protocol (PP) analysis was performed, 95% confidence intervals (CI) were calculated and significance of differences was assessed by Chi square test.

Results: Ten pts in BQ group, 6 pts in CT10d group and 3 pts in CT14d discontinued therapy because of side effects; 2) ITT and PP eradication rates in BQ were 184/201 (91.5%, 95%CI 86.8-95) and 183/191 (95.8%; 85% CI 91.9-98.2), respectively; 3) ITT and PP eradication rates in CT10d were 80/100 (80%; 95% CI 70.8-87.3) and 80/94 (85.1%; 95% CI 76.3-91.6), respectively; ITT and PP eradication rates in CT14d were 99/103 (96.1%; 95% CI 90.3-98.9) and 97/100 (97%; 95% CI 91.5-99.4), respectively; 4) BQ vs CT10d: p< 0.004 and p< 0.001 (ITT and PP, respectively); BQ vs CT14d: p:ns (ITT and PP); CT14d vs CT10d: p< 0.001 and p=0.003 (ITT and PP, respectively); 5)Prevalence of TRAEs was 26.9%, 26%, and 22.3% in BQ, CT10d and CT14 d, respectively (p:ns); 6) Treatment discontinuation due to TRAEs was 5.5%, 6%, and 2.9% in BQ, CT10d and CT14d, respectively (p:ns).

Conclusion:
1) In an area of high prevalence of CLA and dual resistance BQ and CT14d are highly and equally effective in the treatment of H. pylori infection in pts naïve to treatment and significantly superior to CT10d;
2) No significant differences as to compliance or incidence of TRAEs between treatment was detected;

3) Prescribing therapy based on knowledge of previous exposure to CLA may represent a winning strategy.

Disclosure: Nothing to disclose

P1337 HIGH INCIDENCE OF *H. PYLORI* RESISTANCE IN AN IRISH CENTRE WHICH NEGATIVELY IMPACTS TREATMENT

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Introduction: Helicobacter pylori is a gram-negative bacterium responsible for many gastric conditions. Due to increasing antimicrobial resistance, eradication rates employing currently available treatment options, have significantly declined. Local antimicrobial surveillance is needed to guide therapies and improve outcomes.

Aims & Methods: To evaluate the prevalence of *H. pylori* primary, secondary and multidrug resistance and the impact on treatment outcome. Following ethical approval and informed consent, antral and corpus biopsies were prospectively obtained from patients undergoing routine endoscopy who required *H. pylori* testing at Tallaght University Hospital during 2018-2019. Culture samples were processed if subjects were CLO positive. Antimicrobial susceptibility to seven antibiotics: Metronidazole, Clarithromycin, Amoxicillin, Levofloxacin, Rifampicin, Tetracycline, Moxifloxacin was tested as standard by Etest strips. The minimum inhibitory concentration (MIC) was evaluated and susceptibilities were assigned according to the EUCAST clinical breakpoints. Patients were treated with standard eradication regimes and success was determined by $C^{13}UBT$ with a Delta value of < 4.0.

Results: 66 patients were recruited, mean age 51 (31-81) years, 19 (56%) females. Culture was successful in 33 (50%). 61% (20/32) with no prior treatment (PR= primary resistance) and 39% (13/33) (SR= secondary resistance) having failed prior treatment. PR and SR groups were demographically similar.

Few individuals were sensitive to all antibiotics; 4/20 (20%) PR vs 1/13 (8%) SR.

Primary resistance rates were high; Metronidazole 12/20 (60%), Clarithromycin 9/20 (45%), Amoxicillin 7/20 (35%), Levofloxacin 6/20 (30%), Rifampicin 9/20 (45%), Tetracycline 5/20 (25%), Moxifloxacin 2/20 (10%). Unexpectedly, secondary resistance rates were similar; Metronidazole 11/13 (85%) p=0.1, Clarithromycin 9/13 (69%) p=0.2, Amoxicillin 6/13 (46%) p=0.4, Levofloxacin and Tetracycline 4/13 (31%) p=0.6 and p=0.5, Rifampicin 2/13 (15%) p=0.08, Moxifloxacin 3/13 (23%) p=0.3.

Dual resistance to Metronidazole and Clarithromycin was common 52% (17/33) and similar in PR and SR groups (9/20 45% and 8/13 62%) p=0.3. The multidrug (>3 antibiotics) resistance rate was 48% (16/33) and was also similar in PR and SR groups, 45% and 54% respectively.

Overall our eradication rate was disappointing 39% (13/33) and did not differ between PR and SR groups; 45% (9/20) and 31% (4/13) (p=0.48). Successfully eradicated patients had similar resistance rates to Clarithromycin, Metronidazole and Amoxicillin (46%, 54%, 31%) compared to non-eradicated patients (60%, 80%, 45%).

Conclusion: Primary, secondary, dual and multidrug *H. pylori* resistance is very high in our cohort and has increased significantly from previous published Irish data. Unsurprisingly, our high resistance rates were reflected in poor overall, first line and second line eradication rates. The very high levels of primary resistance account for the lack of difference in the eradicated vs non-eradicated groups. Based on this data novel approaches to eradication in Ireland are warranted.

Disclosure: Nothing to disclose

P1338 COMPARISON OF EFFICACY OF BISMUTH-CONTAINING QUINTET THERAPY AND MOXIFLOXACIN-BASED SEQUENTIAL THERAPY AS FIRST-LINE ERADICATION REGIMEN FOR *HELICOBACTER PYLORI* INFECTION

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Introduction: Recently, the eradication rate of *Helicobacter pylori* (*H. pylori*) infection has been decreasing. We investigated the efficacy of bismuth-containing quintet therapy compared with moxifloxacin-based sequential therapy as a first-line eradication treatment.

Aims & Methods: We enrolled 164 patients with *H. pylori* infection from October 2015 to October 2016, and randomly assigned into 2 groups: bismuth-containing quintet therapy (BCQT group; rabeprazole 20mg bid, amoxicilline 1g bid, metronidazole 500mg bid, moxifloxacin 400mg qd, and tripotassium dicitrato bismuth 600mg bid for 7 days) or moxifloxacin-based sequential therapy (MBST group; rabeprazole 20mg bid and amoxicillin 1g bid for 7 days, followed by rabeprazole 20mg bid, metronidazole 500mg bid, and moxifloxacin 400mg qd for 7 days). Successful eradication was defined as negative for ^{13}C-urea breath test after 4 weeks of treatment.

Results: The eradication rates by intention-to-treat analysis were 76/82 (92.7%, 95% confidence interval [CI] 89.8-95.6%) in the BCQT group and 70/82 (85.4%, 95% CI 81.5-89.3%) in the MBST group (*p* = 0.066). The eradication rates by per-protocol analysis were 76/79 (96.2%, 95% CI 94.0-98.4%) in the BCQT group and 70/80 (87.5%, 95% CI 83.8-91.2%) in the MBST group (*p* = 0.043). Compliance was good (100%) in both groups. The adverse event rates were lower in the BCQT group (9/79, 11.3%) than in the MBST group (12/80, 15.0%) (*p* = 0.048).

Conclusion: The bismuth-containing quintet therapy was more effective and safe compared to the moxifloxacin-based sequential therapy as a first-line eradication treatment of *H. pylori* infection.

Disclosure: Nothing to disclose

P1339 PROSPECTIVE RANDOMIZED AND CROSSOVER STUDY COMPARING TEN DAYS CONCOMITANT TREATMENT TO 10 DAYS BISMUTH BASED THERAPY FOR HELICOBACTER ERADICATION IN A LEBANESE NAÏVE POPULATION

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Introduction: Concomitant therapy and bismuth quadruple therapy are both recommended as 1st line treatment regimens for the empiric treatment of Helicobacter pylori, especially after the increased resistance to clarithromycin. Our goal is to compare both of the treatment regimens among a representative sample of the Lebanese population to eventually conclude whether or not one of these therapies has a higher efficacy as a 1st line treatment regimen. This study also aims to compare the efficacy of these regimens when given as 2nd line therapy after crossover.

Aims & Methods: It is a randomized, prospective and crossover study, started from March 2016 to December 2018. Participants were randomly chosen and diagnosed with active Helicobacter pylori through histology. None of them had a prior eradication therapy or had a recent exposure to antibiotics. Patient were randomized into two equal groups: patients in the first group received 10 days of concomitant therapy (Esomeprazole 40mg twice a day, Amoxicillin 1g twice a day, Clarithromycin 500mg twice a day and Metronidazole 500mg twice a day), while patients in the second group received 10 days of bismuth quadruple therapy (Esomeprazole 40mg twice daily, and a capsule containing all three components: Bismuth, Tetracycline and Metronidazole) 3 capsules were taken four times a day. Eradication was evaluated by the 14C urea breath test done 6 weeks after the end of antibiotic use. Esomeprazole was also stopped for at least two weeks prior to testing. A negative breath test indicated a successful eradication. All patients with a positive breath test were switched to the other treatment regimen for 10 days and then re-evaluated for eradication according to the same protocol.

Results: The eradication rate was 91.43% in the concomitant group and 94.25% in the Bismuth group (NS). 14 out the 15 patients who failed eradication after concomitant treatment as first line, achieved eradication after crossover. All 10 patients who failed Bismuth based first line treatment and received concomitant second line regimen, had a negative breath test at the end of the study.

Conclusion: Bismuth quadruple therapy and concomitant therapy are equally effective as 1st line treatment regimens for Helicobacter pylori eradication in a naïve Lebanese population. They are also highly and equally effective when used as 2nd line after crossover.

Disclosure: Nothing to disclose

P1340 PAN-EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG): ANALYSIS OF 4,388 SECOND-LINE TREATMENTS

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Introduction: After a failed eradication attempt, *H. pylori* treatment's efficacy is compromised due to the selection of resistant strains.

Aims & Methods: To evaluate the efficacy by intention-to-treat (ITT) and per-protocol (PP) of second-line treatments in Europe.

A systematic prospective registry of the clinical practice of European gastroenterologists regarding *H. pylori* infection and treatment (27 countries and 300 recruiting investigators). An e-CRF was created on AEG-REDCap to systematically register all adult patients infected with *H. pylori*. *Variables included*: Patient's demographics, previous eradication attempts, prescribed eradication treatment, adverse events (AEs), and outcomes (cure rates, compliance, follow up, etc.). *Data extraction:* All cases with treatment failure after just one eradication attempt. *Analysis:* Cases with an empiric treatment were evaluated separately from those with a tailored therapy.

Results: Overall, 4,388 second-line patients were included. Culture was performed in 9% of the total of cases. Resistance rates (when available) were: 63% to clarithromycin, 52% to metronidazole, and 40% to both. In total 4,019 were treated empirically: mean age was of 50 years, 64% were women and 5% had penicillin allergy. 58% of indications were dyspepsia and 17% gastroduodenal ulcer. ^{13}C-UBT was used in 49% of the cases to diagnose the infection. Mean efficacy was 77% (by ITT) and 83.5% (by PP). 7 and 10-days regimens did not reach optimal efficacy except for single-capsule bismuth quadruple therapy (>90% PP). 14-days regimens with double doses esomeprazole reported better results (>90% PP) when quinolones were used in triple regimens and bismuth quadruple therapies. After non-bismuth quadruple failure, efficacy was reported higher when the triple therapy with moxifloxacin or the bismuth quadruple therapy with levofloxacin were used. Over 97% of patients were compliant. AEs were reported in 29% of the cases and tolerance was similar among therapies. Most frequent second-line use and efficacy per antibiotic combination is shown in the table.

Treatment	N	% Use	N (ITT)	ITT (%)	(95% CI)	N (PP)	PP (%)	(95% CI)
Triple-A+L	1,449	36.1	1,349	77	(75-79)	1,271	81	(79-83)
Pylera	510	12.7	466	87	(84-90)	442	91	(88-94)
Quadruple-A+L+B	459	11.4	446	88	(85-91)	421	90	(87-93)
Triple-C+A	414	10.3	358	51	(46-56)	221	79	(74-84)
Quadruple-M+Tc+B	179	4.5	167	81	(75-87)	158	84	(78-90)
Quadruple-C+A+M	145	3.6	133	83.5	(77-90)	131	84	(78-90)
Triple-A+Mx	140	3.5	138	88	(83-93)	134	91	(86-96)
Triple-A+M	85	2.1	79	56	(45-67)	73	59	(48-70)
Total	3,966	98.7	3,689	77	(76-78)	3,346	83	(82-8)

ITT - intention to treat, PP - per-protocol, 95%CI - 95% confidence interval, PPI - proton pump inhibitor, C - clarithromycin, M - metronidazole, T - tinidazole, A - amoxicillin, L - levofloxacin, B - bismuth salts, Tc - tetracycline, Mx - moxifloxacin, N - Total of patients receiving an empiric treatment

[Most frequent second-line use and efficacy per antibiotic combination]

Conclusion: Second-line triple therapies generally provide low eradication rates except when prescribing moxifloxacin for 14 days. Bismuth-containing quadruple therapies seem to provide higher efficacy, especially the combination of bismuth with a PPI, levofloxacin and amoxicillin or single capsule bismuth quadruple therapy.

Disclosure: Nothing to disclose

P1341 HELICOBACTER PYLORI INFECTION INCREASED ACCUMULATION OF *ADVANCED GLYCATION END PRODUCTS* IN PATIENTS WITH TYPE 1 DIABETES

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Introduction: Helicobacter pylori (HP) infection is significantly more frequently diagnosed in patients with diabetes. Patients with type 2 diabetes infected with HP showed higher values of estimated Homa insulin resistance factor (HOMA-IR) than those without coexisting infection. Insulin

resistance in patients with type 1 diabetes (DMT1) is associated with thickening of the intima media complex thickness complex (IMT), accumulation of *advanced glycation end products (AGEs)* in the skin and progression of chronic complications.

Aims & Methods: The aim of this study is to assess the relationship between the incidence of H. pylori infection and the accumulation of *AGEs* in the skin in patients with type 1 diabetes.

The study included 103 patients with DMT1 meeting the criteria for inclusion. Inclusion criteria were: age > 18 years, caucasian, duration of DMt1 >5 years. Exclusion criteria: treatment with proton pump inhibitors, H2 blockers and bismuth preparations, steroids, non-steroidal anti-inflammatory drugs and antibiotics within one month prior to the start of the study, pregnancy, and other chronic gastrointestinal diseases. A fast, qualitative, one-step test was performed to detect the HP antigen in faecal samples (Helicobacter Antigen Test by Hedrex). The content of AGEs in the skin was estimated using an AGE Reader device (DiagnOptics). The AF score was calculated automatically (the amount of light emitted by the skin to the amount of light emitted by the device).

Anthropometric parameters (height, body weight, BMI, waist and hip circumference, WHR index) were analysed. Basic laboratory parameters: glycated haemoglobin value (HbA1c), lipid profile, inflammatory marker (C-reactive protein) ALT, AST, creatinine and eGFR (MDRD) were also evaluated.

Results: HP positive (n=72) and HP negative (n=31) groups did not differ in age, sex, duration of diabetes, metabolic control and inflammatory response markers. The studied groups differed in the amount of AGEs in the skin. This relationship between H Pylori infection and increased AGEs content in the skin was confirmed in a multifactor regression model taking into account age, sex, DM duration, HbA1c, BMI, LDL cholesterol and the presence of hypertension and tobacco use.

Conclusion: Increased accumulation of *AGEs* in the skin in patients with DMT1 with coexisting H. pylori infection, may be an indication to pay special attention to eradication treatment in this group of patients.

References: -

Disclosure: Nothing to disclose

P1342 LOW RATE OF Helicobacter Pylori TEST AND ERADICATION IN PATIENTS WITH GASTRIC CANCER

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Introduction: *Helicobacter pylori* (HP) infection is well known to contribute to the development of gastric cancer (GC). Eradication after endoscopic treatment of early GC is recommended to prevent metachronous cancer in the remnant stomach. In addition, HP eradication therapy after surgical treatment of GC can improve the survival rate of GC patients. In this study, we aimed to investigate the rate of HP diagnosis and eradication treatment after GC surgery in a tertiary institute in Korea.

Aims & Methods: Patients who received surgical treatment after diagnosis of GC at Seoul National University Bundang Hospital from 2003 to 2017 were retrospectively analyzed using Electronic Medical Recording and Clinical Data Warehouse (CDW). HP examinations (histology CLO test, and urea breath test) before and after surgery, prescription for eradication, and follow-up examination results are reviewed in detail.

Results: Total 3,734 patients were diagnosed with GC and received surgical treatment. 2,272 patients (60.8%) were tested (1,372 patients preoperatively; 905 patients after surgery) (Fig.). 1,283 patients (56.5%) were positive for HP infection. Among HP+ GC patients 354 patients (27.6%) received eradication treatment and 89 patients were followed-up loss. 237 of 265 patients (89.4%) were finally successfully eradicated, but 28 patients were failed to eradicate. Among 929 HP+ GC patients who did not receive HP treatment 345 showed spontaneous negative conversion during follow-up tests. 71 patients showed fluctuation of test results without eradication (dynamic changes for HP), and 989 patients were persistently negative for HP (Fig.).

Conclusion: Both diagnostic test and eradication treatment rates in patients received GC surgery were significantly low, about one-third patients were not tested even once, and only about 20% of HP-positive patients were successfully eradicated. Considering the high prevalence of GC in Korea and potential benefits of eradication therapy in GC patients, these low rates are disappointing. More attentions and interests of clinicians for GC patients with surgery are needed in terms of HP eradication.

Disclosure: Nothing to disclose

P1343 RISK FACTORS FOR METACHRONOUS CANCER IN THE REMNANT STOMACH AFTER GASTRIC CANCER SURGERY

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Introduction: Early gastric cancer patients have a good prognosis after radical resection. However, there is risk of metachronous gastric neoplasm (MGN) if the patients have a gastric remnant after the surgery. The aim of this study was to clarify the risk factors for MGN after partial gastrectomy for gastric cancer.

Aims & Methods: Data of 680 patients who received surgical treatment after diagnosis of gastric cancer (GC) at Seoul National University Bundang Hospital from 2003 to 2017 were retrospectively analyzed using Electronic Medical Recording and Clinical Data Warehouse (CDW). A univariate Cox proportional hazards model was used to identify possible covariates as significant risk factors for MGN. Then, the variables with p< 0.2 were subjected to multivariate Cox proportional hazards model to identify independent contribution. In addition, the variables which were considered to be possible risk factors for MGN based on the previous studies were also analyzed in multivariate model.

Results: Total 680 patients were diagnosed with GC and received surgical treatment, and 524 patients who received subtotal, proximal, or distal gastrectomy for curative purposes were enrolled. Baseline characteristics of the patients were shown in Table 1. Among these patients, 11 patients (1.6%) were diagnosed as having MGN in the gastric remnant. Clinicopathologic characteristics of MGNs were summarized in Table 2. 6 of 11 (55%) were treated by endoscopic resection, and 4 of 11 (36%) were received surgery. Statistical analysis showed that male sex was the only independent risk factor (Table).

Variable	Patients with MGN (%) (n=11)	Patients without MGN (%) (n=513)	P value
Sex: Female Male	0 (0%) 11 (100%)	198 (39%) 315 (61%)	*0.01
Family history of GC: No Yes	6 (55%) 5 (45%)	107 (21%) 406 (79%)	0.06
Smoking status: No Yes	2 (18%) 9 (82%)	205 (40%) 308 (60%)	0.21
Alcohol drinking: No Yes	3 (27%) 8 (73%)	168 (33%) 345 (67%)	1.00
Gastric Atrophy: Absent or mild Moderate or severe	11 (100%) 0 (0%)	458 (89%) 55 (11%)	0.62
Intestinal Metaplasia: Absent or mild Moderate or severe	7 (64%) 4 (36%)	412 (80%) 101 (20%)	0.24
HP status: Never Past Current	6 (55%) 3 (27%) 2 (18%)	170 (33%) 138 (27%) 205 (40%)	0.25
Type of initial GC: EGC AGC	8 (73%) 3 (27%)	322 (63%) 191 (37%)	0.75

MGN, metachronous gastric neoplasm; H. pylori, Helicobacter pylori; IM, intestinal metaplasia.
*Results were considered statistically significant when p-values were less than 0.05

[Table 1. Clinicopathological characteristics of patients with and without MGN.]

There is a possibility that family history of GC might be also a risk factor for MGN, but the probability value was not statistically meaningful (p=0.06) mainly because the recurrence number was low.

Conclusion: Our data suggested that more intensive surveillance including follow-up endoscopy is needed for the remnant stomach in patients with these risk factors to detect MGN at its early stage. Further analysis in undergoing.

Disclosure: Nothing to disclose

P1344 HELICOBACTER PYLORI -NEGATIVE EARLY GASTRIC CANCER: PROPOSAL FOR A NEW HISTOPATHOLOGICAL CLASSIFICATION

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Introduction: Helicobacter pylori (Hp) infection is widely known as a main cause of gastric cancer. In the past, most gastric cancer cases were infected with Hp. Therefore, Hp-negative gastric cancer (HPNGC) cases were uncommon, most of which were undifferentiated adenocarcinoma (UDA=diffuse-type adenocarcinoma in Lauren classification). Nowadays, the rate of Hp infection is decreasing with passing generations in Japan. HPNGCs, which were considered rare, are now being reported more often including specific histological types of cancers like gastric adenocarcinoma of fundic gland type (GAFG) and UDA [1,2]. However, the histological classification, and the endoscopic and clinicopathological features of HPNGC have not been fully described.

Aims & Methods: HPNGCs were extracted from 849 lesions of early gastric cancers resected endoscopically from April 2009 to January 2019. The samples were classified histologically, and their endoscopic and clinicopathological features were analyzed retrospectively.

Results: We found 51 cases (55 lesions) of HPNGC (6.5%) which were classified into: GAFG, gastric adenocarcinoma of fundic gland mucosal type (GAFGM), gastric-phenotype differentiated adenocarcinoma (G-DA), gastrointestinal-phenotype differentiated adenocarcinoma (GI-DA), and UDA=25/4/6/11/9 lesions, respectively (differentiated adenocarcinoma = intestinal-type adenocarcinoma in Lauren classification). GAFG was found in 13 males and 12 females with a mean age of 66.6 years (location: U/M/L=21/3/1, tumor size:7.4mm, color: white(W)/red(R)=22/12, macroscopic type: elevated/flat or depressed=17/8; invasion depth: mucosa(M)/submucosa(SM)=7/18). GAFGM was found in 3 males and 1 female with a mean age of 51.7 years (location: U/M/L=4/0/0, tumor size: 8.7mm, color: W/R=1/3, macroscopic type: elevated/flat or depressed=4/0, invasion depth: M/SM=1/3). G-DA was found in 4 males and 2 females with a mean age of 57.8 years (location: U/M/L=3/3/0, tumor size: 6.9mm, color and macroscopic type: 5 reddish protruded lesions like a raspberry and 1 whitish flat-elevated lesion). A total of 4 out of 5 raspberry-shaped lesions were disappeared by biopsy and their invasion depth could not be measured. The invasion depth was M in the other 2 cases. GI-DA was found in 6 males and 5 females with a mean age of 56.8 years (location: U/M/L=3/1/7, tumor size: 9.2mm, color: W/R=2/9, macroscopic type: elevated/flat or depressed=6/5, invasion depth: M/SM=11/0). UDA was found in 6 males and 3 females with a mean age of 54.9 years (location: U/M/L=0/6/3, tumor size: 7.9mm, color: W/R=8/1, macroscopic type: elevated/flat or depressed=0/9, invasion depth: M/SM=9/0). All of UDA were signet-ring cell carcinoma. No vascular invasion and relapse-free survival was confirmed in patients with cancer of all histological types. Magnifying endoscopy with narrow-band imaging (M-NBI) was performed in 51 out of the 55 lesions at maximum magnification. Of these, 33 lesions were diagnosed as non-cancer by M-NBI (33/51; 64.7 %).

Conclusion: This study clarified the characteristics of HPNGCs, such as location, color, and macroscopic findings differed by their histological type as follows: (1) GAFG, GAFGM, and G-DA tended to occur in U/M as red or white elevated lesions; (2) UDA tended to occur in M/L as white flat or depressed lesions; and (3) GI-DA tended to occur in U/M/L as red elevated or depressed lesions. There were many lesions difficult to diagnose as cancer by M-NBI. We conclude that understanding the endoscopic and clinicopathological features of each histological type may provide more precise endoscopic diagnosis of HPNGC.

References: 1. Ueyama H, Yao T, Nakashima Y, et al. Gastric adenocarcinoma of fundic gland type (chief cell predominant type): proposal for a new entity of gastric adenocarcinoma. Am J Surg Pathol 34: 609 -619, 2010 2. Yoshimura D, Yoshimura R, Mizutani T, et al. Clinical and pathological characteristics of gastric cancer without Helicobacter pylori infection and its background gastric mucosa. Gastroenterology 152: S260-261, 2017

Disclosure: Nothing to disclose

P1345 THE LONG-TERM FOLLOW-UP OF SERUM PEPSINOGENS IN PATIENT WITH GASTRIC CANCER AND DYSPLASIA AFTER Helicobacter pylori ERADICATION

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Introduction: Recently we have shown reversibility of atrophic gastritis and intestinal metaplasia after Helicobacter pylori eradication up to 10-year follow-up study. Only a few studies have evaluated pepsinogen (PG) change after eradication of H. pylori but there was no study regarding this issue in patients with gastric cancer (GC) and dysplasia.

Aims & Methods: The aim of this study is to evaluate the effect of H. pylori eradication on PG in GC and dysplasia patients in comparison to control group with a long-term follow-up. From March 2003 to February 2019, we prospectively enrolled 368 subjects with GC and dysplasia and 610 subjects with non-GC and non-dysplasia as control group. All of GC and dysplasia patients were treated by enodoscopic mucosal resection or submucosal dissection. H. pylori tests (Giemsa stain, CLOtest and culture) were performed to evaluate HP status. Serum PG levels were measured using a Latex-enhanced Turbidimetric Immunoassay (Shima Laboratories, Tokyo, Japan) before and after eradication, compared by using linear mixed model and student's t-test. The follow-up points were classified as 1-11 months, 12-23 months, 24-35 months and more than 36 months.

Results: Among 368 GC/dysplasia patients, 102 (27.7%) were H. pylori-negative, 179 (48.6%) were H. pylori-eradicated, and 87 (23.7%) were H. pylori non-eradicated/eradication failure. Among 610 control group patients, 373 (61.1%) were H. pylori-negative, 168 (27.6%) were H. pylori-eradicated, and 69 (11.3%) were H. pylori non-eradicated/eradication failure. In GC/dysplasia there were not significantly different in PG values in H. pylori-negative and H. pylori non-eradicated/eradication failure group at all follow-up points compared to those at baseline (Table).

	Before	1-11 months	p-values	12-23 months	p-values	24-35 months	p-values	≥36 months	p-values
Control	168	98		65		22		19	
PG I	75.6 (3.18)	64.0 (3.73)	0.006	55.2 (4.59)	<0.001	44.4 (7.70)	0.001	49.2 (8.67)	0.037
PG II	23.5 (1.07)	11.7 (1.34)	<0.001	10.4 (1.67)	<0.001	8.93 (2.86)	<0.001	10.8 (3.12)	0.001
PG I/II ratio	3.94 (0.16)	5.99 (0.20)	<0.001	5.38 (0.25)	<0.001	5.09 (0.42)	0.106	4.65 (0.47)	1.000
GC/ Dysplasia	179	76		89		51		57	
PG I	55.7 (2.65)	41.0 (3.68)	<0.001	40.3 (3.56)	0.002	36.8 (4.55)	0.003	40.8 (4.53)	0.043
PG II	20.7 (0.70)	10.6 (1.05)	<0.001	9.12 (0.98)	<0.001	8.75 (1.29)	<0.001	10.4 (1.23)	<0.001
PG I/II ratio	2.80 (0.12)	4.04 (0.16)	<0.001	4.38 (0.15)	<0.001	4.59 (0.19)	<0.001	4.19 (0.20)	<0.001

[Table. Comparison of gastric cancer and dysplasia with control in pepsinogen levels before and after eradication of H. pylori]

In contrast H. pylori-eradicated group of GC/dysplasia mean serum PG I (55.7 vs. 41.0, p< 0.001) became significantly lower and mean PG I/II ratio (2.80 vs. 4.04, p< 0.001) became higher at 1-11 months after eradication compared to those at baseline (Table). This improvement of PG values after eradication maintained during all follow-up points with no significant

differences between *H. pylori*-eradicated and *H. pylori*-negative group. However, mean serum PG II did not show any change in both of control or GC/dysplasia group. Control group showed similar tendency to the GC/dysplasia (Table).

Between the control and GC/dysplasia groups significant difference in mean serum PG I and mean PG I/II ratio were observed at 1-11 months (PG I: 41.0 vs. 64.0, *p*<0.001, PG I/II ratio: 4.04 vs. 5.99, *p*<0.001) and 12-23 months (PG I: 40.3 vs. 55.2, *p* = 0.01, PG I/II ratio: 4.38 vs. 5.38, *p* = 0.001) after eradication. These differences disappeared from ≥ 24 months of follow-up

Conclusion: Considering the PG I and PG I/II ratio of GC/dysplasia group become similar to those of control group at the long-term follow-up after eradication, *H. pylori* eradication plays an important role in the prevention of metachronous cancer/dysplasia development.

Disclosure: Nothing to disclose

Small Intestinal II

09:00-17:00 / Poster Exhibition - Hall 7

P1346 THE PREVALENCE OF SMALL INTESTINAL BACTERIAL OVERGROWTH IN PATIENTS WITH HYPERLIPIDEMIA

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Introduction: Microorganisms which colonize the intestine are capable to impact on cholesterol metabolism by affecting the key stages of its synthesis. Excessive microbial growth of anaerobes in the jejunum, which is typical for syndrome of bacterial overgrowth (SIBO), leads to its damage, with the development of system inflammation, that causes early deconjugation of bile acids with the formation of their toxic salts and impaired enterohepatic circulation. In this case, induction of hypercholesterolemia is possible, especially in individuals with hereditary predisposition.

Aims & Methods: The aim of this study was to determine the prevalence SIBO in a series of patients with hyperlipidemia and in controls. 30 patients with hyperlipidemia (14 men and 16 women) average age 33,69±1.73 years with average BMI 24,4±1.54 were examined in "Medicover Ukraine" (Lviv, Ukraine). The diagnostic criteria were: BMI not more that 25, waist circumference < 94 cm for male,< 80 cm for female, no significant alcohol consumption. 20 control subjects (8 men and 12 omen), an average 29,9±0.68 years, BMI 24,2±1.21 were matched with main group patients. All controls had normal lipid range. Both groups of patients underwent biochemical evaluation - lipid profile, C-reactive protein, ALT, AST, GGTP, bilirubin, apoB. Ultrasound examination was proved to all patients of both groups. with aim to exclude the patients with fatty liver disease as one of the reasons of increased lipids level. All subjects were examined by a lactulose breath test.

Results: The prevalence of SIBO in hyperlipidemia group was 78.9%. Small intestinal transit time amounted 100 minutes. Meanwhile, the SIBO occurrence in controls was 40% with average time of small intestine transit 140 minutes. The measurement of SIBO by lactulose test showed the equal result of the basal dose of hydrogen in both groups. In contrast, the maximal dose was particularly higher in patients with hyperlipidemia in comparison with control group (94,7±13,69 vs. 36,13±5,4) . There was remarkable positive connection between LDL, TG, VLDL and the dose of exhaled hydrogen on 120 minute (r=0.6, r= 0.62, r=0.7 respectively) and strong negative correlation between HDL and 120 minutes dose (r=-0.74) in main group. Surprisingly, CRP did not interrelate with bacterial overgrowth in both groups. In contrast, there was strong correlation relationship between AST and AST/ALT ratio and SIBO existence.

Conclusion: The prevalence of SIBO in patients with hyperlipidemia is predominantly higher than in patients without lipid metabolism disturbance. The hydrogen level is significantly higher in patients with hyperlipidemia in comparison with controls. There is an axis between high LDL, VLDL and TG level and hydrogen rate in patients with hyperlipidemia.

References:
1. Adkins c., Rezaie A. Small intestinal bacterial overgrowth and coronary artery disease: what is in the cards? Digestive diseases and sciences, 2018, 63(2) : 271-272

2. Lefebvre P, Cariou B, Lien F, Kuipers F, Staels B. Role of bile acids and bile acid receptors in metabolic regulation. Physiol rev., 2009; 89 : 147-191.
3. Dukowicz A., Lacy B., Levine G. Small intestinal bacterial overgrowth. A comprehensive review. Gastroenterol hepatol., 2007, 3(2) : 112-122.
4. Rhodes Jm, Middleton P, Jewell Dp. The lactulose hydrogen breath test as a diagnostic test for small-bowel bacterial overgrowth. Scand j gastroenterol., 1979; 14 : 333-336.
Disclosure: Nothing to disclose

P1347 *AKKERMANSIA MUCINIPHILA* PLAYS AN IMPORTANT ROLE ON THE SMALL INTESTINAL INJURY CAUSED BY THE COMBINATION OF ASPIRIN AND PROTON PUMP INHIBITOR, WHICH IS AMELIORATED BY *BIFIDOBACTERIUM BIFIDUM* G9-1 IN THE NOVEL ANIMAL MODEL

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Introduction: Although aspirin (ASA) is widely used all over the world to prevent cardiovascular diseases, ASA is well known to cause peptic ulcer. Proton pump inhibitor (PPI) is also used to prevent ASA induced peptic ulcer. However, with the recent development of enteroscopy, it has been reported that not only ASA causes small intestinal injury, but also PPI deteriorates the injury in human. Establishing the animal model of ASA induced small intestinal injury has been difficult since administration of ASA cannot stably induce mucosal injuries in mice. The animal model should be established to reveal the mechanisms underlying the deterioration due to PPI in order to establish possible treatment.

Aims & Methods: Our aims are to establish the mouse model of ASA induced small intestinal injury, to investigate the effect of PPI on gut microbiota, and to find the possible treatment using probiotics.

Male C57BL/6JJcl mice were fed with 60% fructose diet for 9 weeks, and administered 200mg/kg of ASA 3 hours before sacrifice. To investigate the effect of PPI on ASA induced small intestinal injury, 20mg/kg of omeprazole was administered intraperitoneally once a day. *Bifidobacterium bifidum* G9-1 was administered orally (1×10^9 CFU / head) from 1 week before sacrifice until the end. The degree of small intestinal injury was assessed using histological score. *Akkermansia muciniphila* was administered (1×10^9 CFU / head) orally for 9 weeks instead of PPI.

Results: By feeding high fructose diet, ASA induced small intestinal injury was successfully created. On the other hand, no damage was found in the mice fed with basal diet. These intestinal damages were exacerbated with PPI, whose histological score was higher than that of ASA without PPI group. As PPI has been reported to cause gut dysbiosis, we investigated gut microbiota in small intestine. *Bifidobacterium* was decreased by PPI administration, and was decreased when mice were fed with high fructose diet compared to the mice fed with basal diet. The relative abundance of *Akkermansia* in jejunum dramatically increased from 0.08% to 2.5% after the administration of ASA and PPI (p < 0.05), but was significantly suppressed from 2.5% to 0.3% after the administration of *Bifidobacterium bifidum* G9-1 with ASA and PPI (p < 0.05).

Furthermore, when administered ASA and PPI, the thinning of mucus layer in jejunum was significantly induced. It was also observed in the mice that received an oral administration of *Akkermansia muciniphila* instead of the administration of PPI. On the other hand, when administered *Bifidobacterium bifidum* G9-1, thinning of mucus layer was ameliorated. While the number of goblet cells in jejunum were significantly lower in ASA + PPI group than that of vehicle group (p < 0.05), reduction of goblet cells was significantly improved with the administration of *Bifidobacterium bifidum* G9-1 (p < 0.05).

	vehicle	ASA	ASA+PPI	ASA+PPI+G9-1	Akkermansia
Injury	-	+	++	-	
Thinning of mucin layer	-		+	-	+

[Small intestinal injury and thinnning of mucin layer]

Conclusion: These results suggest that gut dysbiosis caused by PPI such as increase of *Akkermansia* and reduction of *Bifidobacterium*, leads to the thinning of mucus layer through the reduction of goblet cells in small intestine. That may cause dysfunction of intestinal barrier, which results in the susceptibility to ASA induced small intestinal injury.
Disclosure: This study was funded by Biofermin Pharmaceutical Co., Ltd.

P1348 POLYUNSATURATED FATTY ACIDS IN A WESTERN STYLE DIET TRIGGERS INTESTINAL INFLAMMATION IN GENETICALLY SUSCEPTIBLE HOSTS

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Introduction: Genome wide association studies identified a plethora of risk genes for the development of Crohn's disease (CD) one of which is glutathione peroxidase 4 (GPX4) (1). Its main function is to maintain cellular homeostasis by reducing lipid peroxides (LPO) in cellular membranes (2) and to prevent cell death. The prime substrate for LPO are polyunsaturated fatty acids (PUFA) in cellular membranes. The increasing consumption of specific PUFAs, such as AA and DHA, due to an increasing consumption of a western style diet was paralleled by a rising incidence of IBD during the last decades. However, the impact of increased PUFA uptake on the development of CD remains elusive.
Aims & Methods: The aim of the study was to analyse the influence of dietary lipids in a genetically susceptible host. We crossed *Gpx4^flox/flox* (3) mice with *Villin-Cre^+/-* mice to obtain *Gpx4^flox/wt;Villin-Cre^+/-* (*Gpx4^+/-IEC*) mice, that specifically delete one allele of *Gpx4* in the intestinal epithelium. WT and *Gpx4^+/-IEC* littermates were fed a western style diet (WD) or a PUFA enriched western style diet (PUFA WD) for 3 months. Inflammation was assessed on H&E tissue sections. Staining for neutrophils was done with MPO and GR1. Microbiota was analysed in fecal samples by 16s amplicon sequencing.
Results: *Gpx4^+/-IEC* mice on a PUFA enriched western style diet developed small intestinal inflammation while WT littermates were unaffected. The inflammation mainly occurred in the jejunum while other parts of the small intestine and as well as the colon were not affected. Inflammation was characterised by infiltrating neutrophils and mononuclear cells as well as the formation of granuloma like lesions. Additionally, increased levels of the IL-8 homologue CXCL-1 were found in epithelial cell scrapings of *Gpx4^+/-IEC* mice. The fecal microbiota analysis revealed a decreased a-diversity in PUFA WD fed mice as well as a distinct ß diversity when compared to WD fed mice. However, we found no differences between WT and *Gpx4^+/-IEC* mice.
Conclusion: Here we show that PUFAs in a western style diet evoke small intestinal inflammation in GPX4 deficient hosts, independent from microbiota alterations. We identified these PUFAs as a non toxic dietary component that evokes CD like inflammation in the small intestine.
References: 1 L. Jostins et al., Host-microbe interactions have shaped the genetic architecture of inflammatory bowel disease. Nature 491, 119-124 (2012). 2 Dixon et al., Ferroptosis: An Iron-Dependent Form of Nonapoptotic Cell Death. Cell 149, 1060-1072, (2012) 3 S. E. Yoo et al., Gpx4 ablation in adult mice results in a lethal phenotype accompanied by neuronal loss in brain. Free radical biology & medicine 52, 1820-1827 (2012).
Disclosure: Nothing to disclose

P1349 OXIDATION OF POLYUNSATURATED FATTY ACIDS TRIGGERS A PRO-INFLAMMATORY RESPONSE IN GENETICALLY PRONE INTESTINAL EPITHELIAL CELLS

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Introduction: Genetic variation of Glutathione peroxidase 4 (GPX4) is associated with the development of Crohn's disease (CD) (1). GPX4 is an antioxidative acting enzyme particularly reducing lipid peroxides (LPO) within biomembranes, and particularly polyunsaturated fatty acids (PUFAs) which are prone to oxidation due to their carbon-carbon double bond backbone (2).
PUFAs are essential fatty acids and enriched in a common western style diet rich in red meat, eggs and oils. Dietary enrichment of arachidonic acid, an ω-6 PUFA, paralleled a rising incidence of inflammatory bowel disease (3). How dietary PUFAs affect the development of CD remains currently unknown.
Aims & Methods: In MODE-K cells, a small intestinal epithelial cell line (IECs), *Gpx4* siRNA silencing was established. Silenced cells were stimulated with palmitic acid, a saturated fatty acid, oleic acid and palmitoleic acid, two monounsaturated fatty acids as well as a range of ω-3 and ω-6 PUFAs (stearidonic acid, eicosapentaenoic acid, docosapentaenoic acid, arachidonic acid, docosahexaenoic acid), respectively. LPO was measured with BODIPY 581/591 C11 by flow cytometry and cytokine production was assessed and confirmed by a multiplex ELISA in the supernatant.
Results: Gpx4 silencing led to increased levels of LPO, which was further aggravated by the stimulation with ω-6 PUFA arachidonic acid and a range of ω-3 PUFAs. Stimulation with the same PUFAs led to an increased release of IL-6, CXL-1 as well as other pro-inflammatory cytokines and chemoattractants only in GPX4-deficient IECs. The addition of α-tocopherol, a lipophilic reactive-oxygen species scavenger, prevented the formation of LPO and the release of cytokines. Interestingly saturated and monounsaturated fatty acids neither induced cytokine production nor aggravated LPO in *Gpx4*-silenced IECs.
Conclusion: Our data provides evidence that specific non-toxic dietary lipids, which are enriched in a western-style diet, induce cytokine production in GPX4-deficient IECs which is accompanied by increased levels of LPO which could be reversed by LPO scavenging.
References: 1. Jostins L, Ripke S, Weersma RK, Duerr RH, McGovern DP, Hui KY, et al. Host-microbe interactions have shaped the genetic architecture of inflammatory bowel disease. Nature. 2012;491(7422):119-24. 2. Ayala A, Munoz MF, Arguelles S. Lipid peroxidation: production, metabolism, and signaling mechanisms of malondialdehyde and 4-hydroxy-2-nonenal. Oxid Med Cell Longev. 2014;2014:360438. 3. Patterson E, Wall R, Fitzgerald GF, Ross RP, Stanton C. Health implications of high dietary omega-6 polyunsaturated Fatty acids. J Nutr Metab. 2012;2012:539426.
Disclosure: Nothing to disclose

P1350 *LACTOBACILLUS RHAMNOSUS STRAIN* AFFECTS STRESS-RELATED INTESTINAL PERMEABILITY, SYMPTOMS AND FECAL MICROBIOTA DIVERSITY IN HEALTHY ADULTS: RESULTS FROM A RANDOMIZED, DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL (PROSPER)

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Introduction: Potential probiotic strains protect the intestinal barrier in animal models, but human data are lacking. We aimed to study the effect of *Lactobacillus rhamnosus CNCM I-3690* on intestinal hyperpermeability, occurring during public speech (1), and the relation with stress-related symptoms and fecal microbiota diversity.

Aims & Methods: Healthy students were randomized to the *L. rhamnosus* fermented milk or placebo (acidified milk) consumed daily (2 x 125g) for 4 weeks prior to public speech (exam) and 2 more weeks until NSAID-administration (indomethacine 125mg; positive control). Small intestinal permeability was quantified by a 2h lactulose-mannitol ratio (LMR), fractional excretion of mannitol (FEM) and lactulose (FEL) at baseline and after the exam. Salivary cortisol was measured with ELISA and the State-Trait Anxiety Inventory (STAI) and Perceived Stress Scale (PSS) were completed at both visits. Stool samples were collected for 16S sequencing in a subset of subjects (n= 76) at both visits. Primary outcome was the change during stress vs. baseline of LMR between treatment groups. Mixed models with contrasts between groups were applied with correction for multiple testing for secondary endpoints only. Within-group changes were compared to nominal alpha 5%.

Results: In total, 92 students (55 female, mean age 23±1.9 years) were included (46 per group). No differences between groups were found for change in LMR (delta=-0.003, 95%CI [-0.01;0.005], p=0.51), FEL or FEM. Within-group analyses showed similar LMR and FEL but an increase of FEM during exam vs. baseline for placebo but not *L. rhamnosus* (Table 1). LMR and FEL increased in both groups after NSAIDs (all p< 0.001) with a trend for an increase in FEM in the placebo (p=0.07) but not *L. rhamnosus* group (p=0.39). Salivary cortisol increased during exam vs. baseline in the placebo and *L. rhamnosus* group with no difference between groups. The increase in STAI before the exam vs. baseline was significant in the placebo and *L. rhamnosus* groups with a lower increase in *L. rhamnosus* vs. placebo (delta=-4.73, 95%CI [-8.84;-0.62], p=0.02). The increase in PSS before the exam vs. baseline was significant in the placebo and not *L. rhamnosus* group with a trend for a lower increase in *L. rhamnosus* vs. placebo (delta=-2, 95%CI [-4.24;0.32], p=0.09). Preliminary analyses of the fecal microbiota suggested an increase of the alpha-diversity in the *L. rhamnosus* group vs. placebo group after the exam. No serious adverse events occurred.

Conclusion: Despite the primary endpoint was not reached, *L. rhamnosus* CNCM I-3690 seems to prevent stress-induced hyperpermeability to mannitol, a pathway that differs from NSAID-induced hyperpermeability to lactulose. Subjective but not objective stress-markers were reduced suggesting gut-brain mediated effects via the microbiota, for which preliminary analyses suggested an increase of the alpha-diversity upon consumption of the *L. rhamnosus* vs placebo.

	Placebo (n= 46)			L. rhamnosus (n= 46)		
Variable	baseline	exam	p-value	baseline	exam	p-value
LMR	0.03±0.01	0.03±0.01	0.78	0.03±0.02	0.03±0.01	0.54
FEL (%)	0.10±0.05	0.12±0.07	0.28	0.12±0.05	0.12±0.05	0.76
FEM (%)	9.3±2.5	10.6±3.7	0.02	9.5±3.9	10±4	0.23
Cortisol (ng/ml)	5.8±5.4	13.9±7.1	<0.0001	4.9±3	12.6±6.2	<0.0001
STAI	28.7±6.4	45.2±1.4	<0.0001	29.8±5.7	41.8±1.7	<0.0001
PSS	7.8±4.9	10.3±5.1	0.002	7.9±4.7	8.4±5.4	0.58

[Table 1]

References: (1) Vanuytsel et al., Gut 2014

P1351 MUCOSAL IGG PRODUCTION AND PLASMA CELLS-NERVES INTERACTION: POTENTIAL MECHANISMS OF GUT-BRAIN AXIS DYSFUNCTION IN DIARRHOEA-PRONE IRRITABLE BOWEL SYNDROME

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Introduction: Irritable bowel syndrome (IBS) is a chronic gastrointestinal disorder characterized by recurrent abdominal pain associated with altered bowel motility and high frequency of mental comorbidities such as psychological stress, anxiety and depression. IBS remains a chronic debilitating disorder with undefined pathophysiological mechanisms for which specific biomarkers are lacking. Enhanced humoral immunity has been identified in the intestinal mucosa; however, the role of plasma cells has not been addressed.

Aims & Methods: Our aim is to characterize the antibody-mediated response and its association with IBS pathophysiology. Mucosal jejunal biopsies and stool samples were obtained from diarrhoea-IBS (IBS-D; n = 18) patients meeting Rome III criteria and age-matched healthy volunteers (H; n = 18) as the control group. Bowel movements, stool consistency and abdominal pain were monitored (10 days prior to biopsy). Psychological stress and depression were assessed by validated questionnaires. The number and the activation of mucosal plasma cells were determined by transmission electron microscopy. Luminal immunoglobulins (Ig) were determined in faecal content by ELISA.

Results: Mucosal plasma cells were found in the subepithelial area and located in proximity to nerve endings. This distance was significantly lower in samples from IBS-D compared to H (IBS-D: 1.26 (0.21-4.25); H: 2.13 (0.26-7.06) micrometers; P< 0.05). Plasma cells showed morphological signs of activation such as enlarged cytoplasm and expanded endoplasmic reticulum cisterna, features mainly observed in IBS-D. Moreover, while individual plasma cells were observed scattered in control group, clusters of long-lived plasma cells featured the jejunal mucosa of IBS-D. The number of plasma cells was higher in IBS-D respect to H (IBS-D: 1,407±257; H: 336 ± 83.9 plasma cells/mm², P< 0.05) as previously reported (Gut, 2015) and significantly correlated with proximity to nerve endings (r²=-0.63, P< 0.01). The quantification of Ig in faeces revealed no differences in sIgA, IgM and IgE concentration between groups, while IBS-D showed significantly higher concentration of total IgG (IBS-D: 11.38 (1.5-45.82); H: 3.68 (0.61-35.34) ng/mg protein; P< 0.05), IgG2 (IBS-D: 0.71± 0.53; H: 0.40 ± 0.29 ng/mg protein; P< 0.05) and IgG3 respect to H, the later not reaching statistical significance (IBS-D: 1.05 (0.28-3.65); H: 0.91 (0.19-1.83) ng/mg protein; P=0.08). Both, H and IBS-D groups had equivalent concentration of IgG1 and IgG4. Notably, luminal IgG positively correlated with abdominal pain (r²=0.50; P< 0.05) and distance of plasma cells to nerves negatively correlated with psychological stress (r²=-0.55; P< 0.05) and depression (r²=-0.46; P< 0.05).

Conclusion: Mucosal humoral immunity and its interaction with nerves are identified as potential factors associated with brain-gut axis dysfunction in IBS-D. Studies aimed at determining the underlying mechanisms warrant further investigation.

References: Vicario M, González-Castro AM, et al. Increased humoral immunity in the jejunum of diarrhoea-predominant irritable bowel syndrome associated with clinical manifestations.Gut. 2015 Sep;64(9):1379-88. doi: 10.1136/gutjnl-2013-306236. Epub 2014 Sep 10.

P1352 EXPLORING IMMUNE CELL HETEROGENEITY IN POST OPERATIVE ILEUS USING SCRNA SEQ REVEALED A PRO RESOLVING ROLE FOR MYELOID CELLS EXPRESSING ARGINASE-1

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Introduction: Patients undergoing open abdominal surgery often suffer from a transient episode of intestinal dysmotility referred to as postoperative ileus (POI). Intestinal manipulation (IM) during the surgery evokes tissue damage and consequently an inflammatory response leading to impaired gastrointestinal (GI) motility. Recently our lab revealed a critical role for monocyte-derived macrophages (MΦs) in supporting neuromuscular function and restoring intestinal homeostasis after surgical trauma. Blocking monocytes recruitment to the muscularis externa (ME) after IM increased neutrophil-mediated immunopathology and prolong the clinical outcome of POI.

Aims & Methods: Despite significant advances in our understanding of MΦ regulation and function during intestinal inflammation, the factors and the effector molecules responsible for the pro-resolving MΦ-effect remain not well defined. To answer these questions, we have employed state of the art single cell RNA sequencing (sc-RNA seq) of different subset of intestinal MΦs at the steady state and during the acute and resolution phase of POI.

Wild-type female mice (WT; C57BL/6JOlaHsd) and Csf1rCreERT2/+ Arg1fl/fl were subjected to IM to induce POI. The severity of POI was evaluated by assessing GI transit, and ME inflammation via flow cytometric analysis of recruited immune cells. Immune cells infiltrating the muscularis externa of naïve mice and of mice 1 day and 3 days after IM were analysed by sc-RNA seq. Sc-RNA seq was performed on the Chromium Single Cell Gene Expression Solution (10x Genomics). Seurat R package was used for graph-based clustering and visualizations.'SingleR' package was used for immune cell type annotations. Trajectory analysis was performed with Monocle2. Gene set enrichment analysis (GSEA) was done on the average expression of the cell clusters using java GSEA Desktop Application.

Results: Sc-RNAseq of immune cells from the naive, inflamed and resolving muscularis revealed a complex immune cell landscape during different phases of POI. Resident immune cell populations including muscularis MΦs were seen in naive ME as expected. At day 1 post IM, myeloid cell infiltration was apparent including mainly monocytes and neutrophils. At day3 post IM, most of the infiltrated myeloid cells seemed to be cleared as the inflammation resolves. The heterogeneity between the myeloid cell types seen on Day1/Day3 go beyond the current understanding by using conventional cell surface marker-based flow cytometry. Trajectory analysis revealed possible differentiation trajectory of classical monocytes to give rise to mature MΦs via multiple intermediate phenotypes. GSEA analysis showed that PPAR-γ targets are differentially upregulated between the cells at the beginning and end of the trajectory hinting at a possible role for PPAR-γ in driving the differentiation of monocytes towards mature MΦs. During this differentiation, the monocyte derived Ly6C low and MHCII low MΦs express the major pro- resolving MΦ factor Arginase 1. Mice lacking Arginase 1 in myeloid cells failed to recover gastrointestinal transit after IM. Hence, the Arg1 expressing myeloid cells could be directly responsible for supporting the recovery of gastrointestinal motility after damage.

Conclusion: Our study reveals a critical role for monocyte-derived MΦs in restoring intestinal homeostasis after surgical trauma. The specific functions of each of these myeloid sub populations has to be further analysed to deepen our understanding of the intestinal inflammatory cascade and the process of resolution of inflammation which could be key in developing novel therapy.

Disclosure: Nothing to disclose

P1353 DIAGNOSTIC YIELD AND ACCURACY OF SMALL BOWEL ULTRASONOGRAPHY COMPARED TO CAPSULE ENTEROSCOPY FOR THE DIAGNOSIS OF SMALL BOWEL DISEASES

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Introduction: Video capsule enteroscopy (VCE) is considered the reference standard for the assessment of small bowel disorders since it has the highest diagnostic yield for the detection of luminal and mucosal alterations. There are no studies comparing VCE with small bowel ultrasonography (B-US). The aim of this study is to compare the diagnostic yield of VCE and B-US in the diagnosis of small bowel disorders.

Aims & Methods: The aim of this study is to compare the diagnostic yield of VCE and B-US in the diagnosis of small bowel disorders.

We retrospectively enrolled 159 patients undergoing VCE and B-US for the following indications: obscure gastrointestinal bleedings, suspect or follow-up of known complicated celiac disease, chronic diarrhea or malabsorption syndromes. The interval between the two exams had to be inferior to one year. We evaluated the diagnostic yields of the two techniques. The accuracy of small bowel ultrasonography was determined using VCE as the reference standard.

Results: The diagnostic yields calculated in the whole sample were 55% for VCE and 33% for B-US (p< 0,05). The subgroups analysis showed that VCE ability to detect pathological signs is higher; there was a statistical significant difference between the diagnostic performances of the two techniques in patients with OGIB (62% vs 14%, p< 0,05) and suspect or known complicated celiac diseases (55% vs 35%, p< 0,05), while the difference was not statistical significative among patients with chronic diarrhea and malabsorption syndromes (51% vs 46%, p=0,8).

Conclusion: Compared to B-US, VCE is more accurate to detect lesions in patients with OGIB and suspect or known complicated celiac disease. B-US could have a role in the screening of celiac disease complications, since it was able to detect patients with severe complications (RCD II, EATL, adenocarcinoma).

In patients with chronic diarrhea and malabsorption syndromes, B-US was able to detect signs suggestive for enteropathies, especially in patients with Chron's disease.

Disclosure: Nothing to disclose

P1354 COULD NEUTROPHIL-TO-LYMPHOCYTE RATIO PREDICT ULCERATIVE COLITIS FLARE DURING PREGNANCY?

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Introduction: Women with ulcerative colitis (UC) in remission, frequently suffer from flaring of disease activity during pregnancy. Predicting such problem early in pregnancy, would arouse not to decrease the dose or number of medications used to maintain remission, and hence UC relapse could be avoided. Serum neutrophil-to-lymphocyte ratio (NLR) is a promising simple marker of systemic inflammation.

Aims & Methods: The aim of this study was to assess the value of neutrophil to lymphocyte ratio (NLR) in predicting UC flare during pregnancy. In this study, clinical and laboratory data of 27 female patients with UC who got pregnant while in remission were retrospectively analyzed. Baseline serum measurements (early at first trimester) of NLR and other inflammatory markers were recorded. Disease activity during pregnancy was assessed using Truelove and Witts criteria.

Results: Flare up of UC throughout pregnancy was noticed in ten patients (10/27, 37.0%), and was significantly associated with increased mean baseline values of platelets count, ESR, CRP and NLR ($P=0.035$, $P=0.014$,

P=0.006 and *P*< 0.001, respectively). Using logistic regression analysis, baseline NLR was the only independent predictor of UC flare (*P*=0.002). Spearman's correlation analysis showed significant positive correlation between NLR and each of CRP (r =0.418, *P*=0.030) and ESR (r =0.522, *P*=0.005). The sensitivity and specificity of NLR (90.0% and 88.2%, respectively), at a cut-off level ≥2.85, for prediction of UC flare (area under the curve [AUC]=0.915, *P*< 0.001), are much higher than that of CRP and ESR.
Conclusion: The NLR is an effective, simple and readily available biomarker for prediction of UC flare during pregnancy.
Disclosure: Nothing to disclose

P1355 GUT MICROBIOTA AND SMALL BACTERIAL OVERGROWTH IN PATIENTS WITH HYPERLIPIDEMIA

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Introduction: Current data suggests that the intestinal microbiota is involved in the cardiovascular disease occurrence with the host-microbe interaction regulating metabolic pathways. Microorganisms which colonize the intestine are capable to impact on cholesterol metabolism by affecting the key stages of its synthesis. Excessive microbial growth of anaerobes in the jejunum, which is typical for syndrome of bacterial overgrowth (SIBO), leads to its damage, with the development of system inflammation, that causes early deconjugation of bile acids with the formation of their toxic salts and impaired enterohepatic circulation. In this case, induction of hypercholesterolemia is possible, especially in individuals with hereditary predisposition.
Aims & Methods: The aim to evaluate the SIBO prevalence in patients with hyperlipidemia. One more idea was to examine the prevalence of SIBO in such patients. 96 patients with hyperlipidemia (average age 43.03±2.67 and BMI 26.15±0.67) were examined in "Medicover Ukraine". 47 control subjects, an average age 48.25±2.47 and average BMI 24,2±1.21 were matched with main group by metabolic characteristics. All control subjects had normal lipid range and no history of coronary disease. The average waist circumference in main group was 98.6±1.09 cm (in men), 86.3±0.65 cm (in women), in controls - 91.2±2.1 cm in men, 82.7±1.8 in women. .Both groups of patients underwent biochemical evaluation of serum that included blood cell count, lipid profile, C-reactive protein, ALT, AST, GGTP, bilirubin, apo B, apo A. Determination of microbial composition at the level of major microbial phyla was carried out by identification of total bacterial DNA, and DNA of Bacteroidetes, Firmicutes and Actinobacteria was performed with quantitative real-time PCR (qRT-PCR), using gene-targeted primers. All subjects were examined by a lactulose breath test what is one of the most diagnostically valuable methods for determining excessive bacterial growth.
Results: The prevalence of SIBO in hyperlipidemia group was 78.9%. Meanwhile, the SIBO occurrence in controls was 40%. The composition of microbiota was not significantly different between main group and control - Bacteroidetes, Firmicutes, Actinobacteria, Firmicutes/Bacteroidetes ratio was equal in both groups (p³0,05). Strong negative correlation between Bacteroidetes and Firmicutes (r=-0.74), and Bacteroidetes and Firmicutes/Bacteroidetes index (r=-0.69) was marked in patients of main group. Moreover, there was strong positive correlation among Firmicutes and CRP (r=0.6) and apo B (r=0.8). Meanwhile, Actinobacteria in patients with hyperlipidemia had the negative correlation within total, direct, indirect bilirubin (r=-0.52, r=-0.75, r=-0.52 respectively), CRP (r=-0.86) and apo B (r=-0.52). BMI strongly correlated with different phyla of bacteria - there was negative correlational relationship between BMI and Bacteroidetes and Actinobacteria (r=-0.98), and positive association between BMI and Firmicutes (r=0.98).
Conclusion: The prevalence of SIBO in patients with hyperlipidemia is predominantly higher than in patients without lipid metabolism disturbance. The decreasing of Bacteroidetes leads to Firmicutes increasing on the background of hyperlipidemia. The growth of Firmicutes level influences on the CRP and apo B level increasing in patients with hyperlipidemia. The increasing of Actinobacteria leads to the bilirubin, CRP and apo B level decreasing in patients with hyperlipidemia. BMI in patients with hyperlipidemia interrelates with gut bacteria.
Disclosure: Nothing to disclose

P1356 CONDITIONED MEDIUM DERIVED FROM BONE MARROW MESENCHYMAL STEM CELLS WITH INFLAMMATORY ACTIVATION REGULATES INFLAMMATORY RESPONSE TO ACUTE RADIATION-INDUCED INTESTINAL INJURY

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Introduction: Bone marrow mesenchymal stem cells (MSCs) have powerful anti-inflammatory and imm) could improve the structural and functional repair of the small intestine afterunomodulatory properties. Our previous experiments have demonstrated that conditioned medium from bone marrow MSCs with inflammatory activation (MSC-CM[IEC-6(IR)] acute radiation-induced intestinal injury, but its effects on the inflammatory response to acute radiation-induced intestinal injury have not been defined.
Aims & Methods: To investigate the effects of MSC-CM on the inflammatory response to acute radiation-induced intestinal injury.Eighty Sprague-Dawley rats (provided by the experimental center of the North Campus of Sun Yat-Sen University in China) were randomly divided into four groups (n=20/group): control group, irradiation (IR) group, irradiation+MSC-CM[IEC-6(NOR)] group (IR+MSC-CM[IEC-6(NOR)] group) and irradiation+MSC-CMIEC-6(IR) group (IR+MSC-CMIEC-6(IR) group), followed by continuous administration via the tail vein and abdominal cavity. Intestinal tissue and serum samples were collected 1, 3, 5, 7 days after radiation for hematoxylin-eosin staining and analysis of the concentrations of inflammatory factors via ELISA. Mesenteric lymph nodes were collected 3 days after radiation for analysis of the percentage of CD4+Foxp3+Treg cells via flow cytometry.
Results: Compared with the IR group and IR+MSC-CMIEC-6[(NOR)] group, the intestinal structure (small intestine epithelial villi and crypt) was significantly improved and the pro-inflammatory factors such as interleukin-1β, interleukin-6 and tumor necrosis factor-α in the small intestine were significantly decreased in the IR+MSC-CMIEC-6[(IR)] group, whereas the level of anti-inflammatory factor interleukin-10 was significantly increased. Similarly, the levels of pro-inflammatory factors such as Activin A, interleukin-1β, interleukin-6 and tumor necrosis factor-α in the serum samples were significantly decreased and the level of anti-inflammatory factor IL-10 was significantly increased. The changes in the levels of inflammatory factors were most significant at 3 days after irradiation. The number of CD4+Foxp3+ Treg cells in mesenteric lymph nodes in the IR+MSC-CMIEC-6[(IR)] group was significantly higher than that in control group and IR+MSC-CMIEC-6[(NOR)] group.
Conclusion: These results suggest that MSC-CMIEC-6(IR) can regulate the balance of pro-inflammatory factors and anti-inflammatory factors, and increase the number of CD4+Foxp3+ Treg cells in mesenteric lymph nodes, thus inhibiting the inflammatory response at systemic and mucosal levels in acute radiation-induced intestinal injury and promoting the repair of small intestinal mucosal injury.
Disclosure: Nothing to disclose

P1357 EFFECT OF PROBIOTIC SUPPLEMENT IN SYMPTOMATIC CELIAC DISEASE PATIENTS ON LONG-TERM GLUTEN-FREE DIET; A PILOT STUDY

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Introduction: A strict gluten-free diet (GFD) is currently the only recommended treatment for celiac disease (CD). Despite apparent compliance with the diet, 30-50% of treated patients have gastrointestinal (GI) symptoms. We explore the effect of a three-month course probiotic supplement on persistent symptoms in patients with CD following a long-term GFD.
Aims & Methods: We conducted a prospective, randomized, double-blind, placebo-controlled trial. Adult patients were enrolled if they were on a GFD for at least two years and were symptomatic at screening according to the GI symptom rate score (GSRS). 31 patients were randomized to receive probiotic (n=16) or placebo (n=15) for 12 weeks. Patients who answered "considerably relieved" or "completely relieved" over the 12 weeks of intervention were defined as responders.
Results: Thirty one patients including 16 in probiotic group (with mean age= 31±15, 50% female) and 15 in placebo group (with mean age= 39.5±20, 53.3% female) were enrolled. At the baseline analysis, there were no significant differences in the total score and subscales comparing probiotics vs. placebo. After 12 weeks trial, there was statistically significant relief in symptoms for diarrhea (46.7% vs. 12.5%, p=0.04) and fatigue (40% vs. 6.2, p= 0.03); But there were no significant differences for abdominal cramp (93.3% Vs. 93.75%, p=0.38), bloating (86.7% Vs. 87.5%, p=0.25), fatty diarrhea (93.3% Vs. 87.5%, p=013), gas feeling (93.3% Vs. 81.25%, p=0.38), weight loss (80% Vs. 81.25%, p=0.38), heartburn (93.3% Vs. 81.25%, p=0.82), muscle pain (73.3% Vs. 81.25%, p=0.96), nausea/vomiting (33.3% vs. 31.2%, p=0.90), and bloody diarrhea (6.7% vs. 6.2%, p=0.97), anemia (46.7% Vs. 37.5 %, p=0.72), depression mood (13.3% Vs 50.0%, p=0.09) and stress (53.3% Vs 81.2%, p=0.12) between two groups.
Conclusion: This experimental study suggests that probiotic supplement may improve specific CD symptoms in a subgroup of treated patients with higher symptomatic burden despite adherence to the diet. Further studies are require to confirm these findings.
Disclosure: no conflict of interest

P1358 MARSH SCORE AT THE DIAGNOSIS OF COELIAC DISEASE PREDICTS THE PRESENCE OF OSTEOPENIA AND OSTEOPOROSIS

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Introduction: Patients with coeliac disease (CD) frequently have mineral bone density (MBD) alterations. Implications of this alterations and the best way to monitor them are yet to be defined. Our objective was to evaluate the prevalence of MBD alterations at the diagnosis of CD and the associated risk factors.
Aims & Methods: A retrospective study of 96 patients (median age 25 years old; 79,6% women) with MBD evaluation at the diagnosis of CD was performed. Patients were divided into three groups: normal MBD (t score > -1.0), osteopenia (t score -1.0 to -2.5) and osteoporosis (t score < -2.5). Different clinical, serologic and histopathologic data were analyzed. Logis-

tic regression of the variable with statistical significance was performed. In patients with MBD alterations and subsequent follow-up, associations with MBD normalization were also searched.
Results: Osteopenia was present in 53,1% of the patients and osteoporosis in 7,3%. Osteopenia group presented more frequently Marsh score >2 when compared with normal MBD group. The osteoporosis group was older (p=0,011) and had more frequently Marsh score > 2 in histopathologic analysis (p=0.019) and vitamin D deficiency (p=0.039), when compared with normal MBD group. In logistic regression, Marsh score >2 (OR 1.4, p=0.005) was statistically significant in the osteopenia group. Age >45 years old (OR 3,19; p=0,036), male gender (OR 3,51; p=0,027) and Marsh >2 (OR 2,17; p=0,001) were statistically significant in the osteoporosis group. MBD normalization occurred in 25% in subsequent follow-up. Anti-transglutaminase antibody normalization was associated with MBD normalization (OR 2,5; p=0.012).
Conclusion: MBD is frequently decreased at the time of CD diagnosis. Osteoporosis had an association with older age, male gender and marsh score >2. Osteopenia presented an association with Marsh >2. In face of this evidence, MBD should be performed at the diagnosis of CD, especially if the patient presents a Marsh score >2. Normalization of anti-transglutaminase antibody is associated with MBD normalization.
Disclosure: Nothing to disclose

P1359 SCREENING FOR COELIAC DISEASE IN ELDERLY PATIENTS PRESENTING WITH IRON DEFICIENCY ANAEMIA

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Introduction: Iron deficiency anaemia (IDA) is a common indication for referral to gastroenterology. Gastrointestinal blood loss from colonic or gastric cancers as well as malabsorption in coeliac disease are the main causes of IDA in developed countries. Screening for coeliac disease in all patients with IDA is recommend by national guidelines[1].
Aims & Methods: The aim of our study was to assess whether screening for coeliac disease is routinely performed for elderly patients with IDA. We retrospectively reviewed the electronic health records of all patients ≥65 years with IDA who underwent colonoscopy at our hospital between 01 October 2018 and to 31 March 2019. We collected data on demographics, cancer findings and tests for coeliac disease, either serology or histology of duodenal biopsies.
Results: A total of 291 patients with an average age of 74.7 years (range 65 to 93) were included in our study. There were 19 (6.5%) cases of cancer in this cohort. 225 patients (77.3%) had a duodenal biopsy or coeliac serology as part of investigation for IDA. Of those screened, five patients (2.2%) were tested positive for coeliac disease. There were no cases of cancer and coeliac disease in the same patient in this cohort.
Conclusion: Coeliac disease remains an important cause of IDA, even in the elderly patients. However, we found that over twenty percent of elderly patients who presented with IDA at our hospital were not screened for coeliac disease, which might potentially lead to unnecessary further investigations for their IDA.
References: 1. Gut 2011;60:1309e1316
Disclosure: Nothing to disclose

P1360 COELIAC DISEASE, BUT NOT NON-COELIAC WHEAT SENSITIVITY IS STRONGLY ASSOCIATED WITH PSORIASIS: A POPULATION-BASED STUDY OF 3542 RANDOMLY SELECTED SUBJECTS

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Introduction: Patients with psoriasis are at approximately 3-fold increased risk of coeliac disease (CD) (1). Psoriasis has also been linked with non-coeliac gluten or wheat sensitivity (2). Anti-gliadin antibodies (AGA) have been shown to correlate with psoriasis severity and those with psoriasis and AGA antibodies experience improved symptoms on a gluten free diet (3). Our aim was to determine the link between coeliac disease, self-reported non-coeliac wheat sensitivity and psoriasis in a population study.
Aims & Methods: A total of 3542 people randomly selected from the Australian population returned a survey (the Digestive Health and Wellbeing Survey, response rate = 43%) which contained questions on GI symptoms, such as heartburn, epigastric burning, pain, swelling and bloating in the last 3 months and included a self-reported physician diagnosis of coeliac disease and/or psoriasis. Wheat sensitivity was defined as those with GI symptoms on wheat ingestion without a formal diagnosis of CD. There was minimal response bias. Associations between categorical variables were evaluated using Pearson chi-squared test. A total of 3542 people randomly selected from the Australian population returned a survey (the Digestive Health and Wellbeing Survey, response rate = 43%) which contained questions on GI symptoms, such as heartburn, epigastric burning, pain, swelling and bloating in the last 3 months and included a self-reported physician diagnosis of coeliac disease and/or psoriasis. Wheat sensitivity was defined as those with GI symptoms on wheat ingestion without a formal diagnosis of CD. There was minimal response bias. Associations between categorical variables were evaluated using Pearson chi-squared test.
Results: The prevalence of psoriasis by self-report was 4.5%. Of those with psoriasis 22.5% reported coeliac disease compared to only 4.2% who did not have CD (unaffected cohort) (OR 6.5, 95% CI 2.95-13.4). There was a significant association between psoriasis, CD and frequent bloating (p=0.027). In those with CD and psoriasis, 36% reported bloating on more than one day per week compared to only 13% in those with CD only. There was no significant association with other GI symptoms. There was no significant association between non-coeliac wheat sensitivity and psoriasis with 16.0% of patients with wheat sensitivity reporting psoriasis compared to 13.4% reporting no psoriasis (p=0.349). There was a significant association between having CD, psoriasis and other autoimmune disorders. These included rheumatoid arthritis (p=0.004), asthma (p=0.0001) and scleroderma (p=0.0001). The prevalence of self-reported wheat sensitivity in this cohort was 14.9% (95% CI 13.7-16.2) and CD, 1.2% (95%CI 0.8-1.6) (4).
Conclusion: In this cohort, coeliac disease, but not self-reported non-coeliac wheat sensitivity, is strongly associated with psoriasis. Those with coeliac disease who report bloating are more likely to report psoriasis. Those with other autoimmune diseases and psoriasis are more likely to have coeliac disease. It may be worthwhile screening such patients by serology and asking whether ingesting wheat worsens their symptoms to improve diagnosis of coeliac disease in this population.

References: 1. Ungprasert P et al Indian J Dermatol. 2017 62:41-46. 2. Carroccio A et al. Gastroenterology. 2015 149:596-603 3. Michaelsson G et al. Br J Dermatol. 2000;142:44-51. 4. Potter MDE, et al Am J Gastroenterol. 2018;113:1036-1044

Disclosure: Nothing to disclose

P1361 DUODENAL BIOPSIES ARE UNNECESSARY FOR THE EXCLUSION OF COELIAC DISEASE IN PATIENTS WITH A NEGATIVE TRANSGLUTAMINASE (TTG)

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Introduction: The British society of Gastroenterology guidelines (BSG) recommend that if coeliac serology (tissue transglutaminase (tTG) antibody 27 or endomysial antibody) is negative, small-bowel biopsies need not be performed unless there are other features which make a diagnosis of coeliac disease more likely.
Aims & Methods: Patients undergoing oesophagogastroduodenal (OGD) endoscopy between November 2018 and March 2019 for iron deficiency anaemia were identified. Demographics and investigations for anaemia and coeliac disease (Hb, MCV, ferritin, tTG antibodies, endomysial antibody, IgA levels) were collected. Electronic clinic letters were opened to identify patients who had diarrhoea, making a diagnosis of coeliac disease more likely. The OGD report, number of duodenal biopsies and histopathology results were collected. Sensitivity and specificity of tTG levels for coeliac disease were calculated.
Results: There were 120 patients identified. Mean age was 68 years, male to female ratio of 30:90. Mean haemoglobin, MCV and ferritin was 105 g/l, 81 fl/red cell, and 27 ng/ml respectively. Ninety (75%) patients had tTG levels tested. Endomysial antibody and IgA levels were measured in 7 (6%) and 71 (59%) patients respectively. The tTG levels and endomysial antibodies were positive in 3 patients. There were no patients with IgA deficiency. All 120 patients had duodenal biopsies regardless of the tTG or endomysial antibody result. Eighty-seven (97%) of the patients undergoing tTG levels had a negative result. Of these, 12 patients had diarrhoea necessitating biopsy. No patients with a negative tTG was found to have coeliac disease from duodenal biopsy histology. Of the 3 positive tTG and endomysial antibody tests for coeliac disease (3%), two were confirmed with duodenal biopsy as coeliac disease and one patient had suboptimal biopsy which showed likely coeliac disease. There was a mean of 3 duodenal biopsies per patient (range 1-7). In this series tTGA was 100% sensitive and specific for coeliac disease. Seventy-five patients (63%) had an inappropriate biopsy according to the BSG guidelines.
Conclusion: Small bowel biopsy is not necessary to confirm a negative tTGA result in patients with iron deficiency anaemia. There was no increased yield of coeliac disease detection in the context of diarrhoea. These results support the BSG guidance stating biopsies should be reserved to confirm a positive tTG result or where tTG levels have not been performed.
Disclosure: Nothing to disclose

P1362 OCCASIONAL INGESTIONS OF GLUTEN ARE TOLERATED IN A GROUP OF PATIENTS WITH CELIAC DISEASE

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Introduction: Gluten free diet (GFD) decreases the quality of life of patients with celiac disease (CD) who frequently ask to occasionally ingest gluten containig food.
Aims & Methods: We evaluated CD patients reporting voluntary and occasional transgressions to the GFD. CD patients undergoing annual follow-up were enrolled and divided in two groups:
i) patients reporting an occasional and voluntary gluten ingestions (GFD-transgression) and;
ii) patients following a strict GFD (GFD-adherent).

Patients underwent clinical examination, blood tests, duodenal biopsy. In the GFD-transgression group a capsule enteroscopy, a validated food-frequency questionnaire (FFQ) assessing the frequency and quantity of gluten intake and mortality were assessed.

Results: 197 patients were included into the study (age 45 ± 16 years, age at diagnosis 30 range 6-49 years, 38 females). In patients not adhering to the GFD (n=48), mean gluten intake was 185.2 ± 336.9 g/year, duration of GFD transgression was 8.6 ± 6.9 years. Most of the patients reported an ingestion of gluten per week or per months. Among uncompliant patients, 23(47%) did not present any histological alteration; Marsh score profile was not different among the two groups. 75% of patients did not report any gastrointestinal symptoms after gluten ingestion. 23% of patients in the GFD-transgression group presented positvie tTG-IgA vs none in the GFD-adherent group (n=149). No association was found between gluten intake, clinical symptoms and biomarkers. Mortality was not different between groups and general population.

Conclusion: Our results showed that a group of CD patients with a long-term gluten intake does not show significant clinical symptoms or histological abnormalities, suggesting that a degree of tolerance towards gluten consumption can be reached. Although a strict GFD remains the only treatment available for CD patients, its tolerance should be accurately monitored over time.

Disclosure: Nothing to disclose

P1363 OUTCOMES OF PATIENTS ADMITTED WITH CELIAC DISEASE DIAGNOSED WITH Clostridioides Difficile

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Introduction: Patients with Celiac disease (CD) are at increased risk of infections, as evidenced by increased prevalence of tuberculosis, influenza, and sepsis. Alterations in immunity and microbiota can contribute to this predisposition. Although the prevalence of *Clostridioides difficile* (C.Diff) continues to increase in the US, there is little data on the association and outcomes in patients with CD.

Aims & Methods: Therefore, the aim of this study was to assess inpatient prevalence, outcomes and resource utilization of patients with CD and C.Diff infection in the US in the past decade.

This was an observational retrospective cohort study using the NIS 2007 to 2016, the largest publically available inpatient database in the US. All patients with CD were included using ICD9-10CM codes. The cohort was stratified according to the coexistence of CDiff infection. No patients were excluded. The primary outcome was determining the association of CD with C.Diff infection. Secondary outcomes were determining the CDiff inpatient prevalence trend in the CD patients, as well as mortality, morbidity, length of hospital stay (LOS), total hospital charges and costs, which were adjusted for inflation using the Consumer Price Index. Multivariate regression was used to adjust for age, gender, income in patient zip code, Charlson Comorbidity Index, hospital region, location, size and teaching status.

Results: A total of 337,201 patients with CD were identified, of which 5,500 had associated C.Diff. Mean age was 55 years and 71% were female. The inpatient prevalence of C.Diff in patients with CD increased from 0.9/100,000 admissions in 2007 to 1.65/100,000 admissions in 2016. After adjusting for confounders, patients with CD displayed increased adjusted odds (aOR:1.56, p< 0.01) of having coexisting C.Diff compared to patients without CD. In addition, patients with CD had lower odds of mortality, ICU, shock, multiorgan failure, but increased odds of requiring TPN. Patients with CD also had lower adjusted mean hospital costs, charges, and LOS than the general admitted population with C.Diff. All outcomes are displayed in tables 1 and 2.

Conclusion: Patients with Celiac Disease had higher odds of C.Diff compared to non-CD patients, which could be attributed to CD-related gut mucosal integrity, immunological or microbiome alterations. The inpatient prevalence of C.Diff in patients with CD increased from 2007 to 2016. This may be a reflection of the general increase of C.Diff cases in the inpatient population coupled with improved CD diagnostic modalities. Overall, patients with CD and C.Diff infection did show decreased morbidity/mortality and resource utilization, suggesting that the clinical course is less severe.

Further studies should continue to assess the gut immunological and microbiome changes in CD to further clarify potential factors associated with increased C.Diff infections.

Disclosure: Nothing to disclose

Variable	Adjusted Odds Ratios / Adjusted Means	95% CI	p-value
C.Diff	1.56	1.46-1.67	<0.01
Mortality	0.44	0.30-0.65	<0.01
ICU	0.47	0.35-0.62	<0.01
Shock	0.65	0.49-0.85	<0.01
Multiorgan failure	0.83	0.71-0.97	0.02
TPN	1.69	1.32-2.18	<0.01
Additional Hospital Costs	-$6,261	-8632,-3890	<0.01
Additional Hospital Charges	-$24,995	-32572,-17417	<0.01
Additional Length of Stay	-2.0	-2.8,-1.2	<0.01

[Adjusted means and odds ratio for the evaluated parameters comparing patients with CD compared to patients without CD. a=adjusted.]

P1364 THE MILANO QUESTIONNAIRE: A NEW DIETARY SCORE FOR EVALUATION OF COMPLIANCE TO GLUTEN FREE DIET IN PATIENTS WITH CELIAC DISEASE

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Introduction: Gluten free diet is the only recognized treatment for patients with celiac disease. Follow up for these patients is not standardized and the adherence to gluten free diet is not always easy to monitor.

Aims & Methods: We aimed to develop a novel questionnaire to monitor adherence to gluten free diet
in celiac disease.

The 'Milano' questionnaire is composed of 9 items: 6 questions are based on a visual analogue scale (VAS, obtaining continuous variables) and 3 of them are yes/no questions. Questions have been expressly formulated in order to investigate factors strictly connected with adherence to gluten free diet (GFD). In particular: voluntary gluten assumption, accidental gluten assumption (i.e. possibility of contaminations) and attention paid on the control of nutritional labels of GF products.

Two questions evaluate the presence and severity of symptoms experienced in case of accidental or voluntary gluten assumption. The questionnaire was compared to tTGA titres and duodenal histology.

Results: The Milano questionnaire was administered to 285 patients (209 females and 76 males). We observed a significant correlation between the score obtained and serological status of the patients. In particular lower scores obtained were associated with higher probability of positivity to tTGA, suggesting a score of 30 as a cut off value. In particular, among the questionnaire items, 3 of them resulted significantly different between the groups based on tTGA positivity: question number 1 about general attention to GFD, question number 2 concerning the frequency of voluntary assumption of gluten and question number 7 about the eventual check of nutritional labels of products. We also observed a positive correlation between a score minor than 30 and the grade of villous atrophy at biopsy obtained during GFD.

Conclusion: This study shows that a new dietary questionnaire, the Milano questionnaire, is an useful tool to evaluate compliance to the GFD of celiac patients during clinical follow up.

Disclosure: Nothing to disclose

P1365 WITHDRAWN

P1366 CELIAC HEPATITIS: IS THERE A RELATIONSHIP WITH CELIAC DISEASE NUTRITIONAL DEFICIENCIES?

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Introduction: Celiac hepatitis characterized by gluten-responsive mild elevation of transaminases is the more common liver manifestation of celiac disease (CD). It has been assumed that celiac hepatitis is related with the disruption of the "gut-liver axis". In the same way, a nutritional deficiency in CD is an indirect marker of intestinal absorptive function damage, as well as a possible precipitant of the systemic inflammatory cascade.
Aims & Methods: We aimed to study the relationship between nutritional deficiencies and the presence of abnormal liver function tests at the time of CD diagnosis.
A retrospective analysis of a CD cohort followed in a specialized outpatient clinic was performed. For each case, clinical and laboratory data at the time of diagnosis was collected. Within laboratory values, ferritin, folic acid, calcium, magnesium, phosphorus and vitamins A, B12, D and E were recorded. The correlation between continuous variables was established by Spearman's correlation; statistical differences between medians was assessed with the Mann-Whitney U test.
Results: We included 161 cases (mean age 35.5 ± 13.9 years old, 78.3% female) with an average follow-up of 10.6 ± 9.7 years. At diagnosis, 14.9% (n=24) of the patients had abnormal liver tests compatible with celiac hepatitis [median ALT 54 (IQR 41-62) IU/L; median AST 43 (IQR 39-53) IU/L; median GGT 15 (IQR 10-26) IU / L; median FA 99 (72-127) IU/L; median total bilirubin 0.55 (IQR 0.42-1.73) mg/dL].
At the time of CD diagnosis, the value of ALT showed a significant correlation with the value of anti-transglutaminase immunoglobulin A (TTG-IgA) (k=0.23; p=0.02).
Using regression analysis, the presence of abnormal liver tests was associated with iron-deficiency anemia (OR 3.12; CI95% 1.31-8.24, p=0.04).
The median value of ALT was significantly higher in the presence of folic acid deficiency (median 34 (IQR 20-39) vs.18 (IQR 14-29), p=0.02] and vitamin D deficiency [median 21 (IQR 16-37) vs.16 (IQR 14-25), p=0.02]
Conclusion: We found a statistically significant relationship between the presence of celiac hepatitis and iron deficiency anemia. Also, the serum value of ALT was significantly increased in folic acid and vitamin D deficiency. Gut dysfunction leading to an increased intestinal permeability and consequent liver tissue exposure to endotoxins may explain the previously mentionted relationship
Disclosure: Nothing to disclose

Nutrition II
09:00-17:00 / Poster Exhibition - Hall 7

P1367 PROGNOSTIC FACTORS ON BODY WEIGHT LOSS BY AN INTRAGASTRIC BALLOON THERAPY

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Introduction: Intra-gastric balloon therapy (IGBT) is a non-invasive modality of the bariatric therapy and can reduce 10 to 14 % of total body weight (TBW) before the therapy [1]. FDA recommends that doctors should indwell the balloon during only 6 months in stomach and then excrete it after therapy. If we can estimate the effect of bariatric balloon therapy before the therapy, it is clinically very useful.
Aims & Methods: Our aim is to clarify the key factors which can maximize the body weight loss by IGBT. We analyzed the correlation between TBWL (TBW loss) and BMI, visceral and subcutaneous fat amount, leptin, insu-

lin in sera, liver dysfunction, metabolic complications and its drugs, gut microbiomes before therapy in our clinical trial [UMIN 0008675] which enrolled 25 patients with obesity. On analyzing, we took some biases (sex, age) into account. In multivariable logistic regression analysis, TBWL (1: ≥10%, 0:< 10%) was assigned for independent variables and afore-mentioned factors were assigned for dependent variables.
Results:
1) Visceral fat amount was closely correlated with TBWL (correlation coefficient: 0.76). On the other hand, subcutaneous obesity group and high BMI>40 group could not reduce TBW over 5%.
2) Obese patients complicated with diabetes realized nearly 14~18% TBWL after 6 months therapy if their primary diabetes were regulated very well.
3) The patients with hyperleptinemia could reduce only 4.3% of TBW before therapy.
4) Patients with NAFLD could reduce 13.2% of TBW and improve the liver function adequately by IGBT.
5) HR was higher in visceral fat, complication and drug, anti-obesity microbiota.
Conclusion: Visceral fat amount and metabolic complication have possibility of becoming better prognostic factors in bariatric balloon therapy.
References: [1] Abu Dayyeh et al. "Endoscopic bariatric therapies" Gastrointest. Endosc. 2015, No.5, 1073-86
Disclosure: Nothing to disclose

P1368 HEPATIC STEATOSIS AND LIVER FIBROSIS EFFECTS AFTER ENDOSCOPIC SLEEVE PLICATION (ESP) FOR TREATMENT OF OBESITY I-II. PRELIMINARY RESULTS WITH THE NEW PATTERN FOR GASTRIC EMPTYING DELAY

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Introduction: Obesity and hepatic steatosis are major diseases with high morbidity. Treatment for patients (px) with hepatic steatosis (HS) with or without liver fibrosis is weight loss. Intragastric balloon is the endoscopic gold standard on short time weight loss. Endoscopic plicature can offer better middle long-term results than balloon for its durability. Liver stiffness (LS) and hepatic steatosis (HS) can be estimated with transient elastography (TE) and controlled attenuation parameter (CAP).
Aims & Methods: Multi-center, prospective pilot study intended to evaluate the safety and efficacy of the Gastric Endoscopic Sleeve Plication procedure (mid & distal body plications) (GESP) and its effect on hepatic fibrosis and steatosis.
Study was approved by ethic committee at both institutions. Px signed a written consent. Px with grade I-II obesity were included for the procedure. Use of the Incisionless Operating Platform (IOP)™ (USGI Medical, San Clemente, CA, USA) with a defined new pattern of disposition of the transmural plications with the g-cathTM EZ suture anchors in the greater curvature shortening and tubulizing the stomach to potentially delay gastric emptying and reduce gastric volume/accommodation for an enhanced physiological effect.
LS and CAP was measured with Fibroscan® device provided with M or XL probe (Echosens, France) by experienced personnel. Quality criteria for LS by TE were: 10 measurements obtained with a success rate ≥ 60% and a IQR≤30% of the median. Blood test was evaluated at baseline (BL) and 6 months post-GESP.
Results: 39 px were included in these multicenter-trial. 17 pxs (44%) from Centro Medico Teknon (CMT) were analyzed. 17 GESP in 17 pxs were successfully performed in CMT (59% females) without serious adverse events. LS+CAP was successful in all px (82% with XL probe).
Preliminary data on LS+CAP was obtained in 16 px (94%) at 2 months and in 7 px (42%) at 6 months. Body weight loss at 2 (n=14) and 6 months (n=8) was 14±4% (13.1±4.2 kg) and 19±11% (15.8±7.2 kg).
At BL, 11 px had absent/mild fibrosis (F0-F1), 4 px had significative fibrosis (F2), 1 px had severe fibrosis (F3) and 1 px cirrhosis (F4), with a mean LS of 4.1±0.9, 8.2±0.4, 9 and 12.3 kPa, respectively; HS S0, S1, S2, S3 was present in 4, 2, 3 and 8 px, with a mean CAP of 205±19, 248±5, 285±8 and 342±21, respectively.

At 2 months, 3 px (19%) with BL F2 (mean LS 8±0.4 kPa) had a statistically significant improvement of LS (mean LS 6.6±0.2, p=0.007). In regard to HS, 50% (n=8) of px had a reduction of HS in 2 stages and 19% (n=3) in 1 stage; 4 S0 at BL and 1 (6%) S3 at BL had no variation. A total of 5 px (31%) with BL HS (3 S2 and 2 S1) achieved S0. The only px with BL cirrhosis had a mild improvement of LS (12.3 vs 11.3 kPa) with an associated reduction in 2 stages of HS (S3 to S1); unfortunately, we still not have data on 6 months evaluation of this patient.

At 6 months, all 7 px had BL F0-F1 and showed a significant reduction in HS (303±47 vs 221±24, p=0.001) along with lower ALT levels (34±20 vs 17±4 IU/L, p=0.46) and elevation of HDL cholesterol (53±15 vs 60±19, p=0.036). LS, hemoglobin, platelets, creatine, total and LDL cholesterol, triglycerides, AST and total bilirubin were no significant different.

Conclusion: Preliminary results with reduction of weight loss with GESP procedure are promising for treatment of hepatic fibrosis and steatosis in patients with grade I-II obesity. Long term follow-up its necessary to assess its value for treatment of HS and LS.

Disclosure: Nothing to disclose

P1369 BRAZILIAN MULTICENTER STUDY OF ENDOSCOPIC SLEEVE GASTROPLASTY WITH OVERSTITCH USE - INITIAL RESULTS

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Introduction: With the current picture of obesity pandemic, the Endoscopic Sleeve Gastroplasty technique (ESG) has become an important tool as an option for treatment[1]. The therapeutic success rates described in literature vary from 50% to 100%, with little or no complication during or after the procedure, without cases of mortality, as well. This study was developed to analyze the results obtained by the respective technique in different treatment centers for obesity.

Aims & Methods: Three treatment centers for obesity from the main capitals of Brazil participated in this study. All patients were instructed on the ethical aspects of the research, and were followed for eighteen months after the procedure by a multidisciplinary team. Since July 2017, a total of 126 patients (109 submitted to full-thickness U-shaped sutures = SU; 17 submitted to full-thickness U-shaped sutures + Reinforcement = SUR) were randomly assigned to the study. Among the seventeen patients in the SUR group, only eight reached six months of follow-up.

Results: The sample profile consists of young adults with a mean age of 41.3 ± 10.5 years, being most of them women (63.5%). Initially, the patients presented mean weight: 97.4 ± 20.6 kg and mean BMI: 34.3 ± 4.9 kg / m. There was a significant* mean decrease of weight (6 months: 10.3± 5.1 kg, 12 months: 17.5± 8.6 kg, 18 months: 23.1± 8.2 kg) and BMI (6 months: 3.6±1.6 kg / m, 12 months: 6.5±2.6 kg / m; 18 months: 7.9±2.4 kg / m).

The results observed for the TBWL % (Total Body Weight Loss percentage) parameters were: 6 months = 10.3 ± 3.9; 12 months = 16.6 ± 6.2; 18 months = 21.3 ± 5.1. And the mean EWL % (Excessive Weight Loss percentage) was 41.8 ± 21.2, 64.1 ± 29.3 and 73.3 ± 27.6 at 6 months, 12 months and 18 months respectively.

Patients submitted to SUR presented superior results in EWL % (when compared to patients submitted to SU in 6 months of follow-up: SU = 38.1 ± 19.6, SS = 43.9 ± 15.9. A mean of 62.5 ± 6.1 and 89.2 ± 4.9 bites per suture was observed, with a mean of 4.6 ± 0.5 and 7.2 ± 0.5 threads respectively for SU and SUR suture. There was no case of complication during or after the procedure.

* Parametric t test; p < 0.05

Conclusion: The results described in this sample confirm the data pointed out in the literature[1], [2], ESG is a safe procedure and with high rates of therapeutic success. The results also showed that SUR procedures clinically imply double the rates of long-term therapeutic success. In this sample, 100% of patients submitted to SUR at 06 months had lost almost 45% of excess weight and no weight regain was observed in this group. We believe that these findings may be due to the mechanical response of SUR, as it promotes an even greater reduction of the lumen of the gastric tube, inducing with more intensity and for a longer time the delay of the gastric emptying and increasing the satiety.

It is important to emphasize that the high success rates described in this study are a direct consequence of a precise and adjusted interaction of the multidisciplinary support team. The data presented in this study are part of a larger ongoing study.

References: 1. Jain D et al. Endoscopic Sleeve Gastroplasty - A New Tool to Manage Obesity. Clin Endosc. 2017 Nov; 50(6): 552-561. 2. Bazerbachi F, Vargas Valls EJ, Abu Dayyeh BK. Recent clinical results of endoscopic bariatric therapies as an obesity intervention. Clin Endosc 2017;50:42-50. 3. Abu Dayyeh BK, Rajan E, Gostout CJ. Endoscopic sleeve gastroplasty: a potential endoscopic alternative to surgical sleeve gastrectomy for treatment of obesity. Gastrointest Endosc 2013;78:530-5.

Disclosure: Nothing to disclose

P1370 WEIGHT REGAIN AFTER BARIATRIC SURGERY - ENDOSCOPIC SUTURE WITH OVERSTITCH USE FOR GASTROINTESTINAL ANASTOMOSIS DECREASE - INITIAL RESULTS - BRAZILIAN MULTICENTER STUDY

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Introduction: Weight regain has been a constant concern, as reports in literature indicate that rates can reach up to 50%, especially in patients who have undergone bariatric surgery. However, it is not yet clear how weight regain occurs because it is a variable that undergoes various intrinsic and extrinsic interferences of the individual. The technique to reduce the anastomotic size has been successfully developed around the world. Thus, this paper aims to describe the initial results of a long-term clinical study in Brazil.

Aims & Methods: Three treatment centers for obesity from the main Brazilian capitals participated in this study. All patients were instructed on the ethical aspects of the research, and were followed for eighteen months after the procedure by a multidisciplinary team. Thirty-one patients (twenty-one submitted to full-thickness Z-shaped sutures and ten submitted to full-thickness Z-shaped sutures + Reinforcement) participated in this study, since July 2017, and were followed up for eighteen months.

Results: Thirty-one patients with a mean age of 42.9 ± 8.7 years participated in this study, most of them women (84.4%). Pre-intervention data: Weight: 103.7 ± 17.9 kg and BMI: 36.2 ± 6.1 kg / m. A mean of 28.9 ± 9.3 bites per suture and 2.1 ± 0.7 threads were used in the procedure. There was a significant* mean reduction of 11.9 ± 5.3 kg, 15.2 ± 6.1 kg and 19.3 ± 8.9 kg at 6 months, 12 months and 18 months respectively. A mean reduction of 4.1 ± 1.5, 5.5 ± 2.1 and 6.7 ± 2.5 points in the BMI parameter was observed for follow-up times of 6 months, 12 months and 18 months, respectively. There was progressively an increase of TBWL % (Total Body Weight Loss percentage) = 11.3 ± 3.6, 14.6 ± 3.8 and 17.7 ± 4.5 for 6, 12 and 18 months respectively. The Excessive Weight Loss was significant at 6 months (EWL % = 40.4 ± 13.5), at 12 months (50.3 ± 17.7) and 18 months at follow-up (56.3 ± 8.6). No complications were observed during or after the procedure.

Conclusion: The data so far have shown very significant results in relation to the main outcome (EWL %), as this study presented an approximate loss of 50% of the excess weight in the first 12 months. There was a slight increase in this parameter in later follow-up. There should be pointed out that between one year and a year and a half, the weight loss was kept going on. In this initial cut of the study, no complications were observed during or after the procedure. These results are due in large part to the multidisciplinary work employed throughout the follow-up of these patients.

References: [1] Jain D et al. Endoscopic Sleeve Gastroplasty - A New Tool to Manage Obesity. Clin Endosc. 2017 Nov; 50(6): 552-561. [2] Bazerbachi F, Vargas Valls EJ, Abu Dayyeh BK. Recent clinical results of endoscopic bariatric therapies as an obesity intervention. Clin Endosc 2017;50:42-50. [3] Abu Dayyeh BK, Rajan E, Gostout CJ. Endoscopic sleeve gastroplasty: a potential endoscopic alternative to surgical sleeve gastrectomy for treatment of obesity. Gastrointest Endosc 2013;78:530-5.

Disclosure: Nothing to disclose

P1371 ENDOSCOPIC GASTRIC MUCOSAL RESECTION FOR WEIGHT LOSS AND SUPPRESSING SYSTEMIC GHRELIN LEVELS IN VIVO MODEL

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Introduction: Obesity is a chronic metabolic disorder that is challenging to control. Ghrelin may be involved in the occurrence of obesity and associated with weight-loss resistance [1]. Endoscopic gastric mucosal resection (EGMR) is performed by the combination of endoscopic submucosal dissection (ESD) and endoscopic mucosal resection (EMR).
Aims & Methods: The aim of this study was to analyzed the impact of EGMR on body weight and ghrelin levels to explore its potential as a novel weight-loss technology. EGMR procedure was carried out to resect the mucosal layer of the fundus and body of the stomach in five healthy pigs, while another five were untreated as controls. Weight was monitored continuously for 12 weeks and fasting plasma ghrelin levels were analyzed by enzyme-linked immunosorbent assay (ELISA) within 1 and 2 months after the EGMR procedure.
Results: Compared with the control group, pigs in the experimental group exhibited reduced gastric volume and weight-loss with time after the EGMR procedure. The average weight in the experimental group was 51.6±17.27 kg at 12 weeks after the EGMR procedure and 64.00 kg±11.86 kg in the control group (P = 0.0001). There were significant differences in ghrelin levels. Compared with baseline, ghrelin levels decreased to 250.72±15.57 pg/ml at 1 month after the EGMR procedure, and continued to decrease to 169.15±17.93 pg/ml at 2 months after the EGMR procedure. In contrast, there were no obvious changes in the ghrelin levels between the experimental and control groups (F = 90.11, P = 0.0007).
Conclusion: EGMR procedure can effectively reduce stomach volume permanently and suppress ghrelin, indicating the potential of this approach as a novel weight-loss technology.
References: 1. Pereira JADS, da Silva FC, de Moraes-Vieira PMM. The Impact of Ghrelin in Metabolic Diseases: An Immune Perspective. J Diabetes Res. 2017; 2017:4527980.
Disclosure: Nothing to disclose

P1372 LARGEST MUCOSAL RESECTION IN THE WORLD FOR WEIGHT LOSS

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Introduction: Obesity is one of the most ubiquitous chronic diseases[1]. Inspired by the complication of esophageal stenosis after endoscopic submucosal dissection (ESD)[2], we hypothesized that resection of a sufficiently large area of the gastric mucosa should result in contracture and a reduction in gastric volume and provide a new strategy for medical treatment of obesity.
Aims & Methods: The aim of this study was to evaluate large gastric mucosal resection using combination methods of ESD and endoscopic mucosal resection (EMR) procedures for weight loss. A cap-based single-channel endoscope was used to resect 80% of the circumference of the anterior, posterior, greater curvature mucosal layer of the stomach. Small portions of mucosa (mucosal islands) were left to promote wound healing and regeneration of the gastric mucosa after the procedure. Finally, coagulation forceps were used to coagulate the bleeding or potential bleeding sites in the submucosal and muscular layer to prevent recurrent bleeding.
Results: From December 2015 to March 2019 a total of eight patients (n=8) underwent gastric mucosal resection procedure for weight loss and two patients (n=2) were associated with type 2 diabetics. The mean initial body weight was 108.56 kg (range, 75-135kg). One week after the procedure, gastroscopy showed a large area of ulceration on the greater curvature of the stomach covered by yellow plaque. One month after the procedure, the area of the ulcer was noticeably smaller, the mucosal islands were wider, and the plaque was white and clean. The mean BMI was decreased to 32.24 kg/m² from 37.13 kg/m². Eighteen months after the procedure, gastroscopy confirmed ulcer healing completely with a normal appear-

ing mucosa. CT scan confirmed that the gastric volume was reduced. The mean follow-up time was 12.66 months (range, 3-30 months). All patients experience early satiety after eating and lost most of the excess weight. Following the procedure, the mean BMI reduction was 29.73 kg/m², 28.05 kg/m², 27.59 kg/m², 27.15 kg/m², and 27.19 kg/m² at three months (n=8), six months (n=8), twelve months (n=6), twenty-four months (n=2), and thirty months (n=2), respectively. One patient (n=1) had recurrent vomiting and could not take food one month after the procedure, and received stent implantation in our hospital. There were no others major adverse effect intra-procedure or during 30 months follow-up period. The blood glucose level was decreased to normal and no therapy was needed.
Conclusion: This new procedure appears to be an effective, safe, and less invasive restrictive-type bariatric procedure with low technical complexity and complications.
References: 1. Hruby A, Hu FB. The Epidemiology of Obesity: A Big Picture. Pharmacoeconomics. 2015; 33: 673-689 2. Kakushima N, Kawata N, Tanaka M et al. Complications of endoscopic dilation for esophageal stenosis after endoscopic submucosal dissection of superficial esophageal cancer. Surg Endosc 2015; 29:2953
Disclosure: Nothing to disclose

P1373 MULTI-STRAIN PROBIOTIC INCREASES THE GUT MICROBIOTA DIVERSITY IN OBESE PREGNANT WOMEN: RESULTS FROM A RANDOMIZED, DOUBLE-BLIND PLACEBO-CONTROLLED STUDY

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Introduction: Maternal obesity is associated with adverse pregnancy outcomes with both maternal and neonatal complications. Probiotic supplementation during pregnancy may have positive effects on maternal blood glucose, gestational weight gain (GWG), and the risk of gestational diabetes mellitus (GDM).
Aims & Methods: The primary aim of this study was to determine the feasibility of probiotic intervention in obese pregnant women from the early second trimester until delivery. The secondary aim was to investigate the effect of daily probiotic supplementation on GWG, maternal glucose homeostasis, infant birthweight, and maternal gut microbiota.
We carried out a randomized double-blinded placebo-controlled study in 50 obese pregnant women with pre-pregnancy body mass indices between 30 and 35 kg/m². Participants were randomly allocated to two treatment groups, Vivomixx (n=25) or placebo (n=25) at 14-20 weeks of gestation (baseline) and followed with two pre-delivery visits at gestational week 27-30 and 36-37 and with one post-delivery visit 2-3 days after birth. All visits included blood and fecal sampling. An oral glucose tolerance test was performed at baseline and gestational week 27-30.
Results: Forty-nine participants completed the study, Vivomixx (n=25), placebo (n=24). Thirty-eight participants took more than 80% of the capsules, Vivomixx (n=21), placebo (n=17). There was no significant difference in HbA1c levels and the occurrence of GDM between groups. There was, however, a trend towards lower GWG and lower infant birthweight in the probiotic group. Fecal microbiota analyses showed an overall increase in α-diversity over time only in the Vivomixx group (p=0.016).
Conclusion: Administration of probiotics is feasible, and a multi-strain probiotic were able to increase α-diversity during pregnancy in obese women. A larger study population is needed to uncover whether the trends found regarding probiotic effects on GWG and lower infant birthweight become significant.
Disclosure: Both the probiotic and placebo capsules as well as half a year's salary to the study have been donated to Copenhagen University Hospital Hvidovre by Next Gen Pharma India Pvt. Ltd., H. No. 331, 1st Floor, Sector 15A, Noida 201301, National Capital Region, India. The funding source

had no role in the study design, data collection, interpretation of analysis, writing of the manuscript, or decision to submit the publication. Anders Elm Pedersen is affiliated with Merck A/S, Denmark. The present work is not related to this affiliation. The study was financed by grants from the following private foundations; Jeppe Juhls og hustru Ovita Juhls Mindelegat, Else og Mogens Wedell-Wedellborgs Fond, Aase og Ejnar Danielsens Fond, Knud og Edith Eriksens Mindefond, Toyota-Fonden Denmark, and Next Gen Pharma India Pvt. Ltd. The study was co-financed by the Faculty of Health and Medical Sciences, University of Copenhagen. All funding sources had no role in the study design, data collection, interpretation of analyses, writing of the manuscript, or decision to submit the publication.

P1374 PHASE ANGLE AS MARKER OF NUTRITIONAL STATUS IN PATIENTS WITH CROHN'S DISEASE: A CROSS SECTIONAL STUDY

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Introduction: The assessment of body composition (BC) can offer a practical approach to identify malnutrition, frequently observed in patients with Crohn's disease (CD). Bioelectrical phase angle (PhA) provides crucial information on cell mass quality and hydration status.

Aims & Methods: The aim of this study was to assess BC, PhA and muscle strength in CD patients as indicators of both nutritional and functional status.

Consecutive adult CD patients aged between 18-65 years were recruited for this cross-sectional study. Disease activity was clinically defined by Crohn's Disease Activity Index (CDAI) in active (>150) and quiescent (< 150) phase. All participants underwent anthropometry, BC and handgrip-strength (HGS) measures; additionally, biomarkers involved in the nutritional status were assessed. Data from CD patients were also compared with a group of healthy subjects age-, sex- and BMI- matched.

Results: A total of 140 CD patients with a mean age of 38.8 ±13.9 years and an average body weight of 64.9±12 kg were recruited and compared to controls. Findings showed that all nutritional parameters, especially PhA (CD: 6.35±0.94° vs. Controls:6.81±0.79°; p=0.000), were lower in CD patients, especially in the active group, compared to controls. Active-CD patients had also a lower body weight and fat mass compared both to the quiescent and control groups. PhA was also negatively correlated with age (r=-0.362; p=0.000) and CDAI (r=-0.315; p=0.000), whereas was positively associated with FFM (r=0.443; p=0.000) and HGS (r=0.539; p=0.000). Similarly, serum protein markers are lower for active-CD patients compared to the quiescent group (p< 0.05); while, CRP meaningfully increased.

Conclusion: Overall, nutritional indicators tend to be lower in CD patients compared to controls. Specifically, PhA-values impaired with increasing of disease activity, being a sensitive marker of nutritional status. Therefore, the assessment of BC should be recommended in clinical practice for screening and monitoring nutritional status of CD patients.

Disclosure: Nothing to disclose

P1375 A PROSPECTIVE MULTI-CENTER STUDY ON THE PREVALENCE OF FRUCTOSE MALABSORPTION IN PATIENTS WITHCHRONIC INFLAMMATORY BOWEL DISEASE

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Introduction: Patients with chronic inflammatory bowel disease (IBD) might have a greater likelihood of also being fructose malabsorbers as compared to healthy controls. The aim of this study was to determine the prevalence and symptom severity of fructose malabsorption in patientswith active and inactive IBD compared to healthy controls.

Aims & Methods: The present study was a multi-center non-interventional diagnostic pilot trial approved by the Ethics Committee of the Christian-Albrechts-University Kiel, Germany. Fifty-seven patients with active IBD, 93 patients with IBD in remission, and 101 healthy controls admitted to twelve different out-patient clinics for Internal Medicine in Germany were included prospectively. Fructose malabsorption was diagnosed by hydrogen breath testing after the ingestion of 50g fructose diluted in 300ml water and defined as an increase in H_2 levels by at least 20 parts per million compared to baseline. Patients diagnosed with bacterial over-population as diagnosed by the glucose breath test and non-H2 producers as diagnosed by the lactulose breath test that were tested negatively on fructose as well as lactose were excluded from the analyses.Gastrointestinal symptoms during the breath tests were evaluated using four-point items to determine subjective severity of bloating, abdominal pain and diarrhea.

Results: 251 participants were included in the study (table 1). 205 patients (45 with active IBD, mean age 39.20 ± 13.48 years, 55.6% female; 80 with IBD in remission, mean age 43.03 ± 11.79 years, 58.8% female; 81 healthy controls, mean age 28.92 ± 8.81 years, 61.7 % female) remained after diagnosing for bacterial over-population and non-H2 producers. The number of patients diagnosed with fructose malabsorption - 35/44 (79.6%) in patients with active IBD, 59/80 (73.8%) in patients with inactive IBD, and 66/81 (81.5%) in healthy controls - did not differ between the three groups (χ^2(2, N= 205) = 1.48, p= .48). Abdominal pain was more frequent in patients with active IBD than in patients with IBD in remission (z = -2.936, p= .010) and diarrhea was more frequent in patients with active IBD than in healthy controls (z = 2.489, p= .038).

Conclusion: Within the present study, fructose malabsorption is not more common in patients with IBD than in healthy subjects. However, the stronger symptoms of the patients with IBD may have pathological and therapeutic relevance.

Disclosure: Lecture and consulting fees: AbbVie, MSD, Ferring, Falk Foundation, Takeda, Mundipharma, Hospira, Vifor Pharma

P1376 LACTOSE SENSITIVITY AND LACTOSE MALABSORPTION. THE TWO FACES OF LACTOSE INTOLERANCE IN PATIENTS WITH FUNCTIONAL BOWEL DISORDERS

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Introduction: In France, 30 to 50% of adults have incomplete digestion of lactose. The importance of the symptoms is a function of the residual lactase activity and the amount of lactose ingested. These symptoms are more frequent in postprandial period, 30 minutes to 2 hours after ingestion of food containing lactose. They are not specific, evocating bowel disorders,(gas, bloating, abdominal cramps, diarrhea, nausea, vomiting) or general disorders. They are frequently confused with irritable bowel syndrome, that may delay the prescription of an adapted regime.

Aims & Methods: The purpose of this study is to evaluate the frequency of lactose malabsorption and the frequency of lactose sensitivity in patients with functional bowel disorders, with symptoms revealed or increased after lactose ingestion.

We included 142 consecutive patients (104 women, 73%) with functional bowel disorders. In all patients, the search for a small intestine bacterial overgrowth by glucose breath test was negative. These patients have completed a Rome III questionnaire and performed the lactose absorption test that measures the blood glucose before and 15, 30, 45 and 60 minutes after ingestion of 50 g of lactose. A malabsorption was diagnosed when the peak blood glucose level was below 0.20 g / l and a lactose sensitivity was registered if digestive signs appeared during the test.

Results: Lactose sensitivity without malabsorption was present in 58 patients (group I, 41%), a malabsorption without lactose sensitivity was found in 14 patients (group II, 10%) and 23 patients (group III, 16%) exhibited at the same time lactose malabsorption and lactose sensitivity. 47 patients (Group IV, 33%) showed neither malabsorption nor sensitivity to lactose Compared with group IV patients, patients in group I were younger (38.8

± 1.5 vs 44.4 ± 2.7 years, P = 0.039) and complained of greater incidence of chest pain (29% vs. 26%, P = 0.042). Other demographic parameters, frequency of other symptoms (esophageal, gastroduodenal, intestinal and anorectal according to Rome III) were similar in the four groups of patients.

Conclusion: The joint study of lactose absorption and lactose sensitivity is useful to eliminate the pathogenesis of this sugar in patients with disorders intestinal function and justify the establishment of a lactose-free diet. In symptomatic patients after ingestion of lactose, we suggest distinguish patients suffering from malabsorption of lactose by decreased Intestinal lactase activity from patients with lactose sensitivity characterized by the appearance of symptoms without decrease of lactose absorption.

Disclosure: Nothing to disclose

P1377 PATTERNS OF FIBER INTAKE AMONG BRAZILIAN ADULTS: A NATIONWIDE WEB-BASED SURVEY

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Introduction: Adequate fiber intake has been directly linked to physiological gut balance and is recognized as essential for human health. The World Health Organization (WHO) recommends for adults a daily fiber consumption of ≥25 g, but previous studies observed a fiber intake in Brazil lower than recommended.
Aims & Methods: We aimed to describe fiber intake among adults in Brazil, through a nationwide web-based survey. Data was collected in September 2018 using an online platform with closed-ended questions. A representative sample of Brazilian internet users stratified by sex, age, socioeconomic status and geographic region was adopted. Sample size was calculated using a 2% error margin and 95% confidence interval (n=2,000). Data was descriptively analyzed using measures of frequency, central tendency and dispersion.
Results: Sample included 2,000 individuals who were well-balanced in terms of sex (51% female), with mean age of 36 years (most represented age group was 35-54 years, 40%) and from all country geographic regions (49% from Southeast). Most subjects (64%) were classified as having low socioeconomic status/income, consistent with Brazilian general population. 70% of them consider their usual diet as healthy and 78% reported consuming fibers regularly. Fibers from natural sources are consumed at least once a day by 69% of the sample, while daily fiber supplements were reported by 30%. Absence of regular fiber intake was reported by 22% of respondents and the most common reason was "lack of knowledge about fiber sources" (39%), followed by "daily inclusion of fibers would be expensive" (30%) and "lack of time" (22%). Fibers sources with higher frequency of daily intake in the sample were: beans and pulses (67%), whole grains (57%), and vegetables (56%). Nuts were the least frequent group with only 13% of daily intake (18% never consume). 74% of the sample informed that they knew about the role of fibers in improving intestinal function, but only 30% knew the difference among soluble and insoluble fibers. When informed about the food sources of each type of fiber (soluble and insoluble) and asked about the regular intake of each type, only 2% answered that they do not consume any of them regularly (as opposed to 22% before receiving information about specific fiber sources). 87% of the individuals who reported taking regular fiber supplements classified their intestinal function as normal. Men reported having better intestinal function than women.
Conclusion: Our findings indicate that fiber intake in Brazil is probably insufficient with a high proportion of individuals reporting irregular or absent ingestion of fiber sources in their daily lives. Lack of knowledge about fiber sources and fiber types seems to play a role in this inadequate intake, highlighting the need for nutritional education to achieve healthy dietary patterns in the country.
Disclosure: Maria do Carmo F. Passos is a global member's advisory board for Takeda Pharmaceuticals, Mantecorp, EMS and Speaker for Aché, Nestlé, Danone, Hypera, EMS, Janssen. Luciana S Guedes is Sr Medical Manager at Takeda Pharmaceuticals

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P1378 IRREGULAR DIETARY HABITS WITH A HIGH INTAKE OF CEREALS AND SWEETS ARE ASSOCIATED WITH MORE SEVERE GASTROINTESTINAL SYMPTOMS IN IBS PATIENTS

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Introduction: Dietary advice constitutes one of the first choices of treatment for irritable bowel syndrome (IBS). However, almost 50% of the IBS population do not improve their symptoms following accepted recommendations such as the NICE guidelines or a low FODMAP diet. The sucrase-isomaltase (SI) genes are responsible for the enzymatic breakdown of starch and sucrose in the small intestine. Recently, we have recognized that an increased prevalence of functional SI gene variants can be seen in patients with IBS, resulting in enzymatic defects and possible difficulty digesting starches and sucrose [1].
Aims & Methods: The primary aim was to examine participants' dietary habits at baseline, and to correlate the dietary habits with gastrointestinal (GI) symptoms and blood levels of minerals and vitamins. Secondly, we wanted to examine the effect of a starch- and sucrose-reduced diet (SSRD) on GI symptoms. IBS patients, without any organic GI disease, and total IBS-SSS score >175, were randomized to either the dietary intervention group (n=80); following a SSRD for 2 weeks or to the control group (n=25) who continued with their ordinary eating habits. The main dietary advise was to decrease the intake of cereals, sweets/soft drinks, and to avoid vegetables and fruits with high content of starch (2). All subjects had blood samples drawn and completed questionnaires regarding GI symptoms (visual analog scale for irritable bowel syndrome (VAS-IBS), irritable bowel syndrome symptom severity scale (IBS-SSS) and Rome IV), and two 4-day food diaries, at baseline and after 2 weeks. The food intake was categorized into regular (3-6 meals/day) or irregular food habits, the intake frequency of fast food and soda was counted, and an on-going current diet was registered. Food items were categorized into meat, fish, vegetables, fruits, dairy products, cereals, and sweets/soft drinks.
Results: Patients with regular dietary habits exhibit less pronounced GI symptoms, measured as total IBS-SSS score, than patients with irregular habits (p=0.029). Intake frequency of sugar-rich soda correlated with total IBS-SSS score, vomiting and nausea and intestinal symptoms' influence on daily life. Women with an on-going diet had lower levels of ferritin than women without diet (p< 0.029, adjusted for age). A majority of the patients had serum levels of 25-OH vitamin D below reference values. IBS patients randomized to the intervention group showed significant improvement of several symptoms after the 2-week dietary intervention, in contrast to controls, with 31.1% of subjects in the intervention group being responders (>50% decrease in total IBS-SSS score). The change in GI symptoms between 2 weeks and baseline, delta values, differed between the intervention and control group regarding total IBS-SSS score (p< 0.001, abdominal pain (p=0.001), diarrhea (p=0.002), bloating and flatulence (p=0.005), psychological well-being (p=0.048), intestinal symptoms' influence on daily life (p< 0.001). The decreased intake of cereals and sweets/soft drinks correlated with decreased scores of total IBS-SSS, abdominal pain, diarrhea and bloating and flatulence. The dietary advice was easy to adhere to.
Conclusion: Dietary habits affect the experience of GI symptoms and blood levels of minerals and vitamins in patients with IBS. A starch-and sucrose-reduced reduced diet with reduced intake of cereals and sweets/soft drinks has marked effect on reducing GI symptoms in this cohort. The pathologic mechanisms behind this improvement need to be further researched in future studies.
References: 1. Garcia-Etxebarria, K.; Zheng, T.; Bonfiglio, F.; Bujanda, L.; Dlugosz, A.; Lindberg, G.; Schmidt, P.T.; Karling, P.; Ohlsson, B.; Simren, M.; Walter, S.; Nardone, G.; Cuomo, R.; Usai-Satta, P.; Galeazzi, F.; Neri, M.; Portincasa, P.; Bellini, M.; Barbara, G.; Jonkers, D.; Eswaran, S.; Chey, W.D.; Kashyap, P.; Chang, L.; Mayer, E.A.; Wouters, M.M.; Boeckxstaens, G.; Camilleri, M.; Franke, A.; D'Amato, M. Increased Prevalence of Rare Sucrase-isomaltase Pathogenic Variants in Irritable Bowel Syndrome Patients. Clin Gastroenterol Hepatol 2018;16:1673-1676. 2.Sucrose Intolerance. Genetic Sucrase-Isomaltase Deficiency [cited 2018-07-10]. Available from: https://www.sucroseintolerance.com/choosing-your-foods
Disclosure: Nothing to disclose

P1379 COMPARISON OF NUTRIENT INTAKES BETWEEN PATIENTS WITH DIFFERENT PANCREATIC DISEASES

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Introduction: The last decade has seen a steady increase in the number of persons with pancreatic pathology, which is becoming an important social and economic problem. Both acute and chronic pathology of the pancreas can lead to the development of endocrine and exocrine pancreatic insufficiency, disrupting the processes of digestion, absorption.
Aims & Methods: Compare nutrient intake for patients with pancreatic cancer (PC) , acute pancreatitis (AP) and chronic pancreatitis (CP).
166 patients were examined in the clinical study. Of these, 43 patients with pancreatic cancer (62.8 ± 4.7 years) and 123 patients with acute pancreatitis (AP) and chronic pancreatitis (CP), the average age of patients with pancreatitis is 50.4 ± 2, 2 years. Of these, 42 patients with acute pancreatitis and 81 patients with chronic pancreatitis. All patients underwent an ultrasound examination of the pancreas, liver and biliary tract, patients with PC were performed computed tomography of the pancreas. A survey of patients with AP was conducted in the first 5-10 days from the day of hospitalization, patients with CP - during the exacerbation. The actual nutrition was assessed using a questionnaire, including 142 product names indicating the portions of this product and the frequency of consumption over the past 3 months. Indicators of consumption of basic nutrients were calculated in grams and as a fraction of the daily caloric value they provide. The nutrient set was compared with the "Norms of physiological needs for energy and nutrients" (V. Tutelyan, 2009).
Results: The total caloric content of the daily diet of patients with various pathologies of the pancreas did not differ. The energy of the diet was: in patients with PC - 2593.7 ± 309.1 kcal / day, in patients with CP - 2553 ± 586.7 and in patients with AP - 2438 ± 224.2 kcal / day.
The diet of patients with pancreatic pathology was unbalanced by the fat and carbohydrate components. The high proportion of total fat intake (PC - 48.5% of kcal / day, CP - 46.2%, AP - 47.8%) and insufficient consumption of carbohydrates (35.3% of kcal / day, 39.1% and 38.0%, respectively). In individuals with pancreatic cancer, the diet included 135.2 ± 18.1 g / day of total fat and 235.3 ± 27.2 g / day of total carbohydrates.
The proportion of protein in the diet of patients with PC was 102.3 ± 12.2 g / day, which is higher than the recommended physiological intake rate - 16.2% of kcal / day, as well as in patients with CP and AP - 14.7% and 14 , 2%. The content of vitamins B1, B2, PP in the diet of patients with various pathologies of the pancreas is within the recommended standards, but there is a significant excess of the norms of consumption of vitamins A and C in the diet of patients with prostate cancer (1787.8 ± 558.4 mkg ret. Equiv. and 335.5 ± 84.1 mg, respectively, p < 0.05), and in patients with AP, the content of beta-carotene in the diet is reduced (3.6 ± 0.9 mg / day).
Conclusion: The levels of nutrient intake in individuals with different pathologies of the pancreas were significantly different, the daily diet was unbalanced. The consumption of proteins, fats, vitamins A and C exceeds the recommended consumption rates. The share of total carbohydrate intake reduced in patients with cancer of the pancreas and in patients with acute and chronic pancreatitis. Probably, this can be regarded as an indirect sign of low adherence of patients with pancreatic diseases to compliance with medical recommendations, including dietary recommendations.
Disclosure: Nothing to disclose

Women in GI
09:00-17:00 / Poster Exhibition - Hall 7

P1380 CURRENT CHALLENGES FACING JAPANESE FEMALE DOCTOR IN THE FIELD OF GASTROENTEROLOGY: HOW DO WE MOVE FORWARD?

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Introduction: The number of women entering medical school increased remarkably over the past several decades and nearly a third of the graduates are female in Japan. However, the percentage of female gastroenterology fellows has remained stable at approximately 10%. Therefore, the Japanese society of Gastroenterology (JSGE) organized the Supporting Women in Gastroenterology group at each 10 regional bureau nationwide in 2016 and started to discuss this issue.
Purpose: The purpose of this study was to clarify the current situation and how to get more females in the field of gastroenterology area in Japan.
Aims & Methods: We conducted a survey by questionnaire for female member of JSGE Tohoku branch from October to December in 2016. That includes ; age distribution, marital status, specialized field, working hours, working condition during pregnancy and child care or elderly care, evaluation of current working environment, and desired support measures for continuous service.
Results: Of 233 female doctors in gastroenterology, 120 (53.8%) returned the questionnaire. The results are as follows ; age distribution (-29 years old ; 8.3%, 30-39; 41.7%, 40-49; 29.2%, 50-59; 15.0 %, 60-; 5.8 %), marital status (married; 68.3%, unmarried; 31.7%), specialized field (gastroenterology; 78.3%, surgeon ; 4.2%, others; 17.5%), working hours (8-10 hours per day ; 30.8%, 10-12 ; 17.5%, more than 12; 19.2%), approximately 90% of them came back to work soon after short maternity leave and 91% of those who were entitled to didn't take elderly-care leave. Many working mothers feel that they aren't fully understood by their colleagues. On the contrary, some unmarried female doctors complained of heavier workload due to other person's maternity leave and/or exemption from their duties. Most of the respondents thought that the understandings and supports from their boss and colleagues, working flexibly and/or sharing their work are essential for continuing their work.
Conclusion: Current working environment of women in gastroenterology field in Japan are tough. To get more female to this area and enable them to work with less burden, improvement of long working hours and change in awareness of their boss and colleagues are very important.
Disclosure: Nothing to disclose

Paediatric: Upper GI II

09:00-17:00 / Poster Exhibition - Hall 7

P1381 TREATING FUNCTIONAL GASTROINTESTINAL DISEASES IN THE PAEDIATRIC POPULATION: ARE HERBALS AN OPTION? A SYSTEMATIC REVIEW

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Introduction: Functional gastrointestinal diseases describe a spectrum of gastrointestinal dysfunctions, mainly functional dyspepsia (FD) and irritable bowel syndrome (IBS). Symptoms include abdominal pain, nausea, fullness and stool irregularities, leading to a severely impaired quality of life (1).

Aims & Methods: Given the high medical need in these indications especially in children (2), there is a requirement for effective and well-tolerated treatment options in this age group.
A PubMed-Medline search for clinical studies and reviews regarding FD and IBS in children in compliance with the PRISMA statement was conducted and complemented by hand searching and cross-referencing.

Results: The search gained 79 hits for FD in children, thereof 13 on pharmacological treatment options, 2 of which were herbals. For IBS, it gained 321 hits, including 23 on pharmacological treatments, thereof 5 herbals. These were Psyllium, Peppermint oil and STW 5 as well as Turmeric, Cannabis, Aloe vera and Ginger, with clinical studies in children mentioned only for Psyllium, STW 5 and Peppermint oil (1-5). For FD, Hippophae rhamnoides and STW 5 were identified, both with clinical evidence (1, 6). Only STW 5 was mentioned for both diseases.
A closer look into the evidence for this preparation showed a number of studies supporting the therapeutic usefulness in children of all ages, retrospectively (7, 8) as well as prospectively (9-14). These included 44.488 children, showing an excellent safety profile with only few mild side effects in this age group, and a convincing rating of the therapeutic usefulness.

Conclusion: Functional GI diseases are an important indication especially in children, where herbal preparations provide effective treatment options with a low risk profile and therefore play a prominent role in their management. Grades of evidence are different and most convincing for STW 5 likewise in FD and IBS, while Psyllium and Peppermint oil as well as Hippophae rhamnoides show evidence only for IBS or FD, respectively.

References: 1. Malfertheiner, Dig Dis. 2017, 35 Suppl 1: 25-29; 2. Shulman et al., Clin Gastroenterol Hepatol. 2017, 15: 712-719; 3. Charrois et al., Pediatr Rev. 2006, 27: 49-51; 4. Grigoleit and Grigoleit, Phytomedicine 2005, 12: 601-6; 5. Fifi et al., Nutrients 2018, 10:E1715; 6. Xiao et al., Hell J Nucl Med. 2013, 16: 38-43; 7. Kelber Z Phytother, 2010, 31: 40-47; 8. Gundermann and Hänicke, Päd. 2004, 10: 408; 9. Vinson and Radke, Gatroenterol. 2011, 140: 102; 10. Nazarenko et al., Med. novosti 2008, 10: 79-83; 11. Aryaev and Kozhevin, Modern Pediatrics, 2009, 5: 151-154; 12. Shadrin et al., Modern Pediatrics, 2012, 6: 161-165; 13. Bovbel and Maljugin, Med. novosti, 2009, 4: 51-54; 14. Ermakova et al., Med. novosti, 2009, 8: 72-78

Disclosure: OK is employee at Steigerwald Arzneimittelwerk GmbH. JM is intern at Steigerwald Arzneimittelwerk GmbH.

P1382 DIAGNOSIS OF RUMINATION SYNDROME IN CHILDREN WITH AMBULATORY IMPEDANCE-PH MONITORING

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Introduction: According to the Rome IV criteria the diagnosis of rumination in children is based on typical symptoms during clinical evaluation. High resolution manometry/impedance (HRM/Z) can be used to confirm the clinical suspicion of rumination but is rather poorly tolerated in children and only records one postprandial period.

Aims & Methods: The **aim** of our study was to identify a specific diagnostic pattern of rumination during ambulatory Impedance-pHmetry (MII-pH). We retrospectively assessed MII-pH tracings from children with clinical diagnosis of rumination syndrome confirmed by HRM/Z (minimal 2 typical rumination episodes in postprandial evaluation). We then compared the MII-pH parameters of these patients with those from children with GERD and "non-GERD" children (investigated for possible GERD but with normal MII-pH). We established cut-off levels for significant MII-pH parameters and developed a rumination-specific scoring system. We then validated the scoring system on another group of patients who underwent both HRM/Z and MII-pH (traces scored blindly).

Results: We identified 12 children with confirmed diagnosis of rumination based on HRM/Z findings (median age: 13.9 years, 6M:6F). Another 18 children were identified with GERD (median age: 8.1 years, 8M:10F) and 12 children with non-GERD (median age: 12.4 years, 6M:6F). Children with rumination had significantly higher number of total reflux events (RE)/24 hrs, total number of proximal RE/24 hrs (p< 0.0001) and postprandial non-acid RE/hr (p=0.0072) compared to GERD and non-GERD groups. The SAP for regurgitation/reflux/vomiting was significantly higher in the rumination group (p=0.0009). The scoring system includes: 1)Total proximal RE/24hrs >57.5, 2)Postprandial non-acid RE/hr >2, 3)SAP for regurgitation/reflux/vomiting >97.5. Each parameter scores 1 and rumination is diagnosed if the score is < 2. We validated the scoring system in a group of 18 children who underwent both a HRM/Z and MII-pH (8 diagnosed with rumination - 3M:5F, median age: 13 years - and 10 with a negative HRM/Z - 4M:6F, median age:8.5 years). The sensitivity and specificity of the score is 75% and 80% respectively.

Conclusion: Children with rumination have many more symptomatic reflux episodes (SI/SAP positive) with high proximal extent, particularly during postprandial periods compared to GERD and controls. Our scoring system allows for early identification of children with rumination syndrome.

Disclosure: Nothing to disclose

P1383 ADULT ABDOMINAL PAIN CAN BE PREDICTED FROM EARLY CHILDHOOD SYMPTOMS AND PSYCHOSOCIAL FACTORS

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Introduction: Early childhood factors have been implicated in the development of chronic functional gastrointestinal (GI) symptoms in adulthood, including the irritable bowel syndrome. A number of specific factors have been suggested, including early GI symptoms[1], early life events[2] exposure to immune-activating events[3] and the child's psychosocial environment[4]. However most of these studies are based on recall of childhood events after the individual has reached adulthood and hence may be subject to recall bias. In a prospective birth cohort our group recently demonstrated that mode of delivery and early psychosocial factors influenced the development of abdominal pain to 12 years of age[5] but were unable to confirm other factors such as early immune-activation by exposure to environmental factors such as pets in the household.

Aims & Methods: We now report on additional data collected on the birth cohort at average age 20 years, aiming to identify early childhood factors that are associated with the prevalence of abdominal pain. 5478 individuals (response rate 32%) were able to be contacted and agreed to participate in a follow-up. Factors recorded during early childhood and previously identified as associated with adult FGIDs were evaluated using logistic regression.

Results: 55% of the sample was female. Overall the prevalence of GI pain was 20% (95% confidence interval 19-21%). Increased abdominal pain in adulthood could be predicted from GI pain reported by parents as early as two years of age although the predictive ability improved when measured later in childhood (Table 1). In addition, poor appetite reported by parents at age five was also associated with increased prevalence of GI pain in adulthood (Table 1). The occurrence of serious life events in the child's year of birth and parental concerns for the child as early as two years of

age were all associated with increased prevalence of GI pain in adulthood, in addition to female gender (Table 1). In contrast, neither number of pets in the household at age 1 (OR=1.04, p=0.4) nor age 5 (OR=0.98, p=0.7) were associated with adult abdominal pain. We also considered early (< 5 years) allergy to milk, eczema and asthma, social support, marital status of parents, mental health conditions, temperament, antibiotic use, mode of delivery at birth and duration of breast feeding but none of these were associated with adult abdominal pain.

Factor	GI pain +	GI pain −	Odds ratio	95% CI	p-value
Female gender (%)	71	51	2.42	2.10, 2.80	<.001
GI pain at 2 years (%)	8	5	1.74	1.24, 1.44	.001
GI pain at 5 years (%)	12	9	1.42	1.05, 1.93	.02
GI pain at 8 years (%)	17	9	2.15	1.53, 3.02	<.001
GI pain at 12 years (%)	21	10	2.36	1.74, 3.20	<.001
Life events (%)	6	4	1.49	1.04, 2.15	.03
Parent worries at 2 years (mean/SD)	2.57 (1.21)	2.45 (1.14)	1.10	1.02, 1.18	.02
Parent worries at 8 years (mean/SD)	2.39 (1.00)	2.22 (0.98)	1.18	1.05, 1.32	.006

[Table 1. Early childhood factors univariately associated with adult abdominal pain prevalence]

Female gender (OR=2.39, 95% confidence interval 2.07, 2.76, p< .001) and GI pain at eight years (OR=1.35, 95% confidence interval 1.09, 1.67, p=.006) were statistically independent predictors of adult GI pain.

Conclusion: GI pain experienced in adulthood appears to result from a process that starts early in a child's development and is influenced by its psychosocial environment. Greater attention to signs evident as early as infancy may have long-lasting benefits to patients. In contrast to previous findings, the child's physical environment appears to be less relevant, in including the presence of immune-stimulating factors.

References: 1. Lowman BC, Drossman DA, Cramer EM, McKee DC. Recollection of childhood events in adults with irritable bowel syndrome. Journal of clinical gastroenterology. 1987;9(3):324-330. 2. Bradford K, Shih W, Videlock EJ, et al. Association between early adverse life events and irritable bowel syndrome. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association. 2012;10(4):385-390 e381-383. 3. Koloski NA, Jones M, Weltman M, et al. Identification of early environmental risk factors for irritable bowel syndrome and dyspepsia. Neurogastroenterology & Motility. 2015;27(9):1317-1325. 4. Tanaka Y, Kanazawa M, Fukudo S, Drossman DA. Biopsychosocial model of irritable bowel syndrome. J Neurogastroenterol Motil. 2011;17(2):131-139. doi:10.5056/jnm.2011.17.2.131 5. Jones MP, Faresjö Å, Beath A, Faresjö T, Ludvigsson J. Abdominal Pain in Children Develops With Age and Increases With Psychosocial Factors. Clin Gastroenterol Hepatol in press https://doi.org/10.1016/j.cgh.2019.04.036
Disclosure: Nothing to disclose

P1384 CLINICAL AND PROGNOSTIC VALUE OF THE FECAL ZONULIN IN EXTREMELY PREMATURE BABIES

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Introduction: The state of integrity of the intestinal barrier is significant in the development of conditions associated with digestive disorders of varying severity, especially in premature babies. Increased zonulin in the tissues of the intestine leads to the expansion of intercellular contacts and an increase in intestinal permeability. [1-6]

Aims & Methods: The aim of the study is to evaluate the clinical and prognostic significance of fecal zonulin in extremely premature babies up to 32 weeks.

Material and methods: We examined 108 premature babies with gestational age at birth from 22 to 32 weeks and 27 full-term newborns who constituted the control group. Studies of fecal zonulin were carried out in

dynamics on the 3rd, 7th and 14th days of life. The content of zonulin in feces was determined using Immunodiagnostik (Germany) reagents (ELISA) by enzyme-linked immunosorbent assay.

Results: We found an increase in the level of fecal zonulin (FZ) in 17 times on the third day of life, 8 times on the 7th day of life and almost 5 times on the 14th day of life compared to the control group, whose values were -28.5 ± 3 on the 3rd day, 6 ng / ml, on day 7 - 61.1 ± 5.1 ng / ml and 14 days of life - 89.8 ± 5.8 ng / ml. To identify parallels between the values of the FZ and other clinical and laboratory parameters, we divided all children into clusters with certain limits of fluctuations of the values of the FZ. Cluster A consisted of patients with fecal zonulin values up to 500 ng / ml (n = 52), cluster B - children with values from 500 to 1000 ng / ml (n = 40) and cluster C - 16 children with fecal zonulin values (more than 1000 ng / ml). In cluster B, on the 7th day of life, along with higher rates of fecal zonulin, the marker of the inflammatory process − C-reactive protein (respectively, cluster A-9.6 ± 1.0 and B-18.0 ± 2.7 , t-2.94, p < 0.001). The hemoglobin values determined on the first day of life in newborns in cluster B had significantly lower values than in cluster A. (175.1 ± 2.7 g / l and 152.5 ± 4.2 g / l, t-2.31, p < 0.001).

On day 14 of life in cluster A, the mother's prothrombin index was significantly lower than in cluster B (cluster A-82.0 ± 1.4%, cluster B-96.0 ± 1.9%; t-5.89, p < 0,001).

To study the relationship between the values of fecal zonulin and the prognosis of necrotizing enterocolitis, we divided all patients into 2 groups. The first group consisted of 10 children who developed necrotizing enterocolitis by 10.2 ± 4.5 days of life and 81 children entered the 2nd group without necrotizing enterocolitis.

In the group of children with NEC on the 7th day of life, we observed an almost twofold, significantly significant increase in zonulin values compared with the compared group without NEC (343.5 ± 76.7 and 618.4 ± 89.9 with p < 0.05).

Conclusion: The dynamics of fecal zonulin in premature babies revealed a multiple increase in its values within 14 days of life compared with healthy full-term babies. The level of faecal zonulin on day 7 of life is a predictor of the development of NEC in very premature babies.

References: 1. Fasano A, Not T, Wang W, Uzzau S, Berti I, Tommasini A, Goldblum SE.Zonulin, a newly discovered modulator of intestinal permeability, and its expression in coeliac disease. Lancet 2000 Apr 29;355(9214):1518-9. DOI: 10.1016/S0140-6736(00)02169-3 2. Drago S1, El Asmar R, Di Pierro M, Grazia Clemente M, Tripathi A, Sapone A, Thakar M, Iacono G, Carroccio A, D'Agate C, Not T, Zampini L, Catassi C, Fasano AGliadin, zonulin and gut permeability: Effects on celiac and non-celiac intestinal mucosa and intestinal cell lines Scand J Gastroenterol. 2006 Apr;41(4):408-19. DOI: 10.1080/00365520500235334 3. El Asmar R1, Panigrahi P, Bamford P, Berti I, Not T, Coppa GV, Catassi C, Fasano A, Host-dependent zonulin secretion causes the impairment of the small intestine barrier function after bacterial exposure. Gastroenterology. 2002Nov;123(5):1607-15. doi: 10.1053/gast.2002.36578 4. Anna Tarko,1 Anna Suchojad,1 Marta Michalec,1 Małgorzata Majcherczyk,1 Aniceta Brzozowska,2 and Iwona Maruniak-Chudek1 Zonulin: A Potential Marker of Intestine Injury in Newborns Disease Markers Volume 2017, Article ID 2413437, 6 pages https://doi.org/10.1155/2017/2413437
Disclosure: Nothing to disclose

P1385 THE USEFULNESS OF PROBIOTIC ADMINISTRATION IN OBESE CHILDREN WITH NONALCOHOLIC FATTY LIVER DISEASE

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Introduction: The increasing rate of pediatric obesity imposed nonalcoholic fatty liver disease (NAFLD) as the most frequent cause of chronic liver conditions in children. It includes simple liver steatosis and may progress to non-alcoholic steato-hepatitis and cirrhosis. Recent studies suggested that intestinal dysbiosis and gut-derived endotoxins may be important in this progression, therefore probiotics may have a positive role in improving liver parameters.

Aims & Methods: The aim of this paper was to evaluate the usefulness of probiotics administration to obese children with NAFLD to optimize metabolic parameters and to reduce intestinal dysbiosis. Methods: 102 obese children aged 10-18 years were enrolled in this double-blind,

placebo-controlled study. NAFLD was assessed in all children using abdominal imaging and laboratory findings. All children underwent clinical and anthropometric evaluation, liver and renal function tests, glycemia, insulinemia and lipid metabolism assessment. Glucose hydrogen breath test was performed for small intestinal bacterial overgrowth (SIBO) assessment at baseline and after 12 weeks of probiotic intervention. NAFLD subjects were equally randomized to receive either probiotic Lactobacillus reuteri (10^8 CFU/day) or placebo for 12 weeks add on hypo-caloric diet and increased physical activity.

Results: 36/102 (35%) of obese children presented NAFLD. Children who received probiotic supplementation had a significant higher reduction of body mass index after 12 weeks compared to placebo group (P< 0.01). There was a significantly higher reduction of intestinal dysbiosis, aminotransferases level and serum triglycerides levels after the intervention period in the probiotic group compared to placebo (P< 0.05).

Conclusion: In this study, decreasing in body mass index was higher in the group receiving probiotics compared to placebo. Lactobacillus reuteri added to proper diet had a beneficial effect on lipid profile and transaminases level and significantly decreased the intestinal dysbiosis in obese children with NAFLD.

Disclosure: Nothing to disclose

P1386 IMPORTANCE OF METABOLIC COMPLICATIONS IN SEVERE OBESITY COMPARED TO OBESITY IN THE REGION WHERE THE OBESITY EPIDEMIC SHOWED MODERATE INCREASE

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Introduction: The prevalence of obesity is increasing worldwide among children and adolescents. Although obesity in children has a relatively low risk of metabolic complications, those with more severe types of obesity may be at higher risk in adults. In many countries with moderate increase of the obesity epidemic, the association between severe obesity and metabolic complications has been rarely reported in pediatric populations.

Aims & Methods: The purpose of this study is to assess the prevalence of severe and extremely severe obesity and each metabolic complication using a nationally representative data in Korea and to identify proper monitoring tools for assessing the current obesity epidemic.
A total of 790,653 student (380,580 female) aged 5-19 years were recruited from the Korean student health examination, 2011-2018. Obesity was defined by age- and sex-specific BMI reference according to the WHO Growth reference data (2007). Obesity was defined by using the skinner's new classification: Class I obesity (BMI ≥ 100% of 95th percentile), Class II (severe obesity, BMI ≥ 120% of 95th percentile), and Class III (extremely severe obesity, BMI ≥ 140% of 95th percentile). Metabolic complications included hypertension, hyperglycemia, hypercholesterolemia, and elevated aminotransferase. All analyses were performed using SAS software (Version 9.4).

Results: Comparing 2011 and 2018, the overall prevalence of Class II (severe) obesity have increased by 63% (from 3.0% to 4.9%) (p< 0.0001) and Class III (extremely severe) obesity increased by 100% (from 0.4% to 0.8%) (p< 0.0001), whereas Class I (conventional) obesity increased by 28.7% (from 15.7% to 20.2%) (p< 0.0001). In logistic regression analysis, the adjusted odds ratios (ORs) for Class III obesity were calculated according to each metabolic complications; hypertension was 10.3 times higher than non-obese group (p< 0.001), hyperglycemia was 2.6 times higher (p< 0.001), hypercholesterolemia was 2.1 times higher (p < 0.001), and elevated aminotransferase was 12.7 times higher (p < 0.001). The mean numbers of metabolic complications in each obesity group was 1.14 in Class III obesity, 0.76 in Class II, 0.5 in Class I, and 0.29 in non-obese group. (Table 1)

Obesity group	The number of metabolic complications (%)					mean (95% CI)	mean difference1 (95% CI)	p-value
	0	1	2	3	4			
Non-obese	75.7	20.3	3.7	0.3	0.1	0.29 (0.27, 0.31)		
Class I Obesity	60.1	30.8	8	1	0.02	0.5 (0.49, 0.51)	0.21 (0.19, 0.24)	<.0001
Class II Obesity	43.7	39.5	14.3	2.3	0.16	0.76 (0.73, 0.78)	0.47 (0.44, 0.5)	<.0001
Class III Obesity	22.8	47.9	22.8	5.6	0.9	1.14 (1.08, 1.2)	0.85 (0.79, 0.92)	<.0001

[Table 1. The mean numbers of metabolic complications in each obesity group, 2011-2018]

Conclusion: We found that the prevalence of Class II and III obesity (severe and extremely severe) is highly increasing and the risk of metabolic complication is sharply increasing according to severity of obesity in childhood. Close monitoring of metabolic complications is important to track severe obesity. Further longitudinal studies are needed to verify childhood obesity at the highest metabolic risk.

Disclosure: Nothing to disclose

Liver and Biliary III

09:00-14:00 / Poster Exhibition - Hall 7

P1387 IS ADIPONUTRIN STILL A FACTOR IN HCV? PNPLA3, STEATOSIS AND FIBROSIS PROGRESSION IN CHRONIC HEPATITIS C

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Introduction: There is an established correlation between the PNPLA3 rs738409 C>G single nucleotide polymorphism (SNP) and hepatic steatosis and fibrosis in HCV infected patients. However not all data is convergent regarding the exact impact of this SNP on the pattern of disease progression in different clinical settings.

In this study, **we aimed** to further bridge the knowledge gap on this topic by investigating the role of the G allele in promoting steatosis, fibrosis and disease progression in relation to other metabolic and anthropometric host factors.

Aims & Methods: Two hundred and fifty consecutive patients, previously diagnosed with chronic hepatitis C (CHC) underwent liver biopsy. Histology was assessed using the Metavir scoring system. Transient elastography was used for follow-up. Ninety-eight patients were genotyped for PNPLA3 rs738409 and followed up for fibrosis progression.

Results: PNPLA3 rs738409[G] allele was significantly correlated with severe steatosis ($p = 0.04$), severe fibrosis at the time of enrollment ($p = 0.0005$) and fibrosis progression with an OR of 10.31 (95% CI 1.06-99.59, $p=0.04$), after a mean follow-up time of 62.85 (95%CI: 52.21-76.15) months. Severe steatosis at the time of enrollment had an OR of 11.02 (95% CI 1.48-82.09, $p=0.01$) for the association with fibrosis progression. The HOMA-IR index was also positively correlated with severe fibrosis ($p=0.03$) and fibrosis progression on univariate analysis ($p=0.02$).

Conclusion: PNPLA3 rs738409[G] allele is a reliable predictor for steatosis and fibrosis in CHC. The presence of G allele, along with severe steatosis and insulin resistance are significant predictors for fibrosis progression.

Disclosure: Nothing to disclose

P1388 NON-INVASIVE MARKERS OF LIVER FIBROSIS AND TRANSIENT ELASTOGRAPHY IN PATIENTS WITH NON-ALCOHOLIC STEATOHEPATITIS: WHICH FORMULA SHOULD WE USE TO MONITOR FIBROSIS?

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Introduction: Transient hepatic elastography is widely used in staging and monitoring of fibrosis in patients with non-alcoholic steatohepatitis (NASH). According to the European Association for the Study of Liver (EASL) recommendations, the evaluation of transient elastography should be complemented with non-invasive markers to improve its accuracy.

Aims & Methods: We aimed to evaluate the correlation between the variation of the transient elastography (TE) and noninvasive fibrosis markers in a historical cohort of biopsy-proven NASH patients.

For this, we performed an observational and retrospective study in a random sample of NASH patients in whom diagnosis was established by liver histology. For each case, TE and NAFLD activity score, fibrosis-4 index for liver fibrosis (FIB-4), AST to platelet ratio (APRI) and AST/ALT ratio data were documented at the time of the diagnosis and at the date of the last clinical contact. The difference between the final and initial values was calculated for each variable (Δ, "delta"). The statistical relationship between the ΔTE and variation in noninvasive fibrosis markers was established in a linear regression model.

Results: We evaluated 62 cases (mean age at diagnosis 49.9 ± 12.9 years, 56.5% of the male gender) with an average follow-up time of 3.54 ± 1.54 years. Liver disease was diagnosed in the cirrhotic stage in 16.1%.

During follow-up, we observed the presence of an acute cardiovascular event in 5 patients; one case developed hepatocellular carcinoma. The therapeutic goals of weight reduction and regular physical activity were reached in 30.6% and 27.4% of the patients, respectively.

The mean ΔTransient Elastography value was -0.38 ± 7.6 kPa. Bivariate correlation test showed a statistically significant correlation between the ΔTransient Elastography and ΔNAFLD activity score (k = 0.48, p < 0.01), ΔFIB-4 (k = 0.65, p < 0.01) and ΔAST/ALT ratio (k=0,37, p=0.2). After adjustment of the Δ values for the follow up time in a linear regression multivariate model, this significant relationship was maintained (NAFLD activity score: β3.01, p < 0.01; FIB-4: β3.36, p < 0.01; AST/ALT ratio: β=8.38, p = 0.2).

Conclusion: In this sample of NASH patients, the variation of the NAFLD activity score, FIB-4 and AST/ALT ratios was correlated with the variation of EHT values. Among the formulas, the variation in FIB-4 values presented a better correlation with the transient elastography values.

Disclosure: Nothing to disclose

P1389 HEMATOLOGICAL SCALES - POTENTIAL NONINVASIVE TOOLS IN THE ASSESSMENT OF LIVER FIBROSIS IN ALCOHOLIC LIVER CIRRHOSIS AND NON-ALCOHOLIC FATTY LIVER DISEASE PATIENTS - A SINGLE-CENTER EXPERIENCE

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Introduction: Advanced liver fibrosis was proved to correlate positively with mean platelet (PLT) volume (MPV) to PLT ratio (MPR) and neutrophil to LYM ratio (NLR) and negatively with PLT to LYM ratio (PLR). However, the number of available analyses in this field of hepatology is still limited.

Aims & Methods: The aim of our investigation was to evaluate the diagnostic accuracy of MPR, NLR and PLR in the assessment of liver fibrosis in alcoholic liver cirrhosis (ALC) and non-alcoholic fatty liver disease (NAFLD) patients and to compare it with serological: indirect and direct markers of liver fibrosis. Another goal was to assess relationships between abovementioned hematological indices and clinical progression of ALC. Three hundred and two participants were recruited to the study: 142 patients with ALC, 92 with NAFLD and 68 healthy volunteers in control group. Hematological indices (MPR, NLR and RLR) were measured in each person. Indirect markers of liver fibrosis were also obtained: AAR [aspartate aminotransferase (AST) to alanine aminotransferase (ALT) ratio], APRI (AST to PLT Ratio Index), FIB-4 (Fibrosis-4) and GPR (γ-glutamyl-transferase to PLT ratio). Among direct indices of liver fibrosis, procollagen I carboxyterminal propeptide (PICP), procollagen III aminoterminal propeptide (PIIINP), platelet-derived growth factor AB (PDGF-AB), transforming growth factor-α (TGF-α) and laminin were assessed. The assessment of clinical progression of liver failure in ALC patients was done with MELD score. NAFLD fibrosis score and BARD score were calculated in NAFLD patients. Achieved results were compared to controls and between ALC and NAFLD groups. Then a correlation between evaluated indices was done. Diagnostic value of each assessed haematological parameter together with proposed cut-off in research group were measured with AUC (area under the curve).

Results: MPR and NLR values in ALC patients were significantly higher in comparison to controls (p<0.0001); PLR level was significantly lower (p<0.0001). MPR and PLR correlated positively with indirect markers of liver cirrhosis (APRI, FIB-4; p<0.001). Positive (but weaker) relationships were found between NLR and both: AAR and GPR (p<0.05). MPR correlated negatively with PDGF-AB (p<0.0001); positive relationship was observed between PLR and PDGF-AB (p<0.01).

Additionally, NLR correlated negatively with PIIINP (p<0.05). MELD score correlated positively with NLR (p< 0.0001) and negatively - with PLR (p<0.001). NLR level in NAFLD patients was significantly higher in comparison to controls (p<0.0001). MPR and PLR valued did not differ significantly. MPR correlated positively with indirect markers of liver fibrosis - APRI (p<0.0001), FIB-4 (p<0.0001) and GPR (p<0.01).

A strong positive relationship between MPR and NAFLD fibrosis scale was noted, too (p<0.0001). MPR and NLR values were significantly higher in ALC patients compared to NAFLD group (p<0.0001); PLR level was significantly lower (p<0.0001). AUC values and proposed cut-offs for MPR, NLR and PLR in ALC patients were: 0,929 (>0.048), 0.821 (>2.227) and 0.675 (<70.445), respectively. AUC values and proposed cut-offs for MPR, NLR and PLR in NAFLD patients were: 0.547 (>0.038), 0.725 (>2.034 %) and 0.528 (>97.101 %), respectively.

Conclusion: PLR and NLR turned out to be the most powerful markers of liver fibrosis in ALC patients. Moreover, they also correlated with clinical progression of the disease. Diagnostic accuracy of MPR, NLR and PLR was found to be weaker in examined NAFLD patients.

References: 1. Kalra A, Wedd JP, Bambha KM i wsp. Neutrophil-to-lymphocyte ratio correlates with proinflammatory neutrophils and predicts death in low model for end-stage liver disease patients with cirrhosis. Liver Transpl. 2017; 23: 155-65 2. Lai Q, Melandro F, Larghi Laureiro Z i wsp. Platelet-to-lymphocyte ratio in the setting of liver transplantation for hepatocellular cancer: a systematic review and meta-analysis. World J Gastroenterol. 2018; 24: 1658-65 3. Iida H, Kaibori M, Matsui K i wsp. Ratio of mean platelet volume to platelet count is a potential surrogate marker predicting liver cirrhosis. World J Hepatol. 2018; 10: 82-7

Disclosure: Nothing to disclose

P1390 LIVER MICRORNA-34A IS ACTIVATED IN MULTIPLE ANIMAL MODELS OF NAFLD AND CORRELATES WITH KEY DISEASE HALLMARKS IN HUMAN PATIENTS

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Introduction: Non-alcoholic fatty liver disease (NAFLD) comprises a spectrum of stages from simple steatosis to non-alcoholic steatohepatitis (NASH). Recent evidence supports a functional role for microRNAs (miRNA/miRs) in regulating NAFLD progression. In particular, pro-apoptotic miR-34a expression has been reported to sequentially increase during disease progression in both experimental and human NAFLD.

Aims & Methods: We now aimed to elucidate whether modulation of miR-34a in NAFLD constitutes a key, primary event and which disease hallmarks correlate with its expression, hinting at its multiple roles in disease pathogenesis.

C57BL6 mice were fed five different NAFLD-inducing diets, namely a methionine and choline-deficient diet for 2 and 8 weeks; a high-fat choline-deficient diet for 14 weeks; a high fat, 2% cholesterol diet with high fructose for 25 weeks; a high-fat/calorie diet with high fructose/glucose in drinking water for 16 weeks; and a choline-deficient amino acid-defined diet for 32 weeks. Liver biopsies were obtained from a cohort of 166 NAFLD patients, histologically and metabolically characterized (NAS 0 to 4: n=89; NAS > 4: n=77). Human liver total RNA was used for analysis of miR-34a by Taqman Advanced Real-Time RT-PCR.

Results: Mice fed with any of the five diets developed different degrees of NASH, paralleling liver triglyceride deposition, steatosis, inflammation and weigh gain. Mild-to-severe fibrosis was observed in all animals, except for mice fed the high fat, 2% cholesterol diet, where fibrosis was ab-

sent. Nonetheless, miR-34a expression levels were significantly increased in the livers of all these mice (at least *p*< 0.05), comparing with control diets-fed animals.

NAFLD patients exhibited different degrees of steatosis and NASH, with or without the presence of fibrosis and concomitant diseases, including diabetes, arterial hypertension and cholelithiasis. Liver miR-34a expression was found to progressively and significantly increase with the raise of steatosis, lobular inflammation and NAS score (at least *p*< 0.05). Furthermore, miR-34a expression levels were also significantly higher in patients with bridging fibrosis and cirrhosis (at least *p*< 0.05), as well as in those with concomitant diabetes, arterial hypertension and cholelithiasis (at least *p*< 0.05). Finally, liver miR-34a expression levels positively correlated with histological analysis (steatosis, lobular inflammation, fibrosis and NAS score), serum hepatic enzymes (AST and ALT), hepatic triglyceride content and age (at least *p*< 0.05).

Conclusion: In conclusion, liver miR-34a appears to be a key player in NAFLD pathogenesis and progression, correlating with several well-characterized disease hallmarks. A better understating of the overlapping roles of miR-34a in NAFLD development may help in establishing novel and appealing therapeutic targeting options (Gilead Sciences International - Research Scholars Program in Liver Diseases; PTDC/MED-PAT/31882/2017 and SFRH/BD/104160/2014, FCT, Portugal).

Disclosure: Nothing to disclose

P1391 ESTABLISHMENT OF A NOVEL DIETARY-INDUCED MOUSE MODEL SHOWING STEATOHEPATITIS WITH SEVERE FIBROSIS

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Introduction: Experimental induction of liver fibrosis is still difficult in rodents. Carbon tetrachloride-induced fibrosis is secondary to hepatocellular necrosis that is similar to human viral hepatitis, while nonalcoholic steatohepatitis (NASH) is characterized by perivenular-pericellular fibrosis with elongation of delicate fiber rather than remarkable necrosis.

Aims & Methods: We previously made a model of NASH-related cirrhosis mimicking human fibrotic pattern of NASH using a rat fed with a high-fat and cholesterol (HFC) diet; thus, the aim of this study was to establish a mouse model of liver fibrosis. Six-week-old male Tsumura-Suzuki obese diabetes (TSOD) mice, a model of spontaneous metabolic syndrome and NASH, and Tsumura-Suzuki non obese (TSNO) mice that are control of TSOD mice were fed with a HFC diet and normal diet for 12 months. Blood and liver were collected at 20, 32, 44 and 56 weeks of age.

Results: TSOD mice fed the HFC diet showed obesity, diabetes and steatohepatitis with slight fibrosis. On the other hand, TSNO mice of normal control did not show obesity and diabetes but exhibited severe fibrosis in addition to steatohepatitis. The pattern of fibrosis in TSNO mice resembled human NASH, namely, delicate perivenular and perisinusoidal fibrosis. We initially hypothesized that hepatic fibrotic change of TSOD mice could be enhanced by intake of the HFC diet due to their background of spontaneous metabolic syndrome, however, TSNO mice showed much more severe fibrosis. It is speculated that fibrosis-prone traits may be enriched in the process of selective breeding of non-obese and non-diabetic mice. The fibrotic lesions in TSNO mice lasted until 56 weeks of age, but there was only one case of onset of liver tumor. It is known that carcinogenesis attenuates background liver pathology including fibrosis and tumor onset provides endpoint in experiments assessing fibrosis. Receptor interacting protein 3 which promotes cell death by necroptosis was positive in the liver of TSNO mice fed with the HFC diet, suggesting that necroptosis pathway might upregulate and resulting in low occurrence of liver tumor in this model. Because our model persists in fibrosis over a long period without carcinogenesis, it can be considered to be a useful model not only for preventive but also for therapeutic experiments.

Conclusion: The HFC diet-loaded TSNO mice developed NASH with marked fibrosis with quite similar pattern of human fibrotic NASH. Our model induced by not genetically modification but simple diet that imitated human dietary habits has many advantages that can simply analyse the mechanism of development of liver fibrosis.

Disclosure: Nothing to disclose

P1392 IDENTIFICATION OF NOVEL MIRNAS ASSOCIATED WITH EXPERIMENTAL NAFLD PATHOGENESIS

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Introduction: microRNAs (miRNAs) are modulated in non-alcoholic fatty liver disease (NAFLD) and are being studied as putative diagnostic and prognostic biomarkers. Further, as post-transcriptional modulators of gene expression, miRNAs appear to contribute to NAFLD pathogenesis by regulating distinct cellular pathways, impacting on lipid and glucose metabolism, energy homeostasis, cell death, cell proliferation and differentiation, among others.

Aims & Methods: Here, we aimed to identify and validate novel metabolism-associated miRNAs modulated during experimental NAFLD. C57BL/6N male mice were fed distinct NAFLD-inducing diets, namely a methionine and choline deficient diet (MCD; n=30) for 2 and 8 weeks; a high fat, 2% cholesterol diet with high fructose - fast-food diet (FF; n=12) - for 25 weeks; and a choline-deficient amino acid-defined diet (CDAA; n=28) for 32 and 66 weeks. Liver samples were collected and processed for histological and miRNA analyses. Liver RNA from 8 week MCD-fed mice was analysed using TaqMan™ array microRNA cards, containing sequences for ~740 of the most relevant human or rodent miRNAs. qPCR array data was analysed using the HTqPCR package in Bioconductor. We found significant differences in the expression of 52 miRNAs, with 25 miRNAs increasing and 27 miRNAs decreasing in the liver of MCD diet-fed mice, comparing with chow-fed animals. Differentially expressed miRNAs were subjected to an *in silico* analysis to exclude previously reported associations with NAFLD or related metabolic liver diseases. Based on this, a panel of different upregulated (miRNA-127, miRNA-136, miRNA-411) and downregulated (miRNA-107, miRNA-455) miRNAs was selected for downstream validation analyses.

Results: miR-136 was found to be up-regulated in MCD-fed animals alone. In turn, both miRNA-127 and miR-411 were found consistently upregulated in both MCD and CDAA diets, but unaffected in the FF diet, suggesting a possible association with liver damage rather than overall metabolism. Interestingly, miRNA-107 and, in particular, miRNA-455, were consistently downregulated in all diets, comparing with control diet-fed animals, suggesting that they may constitute major regulators of disease pathogenesis.

Conclusion: In conclusion, we have identified novel miRNAs modulated during experimental NAFLD, associating with distinct pathogenic signalling pathways. A better characterization of the role of these miRNAs in disease could translate into prospective therapeutic strategies as well as putative biomarkers in NAFLD.

Disclosure: Nothing to disclose

P1393 IL-2, IL-15 AND STEM CELL FACTOR ENHANCE CYTOTOXICITY OF CD3⁻CD56⁺CD16⁺ NK CELLS AGAINST HUMAN HEPATOCELLULAR CARCINOMA CELL LINES

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Introduction: Liver cancer is a kind of malignant tumor, which seriously affects people's health.

Aims & Methods: To investigate the effects of IL-2, IL-15 and stem cell factor (SCF) on the efficiency of expansion, expression of NKG2D and the cytotoxicity of CD3⁻CD56⁺CD16⁺ NK cells against human hepatocellular carcinoma cell lines. The CD3⁻CD56⁺CD16⁺ NK cells purified by the sorting method of MACS (magnetic microbeads activated cells sorting) were expanded in the presence of IL-2 or IL-15 or IL-2/IL-15/SCF with or without anti-NKG2D monoclonal antibody. The efficiency of expansion, the expression of NKG2D and the cytotoxcity of CD3⁻CD56⁺CD16⁺ NK cells against HepG2, SMMC-7721 were determined using trypan blue staining, flow cytometry and CCK-8 assay, respectively.

Results: The efficiency of expansion, the expression of NKG2D and the cytotoxcity of CD3⁻CD56⁺CD16⁺ NK cells treated with IL-2/IL-15/SCF were significantly increased than those in other groups. Most interestingly, the cytotoxic effects of CD3⁻CD56⁺CD16⁺ NK cells on HepG2 cells were significantly reduced by the pretreatment with anti-NKG2D monoclonal antibody. However, the treatment with the same antibody had little influence on the cytotoxicity of CD3⁻CD56⁺CD16⁺ NK cells against SMMC-7721 cells.

Conclusion: IL-2/IL-15/SCF enhances the efficiency of expansion, the expression of NKG2D and the cytotoxicity of CD3⁻CD56⁺CD16⁺ NK cells against human hepatocellular carcinoma cell lines.. NKG2D plays an important role in mediating the cytotoxicity of NK cells on specific types of tumor cells.

Disclosure: Nothing to disclose

P1394 GYNECOLOGICAL HISTORY AND PREGNANCY OUTCOMES IN WILSON'S DISEASE PATIENTS UNDER THERAPY – A BICENTRIC CONTROLLED STUDY

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Introduction: Untreated Wilson Disease (WD) is associated with menses irregularities and obstetric complications. Research in this area is scarce and most studies narrowly focus on pregnancy outcomes comparisons between WD patients with and without treatment.

Aims & Methods: Aims: Identify menses irregularities in WD; evaluate the impact of under treatment WD in pregnancy, compared with two control groups (with and without liver disease).

Data collection was carried in two hospital centers in order to identify the maximum number of women diagnosed with WD. For the control groups, women with Hepatitis C (controls with liver disease) and women with other gastrointestinal conditions (controls without liver disease), were consecutively identified from the hepatology and gastroenterology clinics. Sociodemographic characterization and gynecological history were collected. Statistics: chi-square test, multinominal logistic regression.

Results: We identified 18 women ongoing treatment for WD (11 pregnancies) and 20 women for each control group. Stage of liver disease between controls and the study group was adjusted (p = 0.65).

The incidence of menses irregularities was higher in the WD group (late menarche, 15 vs. 2 vs. 2 [p < 0.01]), irregular cycles, 18 vs. 4 vs. 4 [p < 0.01], amenorrhea, 12 vs. 2 vs. 1 [p < 0.01]).

The logistic regression model identified the WD group as a predictor of miscarriage and low birth weight (odds ratio: 9.0 [1.4-57.1], p = 0.02). Concerning "fetal malformations", the WD group had the highest rate of events (3/11) but the difference was not significant (p = 0.51). The type of therapy (D-Pencillamine or zinc acetate), and the clinical presentation of the disease (hepatic or/and neurological) was not associated with the identified obstetric complications in WD.

Conclusion: There was a higher incidence of menses irregularities in the WD group. Also, this work adds to the literature as it suggests that WD under therapy still maintains a higher risk of spontaneous abortion and low birth weight, compared to control groups with and without liver disease. Despite the theoretical teratogenic potential of the drugs, the risk of fetal malformations under chelation therapy (D-Pencillamine 300mg) or zinc acetate (150mg) was not significant, which reinforces the need to maintain therapy throughout pregnancy.

Disclosure: Nothing to disclose

P1395 WHY GASTROENTEROLOGISTS MUST LOOK FOR TYPE 2 DIABETIC PATIENTS?

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Introduction: Non-alcoholic fatty liver disease and type 2 diabetes commonly coexists. The risk of developing NAFLD in these patients is high due to high prevalence of obesity.
Aims & Methods: The **aim** of the study was to assess the severity of liver fibrosis and steatosis in a cohort of pure type 2 diabetic patients, using non-invasive methods: Transient Elastography (TE) and Controlled Attenuation Parameter (CAP).
The study included 704 type 2 diabetic patients, who were prospectively randomized evaluated in the same session by means of TE and CAP (FibroScan EchoSens) to assess both liver fibrosis and steatosis. Reliable liver stiffness measurements (LSM) were defined as the median value of 10 LSM with an IQR/median < 30%. A cut-off value of 10.1 kPa[1] was used to define severe fibrosis (F≥3). For differentiation between stages of steatosis we used the following cut-off values proposed by the manufacturer: S1 (mild) 230-275, S2(moderate) 275-300 db/m, S3(severe) > 300 db/m.
Results: Out of 704 diabetics screened we excluded those with associated viral hepatitis, those with an AUDIT-C score ≥8 and those with unreliable LSM. 14 patients had associated viral B or C hepatitis (1.9%) ,17 patients an AUDIT-C score ≥8 (2.4%) and 15 patients (2.1%) had other hepatopathies (autoimmune, toxic, cholestatic). After excluding those with unreliable LSM, the final analysis included 546 diabetic patients without other hepatopathies (53.8% women, mean age 60 ±9.5; BMI=31.6± 6.1 kg/m²). 59.9% of them had BMI ≥ 30kg/m². Mild, moderate and severe steatosis by means of CAP was found in 17 %, 14.5 % and 58.8% cases respectively. The median CAP value of patients with mild, moderate and severe steatosis was 260 db/m, 287 db/m and 356 db/m. Severe fibrosis was detected by means of TE in 19% (104/546) of subjects and the median value was 12.5 kPa.
Conclusion: In our group, approximately 77.6% were diabetic patients with reliable LSM. Presence of steatosis was found in 90.3% of patients by means of CAP and 19% of them had severe fibrosis suggesting the need for further assessment.
References: 1. Petta S et al. Improved Noninvasive prediction of Liver Stiffness Measurement in Patients with Nonalcoholic Fatty Liver Disease Accounting for Controlled Attenuation Parameter Values. Hepatology 2016. Doi:10.1002/hep.28843
Disclosure: Ioan Sporea: Speakers fees: AbbVie, BMS, Gilead, Janssen, Philips, General Electric; Advisory boards: AbbVie, Merck; Siemens, Canon Toshiba. Research support: Philips, General Electric Roxana Sirli and Alina Popescu had the following conflict of interests: Philips, General Electric, Abbvie, AstraZeneca, Zentiva, Neola, Dr. Reddy, BMS, MSD, Mylan.

P1396 RELATIONSHIP BETWEEN COFFEE CONSUMPTION AND NONALCOHOLIC FATTY LIVER DISEASE

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Introduction: There is emerging evidence for the positive effects of coffee consumption in patients with liver disease. Our aim was to determine the effects of coffee intake on a liver enzymes, inflammation parameters, non-invasive elastographic markers of liver steatosis and fibrosis, as well as to degree of NAFLD detect by liver biopsy.
Aims & Methods: In this cross-sectional study we have analyzed 575 patients with NAFLD. There was 273 (47.5%) man and the mean age was 59±13 years. NAFLD was detected by controlled attenuation parameter (CAP) and liver stiffness measurements (LSM) assessed by transient elastography (TE). In part of the patients (113) the liver biopsy was done as well. Coffee drinking was recorded using semi-quantitate questionnaire and categorized as yes vs. no and as 0, 1, 2, ≥3.
Results: The great majority were coffee drinkers (77.6%). Patients were divided into four subgroups of patients depending on the number of cups of coffee per day (0, 1, 2, ≥3). Firstly we have analyzed the influence of coffee drinking on the elastographic parameters of liver steatosis and fibrosis (CAP and LSM). Interestingly, patients that were drinking more cups of coffee had higher CAP, while the same group of patients had lower LSM values in comparison to nondrinkers or those who were drink only one cup of coffee per day, although that was not statistically significant. Next we have investigated the influence of coffee drinking on biopsy findings. There was no significant difference in the degree of NASH, although patients who were not coffee drinkers had lower degree. On the other hand those who drank more coffee had the lowest degree of fibrosis, although this difference is not statistically significant. Furthermore, drinking coffee had no influence on liver enzyme levels. Finally, drinking coffee had beneficial influence on ferritin and CRP values as inflammation parameters.
Conclusion: According to our results drinking coffee have beneficial effect on degree of fibrosis detected by TE (LSM) and liver biopsy, as well as on inflammation parameters.
Disclosure: Nothing to disclose

P1397 GENDER BIAS IN POLYCYSTIC LIVER DISEASE: ESTRADIOL STIMULATES PROLIFERATION AND INFLUENCES ESTROGEN RECEPTOR EXPRESSION IN PRKCSH KNOCKOUT CHOLANGIOCYTES

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Introduction: Polycystic liver disease (PLD) is a rare genetic disease and *PRKCSH* has been identified as one of the causative genes. In large cohort studies, over 80% of patients are female. In addition, the severity of PLD correlates with the use of exogenous estrogens [1]. We aimed to find experimental evidence for the effect of estradiol on proliferation of cholangiocytes *ex vivo*. Furthermore, we studied the expression of estrogen receptor (ER)-α, ER-β and the G protein-coupled estrogen receptor (GPER) in cholangiocyte cell lines, organoids and hepatic cyst tissue.
Aims & Methods: We used H69 wild type (WT) and H69 *PRKCSH* knock out (KO) cholangiocyte cell lines, patient-derived organoids (n=10) and hepatic cyst tissue (n=9). H69 cell lines were incubated in a dilution series of estradiol. A possible additive effect of progesterone was also assessed in a dilution series. With the use of WST-1 assays, the effect of the hormones on the relative proliferation between treated and non-treated WT and KO cholangiocytes was determined. PCNA expression was used to identify proliferative effects in organoids. For RNA isolation we cultured WT and

KO cholangiocytes, and organoids in medium with either the optimal hormone concentration for proliferation, or vehicle. RNA was isolated using Trizol to determine the expression of estrogen receptors (ER-α, ER-β and GPER) and PCNA by quantitative polymerase chain reaction (qPCR). The relative expression fold change ($2^{-\Delta\Delta Ct}$) between WT and KO cholangiocytes, and treated and non-treated cholangiocytes and organoids was measured. Finally, we studied the expression of estrogen receptors in hepatic cyst tissue obtained from surgical fenestration and patient-derived organoids. The organoids were derived from cyst fluid obtained during aspiration or tissue during fenestration of hepatic cysts.

Results: We found that mainly estradiol, but also progesterone to a minor extent, stimulates proliferation in *PRKCSH* KO and WT cholangiocytes. The optimal estradiol concentration was 10 nM. Without estradiol, GPER expression was higher in KO cholangiocytes compared to WT ($2^{-\Delta\Delta Ct}$ = 6.19). When treated with estradiol, the relative expression decreased, but was still higher in KO compared to WT ($2^{-\Delta\Delta Ct}$ = 2.47). This is explained by an increase in GPER expression in WT ($2^{-\Delta\Delta Ct}$ = 1.58) and reduction of GPER expression in KO ($2^{-\Delta\Delta Ct}$ = 0.63) after estradiol treatment. ER-α and ER-β were not detectable with qPCR in the cell lines, nor did we detect any estrogen receptor expression in organoids. After addition of estradiol to organoids, PCNA expression was 6 times higher, which is indicative of a proliferative effect. In 7/9 (78%) cyst tissue samples, expression of any estrogen receptors was found. In 6/9 (66%) samples ER-α was expressed, in 3/9 (33%) ER-β and in 7/9 (78%) GPER. We detected both GPER and ER-α in 5/9 (56%) samples.

Conclusion: In this study we provide evidence for the proliferative effect of estradiol on cystic cholangiocytes, which may be regulated by multiple estrogen receptors in cystic epithelia. With the results of this study, we confirm that gender bias in polycystic liver disease is to some extent explained by estradiol exposure.

References: 1. Sherstha, R., et al., Postmenopausal estrogen therapy selectively stimulates hepatic enlargement in women with autosomal dominant polycystic kidney disease. Hepatology, 1997. 26(5): p. 1282-1286.

Disclosure: Nothing to disclose

P1398 NONALCOHOLIC FATTY LIVER DISEASE (NAFLD) AND GASTROESOPHAGEAL REFLUX DISEASE

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Introduction: According to current data connection between nonalcoholic fatty liver disease
(NAFLD) and gastroesophageal reflux disease (GERD) is controversial. Our aim was to analyze relationship between GERD and NAFLD.

Aims & Methods: In this cross-section study we have analyzed 436 patients mean age 63.3±13.5 in whom upper gastrointestinal endoscopy (GE) was done. There were 215 (49.3%) male patients. On upper GE endoscopy we were interested to analyze presence of hiatal hernia, cardiac insufficiency and the presence and degree of GERD. NAFLD was diagnosed by liver enzymes and transient elastography [controlled attenuation parameter (CAP) for detection of liver steatosis and liver stiffness measurements (LSM) for liver fibrosis detection]. In part of the patients the liver biopsy was done.

Results: Firstly we have analyzed difference between patients with mild steatosis (first group had CAP< 268 db/m) and advanced steatosis (second group had CAP≥268 db/m). As we expected patients with advanced steatosis had higher values of anthropometric parameters of obesity, the XL probe was dominantly used and they had higher incidence of dyslipidemia. There was no significant difference due to GERD frequency and degree as well as frequency of hiatal hernia between two group of patients, but patients with advanced steatosis had higher incidence of cardiac insufficiency (p=0.04). Next, we were interested to analyze is there a difference in upper GI endoscopy findings between NAFLD patients with normal and elevated LSM values. There was no difference in anthropometric parameters of obesity between NAFLD patients with normal LSM values and those with elevated LSM values, while second group of patients had higher

incidence of other components of the metabolic syndrome. Interestingly we didn't find any significant difference in upper GI endoscopy between two groups of patients. Finally we have analyzed what are the difference in liver enzymes, elastographic and liver biopsy findings between patients with GERD and those without GERD. We didn't find any significant difference in liver enzymes, elastographic parameters of steatosis (CAP) and fibrosis (LSM) and liver biopsy findings among two group of patients.

Conclusion: According to our results and in contrary to recent data, we didn't find the connection between frequency and degree of GERD and degree of NAFLD diagnosed by liver enzymes, elastographic parameters of steatosis (CAP) and fibrosis (LSM) and liver biopsy findings, except patients with advanced steatosis defined by CAP values had higher incidence of cardiac insufficiency.

Disclosure: Nothing to disclose

P1399 SIMPLE BIOLOGICAL SCORE FOR DIABETOLOGISTS TO IDENTIFY NAFLD PATIENTS WITH SIGNIFICANT FIBROSIS

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Introduction: Non-alcoholic fatty liver disease is becoming the most common cause of chronic liver disease.

Aims & Methods: The aim of this study was to identify factors associated with significant liver disease in a cohort of type 2 diabetes patients and to develop a simple score for clinicians to identify more easily patients at risk. Patients were recruited prospectively in the study. Every first 6 patients who were referred to the Metabolic Disease Outpatient Clinic on a consultation day. Evaluation of liver fibrosis (stiffness) was made using Transient Elastography (FibroScan), performed in fasting conditions, with M and XL probes. Each patient was evaluated biologically for the presence of viral hepatitis (B and C) and an AUDIT-C score was performed to exclude alcohol abuse. Also subjects characteristics, epidemiological data and biochemical tests were recorded. Variables tested for the association with advanced liver fibrosis were: age, body mass index (BMI), abdominal circumference, hypertension, years after diagnosis of diabetes, glycemia, glycosylate hemoglobin, AST, ALT. Logistic regression was used for multivariate model to assess the association between advanced liver fibrosis and other variables. The cut-off value for significant fibrosis was >8.4 kPa [1].

Results: The total number of diabetics evaluated was 641. After the exclusion of others conditions, 468 patients with NAFLD were included, mean age 60.2±9.2, 55% women and 45% men. Advanced fibrosis was found in 29.4% (138/468) patients. To assess the advanced fibrosis predicting score, all clinical variables associated with significant fibrosis, with p < 0.05 in the univariate analysis were considered in a multivariate regression model (BMI, glycemia, glycosylate hemoglobin, AST, ALT, abdominal circumference) and gave us the following predicting score: 1 point for AST> 30 U/l, ALT>35 U/L, BMI> 30, abdominal circumference and 2 points for HbA1c > 7.5%, glycemia>200mg/dl. The score ranged from 0 to 8 with maximum predictability at 8. The best cut-off value for predicting significant fibrosis was ≥4, with a sensitivity of 83.3%.

Conclusion: A simple score consisting of body mass index (BMI), abdominal circumference, glycemia, glycosylate hemoglobin, AST, ALT can identify NAFLD patients with significant fibrosis.

References: 1.Petta S. et al, The combination of liver stiffness measurement and NAFDL fibrosis score improves the non-invasive diagnostic accuracy for severe liver fibrosis. Liver Int 2015.

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P1400 ASSESSMENT OF NONALCOHOLIC FATTY LIVER DISEASE USING SERUM TOTAL CELL DEATH AND APOPTOSIS MARKERS - COMPARISON WITH THE LIVER BIOPSY

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Introduction: The diagnosis of non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH) and fibrosis relies on liver biopsy. Non-invasive assessments are urgently needed. Thus, our aim was to evaluate cell apoptotic marker cytokeratin-18 M30 and total cell death markers cytokeratin-18 M65 for the assessment of NAFLD.

Aims & Methods: A cohort of 136 patients mean age 58.3±11.3 with biopsy-proven NAFLD were enrolled. There was 69 (50.7%) male patients. NAFLD was by transient elastography [controlled attenuation parameter (CAP) for detection of liver steatosis and liver stiffness measurements (LSM) for liver fibrosis detection]. NASH diagnosis was based on Brunt's criteria and the NAFLD activity score (NAS) and the presence of fibrosis were determined. The diagnosis of NASH was based on NAS≥5. Biomarkers were determined by enzyme-linked immunosorbent assay.

Results: Of 136 analyzed patients, 67 patients had NAS≥5 defined as NASH (according to the NAS score). Interestingly, there was no significant correlation between the M30 and M65 levels and CAP measurements. On the other hand, there was significant positively correlation of M65 and LSM measurements (r=0.228; p=0.007), while the correlation between M30 and LSM didn't reach the significant level (r=0.156; p=0.06). There was significant positive correlation between NAS score and M30 (r=0.193; p=0.02) and M65 (r=0.300; p=0.0004). M30 levels were significantly higher in NASH group of patients in the comparison to the non-NASH patients according to the NAS score (351.2±655.6 vs. 90.1±62; p=0.001) (figure 1a). Also, M65 levels were significantly higher in NASH group of patients in the comparison to the non-NASH patients according to the NAS score (585.1±886.5 vs. 207.2±33.2; p=0.0006). M30 levels was a moderate predictor of NASH on biopsy with an area under the curve (AUC) of 0.722 (95% Cl 0.639 to 0.795). A M30 cut-off of >74 had a sensitivity of 52.2%, specificity of 90%in NASH diagnosis. Similar, M65 level was a moderate predictor of NASH on biopsy with an area under the curve (AUC) of 0.781 (95% Cl 0.595 to 0.759). A M65 cut-off of >274 had a sensitivity of 38.8%, specificity of 97.1% in NASH diagnosis. Interestingly, M30 levels were significantly higher and in patients with significant fibrosis (grade 2-4) in comparison to the patients without fibrosis and to those with mild fibrosis (grade 1) (303.6±658.4 vs. 143.3±197.4; p=0.05). Also, M65 levels were significantly higher in patients with significant fibrosis (grade 2-4) in comparison to the patients without fibrosis and to those with mild fibrosis (grade 1) (494.9±802.7 vs. 295.6±317.4; p=0.05).

Conclusion: Serum biomarkers M30 and M65 had a moderate accuracy in detecting NASH. Combination of non-invasive marker could improve the sensitivity.

Disclosure: Nothing to disclose

P1401 TREATMENT OF NONALCOHOLIC FATTY LIVER DISEASE WITH VITAMIN D: A DOUBLE- BLINDED, RANDOMIZED, PLACEBO-CONTROLLED PILOT STUDY

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Introduction: Nonalcoholic fatty liver disease is the most commmon form of chronic liver disease that affects around 25% of population. No licensed mediacal treatment exists. We investigated efficacy and safety of a 48-week treatment with vitamin D in patients with transiet elastography (TE) defined NAFLD.

Aims & Methods: TE defined NAFLD pataients with decreases 25-OH vitamin D level at baseline recieved vitamin D (1000 IU/per day) or placebo orally over a 48-week period. The primary endpoint of this study was the changes of elastographic parameter of liver steatosis (controller atenuation parameter - CAP) and fibrosis (liver stifness measurements - LSM) from the baseline to the end of treatment. The secondary aim was tthe changes of liver enzymes (AST, ALT, GGT) from the baseline to the end of treatment.

Results: Patients were randomly assigned to intervention (N=175) or placebo group (N=90). Average age of population was 62.4 years with 42% of male participants. There was no significant differences in intervention or placebo group in baseline age, gender, BMI, waist, hip and thigh circumference, but also there was no significant difference in baseline serum vitamin D levels in intervention and placebo group (55.7±30.3 vs 50.7±27.9, P=0.22). There was significant decrease in CAP (dB/m) values in intervention group through follow up of 12 months (317.5±39.6 vs 277.01±53.35, P< 0.0001) comparing to placebo group where there was significant increase in CAP values (309.2±41.7 vs 323.8±41.5, P=0.019). We have not noticed significant changes in LSM (kPa) values in placebo or intervention group, however it is important to notice that there was a trend towards lower values of LSM in intervention group in the follow-up period (6.23±3.73 vs 5.65±3.26, P=0.12) comparing to the placebo group (6.13±3.85 vs 6.17±2.7, P=0.931).

Conclusion: Treatment with 1000 IU of vitamin D over 48 weeks was well tolerated and led to a significant improvement of CAP values.

Disclosure: Nothing to disclose

P1402 TRANISET ELASTOGRAPHY IN THE PROSPECTIVE EVALUATION OF FATTY LIVER DISEASE

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Introduction: The aim of this prospective study was to monitor the progression of elastographic parameters of liver steatosis [controlled attenuation parameter (CAP)] and fibrosis [liver stiffness measurement (LSM)] in patients with elastography proven NAFLD using Fibroscan 502 Touch. Furthermore, using elastographic parameters in patients with one or more MetS components and NAFLD, we were estimating the effects of clinical

and laboratory parameters on progression of elastographic parameters of steatosis and fibrosis (CAP and LSM). Finally, according to different BMI categories.

Aims & Methods: For the time period between May 2014 and October 2014 there were 606 consecutives ambulatory NAFLD patients enrolled in this prospective study. During each visit, that is every three months, Transiet elastography (TE) examinations were performed in each patient. First of all, we were interested in analyzing the time to CAP (i.e. elastographic parameter of steatosis) and LSM (i.e. elastographic parameter of fibrosis) progression by at least 20% in total population and in identifying independent predictors of CAP and LSM progression in total population. Secondly, we were interested in analyzing the time to CAP and LSM progression by 20% in different BMI categories.

Results: This cohort consisted of 507 patients, 53.3% males. Median age was 62 (63-68) years and median BMI was 29.6 kg/m2, with relatively high proportion of overweight (41%, n=208) and obese (45.8%, n=232) patients and only 13.2% (n=67) having BMI< 25. There was a high proportion of patients with hypertension (71%), T2DM (39.1%), hyperlipidemia (68.6%), CKD (24.9%) and MetS (44.6%). Median values of CAP were 305 (269-337) and liver stiffness 5.3 (4.3-6.9). The cohort was followed for a mean period of 15.46 months (±11.3, range 0.4-41.4 months), corresponding to 663.58 person years.

During follow-up in 84 patients (16.5%) progression of liver steatosis for 20% occurred. On the other hand, in more patients, 201 (39.6%), occurred progression of liver fibrosis for 20%. After that we analyzed patients divided into three groups based on BMI status; < 25 (lean), 25-29.9 (overweight), and≥30 kg/m2 (obese). When stratified for BMI category, significant difference was found in occurrence of fibrosis progression, with obese patients having the highest proportion. There was no difference in occurrence of steatosis progression, or time to steatosis or time to fibrosis progression.

Obese patients have 1.66 (1.23-2.25) higher risk of developing fibrosis progression compared to overweight patients which were taken as the reference category. Kaplan-Meier survival curves stratified per BMI category were different (P=0.023) with obese patients having the highest risk of liver fibrosis progression. This was not the case for progression of liver steatosis. In multivariate Cox-regression analysis significant predictor of fibrosis progression was HOMA-IR.

Conclusion: By this study we have shown that for the progression of elastographic parameters of steatois and fibrosis (I.e. CAP and LSM) are important the same factors (i.e. MetS and its individual components) that were reported to be associated with NAFLD progression detected by other methods. Thus, indicating that by this method we could monitor NAFLD progression in everyday clinical practice by patient-friendly method. However further studies are needed.

Disclosure: Nothing to disclose

P1403 THE PSYCHOLOGICAL ASPECTS AND HEALTH-RELATED QUALITY OF LIFE IN OBESE PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE WITH MILD FIBROSIS

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Introduction: The non-alcoholic fatty liver disease (NAFLD) is considered to be the most common liver disease in the world in recent years. It is closely linked to metabolic disorders and, in the first place, with obesity. This greatly impairs the quality of life of the patients, and may also be accompanied depressive disorders.

Aims & Methods: The aim of the study was to assess depressive disorders and health related quality of life of obese patients with NAFLD in the initial stages of liver fibrosis(non-cirrhotic NAFLD). 45 patients (20 men and 25 women, aged 23- 78 years, mean BMI 30,47 kg/m^{2}) were devided into 4 groups : 10 obese without fibrosis(age 48,6±18,4, BMI 32,2±2,4 kg/m^{2}), obese with 1 stage of fibrosis(age 55,8±13,6, BMI 32,7±4,7 kg/m^{2}), 11 obese with 2-3 stage of fibrosis(age 63±3,7, BMI 34,8±3,7 kg/m^{2}), and 11 lean

without fibrosis(control group) (age 49,6±17,7, BMI 22±2,1 kg/m^{2}). Liver stiffness was measured by share wave elastography, HRQOL was measured using the Ukrainian version of the SF-36 Health Survey.

We assessed the depression with the help of The Beck Depression Inventory (BDI).

Results: Main domains of the HRQL score were significantly lower in obese patients with NAFLD in comparison to the lean patients: comparing of three groups of obese patients with different stages of fibrosis with lean patients we found statistically significant difference in Physical health: control- F0(t=2,6 p=0,017), in control -F1(t=3,6 p=0,002) and in control - F-2-3 groups (t=3,53 p=0,002). Datas of Mental health in the comparing group control- F0(t=2,7 p=0,013), control- F1(t=2,5 p=0,019). In comparing group with advanced fibrosis no statistically significant difference in Mental health control F2-3 (t1,27 p 0,216).

The depression level is higher in the group of obese patients comparing to the lean ans it's stage is the highest in the F2-F3 group.

Conclusion: In obese people HRQL is lower than in lean and it decreases with the stage of fibrosis. We suppose that our datas show deterioration of the critical assessment of their condition in patients with advanced fibrosis.

Disclosure: Nothing to disclose

P1404 THE EFFECT OF SILYMARIN AND VITAMIN E IN THE TREATMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE: A RANDOMIZED, DOUBLE-BLIND CLINICAL TRIAL

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Introduction: Lifestyle modification is the only currently recommended treatment for nonalcoholic fatty liver disease (NAFLD). Preliminary studies of vitamin E and silybin showed beneficial effects on liver function. We report on a double-blind clinical trial the effect of Sylimarin and vitamin E in patients with NAFLD.

Aims & Methods: Randomized, double-blind, clinical trial conducted at 2 university clinical research centers in 80 patients (aged years) with NAFLD conducted between September 2014 and March 2015. All patients were randomized to receive vitamins E (400 IU) and Silymarin 280mg daily for 4 months. Additionally, all patients were given standard weight-loss counseling and encouraged to follow a low fat diet (< 30 fat g/day). Patients were obtained at baseline and on after 4 months for measurement of ALT and ultrasonography. Given the two planned primary comparisons, P values of less than 0.05 were considered to indicate statistical significance.

Results: There was no significant difference in terms of sex and BMI between the groups. At the end of the 12-week treatment period there was a significant decrease in the serum ALT levels in both treatment groups. The mean change in ALT level from baseline to 4 months was 31.6 U/L with Sylimarin group vs. -15.1 U/L with vitamin E (P =.07). Therefore, effects in the Sylimarin were larger than vitamin E (p < 0.0001). The mean ALT levels changed to normal 55.0% (22 of 40 cases) in the Sylimarin group and 45.0% (18 of 40 patients) vitamin E group (P=0.04). Based ultrasonography findings after 4 months in the vitamin E group 4 patients and in the Sylimarin group 2 cases were normalized. Adverse events (AEs) were generally transient and included diarrhea, dysgeusia, and pruritus; no serious AEs were recorded.

Conclusion: In Sylimarin and vitamin E treatment appears to be significantly effective in biochemical improvement in decreasing the ALT and ultrasonographic measurement, respectively

Disclosure: Nothing to disclose

P1405 SYMPATHETIC OVERACTIVITY AND EARLY SODIUM RETENTION IN EXPERIMENTAL LIVER CIRRHOSIS: A ROLE FOR RENALASE

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Introduction: Sympathetic overactivity promotes sodium retention and functional renal failure in liver cirrhosis. Renalase, 38 kDa amine oxidase with just 13% aminoacid identity with monoamine oxidase A, is secreted into the blood by the kidney and is the only identified form of amine oxidase that clears plasma of circulating catecholamines.

Aims & Methods: To study plasma and tissue content and function of renalase in experimental preascitic and ascitic cirrhosis. In normal rats (group G1), rats with CCl_4-dependent liver cirrhosis without ascites (G2) and with ascites (G3) we evaluated: renalase levels and activity in plasma, liver and kidney; renalase gene transcription and immunohistochemical localization in liver and kidney; liver histology and matrix deposition, hormonal status and kidney function.

Results: In plasma, mature (38 kDa) contents and activity, well detected in normal rats, were virtually absent in rats with compensated or ascitic cirrhosis (all P< 0.01 vs. G1). In G2 and G3 rats, but not in G1, we found large amount of enzymatically active high-molecular-weight (78 kDa) renalase and very little 38 kDa protein in hepatocytes of regenerative nodules of the cirrhotic liver and in kidney tubules. RT-PCR confirmed higher levels of renalase gene transcription in both liver and kidney of G2-3 (P< 0.03 vs. G1). Rats with preascitic liver damage showed increased plasma catecholamines, normal renin-angiotensin system activation and sodium retention, while ascitic rats had both secondary aldosteronism and increased adrenergic activation.

Conclusion: High-molecular-weight forms of functional renalase accumulates in diseased liver and kidney, but tissue processing and release into blood of mature (38 kDa) renalase is almost absent, contributing to increased levels of plasma catecholamines and sodium retention in both preascitic and decompensated cirrhosis.

Disclosure: Nothing to disclose

P1406 BLUNTING OF ADRENERGIC FUNCTION HAS AQUARETIC EFFECTS IN EXPERIMENTAL ASCITIC CIRRHOSIS

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Introduction: Catecholamines promote proximal tubular fluid retention and decrease Na^+ and water delivery to the diluting segment of the Henle's loop, thereby reducing renal excretion of solute-free water. In advanced cirrhosis, non-osmotic hypersecretion of vasopressin (ADH) has a role in causing dilutional hyponatremia, but the advantage of ADH V_2 receptor antagonists is controversial in the treatment of ascites.

Aims & Methods: By means of the use of sympatholytic agents ($\alpha2_A$ adrenergic receptor agonists), we assessed the hypothesis that adrenergic hyperfunction might contribute to water retention in experimental ascitic cirrhosis. Hormonal status, renal function and tubular free-water reabsorption (TFWR) were evaluated in four groups of rats with ascitic cirrhosis: rats with cirrhosis due to 13 weeks of CCl_4 (group G1); cirrhotic rats receiving, from 11th to 13th CCl_4 week, daily diuretics alone (0.5 mg/kg furosemide plus 2 mg/kg K^+- canrenoate) (G2), or diuretics plus guanfacine oral prodrug ($\alpha2_A$ adrenergic receptor agonist and sympatholytic agent) 2 mg/kg (G3). Group G4 received diuretics plus SSP-004240F1 (V_2 receptor antagonist) 1 mg/kg.

Results: Compared to G2, guanfacine plus diuretics (G3) reduced serum norepinephrine from 423 ± 22 to 211 ± 41 ng/L and plasma renin activity from 35 ± 8 to 9 ± 2 ng/mL/h (all P< 0.03). Compared to G1 and G2, TFWR was significantly reduced, and to the same extent, with low-dose guanfacine plus diuretics (G3) and with V_2 antagonist plus diuretics (G4) (all P< 0.03). TFWR correlated with plasma aldosterone (r=0.51, P< 0.01) and urinary potassium excretion (r=0.90, P< 0.001).

Conclusion: In ascitic cirrhosis, reduced volaemia, secondary aldosteronism and adrenergic hyperfunction, especially when exacerbated by potassium-depleting diuretics (furosemide), contribute to tubular retention of water and dilutional hyponatremia. Low-dose sympatholytic agents are as effective as V_2 antagonists to achieve aquaretic effects in this setting.
Disclosure: Nothing to disclose

P1407 REBALANCED HEMOSTASIS IN LIVER CIRRHOSIS

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Introduction: Traditional concepts of liver cirrhosis believed that it presented a pro-haemorrhagic tendency, thought to be the result of laboratory abnormalities such as thrombocytopenia and prolongation of the international normalised ratio (INR). However, recent evidence indicates that the hemostasis in liver cirrhosis is more complex that previously thought. Production of both procoagulant and anticoagulant factors is affected, leading to a delicate hemostatic rebalance, where a higher risk for both bleeding and thrombosis coexists.
Aims & Methods: We aimed to investigate the coagulation abnormalities in patients with acute decompensated cirrhosis. We conducted a prospective observational study including patients admitted with acute decompensated cirrhosis. Measurement of serum level of platelets, von Willebrand factor antigen (vWF), prothrombin time (PT), INR, coagulation factors II, V, VII, VIII and procoagulant protein C (PC) and antithrombin (AT). Statistical analysis with SPSS v25.
Results: 55 patients included (91% male; mean age of 61±10 years; 93% alcoholic etiology; mean MELD 17±5,6 points; Child-Pugh C 62%). Mean serum level values: platelets 115000±64000; PT 20,9±6,9; INR 1,42±0,27; FII 43,3±15,2 (reference value 50-150); FV 49±22,3 (62-139); FVII 33,5±31,2 (50-129); FVIII 231±186 (50-150); vWF 491±236 (42-176,3); PC 29,1±17,5 (70-140), AT 45,1±25 (83-128).
Patients with platelet levels below 100 000/uL had higher values of vWF (562 vs 405; p<0,05). There was a moderate inverse correlation between INR and PC (p<0,05; R=-0,462) and AT (p<0,05; R=-0,434); and there was a strong positive correlation between INR and vWF (p<0,001; R=0,544). There was also a strong positive correlation between AT and factors V (p<0,01; R=0,759) and VII (p< 0,01; R=0,657).
Conclusion: This study corroborates the concept that the patient with liver cirrhosis presents a complex and fragile hemostatic profile, with prohemostatic and antihemostatic factors that tend to rebalance. Thrombocytopenia and prolongation of the INR are compensated by an increase in vWF values; a reduction of procoagulant factors (V and VII) is counterbalanced by a decrease in PC and AT.
Disclosure: Nothing to disclose

P1408 CHANGES IN PLASMA CIRCULATING MICROVESICLES IN PATIENTS WITH HCV-RELATED CIRRHOSIS AFTER TREATMENT WITH DIRECT-ACTING ANTIVIRALS

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Introduction: The eradication of HCV infection by direct-acting antiviral agents (DAAs) has been linked to an amelioration of liver synthesis and a regression of fibrosis. Although changes in number and type of circulating microvesicles (MVs) have been reported in cirrhosis, conclusive data on the effect of DAAs treatment on MVs profile in HCV cirrhotic patients remain scarce.
Aims & Methods: To prospectively characterize changes in plasmatic levels of endothelial, platelet and hepatocyte MVs, and MVs expressing versican core protein (VCAN+) in patients with HCV-related cirrhosis at baseline, end of therapy (EOT), at 12, 24 and 48 weeks (W) after EOT by new generation flow-cytometry, and to correlate these changes with clinical outcome.

Results: Fifty-eight patients were enrolled (86% Child's A). MVs were increased at EOT versus baseline, though only platelet MVs revealed a statistically significant difference (p<0.01). MVs levels did not change significantly after EOT notwithstanding a steady downward trend towards baseline levels. In contrast, VCAN+MVs dropped significantly at EOT (p < 0.001) and remained low throughout the follow-up. Hepatocyte MVs significantly correlated with liver stiffness (r 0.40, p 0.0021). Eight composite outcomes occurred during the 1-year follow-up: 3 portal vein thromboses, 2 hepatocellular carcinomas and 3 liver decompensation. Child's B, the presence of F2 oesophageal varices (OR for interaction 19.2 [95%CI 1.45-253.7], p 0.023) and platelet MVs (OR 1.026 [95%CI 1.00-1.05, p 0.023) correlated significantly with clinical outcomes.

Conclusion: VCAN+MVs appear to mirror the profibrotic status of the cirrhotic disease; hepatocyte MVs correlate with liver stiffness and platelet MVs might be associated with a worse clinical outcome.

Disclosure: Nothing to disclose

P1409 SPLEEN AND LIVER STIFFNESS COMBINED MODEL FOR PREDICTING ESOPHAGEAL VARICES IN PATIENTS WITH COMPENSATED LIVER CIRRHOSIS

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Introduction: Ultrasound based elastography methods and biological markers can be used as non-invasive tools for predicting the presence of esophageal varices,

Aims & Methods: The aim of the study was to formulate and assess the usefulness of a new non-invasive score to predict the presence of esophageal varices (EV) in cirrhotic patients.

A prospective study was performed in 77 subjects with compensated liver cirrhosis (diagnosed based on clinical, biological and elastographic criteria -Liver transient elastography>12.5kPa[1]), who underwent upper endoscopy, abdominal ultrasound, spleen and liver stiffness measurements (SSM and LSM, respectively) with a 2D-SWE technique from General Electric (Logiq E9) and biologic tests in the same session. Reliable SSM and LSM were defined as the median value of 10 measurements acquired in a homogenous area with IQR/M< 0.30.

Results: We obtained reliable SSM in 98.7% (76/77) subjects and reliable LSM in 97.4% (75/77). 75 subjects were included in the final analysis, 64% (48/75) with EV. The mean SS, LS, spleen size (cm) were significantly higher in patients with EV (16.77±2.92 kPa vs. 13.2±2.66 kPa, p< 0.0001; 14.12±2.09 kPa vs. 11.5±1.56 kPa, p< 0.0001; 14.49±2.09 cm vs. 13.05±1.86 cm, p=0.004, respectively). Thrombocytes were significantly fewer in patients with EV (90,125±34,425 vs. 135,738 ± 58,905, p=0.0001).

In univariate analysis, SSM, LSM, spleen size and thrombocytes were associated with the presence of EV, all p< 0.0001. In multivariate analysis, the model including SSM, LSM, spleen size and thrombocytes had the following p-values: p=0.01, p=0.01, p=0.03 and p=0.01. Using these factors as predictors, by multiple regression analysis, we obtained the following score: Presence of EV=0.04*SSM + 0.06*LSM + 0.04*spleen size - $1*10^{-6}$*thrombocytes -1.17. The score had a cut-off value >0.48(AUROC=0.9, Se=95.8%, Sp=96.3%, PPV=97.9%, NPV=92.9%) for predicting the presence of EV.

Conclusion: Using the model including SSM, LSM, spleen size and thrombocytes we can rule in the presence of EV with a positive predictive value of 97%.

References: 1. Castera, L., Forns, X. and Alberti, A. Non-invasive evaluation of liver fibrosis using transient elastography. Journal of Hepatology, 2008, 48(5), pp.835-847.

Disclosure: Nothing to disclose

P1410 SPLEEN STIFFNESS FOR THE NONIVASIVE PREDICTION OF PORTAL HIPERTENSION. COMPARASION BETWEEN THE PERFORMANCE OF POINT SHEAR WAVE ELASTOGRAPHY AND 2D-SHEAR WAVE ELASTOGRAPHY

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Introduction: Ultrasound based elastography methods can be used as non-invasive tools for predicting the presence of esophageal varices.

Aims & Methods: The aim of the study was to establish the usefulness of spleen stiffness (SS) values measured by means of two elastographic techniques: point shear wave elastography (pSWE) and 2D-shear wave elastography (2D-SWE) as non-invasive markers for predicting the presence of esophageal varices (EV) and to compare their performances.

A prospective study was performed, including 86 subjects with compensated liver cirrhosis who underwent both upper endoscopy and SS measurements (SSM) by means of two elastographic techniques: pSWE - using virtual touch quantification (VTQ) technology (Acuson S2000-Siemens Medical Solutions); and 2D-SWE (LOGIQ E9-General Electric), in the same admission. Reliable SSM were defined for both techniques as the median value of 10 measurements acquired in a homogenous area with (IQR/M) < 0.30. Compensated liver cirrhosis was diagnosed based on clinical, biological and elastographic criteria (Liver transient elastography>12.5 kPa) [1].

Results: We obtained reliable SSM in 98.8% (85/86) by means of 2D-SWE. GE and in 96.5% (83/86) subjects by means of pSWE-VTQ. 83 subjects were included in the final analysis, 63.8% (53/83) of them with EV. The best SS cut-off value by 2D-SWE.GE for predicting the presence of EV in our study group was 13.4 kPa (AUROC-0.89; sensitivity-85%; specificity- 93.3%; PPV-95.7%; NPV-77.8%), while for pSWE-VTQ it was 2.8 m/s (AUROC-0.65; sensitivity-60%; specificity-70%; PPV-78%; NPV-50%). Based on AUROC comparison, 2D-SWE.GE performed significantly better than pSWE-VTQ to predict the presence of EV (p=0.0011).

Conclusion: Although there are no significant differences between the feasibility of the two methods (p=0.62), it seems that 2D-SWE.GE has a better performance in predicting the presence of EV as compared with pSWE-VTQ (p=0.0011).

References: 1. Castera, L., Forns, X. and Alberti, A. Non-invasive evaluation of liver fibrosis using transient elastography. Journal of Hepatology, 2008, 48(5), pp.835-847.

Disclosure: Nothing to disclose

P1411 IS SPLEEN STIFFNESS SUPERIOR TO LIVER STIFFNESS FOR PREDICTING PORTAL HYPERTENSION?

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Introduction: Liver stiffness (LS) and spleen stiffness (SS) are two most widely accessible non-invasive parameters for predicting esophageal varices (EV), but the reported accuracy of the two predictors have been inconsistent across studies.
Aims & Methods: The aim of the study was to establish the usefulness of spleen stiffness (SS) and liver stiffness (LS) values measured by 2D-shear wave elastography (2D-SWE.GE) as non-invasive markers for predicting the presence of esophageal varices (EV) and to compare their performances. A prospective study was performed, including 90 subjects with compensated liver cirrhosis who underwent both upper endoscopy and spleen and liver stiffness measurements (SSM, LSM) by means of 2D-SWE (LOGIQ E9-General Electric), in the same admission. Reliable SSM were defined as the median value of 10 measurements acquired in a homogenous area with (IQR/M) <0.30. Compensated liver cirrhosis was diagnosed based on clinical, biological and elastographic criteria (Liver transient elastography>12.5 kPa) [1].
Results: We obtained reliable SSM in 96.7% (87/90) and reliable LSM in 97.7% (88/90) by means of 2D-SWE.GE. 85 subjects were included in the final analysis, 63.5% (54/85) of them with EV. The best SS cut-off value by 2D-SWE.GE for predicting the presence of EV in our study group was 13.7 kPa (AUROC-0.88; sensitivity-78%; specificity- 90.3%; PPV-93%; NPV-66.8%), while the best LS cut-off value was 11.1 kPa (AUROC-0.78; sensitivity-98.1%; specificity-52%; PPV-77,9%; NPV-94,1%). Based on AUROC comparison, SS performed significantly better than LS to predict the presence of EV (p=0.0253).
Conclusion: SS seems to be a better tool that LS for predicting the presence of EV in cirrhotic patients.
References: 1. Castera, L., Forns, X. and Alberti, A. Non-invasive evaluation of liver fibrosis using transient elastography. Journal of Hepatology, 2008, 48(5), pp.835-847.
Disclosure: Nothing to disclose

P1412 THROMBOTIC EVENTS IN PATIENTS WITH HEPATITIS C VIRUS LIVER CIRRHOSIS TREATED WITH DIRECT ACTING ANTIVIRALS AND SUSTAINED VIROLOGICAL RESPONSE - FACT OR NATURAL COURSE?

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Introduction: The advent of direct-acting antivirals (DAAs) is a major breakthrough in hepatology representing the therapeutical standard of care in patients with chronic hepatitis C virus infection over the past few years. Despite high rates of sustained virological response (SVR), DAAs therapy doesn't eliminate the risk of thrombotic events.
Aims & Methods: In our study we aimed to assess the occurrence of thrombotic events and clinical presentation in patients treated with DAAs and sustained virological response.
We retrospectively analyzed a cohort of patients with HCV-related liver cirrhosis treated with PrOD ± ribavirin and LED/SOF ± ribavirin for 12/24 weeks, in a tertiary gastroenterology center from Romania, between January 1st 2016 and July 1st 2018. All patients with presumption of thrombosis were evaluated by vascular Doppler, abdominal ultrasound and confirmed by CT scan.

Results: The study included 473 HCV-infected cirrhotic patients treated with PrOD or LED/SOF, with documented SVR, mean age 69,7 ± 5,5 years, predominantly female (59%).Of the total number, 284 (60.04%) received PrOD and 189 (39.95%) patients were treated with LED/SOF. Thrombotic complications were reported in 23 (4.86%) patients: 3 (13.04%)with deep vein thrombosis, 14 (60.86%) with portal vein thrombosis (PVT), 6 (26.08%) with malignant PVT.
All patients had associated cardiovascular (15-65.21%) and metabolic comorbidities (8-34.78%). The main clinical manifestations at diagnosis were: swelling,edema, erythema and lower limb pain in 3 patients, upper digestive haemorrhage in 8 patients, ascitic decompensation in 4 patient, abdominal pain in 5 patients and 3 patients were asymptomatic.
Biologically there was no significant change in prothrombin serum levels(baseline values in patients treated with PrOD was 11.67 ± 0.91 versus 11.70 ± 0.83 at SVR,p=0.993, respectively 11.5 ± 0.84 sec at baseline versus 11.4 ± 0.68 at SVR, p=0.715 inpatients treated with LED/SOF±RBV) and platelet count (126 000 (101 500-162 000) vs. 131000 (101 000-165 000), p= 0.818 in patients treated with PrOD, respectively 94857.14 ± 32 vs. 92428.57 ± 35, p= 0.853, in patients treated with LED/SOF+RBV).
Conclusion: We conclude that thrombotic events in patients with HCV-related liver cirrhosis treated with DAAs are not influenced by the variations of coagulation parameters, rather correspond to the hypercoagulability status and the natural evolution of the cirrhotic patient.
Disclosure: Nothing to disclose

P1413 SPONTANEOUS BACTERIAL PERITONITIS: WILL THE DIAGNOSTIC FOLLOW-UP PARACENTESIS BE ESSENTIAL IN APPROACHING THESE PATIENTS?

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Introduction: Recent studies suggest that follow-up paracentesis, in cases of spontaneous bacterial peritonitis (SBP) should only be performed if there is a clinical and/or analytic worsening.
Aims & Methods: Our aims were to evaluate which patients with SBP benefit from the diagnostic follow-up paracentesis, according to clinical and analytical predictive factors of an inadequate response at the third day of treatment.
Retrospective study conducted in a tertiary center, included the patients with SBP between January 2011 and June 2018. Clinical/analytical data was obtained at baseline and at the third day of antibiotic therapy. An adequate response to therapy, at the third day, was defined by a decrease of ≥25% in neutrophil count of the ascitic fluid.
Results: We included 103 cases of SBP with a mean age of 61±11 years. 30.1% of cases the patients were under antibiotic prophylaxis for SBP. At the third day, 30.1% had an inadequate response to antibiotic therapy.
At admission, the presence of diabetes mellitus (p=0.034), a higher serum neutrophils count (p=0.043), a lesser level of serum total proteins (p=0.040) and a positive culture in ascitic fluid (p< 0.001) were related to inadequate response. At day 3, a higher level of serum urea (p=0.018), creatinine (p=0.030), CRP (p=0.001), a higher count of serum leucocytes (p=0.001) and neutrophyles (p=0.001), the presence of fever (p=0.047) and abdominal pain (p< 0.001) were associated to absence of response, too.
In the multivariate analysis, diabetes mellitus (OR=5.33; 95% CI:1.24-22.96), positive ascitic fluid culture at admission (OR=15.66; 95% CI:2.41-101.94), abdominal pain at day 3 (OR=3.94; 95% CI:0.94-16.45; p<0.06) and CRP at day 3 (OR=1.02; 95% CI:1.00-1.03) were independently and significantly associated to inadequate response at the third day of empiric therapy.
The predictive model presented good accuracy [AUROC of 0.85 (p< 0.001) (Fig. 1)] - a cutoff of 0.055 had a sensitivity, specificity, positive predictive value, and negative predictive value for absence of response to antibiotic of 100%, 35%, 42%, and 100%, respectively.
With this model cutoff, 24% of repeated paracentesis could be precluded in our population sample.

Conclusion: These results evidence that, in approach of SBP, the performance of follow-up paracentesis, three days after the beginning of empiric therapy, should be individualized, according the conjugation of clinical and analytic variables. With our model a considerable number of unnecessary procedures may be avoided.
Disclosure: Nothing to disclose

P1414 TIMED UP AND GO TEST PREDICTS MORTALITY IN A COHORT OF COMPENSATED LIVER DISEASE

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Introduction: Poor muscle function and sarcopenia has previously been shown to be a negative prognostic factor in advanced liver disease (Hanai et al, Nutrition 2015). However, the impact of muscle function on prognosis in compensated chronic liver disease (CLD) is unknown.
Aims & Methods: We aimed to assess the potential prognostic value of muscle performance in a cohort of patients with a variety of common CLDs. Our primary aims were to assess mortality and transplant-free survival.
We followed a consecutively recruited cohort of patients with compensated CLD (Child- Pugh < B/C) that were enrolled in a study on muscle function and CLD in our institution between 2010 and 2014. In all, 270 CLD outpatients accepted inclusion (52±15 years at baseline,59±15 at follow up, mean±SD; 151 females). Twenty-nine patients with a history of hepatic decompensation (e.g., ascites) or Fibrosis 4 score (FIB-4) ≥3.25 indicating cirrhosis were excluded. Diagnoses in the remaining 241 subjects were primary biliary cholangitis (PBC; n=41), primary sclerosing cholangitis (PSC; n=42), autoimmune hepatitis (AIH; n=48), and viral hepatitis (HBV, n=51; HCV, n=59). All subjects performed four validated tests of muscle function: "Timed Up and Go" test (TUG, dichotomized into >10 seconds), walking speed (self-chosen and maximal walking speed, 30 m distance; m/s), handgrip strength with a dynamometer (maximum and average strength over 10 sec; N), and standing heel-rise test (number of heel-rises). In addition, using a seven-grade scale questionnaire for physical activity level, from 0 = no to 6 = regular strenuous physical activity several times/week, we dichotomized the study population into those with levels 0-4 and 5-6. By comparisons with data of an age and gender matched reference population we estimated muscle performance as percentage of normal and dichotomized patients into groups with normal or impaired muscle performance for each muscle test. Follow up data for mortality and liver transplantation was obtained through hospital records and Swedish population registries.
Results: In our population, at baseline muscle function was impaired in several tests: standing heel-rise test (n=16 normal test, 7%), maximum (n=54, 22% normal test) and average grip strength (n=56, 23% normal test), self-chosen (n=169, 70% normal test) and maximum walking speed (128, 53% normal test), TUG>10 seconds (n=42, 17%). Physical activity level 5-6 (n=35, 15%).
During a follow up of a mean of 6.75±1.4 years, 14 patients died (6%) and 10 (4%) patients underwent liver transplantation. TUG over 10 seconds was associated with a lower survival (Kaplan-Meier, log rank test p=0.041), however not with transplant free survival (p=0.248). The other physical functioning tests including physical activity level, self-chosen and maximum walking speed, maximum and average handgrip strength were not significantly associated with mortality or transplant free survival (Kaplan-Meier, log rank test p>0.05 for all).
Conclusion: Timed up and go test was a predictor of mortality in our population of compensated chronic liver disease. The prognostic value of this test in patients with fully compensated liver disease should be evaluated in further trials.
Disclosure: Nothing to disclose

P1415 ANTICOAGULANT TREATMENT FOR CIRRHOTIC NON-MALIGN PORTAL VEIN THROMBOSIS -EFFICACY AND SAFETY

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Introduction: Portal vein thrombosis (PVT) is recognized as one of the complications of liver cirrhosis. Anticoagulation treatment could be indicated in patients with PVT, but the efficacy remains unclear.
Aims & Methods: We aim to investigate the characteristics of PVT and the efficacy of anticoagulation treatment in cirrhotic patients diagnosed with PVT. A total of 116 cirrhotic patients who were diagnosed with PVT between January 2018 and December 2018 were retrospectively analyzed in this study. Complete response (CR) for anticoagulation treatment was defined as repermeabilization of PVT assessed by dynamic imaging.
Results: The baseline characteristics of all patients were as follows : age, 61.26±11.33 years old; platelet counts, 90 × 106 /L; ALT, 30 U/L; albumin, 3.2 g/dL; PT, 64%; D-dimer, 4.6 ng/mL; AT-3 56% and the etiology of the liver cirrhosis (viral B hepatitis/ viral C hepatitis/alcoholic/ NASH/other), 17.2%/33.6%/22.4%/22.4%/4.3%.
Among patients with liver disease, 51 patients (44.0%) had history of liver cancer and the mean MELD score was 15.21±7.11. Almost half of PVT were located in the main trunk of portal vein (61/116.) Twenty seven patients (23.3%) received an anticoagulant treatment.
Most of the patients received low weight molecular heparine (59.3%), followed by acenocoumarol (25.9%) and only 14.8% of the patients received direct oral anticoagulant treatment. During the study period half of the patients 58 (50.0%) remained stationary, 40 patients had improvement of the PVT (34.5%) and in 18 patients PVT worsened. The anticoagulant treatment did not influenced PVT evolution. In 24 patients that received an anticoagulant treatment PVT improved or remained stable.
However, 14 patients (12.1%) died during the study, none of them from bleeding complications. The anticoagulant treatment was not associated with an increased mortality rate (OR 0.899, CI 0.228-3.440, p=0.862).
Conclusion: Anticoagulation treatment for PVT was safe, although did not influenced PVT evolution. Careful management should be necessary after anticoagulation treatment.
References: 1. Sarin SK, Philips CA, Kamath PS, et al. Toward a comprehensive new classification of portal vein thrombosis in patients with cirrhosis. Gastroenterology 2016;151:574-577 2. Lisman T, Porte RJ. Nery F, Chevret S, Condat B, et al. Groupe d'Etude et de Traitement du Carcinome Hépatocellulaire. Causes and consequences of portal vein thrombosis in 1,243 patients with cirrhosis: results of a longitudinal study. Hepatology 2015;61:660-667
Disclosure: Nothing to disclose

P1416 THE RISK OF VARICEAL BLEEDING AFTER STOPPING BETA BLOCKERS IN CIRRHOTIC PATIENTS WITH REFRACTORY ASCITES

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Introduction: The non selective beta-blockant (NSBB) treatment in cirrhotic patients has several limitations regarding side effects, as arterial hypotension or bradicardia. Caution should be taken in cirrhotic patients with refractory ascites, hyponatremia or arterial hypotension, as NSBB could precipitated the development of the acute kidney injury.

Aims & Methods: The aim of this study was to evaluate the risk of variceal bleeding after the NSBB treatment is stopped in patients with refractory ascites. All consecutive patients with liver cirrhosis and refractory ascites admitted to the Institute of Gastroenterology and Hepatology from January 2017 to December 2017 were included in this study. The diagnosis of refractory ascites was established according to the current guidelines.

Results: During the study period a total of 57 patients were diagnosed with refractory ascites. In more than half of them, 29 patients (50.8%), the NSBB treatment was stopped, the main cause of stopping the treatment being systolic blood pressure less than 90 mmHg. The majority of the patients were receiving propranolol (86.2%), and only 4 patients (3.8%) received carvedilol. Out of the 29 patients that stopped the treatment, 21 (72.4%) were Child-Pugh class C, and 5 patients (17.2%) developed variceal bleeding. The risk of variceal bleeding was not increased in cirrhotic patients with refractory ascites that stopped the NSBB treatment (OR 1.207, CI 0.361-4.039, p=0.796).

Conclusion: Stopping the NSBB treatment in patients with refractory ascites is not associated with an increased risk of variceal bleeding , despite the severity of liver disease.

References: 1. Garcia-Tsao G, Abraldes JG, Berzigotti A, Bosch J. Portal hypertensive bleeding in cirrhosis: Risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the study of liver diseases. Hepatology. 2017 Jan;65(1):310-335. doi: 10.1002/hep.28906. 2. Reiberger T, Mandorfer M. Beta adrenergic blockade and decompensated cirrhosis. J Hepatol 2017 Apr;66(4):849-859. doi: 10.1016/j.jhep.2016.11.001. Epub 2016 Nov 15. Review. PubMed PMID: 27864004.

Disclosure: Nothing to disclose

P1417 BAVENO CRITERIA SAFELY IDENTIFY PATIENTS WHO CAN AVOID VARICEAL SCREENING ENDOSCOPY: A DIAGNOSTIC TEST ACCURACY META-ANALYSIS

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Introduction: Baveno criteria safely identify patients who can avoid variceal screening endoscopy: A diagnostic test accuracy meta-analysis.

Aims & Methods: This meta-analysis aimed to quantify the safety and efficacy of these criteria. A systematic search was conducted in nine databases for diagnostic accuracy studies. Eligible papers discussed chronic liver diseases (CLD) and tested Baveno criteria against endoscopic variceal screening. Our main focus was the predictive power of Baveno criteria for varices needing treatment. We calculated pooled spared endoscopy rate, sensitivity, specificity, and negative and positive predictive values with 95% confidence intervals (CIs). Heterogeneity was tested by I2-statistics and explored by subgroup analysis (cACLD) and meta-regression.

Results: The search yielded 27 eligible papers including 6739 CLD cases. Pooled spared endoscopy rate was 26.4% (CI: 21.6-31.5%; I²=95.1%). Pooled negative predictive value proved to be 99.3% (CI: 98.4-99.8%; I²=21.5%). In the subgroup of cACLD, heterogeneity disappeared while negative predictive value was maintained.

Pooled sensitivity was 97.9% (CI: 95.1-99.7%; I²=49.4%), with an I²=9.8% in the subgroup of cACLD. Pooled positive predictive value was 8.1%, (CI: 13.3-23.5%; I²=93.0%). Pooled specificity was 31.0% (CI: 23.5-39.0%; I²=96.5%). Meta-regression proved that body mass index (p=0.042), the percentage of non-alcoholic fatty liver disease (p=0.038), and platelet count (p=0.027) correlated positively with specificity.

Conclusion: The application of Baveno criteria significantly reduces the number of unnecessary variceal screening endoscopies while being safe: patients with liver stiffness < 20 kPa and platelet count >150x10⁹ cells/L carry a very low risk of having varices needing treatment.

Disclosure: Nothing to disclose

P1418 THE ROLE OF LIVER AND SPLEEN STIFFNESS MEASUREMENT IN PREDICTING HEPATIC DECOMPENSATION AFTER HCV ERADICATION WITH DIRECT-ACTING ANTIVIRAL AGENTS THERAPY

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Introduction: To date few evidences are available on the risk of hepatic decompensation (HD) related to portal hypertension (PH) after therapy with new direct-acting antivirals (DAAs) in patients with HCV-related advanced chronic liver disease (ACLD). Furthermore, the predictive role of non-invasive markers of PH, such as liver (LSM) and spleen (SSM) stiffness measurement after DAA therapy is still debated and should be clarified. We previously reported that SSM≥54 kPa was able to predict HD in untreated HCV patients, better than LSM.

Aims & Methods: The aim of this study is to assess the role LSM and SSM in HD prediction after sustained virologic response (SVR).

A cohort study in 146 ACLD patients treated with DAAs and with available LSM and SSM both before and 6 months after end-of treatment (EOT) was performed in our centre. Patients were prospectively followed up from EOT and PH related events were registered. Time-dependent models for HD prediction after SVR were applied to account for changes in LSM and SSM after DAA therapy.

Results: During a follow-up of 33,5 months a total of 20 (13.7%) patients developed at least one episode of HD (among these, 3 presented a second HD event). The first decompensating event was ascites in the majority (17/20, 85%) of patients.

Three patients developed a second episode of HD. Besides HD development, 18 (12.3%) patients developed hepatocellular carcinoma after DAA therapy; 3 (2.1%) developed portal vein thrombosis, 4 (2.7%) underwent high-bleeding risk varices prophylaxes, 3 (2.1%) underwent liver transplantation and 7 (4.8%) patients died.

At the multivariate analysis, previous HD (HR, 8.065; 95%CI 2.806 - 23.180) and SSM≥54 kPa (HR, 4.678; 95%IC 1.307-16.744) were independently associated with a higher risk of HD development after DAAs treatment. Kaplan-Meier curves were estimated and drawn by the SSM cut-off of 54 kPa ; in term of survival, the difference between the two curves was statistically significant (p= 0.0007). The time-dependent model including SSM values at baseline and at 6 months after EOT predicted post-SVR HD development better than the models including LSM and its changes after therapy.

Conclusion: SSM is confirmed to be an accurate surrogate of portal hypertension also after SVR achieved with DAA therapy. Moreover, SSM is able to stratify for the risk of HD development after DAA therapy more accurately than LSM.

References: Nahon P, Layese R, Bourcier V, et al. Incidence of Hepatocellular Carcinoma After Direct Antiviral Therapy for HCV in Patients With Cirrhosis Included in Surveillance Programs. Gastroenterology 2018; Ioannou GN, Feld JJ. What are the Benefits of a Sustained Virologic Response to Direct-acting Antiviral Therapy for HCV Infection? Gastroenterology 2018; Park H, Wang W, Henry L, et al. Impact of all-oral direct-acting antivirals on clinical and economic outcomes in chronic hepatitis C patients in the U.S. Hepatology 2018; Ravaioli F, Colecchia A, Dajti E, et al. Spleen stiffness mirrors changes in portal hypertension after successful interferon-free therapy in chronic-hepatitis C virus patients. World J. Hepatol. 2018;10:731-742. Colecchia A, Colli A, Casazza G, et al. Spleen stiffness measurement can predict clinical complications in compensated HCV-related cirrhosis: A prospective study. J. Hepatol. 2014;60:1158-64.
Disclosure: Nothing to disclose

P1419 ANTICOAGULATION AND LONG TERM PROGNOSIS IN PATIENTS WITH CIRRHOSIS AND PORTAL VEIN THROMBOSIS

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Introduction: Portal vein thrombosis (PVT) is being increasingly recognized in patients with advanced cirrhosis and in those undergoing liver transplantation. Therapy with low molecular weight heparin and vitamin K antagonists has been shown to achieve complete and partial recanalization. Although anticoagulation therapy related bleeding is the most feared complication, studies are showing no increase in the risk of bleeding related to coagulation

Aims & Methods: Clinical, demographic, and biochemical data were retrospectively analyzed from a cohort of 150 consecutive patients with cirrhosis and portal vein thrombosis who presented from 2010 until 2018 in Fundeni Clinical Institute. The patients were followed until death, liver transplantation or last contact. Survival models were built based on univariate and multivariate Cox regression analysis

Results: There were 51% men (77 patients), median age at inclusion 54 years, the main etiology of LC was viral (69%) , 70 patients having VHB or VHB+VHD infection and 34 patients with VHC infection. Portal vein thrombosis was complete in 47 (31%) patients and localised at portal trunk in 72% (109 patients), confluent of the PV 55% (83 patients) and superior mesenteric vein 35%. (56 patients). LT was performed in 22 (14.66%) patients. Therapy with anticoagulants was administered in 80 (53%) patients. Median overall survival from diagnosis of LC was 57.3 months and median survival since diagnosis of PV thrombosis was 16 months. Predictive factors for death identified by univariate Cox regression analysis were: age of the patient, initial lab MELD score at diagnosis of PV thrombosis and after 6 months of follow-up, absence of administration of anticoagulants, progression of PV thrombosis during follow-up, refractory ascites and bleeding complications after PV development. Independent predictors of death identified by multivariate analysis were: increased age of the patient (HR=1.09, p=0.02), increased MELD score at 6 months after diagnosis of PV thrombosis (HR=1.27, p=0.01), occurrence of hemorrhagic complications after PV diagnosis (HR=4.47, p=0.004). There was no statistical association between administration of anticoagulants/type and occurrence of hemorrhagic complications.

Conclusion: Anticoagulant therapy should be administered to all patients with portal vein thrombosis. Lower survival rates should be expected in patients with LC and PV thrombosis that are older at diagnosis and have an accelerated impairment of liver function and portal hypertension after PV development

Disclosure: Nothing to disclose

P1420 WITHDRAWN

P1421 NOVEL RISK SCORE FOR PREDICTION OF HEPATOCELLULAR CARCINOMA AFTER DIRECT ACTING ANTIVIRAL DRUGS

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Introduction: Direct acting antivirals (DAAs) are a novel and completely oral hepatitis C therapy. DAAs are used in most patients being treated for hepatitis C, including those with decompensated cirrhosis. Cirrhotic patients should be closely monitored after treatment. HCC is thought to develop over time as the liver is exposed to inflammation and develops fibrosis.

Aims & Methods:
1. To detect risk factors for HCC in cirrhotic patients after DAAs.
2. To evaluate new score for HCC prediction after DAAs in chronic Hepatitis C.

We retrospectively evaluated 1240 patients treated with DAAs but 124 patients who had fibroscan in virology unit, National Liver Institute, Menoufia University after informed written consent. Pre-treatment laboratory data were collected after multivariate analysis to data we found risk factors for HCC with DAAs (High fibroscan, Diabetus mellitus, low paltates and older age) this data show in novel score to detect HCC (Age >60 equal points 2 or younger 1, Fibroscan > 18.5 kPa equal 2 or other equal 1, presence of DM equal 2 or other equal 1 and paltates < 100 Iu/ml equal 2) and calculated from (4-8 points).

Results: All patients who developed HCC was group (I) (35 patients; 0.028%) and who did not develop HCC group (II), Risk score was calculated from 124 patients who had fibroscan at base line assesment with AUC (0.90) and significant in table (1); after Demographic, clinical and laboratory data were compared between group developed HCC and not developed HCC, Multivariate models showed that Age (Age >60 years) (OR 8.9), CI (2-40.8), presence of DM (OR 8.9) CI(3.1 - 26.1), Fibroscan (OR 37) CI (5.6-257), Platlates (OR 3.2)CI(0.99 - 1.1).

Test Result Variable	Area	Std. Error	Asymptotic Significance	Asymptotic 95% Confidence Interval
Novel score	0.906	0.027	0.000	Lower Bound (0.853); Upper Bound(0.959).

[Novel score Area Under the Curve :]

Conclusion:
1. Novel risk score for HCC after DAAs with cut off level (6) with sensitivity (80%) and specificity (85%) can predict HCC with DAAs.
2. Higher LSM by fibroscan, older age, DM and lower paltates are risk factors for HCC after HCV eradication by DAAs.

Disclosure: Nothing to disclose

P1422 NON-INVASIVE PREDICTION OF HIGH-RISK VARICES IN PATIENTS WITH PRIMARY BILIARY CHOLANGITIS BY TWO-DIMENSIONAL SHEAR WAVE ELASTOGRAPHY

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Introduction: Variceal bleeding is one of the most fatal complication in patients with liver cirrhosis. A screening esophagogastroduodenoscopy (EGD) is recommended in all patients with cirrhosis to detect those patients at risk of variceal bleeding.

However, with the progressive introduction of non-invasive methods for the diagnosis of cirrhosis, an increasing number of patients are diagnosed at an earlier, fully compensated stage of the disease, resulting in a large number of unnecessary screening endoscopies [1]. Thus, there is an urgent need for noninvasive screening methods for varices in patients with chronic liver disease.

Two-dimensional shear wave elastography (2D-SWE) is a promising new type of shear wave-based ultrasound technique for measuring liver stiffness. The shear waves are generated directly within the tissue, allowing measuring stiffness also in patients with ascites. The liver stiffness values can be obtained on the basis of anatomic information to control major measurement bias [2]. This method has equal or superior diagnostic accuracy for the staging of liver fibrosis and portal hypertension in patients with chronic liver disease [3, 4].

Primary biliary cholangitis (PBC) is one of cholestatic autoimmune liver diseases, rare etiology of chronic liver disease. However, there was also no coincident cut-off value for predicting high varices, and only several studies about SWE evaluating the varices in compensated liver cirrhosis, and all of studies with all etiology of cirrhosis and small sample sizes [5, 6].

The aim of this study was to investigate the diagnostic performance of 2D-SWE for predicting high-risk varices in patients with PBC related chronic liver disease.

Aims & Methods: To investigate the diagnostic performance of 2D-SWE for predicting high-risk varices in patients with PBC related chronic liver disease. Clinical data from 182 patients with PBC related chronic liver disease who underwent 2D-SWE and endoscopy were collected consecutively. Liver stiffness (LS) was measured by 2D-SWE. The time interval between 2D-SWE and endoscopy examination no more than 3 months. Comparisons of the accuracy of prediction between groups were made by areas under the receiver operating characteristic curves (AUROCs).

Results: The optimal cutoff value for predicting high-risk varices was 13.65 kPa, AUROC of LS was 0.886(95% CI: 0.837-0.935), sensitivity was 0.759 and specificity was 0.898. The optimal cutoff value for predicting high-risk varices in PBC patients without ascites was 10.2 kPa, AUROC of LS was 0.887 (95% CI: 0.816-0.959), sensitivity and specificity were 0.957 and 0.721, respectively.

Conclusion: LS of 2D-SWE is reliable predictor for predicting presence of high-risk varices in patients with PBC related chronic liver disease. In addition, SWE is a reliable noninvasive tool for predicting esophageal varices with ascites.

References: 1. de Franchis, R., Evolving consensus in portal hypertension. Report of the Baveno IV consensus workshop on methodology of diagnosis and therapy in portal hypertension. J Hepatol, 2005. 43(1): p. 167-76. 2. Muller, M., et al., Quantitative viscoelasticity mapping of human liver using supersonic shear imaging: preliminary in vivo feasibility study. Ultrasound Med Biol, 2009. 35(2): p. 219-29. 3. Elkrief, L., et al., Prospective comparison of spleen and liver stiffness by using shear-wave and transient elastography for detection of portal hypertension in cirrhosis. Radiology, 2015. 275(2): p. 589-98. 4. Paul, S.B., et al., Assessment of liver fibrosis in chronic hepatitis: comparison of shear wave elastography and transient elastography. Abdom Radiol (NY), 2017. 42(12): p. 2864-2873. 5. Petzold, G., et al., Evaluation of liver stiffness by 2D-SWE in combination with non-invasive parameters as predictors for esophageal varices in patients with advanced chronic liver disease. Scand J Gastroenterol, 2019: p. 1-8. 6. Kim, T.Y., et al., Diagnostic Performance of Shear Wave Elastography for Predicting Esophageal Varices in Patients With Compensated Liver Cirrhosis. J Ultrasound Med, 2016. 35(7): p. 1373-81.

Disclosure: Nothing to disclose

P1423 FUNCTIONAL LIVER RESERVE - A PREDICTIVE FACTOR FOR PORTAL VEIN THROMBOSIS IN PATIENTS WITH LIVER CIRRHOSIS- A SINGLE CENTER EXPERIENCE

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Introduction: In liver cirrhosis, especially in advanced stages, portal vein thrombosis(PVT) is one of the most common complications and its prevalence increases with disease severity. PVT is mainly due to hypercoagulable state and altered dynamic of blood flow in the portal vein. Studies reported a prevalence of 10-28% in cirrhotic patients, excluding those with HCC. Association between liver cirrhosis and malignancies, especially HCC, may increase PVT prevalence up to 44%.

Aims & Methods: In our study we aimed to evaluate the prevalence of portal vein thrombosis in a cohort of patients with liver cirrhosis based on Child Pugh score (CPS). We retrospectively analyzed a cohort of pa-

tients with livercirrhosis in a tertiary gastroenterology referral center from North-Eastern Romania, between January 1st 2017 and December 31st 2018. All patients with presumption of thrombosis wereevaluated by abdominal ultrasound and confirmed by CT scan. Were excluded from patientswith thrombophilia.

Results: The study included 2734 cirrhotic patients with mean age 56,7 ± 5,3 years,predominantly female (1558 - 57%). Of the total number, 143 (5.23%) patients presented PVT, of which 21 (14.68%) patients with acute PVT and 122 (85.31%) patients with chronic PVT. The main clinical presentation at diagnosis were variably: upper digestive haemorrhage in 26 (18.18%) patients, ascitic decompensation in 80 (55.94%) patients, abdominal pain in 25(17.48%) patients and 12 (8.39%) patients were asymptomatic. The commonest causes of cirrhosis and PVT were alcoholic liver disease (30, 20.97%), viral hepatitis B±D (13, 9.09%)viral hepatitis C (74, 51.74%), malignant PVT (19, 13.28%) and other causes (7, 4.89%). Of the patients included in study, 12 (8.39%) Child-Pugh class A, 81 (56.64%) class B and 50(34.96%) class C cirrhotic patients. PVT prevalence is 2.1% in compensated liver cirrhosis and up to 23% in decompensated liver cirrhosis. Association between liver cirrhosis and malignancies, especially HCC, increased PVT prevalence to 42%.

Conclusion: Child-Pugh score was higher in patients with PVT, which confirms that the prevalence of PVT increases with the severity of cirrhosis liver. Thus, PVT prevalence is low in compensated liver cirrhosis and is increased in decompensated liver cirrhosis. In addition, in patients with liver cirrhosis and HCC, the PVT prevalence was higher, data confirmed by the literature.

Disclosure: Nothing to disclose

P1424 EPIDEMIOLOGICAL PROFILE OF CIRRHOTIC PATIENTS WITH DIGESTIVE HEMORRHAGE

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Introduction: Digestive hemorrhages (DH) represent high morbidity and mortality clinical emergency[1]. They can manifest in the form of hematemesis, melena, enterorrhagia and hematochezia[2]. The main cause of DH non related to digestive tract affections is the hypertension of the portal system. This clinical syndrome is frequent in the liver cirrhosis and the growth of esophageal varices (EV) is one of its main complications, with predominance in 60% and 80% of the cases[1]. Hemorrhage by rupture of EV constitutes a bad prognosis in cirrhosis, with mortality between 17% and 57%[1]. For proper management, endoscopic treatment is indicated, through sclerotherapy and elastic ligature of the esophageal varices[3].

Aims & Methods: To investigate the clinical and demographic profile of the cirrhosis patient hospitalized with DH in a university hospital in the period from September 2017 to January 2019. This is a retrospective study, made through records' data collection, of 772 patients attended in the Digestive Hemorrhage Department of the Hospital Universitário Evangélico Mackenzie in this period. In September 2017, this hospital became a unique reference for acute cases of GIB sent by the Public Health System in Curitiba (about 3.5 million people). A descriptive and statistical analysis of prevalence by age, sex, transfusion, decease, symptomatology of admission, smoking, alcoholism, medicine, comorbidities, clinical-surgical conduct, endoscopic diagnosis and endoscopic treatment was made.

Results: From the 772 patients with gastrointestinal bleeding, 139 presented with cirrhosis diagnosed. The main etiology was alcoholism (76.2% patients), followed by hepatitis C and hepatitis B. The most prevalent gender was male (107 patients, 77%). The mean age was 55 years old. The age range compromised was between 41-50 years old (29.5%). 43 patients (30.9%) were deceased throughout the internment, 30 men and 13 women. The mortality rate was higher between women, 40.6% against 28% of the men. Red blood cells transfusion was necessary in 81 of the patients (58.2%). The most common entry symptom was hematemesis, with 123 cases (88.4%) and the most common association was hematemesis and melena with 64 cases (46%). The medium level of hemoglobin at admission was 8,9 g/dL (3.2-17.6). Among patients, 76.2% were alcohol-

ism and 28.7% patients were tobacco users. The most frequent comorbidity was systemic arterial hypertension (26.6%) and medication most associated with digestive bleeding was the usage of anti-inflammatory, 9 cases (6.4%). At the endoscopic exam, the most frequent finding was esophageal varices, 71/139 (51%) of which 24 (33.8%) needed endoscopic treatment by elastic ligature. Besides EV, 35 patients (25.17%) presented hypertensive gastropathy and 8 manifested gastric varices (5.75%). Ten patients had liver transplants and 3 (33.3%) dead.

Conclusion: The profile of the patients with hepatic disease and cirrhosis admitted for digestive hemorrhages is represented by a male patient, above 55 years, alcoholics and with high mortality risk. The main symptom observed is hematemesis and presenting esophageal varices.

References: 1. JASMINS, Luís. Rastreio de varizes esofágicas em doentes com hipertensão portal: Haverá lugar para um método não endoscópico? J Port Gastrenterol., Lisboa, v. 19, n. 1, p. 10-11, jan. 2012. Available from: http://www.scielo.mec.pt/pdf/ge/v19n1/v19n1a02.pdf. 2. OLIVEIRA, Mário Ramos de; FANGANIELLO, Mário. Hemorragias de causas digestivas: aspectos fisiopatológicos e clínicos. Revista de Medicina, São Paulo, v.44, n. 4, p. 231-245, nov. 1960. Available from: https://www.revistas.usp.br/revistadc/article/download/57800/60851/ 3. Erwin Biecker, "Gastrointestinal Bleeding in Cirrhotic Patients with Portal Hypertension," ISRN Hepatology, vol. 2013, Article ID 541836, 20 pages, 2013. Available from: https://doi.org/10.1155/2013/541836.

Disclosure: Nothing to disclose

P1425 PREDICTIVE FACTORS FOR EARLY READMISSION AFTER RESOLUTION OF A FIRST BACTERIAL INFECTION IN CIRRHOTIC PATIENTS

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Introduction: Bacterial infections (BI), which are frequent and late complications of cirrhosis, increase the frequency of hospitalizations, morbidity and mortality.

Aims & Methods: Our objective was to determine the prevalence of BI and to identify predictive factors for readmission within 30 days for all causes in cirrhotic patients treated for first BI.

We performed a retrospective analysis of data from consecutive cirrhotic patients hospitalized for an IB, recruited from January 2010 to December 2017.

Results: A total of 252 cirrhotic patients were included. Eighty-one (32,1%) of them were hospitalized for an IB with average age of 61,6 years [37-87] and sex-ratio of 0,39. The etiology of cirrhosis was dominated by viral origin in 47% of cases. The infection was Community-Acquired in 70,3% and nosocomial in 29,6%. These consisted mainly of urinary tract infection (49.4%), respiratory infection (14.1%) and ascitic fluid infection (15,1%) with two cases of ascitic fluid tuberculation. *Escherichia coli* (E. coli) was the most common germ (52%). E.coli ESBL (extended spectrum beta-lactamases) was the predominant germ in nosocomial infections (35,7%). The median hospital stay was 31 days [6-90]. sixteen patients (19,7%) died during hospitalization. During follow-up, 11 patients (13,5%) were readmitted within 30 days of discharge. Predictive factors of early readmission in univariate analysis were: anemia (p=0,02), hepatocellular carcinoma (HCC) (p=0,01), a history of diabetes (p< 0,05), undernutrition (p< 0,05). In multivariate analysis, only anemia and HCC were independent predictors of early readmission.

Conclusion: In our study, BI were dominated by E.coli urinary tract infections. These infections may represent a relatively higher risk of early readmission with anemia and HCC as predictive factors.

Disclosure: Nothing to disclose

P1426 ASSESSMENT OF THE PROGNOSTIC IMPACT OF KIDNEY FAILURE ESTIMATED BY THE ROYAL FREE HOSPITAL CIRRHOSIS GLOMERULAR FILTRATION RATE (RFHCGFR) IN CASE OF VIRAL CIRRHOSIS C

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Introduction: The occurrence of renal failure during viral cirrhosis is frequently associated with a poor prognosis. Since most glomerular filtration rate (GFR) formulas in these patients are often inaccurate due to the inclusion of serum creatinine, a new more specific formula (RFHCGFR) has been proposed.

Aims & Methods: Our objective was to evaluate the prognostic impact of kidney failure estimated by RFHCGFR during viral cirrhosis C.

We performed a retrospective analysis of data from consecutive patients followed in our department for viral cirrhosis C recruited from January 2010 to December 2017. GFR was estimated by MDRD and RFHCGFR. Survival associated with GFR was estimated by Kaplan Meier method using the Log-rank.

Results: A total of 112 patients were included with an average age of 62,9 years [43-83] and sex-ratio of 0,3. Patients were classified by the Child-Pugh (CP) score into CP A in 42,8%, CP B in 41,9% and CP C in 15,1% of cases. The median GFR was 96,3 ml/min evaluated by MDRD and 72.3 ml/min/1,73^2 by RFHCGFR. GFR estimated by RFHCGFR was significantly correlated to GFR estimated by MDRD (p < 0.0001). Using RFHCGFR, the survival at two years was 73,3% in patients with GFR>30 ml/min/1,73^2 and 5,2% in patients with GFR< 30 ml/min/1,73^2 (p=0,02). For the MDRD, there was no difference in survival between patients with GFR>30 ml/min and those with GFR< 30 ml/min (p=0,09). A significant correlation was noted between kidney failure estimated by RFHCGFR and ascitic decompensation (p=0.005), bacterial infections (p=0,05) and early readmission within 30 days (p=0,03).

Conclusion: In our study, renal failure estimated by RFHCGFR was a prognostic factor correlated with survival, ascitic decompensation, bacterial infections and early readmission.

Disclosure: Nothing to disclose

P1427 CIRRHOSIS ASSOCIATED WITH WORSE OUTCOMES IN PATIENTS UNDERGOING BARIATRIC SURGERY

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Introduction: Obesity is directly linked to non-alcoholic steatohepatitis (NASH). Bariatric surgery (BS) has emerged as a successful treatment option for obesity, and used as a way to decrease the BMI and positively influence a patient's NASH. Cirrhosis, a complication of NASH, confers an increased risk for a broad range of surgical interventions. Smaller studies have shown that BS is safe in compensated (Child A) cirrhosis. However, large studies examining bariatric surgical outcomes in patients with cirrhosis with and without PVT lack.

Aims & Methods: The aim of this study is to determine the inpatient outcomes of non-transplant patients with liver cirrhosis undergoing BS. Case-control study using the 2012-2016 NIS, the largest public inpatient database in the US. All patients with ICD9-10CM procedural codes for BS were included. Patients with history of liver transplant (LT) and those who underwent LT during that admission were excluded. The cohort was stratified into two groups: 1) cirrhosis without PVT and 2) cirrhosis with PVT. These groups were compared to non-cirrhotic patients undergoing BS. The primary outcome was determining the odds of inpatient mortality in the two cohorts. Secondary outcomes included determining inpatient morbidity, resource utilization, hospital length of stay (LOS), and inflation-

adjusted total hospital costs and charges. Multivariate regression analyses were used to adjust for age, gender, Charlson Comorbidity Index, income in patient zip code, hospital region, location, size and teaching status.

Results: 965,595 patients underwent BS in the study period, of which 6,470 had cirrhosis without PVT and 160 had cirrhosis with coexisting PVT. The mean age for patients with cirrhosis and no PVT was 58.8 years, while the mean age for patients with cirrhosis and PVT was 59.0 years (53% and 31% were female, respectively). For the primary outcome, patients with cirrhosis and no PVT had increased inpatient mortality odds of 4.03 (p< 0.01), while patients with cirrhosis and PVT had inpatient mortality odds of 13.86 when compared to patients undergoing BS without cirrhosis. For the secondary outcomes, patients with cirrhosis with and without PVT displayed increased odds of shock, ICU stay, AKI, and multiorgan failure. In addition, both cohorts displayed significantly higher additional hospital costs. However only patients with cirrhosis and PVT displayed higher total hospitalization charges and LOS compared to patients without cirrhosis who underwent BS (Table 1).

Variable	Cirrhosis without PVT	Cirrhosis with PVT
Mortality	4.03 (3.24,5.03) <0.01	13.86 (5.44,35.32) <0.01
Shock	2.56 (2.10,3.12) <0.01	9.02 (3.64,22.32) <0.01
ICU	2.25 (1.91,2.65) <0.01	7.81 (3.56,17.16) <0.01
AKI	1.71 (1.46,2.02) <0.01	6.74 (3.07,14.83) <0.01
Multi-organ failure	1.93 (1.67,2.23) <0.01	5.81 (2.66,12.71) <0.01
Additional Adjusted Costs	$2,549 (368,4729) 0.02	$43,334 (24637,62035) <0.01
Additional Adjusted Charges	$8,826 (-742,18394) 0.07	$182,059 (67762,296357) <0.01
Additional Adjusted LOS (days)	0.1 (-0.5,0.7) 0.76	13.3 (7.7,19.0) <0.01

[Adjusted odds ratio and additional adjusted means in patients with cirrhosis and no PVT and cirrhosis with PVT undergoing BS.]

Conclusion: Patients with cirrhosis with and without PVT had higher associated inpatient mortality and morbidity odds during the admission for bariatric surgery compared to patients without cirrhosis. Patients with cirrhosis and PVT had higher mortality and morbidity odds than patients with cirrhosis alone. This reflects the risk that cirrhosis in itself confers to patients undergoing bariatric surgery. Thus, this should continue to be an important consideration in patients with cirrhosis evaluated for bariatric surgery. Prospective studies are required to better understand the impact of cirrhosis, both compensated and decompensated, on bariatric surgical outcomes.

Disclosure: Nothing to disclose

P1428 EVIDENCE-BASED PROTOCOL FOR DIAGNOSIS AND TREATMENT IS INDEPENDENTLY ASSOCIATED WITH LOWER MORTALITY IN PATIENTS WITH HEPATORENAL SYNDROME

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Introduction: Hepatorenal syndrome (HRS) is one of the deadliest complications of cirrhosis and carries a high mortality. It is treated with an association of terlipressin plus albumin. This treatment is very costly, and it is paramount to choose wisely those patients who benefit from it. Our hospital had an evidence-based protocol for treatment of HRS instituted as standard-of-care in 2013.

Aims & Methods:
Purpose: Analyze variables associated to survival in patients diagnosed with HRS.
Study design: Historical cohort.
Methods: A search for every patient who received terlipressin in our hospital from 2010 to 2016 was performed, ranging from three years prior and after the institution of the protocol. Every chart was reviewed in order to determine the diagnosis of cirrhosis and HRS. The data in these charts was reviewed and multiple variables were collected. A cox-regression multivariate analysis was performed to determine mortality.

Results: It was included 46 patients who were diagnosed with HRS, 20 pre-protocol and 26 post-protocol. Mean age was 58 years-old and 80% were male. Most common cause of cirrhosis was alcohol abuse (76%). Respectively, mortality for 30-day, 90-day and 365-day was 75%, 89% and 89% for the pre-protocol period and 61%, 69% and 80% for the post-protocol period. In multivariate analysis, AST > 40, pre-protocol period and Child-Pugh score were associated with higher 30-day and 90-day overall mortality. Also, the total mean dose of terlipressin and albumin used per patient reduced with the institution of the protocol, reducing from 27 to 22 mg of terlipressin and from 236 to 144 g of albumin per patient. This was not associated with higher mortality.

Conclusion: The use of a evidence-based protocol in the treatment of HRS translated in a higher survival. Also, it was associated with lower drug use.

Disclosure: Nothing to disclose

P1429 FACTORS ASSOCIATED WITH AN INCREASE OF LIVER STIFFNESS VALUES IN PATIENTS WITH HCV HEPATITIS WITH SUSTAINED VIROLOGIC RESPONSE

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Introduction: Several studies demonstrated a significant decrease in livers stiffness (LS) values in most, but not all patients following sustained virologic response (SVR).

Aims & Methods: The purpose of this study was to highlight the factors associated with an increase in LS following SVR.
The study included 254 patients with genotype HCV hepatitis who had a SVR following DAA treatment. All were assessed by transient elastography (TE) at the start of treatment and 12 weeks after the end of treatment, when SVR was assessed. In each patient, 10 valid LS measurements were obtained either with M or XL probes. Reliable LSM were defined as median value of 10 measurements with Interquartile range/median (IQR/M)≤30%. Demographic, biologic (including FibroMax), ultrasonographic data were collected and analyzed.

Results: Of the 259 patients evaluated, 47 (22.4%) patients had elevated LS values at SVR12 as compared to start point, but in only 27 all data was available, so the final analysis included 27 patients. In univariate analysis only obesity and elevated transaminases at SVR12 were associated with LS increase at SVR12 (p=0.0007 and p=0.0008, respectively). In multivariate analysis, the presence of steatosis on ultrasound, obesity and elevated transaminases were independently associated to LS increase at SVR12.

Conclusion: Obesity, cytolysis and steatosis were associated with LS increase after SVR in patients with HCV hepatitis treated with DAA.

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P1430 IMPACT OF GENETIC POLYMORPHISMS OF INTERLEUKIN 28B AND ICAM-1 ON RESPONSE TO DIRECT ANTIVIRAL TREATMENT AMONG CHRONIC HEPATITIS C EGYPTIAN PATIENTS

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Introduction: Complete eradication of HCV virus is one of the most important goals for antiviral treatment research. New direct antiviral agent (DAA) therapy has revolutionized for HCV; with higher efficacy and safety than peg IFN-α/RBV. However, easy access to DAAs, availability of reliable HCV prognostic tests, and affordable costs still remain important goals that must be reached to globally eliminate hepatitis C. Genotyping of interleukin-28B (IL28B) and intra-cellular adhesion molecule-1 (ICAM-1) single nucleotide polymorphisms (SNPs) may be helpful to predict response to treatment of HCV infected patients; especially when double or triple therapy can be used. Thus they could have a role in predicting early virological response to DAA.

Aims & Methods:

The aim of the current study was to investigate the impact of IL-28B rs860, rs917 and ICAM-1 rs1437 single nucleotide polymorphisms on response to treatment with sofosbuvir + Daclatsvir ± Ribavirin, among chronic hepatitis C Egyptian patients.

Subjects and Methods: Genomic DNA was extracted from a total of 120 subjects; including 40 healthy volunteers, 80 chronic HCV patients who were subdivided into responder and non-responder to direct antiviral drugs. IL-28B and ICAM-1 SNP was assessed by 5' nuclease assay with a TaqMan MGB (minor groove binder) probe using *StepOne*™ Real-Time PCR System (Applied Biosystems, Life Technologies). Liver functions' tests, Anti-HCV antibodies, quantification of HCV-RNA and HCV Sequence analysis were done for all subjects under the study.

Results: AST and ALT values showed statistically significant increase among non- responder HCV patients compared to the other studied groups (P=0.001*) while serum albumin and ALK levels did not show any statistically significant differences (P=0.173 and 0.076, respectively). All HCV patients were positive for anti-HCV antibodies. All samples of HCV patients were successfully genotyped and sub-genotyped; 72 patients (90%) have HCV genotype 4a, while the remaining 8 cases (10%) have genotype 4l. The frequencies of IL 28B rs860 T and ICAM-1 rs 437 C alleles were higher among HCV patients, either responders or non-responders, when compared to the control group but statistically insignificant (P= 0.280, 0.305, respectively). On the other hand, IL 28B rs917 G allele is more frequent among healthy controls; suggesting their protective role against HCV infection (P= 0.045*). Regarding relation between IL-28B and ICAM-1 polymorphism and response to treatment with DAA, HCV patients with IL-28B rs917 GG alleles showed an early viral responder compared to those carrying TT alleles; these differences were found to be statistically significant (P=0.050*). Also, ICAM-1 rs437 CT alleles were more frequent among responders and control groups but statistically insignificant. On the other hand, for IL 28B rs860 HCV patients with either CT or TT alleles did not show any statistically significant differences among all the studied groups.

Conclusion: IL-28Brs917 represents protective genotypes as HCV infected patients have a statistically significant lower prevalence of IL-28Brs917 GG genotype when compared to uninfected individuals. Considering response to DAA treatment, the higher frequency of ICAM-1 rs437 CT genotypes observed among responder HCV patients elucidate that ICAM-1 rs437 genotyping could be a useful independent tool for predicting outcome of treatment with DAA.

References: Helaly GF, Elsheredy AG, Bedewy ES and Attia NM. Sequence Heterogeneity in the Core and NS5A Region of Hepatitis C Virus (HCV) and IL-28B Polymorphisms in Predicting Treatment Response among Chronic HCV Genotype 4 Infected Egyptian Patients. Int.J.Curr.Microbiol.App.Sci (2017) 6(7): 2382-98. Das D, Pandya M. Recent Advancement of Direct-acting Antiviral Agents (DAAs)in Hepatitis C Therapy. Mini Rev Med Chem.

2018;18(7):584-596. Spengler U. Direct antiviral agents (DAAs) – A new age in the treatment of hepatitis C virus infection. Pharmacol Ther. 2018 Mar;183:118-26. Sakhaee F, Ghazanfari M, Vaziri F, Jamnani FR, Davari M, Gharibzadeh S, et al. The impact of genetic variation in IL28B, IFNL4 and HLA genes on treatment responses against chronic hepatitis C virus infection. Infect Genet Evol. 2017 Oct;54:330-7. Amany A. Ghazy*, Nour M. El-Etreby. Relevance of HLA-DP/DQ and ICAM-1 SNPs among ovarian cancer patients. Front in Immunology 2016 May; 12:202.
Disclosure: Nothing to disclose

P1431 MINIMAL RISK OF HBV REACTIVATION IN RESOLVED HBV-INFECTED PATIENTS DURING IMMUNOSUPPRESSIVE THERAPY

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Introduction: Hepatitis B virus reactivation (HBVr) during immunosuppressive drug therapy (ISDT) is a growing concern; however, prospective long-term follow-up studies are rare.

Aims & Methods: In this cross-sectional, prospective study, we analyzed two groups of patients showing hepatitis surface antibody (anti-HBs) positivity/HBV surface antigen (HBsAg) negativity among 225 patients receiving immunosuppressive therapy and 157 patients receiving antineoplastic therapy in our tertiary care center between January 2016 and January 2018. We also analyzed the associated factors and determined the necessity of prophylactic antiviral treatment. Baseline hepatitis serology, PCR measurements, liver alanine transaminase (ALT) levels and the international normalized ratio (INR) were recorded. Routine monthly follow-up of patients consisted of a complete physical examination and analyses of liver enzymes, the INR and HBV serology. According to the national healthcare policy, HBV-DNA levels were measured by PCR every three months. Patients who were HBsAg (+), HBV-DNA (+), anti-HCV (+), anti-HDV (+) or anti-HBc (-) were excluded. Because HBVr typically occurs during the first six months of ISDT, patients who discontinued treatment because of HBV-unrelated reasons and/or died before the six-month follow-up threshold were excluded and patients with a history of treatment with interferon (IFN) or antiviral drugs were excluded. HBVr criteria defined as: loss of HBV immune control in HBsAg (-) / anti-HBc (+) patients (i) receiving ISDT for a concomitant medical condition; (ii) a rise in HBV-DNA compared to baseline; and (iii) reverse seroconversion (seroreversion) from HBsAg-negative to HBsAg-positive for HBsAg (-) anti-HBc (+). To examine the association between anti-HBs titers and HBVr, anti-HBs (+) patients were divided into three subgroups: (i) anti-HBs > 1000 mIU/mL (Group A), (ii) anti-HBs between 100 and 1,000 mIU/mL (Group B) and anti-HBs between 0 and 100 mIU/mL (Group C).

Results: Among the 579 patients recruited to this study, 144 were excluded according to the above-mentioned criteria (74 patients did not meet the criteria, and 70 patients were either lost to follow-up, discontinued the treatment or died before the 6-month threshold); thus, 435 patients were included The mean follow-up time was 25.8 months. We did not detect any cases of HBVr, even among 86 patients receiving rituximab (49 of which are anti-HBc positive only) and 132 patients receiving tumor necrosis factor inhibitors (84 of which are anti-HBs positive only). Furthermore, we did not find an association between anti-HBs changes and HBVr, although a role for anti-HBs in reactivation has previously been suggested. A subgroup analysis showed that during the study period, the antibody levels did not change in Group A, changed non-significantly in Group B (p=0.25) and significantly declined in Group C (p=0.002). However, despite the marked decline in antibody levels in Group C, we did not observe any cases of HBVr. Changes in the mean ALT and INR levels were not significant (p=0.36 and p=0.54, respectively).

Conclusion: The risk of reactivation of HBV infection by immunosuppressive and antineoplastic therapy is lower than that suspected in published anecdotal reports.

Disclosure: Nothing to disclose

P1432 NON INVASIVE ASSESSMENT OF PORTAL HYPERTENSION IN PATIENTS WITH ADVANCED FIBROSIS DUE TO HEPATITIS C AFTER TREATMENT WITH DIRECT ACTION ANTIVIRALS

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Introduction: Patients with advanced hepatic fibrosis due to chronic hepatitis C (HCV) receive successful treatment for hepatitis with direct-acting antivirals (DAA); however, many of them are still at risk of decompensation, mainly at the expense of portal hypertension. There are data that reflect a lower risk of decompensation in those who achieve sustained viral response (SVR), although they are scarce and in the short term.

Aims & Methods: We want to make a comparison using an innocuous and widely available indirect method such as abdominal ultrasound of the most accessible parameters of portal hypertension before and after treatment with DAA in patients who achieve SVR.

Retrospective study of patients with HCV hepatitis and F4 fibrosis treated in our center between 2015 and 2017. Data was collected in 2019. The diameter of the portal vein (PVD), the superior mesenteric and splenic veins diameter (SMVD, SVD), the bipolar diameter of the spleen (BPSD), and the presence of ascites is compared before (in the previous 12 months) and after the end of treatment at the first, second and third year. The variables PVD, SMVD, SVD, BPSD and ascites are collected as qualitative variables (normal vs. pathological); in the case of pathological PVD and BPSD (≥ 13mm and ≥ 120mm respectively), they are expressed as quantitative variables in millimeters.

Results: There is a decrease in the incidence of splenomegaly after treatment so that those with enlarged BPSD at the start of treatment normalized it by 21.2% in the first year (p = 0.023), 28.2% in the second (p = 0.001), and 30.8% in the third (p = 0.000), so that the prevalence of splenomegaly changes from 46.45% to 40.43% after one year, 37.42% after the second, and 43.63% after the third. Among those with pathological BPSD, a statistically significant decrease of 4.22 (1.50-7.21, 95% CI) mm was observed at the first year (p = 0.006), 5.57 (2.80-8.55, 95% CI) at the second year (p = 0.001), and 6.61 (2.60-10.63, 95% CI) mm at the third year (p = 0.002). With regard to the presence of ascites, among the 10 patients who presented it at the beginning of treatment, only 2 presented it after one year (with 2 new patients who did not present it before), although this difference did not reach statistical significance (p = 0.109). By the second year, only 1 patient of the initially decompensated remained this way, and none of the patients in the third year (with a total of 3 decompensated patients who were not decompensated at the beginning of the treatment in both the second and the third year), these differences are not significant (p = 0.227, and 0.727 respectively).

With respect to PVD, there are no differences before or after treatment, nor are there any differences with SMVD or SVD. Among those with a pathological PVD, its quantitative measurement does not show improvement in the first, second or third year.

Conclusion: An improvement in BPSD (splenomegaly) is observed. This could translate an improvement in the hepatic venous pressure gradient (HVPG) with a lower risk of decompensation in these patients, as an indirect parameter of portal hypertension and predictor of the existence of esophageal varices in cirrhosis. We observed for the first time that this change is maintained in the long term (3 years), which could translate changes in the hepatic architecture with regression of fibrosis.

Likewise, the data seem to suggest a lower incidence of ascites, without being statistically significant. However, other sonographic parameters such as PVD, SMVD, or SVD show no improvement.

References: Thrift AP, El-Serag HB, Kanwal F. Global epidemiology and burden of HCV infection and HCV-related disease. Nat Rev Gastroenterol Hepatol. 2017;14:122- 132. van der Meer AJ, Veldt BJ, Feld JJ, Wedemeyer H, Dufour JF, Lammert F, Duarte-Rojo A, Heathcote EJ, Manns MP, Kuske L, Zeuzem S, Hofmann WP, de Knegt RJ, Hansen BE, Janssen HL. Association between sustained virological response and all-cause mortality among patients with chronic hepatitis C and advanced hepatic fibrosis. JAMA 2012; 308: 2584-2593 Simmons B, Saleem J, Heath K, Cooke GS, Hill A. Long-Term Treatment Outcomes of Patients Infected With Hepatitis C Virus: A Systematic Review and Meta-analysis of the Survival Benefit of Achieving a Sustained Virological Response. Clin Infect Dis 2015;61: 730-740 Libânio D, Marinho RT. Impact of hepatitis C oral therapy in portal hypertension. World J Gastroenterol. 2017;23(26):4669-4674. doi:10.3748/wjg.v23.i26.4669
Disclosure: Nothing to disclose

P1433 GLECAPREVIR/PIBRENTASVIR FOR CHRONIC HEPATITIS C IN LARGE REAL WORLD EXPERIENCE STUDY

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Introduction: Aim was to follow patients profile and effectiveness of chronic hepatitis C (CHC) treatment with glecaprevir/pibrentasvir (GP) a pangenotypic regimen in real world settings.

Aims & Methods: Patients treated with GP were selected from 10 161 included in the EpiTer2 database of treated for CHC between 2015 and 2018. Analysis was carried out in 381 patients which started therapy with GP in 2018, that was compared to data from general population of treated in corresponding period (n=3938).

Results: Gender distribution (51% females) and age (49±14 years) of patients treated with GP were similar to general population. Majority of patients on GP were infected with genotype 1b (51%) or 3 (39%) and these proportions were different than in general population (78% and 13% respectively). Majority of GP patients (69%) were treatment naïve, but it was lower than in general population (85%). Proportions of cirrhotics (14%), decompensation history (0.5%) and Child-Pugh >A (1.2%) in patients treated with GP were similar to general population (15%, 0.8%, 1.1% respectively). Majority of patients received 8 weeks regimen (65%), followed by 12 weeks (28%). Since there were three treatment failures, sustained virologic response rates available in 111 patients for intent to treat and in 110 per protocol analysis, were 96% and 97% respectively, that was similar to general population data. Much more subpopulation analysis, including cirrhotics, genotype 3 infected and failures to previous therapies will be available in mid 2019 for possible presentation at the meeting.

Conclusion: Glecaprevir/pibrentasvir compared to other regimens, was administered more frequently to patients infected with genotype 3 and treatment experienced. Effectiveness of this novel regimen in this real world study reached up to 97%.

Disclosure: Robert Flisiak, Dorota Zarębska-Michaluk, Ewa Janczewska, Krzysztof Tomasiewicz, Anna Piekarska received speakers honoraria from AbbVie, MSD, Gilead, Robert Flisiak, Krzysztof Tomasiewicz, Anna Piekarska were advisors to AbbVie, MSD, Gilead. Robert Flisiak received research grant from AbbVie, Arbutus, MSD, Gilead, Roche Krzysztof Tomasiewicz received research grant from BMS Rafał Krygier - nothing to disclose

P1434 HCVKID-STUDY: COMPARISON FOR PREVALENCE OF EARLY RENAL FINDINGS AMONG HEPATITIS-C POSITIVE AND NEGATIVE POPULATIONS USING URINE AND PLASMA BIOMARKERS

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Introduction: Hepatitis C (HCV) infection is known to cause extrahepatic kidney manifestations, which are typically discovered at a late stage. HCV-related nephropathy may show different histopathologic patterns, as both glomerular and tubulointerstitial damage have been described in the literature. Early identification of patients with kidney derangements would be beneficial to enable treatment and to avoid progression to chronic kidney disease.

Aims & Methods: The primary objective of the prospective, observational HCVKID-study is to evaluate the prevalence of renal manifestations among HCV+ patients in Finland and to compare those findings to HCV-negative

controls complemented by long-term analyses to identify changes from baseline. This is a cross-sectional analysis to compare baseline characteristics between HCV+ patients and healthy controls. 208 HCV-PCR-positive male and female patients (≥ 18 years old) were eligible for the study. The HCV-negative control group (n= 492) was enrolled by an occupational healthcare provider. Exclusion criteria were HIV or Hepatitis B or other underlying diseases that may influence kidney function.

Results: The prevalence of any renal finding (abnormal proteinuria, occurrence of hematuria or serum creatinine over upper normal limit) was significantly more frequent in the HCV+ -population compared to healthy controls (41/208 vs. 45/492), p = 0.0002. Occurrence of abnormal proteinuria as evaluated by various methods was the most common urinary finding among HCV+ patients. Protein dipstick test was positive in 4/201, tubular proteinuria marker A1Miglo in 22/208 and albuminuria marker AlbCrea in 8/208. Elevated serum cystatin-C was also prevalent among HCV+ -patients (72/208), however s-creatinine was abnormal only in 7/208. Glomerular filtration rate (eGFRepi) was significantly lower in the HCV+ population with renal findings, albeit within normal limits. Estimated time from HCV transmission, infection genotype or stage of liver fibrosis were not significantly different between HCV + with renal finding vs. HCV + without renal finding. Baseline blood values and liver parameters were similar among both HCV+ populations. SVR12 data on 97 patients revealed early improvements in liver enzymes and APRI scores, but not in proteinuria markers, serum creatinine or cystatin-C.

Conclusion: HCV seems to influence both renal tubular and glomerular cells as judged by different proteinuria profiles. Tubular cell damage may be the earliest sign of renal dysfunction caused by HCV and could potentially be used to identify patients with a higher risk to develop more severe renal manifestations.

References: Lai T, Lee MH, Yang HI, You SL, Lu SN, Wang LY, Yuan Y, L'Italien G, Chien KL, Chen CJ; REVEAL-HCV Study Group. High hepatitis C viral load and genotype 2 are strong predictors of chronic kidney disease. Kidney Int. 2017; 92(3):703-709. doi: 10.1016/j.kint.2017.03.021. Ozkok A, Yildiz A: Hepatitis C virus associated glomerulopathies. World J Gastroenterol. 2014;20(24):7544-54 Ferri C, Giuggioli D, Colaci M. Renal manifestations of hepatitis C virus. Clin Liver Dis 2017; 21: 487-97

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P1435 DAPS SCORE: PREDICTIVE MODEL FOR SIGNIFICANT FIBROSIS IN IDAHS

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Introduction: Up to 20% of Incidentally Detected Asymptomatic Hepatitis B patients (IDAHS) have significant fibrosis at presentation. Management of IDAHS, especially those with normal Alanine Transaminase (ALT) has been a topic of debate. We aimed to study predictors of significant fibrosis in IDAHS and to develop a composite clinical score for prediction of significant fibrosis.

Aims & Methods: A retrospective review of IDAHS referred to the Liver clinic at King Edward Memorial Hospital from May 2018 to December 2018 was done. Demographic details of the patients were noted. Patients underwent investigations including complete blood count, liver function tests, HBeAg assay, HBV DNA PCR and ultrasound of abdomen. Liver stiffness measurements were taken using the Fibroscan 430 Mini machine (Echosens Ltd., Paris, France) using the M or XL probe attachments after an overnight fast. 10 readings were taken with success rate of >80% and interquartile range of < 30% as standard. Fibroscan values of >8 kPa were classified as significant fibrosis (>F2) as per the APASL criteria and those with values >11 kPa were considered as cirrhosis.

Results: 299 patients were included, of which 63% were male with mean age of 42.6 years. 20% patients were obese as per BMI criteria. 226 (75.9%) were HBeAg non-reactive. 5 patients had concomitant HCV and 4 had HIV infection. Significant fibrosis was seen in 82 (27.4%) patients. 36 patients (12%) were cirrhotic on VCTE. 39 (19.6%) patients with normal SGPT had evidence of significant fibrosis. Higher Age, Higher mean SGPT, lower platelets and presence of Diabetes was associated with significant fibrosis (p<0.05) on Univariate Analysis. HBV DNA levels, HBeAg and presence of obesity were not associated with significant fibrosis. Multivariate analysis revealed higher SGPT, lower platelets, higher age and Diabetes

were associated with fibrosis. Hence prediction model using Platelets (>240000/cu.mm =0, <240000/cu.mm=1 point), Age (<45 yrs =0, >45 yrs =1 point), presence of Diabetes (No=0, Yes= 1 point) & SGPT (<45 U/L=0, >45 U/L=1 point) was developed. Patients were sub-stratified based on cumulative score as low risk (0-2 points) and high risk (3-4 points). Those with high risk had OR of 14.9 (95% CI- 4.89-45.84) over those with low risk for fibrosis. On internal validation, DAPS score had accuracy of 77.3% with specificity of 98.2%.

Parameter	Points= 0	Points= 1
Associated Diabetes Mellitus	No	Yes
Age	<45 years	>45 years
Platelets	>240,000/ cu.mm	<240,000/ cu.mm
SGPT	<45 U/L	>45 U/L
Total score- 0-2 Low risk 3-4 High risk		

[DAPS Score for fibrosis prediction in IDAHS]

Conclusion: High proportion of IDAHS have significant fibrosis (27%) at presentation. 20% patients with normal SGPT have fibrosis on VCTE. In low resource settings where non-invasive assessment of fibrosis is not feasible, DAPS score can be used for prediction of significant fibrosis in IDAHS with high specificity.

References: NA

Disclosure: Nothing to disclose

P1436 USEFULNESS OF SHEAR WAVE ELASTOGRAPHY BEFORE AND AFTER DIRECT-ACTING ANTIVIRAL TREATMENT FOR HEPATITIS C VIRUS

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Introduction: Direct-acting antivirals (DAA) for hepatitis C virus have helped achieve a high sustained virologic response (SVR). While the ideal method of determining the risk of hepatocellular carcinoma (HCC) development is unclear, some studies have shown an association of liver stiffness and Mac-2 binding protein glycosylation isomer (M2BPGi) with liver carcinogenesis. We evaluated the liver stiffness using shear wave elastography (SWE) before and after DAA treatment and examined its usefulness for predicting HCC development.

Aims & Methods: We enrolled 84 patients with hepatitis C virus infection who underwent SWE before and after DAA treatment at our hospital and examined the relationship between the SWE value and fibrosis markers, such as M2BPGi and hyaluronic acid. The SWE value was measured using a Logiq E9 (44 cases; General Electric Company) or an Aplio 500 (40 cases; TOSHIBA). The SWE value was measured with the same device throughout a given patient' course.

Results: The average age was 67 years old (range 43-87), 38 patients were men, and 20 had cirrhosis (23.5%). Nine patients (11%) had a history of HCC. DAA treatment comprised Daclatasvir and Asunaprevir in 27 cases, Sofosbuvir and Ledipsvir in 38 cases, Ombitasvir and Paritaprevir in 1 case, Sofosbuvir and Ribavirin in 15 cases, and Elbasvir and Grazoprevir in 3 cases. The SVR rate with treatment was 92.9%. The pre-treatment SWE values measured with the Aplio 500 were positively correlated with the FIB-4 index (Correlation coefficient, $r = 0.8$, $p < 0.001$), hyaluronic acid level ($r = 0.515$, $p = 0.014$), M2BPGi level ($r = 0.671$, $p = 0.024$), and alpha-fetoprotein (AFP) level ($r = 0.421$, $p = 0.007$). There was a negative correlation with the platelet count ($r = -0.652$, $p < 0.001$) and albumin level ($r = -0.374$, $p = 0.019$). Similarly, the pre-treatment SWE values measured with the LogiqE9 were positively correlated with the FIB-4 index ($r = 0.353$, $p = 0.019$), hyaluronic acid level ($r = 0.345$, $p = 0.042$), and M2BPGi level ($r = 0.474$, $p = 0.013$). The average SWE value with the Aplio500 was 1.94 m/s in cases with an FIB-4 index < 3.25 (equivalent to F0-2) and 2.43 m/s in those with a value ≥3.25 (equivalent to F3 or higher); those respective values with the Logiq E9 were 1.39 m/s and 1.49 m/s. The SWE value decreased in 67.9% of cases after DAA treatment, and the average value before treatment, at the end of treatment (EOT), 6 months after the EOT, 12 months after the EOT and 24 months after the EOT were 2.18, 2.18, 2.01, 1.98, and

1.86 m/s with the Aplio 500, respectively, and 1.45, 1.36, 1.29, 1.28, and 1.19 m/s, with the LogiqE9, respectively. We divided patients with SVR who had no history of HCC into two groups based on whether or not the SWE value decreased after the EOT. We compared the baseline values of alanine aminotransferase, platelet, AFP, and FIB-4 index between these two groups but noted no marked differences. However, in the patients whose SWE value decreased, the M2BPGi level was significantly lower at 6 and 12 months after the EOT than at EOT (p < 0.001, 0.002, respectively), with no such changes noted in the patients whose SWE value did not decrease (p = 0.467, 0.921 respectively).

Conclusion: A decrease in the SWE value after DAA therapy likely reflects improvement in the liver inflammation. However, there were some patients in whom the SWE levels did not decrease after the EOT. In those patients, the M2BPGi also did not decrease, suggesting that these patients may be at risk of liver carcinogenesis.

Disclosure: Nothing to disclose

P1437 STUDY OF THE RESPONSE AND SAFETY OF DIRECT ACTING ANTIVIRAL COMBINATION THERAPY IN HEPATITIS C VIRUS-RELATED CHILD-B LIVER CIRRHOSIS

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Introduction: Direct-acting antiviral drugs (DAAs) have revolutionized the treatment for patients with chronic hepatitis C virus (HCV) infection, with excellent rates of sustained virologic response(SVR). Patients with HCV-related Child -B liver cirrhosis are poorly evaluated in the clinical trials of DAAs.

Aims & Methods: In this cohort multicentral cross-sectional study, we focused on the effectiveness and safety of DAAs for the treatment of Child B- cirrhotic Egyptian patients with chronic HCV infection genotype(GT-4) in a routine clinical practice. Child -Pugh score was calculated for all patients, those with score 7 to 9 was selected(Child-B). All patients' data including demographic, clinical and laboratory measures were recorded. Child B patients (hard to treat) with a total number (n=326);269 naïve and 57 experienced were compared to Child A patients (easy to treat) (n=275), all of them were naive.

Results: In Child A patients, 260 had sofosbuvir (SOF)and daclatasvir (DAC) for 12 weeks,13 had SOF plus simeprevir (SIM) for 12 weeks and 2 had Ritonavir-Paritaprevir-Ombitasvir-Ribavirin for 12 weeks. While, in Child B patients; 86 had SOF-DAC for 24 weeks, 233 patients had SOF-DAC-RVB for 12 weeks. (98.9%) of Child A patients had completed their course and 1.1%stopped treatment due to pregnancy, However, in Child B only (91.1%) had completed their course (P< 0.001); 29 stopped treatment due to complications (hematemesis 2.8%, jaundice 1.8%, ascites0.6% or anemia aggravation2.8%, hepatic encephalopathy0.6%)with statistically significant difference between both groups (P- 0.001).SVR-12 achieved in 98.5%&86.7%in Child A&B, respectively with statistically significant difference(P< 0.001).In both groups, HB, PLT, ALT, AST, s.albumin and bilirubin improved post- than pre-treatment levels(p-< 0.001).Regarding the risk factors for non-SVR-12; increasing age, male gender, experienced patients, with SOF-DAC for 12 weeks, moderate to severe ascites and Child score 9 were highly statistically significant difference (p-value=0.000). At SVR-12 in Child B group,3/297 (1%)patients developed hepatic focal lesions (HFLs), 5(1.7%) developed new jaundice,20% has developed new-onset or a deterioration of pre-existing ascites and 1.2%developed upper gastrointestinal bleeding.

Conclusion: Real-world results of generic DAAs combinations in Egyptian patients with chronic HCV-Child B were very safe and effective with SVR-12 (98.5%&86.7%) with very rare reported complications (0.01%,0.9%) in Child A&B, respectively.

Disclosure: Nothing to disclose

P1438 THE EFFECT OF INTERFERON THERAPY ON NATURAL COURSE OF HEPATITIS D

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Introduction: Hepatitis Delta Virus (HDV) is a defective virus that can only cause hepatitis on hosts already infected with Hepatatis B virus (HBV). Compared with other viral hepatitis; chronic delta hepatitis (CDH) has a higher incidence of end stage liver disease and hepatocellular carcinoma. Treatment goal of HDV infection is either eradication of both HBV and HDV or long-term suppression of disease activity.

Today the only approved treatment opportunity of CDH is alpha interpheron (IFNα). Previous clinical trials claim a high dose long term IFNα treatment has a higher chance of virological, biochemical and histological response with a ameliorated natural course of disease.

Aims & Methods: This study aims to asses long term histological, virological and biochemical outcomes of our patients treated with IFNα. Data of 48 CDH patients who had been treated with IFNα for at least 1 year and who were non cirrhotic at the beginning of follow up were assessed retrospectively. . Demographic characteristics, biochemical, serological and histological parameters of patients were reviewed. Cirrhosis diagnosis was supported with objective findings of portal hypertension. Pre and post treatment liver biopsy Ishak fibrosis staging scale scores were compared. Patients were grouped according to fibrosis score change as increasing, decreasing and steady groups. Histological course, virological and biochemical responses were comparatively analyzed.

Results: 48 patients were followed for mean 7 years. Post treatment follow up was mean 5 years. 24 of 48 patients were observed to be cirrhotic during follow up. Virological response rate of patients treated with classical IFNα was %37 while patients treated with pegylated IFNα had % 41 virological response rate. Sustained virological response (SVR) rate among patients was %37 at the end of follow up. There was statistical correlation in between histological response rates and virological and biochemical responses. Biochemical response is accepted as normalized serum ALT value. Pre – post treatment liver biopsy fibrosis scores of 24 patients who were non cirrhotic at the end of follow up; were compared, the result was statistically non – significant (p=0,979). Patients with decreasing or steady fibrosis scores are accepted as histological responders. 6 patients (%13) were in decreasing fibrosis score group, 10 patients (%21) were in steady fibrosis score group while 8 patients (%16) were in increasing fibrosis score group of total 24 patients with both pre and post treatment liver biopsies.

Conclusion: This study revealed long term natural course of patients treated with IFNα at least for 1 year. IFNα therapy hasn't changed the natural course, however 2 of 3 patients have clinicaly and hystologicaly progressed.

Disclosure: Nothing to disclose

P1439 ADHERENCE TO TREATMENT AND THERAPEUTIC SUCCESS IN PEOPLE WHO INJECT DRUGS WITH HEPATIS C VIRUS INFECTION IN A TERTIARY CARE HEPATOLOGY CENTER

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Introduction: Hepatitis C therapy with directly-acting antiviral agents (DAA) (especially pangenotypic) is associated with a sustained virological response (SVR) >95% in a real world setting with almost no adverse events. The World Health Association published a strategy to eliminate hepatitis C by 2030. People who inject drugs (PWIDs) are often less-compliant to treatment and have a high risk of reinfection. Hepatitis C elimination will be difficult in this group of patients.

Aims & Methods: The aim of this study was to investigate the adherence to treatment, SVR rate and reinfection rate in PWIDs with hepatitis C. Our retrospective study included PWIDs with hepatitis C which were evaluated in our Hepatology outpatients clinic between 2014-2018.

The following information was extracted: presence of positive viral load, HCV genotype, treatment regimen, SVR achievement, reinfection with hepatitis C virus, HIV coinfection, recent (in the last 6 months) i.v. drugs use, ongoing opioid agonist therapy, fibrosis stage according to Transient Elastography -TE (Fibroscan). The following TE cutoff values were used (Tsochatzis et al - JHepatol 2011; 54: 650-659): F≥2: 7 kPa F≥3: 9.5 kPa and F4: 12 kPa

Results: We included 202 PWID with hepatitis C in our analysis with a mean age of 34.1±9.6 years (70.7% male). Intravenously drugs use in the last 6 months was reported in 20.8% of patients and 51.9% of the whole cohort were under opioid substitution therapy. HIV coinfection was diagnosed in 1.9% of patients.

Positive HCV viral load was present in 179/202 patients (88.6%).

HCV genotype distribution was: 1 (subtyping not possible)-1.8%, 1a-30.2%, 1b-8.4%, 2-1.5%, 3-49.8%, 4-2.8%, 6-2.2%, unknown (viral load very low)-2.8%.

TE was available in 145/179 (71.7%) of patients and the following fibrosis grades were observed: F0-1-68.9%, F2-16.6%, F3-4.1%, F4-10.4%.

40/179 (22.3%) of patients with a positive viral load were not treated (2.8% very low viral load with suspicion of acute hepatitis C in healing, 0.5% because of pregnancy and 19% because the patients did not show up to start therapy).

The first treatment-regimen used were: DAA-69.1%, DAA+Ribavirin-23.1%, PegInterferon+Ribavirin-4.3%, DAA+PegInterferon+Ribavirin-3.5%.

SVR12 was documented after first therapy in 76/139 (54.6%) of patients. 6/76 (7.9%) patients presented in follow-up with reinfection with hepatitis C virus.

Currently, the treatment status of our treated patients is: SVR12 -80/139 (57.5%), viral load negative by end of treatment (EOT), but patients did not show up to SVR12 visit - 40/139 (28.8%), viral load negative at EOT and SVR12 visit will follow-10/139 (7.2%), ongoing therapy-5/139 (3.7%), therapy discontinued-3/139 (2.1%)(2/3 patients were on DAA therapy and did not show up after first prescription was given) and relapse - 1/139 (0.7%)(after therapy with PegInterfeon+Ribavirin).

Relapse after DAA+/- Ribavirin therapy was observed by 4 patients (genotype 1a-2 patients and genotype 3-2 patients). 2/4 patient achieved SVR after therapy with another DAA regimen. The other two patients are currently under therapy.

Conclusion: To achieve hepatitis C elimination, better strategies regarding PWIDs are needed. In our cohort, around 20% of the patients with positive viral load are not treated and they can infect other people, especially by sharing needles.

Disclosure: Nothing to disclose

P1441 DO HLA-DP/DQ POLYMORPHISMS AND/OR SERUM IP-10 AFFECT RESPONSE TO DIRECT ANTIVIRAL DRUGS THERAPY AMONG HEPATITIS C EGYPTIAN PATIENTS?

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Introduction: Recent genome-wide studies have demonstrated that antigen-presentation genes, particularly HLA class II gene may play an important role in pathogenesis and response to antiviral therapy among chronic hepatitis C patients. During viral infection, IP-10 is secreted by hepatocytes and correlates with hepatic inflammation due to induction of cellular immunity. It could predict sustained non-response to antiviral therapy.

Aims & Methods: Thus in the current study aimed to investigate the impact of HLA-DP/DQ single nucleotide polymorphisms and serum IP-10 levels on response to treatment with sofosbuvir + Daclatsvir ± Ribavirin, among chronic hepatitis C Egyptian patients.

Subjects & methods: This study was conducted on 80 HCV infected patients (40 responder and 40 non-responder) and 40 healthy volunteers. History taking, thorough clinical examination, CBC, liver functions tests, AFP, anti-HCV antibodies and viral load were done for all subjects under the study. Genomic DNA was extracted from a total of 120 subjects, including 40 healthy volunteers, 40 HCV responder patients, and 40 HCV non responder chronic HCV patients. HLA-DP-rs3077 and HLA-DQ-rs3920 SNP was assessed using 5' nuclease assay with a TaqMan MGB (minor groove binder) probe in a *StepOne™* Real-Time PCR System. Serum Levels of IP-10 were measured in all serum samples, using commercial human IP-10 Instant ELISA kit.

Results: Allelic discrimination of HLA-DP-rs3077 and HLA-DQ-rs3920 SNP revealed a statistical significant correlation between HLA-DP-rs3077 AA genotype and response to treatment (P= 0.001*). Also, there was a statistical significant correlation between HLA-DQ-rs3920 AG variant and HCV infection as it was markedly expressed in both responders and non-responders groups when compared to the controls (P=0.004*); regardless the outcome after treatment.

Moreover, there was statistically significant increase in IP-10 levels among the non-responder group when compared with other groups (P = 0.001*) and IP-10 showed 95% sensitivity and 15% specificity with area under curve (AUC) of 0.889 (95% Confidence Interval=0.776-1.001, P=.00001*); indicating a good negative test that is good for catching actual cases of HCV but it also comes with some false positives. So, it could be considered the excellent for screening test.

Conclusion: Our work provides more detail about HLA-DP/DQ gene polymorphism and serum IP-10 among chronic hepatitis C patients as new independent tools for anticipating HCV infection susceptibility (particularly HLA-DQ-rs3920 AG genotype and IP-10) and response to direct antiviral drugs (especially HLA-DP-rs3077 AA).

Disclosure: Nothing to disclose

P1442 SAFETY AND EFFICACY OF SOFOSBUVIR BASED REGIMENS IN HEPATITIS C VIRUS RECURRENCE POST LIVER TRANSPLANTATION

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Introduction: Hepatitis C virus (HCV) recurrence after liver transplantation (LT) is universal and associated with an accelerated disease course. Second generation direct acting antivirals dramatically improved viral clearance. Their use in the post-transplant still needs to be studied.

Aims & Methods: we aimed in our study to evaluate safety and efficacy of sofosbuvir based regimens in treatment of HCV recurrence after liver transplantation.

Sixty patients with HCV recurrence after LT were included. They received sofosbuvir (SOF) in combination with: ribavirin (SOF/RBV) for 24 weeks (n=20), simeprevir (SOF/SIM) for 12 weeks (n=21), and daclatasvir with or without ribavirin (SOF/DCV±RBV) for 12/24 weeks according to the stage of liver fibrosis and eligibility for ribavirin (n=19). All patients who received (SOF/SIM) were on Tacrolimus or rapamune based immunosuppression

Results: Mean age of the studied patients was 52.5±7.9 years (range 28-68), mostly males (99.7%). All patients achieved end-of-treatment response. Sustained virological response at 12 weeks after cessation of treatment (SVR12) was 100% with the SIM/SOF and SOF/DCV±RBV regimens and 85% (n=17) with SOF/RBV. The commonest adverse event was fatigue, which occurred in 15 (75%), 18 (85.7%) and 0%, followed by hemoglobin drop < 9 g/dl in 3 (15%), 1 (4.8%) and 2 (10.5%), and hyperbilirubinemia in 2 (10%), 2 (9.5%) and 0% in the SOF/RBV, SIM/SOF and SOF/DCV±RBV groups respectively.

Conclusion: Sofosbuvir based combinations are safe and effective in the treatment of recurrent HCV after LT, especially when combined with another directly acting antiviral.

Disclosure: Nothing to disclose

P1443 NUCLEOS(T)IDE ANALOGUES WITHDRAWAL IN AGHBE-NEGATIVE CHRONIC HEPATITIS B: EXPERIENCE OF 2 YEARS OF FOLLOW-UP

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Introduction: The nucleos(t)ide analogues (NUCs) are the mainstay treatment for chronic hepatitis B (CHB). It was recently recommended to stop NUCs in selected patients with HBeAg-positive CHB and without cirrhosis. However, it is not yet defined what is the best moment to discontinue NUCs neither is clear what are the predictors of remission.

Aims & Methods: We aimed to analyse the outcomes after NUC withdrawal in a selected group of HBeAg-positive CHB patients.

Evaluation of all patients that discontinued NUCs and had at least 2 years of follow-up in a hepatology unit of a tertiary care hospital. To stop NUCs the patients had to have at least 3 years of virus load undetectability, no past history of clinical or laboratorial exacerbation of hepatitis and a transient elastography < 6kPa. Relapse was defined as alanine aminotransferase (ALT) elevation over 2 times the upper limit of normal and HBV DNA levels over 20000 UI/mL.

Results: 21 patients were evaluated, 17 men, average age of 59 (±12) years old, treated with NUCs for an average time of 103 (±29) months, with an average time of undetectability of HBV-DNA levels of 85 (±25) months and an average value of ALT before the beginning of NUCs treatment of 187UI/L (range: 52-674UI/L). The average value of qAgHBs at the time of NUCs discontinuation was 2203 UI/mL (range: 2.9-12804UI/mL).

Relapse was observed in 10 (52%) patients, in all cases it occur in the first 6 months after discontinuation of NUCs. These patients had an average value of ALT at the hepatitis *flare* of 349 UI/L (range; 85-873UI/L) and none had liver failure. All these patients were restarted on NUCs and it was observed AgHBs seroconvertion in 20% (2/10) at 20 and at 26 months after NUCs discontinuation.

In the 11 patients without recurrence, in an average follow-up of 28 months, there was one case of seroconversion of AgHbs.

In multivariate analysis, none of the variables analysed (duration of treatment, duration of undetectable viral load, ALT before starting NUCs, qAgHBs before NUCs discontinuation) pointed out any significant predictor for need to restart NUCs or to seroconversion.

Conclusion: The NUCs withdrawal in a selected group of patients with HBeAg-negative CHB was safe, permitted to stop long-term NUCs therapy in most patients and resulted in the seroconversion of the AgHbs in a considerable percentage of patients.

Disclosure: Nothing to disclose

P1444 PERFORMANCE OF ABDOMINAL ULTRASOUND IN THE PREDICTION OF ESOPHAGEAL VARICES

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Introduction: Portal hypertension (PHT) is the main complication and cause of death during cirrhosis. The signs of PHT (collateral circulation) in imaging are sufficient, according to BAVENO VI recommendations, to affirm the presence of a clinically significant PHT (defined by a hepatic venous pressure gradient > 10 mmHg).

Aims & Methods: Our objective was to evaluate the performance of imaging, especially abdominal ultrasound (AU), in the prediction of esophageal varices (OV).

We performed a retrospective study including, between January 2010 and December 2016, all patients with chronic liver disease, followed in our department and who had within 3 months, upper gastrointestinal endoscopy (UGIE) and AU.

Results: We included 198 patients (69 men and 129 women) with an average age of 60.5 years. The main etiologies of chronic liver disease were viral infection C (44.9%) and viral infection B (19.7%). OV were found in 116 patients. Ultrasound signs of PHT were found in 92 patients. A significant correlation was noted between the presence of signs of PHT at AU and the presence of OV at UGIE (p < 0.001). The sensitivity, specificity, positive predictive value, and negative predictive value of AU in OV prediction were 73.8%, 66%, 79.7%, and 58.2%, respectively, with an area under the curve ROC of 0.65 (0.56-0.74).

Conclusion: The good sensitivity of AU, which is a non-invasive examination, in the prediction of OV didn't exempt the UGIE, but could provide a better selection of patients requiring this invasive exploration.

Disclosure: Nothing to disclose

P1445 ROLE OF RISK STRATIFICATION IN PRIMARY BILIARY CHOLANGITIS IN PREDICTING BIOCHEMICAL RESPONSE TO URSODESOXYCHOLIC ACID

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Introduction: Ursodesoxycholic acid (UDCA) remains the mainstay of management of primary biliary cholangitis (PBC). However the course of this disease can be variable. Numerous criteria for predicting outcome of treatment have been studied based on biochemical response to UDCA, though it does not take the stage of the disease into account. More recently the globe score have been validated to identify patients at risk of poor prognosis by estimating transplant-free survival.

Aims & Methods: We aimed to assess the prognostic ability of the GLOBE score alongside with Paris-2 criteria. We performed a retrospective analysis of data from 53 consecutive patients with PBC from 2009 to 2018. We enrolled all patients from our department with PBC and receiving UDCA therapy 13-15mg/kg/day. The diagnosis of PBC was done according to EASL criteria. The response to treatment was evaluated according to Paris-2 criteria at 1 year of treatment. The GLOBE score was calculated in all patients. The parameters of this score are: age at diagnosis and levels of bilirubin, alkaline phosphatase, albumin, platelet count at 1 year of treatment with UDCA.

Results: A total of 53 consecutive patients were included: 45 women and 8 men (sex ratio F/M=5.6). The mean age at diagnosis was 55 years (range 19-78 years). The median follow-up was 6 years. Cirrhosis was present at the diagnosis in 39% of cases (n=21). The mortality rate was 15% (n = 8). Factors associated with poor response to UDCA therapy were: stage of cirrhosis at diagnosis of PBC (p = 0.04), associated autoimmune disease (p = 0.024) and elevated pre-therapy level of total bilirubin (p = 0.01). The average Globe score was 2.05 (extremes -0.91-5.55). This score was significantly correlated with response to treatment (p < 0.001) and mortality (p = 0.04). Patients fulfilling Paris II criteria had a significantly lower score globe than those who did not (mean 0.35 vs 2.28; p = 0.028).

Conclusion: Our study found a significant association between the globe score and the response to the UDCA therapy. The use of this score will allow early identification of patients at risk of poor response in order to optimize treatment, prevent progression to end stage liver disease and improve the prognosis.

References: Scoring systems in primary biliary cholangitis - time to make a move. Yang F, Yang Y, Tang R, Gershwin ME, Ma X. Aliment Pharmacol Ther [2017]

Disclosure: Nothing to disclose

P1446 SERUM AND BILIARY PROTEOMICS AS SURROGATE MARKERS FOR DISEASE PROGRESSION AND RISK FOR BILIARY NEOPLASIA IN PRIMARY SCLEROSING CHOLANGITIS

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Introduction: Primary sclerosing cholangitis [PSC] is a chronic inflammatory disease leading to strictures of intra- and extrahepatic bile ducts, cholestasis and eventually to biliary cirrhosis (1). The chronic inflammation and increased proliferation of biliary epithelial cells are associated with development of biliary dysplasia and cholangiocarcinoma [CCA] (2-3), with the lifetime risk around 10% (4-5). Several serum surrogate markers (6) have been developed to predict the risk for liver cirrhosis, transplantation free survival or death, such as decrease of P-ALP (7), IL-8 (8), and ELF® (9). However, all of these variables are very late endpoints and not suitable for monitoring bile duct inflammation, progression of bile duct disease or development of risk of biliary dysplasia – before development of CCA.

Aims & Methods: The aim of the study is to evaluate the proteomic profiles in serum and bile in PSC patients with

1) non-advanced,

2) advanced bile duct disease or

3) biliary neoplasia to find better markers for disease progression and risk for biliary neoplasia.

In total, 79 patients with confirmed PSC referred for ERC for diagnosis and surveillance of the disease were included (48 females) and another 12 patients with CCA. During ERC bile sample was aspirated using balloon catheter and then stored in -80°C. Brush cytology (BC) was collected both from extra- and intrahepatic bile ducts for Papanicolaou staining for grading dysplasia. Cholangiographic findings are scored according to modified Amsterdam score (Helsinki score). Serum samples are collected at the time of ERC.

Label -free quantitative proteomics from serum and bile from the same individuals was performed UDMSE mode in Synapt G2-Si with nUPLC-TRIZAIC C18 tile as previously described (10).

Results: Quantitative serum and bile proteomics from 43 patients with PSC with a small ERC score < 4 were compared to PSC 36 patients with ERC score of >4 as a marked of disease progression. The bile proteome was significantly different in PSC compared to CCA patients. 93 bile proteins showed were significantly (Mann-Whitney) differentially expressed and the changes were up to 15-fold. These proteins were enriched on the e.g. inflammatory pathways. Concomitantly the serum proteomics showed only mild alterations, with only 14 significantly altered proteins with a maximus 2-fold increase.

Quantitative serum and bile proteomics from 79 patients with PSC, but not dysplasia or CCA were compared to 12 serum from patients with CCA. The bile proteome was significantly different in PSC compared to CCA patients. 156 bile proteins showed were significantly (Mann-Whitney) differentially expressed and the changes were up to 53-fold. Concomitantly the serum proteomics did not show essentially any significantly altered protein expressions between PSC and CCA patients. The upregulated proteins were enriched on e.g. inflammatory and gluconeogenesis/glycolysis.

Conclusion: Analyses of bile proteomics showed significant alterations during the disease progression of PSC. Similarly the bile proteomics was profoundly altered during the progression from an inflammatory disease (PSC) to a malignant process (CCA). While the bile proteome was found to be modified significantly during these disease states the serum proteomics did not display these alterations at the same level.

References: 1. Dyson JK et al Lancet. 2018 2. Bergquist A, et al. J Hepatol. 2002;36:321-7. 3. Manninen P, et al. Scand J Gastroenterol. 2015;50:423-8 4. Boberg KM, et al. Scand J Gastroenterol 2002; 37: 1205-11. 5. Claessen MM. J Hepatol. 2009;50:158-64. 6. Ponsioen CY, et al. Hepatology. 2016;63:1357-67. 7. de Vries EM, et al. Liver Int. 2016;36:1867-75. 8. Vesterhus M, et al.J Hepatol. 2017;66:1214-22. 9 deVries EMG. Liver International. 2017;37:1554-1561. 10 Holm M, et al. PLoS One. 2018;13:e0195354.

Disclosure: Nothing to disclose

P1447 WITHDRAWN

P1448 PRIMARY BILIARY CHOLANGITIS AND AUTOIMMUNE MANIFESTATIONS : CLINICAL ASPECTS AND ROLE IN THE TREATMENT RESPONSE

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Introduction: Primary biliary cholangitis (PBC) is an auto-immune disease characterized by destructing the biliary ducts. It affects women in their fifties. The actual treatment is the ursodesoxycholic acid (UDCA). Association with auto-immunes diseases (AID) has been already established.

Aims & Methods: The aim of this study is to describe the different auto-immune diseases found in a population of PBC and to study their impact on the treatment response.

Methods: Retrospective study from January 2000 to August 2018. All patients hospitalized in the gastroenterology department for PBC were included. PBC diagnosis was based on the EASL criteria. The response to treatment was evaluated by the Paris II criteria at one year of treatment.

Results: We included 53 patients. The sexe ratio M/F was 0,18. The mean age of our patients at the time of the positive diagnosis of PBC was 55 years old. Family history of auto-immune hepatitis was found in 11,3% of the cases. AID were found in the first consult in 60,4% of the patients. The different AID were type 1 diabetes (n=1), celiac disease (n=6), hypothyroidisms (n=10), systemic lupus erythematosus (n=2), vitilio (n=1), Sjogren syndrome (n=13), hemolytic anemia (n=8) and auto-immune hepatitis (n=6). 13 patients had at least two of these associated AID. The influence of the AID on the response to the treatment by UDCA was studied. Diabetes type1, hypothyroidism, and celiac disease influenced significantly the response to treatment (respencively p= 0,024, p=0,001, p=0,024). Generally, the response to UDCA was better in the group with no AID with a difference statistically significant (p< 0,005).

Conclusion: Auto-immune diseases, when associated with PBC influence the response to UDCA. They need to be researched ant treated since the positive diagnosis of PBC to ameliorate the response to the treatment and therefore the survival of the patients.

Disclosure: Nothing to disclose

P1449 EXOME-WIDE SEQUENCING STUDY OF PRIMARY SCLEROSING CHOLANGITIS - A TWO POPULATION STUDY

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Introduction: Primary sclerosing cholangitis (PSC) is a rare and progressive inflammatory disease of the bile ducts with no effective therapy currently available. While the prevalence of PSC has been reported only at 15.3-32/100,000, PSC is the most common cause of liver transplantations in Nordic countries. Additionally, PSC patients are at high risk of cholangio-carcinoma (up to 1000-fold) compared to population control and substantial risk of colorectal cancer. PSC is commonly associated with inflammatory bowel disease (IBD) as ~70% of PSC-patients present with PSC-IBD. When co-occurring with IBD, PSC is most often (80% of cases) associated

with ulcerative colitis (UC). So far it is unclear whether PSC-IBD is an independent entity or whether it only manifests as an IBD subtype, however up to 8% of patients with IBD have diagnostic findings in MRI. A recent (and largest) genome wide association study using imputed array data of 4,796 PSC cases estimated the genetic correlation of IBD and PSC to 29%, while confirming most previously reported variants and identifying 4 new loci, as up to 19 loci have now been associated with PSC.

Aims & Methods: This study aims to assess the (possibly rare and hence not captured by array genotyping and imputation) coding mutations relevant to PSC risk. In this present study, we perform the largest exome-wide association study on PSC to date, to further extend our understanding of genetic determinants of biliary and intestinal inflammation in patients with PSC. We are currently analyzing the largest so far whole exome sequencing (WES) study on PSC, aiming at meta-analyzing > 1100 patients of Finnish (n~720) and European (n~400) ancestry. The Finnish PSC patients represent ~15% of total estimated Finnish PSC population.

In addition to DNA, deep phenotyping and health status information, sequential endoscopic retrograde cholangiographic examinations (ERC), biliary cytology, bile samples have been collected from the Finnish patients.

Results: Our preliminary analysis focused on a Finnish subset and suggests that out of the 19 loci described so far, we identify nominally significant (p<0.05) associations in 8 genes and in 12 loci within a 500kb window of the previously implicated gene (p<0.01). Additionally, we confirm a strong MHC component and replicate 14/312 Finnish signals (p<0.0001) in a non-Finnish-European population (p<0.05).

Conclusion: The summary statistics-level results of a full meta-analysis will be made available online for UEG Week.

Disclosure: Nothing to disclose

P1450 REAL WORLD EXPERIENCE WITH OBETICHOLIC ACID IN PATIENTS WITH PRIMARY BILIARY CHOLANGITIS – MULTICENTRIC AUSTRIAN ANALYSIS

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Introduction: The use of obeticholic acid (OCA) is approved as second line therapy for patients with primary biliary cholangitis (PBC) with insufficient response or intolerance to ursodeoxycholic acid (UCDA).

Aims & Methods: To assess the efficacy and safety of obeticholic acid as second line therapy in patients with PBC (as monotherapy or add-on to UCDA) in a real-world cohort in Austria.

Our study included 33 PBC patients (87.8% women) with a mean age of 60.7 ± 10.8 years from 10 Austrian centers (Klagenfurt, Villach, Salzburg, Linz, Vienna – 2 center, Eisenstadt, Ried, Graz and Innsbruck), who received therapy with OCA because of intolerance or insufficient response to the maximal dose of UCDA (12.2% monotherapy with OCA, 87.8% combination therapy OCA + UCDA).

We evaluated the response of alkaline phosphatase (AP), alanine transaminase (ALT), gamma-glutamyltransferase (GGT) and bilirubin during therapy with OCA. Furthermore, adverse events were assessed.

Fibrosis stage at the start of therapy with OCA was assessed by Transient Elastography -TE (Fibroscan, Echosens, France). The following TE cutoff values were used (Corpechot et al – Hepatology 2012; 56: 198-208): F ≥1: 7.1 kPa, F≥2: 8.8 kPa, F≥3: 10.7 kPa and F4: 16.9 kPa

Results: The median follow up of therapy with OCA was 13 months (between 0.5 and 27 months).

TE was available in 26/33 (78.7%) when OCA was started. The fibrosis stages observed were: F0-19.2%, F1-19.2%, F2-7.8%, F3-26.9% and F4-26.9%. A significant reduction of AP, GGT and ALT was observed with obeticholic acid treatment (Table).

	Baseline values (n=33)	Values after 1 month of therapy (n=32)	Values after 3 months of therapy (n=28)	Values after 6 months of therapy (n=27)	Values after 12 months of therapy (n=18)	p value
AP (U/l) Median (IQR)	237 (204-300)	189 (168-280)	166 (144-244)	156 (116-213)	136 (100-171)	p<0.05 between Baseline and 3,6, 12 months of therapy
GGT (U/l) Median (IQR)	180 (109-432)	98 (53-219)	76 (51-159)	73 (42-152)	41 (20-82)	p<0.05 between Baseline and 3,6, 12 months of therapy
ALT (U/l) Median (IQR)	51 (33-73)	33 (27-48)	35 (23-52)	34 (25-54)	27 (20-32)	p<0.05 between Baseline and 1,3,6, 12 month of therapy
Bilirubin (mg/dl) Median (IQR)	0.7 (0.55-1.11)	0.67 (0.5-1)	0.6 (0.47-0.85)	0.6 (0.47-0.95)	0.47 (0.42-0.74)	p<0.05 between Baseline and 12 month of therapy

[Table]

Adverse events were observed in 18/33 (54.5%) of patients. Adverse events recorded were: pruritus 12/33 (36.3%), fatigue 4/33 (12.1%), joint pain 4/33 (12.1%), abdominal pain 2/33 (6.1%), peripheral edema 1/33 (3.1%), nausea 1/33 (3.1%), exanthem 1/33 (3.1%), and generalized musculoskeletal pain 1/33 (3.1%) of patients. The treatment was stopped in 7/33 (21.2%) patients: in one case because of increase of AP and bilirubin after 7 months of therapy, in one case because non response+pruritus after7 months of therapy and in 5 cases because of adverse events (pruritus -2 cases, severe joint pain and peripheral edema – 1 case, exanthem-1 case and generalized musculoskeletal pain-1 case). One patient was lost to follow-up.

Conclusion: The second-line therapy with obeticholic acid is effective and safe in patients with PBC also in a real-world setting.

Disclosure: Nothing to disclose

P1451 RECURRENCE OF PRIMARY BILIARY CHOLANGITIS AFTER LIVER TRANSPLANTATION: A SINGLE CENTER EXPERIENCE

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Introduction: Primary biliary cholangitis (PBC) is a chronic autoimmune liver disorder that may progress to cirrhosis and eventually to liver failure and death. For those who develop end – stage liver disease, orthotopic liver transplantation (OLT) should be considered. Moreover, recurrent form of PBC (rPBC) appears in significant proportion of patients after OLT. Recurrent PBC is usually characterized by mild clinical course. In minor group of patients however, rPBC may eventually lead to graft loss and liver re – transplantation (re - OLT).

Aims & Methods: The aim of this study was to evaluate outcome of OLT for PBC in our center and to identify recipient risk factors for rPBC. A total number of 82 orthotopic liver transplantations for PBC were performed at Institute for Clinical and Experimental Medicine, Prague between January 1995 and January 2017. The diagnosis of rPBC was based on protocolary and/or on – demand liver graft biopsies. We retrospectively analyzed all relevant medical records from our computed database. Input statistical data were analyzed using JMP software. Survival ratio was determined from Kaplan – Meier curves. Pearson's chi-squared test and Fisher's exact test were used to assess the potential risk factors for rPBC. A *p-value ≤ 0.05* was considered as statistically significant.

Results: Out of 82 transplanted patients with median 158 (23 - 261) months of follow-up, 73 (89 %) were female and 9 (11 %) were male with median age of 56.9 (36 - 71) at the time of OLT. 3/82 (3.7 %) had hepatocellular carcinoma (HCC) in the liver explant. Except 3 (3.7 %) who received split, all patients were transplanted with whole graft. 9/82 (11 %) had overlap-

ping features of autoimmune hepatitis. 1-, 3-, 5-years patient survival was 92.7 %, while 10-years survival was 84.6 %. Graft survival was 91.7 % at 1, 3 and 5 years and 83.7 % at 10 years. 3 (3.7 %) patients received re-transplant: 1 (1.2 %) for primary graft dysfunction and 2 (2.4 %) for rPBC. For analysis of rPBC risk factors, we excluded the patients monitored outside our center and those who died sooner than 3 years after OLT. Out of 74 analyzed patients, 45 (54.9 %) developed rPBC after median time of 46 (11 - 239) months. 22 (29.7 %) received cyclosporin and 52 (70.3 %) received tacrolimus as their primary immunosuppressive agent.

None of the potential risk factors (age, sex, type of immunosuppression, features of AIH prior OLT, AMA and ANA positivity prior OLT) were significantly associated with rPBC (*p > 0.1*). However, the rate of rPBC had statistical tendency to be higher in patients who had HCC in their explants (*p = 0.056*).

Conclusion: Recurrent PBC is frequent but usually not serious clinical condition. In our cohort, rPBC rate was relatively high, presumably due to long median follow - up after OLT.

Disclosure: Nothing to disclose

P1452 WITHDRAWN

P1453 CHARACTERISTICS AND OUTCOME OF AUTOIMMUNE HEPATITIS-PRIMARY BILIARY CHOLANGITIS AND AUTOIMMUNE HEPATITIS-PRIMARY SCLEROSING CHOLANGITIS OVERLAP PATIENTS COMPARED TO AUTOIMMUNE HEPATITIS PATIENTS

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Introduction: In 10% of the autoimmune hepatitis (AIH) patients features of primary biliary cholangitis (PBC) or primary sclerosing cholangitis (PSC) are present, called overlap or variant syndromes. The aim of this study was to characterize AIH-PBC and AIH-PSC patients and compare outcome to AIH patients.

Aims & Methods: In a retrospective cohort study all patients with AIH-PBC and AIH-PSC were included in 3 hospitals. AIH-PBC patients had to fulfil the strict Paris criteria. AIH-PSC patients needed a definite diagnosis of AIH according to the simplified criteria and signs of PSC on ERCP, MRCP or onion ring fibrosis on liver biopsy. Characteristics and outcome were compared to AIH in a case-control design matched on age and cirrhosis.

Results: Twelve AIH-PBC, 25 AIH-PSC and 74 AIH patients were included. AIH-PSC patients were more often males compared to AIH patients (56% vs 28%; p = 0.007) and had large duct PSC in 92%. AIH-PBC patients had higher AF and GGT (p < 0.001 and p = 0.006) and presence of AMA antibodies in 75%. AIH-PSC and AIH-PBC had lower ALAT than AIH at diagnosis (p = 0.014) but IgG levels and SMA antibodies did not differ (p = 0.79; p = 0.58).

Treatment with prednisone, azathioprine and ursodeoxycholic acid (UDCA) was started in all AIH-PBC and AIH-PSC patients, except UDCA in 2 patients. Complete AIH remission was obtained in 8 (67%), 16 (64%) and 61 (82%) of the AIH-PBC, AIH-PSC and AIH patients (p = 0.12).

The median GLOBE score in AIH-PBC patients was -0.41 (range: -1.6 - 2.9) resulting in an expected median 10 year survival of 89% (range: 4-97%). The median Amsterdam Oxford score was 2.45 (range: 0.9-3.8) in AIH-PSC patients resulting in an expected median 10 year survival of 59% (range: 14-88%).

At the end of median follow-up of 107 months (range: 1-353) 4 (33%) AIH-PBC, 8 (32%) AIH-PSC and 8 (11%) AIH patients had progressed to liver transplantation or liver related death (p = 0.023). Four (16%) AIH-PSC developed a cholangiocarcinoma.

Conclusion: In 12 AIH-PBC patients and 25 AIH-PSC patients using strict criteria no difference was found regarding IgG, SMA antibodies and response to therapy compared to AIH patients. Survival was worse in AIH-PSC and AIH-PBC patients than AIH patients. Survival of AIH-PBC patients was worse than expected according to the GLOBE score and survival of AIH-PSC patients was better than expected according to the Amsterdam Oxford score although AIH-PSC patients are at risk for developing cholangiocarcinoma.

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P1454 THE PROGNOSTIC FACTORS FOR PRIMARY SCLEROSING CHOLANGITIS, INCLUDING OXIDATIVE STRESS MARKERS

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Introduction: Primary sclerosing cholangitis (PSC) is a rare chronic liver disease, with 0.95 cases reported per 100,000 people in Japan. Because of its rarity in Japan, the clinical characteristics are still not clear. Recent investigations have shown that general conditions, such as oxidative stress, affect the course of chronic diseases. We investigated the clinical course and oxidative stress-related condition of PSC to determine the prognostic factors of PSC.

Aims & Methods: We analyzed 41 PSC patients who attended our department from June 2008 to June 2018. The clinical characteristics, including concomitant inflammatory bowel disease (IBD) or bile duct carcinoma and liver transplantation experience, were investigated in order to define the prognostic factors. The oxidative stress status was evaluated by two types of markers and the ratio: serum d-ROM (oxidative stress marker, as reflecting serum active-oxygen metabolism) , OXY (antioxidant marker, as reflecting anti-oxidation power) and Oxidative Index (Standardized d-ROM / SD - Standardized OXY / SD).

Results: The median age was 35 years (14-74 years), and male sex was predominant (27:14). The average observation period was 1226 days, and 9 patients died. The Mayo risk score was able to significantly discriminate the poor overall survival (p< 0.001). Significant poor prognostic factors were higher age, higher Mayo risk score, higher FIB-4 index, lower Child-Pugh grade, higher hemoglobin, higher Albumin, lower Bilirubin according to the log rank test. A lower anti-oxidant marker OXY was also included as a poor prognosis-related factor, while d-ROM was not. In a multivariate analysis, while properly excluding confounding factors, FIB-4 index and Mayo risk score were the markers proven to be significant (p< 0.01). A receiver operating characteristic (ROC) analysis revealed the usefulness of Mayo PSC risk score and FIB-4. High AUC (>0.8) indicate FIB-4 index and Mayo risk score were indicated very useful markers for predicting the PSC prognosis.

Conclusion: The FIB-4 index and Mayo risk were shown to be a prognostic factor for PSC in our study. Maintaining antioxidant stress will lead to a good prognosis and suggests the efficacy of antioxidant treatment.

Disclosure: Nothing to disclose

P1455 CLINICAL OVERLAP OF HEPATOBILIARY AND RHEUMATOLOGIC PATHOLOGY: A RETROSPECTIVE STUDY OF PRAVALENCE

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Introduction: The rheumatic manifestations of gastrointestinal pathology, in particular of hepatobiliary diseases, in addition to being a diagnostic challenge, complicate the natural course of the primary disease and worse the prognosis due to the multiorganic affection they often have. The aim of this study is to characterize the prevalence of confirmed rheumatic disease associated with hepatobiliary diseases in a tertiary reference center.

Aims & Methods: All patients with simultaneous diagnosis of hepatobiliary pathology and rheumatologic pathology were retrospectively evaluated between 2007 and 2017. All patients with the following confirmed rheumatologic diagnoses (ICD9) were studied: Rheumatoid arthritis; Undifferentiated polyarthritis; Ankylosing spondylitis; Spondylarthritis; Psoriatic Arthritis; Polymyalgia Rheumatica; Diffuse Connective Tissue Diseases; SLE – Systemic lupus erythematosus; Systemic Sclerosis; Sjögren's Syndrome; Vasculitis; Behçet's disease; Drop; Pseudogout; Osteoarthrosis; with a diagnosis of concomitant confirmed hepatobiliary disease.

Results: From a sample of 2169 consecutive patients, simultaneously in consultation with Gastroenterology and Rheumatology, we were able to identify 51 patients with the above mentioned requirements, and 3 patients were excluded after subsequent exclusion of rheumatologic disease. The majority of the patients were females (58.3%). The mean age at diagnosis was 53.2 years (range 29-91 years).

Hepatitis C was diagnosed in 26 patients (54%), autoimmune hepatitis in 6 patients (12.5%), primary biliary cholangitis in 3 patients (6.25%), primary sclerosing cholangitis in 2 patients (4.2%), non-alcoholic steatohepatitis (4.2%), cryptogenic cirrhosis (4.2%), Wilson's disease (4.2%), and other diagnoses (10.4%) in 5 patients (hepatitis B, alcoholic liver cirrhosis, toxic hepatitis, alpha 1 antitrypsin deficiency and hemochromatosis).

Rheumatoid arthritis was diagnosed in 13 patients (27.1%), spondylarthritis in 13 patients (27.1%), ankylosing spondylitis in 5 patients (10.4%), undifferentiated polyarthritis in 4 patients (8.3%), SLE in 4 patients (8.3%), psoriatic arthritis in 2 patients (4.2%) and other diagnoses (2.1%) in 7 patients (systemic sclerosis, Sjögren's syndrome, vasculitis, Behçet's disease, gout, osteoarthritis and connective tissue diseases).

Particularly, regarding the rheumatologic manifestations of Hepatitis C, we identified rheumatoid arthritis in 6 patients (23%), spondylarthritis in 6 patients (23%), undifferentiated polyarthritis in 4 patients (15.4%), and ankylosing spondylitis in 4 patients (15.4%). %) SLE in 4 patients (15.4%), psoriatic arthritis in 2 patients (4.2%)

It should be noted that 27.1% of this group of patients were currently under biological therapy.

Conclusion: Given that 2.2% of patients, followed in both specialties, present simultaneous digestive and rheumatologic pathology, it is fundamental to characterize the impact and therapeutic repercussions that come from the clinical overlap between pathologies.

Disclosure: Nothing to disclose

P1456 TOTAL GLUCOSIDES OF PAEONY DECREASES APOPTOSIS OF HEPATOCYTES AND INHIBITS MATURATION OF DENDRITIC CELLS IN AUTOIMMUNE HEPATITIS

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Introduction: Total glucosides of paeony (TGP), an active mixture extracted from paeony root, has anti-inflammatory, immune regulatory effects and is widely used for the treatment of autoimmune diseases such as rheumatoid arthritis. However, the role of TGP in autoimmune hepatitis (AIH) is still unknown. Here, we investigate the effect of TGP in concanavalin A (Con A) induced experimental autoimmune hepatitis (EAH) and the molecular mechanisms *in vitro*.

Aims & Methods: C57BL/6 female mice were injected intravenously with Con A (20 mg/kg) to generate a model of EAH. TGP (936mg/kg) was administered by gavage once daily for 3 days before Con A challenge. The levels of serum liver enzymes, variations of immune cells recruited in liver including dendritic cells(DCs), T cells, macrophages and myeloid-derived suppressor cells (MDSCs), liver pathologic examines were determined 12 h after Con A injection. *In vitro*, the LO2 cell lines were used to examine the susceptibility of hepatocyte to Con A and explore the underlying mechanisms.

We treated the hepatocyte with Con A (10μg/mL)and TGP (100mg/L). Mitochondrial membrane potential ($\Delta\Psi$m), reactive oxygen species (ROS) level, apoptosis related proteins including Bax, Bcl2 and cleaved-Caspase3 were detected.

Moreover, immature DCs were generated from mice bone marrow dendritic cells (BMDCs) and then cultured with GM-CSF, IL-4 and β-ME. We then treated the immature BMDCs with Con A (10μg/mL) and TGP(100mg/L) for 24 hours. The expression of major histocompatibility complex II (MHCII), CD11C and CD80 was determined by flow cytometry (FCM).

Results: In Con A- induced EAH mice, pretreatment with TGP reduced the levels of serum liver enzymes including alanine transaminase (ALT), aspartate transaminase (AST). Moreover, decreased histopathological damage was detected in the TGP-pretreated condition. Importantly, the FCM data showed that pretreatment with TGP reduced the infiltration of mature DCs and activated CD4+ T cells in liver.

In vitro, MTT assay showed that TGP(100mg/L) had protective effect on LO2 cell lines as compared with cells treated with Con A alone. Pretreatment with TGP ameliorated $\Delta\Psi$m decline, ROS level imbalance and apoptosis increase of hepatocytes stimulated by Con A. In addition, The expression of Bcl2 was increased during this process, accompanied with decreased level of Bax and cleaved-Caspase3. Therefore, TGP might decrease hepatocytes apoptosis through a mitochondrial apoptotic pathway. In the meantime, the maturation of BMDCs was inhibited by TGP as evidenced by lower levels of MHCII and CD80 as compared with Con A treated cells.

Conclusion: TGP could ameliorate Con A-induced EAH by regulating apoptosis of hepatocytes and maturation of DCs. It might be a potential compound in treating AIH.

Disclosure: Nothing to disclose

P1457 DO NON-INVASIVE MARKERS OF FIBROSIS HAVE A PLACE IN THE EVALUATION OF FIBROSIS IN OVERLAP SYNDROME?

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Introduction: The non-invasive markers of fibrosis are currently validated in viral hepatopathies but less validated in other dysimmune liver diseases. Very few studies have focused on the place of non-invasive markers of fibrosis in the overlap syndrome. The aim of our study is to determine the correlation between non-invasive markers of fibrosis and histological fibrosis scores in overlap syndrome.

Aims & Methods: A retrospective study that collects all patients with an overlap syndrome: primary biliary cholangitis - autoimmune hepatitis or primary sclerosing cholangitis - autoimmune hepatitis. The APRI and FIB-4 scores were calculated at the time of diagnosis and one year after treatment. A liver biopsy specifying the degree of fibrosis according to Metavir was performed at the time of diagnosis. Liver elastography was done after one year of treatment. Fibrosis was considered significant from F2 for hepatic elastography and Metavir score and a cut-off > 1.5 and > 3.25 for APRI and FIB-4, respectively. The Spearman correlation test and the ROC curve were used to analyze the data.

Results: Our study involved 56 patients divided into 52 women and 4 men of average age 51.1 years (30-73 years). Autoimmune hepatitis was associated with primary biliary cholangitis in 89.3% of cases and primary sclerosing cholangitis in 10.7% of cases.Spearman's correlation analysis did not show a correlation between serum markers measured at the time of diagnosis and the degree of histological fibrosis (r = 0.5, p = 0.001). Among the 52 patients who would have significant fibrosis according to the APRI score, 20 patients had no significant histological fibrosis (F0, F1). Among the 48 patients who would have significant fibrosis according to the FIB-4 score, 30 actually had significant fibrosis (> = F2).After one year of treatment, 54 patients underwent hepatic elastography, which showed significant fibrosis in 70.3% of cases (38 patients). Correlation analysis did not show any correlation between serum markers of fibrosis and hepatic elastography. Among the 38 patients with significant fibrosis according to the measurement of hepatic elastography, 16 patients and 12 others were presumed to have no significant fibrosis according to the APRI and FIB-4 scores, respectively.

Conclusion: In our study, we did not find any correlation between the different non-invasive markers of fibrosis and the results of the liver biopsy, which remains to this day the gold standard for assessing liver fibrosis in dysimmunity disorders like overlap syndrome.

Disclosure: Nothing to disclose

P1458 PREDICTION OF THE PROGNOSIS OF ADVANCED HEPATOCELLULAR CARCINOMA PATIENTS BY HTERT PROMOTER MUTATION IN CIRCULATING TUMOR DNA

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Introduction: Human telomerase reverse transcriptase (hTERT) promoter mutation is found in about 50% of hepatocellular carcinoma (HCC), which is the most frequent somatic genetic alteration in HCC. Several clinical studies have revealed that the presence of the hTERT promoter mutation was closely correlated with poor prognosis in solid tumors such as lung and breast cancers. However, the association between the mutation and clinicopathologic features in patients with HCC has not been elucidated well. Recently, cell-free circulating tumor DNA (ctDNA) in plasma/serum has been applied as a noninvasive marker for cancer diagnosis.
Aims & Methods: This study was designed to estimate the clinical utility of ctDNA for detecting hTERT promotor mutation in patients with advanced HCC and to reveal the correlation between hTERT promoter mutation and prognosis. Eighty-six patients with advanced HCC who were treated with sorafenib or lenvatinib at Okayama University Hospital between September 2013 and September 2018 were enrolled in this study. The plasma or serum samples were obtained from their blood prior to the drug administration. ctDNAs extracted from 1ml of plasma or serum samples with QIAamp Circulating Nucleic Acid Kit (QIAGEN, Hilden, Germany) were used to detect hTERT promoter mutations by digital droplet PCR (ddPCR; Bio-Rad, Hercules, CA, USA), and correlations between the presence of the mutation and clinical outcome of the patients were analyzed.
Results: The median follow-up period was 11 months (interquartile range, 6.8-17.7months). The median age of the patients was 73 years and 72% were male. Clinical stages of 4, 11, 31 and 40 patients were II, III, IVa and IVb, respectively. HBs antigen and HCV antibody were detected in 16 (18.6%) and 37 (43.0%) patients, respectively. As for HCC treatments, 71 and 15 patients received sorafenib and lenvatinib, respectively. In the 86 patients examined, 45 patients (52.3%) were positive for hTERT promoter mutation in ctDNA. Presence of the hTERT promoter mutation was correlated with low serum albumin (P=0.048), high aspartate aminotransferase (P=0.016), high alanine aminotransferase (P=0.022), low prothrombin activity (P=0.044), large intrahepatic tumor size (P=0.032), and high PIVKA-II (P=0.032). Overall survival (OS) of the patients with the mutation was significantly shorter than those without it (p=0.001). Median survival time of each group was 11.2 months and 22.2 months, respectively. In univariate analysis with Cox's proportional hazards model, the presence of hTERT promoter mutation [Hazard ratio (HR), 2.13; 95% Confidence interval (CI), 1.20-3.88; P=0.009), low albumin (<3.6 g/dL) (HR, 1.81; 95%CI, 1.03-3.21, P=0.040), high aspartate aminotransferase ($\geqq$25IU/L) (HR, 1.83; 95%CI, 1.45-3.28; P=0.034), Child-Pugh class B (HR, 2.54; 95%CI, 1.22-4.92; P=0.015), vascular invasion (HR, 2.34; 95% CI, 1.29-4.12; P=0.006) were significant factors for poor OS. Multivariate analysis revealed that hTERT promoter mutation (HR, 2.01; 95% CI, 1.09-3.83; P=0.025) and vascular invasion (HR, 2.57; 95% CI, 1.31-4.97; P=0.006) were significant factors for poor OS.
Conclusion: hTERT promoter mutation in ctDNA was associated with short survival and could be a valuable biomarker for predicting prognosis of the patients with advanced HCC treated with molecular target drugs.
Disclosure: Nothing to disclose

P1459 EFFECT OF METFORMIN ON IGF-R-INDUCED APOPTOSIS AND PROLIFERATION IN LIVER CANCER CELLS

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Introduction: Metformin has been well known to have antineoplastic activity in hepatocellular carcinoma (HCC) cells. Studies on AMP-activated protein kinase (AMPK)-related studies and cell cycle inhibition have been reported as HCC inhibitory mechanisms of metformin. Insulin growth factor 1 receptor (IGF-1R) is a receptor involved in cell proliferation, inhibition of apoptosis, angiogenesis and tumorigenesis and tumor-associated inflammation, and targeted therapies for these have been developed and used clinically.
Aims & Methods: This study was performed to determine whether metformin inhibits survival of HCC cells through IGF-1R pathway. HCC cell line HepG2 cells were cultured. In order to investigate the effect of metformin on HepG2 cells according to glucose level, cells were cultured in 5mM glucose and 25mM glucose medium. 3-(4, 5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assays were performed to determine the effect of metformin on the cell proliferation. Apoptosis was measured by a cell death detection enzyme-linked immunosorbent assay and a caspase-3 activity assay. Expression levels of various proteins, with or without specific small interfering ribonucleic acid-induced gene disruption, were measured by Western blot analysis.
Results: Metformin induces apoptosis of HepG2 cells and reduces cell viability. However, the efficacy of metformin-induced apoptosis was reduced in the hyperglycemic environment (25mM glucose). Metformin reduced IGF-1R activity in HCC cells and decreased IRS-1, PI3K, and Akt activities in IGF-1R pathway, leading to increased TSC-2 activity and decreased mTOR activity. When AMPK siRNA was also used to block AMPK function, metformin caused HepG2 cell apoptosis.
In addition, in the normal environment, metformin increased AMPK Thr 172 activity and decreased AMPK Ser 485 activation. However, AMPK Ser 485 activity was increased in hyperglycemic environment as well as AMPK Thr 172.
Conclusion: The inhibitory effect of metformin on HCC cells induces a decrease in IGF-1R activity by metformin and thus promotes apoptosis. In the hyperglycemic environment, the efficacy of metformin on HCC inhibitory effect is decreased, which suggests that the action of mTOR is elevated by AMPK Ser485 phosporylation. Therefore, the use of metformin is helpful in the treatment of liver cancer, especially in hyperglycemia.
Disclosure: Nothing to disclose

P1461 WITHDRAWN

P1460 FIFTEEN YEARS OF HEPATOCELLULAR CARCINOMA, A PARADIGM SHIFT FROM INFECTIOUS TO NON-INFECTIOUS ETIOLOGY

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Introduction: Hepatocellular carcinoma (HCC) is a malignant tumor that is the fifth most common type of cancer and the third leading cause of cancer-related death globally. A study in 2009 concluded that in the Philippines, the most common risk factors leading to the disease were chronic hepatitis b infection and alcoholic liver disease. With an ever-evolving paradigm and change in the trends of diseases, it is imperative to update current knowledge with a more recent collection of data providing essential information on the pre-cursors of Hepatocellular carcinoma.
Aims & Methods: This is a single-center retrospective, descriptive study of all adult patients with hepatocellular carcinoma at Cardinal Santos Medical Center (CSMC) in a fifteen-year span (2003-2018).
Clinical data, including essential demographics such as age, sex, etiology of HCC were obtained and analysis was done using chi-square and t-test, respectively.

Results: Comparison of data showed a statistically significant change in the infectious and non-infectious causes of HCC. Time 1 showed predominance of HCC with infectious etiology, representing 67% of all cases, with most cases from Hepatitis B. Time 2 showed a 22% decrease in this etiology, which could be inferred to be an effect of vaccination readily producing this endpoint. But with a predominantly older age group (mean age 64), a large segment of the population in time 2, specifically 45% had an infectious etiology.

An interesting note is the prominent increase in the number of HCC cases arising from non-infectious causes, with a modest 21% of cases in time 1, to a little over two times of that in time 2. With 73 cases in time 1 and 137 in time 2 representing a statistically significant two-fold increase in these cases, the breakdown shows a shift from a prominent non infectious cause from alcoholic disease towards NAFLD. 72% of non infectious cases in time 2 arose from NAFLD, with ALD, showing significant decrease percentage-wise with the number of cases seemingly overshadowed by the large increase in cases on NAFLD.

N = 674	Time 1 (2003-2010) N=378	Time 2 (2010-2018) N-296	P - Value
Age	63+12.5	66+12.5	1.00
M/F	250/128	255/41	>0.99
HBV	247	104	<0.002*
HCV	7	10	<0.2241
NAFLD	15	99	<0.0000001*
ALD	58	33	<0.035*
Unknown	0	45	NA
DIH	5	0	NA
AIH	0	0	NA

[Table: Results of data from two time periods]

Conclusion: Hepatitis B is still the most common etiology of Hepatocellular Carcinoma. There has been a significant increase in the development of HCC from non-infectious etiologies. Of the non-infectious etiologies, NAFLD seems to be an emerging threat in the development of Liver Cancer.
Disclosure: Nothing to disclose

P1462 C_{60} FULLERENE: ANTIFIBROTIC, ANTITUMOR AND ANTIMETASTATIC NANOTHERAPEUTIC FOR HEPATOCELLULAR CARCINOMA TREATMENT

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Introduction: The excessive production of reactive oxygen species is the main cause of liver cancer initiation and progression, therefore the use of antioxidants could be a promising treatment. Biocompatible pristine C_{60} fullerene is the powerful antioxidant demonstrating low toxicity and ability to be accumulated in liver, so have a prospect as liver disease therapeutic.
Aims & Methods: C_{60} fullerene impact on liver fibrosis, tumor growth and metastasis were aimed to be discovered using rat hepatocellular carcinoma (HCC) model. HCC was initiated by N-diethylnitrosamine (DEN, 200 mg/kg) injection. Two weeks later tumor promotion was achieved by subcutaneous CCl_4 (0.1 ml/100g) injections twice/week continuously. Pristine C_{60} fullerene aqueous colloid solution (C_{60}FAS; 0.15 mg/ml, size of aggregates 1.2-100 nm [1]), was administered daily (0.25 mg/kg) starting in 2 weeks from DEN injection. Its impact on liver fibrosis and cirrhosis was assessed at 10th and 15th week, impact on tumor development and metastasis – at 22nd week. Liver injury was evaluated according to [2], by histological (HE staining) and biochemical (plasma blood markers) methods. C_{60}FAS impact on EGFR and pan-cytokeratin expression was assessed in HepG2 cells (IHC). C_{60} fullerene ability to interact with EGFR, FGFR, PDGFR and VEGFR was assessed by molecular docking and molecular dynamics.

Results: C_{60}FAS attenuated liver steatohepatosis and fibrosis and improved liver state in HCC-rats at 10-week stage (as evidenced by histological and biochemical assay). In HCC-rats at 15-week stage C_{60}FAS also diminished liver injury (as evidenced by liver damage score, depression of elevated serum markers and histological assay) and avoided dysplastic cells appearance in pancreas. In HCC-rats at 22-week stage C_{60}FAS prevented tumor development (no tumors in liver compared to well-developed tumors in non-treated rats), attenuated liver injury (liver enzymes decreased, bilirubin was levelled, morphology was improved) and prevented metastasis (no atypical cells in pancreas compared to neoplastic cells aggregates and even well-developed tumors in non-treated animals). Reference 5-fluorouracil demonstrated less efficacy: small single tumors were observed, liver enzymes remained elevated, bilirubin retained higher than that in control.

	10 weeks		15 weeks		22 weeks		
	HCC	HCC +C60FAS	HCC	HCC +C60FAS	HCC	HCC +C60FAS	HCC +5-fluorouracil
Liver damage score	8.2*	7.25*	9.2*	7.8*	11.33*	9.25*	10.25*
ALT		307	193	215			
AST		268	185	152	74	54	48
Conjugated bilirubin		133		171			56
Non-conjugated bilirubin		74		118			49
ALP		345	273				
LDH		2750	1002	150	67		144
GGT		115	49	380	307		384
α-amilase						-91	-56

*[Parameters of liver state, specified in per cent compared to control; only statistically significant values (p<0.05) are presented, *absolute values]*

C_{60}FAS applying in 10-100 μmol/ml concentration inhibited EGFR and pan-cytokeratin expression in HepG2 cells in a dose-dependent manner (by 39-70%). C_{60} fullerene ability to form complexes with ATP-binding sites of EGFR and FGFR but not VEGFR and PDGFR was also demonstrated, which let us to suggest the possibility of such impact in *in vivo* system.
Conclusion: C_{60}FAS can inhibit fibrogenesis, malignant degeneration and metastasis in liver and maintain its functional activity. C_{60} fullerene ability to inhibit EGFR and pan-cytokeratin expression and to block EGFR and FGFR could contribute to its biological activity.

References: [1] Ritter U, et al. Fuller Nanotub Carbon Nanostruct. 2015;23(6):530-4 [2] Liu X, et al. BMC Complement Altern Med 2013;13:375
Disclosure: Nothing to disclose

P1463 3-MERCAPTOPYRUVATE SULFURTRANSFERASE REPRESSES TUMOR PROGRESSION AND PREDICTS PROGNOSIS IN HEPATOCELLULAR CARCINOMA

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Introduction: The prognosis for hepatocellular carcinoma (HCC) remains dismal in terms of overall survival (OS), and its molecular pathogenesis has not been completely defined. 3-mercaptopyruvate sulfurtransferase (MPST) is one of enzymes to regulate endogenous hydrogen sulfide (H_2S) biosynthesis. The expression and functional role of MPST in HCC has never been investigated. We aimed to clarify the role of MPST in HCC.
Aims & Methods: MPST protein expression in HCC specimens was mainly analyzed by immunohistochemistry (IHC) using a tissue microarray (TMA) containing HCC tumor tissue and matched adjacent tissues from 90 patients. Another 12 paired clinical HCC samples were used for MPST protein determination. The effect of MPST on HCC progression was studied *in vitro* and *in vivo*. A diethylnitrosamine (DEN)-induced liver cancer model was used to evaluate the role of MPST in hepatocarcinogenesis.

Results: TMA in 90 cases revealed that MPST was significantly downregulated in 80 HCC clinical specimens compared to their paired non-tumor tissues by IHC staining, with negative expression in one case. Clinically, a low MPST expression was associated with a worse OS (p < 0.05) and larger tumor size (p < 0.05). Downregulation of MPST protein was further detected in all 12 HCC patients compared with their nontumor counterparts. Downregulation of MPST was also investigated in 5 HCC cell lines compared with normal human hepatocyte by using both qPCR and Western blot analysis. Functional studies showed that overexpression of MPST in HCC cells inhibited cell proliferation, clonogenicity and induced apoptosis.

Furthermore, MPST overexpression significantly suppressed the growth of tumor xenografts in nude mice, whereas silencing MPST by intratumor delivery of siRNA markedly promoted tumor growth. Moreover, DEN-induced murine HCC was aggravated by MPST gene knockout. Mechanistically, MPST overexpression induced G1-phase arrest via inhibition of pRb/E2F1 signaling pathway. Consistently, MPST expression correlated negatively with pRb in HCC specimens and was associated with HCC outcomes.

Conclusion: MPST may function as a tumor suppressor gene that plays an essential role in HCC proliferation and liver tumorigenesis. It is a candidate predictor of clinical outcome in patients with HCC, with possible use as a biomarker and intervention point for new therapeutic strategies.

Disclosure: Nothing to disclose

P1464 VALUE OF SERUM ENDOCAN IN PREDICTION OF POST-ABLATION RECURRENCE OF HEPATITIS C RELATED HEPATOCELLULAR CARCINOMA

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Introduction: Hepatitis C virus (HCV)-related hepatocellular carcinoma (HCC) remains a major global health problem. The recurrence of HCC after curative ablation is common, and mandates frequent costly post-ablation investigations especially triphasic computerized tomography (TCT). Serum endocan (a soluble proteoglycan) has been used as a biomarker to predict prognosis in various inflammatory and neoplastic diseases.

Aims & Methods: The aim of this study was to assess the performance of serum endocan level in prediction of HCC recurrence after curative radiofrequency ablation (RFA), in a subset of patients with HCV-related HCC.

In this prospective study, 56 HCV-related HCC patients treated with curative RFA were enrolled, and tumor recurrence was evidenced by typical radiologic criteria using repetitive TCT (quarter yearly), over a mean follow up period of 23.79±7.56 months. Routine clinical and laboratory assessment, estimation of liver disease severity as class A/B according to Child-Turcotte-Pugh (CTP) scoring, and tumor staging (0/A) using Barcelona Clinic of Liver Cancer (BCLC) system, were performed.

In addition, all studied patients underwent baseline (one month after curative RFA) measurement of suggested serum biomarkers of tumor recurrence including endocan, des-gamma-carboxy prothrombin (DCP) and alfa fetoprotein (AFP).

Results: There were significant associations between HCC recurrence (24/56 patients, 42.86%) and several parameters; tumor size ≥3 cm (p 0.025), multiple tumor foci (p 0.028), BCLC stage A (P 0.042), CTP class B (p 0.005), low serum albumin (p 0.007), high serum bilirubin (p 0.011), as well as increased mean values of endocan (p< 0.001), DCP (p 0.004) and AFP (p 0.039).

Using logistic regression analysis, only serum endocan and DCP were independent predictors of HCC recurrence (p<0.001 and p 0.003, respectively). Serum endocan (at a cut-off level ≥2.09 ng/mL) had the highest sensitivity (95.8%) and specificity (87.5%) for prediction of HCC recurrence (p<0.001), followed by DCP ≥208.5 mAU/mL (sensitivity 79.2%, specificity 71.9%, p 0.003), and lastly by AFP ≥75.0 ng/mL (sensitivity 75.0%, specificity 71.9%, p 0.001). Endocan level ≥2.09 ng/mL carries a significantly high risk of HCC recurrence (Odds Ratio: 161.0, Confidence Interval: 16.8-1542.3, p <0.001).

Using Kaplan-Meier survival analysis, the mean recurrence-free survival time was significantly shorter in patients with endocan level ≥2.09 ng/mL than in those with a level <2.09 ng/mL (16.78 vs. 35.24 months, log-rank

test, p<0.001), and the mean overall survival time was significantly shorter in patients with endocan level ≥2.09 ng/mL than in those with a level <2.09 ng/mL (24.95 vs. 32.58 months, log-rank test, p<0.001).

Conclusion: Serum endocan is a useful biomarker that can significantly predict HCC recurrence and survival after radiofrequency ablation.

Disclosure: Nothing to disclose

P1465 SERUM SEROTONIN AS A POTENTIAL DIAGNOSTIC MARKER FOR HEPATOCELLULAR CARCINOMA

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Introduction: Hepatocellular carcinoma (HCC) is a major health problem in Egypt and its incidence is increasing [1]. Alpha fetoprotein (AFP), the most widely used biomarker for HCC diagnosis, is not sensitive for early HCC detection[2]. So, there was a need for other diagnostic seromarkers to replace, or be used in combination with, AFP

Aims & Methods: We aimed to assess the potential role of serum serotonin level in HCC diagnosis. This study was conducted on 75 Hepatitis C virus (HCV)-positive patients. Twenty five healthy age- and sex-matched subjects were included as a control group. Diagnosis of HCC was done according to the American Association for the Study of Liver Disease (AASLD) guidelines. Staging of patients into early- and late-stage HCC was done according to Barcelona Clinic Liver Cancer (BCLC) criteria.

Subjects were divided into 4 groups:

Group I (late-stage HCC) included 21 patients with late-stage HCC on top of liver cirrhosis.

Group II (Early-stage HCC) included 28 patients with early-stage HCC on top of liver cirrhosis.

Group III (cirrhotic) included 26 patients with liver cirrhosis with no evidence of HCC.

Group IV was the Control group.

Serum serotonin level was determined in all recruited subjects using High Performance Liquid Chromatography (HPLC)-fluorescent detection method.

Results: AFP had a statistically significant elevation in group I (late-stage HCC) with a median of 1300 ng/L (195 - 2544 ng/L) compared to groups II and III (early-stage HCC and cirrhosis) ($P \leq 0.01$). Regarding serum serotonin level, it had a statistically significant elevation in group II (Early-stage HCC) with a median of 275 (204.7-400) compared to groups I, III, and IV (Late-stage HCC, Cirrhosis and control) with median of 33 ng/µL (30-50 ng/µL), 50 ng/µL (30-60 ng/µL) and 102 (85-150 ng/µL), respectively (P=0.001). Receiver operating characteristic (ROC) curve showed that serum serotonin had a sensitivity of 100%, specificity 92.3%, Positive Predictive Value (PPV) 93.3%, Negative Predictive Value (NPV) 96% and accuracy of 96.3%, in discriminating early-stage HCC from cirrhosis. The best values were obtained when using serotonin at cut -off value of 108 ng/µL. There was no correlation between serotonin and AFP.

Conclusion: serum serotonin level is a rapid, sensitive, noninvasive diagnostic biomarker for the detection of early-stage HCC. It may improve the sensitivity of AFP for the detection of early-stage HCC if used in combination.

References: Omar A, Abou-Alfa GK, Khairy A and Omar H (2013): Risk factors for developing hepatocellular carcinoma in Egypt. Chin Clin Oncol. (4):43 Lou, J., Zhang, L., and Lv, S. (2017): Biomarkers for Hepatocellular Carcinoma. Biomarkers in Cancer, 1-9

Disclosure: Nothing to disclose

P1466 VASCULAR ENDOTHELIAL GROWTH FACTOR AS A PROGNOSTIC MARKER IN BOTH CONVENTIONAL AND DRUG ELUTING BEADS TRANSARTERIAL CHEMOEMBOLIZATION FOR UNRESECTABLE HEPATOCELLULAR CARCINOMA

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Introduction: Vascular endothelial growth factor (VEGF) increases in hepatocellular carcinoma (HCC) patients. Many studies had evaluated levels of VEGF in conventional transarterial chemoembolization (cTACE) but assessment of VEGF levels in TACE using drug eluting beads (DEB-TACE) versus cTACE has not been sufficiently studied.

Aims & Methods: Aim of the study was to estimate VEGF levels and their relation to response and recurrence in both DEB-TACE and cTACE in patients with unresectable HCC.

Subjects & methods: This parallel concurrent interventional study included 114 unresectable HCC patients: 58 patients underwent cTACE and 56 patients underwent DEB-TACE. All included patients were classified as Barcelona clinic liver cancer (BCLC) stage B. Three samples of venous blood were obtained from all HCC patients one day before, day 1 and day 30 after TACE for estimation of VEGF levels. According to response after TACE, patients in each group were classified into progressive disease (PD), partial response (PR), and complete response (CR) which was followed for complete one year. The results were statistically analyzed.

Results: VEGF levels at day 1 and day 30 were higher than their basal levels in both cTACE and DEB-TACE groups, while no significant difference was found in VEGF levels between the two groups. Patients with PD after TACE in both groups showed significantly higher VEGF than those with PR and CR.

VEGF levels (basal, day 1 and day 30) at cut off values 97.3, 149.8 and 104.1 pg/ml respectively could discriminate treatment success from disease progression with area under receiver-operating characteristic curves (AUCs) 0.806, 0.775, and 0.771 respectively; sensitivity 88.9%, 88.9% and 77.8% respectively and specificity 62.5%, 64.6 and 66.7% respectively (table 1), but had no relation to HCC recurrence in complete response group after 12 months.

	Basal VEGF	VEGF at day 1	VEFG at day 30
AUC	0.806	0.775	0.771
Diagnostic point	VEGF >97.3 pg/ml have poor prognosis	VEGF >149.8 pg/ml have poor prognosis	VEGF >104.1 pg/ml have poor prognosis
sensitivity	88.9%	88.9%	77.8%
specificity	62.5%	64.6%	66.7%
PPV	96.8%	96.9%	91.4%
NPV	30.8%	32%	27.3%

[Diagnostic performance of different VEGF levels]

Conclusion: VEGF may predict response to therapy in both DEB-TACE and cTACE but it has no relation to HCC recurrence.

Disclosure: Nothing to disclose

P1467 DEVELOPMENT OF A SCORING SYSTEM THAT OUTMATCH OTHER SPECIFIC SCORES IN TRANSARTERIAL CHEMOEMBOLIZATION FOR HEPATOCELLULAR CARCINOMA

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Introduction: Barcelona clinic liver cancer (BCLC) is the most accepted staging system in hepatocellular carcinoma (HCC) in Europe. BCLC recommends treatment with transarterial chemoembolization (TACE) in patients with intermediate-stage HCC (BCLC B). Despite this, TACE is also used in patients with more advanced disease.

Aims & Methods: The aim of this study was to develop a prognostic model of TACE treated patients, that relates to complete response at 1 month after TACE according to the mRECIST criteria, and compare it with other TACE specific staging systems. A cohort of 206 patients treated with TACE was analyzed. Using univariable analysis, different prognostic factors were identified and included in the construction of a prognostic model. Subsequently, we simplified the model by categorizing the albumin and C-reactive protein variables. The model was constructed using backward cox regression. We evaluated the capability of our model to predict complete response at 1 month after TACE according to the mRECIST criteria. Finally, the model was compared with BCLC and established TACE specific staging systems (STATE-score and HAP-score) using ROC curve for prediction of mortality at 1 year.

Results: Our cohort had a median age of 68.75±0,8 year, 77.2% were male; etiology of liver disease was hepatitis C virus in 32%, alcoholic liver disease in 40% and hepatitis B virus in 10%, other causes in 18%. BCLC-A was present in 37,4% of the patients, BCLC-B in 50% and BCLC-C in 12,7%. The median survival time was 18,64 months. Patients with mRECIST complete response at 1 month survived longer than other patients (37.44 vs 23.42 months, p=0.034). In Kaplan-Meier analyses presence of portal thrombosis (p=0.009), up-to 7 criteria (p=0.009), C-reactive protein (p< 0.001) and albumin (p=0.002) were identified as independent prognostic factors and used to construct our model with backward cox regression. By dividing in terciles, we identified three different groups of patients, with median survival times of 37.86, 22.87 and 9.61 month respectively (p< 0.0001). BCLC did not differentiated survival in the Kaplan-Meier analyses (p=0.345). HAP-score (p=0.027) and STATE-score (p< 0.001) differentiated survival. Using this model, we identify differences in the 3 groups for proportion of mRECIST complete response with TACE at 1 month (group A: 19.3%, group B: 18%, group C 2.6%; p=0.018). Unlike HAP-score (p=0.41), BCLC (p=0.135) and STATE-score (p=845) did not related with mRECIST complete response at 1 month. When compared with BCLC (AUC 0.468), HAP-score (AUC 0.549) and STATE-score (AUC 0.601), our model presented a stronger capacity to predict mortality at 1 year (AUC 0,696).

Conclusion: Patients outside the BCLC-B stage might benefit from TACE, since survival in patients with BCLC-C was not different from intermediate-stage in our population. Different staging systems for better patient selection are necessary. We identified prognostic factors for patients treated with TACE. Our model is apparently better at predicting mortality at 1-year when compared with BCLC, HAP-score and STATE-score. This model is also able to identify patients with poor response to TACE according to mRECIST criteria. External validation is necessary to confirm these results.

Disclosure: Nothing to disclose

P1468 LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA IN PATIENTS OVER 65 YEARS OF AGE IN IRELAND: IS THIS THE BEST USE OF OUR GRAFTS?

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Introduction: Liver Transplantation (LT) is an established therapy for patients with hepatocellular carcinoma (HCC) with good long term survival. There are however, an increasing number of effective loco-regional therapies (LRT) available with much lower morbidity and mortality risk. It is not well established whether older HCC patients (≥65 years) have worse outcomes after LT and might be better served with LRT. This might free up grafts for patients with decompensated liver disease and reduce waiting list mortality.

Aims & Methods: 1. Compare the survival of older (≥65 years) and younger (< 65 years) patients that received LT for HCC.

2. Compare the survival of older patients following listing for LT to patients treated only with LRT and resection.

Data was collected retrospectively from both, the prospectively maintained national liver transplantation database from January 1993 to December 2017 and our HCC database from January 2014 to December 2018, in St Vincent's University Hospital. Ethical approval for this study was obtained from the local ethics committee. LRT included transarterial chemoembolization, thermal ablation and selective internal radiation therapy. Survival was compared by using Kaplan Meier curve and log-rank tests.

Results: In total, 156 (n=128 < 65years) patients received LT for HCC in our hospital during the study period. The main aetiology of liver disease were alcohol 26.9% (n=42), viral 39.7% (n=62), haemochromatosis 12.1% (n=19) and non-alcoholic fatty liver 6.4% (n=10). The majority of patients were male (83.9%) and the median age at the time of LT was 59 (IQR 53-63). Most patients were within Milan criteria (n=111, 86.4%) and this proportion was similar in the older and younger age groups (82.1% and 87.4% respectively; p=0.45). Older patients had a worse 4-year survival than younger patients (62% vs 78%, p=0.07). We therefore sought to compare the survival of elderly patients considered for LT from the time of listing, to those treated with LRT or resection only (n=79). There was no survival difference between the groups during the follow period (P>0.05). The survival for both groups was 62% at four years.

Conclusion:
Our data suggest that patients over 65 years have higher peri-operative and early mortality following LT compared to younger patients. LRT or resection has proven to be an effective alternative treatment at least in the short to medium term and offers equivalent survival compared to LT in this group. We therefore question the appropriateness of organ allocation to elderly patients with HCC.

Disclosure: Nothing to disclose

P1469 VALIDATION OF ALPHA FETO PROTEIN MODEL AS A PREDICTOR OF RESPONSE ,RECURRENCE AND SURVIVAL IN EGYPTIAN PATIENTS WITH HEPATOCELLULAR CARCINOMA UNDERWENT TRANS ARTERIAL CHEMOEMBOLIZATION

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Introduction: In Egypt, liver cancer forms 23.81% of the total malignancies.[1] Recently, the French study group for liver transplantation reported on a new predictive model for hepatocellular carcinoma(HCC) recurrence post liver transplant, namely the alpha feto protein(AFP) model which considered superior to Milan criteria in predicting recurrence in a training set of HCC patients, and was subsequently validated in a cohort of French patients followed prospectively under the control of the French organization for organ sharing.[2]

Aims & Methods:
Aim: To validate the use of AFP model as a predictor of response, recurrence and survival in Egyptian patients with hepatocellular carcinoma undergoing trans arterial chemoembolization(TACE).

Methods: This cohort study was conducted at Tropical Medicine department at Ain Shams University Hospitals.We included all newly diagnosed patients with HCC who were fit for TACE according to Barcelona Clinic Of Liver Cancer(BCLC) 2012 starting from January 2012 till January 2016.The AFP model was calculated for each patient enrolled in the study before TACE according to the following (Simplified, user-friendly version of the AFP model)[2]:
Largest diameter of hepatic focal lesion (≤ 3cm, 3-6 cm, > 6 cm took points 0,1, 4 respectively).
Number of nodules (1-3 , ≥4 took points 0 ,2 respectively).
Alpha feto protein level (AFP level (IU/ml) ≤ 100 , 100-1000,> 1000 took points 0,2,3 respectively).
Then the patients were classified before intervention into low risk group for TACE (total points < 2) and high-risk group for TACE (total points of 2 or more).The patients were followed up by AFP level,and triphasic spiral CT performed 1 month after TACE to evaluate the response then at 4 months and 7 months post TACE to evaluate the local and distant recurrence.

Results: One hundred and thirty two patients who underwent TACE were included in the study with mean age 57.28 ± 7.46 years and HCV Ab positive predominance (89.4%).According to alpha feto protein model,the patients were classified into low risk group for TACE(43.2% of patients)with median alpha feto protein model equal zero and high risk group for TACE (56.8% of patients) with median alpha feto protein model equal 3.Complete response was achieved in higher percentage of patients in low risk group(91.2 %)than high risk group(73.3%)but without reaching statistical significance (P=0.057).The one and three years recurrence free survival were 50% and 24.1% in low risk group Versus 29.1% and 16.2%in high risk group respectively.Also,the one and three years overall survival rate were 97% and 37.3% in low risk group Versus 98.1% and 11.6% in high risk group respectively but all without reaching statistical significance. On classifying our patients with alpha feto protein level < 100 IU/ml (79 patients) into low risk patients (57 patients) and high risk patients (22 patients) according to alpha feto protein model, we found that complete response was achieved in significantly higher percentage of patients in low risk group(91.2%)than high risk group(69.6%)(P< 0.05).Also, recurrence occurred in a less percentage of patients in low risk group(71.2%)than high risk group(81.2%)but without reaching statistically significant difference between the 2 groups(P>0.05). Median overall survival was significantly higher in low risk group (18 months) than high risk group (16 months) (P< 0.01).

Conclusion: AFP model could be used as a predictor of response, recurrence and survival in HCC patients undergoing TACE especially in patients with alpha feto protein level less than 100 IU/ml.

References: 1- Holah NS, El-Azab DS, Aiad HA and Sweed DM. Hepatocellular carcinoma in Egypt: epidemiological and histopathological properties. Menoufia Med J .2015; 28:718-24. 2-Andrea N, Richard L, Paolo M, et al. Validation of the AFP model as a predictor of HCC recurrence in patients with viral hepatitis-related cirrhosis who had received a liver transplant for HCC: Journal of Hepatology 2017; 66: 552-559.

Disclosure: Nothing to disclose

P1470 INCIDENCE OF CHOLANGIOCARCINOMA AND RISK FACTORS: AN ANALYSIS OF 403295 CONSECUTIVE PATIENTS

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Introduction: Cholangiocarcinomas (CCAs) are a heterogeneous group of tumors that arise from the biliary tract epithelia, and account for nearly 3% of all gastrointestinal tumors. Although CCA is on the rise in most countries, the epidemiology of these cancers has been poorly understood.

Aims & Methods: We therefore aim to assess the prevalence, demographics and risk factors of patients with new diagnosis of CCA presenting in the Emergency Room (ER) of an Academic Italian Hospital. We retrospectively analyzed all ER cases between January 2010 and December 2017 at Humanitas Research Hospital in Milano Italy.

Results: From January 2010 to December 2017 403295 patients entered the ER, in 203 (0.05%) of them the diagnosis was CCA. CCA cases increased from 38 in the 2010-2011 period (38/102103: 0.03%) to 66 in the 2016-2017

period (66/101337: 0.07%) (p=0.007). The most frequent reasons for hospitalization in patients with CCA were jaundice (n=106, 52%), abdominal pain (n=30, 15%) and abnormal liver function tests (n=13, 6%). During the study period 1224 patients (0.3%) entered the ER for jaundice, CCA accounted for 9% of those cases. Out of the 203 patients with CCA, 109 were male (53.7%), the mean age was 68 years (24-88).

No patient had PSC, only 6 (2.9%) had cirrhosis, while 32 had diabetes (15.7%). The anatomical location of the identified CCA was intrahepatic in 21.6% of the cases, perihilar in 29%, distal in 26.6%, and gallbladder in 21%. Tumor staging was 1 in 27 (13.3%), 2 in 57 (28.1%), 3 in 29 (14.3%) and 4 in 90 patients (44.3%). Treatment of CCA could be analyzed in 135 patients, 51 patients (38%) received best supportive care, 43 received Chemotherapy (32%), while 41 underwent surgery (30%).

The rates of surgery increased during the enrolment period however without reaching significant differences (19.7% in 2010-2011 vs 32.5% in 2016-2017, p=0.3).

Conclusion: CCA is a rare presentation in the ER, however with increasing incidence. CCA was found in 9% of all cases presenting with jaundice. Importantly, none of the identified CCA patients had PSC. Further, the low rate of patients with coexisting liver disease (2.9%), the high prevalence of advanced cancer stage (47%) as well as the low rate of surgical treatment (30%) reported by our study highlights the need for research in the field.

Disclosure: Nothing to disclose

P1471 THE IMPACT OF THERAPY OF HEPATITIS C WITH DIRECT ANTIVIRALS ON THE OCCURRENCE OF HEPATOCELLULAR CARCINOMA - A SINGLE CENTER EXPERIENCE

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Introduction: The advent of direct-acting antiviral agents (DAAs) against hepatitis C virus (HCV) with high-sustained virological response rates, represents a major breakthrough in hepatology. The impact of DAAs on hepatocellular carcinoma risk after obtaining sustained virological response (SVR) in patients with chronic HCV infection and advanced liver fibrosis remains to be clarified.

Aims & Methods: The aim of our study was to assess the incidence of de novo hepatocellular carcinoma in a cohort of patients with SVR after antiviral therapy. We prospectively analyzed a cohort of patients with HCV related liver cirrhosis treated with paritaprevir/ritonavir, ombitasvir and dasabuvir (PrOD) ± ribavirin for 12 weeks. Patients were followed between 01 December 2015 and 01 March 2019, in a tertiary referral center from North-Eastern Romania. All patients were evaluated pretreatment according to our National Protocol.

Results: We enrolled in our study 480 patients (mean age 59.1±8.3 years), predominantly female (54.8%), with no prior history of hepatocellular carcinoma. During the study period we recorded a number of 27 (5.6%) de novo hepatocellular carcinoma cases, predominantly males (68%), mean age 61±5.9 years. The mean period between SVR and hepatocellular carcinoma diagnosis was 28±4 weeks. The sonographic findings revealed the predominance of unicentric lesions in 21 (70%) patients and the predominant localization of the lesions were in the VIII liver segment (23%). During follow-up, the main alpha-fetoprotein levels were significantly higher at the time of hepatocellular carcinoma diagnosis compared to baseline (68.01±5.72 vs 11.22±2.21, p< 0.0001).

Conclusion: In conclusion, obtaining viral clearance does not seem to decrease the risk of hepatocellular carcinoma in patients with HCV-related liver cirrhosis after obtaining SVR with DAAs, the percentage of 5.6% being in the range described for the annual incidence of HCC in untreated HCV cirrhosis (between 3% and 7%). The impact of the DAA therapy impact on hepatocarcinogenesis remains pivotal.

References: 1. European Association for the Study of the Liver; European Organisation for Research and Treatment of Cancer. EASL-EORTC clinical practice guidelines: management of hepatocellular carcinoma. J Hepatol. 2012;56:908-943. 2. Baumert TF, Jühling F, Ono A, Hoshida Y. Hepatitis C-related hepatocellular carcinoma in the era of new generation antivirals. BMC Med. 2017 Mar 14;15(1):52. doi: 10.1186/s12916-017-0815-7. Review. PubMed PMID: 28288626; PubMed Central PMCID: PMC5348895. 3. Gigi E, Lagopoulos VI, Bekiari E. Hepatocellular carcinoma occurrence in DAA-treated hepatitis C virus patients: Correlated or incidental? A brief review. World J Hepatol. 2018;10(9):595-602. doi:10.4254/wjh.v10.i9.595.
Disclosure: Nothing to disclose

P1472 SERUM LEVELS OF SOLUBLE PROGRAMMED CELL DEATH-LIGAND 1 PREDICTS PROGNOSIS IN PATIENTS WITH HEPATOCELLULAR CARCINOMA AFTER CURATIVE TREATMENTS

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Introduction: Immunotherapy in hepatocellular carcinoma (HCC) is a recent and very promising approach, namely the inhibition of the PD/programmed death-ligand 1 (PD-L1) axis. After tumor ablation or surgical treatment the 5 years recurrence rate is beyond 50%. Until now, no serum biomarker has proved to accurately discriminate patients who will develop recurrence from those who will not.

Aims & Methods: In this prospective on-going clinical study we aim to investigate the prognostic value of a soluble form of PD-L1 in HCC patients. During 2016 to 2019 a total number of 267 patients with HCC have been evaluated for possible inclusion in the study. In total 123 patients with Child-Pugh class A, BCLC class 0 or A treated by either ablation (microwave or radiofrequency) or surgery were analyzed. Pre-treatment serum sPD-L1 levels were measured with an enzyme-linked immunosorbent assay (ELISA). Additionally, in 40 out of 123 patients sPD-L1 was also measured 4-6 weeks after ablation or surgery.

Results: Median sPD-L1 concentrations in patients with HCC was 95 (range 47.6-305.4) pg/mL. Using the cut-off value of 95 pg/mL patients were stratified into low (< 95 pg/mL) and high sPD-L1 (³ 95 pg/mL). 108 out of 123 had a minimal follow-up of at least 6 months. After a median follow-up of 18 months the recurrence rate was 10.63% in patients with low sPD-L1 compared to 68.85% in patients with high sPD-L1 (p < 0.001). Disease-free survival was 14.2 months compared to 6.3 months in low vs. high sPD-L1 patients (p=0.001). In 23 out of 40 patients sPD-L1 increased 4-6 weeks after treatment while in 17 out of 40 patients it remained stable or decreased.

Conclusion: We conclude that a high sPD-L1 level is a possible prognostic indicator for a poor outcome in HCC patients after curative treatment. Patients with high sPD-L1 might benefit from combination therapies (e.g. tumor ablation and PD-1/PD-L1 inhibitors). Nevertheless, the predictive value of sPD-L1 levels for a successful anti-PD1/PD-L1 therapy should be investigated in the future.

Disclosure: Nothing to disclose

P1473 BETTER MANAGEMENT OF SORAFENIB RELATED ADVERSE EVENTS IMPACTS ON REASONS LEADING TO DISCONTINUATION AND SURVIVAL

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Introduction: Sorafenib is associated with various adverse events (AEs) potentially leading to permanent drug discontinuation. Common sense suggests that cumulative experience over a long timeframe might improve the

management of drug-related AEs, with a potential benefit to the patients. However, the actual existence and the full extent of this phenomenon have never been investigated.

Aims & Methods: We analyzed a large retrospective-prospective database gathering the clinical data of 201 patients from our Centre, who were consecutively prescribed with sorafenib between 2008 and 2017. We divided these patients in two groups according to the start date of sorafenib (2008-2012 vs 2013-2017), comparing clinical, laboratory and tumor characteristics. In particular, we verified: treatment duration, medium daily dose, reason of sorafenib discontinuation and overall survival (OS).

Results: One-hundred-three and 98 patients started sorafenib in 2008-2012 and 2013-2018, respectively. These groups did not differ in age, sex, performance status, liver function, and tumor staging. Due to more frequent dose reductions, the median average daily dose of sorafenib was lower in the 2013-2018 group (413 vs 518 mg/day, p<0.001). In parallel, the median treatment duration increased in the same group (145 vs 112 day, p=0.027), with no remarkable difference in the cumulative drug dose between the two groups (61.6 vs 58.1 g, p=0.440). The rate of patients permanently stopping sorafenib for intolerance dropped from 23.3% in 2008-2012 to 7.1% in 2013-2017 (p=0.002). The median OS was similar in the two groups (11.1 vs 11.6 months), but the rate of long-survivors (OS>3 year) was higher in the 2013-2017 group (23.4 vs 9.7%, p=0.001).

To reduce the influence of deaths due to early progression, we performed a subgroup analysis of patients who achieved disease control as their best radiologic response. In this case, the OS in the 54 patients treated in 2013-2017 was significantly higher compared to that of the 51 patients treated in 2008-2012 (24.4 vs 20.6 months, HR 0.63, 95%CI 0.42-0.96, p=0.031)

Conclusion: Increased experience in the management of sorafenib-related AEs may lead to increased treatment duration and better outcomes in sorafenib-responsive patients. This factor may be of paramount relevance in the era of sequential treatments based on tyrosine- kinase inhibitors, as these molecules share a common toxicity-profile.

Disclosure: Nothing to disclose

P1474 WITHDRAWN

P1475 A NEW TOOL FOR INTRADUCTAL BILE DUCT TISSUE SAMPLING: EX-VIVO CLINICAL EVALUATION OF CHOLANGIOSCOPY-GUIDED CRYOBIOPSY TECHNIQUE

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Introduction: Indeterminate biliary strictures still represent a major challenge in endoscopic diagnostics today [1], [2]. ERCP, EUS-FNA and cholangioscopic guided biopsy show unsatisfactory sensitivity and may not exclude malignancy [3], [4]. The cryobiopsy technique (CB) is a new method for tissue extraction which is already used for endobronchial biopsies in clinical routine. Several studies have demonstrated that CB is superior to conventional biopsy techniques such as forceps biopsies (FB) [5], [6].

Aims & Methods: The aim of this ex-vivo clinical study was to investigate feasibility and tissue quality of CB in comparison to FB forceps for the retrieval of native and pathologically altered bile duct tissue.

We Included 14 patients with suspected tumor obstruction of the common bile duct who underwent a pancreaticoduodenectomy. Postoperatively, the bile duct was exposed by lengthwise incision. Tissue samples were then taken either from visibly altered areas or, if not visible, from native bile ducts. A new prototype of a cryoprobe with a diameter of 1.1 mm (Erbe Elektromedizin GmbH, Tubingen, Germany) that was connected to a gas supply device (ERBECRYO2) as well as a standard forceps for the gastrointestinal tract (Boston Scientific Radial Jaw 4 Marlborough, Massachusetts, USA) were used for comparison. CB activation time differed from 1 to 6 seconds. A minimum of 3 biopsy attempts per patient were performed with each method. All biopsy specimens were assessed by two pathologists who were blinded to the biopsy method. Data was collected and analyzed for general feasibility, specimen area, and histological as-

sessability (evaluated by using a 7-point Likert scale ranging from 0-6). Samples were defined as representative, if the samples were big enough, had no or negligible crush artefacts and a score ≥2.

Results: In total 76 biopsy attempts were made from 14 patients. Biopsy retrieved a macroscopically sufficient tissue sample in 22/30 (73.33%) attempts using standard forceps and 25/46 (54.3%) using CB (p=0.014). The success rate of CB was 10/11 (90.90%) when carcinoma tissue was sampled compared to FB 6/9 (66.60%; p=0.285). The agreement between the two pathologist regarding representativity was good, with Cohen's Kappa of 0.69.

Significantly larger samples were obtained by CB (5.60 ±5.0mm²) compared to FB (3.23 ±5.00 mm²; p=0.005). Superior histologic assessability scores were achieved by CB (4.58 ±2.51) compared to FB (3.1 ±1.6; p=0.002). More representative samples were obtained by CB (92%) compared to FB (58%; p=0.011).

Conclusion: CB in the bile duct is feasible and the quality of the obtained tissue is high. FB was more successful in retrieving tissue sample from the native bile duct than CB. There was no statistically significant difference in pathologically altered areas. If CB was successful, larger tissue amounts and more representative samples can be retrieved than with a standard biopsy forceps. With these promising results, an in-vivo study is justified.

References: [1] Moura et al. 2018. Endoscopic retrograde cholangiopancreatography versus endoscopic ultrasound for tissue diagnosis of malignant biliary stricture: Systematic review and meta-analysis. Endoscopic ultrasound 7, 1, 10-19. [2] Navaneethan et al, 2015. Comparative effectiveness of biliary brush cytology and intraductal biopsy for detection of malignant biliary strictures: a systematic review and meta-analysis. Gastrointestinal endoscopy 81, 1, 168-176 [3] Navaneethan et al, 2015. Single-operator cholangioscopy and targeted biopsies in the diagnosis of indeterminate biliary strictures: a systematic review. Gastrointestinal endoscopy 82, 4, 608-14. e2. [4] Weilert et al, 2014. EUS-FNA is superior to ERCP-based tissue sampling in suspected malignant biliary obstruction: results of a prospective, single-blind, comparative study. Gastrointestinal endoscopy 80, 1, 97-104. [5] Hetzel et al, 2012. Cryobiopsy increases the diagnostic yield of endobronchial biopsy: a multicentre trial. The European respiratory journal 39, 3, 685-690. [6] Schumann et al, 2010. Cryoprobe biopsy increases the diagnostic yield in endobronchial tumor lesions. The Journal of thoracic and cardiovascular surgery 140, 2, 417-421

Disclosure: Nothing to disclose

P1476 SYNERGISTIC EFFECTS AND PHARMACOTHERAPEUTIC ACTIVITY OF GEMCITABINE AND CISPLATIN COMBINATION THERAPY IN BILIARY TRACT CANCER CELL LINES

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Introduction: Gemcitabine (GEM) and cisplatin (CDDP) combination therapy (GC) is the primary standard chemotherapy for advanced biliary tract cancer (BTC) worldwide; however, its pharmacotherapeutic activity remains unclear. This study aimed to assess the effects of GC in several BTC cell lines.

Aims & Methods: We evaluated the dose-response activity of GEM and CDDP in 17 BTC cell lines; the cell lines were stratified into three groups based on their sensitivity as effective (IC_{50} of <1μM and calculable ≤IC_{70}), resistant (IC_{50} could not be determined), and medium (sensitivity ≤ IC_{70}) using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTS) assay. Eleven cell lines were selected for analysis of GC activity using the MTS assay. Synergistic, antagonistic, and additive effects of GEM and CDDP were determined by the Bliss additivism model (BM) and combination index (CI) at a GEM:CDDP molar ratio of 7:1 based on human renal clearance.

The effect with a CI score of >1.25 was categorized as antagonistic, that with 0.7-1.25 as additive, that with 0.3-0.7 as synergistic, and that with ≤0.3 as strongly synergistic. Pharmacotherapeutic effects were evaluated by comparison of the IC_{50} value of GEM alone and that of GEM plus CDDP at a 7:1 molar ratio.

Results: GEM was effective against four of the BTC cell lines; four cell lines were resistant and three had medium sensitivity. The results of BM revealed GC had synergistic effects against all cell lines. The CI values against GC at a molar ratio of 7:1 revealed that antagonistic, additive, synergism, and strong synergism were 0, 3, 4, 4, respectively. The cell lines, on which GC had strong synergistic effect, were all GEM-resistant, and IC_{50} by GC was >1 μM. In GEM-sensitive cell lines, the IC_{50} at the 7:1 combination ratio was <1μM. The difference in the IC_{50} values for GEM and GC administration was small. If the IC_{50} value is low, the drug therapy is effective. A strong synergistic effect by GC therapy (molar ratio 7:1) was observed against the GEM-resistant cell lines; however, the corresponding sIC_{50} value was high, indicating a discrepancy between the CI and IC_{50} values.

Conclusion: BM and CI show that GC combination treatment has a high synergistic effect. However, the pharmacotherapeutic activity of GC combination treatment did not considerably differ in GEM-sensitive cells. Strong synergy was noted in GEM-resistant cells, but the pharmacotherapeutic effects were not adequate. To treat advanced BTC more effectively, predictive efficacy markers for GEM to select patients who should be treated with GC and a third therapeutic agent in the GC combination are needed.

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P1477 WITHDRAWN

Pancreas III
09:00-14:00 / Poster Exhibition - Hall 7

P1478 BLOOD NEUTROPHIL-LYMPHOCYTE RATIO AND PLATELET-TO-LYMPHOCYTE RATIO CAN BE EARLY PREDICTORS FOR THE SEVERITY OF ACUTE PANCREATITIS

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Introduction: Given the evidence that Neutrophil-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) can early predict the severity and outcome of many inflammation-association diseases and neoplasm. In this study, we aimed to investigate the value of NLR and PLR in early prediction of the severity of acute pancreatitis.

Aims & Methods: Clinical data of 629 acute pancreatitis patients was collected and then NLR and PLR were calculated on the first admission and correlated with subsequent severity. Severe acute pancreatitis (SAP) is defined by persistent organ failure more than 48 hours, while mild severe acute pancreatitis (MSAP) and mild acute pancreatitis (MAP) were defined into Non-SAP.

Results: Among 629 acute pancreatitis patients, 396 were classified into Non-SAP and 233 into SAP. NLR was 6.79 (0.73-46.00) in Non-SAP group and 16.33 (2.91-96.70) in SAP group, respectively. PLR and NLR were the most significant variables after all the data was analyzed. Receiver operating characteristics (ROC) curves of NLR and PLR were performed to determine the optimal cut-off value to predict SAP. NLR (AUC 0.789; 95% CI: 0.755 to 0.820) combine with PLR (AUC 0.770; 95% CI: 0.729-0.807) can get more accurate value (AUC 0.799; 95% CI: 0.760-0.835) for predicting SAP. Then the receiver operating characteristic areas between each predictive model was compared, there was no significant difference between each group, and NLR combined with PLR (N-PLR) did not have a significant better performance than PLR independently. It demonstrated that PLR and NLR were two independent predictors for the severity of acute pancreatitis.

Conclusion: PLR and NLR can be simple and effective indicators for predicting SAP in early stage.

Disclosure: Nothing to disclose

P1479 A MULTICENTER, INTERNATIONAL COHORT ANALYSIS OF 1435 PATIENTS TO SUPPORT CLINICAL TRIAL DESIGN IN ACUTE PANCREATITIS

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Introduction: Despite the lack of specific treatment of acute pancreatitis (AP), there are relatively few clinical trials that investigate this disease. Our aim was to analyze a large, high-quality, multicenter, international cohort to provide necessary information for study feasibility calculation, study design, sample size calculation and primary outcome selection for clinical trials in AP.

Aims & Methods: First, we searched the medical literature for studies which used C-reactive protein level (CRP) or white blood cell count (WBC), to describe their current role in trials on AP. Second, we analyzed the data of 1435 patients in our multinational registry of AP. Data on CRP and WBC: on admission, within 24 hours form the onset of pain and their highest values during hospitalization were analyzed to investigate their correlation with severity and mortality of AP. Descriptive statistical tools as Kruskal-Wallis, Mann-Whitney U, Levene's F tests, Receiver Operating Characteristic (ROC) curve analysis and AUC (Area Under the Curve) with 95% confidence interval (CI) were performed.

Results: Our literature review showed that CRP is used as an inclusion criterion or as a primary outcome or both (17, 10 and 2 studies respectively) in the earlier and current clinical trials on AP. Its use is extremely variable and not well described. In our cohort, CRP levels on admission predicted mortality and severe cases of AP poorly (AUC: 0.669 (CI: 0.569-0.770); 0.681 (CI: 0.601-0.761) respectively). CRP levels measured within 24 hours from the onset of abdominal pain equally failed to predict mortality or severity (AUC: 0.741 (CI: 0.627-0.854; AUC: 0.690 (CI: 0.586-0.793) respectively). The highest CRP and WBC during the entire hospitalization had equally poor predictive accuracy for mortality and severity of AP. However, if CRP within 24 hours from the onset of pain is an inclusion criterion, then it can markedly elevate the combined even rate of mortality and severe cases of AP (13% for CRP>25mg/l and 28% for CRP>200mg/l). WBC did not show the same characteristics as CRP.

Conclusion: We found that increasing the CRP as an inclusion criterion from the onset of abdominal pain can elevate the event rates of mortality, and severity. This novel finding may decrease the number of patients required for clinical trials in the future. Based on our results, CRP should not be used as a primary outcome in clinical trials and WBC should not be used as an inclusion criterion or outcome in clinical trials on AP.
Disclosure: Nothing to disclose

P1480 ENDOSCOPIC MICRODEBRIDER-ASSISTED NECROSECTOMY FOR WALLED-OFF PANCREATIC NECROSIS - A PROSPECTIVE INTERNATIONAL MULTICENTER FEASIBILITY STUDY

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Introduction: Walled-off pancreatic necrosis (WOPN) is a complication of acute pancreatitis that affects approximately 20% of patients and still carries high risk of morbidity and mortality. Endoscopic drainage by either Lumen Apposing Metal Stents (LAMS), Self Expanding Metal Stents (SEMS) or Double Pigtail Stents (DPS) can help to drain the liquid component of WOPN.

However solid debris may remain in the cavity and can act as a source of ongoing infection and sepsis-related multi-organ failure. Therefore endoscopic debridement is usually recommended but a limitation of the approach is the lack of dedicated devices; this results in the need for multiple, repetitive and time-consuming procedures to achieve complete resolution. A new 3.1 mm flexible mechanized microdebrider catheter can now be deployed through a 3.2 mm endoscopic working channel to resect and remove solid debris under direct endoscopic visualization, and may overcome the limitation.

Aims & Methods: The aim of the ongoing prospective international multicenter study is to explore feasibility and safety of necrosectomy with the flexible endoscopic microdebrider in patients with WOPNs. All patients underwent prior CT scan which had to show WOPN of ≥ 6cm and ≤ 22cm in size with ≥30% solid component. Endoscopic drainage (by either LAMS, SEMS or DPS) was carried out at least three days before endoscopic microdebrider-assisted necrosectomy was performed through the gastrostoma under direct visualization.

Adverse events (AE), procedure times, number of procedures until resolution, percentage decrease of solid necrosis per session, decrease of WOPN size on follow-up CT scans (21 days after final session) and time to discharge were documented.

Results: 19 patients with WOPN were screened in the study between November 2018 and March 2019. 12 patients underwent microdebrider-assisted necrosectomy. No microdebrider-associated adverse events, including bleeding were reported. However, one patient died during the study period not attributed to microdebrider use. A mean of 1.8 interventions (range 1-4) were required with an average microdebrider procedure time of 77 minutes and total procedure time of 180 minutes. There was a mean 63.0% reduction of solid necrosis after the first session. The mean decrease of cavity size was 86.8% in the 5 patients so far reported with completed pre- and post-CT scans. Time from microdebrider-assisted necrosectomy to discharge averaged 6 days (range 0-12 days).

Conclusion: Microdebrider-assisted necrosectomy for WOPN seems to be a feasible and safe procedure that can provide very effective endoscopic clearance of solid debris without device-associated adverse events. Compared to endoscopic necrosectomy using conventional, non-dedicated instruments endoscopic microdebrider-assisted necrosectomy appears to be superior with regard to the number of procedures required for resolution and to overall procedure time.

Disclosure: Schlag - speakers fee, advisory board, travel grants and financial study support from Interscope, Olympus, Medtronic, Esocap, Falk Pharma, Adare Pharma; Other authors - no Interscope-related disclosure.

P1481 DIAGNOSIS OF DISRUPTED AND DISCONNECTED DUCT IN ACUTE PANCREATITIS: A SYSTEMATIC REVIEW

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Introduction: Acute (necrotizing) pancreatitis may result in disrupted or disconnected pancreatic duct syndrome, which is associated with a further complicated clinical course. Diagnosis of disconnected pancreatic duct syndrome is not standardized in clinical practice or international guidelines. We therefore performed a systematic review of the current literature on imaging modalities for diagnosing disruption or disconnection of the pancreatic duct in patients with acute pancreatitis.

Aims & Methods: A systematic search was performed in MEDLINE, Embase and Cochrane library databases up to October 2018 to identify all studies evaluating diagnostic modalities for the diagnoses of a disrupted or disconnected pancreatic duct in acute pancreatitis. All data regarding diagnostic accuracy were extracted.

Results: We included twelve studies, evaluating 286 relevant patients, reporting on five different diagnostic modalities. The overall diagnostic accuracy of amylase-measurement in drain fluids for detecting a disrupted pancreatic duct was 65%, with a sensitivity of 100% and a specificity of 50%. One study evaluated endoscopic retrograde cholangiopancreatography (ERCP), as compared with surgically confirmed disruption, showing a sensitivity of 100%, with no reported specificity. In a selected study population, endoscopic ultrasound (EUS) also demonstrated a 100% sensitivity in detecting a disrupted pancreatic duct. The sensitivity of (secretin)-magnetic resonance cholangiopancreatography (MRCP), as compared with several other diagnostic modalities, ranged from 83.3%-100%, with a specificity of 100%. For secretin-MRCP, sensitivity was 83.3% and specificity was 100%. The sensitivity for computed tomography was 68%.

Conclusion: This systematic review suggests that EUS, ERCP and (secretin)-MRCP are all accurate in diagnosing a disruption or disconnection of the pancreatic duct in patients with acute pancreatitis. Given the poor overall visualization of the pancreatic duct on EUS and the invasive nature of ERCP, however, (secretine)-MRCP would be recommended as first diagnostic modality. Further prospective studies are needed to define the optimal timing and diagnostic value of (secretin)-MRCP in different subgroups of patients with acute (necrotizing) pancreatitis.

Disclosure: Nothing to disclose

P1482 LONG TERM RECOVERY OF PANCREATIC FUNCTION AFTER ENDOSCOPIC TRANSGASTRIC DRAINAGE AND NECROSECTOMY FOR ACUTE PANCREATITIS WITH WALLED-OFF NECROSIS

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Introduction: Acute pancreatitis (AP) can lead to both endocrine and exocrine pancreatic insufficiency. Necrotizing pancreatitis is a severe disease that can lead to changes in body composition and earlier findings show that necrotizing pancreatitis is associated with a high risk of exocrine insufficiency.

Aims & Methods: The aim of this study was to investigate the long-term changes in pancreatic function and body composition in patients with AP and walled-off pancreatic necrosis (WON) following endoscopic transgastric drainage and necrosectomy (ETDN).

We prospectively included patients with WON who underwent ETDN. Patients were evaluated during admission and at 1, 3, 6 and 12 months after discharge with faecal elastase (f-elastase), Haemoglobin A1c (HBA1c), C-peptide, and body composition with dual-energy x-ray absorptiometry (DXA). At 12 months Lundh's test was performed to directly assess exocrine function. Before treatment was initiated, all patients underwent a computed tomography (CT) scan, and CT severity index (CTSI) as well as modified CTSI was calculated.

Results: Eighteen patients were included (67% men; median age 63 years; 44% gallstones; 39% alcohol; 17% other). At 12 months follow-up 57% of the patients had exocrine insufficiency based on Lundh's test and 67% based on f-elastase. Two patients (11%) developed signs of endocrine insufficiency, based on both HBA1c and C-peptide, two patients with only HBA1c being affected.

From discharge to up to 3 months after discharge, we found a loss in mean total body mass from 78.2 ± 18.4 kilogram (kg) to 73.9 ± 18.1 kg (p=0.03), in mean total fat mass from 25.9 ± 11.0 kg to 23.5 ± 9.9 kg (p=0.14) and in mean muscle mass from 49.6 ± 10.1 kg to 47.7 ± 10.3 kg (p=0.15). Between 3- and 12-months follow-up, the mean total body mass increased to 78.6 ± 13.7 kg (p=0,001), mean muscle mass to 49.6 ± 9.6 kg (p=0.03) and mean fat mass to 26.4 ± 7.0 kg (p=0.06). We found no correlation between the changes in body composition and endocrine or exocrine function.

Conclusion: More than half of the patients in present study developed exocrine insufficiency one year after treatment for WON with ETDN. Our results support earlier findings, that patients with WON are at risk of developing especially exocrine insufficiency and that a minor group develop endocrine insufficiency. Although exocrine insufficiency is evident, its influence on changes in weight and body composition is questionable as our patients regained their weight on 12 months follow-up. Furthermore, our results question whether enzyme supplement should be supplemented per se in cases of low f-elastase values, or if the clinical decision should include other parameters such as changes in weight and in muscle and fat mass.

Disclosure: Nothing to disclose

P1483 ENDOSCOPIC ULTRASOUND (EUS) FOR EVALUATION OF PATIENTS WITH ACUTE PANCREATITIS WITHOUT OBVIOUS BILIARY ETIOLOGY

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Introduction: Endoscopic ultrasound (EUS) has emerged as an important tool in diagnostic evaluation of patients with acute pancreatitis (biliary or unknown etiology). The current guidelines recommend performance of endoscopic retrograde cholangiopancreatography (ERCP) by patients with acute biliary pancreatitis only in the presence of cholangitis, dilated biliary ducts or confirmed choledocholithiasis.

Aims & Methods: The **aim** of this study was to utility of EUS by patients with biliary or unknown etiology of acute pancreatitis.

Our retrospective study included EUS investigations performed between 06/2017-03/2019 in our newly established GI-Department, which features a centralized endoscopy-service in a University affiliated tertiary care teaching hospital.

EUS was performed in patients with biliary pancreatitis without cholangitis or dilated biliary ducts in order diagnose/exclude choledocholithiasis. Patients with acute pancreatitis of unknown etiology were investigated with EUS in order to identify a possible etiology (especially biliary).

Results: 60 patients were included in this analysis (33 with biliary pancreatitis and 27 with unknown etiology of acute pancreatitis).

Choledocolithiasis was diagnosed in 12/33 (36.3%) patients with acute biliary pancreatitis. All these patients received ERCP and biliary duct stones were removed. In one patient with acute pancreatitis and gallstones, but without choledocholithiasis, EUS also diagnosed a tumor in the pancreatic head (this was not seen in CT scan). A biopsy was performed and showed an adenocarcinoma.

In 1/20 (5%) biliary pancreatitis cases with negative EUS, the patient developed jaundice on follow-up and ERCP with extraction of bile duct stones was performed.

EUS identified an etiology in 16/27 (59.2%) of cases with initially unknown etiology of acute pancreatitis: biliary-11/27 (40.7%), autoimmune pancreatitis - 2/27 (7.4%), pancreatic tumor (undiagnosed in CT scan)- 1/27 (3.7%), pancreaticolithiasis -1/17 (3.7%) and chronic pancreatitis - 1/27 (3.7%).

Magnetic resonance imaging (MRI) was available in 8/11 (72.7%) patients with pancreatitis of unknown etiology and negative EUS. Pancreas divisum was diagnosed in 1/8 cases. In all other cases MRI was also negative.

Negative MRI was present in 3/16 (18.7%) pancreatitis cases with biliary etiology in EUS. No MRI was available in the other cases.

Conclusion: EUS is a very sensitive method for diagnosing choledocholithiasis in patients with biliary pancreatitis and provide an etiology in two thirds of cases with initially unknown etiology of acute pancreatitis.

Disclosure: Nothing to disclose

P1484 TO COMPARE THE CLINICAL OUTCOME OF PATIENTS OF ACUTE PANCREATITIS (AP) HAVING INTRA-ABDOMINAL HYPERTENSION (IAH) WITH THAT OF PATIENT WITH NORMAL INTRA-ABDOMINAL PRESSURE (IAP)

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Introduction: Acute pancreatitis patients, mainly severe acute pancreatitis, tends to have elevated intra-abdominal pressure which may progress to intra-abdominal hypertension (IAH) and abdominal compartment syndrome (ACS). ACS is shown to correlate with poor outcome and increased mortality in AP. However, outcome of AP with IAH is rarely studied.

Aims & Methods: Study was aimed to compare the clinical outcome of patients of AP with IAH with those with normal IAP. Retrospectively data was analysed of 105 patients of AP from Jan 2016 to May 2018. Parameters

measured included the demographic profile, clinical severity scores, CT severity score (CTSI), persistent organ failure (OF), hospital and ICU stay, need and outcome of percutaneous catheter drainage (PCD), surgery requirement and mortality. Patients were divided into two group based on presence or absence of IAH and were analysed.

Results: Among 105 patients of AP, IAH was present in 48 (45.7%) patients. Both the groups were comparable for clinical characteristics. Patients with IAH had more often severe disease, BISAP ≥2, higher APACHE II scores and CTSI. IAH group had more often OF (87.5% vs. 70.2%, p value=0.033), prolonged ICU stay (12.5 vs. 6.75 days, p value=0.007) and higher mortality (52.1% vs. 15.8%, p value < 0.001). In the IAH group, reduction of IAP by less than 35% at 48hours post-PCD compared to baseline correlated with higher mortality (81.2% vs. 37.5%, p value = 0.004) while in patients with normal IAP no correlation with decrease in IAP and mortality was noted. Need for PCD, surgery and hospital stay were similar in two groups. On multivariate analysis, presence of IAH and CVS failure at presentation were independent predictors of mortality (p value < 0.001 and 0.004, respectively). APACHE ≥10 and CTSI ≥8 at presentation was found to predict the development of IAH (p value 0.014 and 0.019, respectively) on multivariate analysis.

Conclusion: IAH is an independent predictor of mortality in AP. Patients with APACHE ≥10 and CTSI ≥8 at presentation are likely to develop IAH and require IAP monitoring.

Disclosure: Nothing to disclose

P1485 PROGNOSTIC AND DIAGNOSTIC ROLE OF ABDOMINAL PAIN ON ADMISSION IN ACUTE PANCREATITIS

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Introduction: Pain is the most common symptom in acute pancreatitis (AP), and is part of the diagnostic criteria. However, its clinical characteristics in AP have not been detailed in the literature. Our aim was to objectify the diagnostic and prognostic role of acute abdominal pain in AP.

Aims & Methods: Our aim was to objectify the diagnostic and prognostic role of acute abdominal pain in AP. The Hungarian Pancreatic Study Group (HPSG) has prospectively collected multicenter clinical data of 1432 adult patients between 2012 and 2017. The specific pain questionnaire contained data in four categories: intensity of pain (Visual Analog Scale; 1-10, mild [mild]: 1-3, moderate [modP]: 4-6, severe [sevP]: 7-10), duration of pain prior to admission (hours), localization of pain (9 regions of the abdomen), and type of pain (sharp, dull, or cramping). These data were compared to parameters on admission and with the outcome of AP. Statistical analyses were performed accordingly.

Results: Pain contributed to the 'on admission' diagnosis in 99.6% (n=1426) of cases. It was mostly severe (mildP: 5%, n=38; modP: 25%, n=178; sevP: 70%, n=511), cramping (61%, n=705), and epigastric (48%, n=687). Severe pain was associated with a more severe disease course (p< 0.05); however, it failed to predict mortality (p=0.826). Sharp pain was associated with AP severity (p< 0.001), mortality (OR=2.263, 95% CI: 1.199-4.059), and systemic complications (OR=2.263, 95% CI: 1.550-3.970). Localization of pain was not associated with the main outcomes. Thrombocyte (r=0.074, p< 0.05), CRP (r=0.322, p< 0.001) alkaline phosphatase (r=0.171, p< 0.001), γ-GT (r=0.071, p< 0.05), and total bilirubin (r=0.147, p<

0.001) were positively correlated with duration of pain prior to admission, whereas amylase (r=0.212, p< 0.001), lipase (r=0.257, p< 0.001), hemoglobin (r=0.090, p< 0.05) and triglyceride (r=0.892, p< 0.05) showed negative correlation with the duration of pain. Pain within the first 24 hours was accompanied by elevated amylase levels in 78% of cases on admission. If pain lasted more than 72 hours, amylase was only increased in 62% of cases on admission. Furthermore, longstanding (>3 days) pain was associated with milder (p< 0.001) and rather dull pain (p< 0.05), localized in the right abdomen (p< 0.005).

Conclusion: Pain was associated with the main outcomes and different, prognostically or diagnostically important laboratory parameters. Pain later in the disease course becomes atypical, and amylase or lipase reach the diagnostic level less frequently. Our work comprehensively objectified the diagnostic and prognostic role of pain in AP.

Disclosure: Nothing to disclose

P1486 DUAL CENTER EXPERIENCE OF EARLY PANCREATIC NECROSIS LOCATION AND ACUTE PANCREATITIS SEVERITY

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Introduction: Acute pancreatitis is a severe and frequently a life-threatening disease, which can lead to pancreatic necrosis, acute lung injury, SIRS and MODS. In this study, we hypothesized that the early radiologically determined location of pancreatic necrosis can serve as a determinant of acute pancreatitis severity, thus lead to more systematic complications.

Aims & Methods: Acute pancreatitis (n=100) patients in two institutions were studied. Contrast CT scan was performed either on admission or between Days 3-10 during the hospital stay. In addition, CT index, percentage of non-enhancement pancreas, Balthazar score, CTSI score and modified CTSI score were evaluated. A particular emphasis was to the location of non- enhancement pancreas and pattern of pancreatic necrosis. Other findings, such as pleural complications, ascites, pericardial effusion, vascular complications, peripancreatic collections, wall and shape of necrosis and extra-pancreatic organ involvement were evaluated. All CT scans were evaluated by two different radiologists in both institutions.

Results: The subjects were selected based on confirmation of acute pancreatitis diagnosis. We report the preliminary results of the first ten (10%) patients from our cohort. Balthazar score- E-7/10, D-3/10 and CTSI score of 10-10%, 6-40%, 8-10%, 4-10%, 3-20% subsequently. While modified CTSI score of 10-30%, 8-40%, 6-30%, 8-20%, 4-10% accordingly. The presence of pancreatic necrosis was determined by four types of spread patterns based on location. Our data demonstrate location of collections as: bilateral- 4 (40%), central-7 (70%), right-sided-2 (20%), scattered necrosis-3 (30%), left sided-2 (20%), right sided-1 (10%), extension below iliac crest-2 (20%), thus 2 (20%) patients had hyperdense adrenals as sign of shock. In addition, non-enhanced pancreas >50%- 1/10, < 30%- 4/10, while subtotal necrosis >90%-2/10 patients.

Conclusion: Further studies are now underway to analyze the remaining cohort to determine whether early identification of location of pancreatic necrosis can determine severity of acute pancreatitis disease course, thus prevent systemic complications.

References: Types of spread patterns of EXPN (based on the dominant pattern observed, modified from Madry et al 1994 and Ishikawa et al 2006); right EXPN, central EXPN, left EXPN, and bilateral EXPN.

Disclosure: Nothing to disclose

P1487 NECROTIZING PANCREATITIS: CAN DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING HELP IN DETERMINING INFECTION?

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Introduction: Acute pancreatitis is a common disease worldwide, with the majority of patients having a rapidly favorable outcome. Nevertheless, 20% will develop moderate to severe disease with a high risk of infection of necrosis and organ failure; in these cases mortality can reach 15%. Infected necrosis requires management with antibiotics and invasive interventions. However, differentiating sterile from infected necrosis can be challenging. Diffusion-weighted magnetic resonance imaging (DW-MRI) has shown promising results regarding the presence of infection or not in pancreatic pseudocysts. These results have not been generalized to pancreatic necrosis or walled-off necrosis (WON). On the other hand, there is limited data regarding microbiology and antibiotic use in these patients.

Aims & Methods: The aim of the study is to assess the diagnostic potential of DW-MRI to detect infected necrosis, as well as determining the microbiology and antibiotic use in patients with necrotizing pancreatitis.This is a retrospective study on patients with necrotizing acute pancreatitis admitted from 2010-2018, having undergone invasive interventions and MRI before intervention. Patients with chronic pancreatitis were excluded. Microbiology results based on fluid collected during drainage and sequential antibiotic use were recorded. Gold standard for an infected collection was considered when the culture of fluid collected during the initial drainage was positive. MRIs were reviewed and infection of the necrosis or WON was considered in case of a restricted diffusion signal.

Results: Sixty-seven patients were identified. The majority (67.2%) were men, and the main etiology was alcoholic in 30/67 (44.6%). Intensive care unit admission was required for 37/67(53.8%) who presented with organ failure for a median duration of 12 (1-121) days. Median hospital stay was 70 (15-345) days. All patients had, at least, one endoscopic drainage (overall 2(1-8)). Endoscopic necrosectomy was required in 24/67 (36%) and combined percutaneous drainage in 18 (26.9%). DW-MRI was performed in 56 patients; sensitivity of DW-MR to detect infection was 67% and specificity 58%. CT revealed air bubbles in 8 patients; sensitivity and specificity of this sign was respectively 19% and 100%. Cultures collected during the first drainage were positive in 57/67 patients (85%). Microbiology results from the first drainage revealed more frequently gram-negative rods: E.Coli (n=15), Klebsiella Pneumoniae (n=6) and Pseudomonas aeruginosa (n=3) with already 9 multidrug resistant bacteria, whereas fungi were found in 17 patients (candida albicans n=13). All patients were treated with antibiotics with a median duration of 43 (1-137) days, with 3 (0-12) adaptations according to clinical evolution or further bacteriological findings. Amoxicillin-clavulanic acid was the most used first choice antibiotic (n=22), followed by piperacillin-tazobactam (n=14). 35 patients (52%) were treated with antifungal therapy, mostly Fluconazole. Mortality during the initial hospitalization occurred in 12/67(17.9%) patients.

Conclusion: DW-MRI could be a useful additional tool to distinguish between sterile and infected necrosis. Antibiotics are overused in patients with necrotizing acute pancreatitis with suspected infection, resulting in an increase of multidrug resistant bacteria and fungal infections.

Disclosure: Nothing to disclose

P1488 PATIENT CHARACTERISTICS AND PREDICTORS OF DISCHARGE AGAINST MEDICAL ADVICE IN ACUTE PANCREATITIS POPULATION

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Introduction: Discharge Against Medical Advice (DAMA) which is the patient's discontinuation or refusal of medical care is a health problem in the United States (U.S) contributing to worse morbidity, mortality and frequent re-hospitalizations. Despite the significant burden DAMA imposes on healthcare cost and utilization, there is a lack of understanding of the characteristics of patients who DAMA and factors associated with DAMA especially among hospitalized gastrointestinal patients. Acute pancreatitis (AP) on the other hand, is the most frequent gastrointestinal reason for hospitalization in the U.S. We therefore aim to examine the characteristics of patient who DAMA and determine factors associated with DAMA among patients admitted with AP.

Aims & Methods: A retrospective study utilizing the 2014 National Inpatient Sample (NIS) database was performed. All adult patients admitted with a primary or secondary diagnosis of AP were included in this study. Patients who died during index hospitalization or transferred to another facility were excluded. Patient and hospital level characteristics were obtained. Discharge diagnosis and DAMA outcome data were collected. Patient and population characteristics of patients who DAMA were examined using descriptive analysis. Multivariable logistic regression was used to determine factors associated with DAMA in this population. We adjusted for patient and hospital-level characteristics, possible etiologies, type of procedure, and complications.

Results: A total of 51,607 discharge records met our inclusion criteria. N=1,893 (3.5 %) of all discharges were against medical advice. 69% of patients were in the 35-65 years age bracket and 60% were Whites. A total of 58% had some type of government insurance (Medicare or Medicaid) and patients with ≥ 3 co-morbidities had the highest proportion of DAMA (43%).

After adjusting for covariates, patients who use tobacco (OR 1.54, 95% CI 1.31 -1.80), cannabis (OR 1.26, 95% CI 1.01 - 1.59), and other illicit drugs (OR 1.50, 95% CI 1.27 - 1.77) were more likely to DAMA compared to non-smokers, non-cannabis and non-illicit drug users. Patients on government insurance (OR 2.28, 95% CI 1.98 - 2.62), and self-pay (OR 2.34, 95% CI 1.99 -2.78) were more likely to DAMA compared to patients with private health insurance. Interestingly, patients with a diagnosis of gallstone (OR 2.76, 95% CI 1.89 - 4.03) and alcoholic AP (OR 2.31 95% CI 2.01 -2.66) were found to be more likely to DAMA compared to AP from other etiologies. Other factors associated with DAMA in this population include males (OR 1.36, 95% CI 1.51 - 1.23), younger patients and patients with less than 3 comorbidities (OR 1.51, 95% CI 1.79-1.28).

Conclusion: In the acute pancreatitis population, factors associated with DAMA include younger male patients, the use of tobacco and illicit drugs, patients on government insurance, patients with gallstone, alcohol-induced pancreatitis and patients with fewer number of comorbidities. Understanding the characteristics of patients discharged against medical advice and the factors that may influence the decision to DAMA may help identify specific populations for pre- and in-hospital intervention to help reduce the incidence of DAMA and its associated morbidity and mortality, as well as reduce the overall cost related to re-hospitalizations in this patient population.

Disclosure: Nothing to disclose

P1489 SPECIFIC CRYSTALLOID SOLUTIONS VERSUS NORMAL SALINE FOR ACUTE PANCREATITIS – META-ANALYSIS WITH TRIAL SEQUENTIAL ANALYSIS

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Introduction: Intravenous fluid resuscitation is a cornerstone of treatment for pts with acute pancreatitis (AP) directed to prevent hypovolaemia and organ hypoperfusion. Specific crystalloid solutions with additional potential anti-inflammatory and buffer agents such as lactate or acetate, and lower chloride levels have been researched in different critically-ill pts compared to the use of normale saline, showing potential superiority.
Aims & Methods: We aimed to evalute the effects of these specific crystalloids in AP pts and assess the level of available evidence. We performed electronic searches of Medline, Web of Science, Scopus, and The Cochrane Library for randomized controlled trials assessing the use of specific crystalloid solutions for treatment of AP. Mortality and organ failure (OF) were assessed as primary outcomes. Secondary outcomes included SIRS, pancreatic necrosis (PN), infected pancreatic necrosis (IPN), local complications (LC), and length of hospital stay. TSA was performed for the primary outcomes, and secondary outcomes showing a significant result in meta-analysis, with alpha of 5%, and power of 80%. Results for dichotomous outcomes were expressed as risk ratios (RRs) with 95% confidence intervals (CIs), and continuous results were expressed as mean differences (MDs) with 95% CIs.
Results: Three RCTs with a total of 127 patients were included in the analysis. All trials compared the use of RL (n=) compared to NS (n=). The mortality and OF rates were similar in both groups with RRs 0.36 (95% CI 0.04 to 3.30;I2=0%) and 0.39 (95% CI 0.09 to 1.76;I2=0%), respectively. Development of PN was reduced with RL (RR 0.28; 95% CI 0.09 to 0.91;I2=0%). SIRS rates at 24h were lower among pts receiving RL (RR 0.38;95% CI 0.15 to 0.98;I2=36%) and the length of hospital stay was shorter (MD -0.80;95% CI -1.23 to -0.37;I2=78%). TSA was not performed for mortality due to too little information available. To detect a RR reduction (RRR) for OF of 30% and a rate of 20% among controls, a total of 1231 pts are required. A 30% RRR with 30% PN rate among controls would require a 1151 pts, while a 30% RRR with 40% SIRS rate among controls would require 2227 pts. A required information size of 218 pts was calculated based on a minimal relevant effect of reducing hospital stay for 1 day (SD=1.52). To detect All TSA analyses were performed for the total of 127 randomized pts.
Conclusion: Evidence favoring use of Ringer's lactate over normal saline for treatment of AP is very low. We couldn't identify RCTs evaluating other specific and balanced crystalloid solutions. Further research is needed.
Disclosure: Nothing to disclose

P1490 EXPERIENCE OF HOT-AXIOS STENT INSERTION IN A TEACHING HOSPITAL IN WEST LONDON

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Introduction: Pseudocysts are a known complication of acute or chronic pancreatitis which can require intervention if symptomatic. The drainage can be achieved endoscopically, surgically or by Interventional Radiology. The endoscopic approach has been shown to be associated with less complications than the other routes.
Aims & Methods: We have analysed data from January 2016 to February 2019 of patients that underwent Hot Axios stent insertion. The data were stored in the electronic endoscopic and patient's record. We collected data on gender, age at stent insertion, patient's background, symptoms that led to endoscopy, hospital stay length and outcome.
Results: Total of patients that had Hot Axios inserted were 41.
Mean age at diagnosis was 53 years. 17 (41%) were females and 24 (59%) were males. 44% patients presented with abdominal pain and vomiting and 22% had associated weight loss. 17% (n 7) had chronic pancreatitis and 5% (n 2) had underlying cancer. Length of hospital stay median of 7

days (0-135). 20 patients had no complications (49%), 4 (10%) reported pain, 9 (22%) sepsis, 2 (5%) bleeding. Sepsis was controlled with repeat necrosectomies and antibiotics.
All patients had resolution of symptoms necessitating cystgastrostomy.
In our cohort there were 2 deaths (5%) which were not related to the stent insertion.
Conclusion: We described our experience over 3 years in a London teaching hospital which receives referrals from all over the region. Sepsis appears to be a relatively common complication of Hot Axios pancreatic pseudocyst drainage necessitating further endoscopic procedures. Accurate selection of patient may help to improve clinical outcome and decrease the complication rate.
Disclosure: Nothing to disclose

P1491 PERFORMANCE OF FAECAL ELASTASE 1 TEST AGAINST THE "GOLD STANDARD" 3 DAY FAECAL FAT COLLECTION TEST FOR THE DIAGNOSIS OF PANCREATIC EXOCRINE INSUFFICIENCY (PEI) IN PATIENTS WITH CHRONIC PANCREATITIS: IT IS TIME TO CHANGE TO CUT-OFF VALUE!

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Introduction: Correct diagnosis of pancreatic exocrine insufficiency (PEI) is very important as pancreatic enzyme replacement therapy improves patient's outcomes. Faecal elastase 1 test is increasingly use as the test of choice for establishing the diagnosis, with the cut-off value varies between >200 and >100mcg/g. With such cut-off values, although the prevalence of PEI in relative benign conditions such as irritable syndromes, diabetes mellitus and age has been reported up to 15%, a majority of these patients did not have pancreatic abnormality on further evaluation. These findings question the validity of the FE1 test and its cut-off values. Validating data of FE1 test against the gold-standard 3-day faecal fat test are lacking.
Aims & Methods: To assess the performed of FE1 test against the gold standard 3-day faecal fat test for diagnosing PEI in patients with chronic pancreatitis.
This was a multicenter study (NCT03481803) that evaluated the presence of PEI in patients with a known history as well as imaging changes of chronic pancreatitis. All patients underwent a screening test for PEI using the FE1 test, which was defined as FE1 < 100mcg/g. Only patients who had FE1 value of less than 100mcg/g underwent further testing with an in-patient 3-day faecal fat test with standardized high fat meal. Both FE1 and 3-day faecal fat tests were evaluated in a centralized laboratory (Sonic, Australia). The 3-day faecal fat test was further validated by another tertiary laboratory in France. Coefficient of Fat Absorption (CFA) is calculated and value of less than 50% indicates the presence of PEI. Descriptive statistics as well ROC analyses were performed.
Results: Of a total 56 patients with clinical and imaging diagnosis of chronic pancreatitis, only 24 (43%) patients had FE1< 100mcg/g. Based on the 3-day faecal fat test, only 5 (21%) patient had PEI, with 11 patients had CFA≥80% and 8 patients had 80%>CFA≥50%. Even if PEI is defined as CFA of less than 75%, PEI is presence in only 9 (37.5%) patients. This would give a false positive PEI diagnostic rate by FE1 test of 79% and 64.5%, respectively. Whilst all patients with CFA< 50% had FE1 of less than 20mcg/g, 10/19 (53%) patients with CFA>50% had FE1< 50mcg/g. Using the ROC analyses, the cut-off value of 37.5mcg/g given the best sensitivity (65%) and specificity (100%).
Conclusion: In patients with clinically proven chronic pancreatitis, only 21% of patients with FE1 < 100mcg/g have PEI. Even if the PEI cut-off value for PEI is lowered to 50mcg/g, the false positive rate is still 53%. Our study suggests that the cut-off value of FE1 to define PEI should be lowered, and a value of less than 37.5mcg/g gives the best diagnostic performance and negate the risk of false positivity.
Disclosure: Nothing to disclose

P1492 PANCREAS VOLUME AND FECAL ELASTASE-1 AS PROGNOSTIC MARKER FOR PANCREATIC EXOCRINE INSUFFICIENCY FOLLOWING PANCREATIC RESECTION

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Introduction: Pancreatic resection can lead to pancreatic exocrine insufficiency (PEI). Fecal elastase-1 (FE-1) test is an effective marker for assessment of PEI in patients who underwent pancreatic resection. We measured pancreas volume, FE-1 level, and BMI of 36 patients who underwent pancreatic resection. The aims of this study ware (1) to assess the relevance between reduced pancreas volume and decreased FE-1 level, (2) to assess the effectiveness of FE-1 level as predictive marker on underweight caused by PEI in patients with pancreatic resection.

Aims & Methods: 36 Patients who underwent pancreatic resection at Kyungpook national university hospital between April 2015 and December 2018 were enrolled. Pancreas volume, FE-1 level and BMI were measured in all 36 patients after pancreatic resection. Patients were divided into three groups according to FE-1 level: "normal" (≥200 μg/g), " intermediate decrease" (15-199 μg/g), "severe decrease" (< 15 μg/g). The association of pancreas volume, FE-1 level, and BMI was analyzed respectively.

Results: Mean FE-1 level was 100.3 μg/g. 7 patients (19%) had normal pancreatic exocrine function and 29 patients (81%) had PEI in patients who underwent pancreatic resection. In PEI patients, 19 patients had "intermediate decrease" FE-1 level and 10 patients had "severe decrease" FE-1 level. 8 patients had underweight on BMI (BMI < 18.5). Reduction of pancreas volume was not significantly associated with decrease of FE-1 level and body weight loss as indicated by BMI (P= .14, P= .33, respectively). And also, FE-1 level was not significantly associated with BMI (P= .80). However, decreased FE-1 level has weak correlation with decrease of BMI (P= .16). Especially, "severe decrease' of FE-1 level has the greater correlation with decrease of BMI (P= .15).

Conclusion: Decrease of FE-1 level is a simple and useful predictive marker for PEI in patients who underwent pancreatic resection.

Disclosure: Nothing to disclose

P1493 NEW INSIGHTS INTO THE DEFINITION OF CHRONIC PANCREATITIS

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Introduction: Early diagnosis of chronic pancreatitis (CP) would be important in order to stop the disease progression in time. Unfortunately, neither definitions nor biomarkers of early CP are available. It has been reported that recurrent acute pancreatitis (RAP) can lead to CP, therefore, the number of previous attacks or RAPassociated parameters may be suitable for characterizing early CP. The main aim of this study is to identify biomarkers which are significantly different in acute pancreatitis (AP), RAP, and CP. Another aim is to understand the modifying effect of the number of acute episodes which could be considered as early CP.

Aims & Methods: The Hungarian Pancreatic Study group has built up a prospective register of subjects with AP. In the last six years, precise clinical data were collected from 1435 patients. In this study, data on the number of episodes from 1315 patients with high data accuracy were analyzed.

Results: In our cohort, 983 (74.75%), 270 (20.53%), 62 (4.72%) patients had a single episode of AP, RAP, and CP, respectively. In the RAP group, 173 patients (64.07%) had 2 episodes, 43 (15.93%) had 3 episodes, 24 (8.89%) had 4 episodes, and 30 (11.11%) had 5 or more episodes. Thirteen biomarkers were significantly different in the first attack of AP and CP. The significant difference between AP and CP disappeared after the second episode of AP concerning 8 biomarkers (gender, age, biliary etiology, alcohol consumption, pseudocyst development, gammaGT, amylase, and red blood cell count), as did after the third episode concerning 3 biomarkers (biliary etiology, body mass index, ASAT) as did after the fourth and fifth episodes concerning 2 biomarkers (ALAT and smoking). As an average, the significant differences between AP and CP disappeared from 2.63 attacks. The average number of acute episodes of patients with preexisting morphological alterations of the pancreas (CP group) was 4.77.

Conclusion: A definition of early CP may be 3 or more previous attacks of AP without chronic morphological alterations in the pancreas.

Disclosure: Nothing to disclose

P1494 PHENOTYPIC AND GENOTYPIC PROFILES IN CHRONIC PANCREATITIS ASSOCIATED WITH CYSTIC FIBROSIS GENE CARRIER STATUS

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Introduction: Pancreatic function has been used in the literature to assess the severity of Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene mutations. The mutations are classified from I to VI; Class I produce no protein, in class II the protein fails to reach the apical membrane, and class III produce protein that fails to respond to cAMP. Classes I to III are called severe mutations and associated with pancreatic insufficiency. Class IV (reduced conductance) and class V (reduced protein synthesis or partially defective) are mild mutations and associated with pancreatic sufficiency.

Aims & Methods: To examine the relationship between cystic fibrosis mutations classifications and pancreatic function in a cohort of patients with chronic pancreatitis and CFTR gene mutations. We conducted a retrospective analysis of all the genetic and the pancreatic function data for all the patients in Manchester Royal infirmary Pancreatology Unit with Chronic pancreatitis and CFTR gene carrier status between 1999 to 2018.

Results: Analysis of pancreatic function was carried out in 42 chronic pancreatitis patients with CFTR mutations. 36 were heterozygous and 6 compound heterozygous. In the heterozygous cohort 30 genes were identified as severe mutations (22 F508. 2 G551 1. I148T/7T, 2 D1152H 1. TG115T5, 1. 1679G, 1 R553X). The overall prevalence of PI was 50%. There was no statistical difference in this prevalence on further subdividing the genes to class I, II, and III. The majority presented as pancreatic sufficient (99%) and later on developed PI. The remaining 6 in the heterozygous group carried mild mutations (Arg117) class IV. PI prevalence was 66%, 33% were pancreatic insufficient at presentation. The prevalence of PI in the 6 compound heterozygous group was 66% (4), 3 were combination of severe and mild mutations F508/Arg117 the other 3 combination of severe and severe mutation (D1151/F508del and F508/G511). Both groups had the same prevalence of PI.

Conclusion: Pancreatic function does not correlate with the class or the severity type of the mutation in both the heterozygous and the compound heterozygous in CFTR patients. In this cohort of patients Presenting with pancreatitis most are pancreatic sufficient which implies additional factors might play a role in the development of pancreatic insufficiency.

Disclosure: Nothing to disclose

P1495 ETIOLOGY AND MORPHOLOGY IMPACT CLINICAL COURSE OF CHRONIC PANCREATITIS

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Introduction: Symptoms caused by chronic pancreatitis (CP) are common but often elusive hampering therapeutic decisions. Though correlations of morphologic findings in imaging and clinical appearance remain vague. We aimed in investigating whether a distinct combination of clinical parameters can better define the extent of pancreatic insufficiency and disease burden.
Aims & Methods: The aim of the study was to assess the impact of etiology and endosonographic morphology on the clinical course of chronic pancreatitis. Data from 350 CP patients were evaluated retrospectively from a single center data base following predefined criteria:
(i) Confirmed CP,
(ii) endoscopic ultrasound (EUS) plus
(iii) fecal elastase-1 testing,
(iv) age >18 years,
(v) Cambridge Score >1 on EUS evaluation.
Results: In total 182 patients (137 male, 45 female) fulfilled criteria. Median age was 52 years (range 19-88 years). Etiology distributed as follows: idiopathic 50%, alcohol 42.3%, autoimmune 7.7%. 56.6% of patients suffered from chronic pain that was significantly associated with male sex and younger age. Stool elastase-1 activity discriminated exocrine pancreatic function in Cambridge IV significantly better than in lower stages. Similarly, the endocrine function was significantly more reduced in Cambridge IV CP.
Conclusion: A high disease burden is linked to extensive morphological alterations in EUS while pain is more frequent in younger and male patients. The etiology of CP is a predictor for the extent of exocrine impairment.
Disclosure: Nothing to disclose

P1496 IGG4-RELATED DISEASE RESPONDER INDEX BUT NOT SERUM IGG4 CORRELATES WITH DISEASE ACTIVITY AND THE RISK OF 1 YEAR RELAPSE IN TYPE 1 AUTOIMMUNE PANCREATITIS

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Introduction: Type 1 autoimmune pancreatitis (AIP) is one of the possible manifestation of IgG4 related disease (IgG4-RD). A score system to evaluate the IgG4-RD activity (IgG4-RD
responder index - IgG4-RD RI) has been recently published. IgG4-RD RI can be used as an outcome measure both for clinical assessment and for the evaluation of drug response in clinical trials.
Aims & Methods: Aim of the study was to establish the reliability of IgG4-RD RI before and after steroid treatment compared to clinical remission and 1 year relapse.
We retrospectively studied all patients observed in our center with a diagnosis of type 1 AIP based on International Consensus Diagnostic Criteria (ICDC) from January 2012 to December 2016. IgG4-RD RI was calculated at baseline (before steroid treatment - time 0), 1 month after the beginning of the treatment (time 1) and at the end of steroid therapy (time 2). We excluded patients who did not undergo MRI and serum IgG4 dosage at any time.

Results: 33 patients (27 males, 6 females, mean age 60.2±17.2 years) were included. IgG4-RD.
RI was 8.9±4 at baseline, 2.5±3.4 at time 1 (p< 0.0001 vs. time 0), and 4.5±3.9 at time 2 (p=0.029 vs. time 1). IgG4-RD RI was higher at time 0 in 14 patients who relapsed within 1 year (10.9) vs. 19 who did not (7.4) (p=0.009). This difference was not observed at time 1 (3.1 vs. 2.1; p=ns), but it was again documented at time 2 (7.1 vs. 2.5; p=0.002). Serum IgG4 levels were similar at any time in patients who relapsed and in those who did not.
Conclusion: IgG4-RD RI is a useful tool for the management of patients suffering from IgG4-RD, especially for the early detection of disease relapse within 1 year. Its levels seem to correlate with disease activity, whereas serum IgG4 levels are not associated neither with disease activity nor with the risk of disease relapse. Prospective studies with larger cohorts of patients are needed to confirm our data.
Disclosure: Nothing to disclose

P1497 DIAGNOSTIC YIELD OF INTERNATIONAL GUIDELINES ON PREDICTING ADVANCED HISTOLOGY IN BRANCH DUCT PANCREATIC INTRADUCTAL MUCINOUS NEOPLASMS (BD-IPMN): A REAL-LIFE STUDY

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Introduction: The timing and frequency of Branch Duct Pancreatic Intraductal Mucinous Neoplasms (BD-IPMN) malignant progression is unknown. Knowledge of predictive features of advanced histology is fundamental in BD-IPMN management (as an indication for resection surgery). In addition to the American Gastroenterological Association (AGA) guidelines, it was recently published the Fukuoka (2017) and the European Study Group on Cystic Tumors of the Pancreas (ESGCTP, 2018) recommendations.
Aims & Methods: We aimed to compare the diagnostic yield between AGA, Fukuoka and European recommendations in the prediction of advanced histology features in patients with BD-IPMN.
For this, we performed a retrospective analysis of the surgical referral criteria according to the previous mentioned guidelines in the cases of BD-IPMN submitted to surgical resection in a tertiary center between 2010-2018. Advanced Histology was defined by the presence of either high grade dysplasia or adenocarcinoma in the surgical specimen.
Results: We reviewed 54 cases (mean age 63.9 ± 14.6 years, 67% were female). Two-thirds of the lesions were diagnosed incidentally, with a mean diameter of 32.3 ± 15.8 mm. After surgical resection, 17 lesions (31.5%) met criteria for advanced histology.
The Fukuoka and AGA guidelines presented a similar probability ratio for the presence of advanced histology features (Fukuoka: OR 26.81, p < 0.01; AGA: OR 29.87, p < 0.01).
The presence of a relative or an absolute criteria of the European guidelines presented the highest sensitivity for the diagnosis of advanced histology between the three guidelines (Fukuoka 76.5%, AGA 82.4%, ESGCTP 100%), with the lowest positive predictive value (PPV) (Fukuoka 76.5%, AGA 74.7%, ESGCTP 50%).
When considering only the presence of an absolute criteria for surgical resection, European guidelines had greater specificity, PPV and odds ratio (sensitivity 52.9%, specificity 97.3%, PPV 90%, OR 40.5, p < 0.01). However, it also had the higher number of "false negatives" results (Fukuoka n = 4, AGA n = 3, ESGCTP n = 8).
All cases with European absolute criteria also presented with AGA and Fukuoka criteria for surgical resection.
Conclusion: The new European criteria presented the highest specificity for the presence of advanced histology features in the surgical specimen. The combination of the European guidelines criteria with Fukuoka or AGA criteria allowed the optimization in sensitivity/PPV of the European guidelines absolute criteria.
Disclosure: Nothing to disclose

P1498 COLONOSCOPY FINDINGS IN IPMN PATIENTS

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Introduction: Intraductal papillary mucinous neoplasms (IPMNs) of the pancreas are being increasingly detected on an incidental basis given the widespread use and availability of cross-sectional imaging. Given the increased risk of metachronous development of pancreatic cancer, the recommendations for follow-up pancreatic imaging are becoming clearer. However, the association between IPMNs and colorectal polyps and adenocarcinoma is not as clear, resulting in an uncertain recommendation for endoscopic examination.

Aims & Methods: This retrospective study aims to establish the prevalence of endoscopic findings such as polyps and colorectal adenocarcinomas on colonoscopy in IPMN patients. The indications for colonoscopy included screening in asymptomatic individuals and investigation of non-specific abdominal pain. This study also aims to determine whether IPMN characteristics differ according to colonoscopy findings. All IPMNs incidentally identified on cross-sectional imaging between 2007 and 2017 in a single-centre in Malta were included. For those patients who underwent a colonoscopy, endoscopic and histology findings were noted. The respective IPMN classification (branch-duct: BD or main-duct: MD), size and location were recorded.

Results: A total of 355 patients with an IPMN were enrolled, 72 of which underwent a colonoscopy. Adenomatous polyps found in 50% (n=36) of colonoscopies, the majority of which had low-grade dysplasia: 11% had either moderate or high-grade dysplasia. Benign hyperplastic polyps were present in 14% (n=10), while colorectal adenocarcinoma was present in 15% (n=11). Colonoscopy was normal in 21% (n=15).

	Colonoscopy Finding			
	Adenomatous Polyps	**Hyperplastic Polyps**	**Colorectal Adenocarcinoma**	**Normal Colonoscopy**
Frequency of finding on colonoscopy (%)	50 (n=16)	14 (n=10)	15 (n=11)	21 (n=15)
Average age (min-max)	70; (58-85)	66; (55-80)	69; (49-84)	67; (54-86)
Male:Female ratio	1.4:1	1.5:1	1.2:1	1:2
IPMN classification	86% BD-IPMNs; 8% MD-IPMNs; 6% Mixed-IPMNs	100% BD-IPMNs	100% BD-IPMNs	100% BD-IPMNs
Average IPMN size (mm); (min-max)	16; (5-46)	12; (5-21)	18; (7-50)	12; (5-23)
IPMN location - head & neck of pancreas (%)	50 (n=18)	60 (n=6)	64 (n=7)	73 (n=11)
IPMN location - body of pancreas (%)	31 (n=11)	0 (n=0)	27 (n=3)	0 (n=0)
IPMN location - tail of pancreas	19 (n=7)	40 (n=4)	9 (n=1)	27 (n=4)

[IPMN Characteristics According to Colonoscopy Finding]

All IPMN patients with a colonoscopy revealing colorectal adenocarcinoma underwent follow-up imaging (staging and monitoring response to treatment). No change in IPMN size was noted over an average follow-up period of 22 months. 46% (n=5) of adenocarcinomas were located in the caecum and ascending colon, 9% (n=1) in the transverse colon, 18% (n=2) in the descending and sigmoid colon, whilst 27% (n=3) were present in the rectum.

Conclusion: The diagnostic yield of a colonoscopy for an adenomatous polyp or adenocarcinoma in a patient with IPMN is around 65% in our cohort of patients. The IPMNs in these patients tend to be of a larger size when compared to those with a normal colonoscopy or benign hyperplastic polyp. Female IPMN patients are twice as likely to have a normal colonoscopy when compared to males. The location of the IPMN itself does not vary significantly between the different groups. These findings are derived from a retrospective study and hence are subject to bias, however, given the fact that both colorectal adenocarcinomas and IPMNs are epithelial neoplasms within the gastrointestinal tract, a possible association between the two entities remains to be investigated further with prospective studies. At present, recommendations for colonoscopy remain based on conventional practice in gastroenterology.

Disclosure: Nothing to disclose

P1499 RELEVANCE OF ENDOSCOPIC ULTRASOUND WITH FINE NEEDLE ASPIRATION IN PANCREATIC CYSTIC LESIONS SMALLER THAN 3 CM. A RETROSPECTIVE STUDY

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Introduction: Pancreatic cystic lesions (PCLs) are frequent findings frequently require repeated imaging surveillance. Endoscopic ultrasound with fine-needle aspiration (EUS-FNA) for CEA and cytology in pancreatic cystic fluid (PCF) is an accurate diagnostic method. Current guidelines recommend EUS-FNA in PCLs with at least one of these worrisome features (size≥3 cm, mural nodule< 5mm, main duct dilation 5-10mm). The value of pancreatic cystic fluid (PCF) analysis in small PCLs is not clear.

Aims & Methods: To evaluate if patients with PCLs < 3cm, submitted to EUS-FNA for cystic fluid analysis with CEA, amylase and cytology, had adequate cyst classification and an alteration in clinical decision.

Methods: Retrospective analysis of a EUS database including 167 patients with PCLs < 3 cm evaluated by EUS from 2007-16, of which 115 had additional FNA performed for PCF analysis. Clinical, imaging, PCF features (cytology, CEA level, amylase), and clinical decision were prospectively registered. We defined two groups of lesions, Group A (without mural nodule/mass) and Group B (with mural nodule/mass).

Results: In 115 patients, 65% were females, with a mean age of 63 ± 12 years old (33-86), and a mean follow-up time of 37±30months (6-134). Cyst location in: head/body/tail/multiple: 45/42/23/5. Mean cyst size=19±6mm, with percentage of cysts by size (mm): < 10/10-20/>20 in 8,7%/48,7%/42,6. Mass/mural nodule present in 27% (31/115) of PCLs. PCF analysis, with CEA level < 5/5-192/>192 in 18,2%/42,4%/39,4%, amylase< 250 in 40%, and with cytology acellular/benign or inflammatory/LGD/malignant or atypical or NET, in 65%/17%/3%/15% of PCLs. Strategy before EUS-FNA: Imaging surveillance/surgery/other: 71%/18%/11%. Strategy after EUS-FNA: Stop imaging surveillance/imaging surveillance/surgery/other: 6%/66%/17%/11%. A total of 19 patients, were referred for surgery, including 10 in Group A and 9 in Group B. Surgical pathology diagnosis (Group A + Group B): PDAC (0+1), IPMN-ADC (1+1) + NETs (2+0), IPMN (3+3), MCN (1+1), SCA (2+2), lymphangioma (1+0), pseudocyst (0+1), what corresponds to 3 vs 2 malignant, 4 vs 4 pre-malignant cysts, and 3 vs 2 benign cysts in Groups A and B, respectively. CEA was < 5 ng/mL in 20% and 14% of patients in Groups A and B, respectively. Comparing the group of patients referred for surgery with other patients, there was a statistically significant difference with a positive cytology and presence of a mural nodule or mass in the surgery group, but no significant differences in age, cyst size, and presence of septations or CEA level between groups. In Group A, older age and malignant/suspicious cytology but not size, CEA or amylase level in PCLs were related with a malignant final diagnosis and in Group B only a positive cytology correlated with a malignant final diagnosis. In Groups A and B, 29% and 22% of PCLs referred for surgery were malignant, corresponding to 3/84 (3.6%) in group A and 2/31(6.5%) in Group B.

Conclusion: EUS-FNA in small PCLs (< 3cm) allows cytological confirmation of malignancy prior to surgery, even in pancreatic cysts without worrisome features (mural nodule or mass) and it should not be delayed in small cysts because 26% of surgical specimens were malignant lesions. On the other hand, low CEA (< 5ng/mL) occurred in about 1 in every 5 patients, with a possible opportunity to stop surveillance, particularly in PCLs without mural nodules, but in clinical practice surveillance stopped for 6% of patients only.

Disclosure: Nothing to disclose

P1500 PANCREATIC CYSTS: DOES EUS-FNA ADDS VALUE OVER EUS MORPHOLOGY AND MRI? EXPERIENCE OF A TERTIARY-CARE ACADEMIC MEDICAL CENTER

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Introduction: Endoscopic ultrasound (EUS) and magnetic resonance imaging (MRI) are valuable tools in the assessment of cystic pancreatic lesions (CPLs). However, achieving a preoperative diagnosis of CPLs still remains a challenge. EUS-guided fine needle aspiration (FNA) provides a method to obtain cyst fluid for analysis to gain additional information.
Aims & Methods: The aim of our study was to compare the concordance between the diagnosis of the cyst by FNA, with that obtained by two diagnostic imaging methods (EUS morphology and MRI). In addition, evaluate if EUS-FNA offered any benefit in cases of inconclusive MRI.
We performed a retrospective analysis of a prospectively collected database at a tertiary-care academic medical center between January 2015 and December 2018. All patients who were referred for EUS were reviewed, and patients with diagnosis of pancreatic cysts were included. Imaging, pancreatic cyst fluid (PCF) and follow-up were analyzed. Cysts were classified as mucinous or non-mucinous based on any of the following parameters: 1) PCF was grossly mucinous on examination (string sign positive) 2) positive citology 3) CEA level was >192 ng/mL.
Results: A total of 2238 EUS were performed during the study period and 319 of them had a final diagnosis of pancreatic cysts (70% women, mean age 64.46 +/- 13.35 SD). The most frequent indication was surveillance of already known lesions (56%) and inconclusive findings in previous images (32%). The most frequent cystic lesions were IPMN 2 and serous cystic neoplasms (50% and 17% by EUS and 53% and 17% by MRI). FNA was performed on 139 cysts (37%), according to the presence of suspicious signs of malignancy, or at the request of the attending physician. From 139 FNAs, 62 were diagnosed as mucinous by PCF . The agreement between the diagnosis of the cyst by FNA, with that obtained by EUS morphology was 89.2% (Kappa 0.78, P < 0.001). The concordance between the diagnosis of the cyst by FNA and that obtained by MRI was 72.66 (Kappa 0.41. P < 0.001). In the correlation with the images, of the 62 patients with mucinous cysts, 55 had a diagnosis of mucinous by EUS morphology (88% CI 95% 78.1-95.3), while only 27 had mucinous diagnosis by CRMN (43.5% CI 95% 31-56.7).
From the 319 patients with pancreatic cysts 60 (18.8%) had inconclusive results on MRI and EUS morphology was able to make a diagnosis in 31 of them. When we analysed the 139 punctured cysts, MRI was indeterminate in 40 patients and FNA diagnosed 36 of the 40 patients (90%): 13 mucinous, 18 serous, 4 cystic neuroendocrine tumors (NET) 1 pseudocyst.
Conclusion: In our study, EUS with or without FNA was superior to MRI specially in cases of inconclusive MRI.
Disclosure: Nothing to disclose

P1501 WITHDRAWN

P1502 ASPIRIN IS ASSOCIATED WITH INCREASED RISK OF CANCER RELATED DEATH AFTER SURGERY FOR INTRAPAPILLARY MUCINOUS TUMORS OF THE PANCREAS: A LARGE SINGLE CENTER COHORT STUDY

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Introduction: Intraductal papillary mucinous neoplasms (IPMNs) are increasingly considered "the polyps of the pancreas", possibly harboring several degrees of cellular atypia up to invasive cancer. If high-grade dysplasia/cancer is suspected, the patient should be considered for surgical resection. No diagnostic tool can preoperatively predict the degree of dysplasia and, on the contrary of other cancer types, no chemoprevention is available to slow progression and cancer related death. Aspirin (ASA), Ace Inhibitors/Sartans (ACEI/ARB) and Statins (STAT) are widely used in the setting of primary and secondary cardiovascular prevention. Such drugs seem to play a role in modulating incidence and prognosis of different type of tumors such as colon cancer. Such drugs have been suggested to possibly influence also pancreas cancer incidence and prognosis by inhibiting respectively COX 1-2, VEGFR and MAPK cascades. No study has previously evaluated their effect on operated IPMNs.
Aims & Methods: to evaluate the effect of ASA, ACEI/ARB and STAT on cancer related death in a cohort of operated IPMNs patients.
Results: single-center retrospective cohort study on prospectively collected patients operated for pancreatic IPMN. Known risk factors for PDAC and exposure to the target drugs were retrospectively collected. Chi-square, t-test, univariate and multivariate logistic and cox hazard regression analysis were applied when needed.
Results, among 274 operated IPMNs patients, 210 were included in the final analysis, 47.61% males. ASA, ACEI/ARB and STAT were used respectively in 29.18%, 51.90% and 36.84% of cases. At univariable cox hazard regression analysis ASA users displayed a borderline significantly higher risk of cancer related death HR 2.11 (0.90-4.94, 95% CI, p=0.08) while STAT and exclusive ACEI/ARB users did not (respectively HR= 0.77, 95% CI 0.32-1.89, p=0.58 and HR= 1.18, 95% CI 0.49-2.82, p=0.69). At multivariable cox hazard regression analysis adjusted for sex, age, clinical factors associated with both pancreas cancer and cardiovascular risk (such as smoking, diabetes, first degree family history, overweight/obesity and elevated Ca19.9) ASA users were confirmed to be associated with increased risk of cancer related death (HR=2.70, 95% CI 1.10-6.59, p=0.02).
Conclusion: The use of ASA but not STAT and ACEI/ARB is associated to cancer related death after surgical resection for pancreatic IPMNs. Further studies are needed to investigate if this association is the result of an underling pathophysiologic mechanism or the result to a common and yet unknown risk factors exposure.
Disclosure: Nothing to disclose

P1503 VON HIPPEL-LINDAU (VHL) SYNDROME - PRESENTATION AND PANCREATIC FINDINGS OF OUR CASE SERIES

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Introduction: Von Hippel-Lindau (VHL) disease is a rare autosomal dominantly inherited familial syndrome with an incidence of 2-3 cases per 100,000 population. This disease is associated with a high morbidity and mortality involving different organs and have varying phenotypes from family to family. Central nervous system, retina, kidneys and pancreas are the main organs affected by the disease. Pancreatic lesions may range from benign cystic lesions to malignant solid neoplasms. The discovery of any of the syndrome components should raise suspicion of this disease and other organ involvements should be investigated.

We present seven cases of Von Hippel Lindau syndrome evaluated in our pancreas clinic.

Aims & Methods: We present seven cases of VHL disease who were admitted to our pancreas clinic between 2008 and 2018. Three of the seven patients referred to us by neurosurgery department following the cranial hemangioblastoma diagnosis. Three patients already had a family history of VHL disease in their first or second degree relatives. One patient was referred to us due to the pancreatic cystic lesions incidentally diagnosed with transabdominal ultrasound and endoscopic ultrasound (EUS) showed multiple cysts in pancreas varying in size.

Results: In our case series, all the patients were female and they were evaluated using a linear array EUS prob. Most common pancreatic manifestation was multiple cysts with clear fluid content without any solid component or debris or calcification in 6/7 patients. Cysts were scattered almost all parts of the organ. Their highest diameters range from 21 to 51 mm. One patient had side branch intraductal papillary mucinous neoplasm (IPMN) with solid components. None of the cases had any pancreas related mortality throughout our follow up period that range from 6 months to 10 years. Their age on application to our pancreas clinic range from 28 to 61 years. One patient had a history of recurrent acute pancreatitis while the rest of them were asymptomatic regarding pancreatic disease. 3/7 patients had accompanying renal cysts.

Conclusion: The hemangioblastomas of the CNS are the most frequent lesions in VHL disease seen in 60 - 84% of the cases while it was diagnosed in 42% of patients in our series. The average age of diagnosis is 29 years, mostly presented as single tumor (58%). Multiple tumors are always associated with the VHL syndrome. Pancreatic cysts are the most common form of presentation in the VHL syndrome. Pancreatitis and pancreatic insufficiency are rare complications. In our series only 1 patient was symptomatic with recurrent pancreatitis history. The identification of the VHL is important as the syndrome cause high risk of complications that can be avoided with a proper diagnosis and early treatment. Early recognition of unaffected family members of patients via genetic testing has contributed to the improved prognosis of these patients. Nevertheless, our results showed that cysts constitute main pancreatic finding and they live uneventful with regard to their pancreatic lesion. One side branch IPMN case in our study represent an unusual pancreatic manifestation of VHL disease. Therefore, it is wise to avoid unnecessary cyst sampling or drainage attempts in VHL disease patients as those interventions may pose risk of infection, hemorrhage etc. to the patient unless the suspicion of malignancy is positive.

Disclosure: Nothing to disclose

P1504 IMPACT OF POST-OPERATIVE INFECTIOUS COMPLICATION ON HEMATOGENOUS LIVER METASTASIS AFTER CURATIVE RESECTION FOR GASTRO-INTESTINAL CANCERS: ESPECIALLY IN TERMS OF PRE-METASTATIC NICHE FORMATION THROUGH IMMUNE-THROMBOSIS IN THE LIVER

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Introduction: Post-operative infectious complications including anastomotic leakage are well known to increase hematogenous liver metastasis and long-term mortality after curative resection for gastro-intestinal cancers. Many strong innate immune cells including Kupffer, NK, NKT, and γδT cells can exist in the liver and eliminate circulating tumor cells (CTC). However, liver metastasis often occurs in such a situation and not much is known about the mechanism of immune escape of cancer cells.

Aims & Methods: We investigated the crucial mechanism of immune escape of cancer cells in the liver. First, in vitro experiment, we co-cultured human pancreatic cancer cell line, BxPC-3 (CD44v and epithelial phenotype) or BxPC3 treated with 10 nM TGF-β (CD44s and mesenchymal phenotype) with activated platelets from both human and mouse, in order to clarify the molecular mechanisms of interactive cell to cell adhesion manner between cancer cells and activated platelets, because it is well known that activated platelets can express p-selectin on the cell surface and can adhere to CD44s, a ligand of p-selectin.

Next, in vivo experiment using immuno-competent mice (n=10), we examined whether LPS (1 mg/kg)-mediated intraperitoneal infection could induce neutrophil extracellular trap (NETs) in the liver sinusoid and form the immuno-thrombosis cooperatively with activated platelets. In addition, 24hrs after intraperitoneal injection of LPS (1 mg/kg) in immune-competent mice (n=20), BxPC3 xenografts (n=10) or BxPC3 treated with 10 nM TGF-β (n=10) were transplanted intrasplenically.

Then, each mouse was sacrificed at each time point of 10 min and 90 min after transplantation of xenografts and subjected to the pathological examinations.

Results: In vitro experiment, numerous activated platelets from both human and mouse could be adherent to BxPC3 treated with TGF-β, but not much adherent to parental cell line BxPC-3. In vivo experiment using immune-competent mice, the heterogeneous NETs formation in the liver sinusoid was found in LPS group (n=5), although the liver was not the organ of surgical site infection. Numerous activated platelets were also present around NETs. However, in saline group (n=5), NETs were not found in the liver. In addition, in mouse model of transplanting parental cell line BxPC-3 xenografts intrasplenically (n=10), these xenografts were entirely eliminated by the innate immune surveillance at the time point of 90 min after transplantation, although xenograft cancer cells were present in the liver at the time point of 10 min after transplantation. In contrast, some clusters of BxPC-3 treated with 10 nM TGF-β were surprisingly found to be vigorous in the liver at the time point of 90 min after transplantation and these xenografts were surrounded by numerous activated platelets even in immune-competent mice (n=5).

Conclusion: We demonstrated that intraperitoneal injection of LPS could induce NETs in the liver sinusoid and form the immuno-thrombosis cooperatively with activated platelets, resulting in the formation of pre-metastatic niche in the liver through a lot of alarmin which were well known to be released from NETs and activated platelets, and have a function to recruit myeloid derived suppressor cells (MDSC) from the bone marrow. In addition to such a pre-metastatic niche formation as the "soil", the induction of epithelial mesenchymal transition (EMT) of cancer cells was considered to be necessary as the "seed" in order to preferably adhere to the activated platelets and escape the innate immune surveillance of the liver as a first step of hematogenous liver metastasis.

Disclosure: Nothing to disclose

P1505 DECIPHERING THE ROLE OF RINT-1 IN REGULATING PANCREATIC DUCTAL ADENOCARCINOMA (PDAC) HOMEOSTASIS

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Introduction: RINT-1 (RAD50-interacting protein 1) is a multifunctional protein playing a role in cell cycle regulation, genomic stability, telomere maintenance, ER-Golgi trafficking and autophagy. Beside facilitating cellular homeostasis, rare missense mutation found in RINT-1 and overexpression of RINT-1 were associated to increase the risk of development of different kind of tumors including breast cancer, colorectal cancer, and Lynch-syndrome type cancers.

Aims & Methods: To characterize more in details the mechanisms of RINT-1 regulation and to ultimately identify RINT1-dependent pathways that could be targeted in PDAC, an extensive interaction study through yeast-two hybrid assay and mass spectrometry was preliminary performed.

Results: We discovered hundreds of new RINT1-interaction partners including E3 ligases interacting with RINT-1 allowing a better understanding of RINT-1 biological function. In addition, we identify several post-translational modifications including ubiquitination and sumoylation and demonstrated that ubiquitination is a key regulator of RINT-1 stability and biological function.

Hereby, we show that RINT-1-depletion in PDAC cell lines leads to severe growth defects in vitro and in vivo associated with massive Golgi fragmentation and G2 cell cycle arrest followed by ER-stress and autophagy. Complete collapse of cellular homeostasis finally results in activation of apoptosis. In addition, subcutaneous xenografts showed strong infiltration of B220+ immune cells in RINT- 1-deficient tumors.

Conclusion: These data suggest that RINT-1 homeostasis is essential for PDAC survival and represents therefore a putative therapeutic target. Altogether, these data reveal the key role of RINT-1 in PDAC homeostasis.

Disclosure: Nothing to disclose

P1506 DESIGNER PANCREATIC CANCER GENERATED FROM HUMAN PLURIPOTENT STEM CELL DERIVED DUCTS

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Introduction: Cell bioengineering approaches not only hold great promise to replace and regenerate dysfunctional tissue for improved life quality of the diseased patient but may also provide more sophisticated disease models. Engineering approaches to build human pancreatic tissue resembling acinar, ductal and endocrine tissue have been hampered by the complexity of the pancreas. Human pluripotent stem cells (PSCs) may provide the appropriate bioengineering platform for developmental and biomedical studies due to their capability to differentiate into every cell type in the human body.

However, PSCs typically yield heterogeneous population, while certain disease models require homogenous populations. Our initial protocol was powered to generate virtually pure cultures of human pancreatic progenitor cells followed by spontaneous differentiation in a 3D-culture environment to allow acinar ductal commitment (Hohwieler, GUT, 2017). Here, we have implemented signals controlling embryonic lineage fate bifurcations to efficiently yield the desired cell types through exclusion of alternate fates.

Aims & Methods: Here, we have implemented signals controlling embryonic lineage fate bifurcations to efficiently yield the desired cell types through exclusion of alternate fates: Specifically, we applied signaling molecules and growth factors inducing ductal cells, while inhibiting the respective counter lineage with inhibitors. Afterwards, we genome edited human PSCs to specifically design the core machinery of the pancreatic cancer genome. Orthotopic transplantation was additionally incorporated into the experimental work flow.

Results: This approach yields virtually pure pancreatic duct-like cells generated from human PSCs resembling key features of adult human pancreatic ducts: A robust test battery including functional Carbanhydrase and CFTR activity and homogenous ductal marker expression underpinned ductal identity. Transcriptional profiles of engineered ducts match the one of human mature ducts. In line orthotopic transplantation reveals human untransformed ducts in the murine host. Pluripotent stem cells armed with oncogenic KRAS were similarly differentiated to the ductal lineage followed by oncogene activation *in vitro* and *in vivo*. Here, mutant KRAS alters ductal organoid polarity as early sign of dysplastic growth *in vitro*, followed by the generation of moderately differentiated human PDAC in vivo.

Conclusion: Summarized, this novel and unique differentiation platform generates human untransformed ducts allowing modelling of plasticity, dysplasia and cancer formation in a human and genetically defined background in the pancreas. Thereby, we also show that human ducts are indeed permissive to generate human PDAC. Tailored genome editing strategies mimicking the mutational make-up of human PDAC will open novel opportunities to provide a unique and valuable human PDAC model.

Disclosure: Nothing to disclose

P1507 THE ROLE OF MMP9 AND HIF1 EXPRESSION IN TUMOR-INFILTRATING LYMPHOCYTES (TIL) IN PANCREATIC DUCTAL ADENOCARCINOMA (PDAC)

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Introduction: Pancreatic ductal adenocarcinoma (PDAC) has high invasiveness, tendency to locally infiltrate and to show nodal and distant metastasis.

MMPs' overexpression is frequently associated with high invasiveness related to ECM degradation. Also HIF1 overexpression, caused by hypoxia adaption, is involved in malignant behavior.

Aims & Methods: Aim of this study is to explore the relationship between MMP9 and/or HIF1 expression and grading, nodal metastasis, perineural and angiolymphatic invasiveness.

Based on records from Parma's Department of Pathology, a database was created collecting a series of 73 surgical samples of PDAC, from 2007 to 2017. On these samples an histological evaluation was performed considering grading, nodal metastasis and perineural and angiolymphatic invasiveness. In addition, to investigate MMP9 and HIF1α histological expression, an immunohistochemical evaluation was carried out. The positivity was evaluated as Tumor-Infiltrating Lymphocytes (TIL) considering three grades observing the number of cells/high power field (TIL1< 30/HPF 40x; TIL2=30-60/HPF 40x; TIL3>60/HPF 40x).

Results: In the assessment of MMP9, TIL1 was 38 (52.1%), TIL2 19 (26%) and TIL3 16 (21.9%).

Sorting by tumor grading, 13 out of 16 (81,25%) TIL3 were G3 and all G1 samples were TIL1 (p=0.03). Perineural infiltration was shown in 55,2% of TIL1, 73,6% of TIL2 and 81,25% of TIL3; angiolymphatic invasiveness was shown in 26,3% of TIL1, 57,8% of TIL2 and 62,5% of TIL3 (p=0.014). Nodal metastasis were detected in 36.8% of TIL1, 57.9% of TIL2 and 68.7% of TIL3 (p=0.06).

In the achievement of HIF1α, TIL1 was 29 (39.7%), TIL2 21 (28.7%) and TIL3 23 (31.5%).

Sorting by tumor grading, there were no statistical significance because all the gradings were equally distributed. Perineural infiltration was shown in 27.5% of TIL1, 52.3% of TIL2 and 52.1% of TIL3; angiolymphatic invasiveness was shown in 48.2% of TIL1, 71.4% of TIL2 and 82.6% of TIL3 (p=0.01). Nodal metastasis was in 31% of TIL1, 52.3% of TIL2 and 69.5% of TIL3 (p=0.03).

Moreover, the more MMP9 and HIF1 positivity increase, the more malignant pattern such as perineural and angiolymphatic infiltration and nodal metastasis can be detected.

Conclusion: The results show that TIL evaluated both with MMP9 and HIF1 could exert a relevant role in neoplastic invasiveness phenotype, in particular considering perineural and angiolymphatic infiltration and tendency to nodal metastasis. Finally, MMP9 and HIF1 both expressed could characterize a more malignant phenotype.

Disclosure: Nothing to disclose

P1508 ANGIOGENESIS ASSESSMENT OF PANCREATIC ADENOCARCINOMA BY CONFOCAL LASER ENDOMICROSCOPY

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Introduction: Pancreatic cancer (PC) represents one of the major therapeutic challenges because most of the patients are diagnosed in an advanced stage, when available therapies barely influence the overall survival rate. In PC the vascularization is characterized by a high microvascular density and poor perfused vessels with heterogenenous distribution. Confocal laser endomicroscopy (CLE), with various miniprobes available is accessible tool for different lesions providing a live diagnosis.

Aims & Methods: Angiogenesis assessment in pancreatic adenocarcinoma (PDAC) by fluorescently labelled antibodies with confocal laser endomicroscopy on fresh harvested samples immediately after surgery.

Materials and method: Ten consecutive patients diagnosed with PDAC following fine needle aspiration - endoscopic ultrasound underwent curative therapy with tumor resection. Fresh specimens from both normal and tumor tissue were washed in saline solution and incubated for one hour in the dark at 37 °C, with Alexa-Fluor 488 anti-CD105/Endoglin antibody (mouse anti-human IgG2a, Exbio Prague, Czech Republic). And CLE imaging was performed to assess the microvascularazation in an ex vivo setting by direct contact with the specimen. We all tested mesothelin as a potential marker to differentiate between normal and tumor pancreatic tissue.

All aquired images were assessed with a dedicated processing software to obtain a Z projection of confocal serial stacks. Next we measured the vascular density and vessel diameters within 50 μm × 475 μm rectangular regions previosuly chosen. We also compared the results with clasic immunohistochemistry technique.

Results: CD105 expression on CLE was present within PDAC samples with a microvascular density of 13.56 ± 6.88 compared to normal pancreatic tissue 1.1 ± 0.857 (p< 0.001). Mesothelin was clearly proved to be present in every PDAC samples suggesting a potential direct target for future oncologic therapies.

Conclusion: This pilot study proves that CLE targeted CD105 for tumoral vascular network might represents a potential tool for future studies regarding PDAC neoangiogenesis and future therapies.

Disclosure: Nothing to disclose

P1509 THE OBESTATIN/G-PROTEIN COUPLED RECEPTOR 39 (GPR39) SYSTEM IS INVOLVED IN THE PROLIFERATION OF PANCREATIC CANCER CELL LINES

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Introduction: Obestatin is a 23-aminoacid peptide derived from pre-proghrelin, was first isolated from stomach in 2005 and binds to the GPR39 receptor. Our group has described obestatin/GPR39 expression in human healthy pancreas, as well as in pancreatic adenocarcinomas. These studies support the hypothesis that this endogenous system plays a regulatory role in the physiology of the exocrine pancreas and in the mechanism of the pancreatic regeneration. In addition, this system seems to be involved in the pathogenesis and/or pancreatic cancer prognosis.

Aims & Methods: The objective of this study is to evaluate the involvement of this system in the proliferation of cell lines of human pancreatic cancer with different degrees of differentiation: PANC-1, which comes from an undifferentiated carcinoma of ductal origin; RWP-1, a well/moderately differentiated ductal adenocarcinoma; and BxPC3, derived from a primary adenocarcinoma, which in nude mice produces well/moderately differentiated adenocarcinomas to poorly differentiated.

In vitro study of the obestatin/GPR39 system expression by using immunocytochemical techniques in tumor the cell lines PANC-1, RWP-1 and BxPC3. In addition, cell proliferation assays were performed after obestatin treatment (100 and 200 nM) by BrdU and manual counting. 10% FBS was used as positive control.

Results: The obestatin/GPR39 system was expressed intensely in the three pancreatic cancer cells. No immunoreactivity was observed in negative controls incubated without primary antibody. Obestatin administration (100 and 200nM) provoked a mitogenic effect in the RWP-1 cell line (46,31±3,45% over control; p< 0,05) although less pronounced than in the PANC-1 cell line at 48 h (64,12±2,64% over control; p< 0,05). In the case of BxPC3, no stimulation of proliferation was observed (-1,05±3,32% over control).

Conclusion: This study offers two main findings: 1) the obestatin/GPR39 system was intensely expressed in the human pancreatic tumor cell lines; 2) exogenous obestatin increased the proliferation of these cell lines. The differences observed in the obestatin mitogenic effect may be due to the expression differences of key molecules in the signaling pathway of the obestatin/GPR39 system, such as the EGF receptor. The obtained results showed that the obestatin/GPR39 system was involved in the proliferative processes of pancreatic cancer.

Disclosure: Nothing to disclose

P1510 MDSCS AND NK CELLS MEDIATE A NOVEL PROMOTING ROLE FOR NEURAL INVASION IN PANCREATIC CANCER

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Introduction: The role of immune cells on the pancreatic cancer microenvironment has increasingly gained attention over the past decade, however, whether the invasion of nerves by cancer cells is regulated by the presence of tumor-infiltrating leucocytes is still unexplored.

Aims & Methods: In this study we aim to uncover novel immune-mediated pathways in the pathogenesis of neural invasion in pancreatic cancer.

We performed a comprehensive histopathological analysis of the intratumoral and perineural immunological infiltration in a cohort of 40 PDAC-patients through immunhistochemical and double immunofluorescence stainings and automated quantification algorithms.

Furthermore, using in vitro migration assays we evaluated the influence of natural killer (NK) cells and myeloid derived suppresor cells (MDSCs) on the chemoattractive gradient towards nerves and analyzed it via digital time-lapse microscopy.

Results: Among the analysed immune cell types, the intratumoral density of MDSCs (p=0,00029), NK cells (p<0,0001) and CD8+ T (p=,0003) cells showed the highest correlation with neural invasion. In the perineural niche, the presence of neural invasion was associated with the infiltration by MDSCs (0,00005562 ± 0,000007588 vs 0,00002839 ± 0,000003435, p=0,0009) and NK cells (0,0001881 ± 0,00003231 vs 0,00007007 ± 0,00001280, p=0,0005). Mechanistically, the migratory behaviour of pancreatic cancer cells towards neurons was significantly enhanced by the interaction with MDSCs (-0,004685 ± 0,0,01074 vs -0,1188 ± 0,01002, p<0,0001) and NK cells (0,09274 ± 0,01496 vs -0,1537 ± 0,009966, p<0,0001).

Conclusion: MDSCs and NK cells raise as the key regulators in the perineural niche promoting neural invasion, constituting therefore attractive targets for immunotherapy aiming to decrease tumor-associated pain and cancer spread.

Disclosure: Nothing to disclose

P1511 SYNERGISTIC TARGETING OF DNA REPAIR PATHWAYS TO DECIPHER PARP-INHIBITOR RESISTANCE IN ATM-DEFICIENT PANCREATIC CANCER

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Introduction: Pancreatic ductal adenocarcinoma (PDAC) is todays 4th leading cause of cancer-associated death in the Western World with an increasing tendency. Thereby it relies on a core of driver mutations and dozens of passenger mutations refining a strong intratumoral heterogeneity. Ataxia-Telangiectasia Mutated (ATM) is the most frequently mutated DNA-damage repair gene and missense mutations can be found in both sporadic and familiar pancreatic cancer. We previously showed that ATM levels inversely correlate with patient's prognosis and the deletion of ATM in a mouse model of pancreatic cancer (AKC) accelerates tumorigenesis, metastasis and leads to genomically instable tumours. The latter characteristic opens vulnerability for a synthetic lethal attack using Parp inhibitors.

Aims & Methods: However, we faced early resistance and tumour control required additional chemotherapy. In the current study, we systematically performed combinational screening for synergistic routes based on actionable perturbations in the DNA damage response to present an ATM null tailored targeted therapy at low dosage.

Results: Synergistic tumour impact was found upon simultaneous inhibition of Parp-, Atr-, and DNA-Pkc-signaling (termed PAD) leading to synthetic lethality in AKC cell lines *in vivo* and *in vitro*.Mechanistically, PAD lead to cytokinesis failure, replication folk stalling, Parp trapping, reversal of Atm-induced track lengthening finally leading to p53-mediated apoptosis. Chemical and genetic targeting of ATM together with PAD in human

PDAC lines and organoid cultures substantiated these data. Additionally, we elaborated consequences of Parp1 inhibitor resistance within the AKC background. Arising cell clones were aneuploid, highly genomically unstable and underwent epithelial-mesenchymal transition to boost an intrinsically program present in Atm-deficient PDAC. These features were associated with the acquisition of a multi-drug resistant phenotype caused by up-regulation of drug-transporters and de-toxification enzymes. Finally, exome-sequencing identified Drg1 loss as an additional crucial mediator in resistant cells.

Conclusion: Thus, we provide coherent understanding of the molecular mechanism occurring upon Atm deletion in PDAC to precisely interfere with tumor characteristic for therapeutic success in mice and men.

Disclosure: Nothing to disclose

P1512 WITHDRAWN

P1513 PREOPERATIVE BILIARY DRAINAGE IN SEVERELY JAUNDICED PATIENTS WITH PANCREATIC HEAD CANCER; A RETROSPECTIVE COHORT STUDY

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Introduction: Based on recent studies, current guidelines recommend against routine preoperative biliary drainage (PBD) in patients with pancreatic head cancer if bilirubin levels are < 250 μmol/l. However, patients with higher bilirubin levels still undergo PBD, despite the lack of clinical studies including these patients. To evaluate the rationale for a different PBD approach in high bilirubin patients, tumor characteristics, PBD technical success- and complication rates, and postoperative complication rates were compared in patients with a bilirubin level ≥250 and < 250.

Aims & Methods: In this retrospective cohort study, patients diagnosed with resectable pancreatic head cancer and cholestasis (bilirubin >40) from 2008 until 2018 were identified in three centers of the Regional Academic Cancer Center Utrecht. Analyses were performed in patients with a bilirubin level ≥250 versus < 250 at diagnosis (1) and prior to PBD and surgery (2) to reflect the moment of clinical decision making (1) and the actual effect of the bilirubin level on procedural outcomes (2). Multivariable logistic regression analyses were performed to identify independent predictors of PBD complications and severe postoperative complications (Clavien-Dindo ≥3), including bilirubin level as a continuous variable.

Results: A total of 244 patients were included, 191 with bilirubin < 250 at diagnosis and 53 with bilirubin ≥250. PBD was performed in 64% (123/191) and 91% (48/53), respectively. Tumor characteristics did not differ between patients with bilirubin ≥250 versus < 250 at diagnosis. In patients undergoing PBD, no differences in technical success (83% vs. 81%, p=0.80) and complication rates (33% vs. 29%, p=0.60) were found between patients with bilirubin ≥250 versus < 250 at diagnosis. The use of metal stents was equal between the two groups (40% vs. 36%, p=0.66).

Ultimately, 212/244 (87%) patients underwent surgery, of which 168 patients had a bilirubin level at diagnosis < 250 and 44 ≥250. PBD was performed in 143/212 (67%) of these patients. The rate of severe postoperative complications did not differ between patients with bilirubin ≥250 versus < 250 at diagnosis (40% vs. 30%, p=0.26). In addition, when analyzing bilirubin levels ≥250 versus < 250 directly prior to PBD and surgery, no differences in PBD technical success and complications and severe postoperative complications were found. Bilirubin level at diagnosis was no independent predictor for PBD complications (OR 1.00 per 1 μmol/l, 95% CI 1.00-1.00),

nor for severe postoperative complications (OR 1.00 per 1 μmol/l, 95% CI 1.00-1.01). Also, no significant association between severe postoperative complications and PBD was found (OR 0.77, 95% CI 0.40-1.51).

Conclusion: Tumor characteristics, PBD technical success and complications, and postoperative complications did not differ between patients with pancreatic head cancer and a bilirubin level ≥250 and < 250. Although cautious interpretation of these data is mandatory given the retrospective nature, our study does not support a different approach regarding PBD in patients with severe jaundice and suggests omitting routine PBD in these patients either.

Moreover, the perioperative benefit of PBD in these patients should be convincing in order to compensate for the serious drainage related morbidity. Whether a subgroup of patients with pancreatic head cancer and cholestasis might benefit from PBD (e.g. in the setting of prehabilitation) needs to be further evaluated.

Disclosure: Nothing to disclose

P1514 METABOLOMIC PROFILING OF PANCREATIC CANCER

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Introduction: With biomarkers lacking specificity and local symptoms appearing late, pancreatic cancer is a silent killer. Although much effort has been invested into modern imaging methods and new treatment approaches in the last decades, the prognosis remains unfavorable, with the 5-year survival rate of only 5-7%. Therefore, intense research has been focusing on the identification of early symptoms and PC-specific markers. Several approaches have been tested, ranging from the inspection of pancreatic stellate cells to the analysis of microRNAs. As the cancerous pathology induces alterations of many essential biochemical pathways, the affected cells and tissues exhibit altered metabolism. This phenomenon may be easily inspected by metabolomics, an analytical platform with the ability to detect metabolites. Metabolites are produced by all bodily cells, thus, their analysis is usually performed using the tissue with suspected pathology or biofluids.

Aims & Methods: To ensure minimal invasiveness and, thereby, a minimal burden for the patient, we used blood plasma for our metabolomics study. The blood plasma is not only easy to obtain, but it also comprises the majority of metabolites produced by the whole body. In our study, the blood plasma of PC patients (stage III-IV) and healthy controls was subjected to two sets of experiments.

First, clinically recognized markers of oxidative stress related to cancerous diseases were detected and quantified. Subsequently, we performed a multi-marker screening, i.e. the identification of other metabolites that might be considered clinically significant for PC.

After initial pre-treatment (extraction, homogenization, centrifugation), the plasma samples were analyzed using high-performance liquid chromatography coupled with electrospray-ionization tandem mass spectrometry in a gradient elution program.

The clinically recognized markers were quantified after measuring their standards; the molecules resulting from the multi-marker screening were identified via Human Metabolome Database.

Results: We detected multiple markers pointing to oxidative stress caused by reactive oxygen species forming during cancer growth, such as ortho-tyrosine or 8-isoprostane, the levels of which were significantly elevated in the plasma of PC patients compared to healthy controls. Damage to the genetic information in DNA/RNA was indicated by higher levels of 8-hydroxy-2'-deoxyguanosine and 8-hydroxyguanosine, respectively. In the PC patients, the multimarker screening revealed enormously decreased levels of lysophosphatidylcholine, which means poor control of cell proliferation and a major disruption of lipid metabolism. Severe disturbances of lipid metabolism during PC were also illustrated by the increase in chenodeoxycholic acid and carnitine derivatives. The presence of docosahexaenoic acid and its metabolites revealed the activation of the immune system.

Conclusion: Apart from markers of oxidative stress, which have been previously clinically recognized for several cancerous diseases, we identified molecules that have not been connected to PC so far. Thus, we believe that metabolomic profiling may serve as a reliable platform for the identification of a panel of potential biomarkers, which would facilitate the diagnosis of pancreatic cancer.

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Disclosure: Nothing to disclose

P1515 PANCREATIC CANCER-DERIVED ORGANOIDS RECAPITULATE CORE FEATURES OF THE PRIMARY CANCER TO PREDICT DRUG RESPONSE

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Introduction: Organotypic cultures derived from pancreatic ductal adenocarcinoma (PDAC) termed pancreatic cancer organoids (PDO) recapitulate the primary cancer and can be derived from primary or metastatic biopsies. Although isolation and culture of patient derived pancreatic organoids have been established several years ago, advantages and constrains for individualized medicine have not been comprehensively investigated yet.

Aims & Methods: We conducted a feasibility study, systematically comparing head-to-head xenografted primary tissue and xenograft-derived organoids by rigorous immunohistochemical and molecular characterization. Subsequently, a drug testing platform has been set-up and validated *in vivo*.

Results: Firstly, PDAC organoids faithfully recapitulate morphology and marker protein expression patterns of the original tumors.

Secondly, quantitative proteomes from the patient-derived xenografts as well as from corresponding organoid cultures showed high concordance.

Thirdly, genomic alterations as assessed by array-based comparative genomic hybridization revealed similar results in both groups.

Fourthly, we established a small-scale, pharmacotyping platform adjusted to operate in parallel considering potential obstacles such as culture conditions, timing, drug dosing and interpretation of the results.

*In vitro*predictions were successfully validated in an *in vivo*xenograft trial. Finally, the organoid phenotyping outcome was compared with the predictive value of gene mutations obtained by panel sequencing.

Conclusion: In conclusion, small-scale drug screening in organoids appears a feasible, robust and easy-to-handle method to allow response predictions in parallel to daily clinical routine. PDO based phenotyping faithfully reflects genotypes. Therefore, our fast and cost-efficient assay is a reasonable approach in a predictive clinical setting.

Disclosure: Nothing to disclose

P1516 THE INFLUENCE OF PATIENT AGE ON TREATMENT AND SURVIVAL OF LOCALLY ADVANCED PANCREATIC CANCER

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Introduction: The treatment options and survival of locally advanced pancreatic cancer (LAPC) have improved in recent years. However, it is unknown whether elderly patients (*i.e.* ≥75 years) have benefited from these improvements. With the ongoing aging of the patient population and an increasing incidence of pancreatic cancer, this patient group deserves more attention. This study aims to assess the influence of age on treatment and overall survival in patients with LAPC.

Aims & Methods: Consecutive patients diagnosed with LAPC were prospectively registered in 14 Dutch centers (April 2015 to December 2017). Patients were divided in three groups according to age (< 65, 65-74 and ≥75 years). We evaluated the influence of age on type of treatment and overall survival by using logistic regression and Cox regression analyses.

Results: Overall, 425 patients with LAPC were included; 163 patients (38.4%) aged < 65 years, 184 patients (43.3%) aged 65-74 and 78 patients (18.4%) aged ≥75 years. Both patients aged < 65 years and 65-74 years were in good condition (WHO ps 0-1 in 88.3% and 73.2% respectively) and were mostly treated with chemotherapy (87% and 81.3%). Elderly patients were in good clinical condition as well (WHO ps 0-1 in 73.2%), 49.9% was treated with chemotherapy and 43.6% received best supportive care. Median overall survival in elderly patients receiving treatment was longer as compared to those receiving best supportive care (9.0 vs 3.0 months). Multivariate logistic regression analysis demonstrated that each additional year in age is associated with a decreasing probability to receive chemotherapy (hazard ratio [HR] 0.948, 95% confidence interval [CI] 0.903-0.994, *p* = 0.028). In multivariate analysis an increase in age was not associated with a decrease in overall survival (HR 1.001, 95% CI 0.987-1.015, *p* = 0.892). A better WHO performance score and receiving treatment were predictors for an increased overall survival.

Conclusion: Elderly patients with LAPC are less often treated with chemotherapy. However, chemotherapy was associated with improved survival in elderly patients and age was not independently associated with lower survival. Therefore, treatment with chemotherapy should probably be considered more often in fit elderly patients with LAPC.

Disclosure: Nothing to disclose

P1517 PROGNOSTIC FACTORS OF UNRESECTABLE PANCREATIC CANCER BEFORE CHEMOTHERAPY

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Introduction: The prognosis of patients with unresectable pancreatic cancer is difficult to predict during the initiation of systemic chemotherapy treatment. In most cases, determining the appropriate chemotherapy drugs and dosages for each patient is challenging. Recent studies have reported that the modified Glasgow prognostic score (mGPS) and neu-

trophil-to-lymphocyte ratio (NLR), as the indices of the inflammatory response of the body and nutritional condition, are associated with cancer prognosis. However, only few studies have demonstrated the use of these indices in predicting the prognosis of patients with unresectable pancreatic cancer.

This report is a retrospective study on the prognostic factors of unresectable pancreatic cancer prior to chemotherapy.

Aims & Methods: In this study, 56 patients with unresectable pancreatic cancer (stages III and IV as per the General Rules for the Study of Pancreatic Cancer, 7th Edition, edited by Japan Pancreas Society) who were treated with chemotherapy from August 2010 to September 2017 were included. In accordance with the mGPS definition, we categorised the patients as follows: both high CRP (>1.0 mg/dL) and low albumin (< 3.5 mg/dL) levels, 2 points; only high CRP level, 1 point and only low albumin level or neither of those, 0 points. We retrospectively discussed sex, age at diagnosis, performance status (PS), CRP, CA 19-9, NLR, platelet-to-lymphocyte ratio (PLR), CRP-to-albumin ratio (CAR), mGPS and overall survival. Furthermore, we predetermined the cut-off value of NLR/PLR/CAR to be 5.0/190/0.09, divided mGPS into 2 groups (0 and 1-2 points).

Results: The subjects included 34 men and 22 women, with a mean age of 69.1 years, at stage III/IV (13/43), PS (27/28/1/0/0) (PS = 0/1/2/3/4). Using univariate analysis for each item (sex, age at diagnosis, CRP, CA 19-9, NLR, PLR, CAR and mGPS), PLR (p = 0.06), CAR (p = 0.03) and mGPS (1, 2) (p = 0.0027) were significantly different. Nonetheless, based on the results of the multivariate analysis, mGPS (1, 2) is the only independent significant factor among the 3.

Conclusion: These findings indicate that mGPS, prior to chemotherapy, can be a predicting factor for the prognosis of patients with unresectable pancreatic cancer.

Disclosure: Nothing to disclose

P1518 ELEVATED CA 19-9 PREDICTS THE PRESENCE OF METASTATIC AORTOCAVAL LYMPH NODES AND IMPAIRED SURVIVAL IN RESECTED PATIENTS WITH BORDERLINE AND LOCALLY ADVANCED PANCREATIC CANCER

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Introduction: Surgery has been shown to improve the survival of patients with borderline and locally advanced pancreatic cancer (BR-LAPC). There are technical, but no clear biologic criteria how to select which patients would benefit from resection.

Aims & Methods: To evaluate the impact of elevated Ca 19-9, mGPS, and positive aortocaval lymph nodes (ACLN) on survival of resected patients with BR-LAPC. Retrospective analysis from a prospectively collected database was done on all patients resected for BR-LAPC at Karolinska University Hospital between 2008-2018. AOCL were routinely sampled for staging, but did not preclude resection.

Results: Overall 270 patients with BR-LAPC were resected with perioperative mortality of 2.6% (n=7). Mean age was 67 years, male:female ratio 1.1:1. Positive AOCL were found in 38 patients (14.1%) and had the strongest association with impaired survival: median, 1-,3-,5-year survival of 11 months, 40%, 7%, 0% and 18 months, 70%, 29%, 19%, respectively. Modified GPS 0, 1 or 2 was neither associated with the presence of positive ACLN nor survival (p=ns). Elevated Ca 19-9 >200, compared to ≤200, showed clear association with the presence of positive ACLN (positive:negative ACLN = 26:58 versus 11:86, respectively, p< 0.05) and impaired survival: median, 1-,3-,5-year survival of 15 months, 56%, 10%, 7% versus 22 months, 69%, 35%, 21% (p=0.0005). Adjuvant, but not neoadjuvant, chemotherapy had significant positive impact on survival: 24 months, 75%, 34%, 23% versus 14 months, 55%, 21%, 12%, respectively (p=0.0004).

Conclusion: Patients with BR-LAPC and elevated Ca 19-9 might need routine sampling of ACLN before decision for resection to better select who would benefit from surgery

Disclosure: Nothing to disclose

P1519 EARLY ONSET PANCREATIC CANCER (EOPC): POST-OPERATIVE OUTCOME AND POSSIBLE RISK FACTORS IN A LARGE CASE-CONTROL STUDY

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Introduction: Pancreas cancer (PDAC) is expected to become the 2nd most common cause of cancer related death within 2030. Its occurrence is higher in the late life, with a peak of incidence is in the seventh decade. Nevertheless, 10% of patients is affected at an age < 50 years. Such population identifies the so called "early onset pancreatic cancers" (EOPC). Although it is known that EOPC are generally diagnosed in a more advance stage of disease and often in a metastatic status already at diagnosis, it is virtually unknown whether this poorer prognosis is the epiphenomenon of a different underling pathophysiological mechanisms, or the result of a merely delayed diagnosis. So far few, small and heterogeneous series have investigated the prognosis in EOPC compared to non-early onset pancreatic cancer (NOPC). None of them through a strict matching for sex and stage of disease (pTNM). Additionally, most of the previous studies relied on non-surgical series describing the clinical outcomes of patients who have not undergone treatments with curative intent.

Aims & Methods: To investigate post-operative survival and possible risk factors worse outcome in EOPC and NOPC patients.

A case-control study on consecutive patients operated for PDAC between 2008 and 2017 at HPB Disease Unit, Karolinska Hospital, Stockholm. Data about demographics, known risk factors for PDAC, exposures, pathological information, treatment and survival were recorded. Cases: PDAC patients aged ≤50 years (EOPC). Controls: 1:5 sex and stage (pTNM) matched patients consecutively recruited in the same period, aged >50 years (NOPC). Chi square was used to analyze categorical variables, t test for continuous ones. Survival was assessed through Kaplan Meier method and statistically significant results were evaluated through univariable and multivariable Cox hazard regression analysis.

Results: 24 EOPC and 120 stage controls were recruited. 1,3,5 years overall survival was similar in cases and controls (respectively 70.8% vs 72.5%; 30.1% vs 28.9% and 24.1% vs 12.5%; p=0.63). The use of adjuvant chemotherapy was confirmed to improve the outcome in both cases and controls (respectively HR=0.30; 95%CI 0.10-0.91, p=0.03 vs HR 0.61; 95% CI 0.36-1.00, p=0.05). No statistically significant difference was found regarding the prevalence of genetic syndromes, exposures and known risk factors for PDAC. At univariable cox hazard regression analysis, diabetes (HR= 1.60; 95CI 0.95-2.69, p=0.07) and underweight (HR=5.59; 95%CI 2.01-15.51, p=0.0009) were significantly associated to an increased risk of cancer related death in controls. Such increased risk was not confirmed in cases. At multivariable cox regression analysis underweight was confirmed to be significantly associated to an increased risk of mortality in controls (HR 4.31; 95%CI 1.51-12.30, p=0.006).

Conclusion: Overall survival is similar in operated EOPC and NOPC patients. Adjuvant chemotherapy was confirmed as a factor positively influencing prognosis in both cases and controls. Metabolic and nutritional status play a role in influencing prognosis in NOPC but not in EOPC.

Disclosure: Nothing to disclose

P1520 SARCOPENIA AS A PROGNOSTIC FACTOR OF SURGICAL OUTCOMES FOLLOWING PANCREATICODUODENECTOMY IN PATIENTS WITH PANCREATIC ADENOCARCINOMA

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Introduction: To assess the impact of sarcopenia on the occurrence of postoperative complications and mortality after pancreatic resection in patients with pancreatic adenocarcinoma.

Aims & Methods: This study included 137 patients with pancreatic adenocarcinoma, who underwent pancreaticoduodenectomy in our institution in the period 2017-2018. Preoperative computed tomography (CT) was performed for all patients. Sarcopenia was quantified using two approaches: the Total Psoas Index (TPI) and the Hounsfield Unit Average Calculation (HUAC). They were measured at the level of the third lumbar vertebral body (L3).

Results: Sarcopenia was diagnosed in 49 (39.8%) patients using TPI. Postoperative complications occurred in 24 (48.9%) patients, in patients without sarcopenia postoperative complications occurred in 23 (31.0%) patients, (c^2 = 4.1, p=0.04). Mortality was 3 (6.1%) and 1 (1.3%) respectively, (c^2 = 0.09, p=0.7).

In 53 (38.7%) patients sarcopenia was diagnosed using HUAC. Postoperetive complications occurred in 25 (47.2%) patients in the group with sarcopenia and in 19 (22.6%) patients in the group without sarcopenia (c^2 = 8.9, p=0.003). Mortality was 3 (5.6%) and 1 (1.2%) respectively (c^2 = 2.2, p=0.1).

In patients with sarcopenia determing by HUAC pancreatic fistula Grade B or C occurred in - 14 patients, delayed gastric empting - in y 3, haemorrhage- in 6, infections complications occurred in 2 patients.

In patients without sarcopenia pancreatic fistula Grade B or C occurred in - 5 patients, delayed gastric empting - in 2, haemorrhage - in 4, infections complications occurred in 5 patients and lymphorrhea occurred in 3 patients. We did not find any significant difference in the increase of delayed gastric empting (c^2 = 0.02, p=0.8), haemorrhage (c^2 = 0.05, p=0.8), infections complications (c^2 = 0.09, p=2.7), but the level of pancreatic fistula Grade B or C was significantly higher in patients with sarcopenia (c^2 = 0.04, p=3.8).

In patients with sarcopenia determing by TPI pancreatic fistula Grade B or C occurred in - 12 patients, delayed gastric empting - in y 2, haemorrhage- in 6, infections complications occurred in 4 patients.

In patients without sarcopenia pancreatic fistula Grade B or C occurred in - 5 patients, delayed gastric empting - in 4, haemorrhage - in 5, infections complications occurred in 9 patients. We did not find any significant difference in the increase in the number of infections complications (c^2 = 2.9, p=0.08), delayed gastric empting (c^2 = 0.74, p=0.3) and haemorrhage (c^2 = 0.07, p=0.8), but the level of pancreatic fistula Grade B or C was also significantly higher in patients with sarcopenia (c^2 = 4.06, p=0.04).

Conclusion: HUAC and TPI could be easily calculated preoperatively in patients with pancreatic cancer. Present results suggest that sarcopenia, determined by HUAC and TPI is a reliable indicator of the surgical outcome and significantly affects the level of postoperative complications and pancreatic fistula. Determination of sarcopenia can be used to improve the selection of patients with pancreatic cancer prior to resection and to predict of pancreatic fistula.

Disclosure: Nothing to disclose

P1521 PANCREATIC RESECTION LEADS TO LOSS OF ADIPOSE TISSUE BUT DOES NOT INFLUENCE MUSCLE WASTING IN PANCREATIC CANCER PATIENTS

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Introduction: Patients with pancreatic cancer are commonly affected by a pronounced perioperative sarcopenia and cachexia, which are associated with poorer overall survival. The aim of this study is to test the impact of pancreatic resection on body composition parameters in pancreatic cancer patients.

Aims & Methods: Body composition parameters were measured using computed tomography (CT) images at L3 vertebral level prior to surgery (timepoint 1, T1) as well as 6 (T2) and 12 months (T3) after pancreatic resection were assessed using Slice-O-Matic® software version 4.3. Following body compositions parameters were estimated: subcutaneous adipose tissue area index (SATI), visceral tissue area index (VATI), intramuscular tissue area index (IMATI), total adipose tissue area index (TATI), as well as skeletal muscle mass index (SMAI).

Sarcopenia was defined by consensus thresholds before surgery with the cut-off points for SMI (skeletal muscle tissue area index) < 52.4 cm²/m² for male and < 38.5 cm²/m² for female patients. 248 patients with pancreatic cancer from cachexia database treated in the Department of Surgery, Klinikum Rechts der Isar, 2006-2019, were screened for this retrospective study.

From 219 resected patients with the presence of preoperative CT, only 63 patients had CTs at T1, T2, and T3. 42 (67%) of these patients were sarcopenic before surgery; 36 (57%) were sarcopenic 6 months after surgery, and 41 (65%) were sarcopenic 12 months after surgery.

Results: Median value of TATI decreased from 95 cm/m2 at T1 to 52 cm/m2 at T2 (p < 0.001) and slightly increased to 62 cm2/m2 at T3 (p < 0.001 T1 vs. T2; p = 0.724 T2 vs. T3). Median value of VATI decreased from 35 cm/m2 at T1 to 20 cm/m2 at T2 (p < 0.001) and slightly increased to 21 cm2/m2 at T3 (p < 0.001 T1 vs. T2; p = 0.913 T2 vs. T3). Median value of SATI decreased from 53 cm/m2 at T1 to 32 cm/m2 at T2 (p < 0.001) and slightly increased to 36 cm2/m2 at T3 (p < 0.001 T1 vs. T2; p = 0.576 T2 vs. T3). IMATI and SMAI did not change significantly after pancreatic resection.

Conclusion: Resected pancreatic cancer patients are affected by a significant adipose tissue loss 6 months after surgery, which doesn't improve until 12 months after surgery. Surprisingly, though the most of pancreatic cancer patients suffer from sarcopenia before surgery, no additional muscle wasting occurs after pancreatic resection.

Disclosure: Nothing to disclose

P1522 WITHDRAWN

Paediatric: Liver, Biliary and Pancreas
09:00-14:00 / Poster Exhibition - Hall 7

P1523 RELATIVE ADRENAL INSUFFICIENCY IN DECOMPENSATED CIRRHOTIC CHILDREN: PROSPECTIVE LONGITUDINAL STUDY

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Introduction: Relative adrenal insufficiency (RAI) is a clinically undetectable predisposing factor of poor outcome in cirrhotics.There are no published studies regarding presence and effect of RAI in children with decompensated cirrhosis.

	Comparison at D1(baseline), n=34				Comparison at D21, n=22		
	Complications (n=18)	No complications (n=16)	p		Complications (n=10)	No complications (n=12)	p
Previous events, n (%)	15 (83)	8 (50)	0.07	Previous events, n (%)	8 (80)	7 (58)	0.38
PELD score	23.5 ± 12.7	6.9 ± 9.9	<0.001	PELD score	22.8 ± 10.7	8.3 ± 9.9	0.004
D1 basal cortisol (nmol/L)	293 ± 98	256 ± 84	0.24	D21 basal cortisol (nmol/L)	290 ± 119	251 ± 113	0.45
D1 peak cortisol (nmol/L)	369 ± 95	341 ± 89	0.39	D21 peak cortisol (nmol/L)	380 ± 114	351 ± 102	0.53
D1 IL-6 (pg/mL)	29 ± 39	39 ± 73	0.63	D21 IL-6 (pg/mL)	63 ± 96	42 ± 65	0.59
D1 TNF (pg/mL)	4.1 ± 5.4	8 ± 12	0.22	D21 TNF (pg/mL)	10 ± 15	4.3 ± 13	0.38
D1 HDL (mg/dL)	14 ± 11	29 ± 12	0.001	D21 HDL (mg/dL)	20 ± 12	36 ± 14	0.009
Death in 180 days, n (%)	7(39)	0(0)	0.008	Death in next 6 month, n(%)	2(20)	0(0)	0.19

[P1523 Table 1: Comparison of decompensated cirrhotic children with relative adrenal insufficiency with and without future complications at baseline and day]

Aims & Methods: We aimed to study
1) prevalence of RAI in decompensated cirrhotic children using low dose short synacthen test,
2) assess the surrogatory markers of RAI [interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α)] and serum high density lipoprotein (HDL), precursor of serum cortisol and
3) assess outcome over 180 days follow-up.
This is a prospective longitudinal observational study enrolled hemodyamically stable cirrhotic patients with ascites after excluding patients on corticosteroids, adrenal insufficiency, terminally ill, concurrent infections and shock. They were sampled for serum basal cortisol (BC), peak cortisol (PC; after 30 minutes of 1 mcg intravenous synacthen), serum TNF-α, IL-6 and HDL levels at D1 and D21. Delta cortisol was defined as difference between BC and PC. RAI was diagnosed as PC< 500nmol/L. Cohort was analysed in terms of severity of liver disease, previous event (hepatic encephalopathy, gastrointestinal bleeding, systemic infection and spontaneous bacterial peritonitis) in past 180 days, complications (new onset organ failures, infection and hospital readmissions) at follow-up and death.
Results: Prevalence of RAI on D1 was 54% in decompensated cirrhosis (n=63). Significant differences of D1-RAI patients (n=34) vs normal adrenal functions (NAF,n=29) were age (135±43 vs 119±53 mo, p=0.18), platelet count (109±63 vs 170±95 x10^3/μL,p=0.003), BC (275±92 vs 517±135 nmol/L,p< 0.001), PC (356±93 vs 673±165 nmol/L,p< 0.001) and delta cortisol (90±84 vs 174±170 nmol/L, p=0.04), complications in follow up (53% vs 24%, p=0.023). D1-RAI, significant varices, hypersplenism, serum albumin, INR, PELD (pediatric end-stage liver disease) score, serum HDL were the statistically significant determinants of follow-up complications on regression analysis in decompensated cirrhotics. Independant factors on multivariate analysis for follow-up complications and mortality were PELD score and hypersplenism. RAI progressed to 61% by D21. Patients with RAI (n=34) with or without complications at follow-up were compared (table 1). In this subgroup, INR, PELD score and serum HDL were risk factors for complications and death. In RAI patients, PELD >7 predicted follow-up complications (AUC: 86%, p< 0.001, sensitivity 100%, specificity 50%) and PELD >11 predicted death (AUC: 86%, p=0.003, sensitivity 100%, specificity 50%).
Conclusion: Half of the decompensated cirrhotic children have RAI. RAI determines the follow-up complications. RAI patients with complications have higher PELD scores, lower HDL levels and higher mortality.
Disclosure: Nothing to disclose

P1524 SCREENING AND FOLLOW-UP OF BILIARY DYSPLASIA IN PRIMARY SCLEROSING CHOLANGITIS PATIENTS WITH DISEASE ONSET IN CHILDHOOD/ADOLESCENCE

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Introduction: The natural history of biliary dysplasia (BD) in children and young adolescents with primary sclerosing cholangitis (PSC) is lacking.
Aims & Methods: Aim of this study was to report the role of endoscopic retrograde cholangiography (ERC) with systematic brush cytology (BC) for screening and follow-up of BD in this setting of patients.
Study design: Retrospective cohort study.
Population, timing, area: All patients with PSC diagnosed in childhood/adolescence between 1993-2017 at Helsinki University Hospital (HUH) were identified.
Disease diagnosis: PSC was diagnosed based on:
1. Elevation of liver enzymes,
2. Liver biopsy,
3. ERC. Notably, ERC with BC is performed in all the patients referred for a suspicious of PSC regardless the severity of the disease in HUH:
1. To confirm/exclude the diagnosis and
2. To assess the individual risk of progression based on BC; patients with a repeatedly confirmed BD are referred for liver transplantation (LT). ERC images were scored using a modified version of Amsterdam PSC score; a global score combing intra- (0-8) and extra- (0-8) hepatic score was obtained (0-4: mild, 5-8: moderate, 9-16: severe changes). Cytology samples were graded as benign (i.e., normal or inflammatory/regenerative atypia), suspicious (for BD or malignancy) or malignant (i.e., CC).
Data: Clinical data and lab tests were reviewed.
End-points: A composite of LT + cirrhosis at last follow-up were evaluated.
Follow-up: All patients were censored by the end of March 2019.
Results: Baseline characteristics: 68 patients (42 males, median age at diagnosis 16, range: 5-21 years) were included; 22 patients (32%) had an overlap with autoimmune hepatitis (AIH) and 57 patients (84%) had concomitant inflammatory bowel disease (IBD).
Follow-up duration: The median follow-up time was 8 (range: 2-25) years. At the last follow-up the median age was 23 (range: 10-43) years.
Screening ERC: At first ERC the global score was: 0-4 in 46 (68%), 5-8 in 8 (12%) and 9-16 in 14 (20%) patients. Gamma-glutamyltranspeptidase (GGT) and Ca 19.9 were higher in patients with more advanced changes (p= 0.05 and 0.01), respectively. Suspicious of malignancy (low-grade dysplasia, LGD) was detected in four patients (6%) (one was cirrhotic, 2 had also aneuploidy): 2 received LT (LGD was confirmed in one and cirrhosis without LGD in one) and 2 LGD were not confirmed on following BC.
Follow-up ERC: A median of 2 (range: 0-11) ERCs with brush cytology were performed. Suspicion of malignancy (LGD) was raised in 5 (3% of the ERC:s): one was transplanted (LGD was not confirmed, but severe cholangitis) and 4 were not confirmed on following BC but one was listed for LT because of cirrhosis. One patient underwent right hepatectomy for a liver mass, consistent with biliary LGD.

End of follow-up: Eight patients (12%) had received LT: 4 for decompensated cirrhosis (one with biliary LGD), one for a markedly increased S-Ca19-9 (cirrhosis on histology) and 2 for suspicion of malignancy. Five patients (7%) were cirrhotic. No cases of CC were detected.

Survival (Logrank test for trend): Probability for the end-point LT + cirrhosis at last follow-up was higher in patients with more advanced bile duct disease at their first ERC (p=0.04).

Multiple linear regression: Elevated GGT (p=0.02), ALP (0.01) and bilirubin (0.05) at first ERC were independent factors for the end point LT + cirrhosis at last follow-up.

Conclusion: In patients with a PSC-onset at childhood/adolescence biliary dysplasia may develop within a median time of 3 years necessitating thorough follow-up.

Disclosure: Nothing to disclose

P1525 ROLE OF GENETIC EVALUATION IN CHILDREN WITH IDIOPATHIC ACUTE RECURRENT PANCREATITIS

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Introduction: Acute recurrent pancreatitis (ARP) is poorly understood in children. Several genetic risk factors have been identified in adults with ARP. However, literature regarding genetics of ARP is sparse in pediatric age group.

Aims & Methods: All children (< 18 years) with ARP from Jan 2016 to May 2018 were prospectively enrolled in the study. Children with a known cause of ARP like obstructive, toxic/metabolic and autoimmune were excluded from the final analysis. Children with idiopathic ARP (IARP)underwent genetic testing for mutations/polymorphisms in genes known to predispose to ARP {SPINK1, PRSS1, CTRC (Chymotrypsin C), CTSB (Cathepsin B), CLDN-2 (Claudin-2) and CFTR}.

Results: A total of 239 children (116 boys, 10.3±3.7 years) were enrolled during the study period. Of these, 204 (85.35%) children were identified as IARP. Themean age of symptom onset and the average number of acute episodes were 8.3±3.7 years and 3.3 ± 1.8, respectively. In 4.6% (11/239) family history of pancreatitis was noted. Pancreas divisum was found in 18.7% (27/144) children. Genetic evaluation was performed in 144 (70.6%) children with IARP. Mutations/polymorphisms in at least 1 gene was identified in 89.5% (129/144) children including SPINK1 in 41.9%, PRSS1 (rs 10273639) in 58.2%, CTRC in 25.6%, CLDN -2 in 72.9% and CFTR in 2.3%. There was no significant in the incidence of genetic mutations/polymorphisms in IARP with or without pancreas divisum (95.7 vs 88.4%; p=0.467).

Conclusion: Genetic mutations are the most common cause of IARP in children. The incidence of genetic mutations is similar in children with or without pancreas divisum. The role of pancreas divisum in causing ARP in the absence of a genetic mutations should be evaluated in future studies.

Disclosure: Nothing to disclose

P1526 PINEAPPLE-R. DATA ANALYSIS OF 46190 PEDIATRIC PATIENTS

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Introduction: The documented incidence of acute pediatric pancreatitis (APP) is low, but it shows a rising pattern from Eastern to Western Europe and the USA. An American study established close correlation between serum pancreas enzyme measurement (sPEM) and the incidence of APP.

Aims & Methods: The aim of the PINEAPPLE-R study is to retrospectively investigate the diagnostic practice for APP and to estimate the incidence of pancreatitis among children suffering from abdominal pain worldwide. PINEAPPLE (Pain IN EArly phase of Pediatric Pancreatits) is a registered (ISRCTN35618458), observational, multinational clinical trial (http://www.ncbi.nlm.nih.gov/pubmed/26641250). The PINEAPPLE-R sub-trial is a retrospective review of pediatric ER medical records, collecting symptoms, results of abdominal imaging and pancreatic enzyme measurements. We have already overviewed 46190 pediatric patient records and obtained the requested data from 4 countries' 15 hospitals for the PINEAPPLE-R trial.

Results: Retrospectively 10.4% (4782/46190) of the children appeared at ER units had abdominal pain. In case of abdominal pain sPEM was performed in 13.8% (662/4782), 23.1% (1104/4782) of the patients had abdominal imaging and the incidence of pancreatitis was 0.2% (11/4782). The number of sPEM decreased from the USA to Eastern Europe (21.6% to 5.6%) and clearly correlated with the incidence of APP (0.5% to 0%, R^2=0.958). The most accurate diagnostic workup has been performed in Israel, where the sPEM was measured in 62.9% (165/262) and the abdominal imaging 41.6% (109/262) of patients with abdominal pain, resulted in 3 (1.14%) diagnosed APP.

Conclusion: The PINEAPPLE-R shows that the incidence of APP is 0.2% based on the current diagnostic practice. Better awareness of APP results 1.14% incidence of APP as a reason of abdominal pain. These data strongly suggest that the majority (86%) of APP is not diagnosed.

Disclosure: Nothing to disclose

Endoscopy and Imaging III

09:00-14:00 / Poster Exhibition - Hall 7

P1527 UNDERWATER ENDOSCOPIC MUCOSAL RESECTION FOR RECURRENT DUODENAL TUMOR: A RETROSPECTIVE CASE SERIES

Shichijo S., Takeuchi Y., Uedo N., Kono M., Fukuda H., Shimamoto Y., Ohmori M., Iwagami H., Matsuura N., Nakahira H., Maekawa A., Kanesaka T., Higashino K., Ishihara R.
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Introduction: Endoscopic resection for superficial non-ampullary duodenal neoplasms (SNADEN) is gradually spreading, and recurrence after endoscopic resection sometimes occurs. However, conventional endoscopic mucosal resection (EMR) for recurrent lesion with submucosal saline injection is difficult because of submucosal fibrosis. Furthermore, endoscopic submucosal dissection (ESD) for duodenal neoplasm accompanies a high risk of perforation, and highly advanced skills are demanded to perform ESD especially on recurrent lesions. Underwater EMR (UEMR) was developed and described by *Binmoeller et al* in 2012. We previously reported the usefulness of UEMR for primary SNADENs.
Aims & Methods: We retrospectively analyzed patients diagnosed with recurrent duodenal neoplasm and treated with UEMR at Osaka International Cancer Institute from 2015 to March 2019. For UEMR procedure, a waterjet endoscope with distal attachment was used. We evacuated air from the affected segment of lumen and infused water until the lumen was complete full, then we performed hot snare polypectomy without submucosal injection.
Results: During the study period, 7 patients (6 men, 1 woman; age, 59-78 years) were treated with UEMR for recurrent SNADENs. All lesions were flat elevated, and located at the descending duodenum. The period from previous treatment to the treatment of recurrence were 1.4 ± 1.1 years. Tumor size was 2 to 11 mm. *En bloc* resection was performed in 5 cases and piecemeal resection in 2 cases without complications during the procedure. The procedure time was 18 ± 17 min. 2 patients presented melena and were performed endoscopic examination 3 and 4 days after UEMR, respectively, and 1 required hemostasis by clipping. Pathological diagnosis was intramucosal adenocarcinoma in 4 cases, and tubular adenoma in 3.
Conclusion: UEMR for recurrent duodenal lesion is feasible and effective, which is difficult to be treated with conventional EMR, or ESD.
Disclosure: Nothing to disclose

P1528 THE DOUBLE-BITE BIOPSY TECHNIQUE IS FASTER AND EQUALLY ACCURATE COMPARED TO THE SINGLE-BITE TECHNIQUE FOR ENDOSCOPIC SURVEILLANCE OF HEREDITARY DIFFUSE GASTRIC CANCER

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Introduction: Germline mutation in the *E-cadherin* gene (*CDH1*) is found in approximately 30% of individuals fulfilling the clinical criteria for hereditary diffuse gastric cancer (HDGC) and is an indication for prophylactic gastrectomy. However, endoscopic surveillance is recommended for those individuals that refuse gastrectomy and prefer to delay it for medical or psychosocial reasons, in order to identify foci of intramucosal signet ring cell carcinoma (SRCC) and inform the best timing of surgery. The recommended endoscopic protocol involves 30 random mapping biopsies in 6 gastric anatomical regions (Cambridge protocol), which is tedious and time-consuming. In order to save time, two specimens could be taken during a single passage of the biopsy forceps ("double-bite" technique). Previous studies on the efficacy of this technique, in both the upper and lower gastrointestinal tract, have generated conflicting results.

Aims & Methods: The aim of this study was to determine the adequacy and utility of the "double-bite" technique for mapping biopsies in patients undergoing surveillance for HDGC. The primary outcome was identification of SRCC foci in the two arms. The secondary outcomes included time to perform biopsy protocol, biopsy size, patients comfort and dose of sedation. Patients were randomized to the single or double-bite arm. Procedures were performed by 3 trained endoscopists with high-resolution white-light and narrow band imaging with targeted biopsies on visible lesions followed by Cambridge protocol biopsies. Randomization was revealed to the endoscopist just before the mapping biopsies. The time taken for the procedure was recorded between the first and last mapping biopsy. A comfort score was assigned by an endoscopy nurse after the procedure, according to the modified Gloucester scale. Biopsy specimens were assessed for size and presence of SRCC foci by two upper GI pathologists, who had significant experience in identification of SRCC and were blinded to study arm.
This study was powered for the secondary endpoint related to the procedural time and we estimated that 13 cases at least in each arm were required to show a difference with a power of 0.95 at a significance level of 0.01.
Results: Twenty-five patients were included in the single-bite and 23 in the double-bite arm. There was no difference in patient demographics, including age and gender. In the mapping biopsies, 2 SRCC foci were detected in the single-bite arm and 5 in the double-bite arm (p=0.24). The Cambridge biopsy protocol in the double-bite arm was significantly faster compared to the single-bite arm (11±2.7min vs 13±2.4; p=0.004). The mean size of the biopsies in the double-bite arm was significantly smaller than in the single-bite arm (2.5 vs 3 mm, p=0.001). There was no difference in sedation dose and comfort score.
Conclusion: The double-bite technique is significantly faster than the single-bite method for performing the Cambridge biopsy protocol in patients undergoing surveillance for HDGC. Despite the smaller size, the double-bite technique does not reduce the yield of SRCC.
Disclosure: Nothing to disclose

P1529 TT-J KNIFE INCREASES SPEED OF PER-ORAL ENDOSCOPIC MYOTOMY: A COMPARISON OF UK AND JAPANESE PRACTICE

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Introduction: Per-oral endoscopic myotomy (POEM) is an effective treatment for achalasia but requires a high level of technical expertise with a steep learning curve limiting its accessibility to select centres. The TTJ knife unlike the conventional TT knife offers an integrated water jet during tunnelling and submucosal dissection.
Aims & Methods: This study aims to determine if the TTJ knife increases the speed of myotomy and could be a beneficial tool for less experienced endoscopists. Procedure data was retrospectively analysed for 107 cases performed at a UK centre (2013-2019) and 1549 cases performed at a more experienced Japanese centre (2008-2019). Case matching was executed between sites for: prior therapies, sigmoid shape oesophagus, knife (TT/ TTJ) and total myotomy length (+/-5cm). Independent samples t-test was undertaken to compare outcome measures (myotomy speed (cm/minute) and procedure time (minutes)) for TTJ and TT knives.
Results: Mean speed of myotomy for all cases was significantly faster for the TTJ knife (0.16 vs 0.21, p< 0.001) and mean procedure time was significantly shorter (68.35 vs 88.81, p< 0.001). Differences in mean myotomy speed by knife (TTJ vs TT) were greater in the UK cohort (0.21 vs 0.14, p< 0.001) than the Japanese cohort (0.21 vs 0.17, p< 0.05) but still significantly faster in both cohorts. Mean procedure time with TTJ was significantly shorter in the UK cohort (57.0 vs 88.7, p< 0.001), while there was no significant difference in the Japanese cohort (79.7 vs 89.0, p=0.17). The speed of myotomy using the TT knife was significantly faster in the Japanese cohort compared to the UK cohort (0.17 vs 0.19, p< 0.05), there was no significant difference by centre for the TTJ knife (0.21 vs 0.20, p=0.72).

Conclusion: The TTJ knife increases the speed of myotomy and reduces procedure time for all levels of operator. The magnitude of this effect appears to be smaller for a high-volume centre, but still significantly different. Furthermore, myotomy speed with TTJ was the same in both groups suggesting a real advantage for a jet-type knife in this scenario.

Disclosure: Nothing to disclose

P1530 OUTCOMES FROM THE UK ENDOSCOPIC SUBMUCOSAL DISSECTION (UK ESD) NATIONAL REGISTRY: MOVING TOWARDS AN ALTERNATIVE APPROACH FOR UNDERTAKING ESD IN A WESTERN SETTING

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Introduction: The practice of endoscopic submucosal dissection (ESD) as a viable technique for resection of early gastrointestinal neoplasia has been growing in the West. However, its uptake has been slow due to a long learning curve, higher complication rate and lack of a reimbursement tariff in many centres.

Aims & Methods: The aim of this study was to analyse the ESD practice in the UK through the development of the country's first national ESD registry. The registry was established in 2016 with 4 major tertiary referral centres performing ESD Data was prospectively collected and captured on a national electronic database for subsequent analysis. Baseline demographics, procedure and lesion details as well as en bloc, R0 resection and complication rates were recorded. Both conventional ESD and hybrid (knife assisted resection or KAR, where a snare is used) techniques were used.

Results: A total of 249 ESD procedures were included. The average age of the patients was 70 years with a male:female ratio of 2:1. The ESD completion rate was 98.4% (245/249). 13.8% of the lesions were scarred from previous endoscopic resection attempts. Of the completed procedures, 70 were undertaken in the oesophagus, 55 rectal, 54 colonic, 64 gastric and 3 in the duodenum. The average lesion size was 3.2cm. The average procedure time was 58, 62, 87 and 127 minutes for oesophageal, duodenal, colorectal and gastric lesions respectively.

The majority of the lesions (177/249, 71.1%) were removed using a standard ESD technique compared to 72/249 (28.9%) using a KAR technique where piecemeal resection was more likely. The table below stratifies the procedure outcomes according to standard ESD versus KAR techniques.

	Standard ESD				Knife assisted resection (KAR)			
	En bloc resection rate	R0 resection rate	Bleeding	Perforation	En bloc resection rate	R0 resection rate	Bleeding	Perforation
Oesophageal (n=70)	60/61 (98.4%)	52/61 (85.2%)	1/61 (1.6%)	0	9/9 (100%)	8/9 (88.9%)	0	0
Gastric (n=64)	56/57 (98.2%)	51/57 (89.5%)	1/57 (1.8%)	3/57 (5.3%)	6/7 (85.7%)	6/7 (85.7%)	0	0
Duodenal (n=3)	N/A	N/A	N/A	N/A	2/3 (66.7%)	2/3 (66.7%)	0	1/3 (33.3%)
Colorectal (n=108)	54/55 (98.2%)	48/55 (87.3%)	2/55 (3.6%)	2/55 (3.6%)	18/53 (33.9%)	18/53 (33.9%)	1/53 (1.9%)	2/53 (3.8%)

[Analysis of ESD by location and resection method]

The overall stricture rate for oesophageal ESD was 8.6% (6/70, with 2 occurring using KAR and 4 using standard ESD). Notably, the complication (bleeding/perforation) rate for oesophageal lesions was lower than that of colorectal despite fewer cases being performed. The en bloc resection rate using KAR for colorectal lesions was low due to piecemeal removal.

Conclusion: This data provides insight into the practice of ESD in the UK through a national registry. Overall en bloc resection rates are high when conventional ESD is undertaken and complication rates low when a KAR approach is used.

Most of the procedures were carried out in the colorectum and oesophagus reflecting the local pathology burden. Bleeding and perforation rates were low and procedure time shortest in oesophageal ESD despite a similar number of rectal, gastric and oesophageal cases being undertaken.

This may provide a basis for training in oesophageal ESD in parallel with rectal and gastric cases rather than the traditional model of Eastern training that advocates step wise progression starting with gastric ESD. Tailoring this model of practice may increase the uptake of ESD as a safe procedure in the West with appropriate training.

Disclosure: Nothing to disclose

P1531 OCCURENCE OF BLACK ESOPHAGUS IN A SINGLE TERTIARY CENTER: A RETROSPECTIVE ANALYSIS OF 11 YEARS

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Introduction: Acute esophageal necrosis so called black esophagus (AEN), is a rare clinical condition characterized by the endoscopic finding of diffuse, often circumferential, black mucosal pigmentation of esophagus, which typically stops at gastro-esophageal junction. Duodenal involvement has been described in this condition. Epidemiological data of AEN are scanty, in fact until now only small case series and case reports are available.

Aims & Methods: To assess the occurrence of AEN in a consecutive endoscopic cohort over an 11 years period.

Results: 15 patients out of 2.515 emergency esophagogastroduodenoscopy [EGDS] (0.59%) were found with AEN. Only 1 out of 23.455 patients were diagnosed during elective EGDS (0.004%). Median age was 75 yrs (range 47-89), 63% were men. Upper gastrointestinal bleeding was the clinical presentation and indication for endoscopy in 13 patients (81.25%). In the other three cases, anemia, persistent vomiting and dysphagia were the indications for EGDS. Only three patients presented hypotension at the time of endoscopy. AEN involved the entire length of esophagus in 7 patients (43%); distal third in 5 patients (32%) and inferior two thirds in 4 patients (25%). Concomitant duodenal abnormalities were reported in 12 patients (75%): 8 patients presented frank duodenal ulcers and 2 patients presented duodenal erosions, whereas the other 2 patients a necrotic aspect of duodenum was found.

Further endoscopic findings included 7 cases of hiatal hernia, one case of Mallory-Weiss lesion, one case of oozing bleeding from the distal esophagus, in one case, a gastric volvulus was diagnosed. No gastric endoscopical abnormalities were described with the exception of one patient presenting necrotic aspect of pylorus.

Laboratory findings showed anemia in 11 patients (68%), neutrophilic leucocytosis in 13 patients (81%) elevated creatinine level reported in 12 patients (75%), hyperglycemia observed in 13 patients (81%).

All patients reported one or more pre existing comorbidities: 7 patients (43%) were diabetic, 5 patients (31%) had history of chronic renal failure, 3 patients (18%) had cardiovascular disease, 2 patients (12.5%) had active malignancy.

Acute events were reported in almost all patients: 7 cases (43%) pneumonia, 6 cases (37%) acute renal failure, 2 cases (12.5%) Clostridium Difficile colitis, 1 case acute myocardial infarction and one patient developed AEN few days after orthopaedic surgery. Two patients developed AEN as first presentation of Zollinger Ellison Syndrome.

Conclusion: AEN is a rare cause of upper gastrointestinal bleeding representing the most common clinical manifestation of this disorder. Concomitant duodenal alterations are associated in two third of cases. Exception-

ally, AEN is observed in elective endoscopy. Combination of acute events and pre-existing comorbities characterize the clinical setting in which AEN may arise.

Disclosure: Nothing to disclose

P1532 WITHDRAWN

P1533 POLYSOMNOGRAPHIC ASSESSMENT OF RESPIRATORY DISTURBANCE DURING DEEP PROPOFOL SEDATION FOR ENDOSCOPIC SUBMUCOSAL DISSECTION OF GASTRIC TUMORS

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Introduction: Although drug-induced sedation can improve outcomes in advanced gastrointestinal endoscopic procedures, sedation-related critical cardiorespiratory complications are of significant concern, and recent guidelines recommend pulse oximetry monitoring during sedation.

Aims & Methods: To investigate that polysomnographic monitoring can accurately evaluate respiratory disturbance incidence during sedation for gastrointestinal endoscopy compare to pulse oximetry alone. This prospective observational study included 10 elderly patients with early gastric cancer undergoing endoscopic submucosal dissection (ESD) under propofol sedation. Apart from routine cardiorespiratory monitoring, polysomnography measurements were acquired. The primary hypothesis was tested by comparing the apnea hypopnea index (AHI), defined as the number of apnea and hypopnea instances per hour during sedation, with and without hypoxemia; hypoxemia was defined as the reduction in oxygen saturation by ≥3% from baseline.

Results: Polysomnography (PSG) detected 207 respiratory disturbances in the 10 patients. PSG yielded a significantly greater AHI (10.44 ± 5.68 hour^{-1}) compared with pulse oximetry (1.54 ± 1.81 hour^{-1}, $p < 0.001$), thus supporting our hypothesis. Obstructive AHI (9.26 ± 5.44 hour^{-1}) was significantly greater than central AHI (1.19 ± 0.90 hour^{-1}, $p < 0.001$). Compared with pulse oximetry, PSG detected the 25 instances of respiratory disturbances with hypoxemia 107.4 seconds earlier on average.

Conclusion: Compared with pulse oximetry, PSG can better detect respiratory irregularities and thus provide superior AHI values, leading to avoidance of fatal respiratory complications during ESD under propofol-induced sedation.

Disclosure: Nothing to disclose

P1534 PHOTODIAGNOSIS OF GASTRIC ADENOCARCINOMA IN RATS

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Introduction: Gastric cancer is one of the most common oncological diseases, which is diagnosed only at the last stage[1]. Photodiagnosis (PDD) is a promising method in the diagnosis of stomach cancer[2]. However, this method has drawbacks: similar spectra for inflammation and cancer[3]. The search for effective diagnostic parameters of PDT can give an impulse for progress in the early diagnosis of gastric cancer and reduce the mortality from this disease. Here we analyzed parameters of PDD that might be effective for early prognosis of gastric cancer in rats.

Aims & Methods: The results were carried out with adult rats using our model of gastric adenocarcinoma[4,5] induced by combination of two factors:
1) stress (overpopulation) and
2) nitrites: toluidine (2g/kg) in food and nitrites (2g/l) in water.
Rats underwent chronic social stress for 9 months. The upper endoscopy was performed using our in-house custom-made multichannel endoscopy system. Histological assay was performed to analyze the changes in the gastric tissues. Biochemical analysis were used for additional confirmation of oncological changes: the levels of sialic acids, TBA-active products, lactic acid were measured by standard methods given in test kits.

Delta-ALA (20 mg/kg) was applied intravenously 2 hours before the spectroscopic observation. Excitation source at 405 nm (AFS-405, Polironik Ltd., Moscow, Russia) coupled with fiber-optical probe with 25 mW output power on the end of the fiber tip was used for induction of 5-ALA-PpIX fluorescence in the lesions under interest. Fluorescence emission of endogenous autofluorescence (420-630 nm) and exogenous 5-ALA/PpIX fluorescence (630-710 nm) was detected using microspectrometer coupled to the fiber probe (USB4000, Ocean Optics Inc., Dunedin, USA).

Results: Our results demonstrated that in 9 months of observation all rats, that underwent chemical and social stress showed development of peptic ulcers. In 38% of rats with peptic ulcers were associated with intestinal metaplasia of goblet cells, which is morphological pre-cancer symptom. Other 62% of rats had gastric adenocarcinoma. Tumor lesions were accompanied by the migration of cancer cells through the lymphatic vessels to the liver and the lungs. The number of metastatic nodes varied from 1 to 5.

Development of gastric adenocarcinoma was confirmed by biochemical analysis of blood serum. Levels of sialic acids, TBA-active products, lactic acid increased significantly in all animals with gastric cancer.

The spectral measurements were made on normal mucosa and suspicious sites. Normal mucosa has significant autofluorescence. The tumor area has reduced autofluorescence signal and well pronounced signal at 635 nm and 704 nm, typical for 5-ALA/PpIX. Inflammatory areas showed intermediate levels of the fluorescence at 635-704 nm. However, the spectral intensity at 635 nm was two times lower than the signal obtained from cancerous sites, which allows to differentiate the areas based on the spectroscopic detection of exogenous fluorophores.

Conclusion: Collectively, our results clearly show that combination of two factors as chronic social stress and nitrites in food provoke gastric adenocarcinoma formation in rats. The intensity of autofluorescence signal is a marker of gastric mucosa injuries. The analysis of two specific maxima of laser at 635 nm and 704 nm in PDD demonstrate more effectiveness of spectral intensity at 635 nm for early differentiation of areas based on the spectroscopic detection of exogenous fluorophores.

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References: 1) Torre, Lindsey A., et al. "Global cancer statistics, 2012." CA: a cancer journal for clinicians 65.2 (2015): 87-108;
2) Namikawa T. et al. Clinical applications of 5-aminolevulinic acid-mediated fluorescence for gastric cancer. World J Gastroenterol. 2015 Aug 7; 21(29): 8769-8775;
3) Borisova E., et al. 5-ALA Mediated Fluorescence Detection of Gastrointestinal Tumors", Adv Opt Tech, ID 862081, 7 pages doi:10.1155/2008/862081 (2008)
4) Ulanova M. et al. "Stress-Induced Stroke and Stomach Cancer: Sex Differences in Oxygen Saturation." Oxygen Transport to Tissue XXXVIII, Advances in Experimental Medicine and Biology 923, DOI 10.1007/978-3-319-38810-6_18.
5) Khorovodov A. et al. The role of stress and nitrosamines in the development of gastric cancer: a new model of adenocarcinoma formation with metastases in rats / United European Gastroenterology Journal. Vol. 5.5_suppl.: A837-A875. 2017.

Disclosure: Nothing to disclose

P1535 PHOTOGRAPHIC DOCUMENTATION OF UPPER GASTROINTESTINAL LANDMARKS AT GASTROSCOPY: HOW GOOD IS IT?

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Introduction: The British Society of Gastroenterology (BSG) and Association of Upper Gastrointestinal Surgeons (AUGIS) recently published a position statement in view of the variability of performance of a high-quality gastroscopy and an unacceptably high rate of failure to diagnose cancer at endoscopy. This set out the minimum expected standards in diagnostic upper gastrointestinal endoscopy. One recommendation is that photo-documentation should be made of relevant anatomical landmarks and any detected lesions. This practice encourages mucosal cleansing, mucosal inspection and ensures a complete examination. The European Society of Gastrointestinal Endoscopy (ESGE) guidelines describe a systematic approach to photo-documentation with a recommendation of eight anatomical landmarks to improve diagnostic endoscopy quality of endoscopy.

Aims & Methods: The aim of this study was to retrospectively assess the photo-documentation at gastroscopy in clinical practice and compare this to the recommended sites as per the ESGE guidelines. This was a single centre, retrospective analysis of 250 consecutive gastroscopies in a district general hospital endoscopy unit in London over a two week period from 2nd April 2019. The gastroscopy reports were scrutinized for photographic evidence of the anatomical landmarks. The images capture on the Uni-soft GI Reporting Tool were analysed and compared to the recommended ESGE guidelines. The patient comfort scores of the procedures (0 = no discomfort, 1 = one or two episodes, 2 = more than 2 episodes, 3 = significant discomfort) were examined in relation to number of photographs obtained.

Results: Of the 250 gastroscopies performed, the eight anatomical landmarks were photographed during only 33 procedures (13%). In these 33 procedures the patient comfort scores were >1 (more than two episodes of discomfort) in 3 patients (9%) compared with 60 (28%) in the 217 patients with suboptimal photo-documentation (p = 0.02). In the 33 procedures where all the landmarks were photographed; 22 patients (66%) had sedation, 11 (33%) patients had xylocaine throat spray.

Anatomical site	Site photographed, n (%)
Upper Oesophagus	77 (31%)
Gastro-Oesophageal	178 (71%)
Fundus in retroflexion	126 (50%)
Body of stomach	130 (52%)
Incisura in retroflexion	70 (28%)
Gastric Antrum	148 (59%)
Duodenal bulb	98 (39%)
Duodenum second part	178 71%)

[Table 1. Frequency of anatomical sites photographed during gastroscopy.]

Conclusion: In this study, photographic evidence of anatomical landmarks as per ESGE guidelines is only documented in 13%. Better comfort scores and procedures under conscious sedation increase compliance with optimal photo-documentation. Photographic documentation improves the diagnostic quality of endoscopy and acts as a medico-legal record of an adequate/complete procedure. There is much room for improvement in the photographic documentation of anatomical landmarks during gastroscopy.
Disclosure: Nothing to disclose

P1536 ODYNOPHAGIA – IS IT A SYMPTOM WORTHY OF URGENT GASTROSCOPY?

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Introduction: Odynophagia is defined as a painful sensation in the oesophageal region that occurs in relation to swallowing. Endoscopy is the gold standard investigation for the diagnosis of mucosal lesions in the oesophagus. Unlike dysphagia, which has historically been an alarm symptom of oesophageal cancer, odynophagia does not form part of the suspected upper gastrointestinal (GI) cancer referral in the UK.
Aims & Methods: We aimed to compare the standard 'red flag' indications for gastroscopy to odynophagia in terms of cancer detection. A retrospective analysis of all patients who underwent upper GI endoscopy for standard upper GI 'two-week-wait' (2WW) criteria compared with odynophagia as a primary symptom over a 14-year period (2005-2019) within an NHS Trust in North London. Data was obtained from the Unisoft Endoscopy reporting software. The findings at endoscopy for all indications were scrutinised.
Results: During the study period, a malignant oesophageal tumour was identified in 21 patients (4%) endoscoped for odynophagia (total 530 patients scoped for odynophagia). This compared to Anaemia (17936 endoscoped and 94 tumours identified (0.5%)); Dysphagia (10954 endoscoped and 562 tumours identified (5%)); Nausea and vomiting (N&V) (6380 endoscoped and 64 tumour identified (1%)); Weight loss (6157 endoscoped and 119 tumours identified (2%)).
Of the 530 patients who were endoscoped for odynophagia during the

study period, 240 (45%) had oesophageal mucosal lesions: Reflux oesophagitis 193 (36%); Barrett's oesophagus 26 (5%); Malignant tumour 21 (4%). 32 (6%) had an oesophageal stricture.

Indication for gastroscopy	Number of endoscopies	Malignant tumour identified (%)
Odynophagia	530	4
Dysphagia	10954	5
Anaemia	17936	0.5
Nausea/Vomiting	6380	1
Weight loss	6157	2

[Table 1. Indication for gastroscopy and percentage of cancers detected]

Conclusion: From this study, almost half of patients endoscoped for odynophagia have a positive endoscopic mucosal abnormality. 4% of patients endoscoped for odynophagia had oesophageal cancer compared with 5% of dysphagia patients. Anaemia (0.5%), weight loss (2%) and N&V (1%) all have inferior cancer pick up rates. We recommend that odynophagia be re-classified as an 'alarm symptom' and those presenting with this significant symptom undergo an urgent upper GI endoscopy to define the exact mucosal abnormality and exclude oesophageal cancer.
Disclosure: Nothing to disclose

P1537 LONG TERM OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC NEOPLASIA: A SINGLE CENTER ITALIAN EXPERIENCE

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Introduction: The endoscopic submucosal dissection (ESD) is the treatment of choice for most gastric superficial neoplastic lesions owing to its potential for a curative en bloc resection and low risk of recurrence. At a minimum, ESD allows a complete histopathological evaluation of the lesion. In recent years, good clinical outcomes from several studies have expanded the indication criteria for gastric ESD.
Aims & Methods: The aim of this study is to report the short- and long-term outcomes of a cohort of patients from a single Italian center who underwent gastric ESD. A retrospective analysis of a prospectively mantained registry of all gastric ESDs performed at Humanitas Research Hospital during a 10-year period (January 2010 - January 2019) was performed. Expanded indication criteria for gastric ESD were used. Demographic, clinical, endoscopic, histological and follow-up data were extracted and analyzed.
Results: During the study period, 158 consecutive gastric lesions were treated by ESD. On final pathology, 91 lesions were adenocarcinoma (57.4%) with a subclassification of pT1a: 56 (61.5%), pT1b: 31 (34.%) and pT2: 4 (4.4%). Thirty-eight lesions were diagnosed as high grade dysplasia (24.%), 23 were low grade dysplasia only (14.5.%) and 6 were non-adenomatous (3.8%). An en-bloc resection was achieved in 136 patients (86%). R0 resection was reported in 116 patients (73,4%), while 30 yielded a R1 resection (19%) and the remaining 12 procedures (7.6%) were classified as Rx. Twenty-two patients (14%) experienced a complication (11 early, 10 delayed, 1 both early and delayed). The most common complication was bleeding (17 patients, 10.7%) while 5 perforations (3%) were reported. All these complications were successfully treated endoscopically except 3 patients who required surgery because recurrent bleeding after failure of endoscopic treatment and radiologic embolization in 1 case and due to early (1 case) or delayed perforation (1 case). No deaths occurred related to the ESD procedure. Overall, 23 patients (14.5%) underwent surgery because of non-curative resections. Thirteen patients (8.2) were lost at follow-up. Mean follow-up was 37.2 months (range 122-3). During follow-up, 6 local recurrences of adenoma with LGD at the previous ESD site were diagnosed while 2 patients developed a cancer in a site different from ESD and were referred to surgery.

Conclusion: In a large western series of ESD for early gastric neoplasia ESD was associated with a significant proportion of curative resection and quite low rate of complications as well as disease recurrence. Overall, surgery was required in 17.7% mostly because of non-curative ESD resection.
Disclosure: Nothing to disclose

P1538 USEFULLNESS OF TRANSNASAL HYBRID ENDOSCOPIC SUBMUCOSAL DISSECTION

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Introduction: Endoscopic Submucosal Dissection (ESD) is technically difficult and time-consuming procedure which is usually performed under sedation. Therefore, ESD has definite risks especially for elderly patients. And due to the physiological constriction, the conventional scope is sometimes not reached to the target lesions. In these situations, transanal hybrid ESD(T-ESD) maybe alternative therapeutic option for superficial gastrointestinal neoplasms.
Aims & Methods: We evaluated the clinical outcome of T-ESD. After informed consent, T-ESD was performed without sedation for elderly patients whose age were over 80 years old or the patient having the trouble of physiological constriction. For this study, the target size was defined 10mm or less intramucosal gastric cancer. And the ulcerative lesions were excluded. Clinical characteristics and outcomes were evaluated retrospectively. 13 gastric lesions were resected by T-ESD between April 2016 and March 2019. All of the T-ESD steps were performed using EG-580NW2 endoscope (Fujifilm, Tokyo, Japan), with a diameter of the distal end of 5.8mm and inner diameter of the instrument channel of 2.4mm and a newly developed multifunctional snare 'SOUTEN' (Kaneka Medics, Tokyo, Japan) which is design to achieve Hybrid ESD which is available through the transnasal endoscope. The knobshaped tip attached to the loop top helps to stabilize the needle-knife, making it less likely to slip during circumferential incision and enables partial submucosal dissection. For hemostasis, RAICHO(Kaneka Medics, Tokyo, Japan) was used which ensure the suction ability of the scope even with the transnasal endoscope.
Results: The mean age was 80.5±6.5 years old, the male to female ration was 8:5. The lesions locations were U/M/L:1/5/7. Mean tumor size and resected specimen size were 10.4±3.2mm and 21.1±6.0mm. And mean procedure time was 15.3±3.1min. En-bloc R0 resection rate were 100% respectively. In all patients, face scale was 1 and oxygen saturation could keep more than 95% during procedure, therefore oxygen administration was not needed. Incidence of perforation and postoperative hemorrhage were 0% and 7.7%(1/13).
Conclusion: We confirmed favorable clinical outcomes of T-ESD. On the other hand, We need pay attention to the fact that the weaker suction ability and lack of the water jet may make hemostasis more difficult to achieve. Though we believe this is a useful therapeutic option, additional studies would be needed to determine if this modality is also useful for beginners.
Disclosure: Nothing to disclose

P1539 INTERNATIONAL MULTICENTER STUDY ON THE MANAGEMENT OF PATIENTS AFTER FAILED PERORAL ENDOSCOPIC MYOTOMY (POEM)

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Introduction: Peroral Endoscopic Myotomy (POEM) is considered a primary treatment for patients with achalasia and a safe alternative to pneumatic dilation (PD) and laparoscopic Heller myotomy (LHM). Although highly effective, clinical failure may occur. It is currently unknown how patients who fail POEM are best managed. Options include conservative management, botulinum toxin injection (BTX), redo POEM, PD, and LHM.
Aims & Methods:
(1) To describe a cohort of patients who failed POEM;
(2) Compare clinical success [Eckardt ≤ 3] and safety [severity of adverse events (AEs) per ASGE Lexicon] of the above described treatment modalities in patients with failed POEM.
This is an international, multicenter, retrospective study at 19 tertiary centers between 1/2012 and 8/2018. All patients who underwent POEM for the treatment of achalasia, esophagogastric junction outflow obstruction (EGJOO), hypercontractile esophagus (Jackhammer), and diffuse esophageal spasm (DES), who failed POEM were included. Patients with an Eckardt score >3 after POEM or during follow-up were considered clinical failures.
Results: A total of 3251 patients underwent POEM and 110 (3.38%) experienced clinical failure (46.46% F, mean age 51yr). Main type of motility disorder was achalasia (82.72 %) and most commonly was type 2 (46.36%). The mean integrated relaxation pressure (IRP) after failed POEM was 15.28±11.97 mmHg. The mean Eckardt score prior to retreatment was 5.64±2.24. A total of 38 (34.5%) patients underwent redo POEM, 28 (25.5%) had PD, 4 (3.6%)had standard balloon dilation, not pneumatic, 8 (7.3%) LHM, 2 (1.8%)BTX, and 30 (27.3%) were treated conservatively (Table 1). Regarding retreatment, in the redo POEM group, the mean length of esophageal and gastric myotomy were 6.77±3.25 and 2.8±1.4 cm, respectively, and mean procedure time was 116.43 ± 65.07 min. In the retreatment with LHM group, the mean length of esophageal and gastric myotomy were 4.4±2.7 and 2.4±0.54 cm, respectively, and the mean procedure time was 135 ±17.32 min. In the PD group, mean dilation diameter and procedure time were 32.31±3.53 mm [1 dilation (n=18), 2 dilation (n=10) sessions] and 20.91±21.2 min. Overall, clinical success was achieved in 40/80 (50%) patients who underwent retreatment during a mean follow-up of 265.76 days. Two (5.2%) patients had AEs during redo POEM [1 muco-

sotomy (mild) and 1 esophageal leak (moderate)]. Mean Eckardt score post retreatment was 2.83±2.38 [2.19±2.2 in Redo POEM, 3.28±2.4 in PD, 4.2±2.8 in LHM]. Clinical success was similar between redo POEM, PD and LHM (p=0.096). PD had the shortest mean procedure time (p< 0.001), and length of hospitalization
(1.1 vs 1.92 vs 2.5 d; p=0.006) (Table 1).

Conclusion: This international study comprehensively assessed a cohort of patients who failed POEM. Redo POEM, LHM, and PD are equally effective and safe retreatment options for these patients.

Disclosure: This abstract has been submitted and accepted for oral presentation at the Digestive Disease Week (DDW) 2019.

P1540 PROSPECTIVE RANDOMIZED STUDY ON THE USE OF A COMPUTER-BASED ENDOSCOPIC SIMULATOR FOR TRAINING IN ESOPHAGOGASTRODUODENOSCOPY

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Introduction: Computer-based endoscopic simulators have been developed in recent years, and their usefulness has been reported. There are a few reports that have evaluated the effectiveness and drawbacks of a computer-based simulator.

Aims & Methods: The present study aimed to assess the effectiveness of a computer-based simulator for basic training in EGD.
The GI-Mentor II simulator was used. The subjects were 16 hospital medical residents. After receiving an explanation regarding the fundamentals of endoscopy, 8 trainees were each randomized into a simulator group and a non-simulator group.
The simulator group received 4h of training with the GI-Mentor II plus bedside training, while the non-simulator group received bedside training. Subsequently, each subject performed endoscopy twice for assessment. Performance was evaluated according to a five-grade scale for a total of 11 items.

Results: The score was significantly higher in the skills required for insertion into the esophagus, passing from the esophagogastric junction (EGJ) to the antrum, passing through the pylorus, and examination of the duodenal bulb and the fornix.

Conclusion: The performance of endoscopy was improved by 4 h of simulator training. The simulator was more effective with regard to the items related to manipulation skills. Computer-based simulator training in EGD is useful for beginners.

Disclosure: Nothing to disclose

P1541 IMPLICATIONS OF RANDOM UPPER GI ENDOSCOPIC BIOPSIES ON COST; A RETROSPECTIVE CLINICAL AUDIT

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Introduction: Oesophago-gastro-duodenoscopy is the major tool for investigation of Upper GI tract symptoms. In view of recent upcoming cancer investigation pathways and campaigns the number of biopsies required is likely to increase[1.] Cancer detection rates remained unchanged by random non-diagnostic biopsies[2].
Non targetted biopsies to investigate Helicobacter Pylori are not cost effective as cheaper non invasive modalities are readily available.Literature review showed that biopsies for weight loss without serological evidence of coeliac disease, is diagnostic in less than 1%[3].

Aims & Methods: This retrospective clinical audit was performed on all diagnostic gastroscopies at the University Hospitals of Leicester within the month of January in 2018. In the initial audit cycle,practice was compared to British Society of Gastroenterology guidelines, recently published recommendations from the Newcastle group as well as our local biopsy protocol [4,5]. All planned therapeutic procedures as well as incomplete or failed procedures were excluded.The local guidelines were updated following

initial audit results and disseminated across the trust. Practice was then re-audited against the updated guidelines. Finally the findings were analysed to evaluate any cost implications.

Results: First cycle: A total 731 gastroscopies were performed during January 2018. Diagnostic biopsies were obtained in 261 out of 570 eligible cases.According to study criteria total of 102 (13.95%) out of 731 patients were biopsied inappropriately.The assumed cost of a single biopsy set was around 145£. The monthly cost of unnecessarybiopsies was 14,790£ (estimated to be 177,480£ annually).
Second cycle: A total of 802 gastroscopies were performed during January 2019.Diagnostic biopsies were obtained in 253 out of 666 eligible patients. According to the study criteria 66 (8.2%) out of 802 biopsies were obtained inappropriately. Keeping the assumed cost for the single biopsy set remained unchanged.The monthly cost was therefore 9,570£ (estimated to be 114,840 annually).

Conclusion: We have detected a sizeable number of inappropriate biopsies resulting from local and national guidelines not being followed. This has a significant cost implication.By updating local protocols and emphasising the importance of avoiding unnecessary non targeted biopsies we have demonstrated potentially significant cost savings.

References: 1.Teriaky A, AlNasser A, McLean C, et al. The utility of endoscopic biopsies in patients with normal Upper Endoscopy.Can J Gastroenterol-Hepatol2016;2016:1-7. 2. Cadman B, Dixon MF, Wyatt JI. Value of routine, non-targeted biopsies in the diagnosis of gastric neoplasia.J ClinPathol1997; 50:832-4. 3.Kotha S, Holohan C, Gera A, et alPTH-032 D2 biopsies in weight loss referrals - is it necessary and cost effective? Gut 2015;64:A420. 4.Beg S, et al. Quality standards in upper gastrointestinal endoscopy a position statement of the British Society of Gastroenterology(BSG) an Association of upper gastrointestinal surgeons of Great Britain and Ireland(AUGIS).Gut 2017;0:1-14. doi:10.1136/gutjnl-2017-314109 5.Gibson V, Needham S, Nayer M, et alDo non-targeted gastric biopsies affect the management of patients, and can a simple protocol and education reduce the rate? Frontline Gastroenterology 2018;9:67-72.

Disclosure: Nothing to disclose

P1542 CORRELATION OF ENDOSCOPIC AND HISTOLOGICAL FEATURES IN ADULTS WITH SUSPECTED CELIAC DISEASE

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Introduction: Clinical presentation of celiac disease is extremely variable and the diagnosis relies on serologic tests, mucosal intestinal biopsy and clinic and serologic response to a gluten-free diet. The aim of our study is to correlate the endoscopic and histological aspects of adult patients with suspicion of celiac disease and to evaluate the correlation with histological findings.

Aims & Methods: A retrospective study was conducted between January 2015 and december 2018. Endoscopic aspects of 61 adult patients were evaluated and correlated with the histological features according the Marsh classification system.

Results: Sixty one patients were included, mean age was 42.9 years[16-83] and sex ratio was 0.8. No statistically significant correlation was showed between the age and gender and pathology features and endoscopy manifestations (p>0.05).
The most prevalent clinical data in patients with histological diagnosis of CD were iron-deficiency anemia (29.5%), chronic diarrhea (9.8%), and malabsorption syndrome (8.2%).
The endoscopic study of the duodenum showed: normal mucosa in 5 cases (8.2%); scalopping folds in 3 (4.9%), and total villous atrophy in 52 (85.2%). Among these patients, histological examination showed CD in 38(23%) ,intraepithelial lymphocytosis in 40(65.5%)and was normal in 9(5.4%) We did not observe a significant correlation between endoscopy results and pathology features (p=0.235).

Conclusion: Our data confirmed Endoscopic markers have disappointing sensitivity. Endoscopic markers of villous atrophy are not useful for screening for celiac disease and duodenal histological assessment remains mandatory

Disclosure: Nothing to disclose

P1543 GASTRIC PER ORAL ENDOSCOPIC PYLOROMYOTOMY (G POEM) FOR REFRACTORY GASTROPARESIS: A SINGLE CENTRE EXPERIENCE

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Introduction: Gastroparesis (GP) is a disorder evidenced by delayed gastric emptying in the absence of mechanical obstruction, commonly idiopathic or secondary to diabetes mellitus. G-POEM has been used to treat refractory gastroparesis and we present our initial experience with this novel endoscopic technique.

Aims & Methods: All patients undergoing G-POEM for refractory GP from May 2018 onwards were included, with data extracted from the hospital electronic patient record. Procedures were performed by one endoscopists at our centre with experience in submucosal endoscopy. Efficacy at 3 months was assessed by reduction of symptom score (Gastroparesis Cardinal Symptom Index; GCSI), with secondary considerations including technical success, procedural complications, hospital length of stay and hospitalisations after treatment.

Results: 10 patients (10F; mean age 40.3± 15.4 y) were included (5 diabetic, 5 idiopathic). Mean duration of disease was 9.5± 5.6 y, with 4 months median duration of follow-up post-procedure. 6 patients had previous treatment with botulinum toxin, and one gastric electrical stimulator. Technical success was achieved in all cases while, at 3 months, 8 had improvement total GCSI (mean scores 3.978 vs 2.076 (p = 0.008)) and each GCSI subtype score: nausea and vomiting (3.63 vs 1.70, p = 0.012); fullness (4.30 vs 2.30, p =0.012); bloating (4 vs 2.22, p = 0.28). Mean hospital stay was 9± 13 d, with 5 patients staying less than 4 days and two with prolonged admission. One significant adverse event was recorded: abdominal collection around the myotomy site requiring a prolonged hospital admission of 18 days for intravenous antibiotics in one patient.

Only one patient required hospitalisation for gastroparesis symptoms after their G-POEM procedure (this was the same patient who did not achieve clinical success with reduction in their GCSI scores).

Conclusion: G-POEM is a promising therapeutic treatment for patients with refractory GP, with significant improvement in symptoms and, in our cohort a dramatic reduction in the need for hospitalisation in short-term follow up. A European sham-controlled study is under way and longer-term data are required to confidently determine its role in the management of such a challenging condition.

Disclosure: Nothing to disclose

P1544 LONG-TERM OUTCOMES AFTER PER-ORAL ENDOSCOPIC MYOTOMY FOR TREATMENT OF ESOPHAGEAL ACHALASIA

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Introduction: Per-oral endoscopic myotomy (POEM) is a relatively novel endoscopic therapy for esophageal achalasia. The outcome and safety of peroral endoscopic myotomy (POEM) in patients with achalasia has been mostly reported with relatively short/mid-term follow-up data. As a matter of fact, studies reporting long-term clinical outcomes and the incidence of gastroesophageal reflux (GER) after POEM are still limited.

Aims & Methods: The aim of this study was to assess the long-term outcomes and the incidence of GER in a cohort of consecutive patients treated with POEM for achalasia between June 2012 and December 2015. A retrospective analysis of a prospectively maintained procedure database was conducted and included clinical assessment in combination with findings at interval upper GI endoscopies, manometry and pH monitoring. Scheduled follow-up included clinical assessment by Eckardt symptoms, high resolution manometry, upper-gastrointestinal endoscopy and pH monitoring at 3-6, 12-24, 36 and 60 months after POEM. A post-POEM Eckardt

score ≤3 was considered a clinical success. Regarding pH monitoring, a percentage of time with esophageal exposure to acid (pH < 4) > 4.2% was considered positive for GER .

Results: A total of 60 achalasia patients (type I 9.8%, type II 82.3% and type III 7.9%) with follow-up longer than 36 months were included. The median age of the patients was 54 years (range 17-86); no patients with ASA class IV were treated with POEM. Nineteen patients had received prior interventional treatment (32.7%) and five patients had a sigmoid esophagus (8,3%).

Adverse events occurred in 7 patients (11.6%); according to the AGA Lexicon classification, 5 were mild, 2 were moderate. Median length of hospital stay was 2.1 days (range 1-9).

The mean pre-POEM Eckardt score was 6.5 (±2.3) and it significantly decreased 3-6 months after POEM (0.75±1.5, p< 0.0001), remaining stable 12-24, 36 and 60 months after POEM (0.74±1.1, 1.11±1.7 and 0.88±1.5, respectively; p< 0.0001). The mean integrated relaxation pressure (IRP) before POEM was 26.12±11.2 mmHg and significantly decreased at 3-6 months after POEM (9.42±3.54 mmHg, p< 0.0001), remaining stable 12-24, 36 and 60 months after POEM (9.81±3.9, 9.6±5 and 10.6±4.5, respectively; p< 0.0001). During follow-up, clinical success was maintained in 95% at 3-6 months, 93.3% at 12-24 months, 91.6% at 36 months and 90% at 60 months after POEM.

Clinical reflux symptoms occurred in 25%, 28.3%, 23.3% and 17.7% of patients, respectively, after 3-6, 12-24, 36 and 60 months after POEM. Upper-GI endoscopy revealed erosive esophagitis in 30%, 28.3%, 31.6% and 35.0% of patients, respectively, at 3-6, 12-24, 36 and 60 months after POEM. Cases of Grade C and D erosive esophagitis were present only 3-6 months after the procedure. There were no confirmed reflux-related post-POEM strictures or diagnoses of Barrett esophagus. Twenty-four hour pH monitoring studies revealed pathological esophageal acid exposure time in 26.3%, 24.2%, 27.6% and 20.0% of patients, respectively, 3-6, 12-24, 36 and 60 months after POEM.

Conclusion: POEM is a highly safe and effective treatment for esophageal achalasia with favourable clinical outcomes up to 60 months post-procedure. GER occurs 20-30% of patients post-POEM. Moreover, our results emphasize the importance of long-term follow-up in all patients after POEM.

References: Cotton PB, Eisen GM, Aabakken L et al. A lexicon for endoscopic adverse events: report of an ASGE workshop. Gastrointestinal Endoscopy;71: 446-454. Werner YB, Costamagna G, Swanström LL et al. Clinical response to peroral endoscopic myotomy in patients with idiopathic achalasia at a minimum follow-up of 2 years. Gut 2016;65(6):899-906. Repici A, Fuccio L, Maselli R et al. GERD after per-oral endoscopic myotomy as compared with Heller's myotomy with fundoplication: a systematic review with metaanalysis. Gastrointest Endosc 2018; 87: 934-43.

Disclosure: Nothing to disclose

P1545 THE "OVER-THE-SCOPE-GRASPER" - A NEW INSTRUMENT FOR FLEXIBLE ENDOSCOPY

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Introduction: Removal of blood clots, necrotic tissue and occasionally foreign bodies is a significant problem in flexible endoscopy. There are no special gripping instruments for the removal of viscous materials and suction alone is often limited.

Aims & Methods: A special gripping instrument (Over-The-Scope-Grasper: OTSG) was designed to overcome those problems. It can be attached to the tip of a conventional gastroscope, similar to a conventional cap. Two excavator-like jaws are attached to the tip of the cap, which can be opened and closed by a pull mechanism running on the outside of the endoscope. Thus, the working channel of the endoscope remains available for suction/irrigation or insertion of additional instruments. The total diameter of the system is 13 mm.

Results: In one patient, the OTSG was used for necrosectomy after the formation of a gastrocystostomy. In another patient, the OTSG was used to remove a large coagulum after ESD in the middle esophagus after removal with a Dormia basket ended frustrantly. The insertion of the endoscope was possible without any problems when the OTSG was closed. By opening and closing the jaws with simultaneous suction, it was possible to remove necrotic material or large parts of the coagulum respectively.

Conclusion: The OTSG was successfully used for the removal of necrotic tissue and blood clots. Further evaluation based on a larger case series is still pending.
Disclosure: Nothing to disclose.

P1546 THE ROLE OF MULTIDISCIPLINARY EVALUATION IN ENDOSCOPIC SLEEVE GASTROPLASTY

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Introduction: Endoscopic sleeve gastroplasty (ESG) is a relatively novel endoscopic procedure that reduces the gastric lumen with proven less complications and almost same 6 months weight loss compared to laparoscopic sleeve gastroplasty (LSG). To our knowledge there are no trials investigating the role of multidisciplinary evaluation (ME) before and after ESG.
The aims of the present study were to evaluate the role of ME prior and after ESG in terms of weight loss outcomes, quality of live improvements and adverse events.
Aims & Methods: From May 2016 to April 2019 all patients that underwent ESG were retrospectively evaluated from a prospective database. Included patients had 2° and 3° degree of obesity or 1° with comorbidities. All patients underwent upper GI endoscopy to exclude pathologies. Until September 2017 before ESG only psychiatric evaluation was requested, while after this date we adopted the guidelines of the Italian Society for Obesity Surgery and all patients were evaluated on a multidisciplinary fashion prior ESG.
The ME team was composed by: gastroenterologist, surgeon, psychiatrist, endocrinologist and dietitian. Patients were divided in two groups: group 1 were patients with ESG done before ME while group 2 were patients with ESG done after ME.
We compared this two groups in terms of weight loss outcomes, quality of life improvements and adverse events. Quality of live was measured with the Bariatric Analysis and Reporting Outcome System (BAROS). ESG was done with the Apollo Overstitch suturing system (Apollo Endosurgery) and a double channel gastroscope Olympus 2TGIF-160 (Olympus Japan) in general anesthesia and with insufflation of CO2.
All patients had ambulatory visit t 1, 3, 6 and 12 months after ESG and weight loss outcomes were measured in terms of Excess Weight Loss (%EWL), the Total Body Weight Loss (%TBWL) and BAROS scale were assessed. Statistical analysis was done with chi-square test and < 0.05 value was considered significant.
The study was approved by the local Ethical Committee (N° 19211/18).
Results: A totally of 89 ESG were performed. Mean procedure time was 51 minutes (range 28-92). Mean number of stitches were 4.7/patient (range 3-8). No procedure related complications were observed. Female were 56 patients; mean age was 45.4 (range 23-73). Mean BMI at inclusion was 41.6 (range 31.6-62.4).
Twelve months follow-up was done in 34 patients, 6 months in 26, 3 months in 10, while in 19 patients follow up was 1-month. Mean %EWL and %TBWL at 12 months was 37.6 and 15.6 respectively, at 6 months was 37.1 and 16.7, at 3 months was 30.6 and 13.8, while for 1 month was 16.9 and 7.8 respectively. Mean Baros score was 4.6 at 12 and 6 months, 3.9 at 3 months, while for 1 month was 2.7.
Comparing the two groups (11 patients in group 1 and 78 patients in group 2) there was significant (P< 0.05) difference in terms of %EWL and %TBWL (Table 1) for all periods of follow-up, with better results in group 2. There was also a significant improvement in the BAROS scale in the patients in group 2 (Table 1).
Conclusion: ME before and after ESG has a fundamental role in terms of better procedure outcomes for both weight loss and quality of live in obese patients.
Disclosure: Nothing to disclose

	WL (Kg)		%EWL		%TBWL		BAROS		
	pre-ME	post-ME	pre-ME	post-ME	pre-ME	post-ME	pre-ME	post-ME	p
1 month follow-up	5.7	10.8	11.5	19.7	5.2	9.1	1.4	3.3	<0.01
3 months follow-up	12.1	18.1	23.7	33.7	11	15.2	2.3	4.7	<0.05
6 months follow-up	14.1	22.4	26.5	42.2	14.7	18.8	2.5	5.7	<0.01
12 months follow-up	14.1	27.5	25.4	48.8	11.7	22	2.5	6.5	<0.01

WL = Weight Loss; EWL = Excess Weight Loss; TBWL = Total Body Weight Loss; BAROS = Bariatric Analysis and Reporting Outcome System.

[Table 1. ESG results on 89 patients pre and post multi-disciplinary evaluation (ME)]

P1547 ENDOSCOPIC RESECTION OF NON-AMPULLARY DUODENAL POLYPS: A RETROSPECTIVE SINGLE CENTRE EXPERIENCE

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Introduction: Current literature estimates that complete endoscopic resection (ER) of duodenal adenomas can be achieved in 79-100% of cases, but complication rates are high and adenoma recurrence is encountered in up to 37% of cases (Basford & Bhandari, 2012). We present our retrospective experience.
Aims & Methods: Data from the electronic patient record was analysed for all patients who underwent duodenal polyp resection from June 2013 were included (excl. familial polyposis cases). Procedures were performed by either one of two endoscopists with experience in endoscopic resection. Accepted definitions of technical success, major adverse events and recurrence were used.
Results: 31 patients (15F; mean age 67.9± 10.4 y) were included. The mean polyp size was 38.8±23.6 mm, with most (n = 26) located within D2. More than half were laterally spreading lesions (n=16). The main method of resection was with piecemeal EMR (n=24), with 5 removed by en-bloc EMR and 2 by ESD. Histology revealed tubular adenoma low grade dysplasia (n = 12), tubulovillous adenoma with low grade dysplasia (n = 11) and neuroendocrine tumour (n = 3). ER was successful in 28 / 31 cases (90.3%). Mean size in 3 incomplete resections was 93mm, with 1 patient referred for surgery, 1 repeat ER and 1 did not proceed due to a more pressing medical diagnosis.
3/31 had peri-procedural complications: endoscopically-treated perforation in 2 (6%) and minor bleeding in 1. 2/31 patients (6%) experienced delayed bleeding, with one patient requiring a repeat OGD but no intervention and the other requiring transfusion of packed red blood cells and observation in hospital. There was no procedure related mortality. At time of writing 4 patients had not yet had surveillance OGD and to date 5 patients (20.8%) had recurrence all treated endoscopically.
Conclusion: ER of duodenal polyps is feasible and safe. Our single centre experience is on par with what is published in the literature in regards to technical success and adverse events. A prospective analysis would be of value to guide patient selection, optimal treatment and surveillance protocols.
Disclosure: Nothing to disclose

P1548 LONG-TERM OUTCOMES OF GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION IN ENDOSCOPIC CURABILITY CRITERIA

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Introduction: Endoscopic submucosal dissection (ESD) is one of the most useful methods for treating early gastric neoplasms, and its indication is becoming expansive. The absolute-indication criteria for gastric ESD have been expanded in the Japanese gastric cancer treatment guidelines 2018. According to the new guidelines, endoscopic curability A (eCura A) is 1) lesions of any size without UL, differentiated-type, and pT1a or 2) lesion size ≤3cm with UL, differentiated-type, and pT1a; whereas endoscopic curability B (eCura B) is 3) lesion size ≤2cm without UL, undifferentiated-type, and pT1a or 4) lesion size ≤3cm, differentiated-type, and pT1b(SM1, <500μm). The eCura A cases are recommended to be followed up by annual EGD, whereas the eCura B cases are recommended to be followed by CT or US in addition to annual EGD. However, few studies have compared the short-/long-term outcomes of gastric ESD between the new endoscopic curability criteria.

Aims & Methods: This study aimed to evaluate and compare the clinical outcomes of ESD in early gastric cancers with eCura A and B lesions. The participants included 476 patients with 554 early gastric cancers, diagnosed as having eCura A or B lesions. All patients underwent ESD at our hospital between June 2007 and August 2018. The patients were divided into 2 groups: eCura A lesions (Group A, 419 patients with 483 lesions) and eCura B lesions (Group B, 70 patients with 71 lesions). We evaluated the clinicopathological findings; short/long-term outcomes including the local, distant, and metachronous recurrence rates, and the overall and disease-specific survival (OS and DSS) rates.

Results: The mean ages of Groups A and B were 72.9 and 68.5 years, respectively, and the male-to-female ratios in Groups A and B were 319/100 and 56/14, respectively. The mean tumor sizes in Groups A and B were 15.5 and 13.6mm, respectively. From the histopathological findings, the rates of differentiated-type were 100% (483/483) in Group A and 62.0% (44/71) in Group B (p< 0.01). Regarding the tumor depth, intramucosal carcinomas were 100% (483/483) in Group A and 38.0% (27/71) in Group B (p< 0.01), and shallow submucosal invasive carcinomas (< 500μm) were 62.0% (44/71) in Group B. The *en bloc* resection rates and curative resection rates were 100% in both groups. Adverse events included the incidence of postoperative hemorrhages of Group A and B were 3.11% (15/483) and 5.63% (4/71), respectively, and perforations during ESD for Group A and B were 0.21% (1/483) and 1.41% (1/71), respectively. Regarding the long-term outcomes, the local and distant recurrence rates were 0.41% (2/483) and 0% (0/483) in Group A, and 0% (0/71) and0 % (0/71) in Group B, respectively (n.s.). The metachronous recurrence rates in Group A and B were 6.83% (33/483) and 5.63% (4/71), respectively (n.s.). Regarding the survival analysis (using the Kaplan-Meier method and long-rank test), the mean follow-up periods for Group A and Group B were 51.6±35.2 and 49.9±35.3 months, respectively. The 3 and 5 y OS rates were 93.1% and 90.0% in Group A, and 100% and 90.6% in Group B, respectively. The 5-year DSS rates were 100% in both groups. There were no significant differences observed for the survival rates.

Conclusion: The eCura B lesions have an excellent long-term prognosis equivalent to that of eCura A lesions. Therefore, the new endoscopic curability criteria are considered apt, and there is a possibility that eCura B lesions could be treated in the same manner as eCura A lesions.

Disclosure: Nothing to disclose

P1549 SEQUENTIAL THERAPEUTIC APPROACH FOR PERSISTENT GASTRO-CUTANEOUS FISTULAS AFTER PERCUTANEOUS ENDOSCOPIC GASTROSTOMY (PEG) REMOVAL IN CANCER PATIENTS

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Introduction: PEG removal in head and neck cancer patients (HNCPs) is required after completion of treatment, in case of tumor remission and after adequate oral intake is resumed. The PEG tract usually closes spontaneously within 48 to 72 hours. Persistent gastro-cutaneous fistula (PGCF) is a rare complication after PEG tube removal. The diagnosis is established in case of persistent gastric leakage through the fistulous tract for more than 30 days after PEG removal.

Aims & Methods: Our goal was to evaluate the incidence and treatment algorithm of PGCF in HNCPs.

This is a retrospective unicentric study of HNPCs referred for PEG removal between 2014-2018. The patients with PGCF were evaluated and their sequential treatment (medical, endoscopic and surgical) was reviewed, and technical and clinical success were assessed.

Results: During the study period, 331 PEG tubes, all with 24 French were removed. There were 313 (94.7%) male patients, with a mean age of 59 ± 11 years (18-85), with 19 PGCF (5.7%). Medical therapy (proton-pump inhibitors, prokinetics and antibiotics in case of infection, for 2 to 8 weeks) was performed with clinical success (definitive closure of the PGCF) in 12 (63.2%) patients. The remaining 7 patients required endoscopic or surgical treatment. In 4 (21.1%), endoscopic treatment had technical and clinical success (3 patients with fulguration of the gastric leak edges with argon plasma coagulation (APC), silver nitrate in the path and external orifice, and closure of the internal orifice with hemoclips: mean number=6,33±0.47 (range: 6 to 7), and 1 (5.3%) with an over-the-scope-clip (OTSC)). Only 3 patients underwent surgery, 1 due to clinical failure of sequential endoscopic therapy (hemoclips + OTSC) and 2 underwent direct surgery (one required surgery for another condition and one had a PEG-site herniation).

Conclusion: PGCF is a rare complication after PEG removal. Medical therapy is usually effective and should be maintained for at least 8 weeks. Endoscopic therapy is an effective second-line option and surgery is rarely required.

Disclosure: Nothing to disclose

P1550 ENDOSCOPIC TREATMENT FOR ZENKER'S DIVERTICULUM WITH THE STAG BEETLE KNIFE (SB KNIFE) - PRELIMINARY RESULTS FROM A SINGLE-CENTER EXPERIENCE

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Introduction: Flexible endoscopic treatment of symptomatic Zenker's diverticulum (ZD) is an established treatment option. Over the years, various techniques have been developed and many devices have been tested with varying results. We report our experience with a scissor-shaped, rotating device with two insulated monopolar blades (SB knife) designed primarily for endoscopic submucosal dissection. Little data are reported about its use for endoscopic treatment of Zenker diverticulum.

Aims & Methods: From Febuary 2014 to April 2019, n = 20 patients (pts) were treated at ASST-Rhodense with the SB knife junior. The two insulated blades allowed to avoid the use of the overtube. The procedures were performed with a cap to better evaluate the diverticulum and the septum. All patients underwent an esophagram before the procedure and post-procedure, to rule out perforation and to assess esophageal transit. Symptoms (dysphagia, regurgitation, and respiratory symptoms) were analyzed

before and at the follow up using a validated scale. Procedure duration, rate of complications, symptom changes after the procedure and rate of relapsing patients during follow up were also recorded.

Results: The procedure was carried out successfully in all patients. The mean size of ZD was 3 cm (1-6 cm). Eighteen out of 20 (90%) patients received one treatment session. The mean procedure time was 28 min (18-60 min). In 4 procedures (20%), one to two clips were prophylactically placed at the bottom of the resection line. Two patients (10%) required a second treatment after a mean of 14 months (2-26) due to symptomatic recurrence; both patients were at the very beginning of our experience (pts n.2 and n.3) and the recurrence of dysphagia was likely to be as a result of an incomplete division of cricopharyngeal fibers of the septum. Two minor intraprocedural bleedings were easily treated by the "coagrasper" use of the device. No major bleeding or late-onset bleeding developed. One minor perforation occurred (minimum free air in the mediastinum, no mediastinitis, no leak of hydrophilic medium per os) and was successfully treated with medical therapy.

During a mean follow-up of 27 months (1-60), a significant symptom improvement was achieved in all the scores (dysphagia; regurgitation; respiratory symptoms).

Conclusion: Flexible endoscopic treatment of ZD with the SB knife is safe, effective, and has lasting effects on symptoms also at long term follow up, with a relatively low recurrence rate.

Disclosure: Nothing to disclose

P1551 PERSISTENT GASTROCUTANEOUS FISTULAS AFTER PERCUTANEOUS ENDOSCOPIC GASTROSTOMY TUBE REMOVAL IN HEAD AND NECK CANCER PATIENTS WITH EARLY FEEDING AND DOUBLE-DOSE PPI: A PROSPECTIVE COHORT STUDY WITH A HISTORICAL CONTROL GROUP

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Introduction: Percutaneous endoscopic gastrostomy (PEG) removal is required in head and neck cancer patients (HNCP), after chemoradiotherapy ends and adequate oral intake is reacquired. The PEG tract usually closes spontaneously within 48-72 hours. Persistent gastro-cutaneous fistula (PGCF) is an uncommon complication of PEG removal.

Aims & Methods: Our aim was to compare the incidence of PGCF in two groups of HNCP removing PEG under distinct protocols.

We performed a prospective cohort study with a historical control group. Group A, with 86 patients who removed PEG in 18-month period (May15-Dec16) and Group B, a historical control group, with 102 patients who removed PEG in a 14-month period (Jan14-Apr15). There were two different PEG tube removal protocols. Group A had 4h of rest and fasting, followed by cold liquid diet 4/4h and omeprazole 40mg bid for 4 weeks. Group B rested for 6h and initiated oral diet 12h after PEG removal. The study primary end-point was the incidence of PGCF in both groups and secondary end-points were to evaluate predictors and treatment of PGCF.

Results: Demographics were identical in Group A and B, 84.9% male with a mean of 56±9 years old and 86.3% male with a mean of 53±11 years old, respectively. In Group A: 67.4% were smokers; 6.9% had diabetes mellitus (DM) and 2.3% used corticosteroids. Median body mass index (BMI) reduction of 2.25 (0.73-4.11) Kg/m2. PEG complication rate of 13.9%, predominantly minor infections. Mean PEG placement time was 8.2±4.5 months, use PEG for nutrition for 2.4 months on average, with 11.6% of the patients not using PEG. Only 2 (2.3%) patients had PGCF after PEG removal, one closure with medical therapy (PPI+prokinetic+antibiotic) and other with through-the-scope (TTS) clips.

In Group B: 50% smokers; 5.9% with DM and 2.9% used steroids. Median BMI reduction of 2.39 (0.71-4.14) Kg/m2. PEG complication rate of 33.3%, most frequently infections. Mean PEG time was 8.5±4.6months, use PEG for nutrition for 4.75 months on average, 9.8% of patients not using PEG. PGCF occurred in 9 (8.8%) patients, with 7 closures with medical therapy, 1 with an over-the-scope clip (OTSC) and 1 with surgery.

By multivariable analysis, PEG time (p=0.006; CI95% 1.05-1.26) and presence of early leak (4h) after PEG removal (p=0.002; CI95% 4.10-9.63) were independent predictors of PGCF. The new protocol reduced the number of PGCF (2 cases versus 9 in the historical control group), nearly reaching statistical significance (p = 0.056, IC95% 0.87-19.57).

Conclusion: The new PEG removal protocol showed a tendency to reduction of PGCF, with less of time in hospital and fewer fasting hours. As PEG time is a predictor of PGCF, early removal of PEG is recommended. Patients with early leak post-PEG removal should be informed that, if PGCF installs, medical treatment is effective, and endoscopy or surgery are rarely required.

Disclosure: Nothing to disclose

P1552 A SUBMUCOSAL FLUID CUSHION PREVENTS MUSCLE LAYER DAMAGE DURING MUCOSAL ARGON PLASMA COAGULATION

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Introduction: Thermal damage to the muscle layer of the gastrointestinal wall can occur during mucosal application of argon plasma coagulation (APC). This injury may be mitigated by creating a fluid cushion within the submucosal layer. This can be achieved during endoscopy by injecting fluids directly into the submucosa, thus creating a cushion effect, using a needle and syringe or a high pressure needleless injection system. The fluid cushion physically separates the mucosal layer from the muscle layer and suppresses unwanted tissue temperature elevation. This in turn protects the muscle layer from thermal damage. The coagulative threshold of muscle proteins is known to be about 60°C, but there are no published systematic assessments of the minimum injection volume needed nor the ideal injectate to prevent thermal damage to the muscle layer during mucosal APC ablation.

Aims & Methods: Our aims were, firstly, to measure the final temperature inside the fluid cushion after mucosal ablation with APC and then to determine any differences in the final temperature between various injectable solutions. Secondly, we sought to determine the minimum volume of injectate required to protect the muscle layer from thermal damage.

All experiments were performed in an ex-vivo porcine gastrointestinal tract model. Five different fluids (normal saline, Glyceol, Gelafundin, Voluven and Eleview) of different volumes (range 0 - 5mL) were injected into the submucosa of the esophagus, stomach (fundus) and rectum to create a fluid cushion. APC was applied to the mucosa for a fixed duration (3s) at different power settings (ranging from 30 - 120W). Immediately after APC treatment, the final temperature was measured by placing a contact thermometer inside the fluid cushion, just on top of the muscle layer. The minimum volume of fluid needed to protect the muscle layer from thermal damage was also determined.

Results: There was no significant difference in the temperature measured at the surface of the muscle layer between elevation with normal saline, Glyceol, Gelafundin, Voluven and Eleview at all 3 tissue locations at equal injection volumes and power settings. The experiments showed that the temperature rose for each injectate with heightened power settings but also decreased with increasing volume of injected fluid. The minimum amount of fluid needed to protect the muscle layer from thermal damage was 2mL for the esophagus, stomach and rectum in the case of a power setting between 30 to 90W and 3mL in the case of 90 to 120W.

Conclusion: Normal saline and four commercially available submucosal injectates possess similar thermoregulatory effects in terms of acting as an insulator of the muscle layer during APC treatment. As opposed to the choice of injectate or anatomic location treated, the volume of fluid injected is the main determinant of the final temperature at the level of the muscularis propria. To reduce the likelihood of thermal damage to deeper layers of the GI tract when APC is applied, a minimum injection volume of 2mL is recommended if < 90W of power is utilized.

Disclosure: Nothing to disclose

P1553 S-POEM IS EFFECTIVE TREATMENT FOR EPIPHRENIC DIVERTICULA ASSOCIATED WITH SPASTIC MOTILITY DISORDERS

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Introduction: Esophageal epiphrenic diverticula are infrequently associated with achalasia and major disorders of esophageal peristalsis. The mainstay of treatment is laparoscopic myotomy and diverticulectomy with anterior fundoplication. However, in case of contraindication and/or disapproval of the procedure by the patient, there are limited ways of alternative treatment. S-POEM (salvage POEM) has gained some evidence as a eligible treatment for achalasia and esophageal epiphrenic diverticula. However, the effectivity of the procedure has yet been demonstrated only in case reports and the data based on the series of patients are lacking.
Aims & Methods: We present a case series of 7 symptomatic patients with achalasia or spastic motility disorders and large epiphrenic diverticulum that have been treated by S-POEM. In these patients Eckhardt score was calculated, barium contrast study was performed and the posture and the size of the diverticulum was recorded before the procedure. High resolution manometry (HRM) was performed and in case of the detection of major disorder of peristalsis according to the Chicago classification v3.0 POEM procedure was performed. Generally, the myotomy was guided on the site opposite to the diverticular sack. After 3 months patients were invited for checkup, during which the general well-being and Eckhardt score was evaluated, upper endoscopy and HRM was performed.
Results: 7 patients (3 men, 4women) met the inclusion criteria. Mean age was 69 years (range 43-80 y.). HRM revealed achalasia in 6 patients, I. type in 5 patients, II type in 1 patient. In one patient we were not able to classify the motility disorder due to previous intervention. Mean radiological size of diverticula was 6 x 4,8cm (range 4x4 - 11x9 cm). The most common complaint was dysphagia (mean partial Eckhardt score for dysphagia 2), followed by regurgitation (mean partial Eckhardt score for regurgitation 2). Posterior POEM procedure was performed in 6 patients, anterior procedure in 1 patient. In 3 months follow up we observed significant decrease of Eckhardt score (6.6 vs. 0.6, p< 0.0001). There was a significant improvement in dysphagia and regurgitation (2 vs. 0.17 p< 0.01, 2 vs. 0.33 p< 0.01). A dramatic decrease of IRP was also observed IRP (31.8 vs. 8.8, p< 0.0001). The average weight gain was 6.8 kg. There were neither complications related to the procedure, nor any aspiration event detected at 3 months follow up.
Conclusion: S-POEM provided effective symptomatic improvement and significant decrease of the LES relaxation pressure in patients with esophageal epiphrenic diverticula associated with achalasia or spastic motility disorders. However, long term follow up in a large cohort of patients is required before it is considered equivalent treatment alternative for these patients. Supported by U01 DK116311 and VEGA 1/0304/19
Disclosure: Nothing to disclose

P1554 QUALITY IN UPPER GASTROINTESTINAL ENDOSCOPY: IMPACT OF CLINICAL PRACTICE GUIDELINES PUBLICATION

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Introduction: Upper gastrointestinal (UGI) endoscopy is the gold standard for the diagnosis and treatment of most esophageal, gastric, and small-bowel disorders. The European Society of Gastrointestinal Endoscopy (ESGE) has identified quality of endoscopy as a major priority and has published performance measures in the field of a quality improvement initiative.
Aims & Methods: Our aim was to evaluate ESGE's performance measures for UGI endoscopy in a tertiary center and assess the effect of their publication on improving the quality of procedures.
Retrospective cohort study included all UGI endoscopies performed in a single center between 2016 and 2018. We performed a global evaluation of performance measures defined by ESGE guideline and a comparative analysis between the period previous (2016) and subsequent (2017-2018) to their publication using Chi² test.

Results: A total of 3289 procedures were evaluated. Regarding key performance measures, proper fasting instructions were received in 99.9%; procedure duration was documented in 97.5%; accurate photo documentation was reported in 70.6%; standardized terminology was used in 35.9%; Seattle protocol in Barrett's surveillance was adopted in 55.9% and immediate and delayed complications were monitored in 99.4% and 77.6%, respectively. As far as minor performance measures are concerned, inspection time in the stomach was appropriate in 72.4%; lugol staining in esophagus for patients at risk of squamous cell cancer was used in 88.9%; biopsy protocol according to MAPS guidelines was applied in 76.1% and 55.6% of Barrett's patients entered a registry to monitor the incidence of dysplasia. Considering comparative analysis between 2016 and 2017-218, we have verified statistically significant improvement in the accurate photo documentation (56.6% vs. 76.7%; p< 0.01); in the standardized terminology use (24.1% vs. 42.7%; p< 0.01) and in the inspection time in the stomach (70.7% vs. 76.3%; p< 0.01).
Conclusion: In our center minimum standards are fulfilled to fasting instructions, documentation of procedure duration and registration of immediate and delayed complications after therapeutic endoscopies. The remaining measures require improvement and subsequent auditing. Disclosure of performance measures, followed by auditing and correction, may allow Gastroenterologists to improve UGI endoscopy quality.
Disclosure: Nothing to disclose

P1555 ARTIFICIAL INTELLIGENCE METHODS FOR DIAGNOSIS OF EARLY GASTRIC CANCER WITH MAGNIFYING NARROW BAND IMAGING ENDOSCOPY

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Introduction: Endoscopic diagnosis of gastric cancer at an earlier stage is the single most effective strategy for reducing gastric cancer mortality. Magnifying narrow-band (M-NBI) imaging endoscopy significantly improves the diagnostic accuracy of gastric epithelial neoplastic lesions [1]. However, effective application of M-NBI endoscopy is difficult due to the presence of various changes of gastric mucosal patterns, and therefore requires appropriate training. Computer-aided decision support systems based on endoscopic image analysis are being designed to assist an endoscopist in enhancing the diagnosis and mastering advanced techniques that require a high level of expertise [2].
Recently convolutional neural networks have become one of the most popular and effective approaches in different fields of endoscopic image analysis.
Aims & Methods: The aim of this study was to develop a system for automatic identification of gastric cancer on M-NBI images using deep learning through convolutional neural networks (CNN). The database of 1293 M-NBI endoscopic images was created. It consisted of 357 M-NBI images of cancerous lesions and 936 M-NBI images of non-cancerous lesions (Olympus Exera II, GIF Q160Z, Lucera GIF, Q260Z, EXERA III, GIF HQ 190). The developed image analysis algorithm was based on the application of the SSD (Single Shot Multibox Detector) architecture of convolutional neural network. The network architecture was implemented using the Caffe framework. The neural network was pre-trained on the ImageNet [3] image database which was used to initialize part of the weights. The weights of the remaining layers were initialized using Xavier initialization. Neural network training was done simultaneously with 8 GPU video cards of the NVIDIA DGX-1 supercomputer. For numerical experiments 100 images were randomly selected from the endoscopic image database: 24 images of cancer and 76 images non-cancerous lesions. The videodata of M-NBI endoscopic procedures (415 frames which were not presented in the database) was blindly analyzed by the designed system and an expert endoscopist to compare it with the doctor's diagnosis. Spatial correlation between automated results and experts opinion was assessed.

Results: Average precision for "cancer" class was 0,827, average precision for "non-cancer" class was 0,923, mean average precision was 0,875. Average intersect over union (IoU) score (area of intersection the expert frame and the frame obtained using algorithm / total area combining these frames) was 0,767 which corresponds to high concordance between automated and expert marking of gastric cancer areas.

Conclusion: The proposed algorithm of image analysis based on deep learning through SSD convolutional neural network allowed to design the automated system for NBI-M endoscopic diagnosis of gastric cancer. The designed system is able to analyze videodata and can be implemented in endoscopic electronic data collecting system for further testing in daily clinical practice.

References: 1. Pimentel-Nunes P., Libânio D., Marcos-Pinto R. et al. Management of epithelial precancerous conditions and lesions in the stomach (MAPS II): European Society of Gastrointestinal Endoscopy (ESGE), European Helicobacter and Microbiota Study Group (EHMSG), European Society of Pathology (ESP), and Sociedade Portuguesa de Endoscopia Digestiva (SPED) guideline update 2019. Endoscopy. 2019 Apr;51(4):365-388. 2. Kuvaev R., Kashin S., Nikonov E., et al. Computer-aided diagnostic system for the real time pathology prediction and clinical decision support during narrow band imaging magnification endoscopy in stomach. United European Gastroenterol J. 2015 Oct; 3(5S):A9 3. Image Net Image Database http://www.image-net.org/.

Disclosure: Nothing to disclose

P1556 TREATMENT OF GASTRIC VARICES BY INTRAVARICEAL INJECTION OF N-2-BUTYL CYANOACRYLATE: RESULTS OF THE FIRST ALGERIAN PROSPECTIVE STUDY

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Introduction: Endoscopic intavariceal injection of cyanoacrylate, especially of N-2-butyl
cyanoacrylate (NBC) is the treatment of choice for bleeding from type 2 gastro-esophageal varices (GOV 2) and isolated gastric varices (IGV), whether in acute phase or in a secondary prophylaxis setting. This endoscopic therapy has not been evaluated in our country. In this study, we evaluated the efficacy of this technique in the secondary prophylaxis of bleeding from VOG 2 and IGV and we have also estimated hemostasis rates and either complications of this technique and predictive factors for recurrence.

Aims & Methods: A prospective analysis of clinical, biological, endoscopic and evolutive parameters was carried out in patients recruited and treated consecutively, which we divided into two non-comparative groups: a group 1 (G1) of patients treated in secondary prophylaxis and a group 2 (G2) of patients treated in acute bleeding phase. Statistical analyses were performed using SPSS software (version 22.0; SPSS Inc., Chicago, IL, United States). Descriptive data are reported as mean ± SD or as percentage. The Student's t test and the χ^2 test were used to assess differences between groups. Forward stepwise logistic regression analyses, both univariate and multivariate, and receiver operating characteristic curve (ROC) analysis were used to determine the correlation between factors and clinical outcomes;The actuarial survival curve was established by the Kaplan-Meir method. The comparisons of survival curves were made using the Logrank test. A P value < 0.05 was considered statistically signifcant.

Results: 75 patients (37 males, 38 females),sex_ratio=0.9 with a mean age of 54.23 ± 3.46 years were enrolled and followed for an average duration of 16.27 ± 2 months, 44 patients were G1 and 31 G2 . Gastric varices (GV) were GOV 2 in 96% of cases and were related to cirrhosis in 55 patients (73%). Immediate and initial hemostasis rates in the G2 were 95% and 90%, respectively, and the failure rate was about 10% (N=3)in the same group. Minor complications were observed in 38.7% in the G2(N=12) and 29.5%cases in the G1(N=12). Major complications were seen in 9.7% in the G2(N=3), including a case of pulmonary embolism and in 2.3%,in the G1 (N=1)

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represented by a single case of spontaneous bacterial peritonitis. Mortality was estimated at 9.7% in the G2 (N=3) and 0% in the G1(N=0). The G1 bleeding recurrence rate was estimated at 0% at six weeks and at 9.1% at 1 year(N=4) and the mean survival without recurrence was evaluated at 22.7 months ± 1.24 [20.26-25.13] .In multivariate analysis only the presence of ascites at the time of endoscopic treatment was a predictive factor of recurrence with an adjusted OR: 13.89 CI 95% [1.07-17.915] .

Conclusion: Our study confirms the efficacy and relative safety of NBC injection in the treatment of GV either in secondary prophylaxis and acute haemorrhage setting. We confirm its feasibility in our environment with satisfactory hemostasis and bleeding recurrence rates and acceptable complications.

Disclosure: Nothing to disclose

P1557 COATING OF METALIC STENTS WITH ACELLULAR BIOMATRIX AND NANOFIBERS BASED SCAFFOLD CONTAINING A STEROID IN PREVENTING ESOPHAGEAL STRICTURE AFTER CIRCUMFERENTIAL ENDOSCOPIC DISSECTION - AN EXPERIMENTAL STUDY

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Introduction: The major drawback of circumferential endoscopic submucosal dissection (CESD) in the esophagus is development of refractory stricture in almost 100% of cases. We have previously shown that a self-expandable metallic stent (SEMS) covered with acellular biomatrix from pig's dermis resulted in reduced stricture severity and improved quality of healing (Dolezel et al. GIE 87.6 (2018): AB266-7).

Aims & Methods: To assess the effect of a newly developed drug eluting SEMS coated with acellular biomatrix and with a nanofibers-based scaffold (from a polymer solution) containing a steroid (Depomedrol 104 mg) in preventing the post-CESD esophageal stricture.
An experimental controlled study. CESD were performed in the mid-esophagus in 14 pigs (control group, A, n=6; interventional group, B, n=8). After completing CESD, SEMS were placed alongside the post-CESD defect and fixed with a lasso technique. SEMS were removed 21 days after CESD. Pigs were euthanatized when a significant stricture developed.

Results: The mean length of the defect was 54 ± 15 mm. Significant strictures developed in all pigs after a mean of 12.8 ± 4.3 days. The length of stricture was 26.6 ± 14.9 mm in the control group and 17.0 ± 10.4 mm in the B group, (p=0.19). The narrowest stricture diameter did not differ between the groups (8.8 ± 4.0 mm (A) vs. 8.6 ± 2.1 mm (B), p=0.45). Macroscopic re-epithelization was not detected in 66% (4/6) of pigs in the control group, while it was always present in the B group, p=0.06. The re-epithelization length (measured as the longest distance of new epithelization from the edge of the defect) was 1100 ± 935 μm in the control group vs. 679 ± 489 μm in the interventional group (p=0.39). The re-epithelization width was 105 ± 115 μm (A) and 236 ± 202 μm in the B group, p=0.24. Thickness of fibrosis was 2.3 ± 1.1 mm (A) and 2.0 ± 0,1 mm (B), p=0.36. Histologically, severe inflammation was present in all pigs in the control A group, while in no pig in the B group (only mild inflammation), p=0,0008.

Conclusion: Depomedrol eluted from SEMS covered with acellular biomatrix was unable to effectively prevent post-CESD esophageal stricture in the experimental model. However, it significantly improved microscopic healing quality in terms of re-epithelization and less severe inflammation. The stent may be a suitable candidate for further development.

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Disclosure: Nothing to disclose

P1558 UNSEDATED UPPER GASTROINTESTINAL ENDOSCOPY: DOES TOPICAL PHARYNGEAL ANESTHESIA MAKE IT MORE TOLERABLE?

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Introduction: In many countries, upper gastrointestinal endoscopy (UGIE) is commonly performed without sedation, which avoids the cost and risk of procedural sedation altogether. Adequate patient tolerance is essential for successful completion of a safe examination. As a result, endoscopists tend to use a topical pharyngeal anesthesia (TPA) as a pretreatment for unsedated UGIE. However its efficiency has not been established.
Aims & Methods: The purpose of this study is to assess the tolerance of unsedated UGIE and to determine whether TPA has an impact on patients' tolerance level. A prospective study during a period of 6 months (November 2018 - April 2019) was conducted. Patients who underwent unsedated UGIE were included and randomly divided into two groups: with and without TPA administration (xylocaine spray).

A comparision of UGIE tolerance between the two groups was performed. Patients who were under psychotropic or analgesic treatment were excluded from this study. The UGIE tolerance evaluation was based on a primary criterion: the patient's acceptance to undergo the examination again under the same conditions.

The secondary criteria were: the occurrence of a suffocation sensation, the occurrence of nausea and the level of pain/discomfort measured using the visual analog scale (VAS) (0 = no pain/discomfort encountered to 10 = extremely painful/uncomfortable).
Results: Seventy patients (female=36, male=34, mean age 50 years [18-82]) were included. UGIE was mostly performed for epigastralgia (48.6%) and iron deficiency anemia (17%). UGIE was well tolerated in 65.7% of patients: forty-six out of seventy accepted to undergo the same procedure. The refusal to repeat the examination was significantly related to suffocation sensation (p< 0.01), nausea (p< 0.01) and the level of pain/discomfort (p< 0.01).

There was no significant difference between the 2 groups in terms of tolerance according to the primary and the secondary criteria. The VAS score was 4.66/10 for patients who received TPA versus 5.49/10 for those who didn't receive TPA. Unsedated UGIE was less tolerable in female patients (p< 0.01) and in less than 40 year-old patients but with no statistical significance (p=0.08). Previous endoscopic experience and longer examination time didn't seem to interfere with patient's tolerance level.
Conclusion: The use of a Topical pharyngeal anesthesia appears to be beneficial for male and for over 40 year-old patients. Otherwise, TPA doesn't seem to improve unsedated UGIE tolerance.
Disclosure: Nothing to disclose

P1559 COMPARISON OF PERORAL ENDOSCOPIC MYOTOMY (POEM) IN ESOPHAGEAL ACHALASIA FOR NAIVE PATIENTS AND PATIENTS WHO FAIL OTHER TREATMENTS. RESULTS OF A MULTICENTER STUDY ON 105 PATIENTS

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Introduction: Peroral Endoscopic Myotomy (POEM) is part of the modern therapeutic arsenal for the management of achalasia. Its effectiveness has been widely demonstrated and it is now often offered as a first-line treatment. Nevertheless, the overall impact of previous processing operations on the results of this intervention remains to be determined in current practice. The purpose of our study was therefore to compare the feasibility, morbidity and efficacy of POEM in naïve and naïve patients.

Aims & Methods: Clinical, manometric and endoscopic data from patients treated for esophageal achalasia with POEM in 2 tertiary centers were collected prospectively and analyzed retrospectively. Esophageal motor disorders were defined according to the Chicago Classification v3.0. Symptoms were assessed using Eckardt's score before POEM, then at 1 and 6 months post-procedure. Esophageal manometry data (before the procedure and at 6 months), gesture data (procedure duration, myotomy length, number of clips), per and postoperative complications (bleeding, infection, hospitalization duration) and efficacy (defined by an Eckardt score ≤3) were collected. The data were compared by matched and unpaired t-test or by Chi2 test.
Results: A total of 105 patients (40 females, 38.1%, median age = 51.2[38.2-64.8] years) were included between July 2015 and October 2018. Twenty-five patients (23.8%) had type I achalasia, 63 (60.0%) type II achalasia, 13 (12.4%) type III achalasia and 4 (3.8%) a variant. Fifty-two (49.5%) patients were naïve to any treatment and fifty-three (50.5%) had previous treatment, (49 patients, had at least one pneumatic dilation, 7 had Heller's myotomy and 4 had botulinum toxin injection). The characteristics of the 2 groups were comparable in terms of sex, age, type of achalasia, Eckardt score, resting pressure of the lower esophageal sphincter (LES) and integrated relaxation pressure (IRP) before POEM.

With regard to the feasibility and the safety of the gesture, no significant differences were found between the two groups concerning: the duration of the intervention (naïve = 45[36-60] minutes vs non naïve = 50[35-65] minutes; p= 0.1647), the length of the myotomy (naïve = 10[8-10]cm vs. non naïve = 9[8-10]cm; p= 0.4275) or the number of clips used to close the submucosal tunnel (naïve= 6[5-7] vs. naïve= 6[6-7]; p= 0.3221). There was no significant difference concerning per and postoperative complications notably for severe complications. Two patients (1.9%) (1 naïve et 1 non naïve, no statistical difference p = 1.00) had a mediastinitis of favourable progression after endoscopic treatment; associated with surgical drainage for one and radiological drainage for the other, without esophagectomy.
Myotomy treatment was considered successful (Eckardt score ≤3) in 77/87 patients (88.5%) at 6 months. The efficacy of POEM at 6 months was comparable between the 2 groups: 39/44 patients (92.9%) in the naïve group and in 38/43 (84.4%) in the non naïve group (p=0.1288) Esophageal manometry data were available for 66/87 patients. There was no significant difference in the post-POEM IRP and lower esophageal sphincter resting pressure between the 2 groups.
Conclusion: This study, conducted on a large number of patients under conditions of routine clinical practice, shows that the feasibility, morbidity and efficacy of POEM in achalasia at 6 months are comparable between naïve and non naïve patients. This technique can therefore be offered to patients with severe esophageal achalasia resistant to other therapies.

References: 1- E. Akintoye, N. Kumar, I. Obaitan, Q. A. Alayo, et C. C. Thompson, « Peroral endoscopic myotomy: a meta-analysis », Endoscopy, vol. 48, no 12, p. 1059-1068, déc. 2016. 2- H. Ø. Kristensen, J. Kirkegård, D. W. Kjær, F. V. Mortensen, R. Kunda, et N. C. Bjerregaard, « Long-term outcome of peroral endoscopic myotomy for esophageal achalasia in patients with previous Heller myotomy », Surg. Endosc., vol. 31, no 6, p. 2596-2601, juin 2017. 3- T. Ling, H. Guo, et X. Zou, « Effect of peroral endoscopic myotomy in achalasia patients with failure of prior pneumatic dilation: a prospective case-control study », J. Gastroenterol. Hepatol., vol. 29, no 8, p. 1609-1613, août 2014.
Disclosure: Nothing to disclose

P1560 SHOULD ROUTINE DUODENAL BIOPSIES ALWAYS BE PERFORMED IN ELDERLY PATIENTS WITH ANEMIA WITHOUT ENDOSCOPIC SIGNS OF BLEEDING?

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Introduction: Anemia, a multifactorial condition, occurs in 12.7% of men and 30.2% of non-pregnant women worldwide. Specifically, iron-deficiency anemia (prevalence 2-5% of men and postmenopausal women in developed countries) is considered a warning sign especially in elderly

(colonic or gastric neoplasia), but it may be also due to benign conditions (coeliac disease (CD), duodenal intraepithelial lymphocytosis (DIL), chronic atrophic gastritis or H.pylori, poor dietary intake, non-steroidal anti-inflammatory drugs. Multimorbidity and polypharmacy may play an additional role. Anemia is found in 80-90% of CD, but the need for routine duodenal biopsies, independently from age or coeliac serology status, is debated. Guidelines from British Society of Gastroenterology recommend duodenal biopsies in individuals undergoing upper endoscopy (EGDS) in whom CD or alternative mucosal cause of malabsorption is suggested.

Aims & Methods: To determine diagnostic yield of routine duodenal biopsies in adult and elderly patients with anemia whose EGDS failed to reveal macroscopic causes of bleeding and to identify predictive features of duodenal histopathological findings. Single center cross-sectional study; between 2015-2018, among consecutive 7968 EGDS performed in our Endoscopy Unit, 744 were for anemia. Patients with manifest GI bleeding or no gastric/duodenal biopsies were excluded. In 469 (F 68%; median age 60yrs), both gastric and duodenal biopsies, were taken.

Clinical, endoscopic and histological features were collected and separately analyzed in the groups with or without histopathological changes of duodenal mucosa (DM). Univariate/multivariate analyses were performed (dependent variable: normal or pathological DM; independent variables: gender, outpatient/inpatient, age, endoscopic findings in stomach or duodenum). Different cut-offs for age were considered (>50, >60, >70, >80yrs).

Results: Of 469 included patients, 40(8.5%) had histopathological changes in DM: 12(2.6%) CD, 25(5.3%) DIL, 3(0.6%) others (2 Giardia Lamblia infection, 1 hypereosinophilia). Compared to patients with normal DM, they were younger (median age 47.5 yrs, range 20-90 vs 62 yrs, range 17-93,p=0.0005) and showed more frequently duodenal endoscopic findings (22.5% vs 6.7%,p=0.0014), while the stomach was endoscopically normal in all cases (0 vs 14.7%,p=0.0182). The frequency of histopathological findings in the DM showed a significantly decreasing trend with increasing age, in patients aged < 40, 41-50, 51-60, 61-70, 71-80, and >80yrs, they were observed in 25%, 30%, 20%, 12.5%, 10%, and 2.5%, respectively (p=0.0010).

Logistic regression models showed that endoscopically normal DM and age >50, >60, and >70yrs were significantly associated with normal DM biopsies. Anemic patients aged >60, >70, or >80yrs with endoscopically normal DM had a 3- to 4-fold higher probability of having normal duodenal histology (OR3.5,95%CI 1.5-82, OR3.6 95%CI 1.6-8.5, OR4.1,95%CI1.8-9.4). The strength of association increased with increasing age. Other independent variables (gender, outpatient/inpatient, gastric findings) were not associated.

Conclusion: In anemic patients without endoscopic signs of bleeding, predictors for histologically normal DM were age and endoscopically normal DM appearance. In over 70yrs anemic patients infrequent or negligible pathological findings in DM were found.

These results suggest that taking routine duodenal biopsies is questionable in elderly anemic patients especially in absence of macroscopic duodenal alterations of other suspected signs of related intestinal diseases.

Disclosure: Nothing to disclose

P1561 INSULATED-TIP KNIFE TUNNELING TECHNIQUE FOR ESOPHAGEAL ENDOSCOPIC SUBMUCOSAL DISSECTION: AN INITIAL WESTERN EXPERIENCE

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Introduction: Esophageal endoscopic submucosal dissection (ESD) can be technically challenging due to the narrow lumen and thin wall of the esophagus. Device and technique innovation is needed to make esophageal ESD easier to perform, especially in the West where experience and procedure volumes are less. The loose submucosa of the esophagus allows easy entry of the entire ceramic tip of an insulated tip (IT) knife within it. This allows for the backside chip (electrocautery blade on the backside of the ceramic tip) to dissect the submucosa, while the ceramic tip protects the muscle layer from injury as the knife is advanced.

This technique is called IT knife tunneling technique and has been described in Japan for esophageal ESD. We evaluated the safety and efficiency of the IT knife tunneling technique for esophageal ESD at our Western endoscopy center.

Aims & Methods: A single center study evaluating consecutive patients who underwent esophageal ESD with IT knife tunneling technique between July 2016-November 2017. This technique was not used on lesions with expected severe fibrosis. All ESDs were performed by a single ESD expert (AB). Primary aim was to determine safety of the technique, particularly regarding perforation, intraprocedural (>2-gram hemoglobin drop < 48 hours after procedure), and delayed (active bleeding from a post-ESD ulcer diagnosed by emergency or planned follow-up endoscopy) bleeding. Procedure time, resection speed, *en-bloc*, R0 (negative vertical and horizontal margins), and curative (R0 resection, well to moderately differentiated histology, absence of lymphovascular invasion, absence of budding, and absence of invasion beyond superficial submucosa (< 500 microns) for adenocarcinoma or no submucosal invasion for squamous cell cancer) resection rates were measured.

Results: 19 patients underwent esophageal ESD with IT knife tunneling technique [Table]. Median lesion size was 3 cm [25-75 IQR: 2.5-3.3], median procedure time 70 min [60.5-96.5], and median resection speed 0.364 cm²/min [0.269-0.482]. No esophageal perforations, strictures, or delayed bleeding. One case with intraprocedural bleeding requiring blood transfusion of one unit. *En-bloc*, R0, and curative resection rate 100% (19/19), 94.7% (18/19), and 73.7% (14/19), respectively. 4/5 of the non-curative lesions were known high-risk lesions; ESD performed because these patients were deemed non-surgical candidates. 17 patients had Barrett's-related neoplasms (5 high-grade dysplasia, 12 adenocarcinoma). Two had squamous cell cancer; these two large resections >2/3 esophageal circumference (6 and 7 cm) were injected with Kenalog and prescribed oral fluticasone to prevent stricture formation.

	IT Knife Tunneling Technique
	N=19
Factor	Statistics
Histology	
1) Barrett's Associated Neoplasm	17/19 (89.5%)
a) Esophageal Adenocarcinoma	12/17
b) High grade dysplasia	5/17
2) Squamous Cell Cancer	2/19 (10.5%)
Size of resected lesion (cm)	3 [2.5, 3.3]
En-bloc resection rate	70 [60.5, 96.5]
R0 resection rate	0.364 [0.269, 0.482]
Curative resection rate	14/19 (73.7%)
Perforations/Strictures	0/0 (0%/0%)
Significant Intraprocedural Bleed	1/19 (5.3%)
Significant Delayed Bleed	0/19 (0%)

[Table 1. Safety and Efficiency of IT Knife Tunneling Technique ESD Resection]

Conclusion: IT knife tunneling technique allowed for safe esophageal ESD of non-fibrotic lesions at our endoscopy center. Further use of this technique in the West is warranted.

Disclosure: Nothing to disclose

P1562 THE EFFECT OF ENDOSCOPIC MUCOSAL RESECTION (EMR) VS ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) TECHNIQUE ON HISTOLOGIC MARGINS FOR ENDOSCOPICALLY TREATED EARLY ESOPHAGEAL ADENOCARCINOMA

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Introduction: Both endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) techniques are used for the treatment of early esophageal cancers. ESD has potential advantages including higher en

bloc and R0 resection rates, which have been demonstrated for squamous cell carcinomas (ESCC) but data for esophageal adenocarcinoma (EAC) is more limited. Histologic determination of the horizontal and vertical margins is important to determine the completeness of resection and risk of recurrence. Larger tumors, especially those that spread laterally may exceed with limits of en bloc resectability using standard EMR techniques.

Aims & Methods:
Aim: To determine the effect of EMR vs ESD techniques on the histologic margins in endoscopically treated early EAC.
Methods: Our institution's endoscopy and pathology databases were queried for patients undergoing endoscopic treatment of early EAC. Endoscopic and histologic characteristics were collected. Pathology slides were re-reviewed by a blinded pathologist to determine status of horizontal and vertical margins. All statistical analyses were performed using SAS (version 9.4, The SAS Institute, Cary, NC) and a $p < 0.05$ was considered statistically significant.

Results: A total of 52 patients with early EAC were analyzed. 23 patients underwent ESD and 29 had EMR. Tumors that underwent ESD were significantly larger compared to those resected with EMR technique (20.0 mm [20.0,28.0] vs 11.0 mm [9.0,13.0], p <0.001). Rates of endoscopic en bloc resection were not statistically different (EMR 89.7% vs ESD 100%, p = 0.25). On the other hand, EMR specimens were significantly more likely to have positive lateral margins compared to ESD specimens (48.3% vs 8.7%, p=0.003) as well as have lower confidence in determining lateral margins. The reason for lower confidence in the EMR group included cautery artifact (37.9%) and difficulty in orientation (20.7%). Interestingly, EMR and ESD had similar rates of positive vertical margins (7.1% vs 8.7%, p = 0.33).

Conclusion: EMR and ESD had similar rates of positive vertical margins but rates of positive horizontal margins were significantly higher in the EMR group, despite a smaller size of lesion resected in the EMR group. We postulate that this is a limitation of the EMR technique and there is a certain lateral size threshold or Paris classification that is unsuitable for EMR as the standard EMR cap assisted technique may not be able to resect enough of a "normal" margin to the tumor compared to ESD. Further analysis is needed to determine if early EAC below a certain size threshold or tumor morphology may be more amenable to EMR technique while other types of tumors should undergo ESD to ensure higher rates of negative margins.

Disclosure: Nothing to disclose

P1563 WHAT IS THE CAUSE OF MISSED GASTROINTESTINAL CANCERS AND DELAYS IN DIAGNOSIS?

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Introduction: A delay in diagnosis in Upper Gastrointestinal Cancer (UGIC) and Colorectal Cancer (CRC) are associated with poor outcomes. Multiple studies have looked at rates of missed cancers at endoscopy, but few have looked at other factors that delay the time to endoscopy. This study looks at systematic factors responsible for this delay, and identifies ways in which we can reduce this delay in both UGIC and CRC.

Aims & Methods: We looked at all patients diagnosed with an UGIC or CRC at King's College Hospital (KCH), London between 2011-2018 inclusive. From this group we identified all patients who were seen by a Gastroenterologist or a Colorectal Surgeon in the 36 months prior to diagnosis, either in clinic or at endoscopy. Each of these cases was looked at in detail to determine whether the cancer was missed due to a 'Systematic Factor' or was a 'Post Endoscopy Cancer'.

Results: 1,073 cases of GI Cancer were diagnosed in the study period. 60 of 797 (7.5%) cases of CRC and 28 of 276 (11.3%) UGICs had been seen in the last 36 months. 61 patients (5.7%) were determined to have a 'missed cancer'. From this group 10 UGICs and 23 CRCs were determined to be 'Post Endoscopy Cancers' (PEC). The remaining 28 cases were determined to be missed secondary to 'Systematic Factors'. Specific causes of delay in diagnosis are shown in Table 1.
The mean length of delay was longer in the 'Systematic Factors' group versus the 'PEC' group (430 vs. 264 days). The 'Systematic Factors' group also showed a more advanced TNM staging compared the 'PEC' group; pT 2.14 vs. 1.39, pN 0.57 vs. 0.45, pM 0.07 vs 0.12. The 'Systematic Fac-

tors' group also showed a higher percentage of patients referred routinely, rather than via an emergency cancer pathway, compared to the PEC group (74.1% vs. 53.8%).

Factor leading to delay	Number of patients
Post Endoscopy Cancers	33
Inadequate Investigation	10
Incomplete endoscopy	2
Poor bowel preparation	5
Missed on radiological investigation	2
Delayed investigation	4
Incomplete Follow up	4
Histology not reviewed	1

[Table 1. Factors leading to Delay of Diagnosis in Gastrointestinal Cancers]

Conclusion: Post Endoscopy Cancers are well-established concept, leading to delays in diagnosing gastrointestinal cancers. However it is important to identify Systematic Factors which also impact on speed to diagnosis. Higher proportions of missed cancer in the routine pathway imply that we are more likely to miss cancers without the pathway driven approach we see in Two Week Wait referrals. Systematic Factors are also more likely to contribute to a longer delay to diagnosis and a more advanced clinical picture as shown by the TNM staging. Therefore, if we are to improve diagnosis of Gastrointestinal Cancers we should focus equally on the Systematic Factors leading up to diagnosis as well as the quality of endoscopy.

Disclosure: Nothing to disclose

P1564 SPECIAL FEATURES OF THE ENDOSCOPIC EXTRACTION OF FOREIGN BODIES INGESTED BY PRISONERS

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Introduction: Ingesting foreign bodies (FB) can be accidental or deliberate. It can be serious because of the location or nature of the FB, which makes their endoscopic extraction urgent. Prisoners represent a population particularly affected by this pathology.

Aims & Methods: The purpose of our study was to describe the modalities of this endoscopic technique as well as to highlight its particularities in the inmates. We conducted a comparative retrospective study of consecutive patients who had undergone upper digestive endoscopy for foreign body extraction between January 1982 and December 2018. We have compared prisoners to non incarcerated patients.

Results: We included 99 patients (74 men and 25 women) with a mean age of 29 years [6 months-66 years]. Endoscopy was performed for all patients. Of these patients, 30.3% were inmates. A psychiatric history was found more frequently among prisoners than non prisoners (90% versus 24.6%, p <0.001). The FB's ingestion circumstance was more voluntary for the detainee (90%, OR = 29, p <0.001). FBs were more numerous among inmates (43.3% versus 13%, p <0.001), with a higher frequency of metallic FB (70% versus 13%, p <0.001) and larger dimensions than non-incarcerated patients (63.6% versus 37.7%, p = 0.02). The success rate of the extraction was 78% with no statistically significant difference between the two groups. Recurrence of FB ingestion was higher in the case of incarceration (13.3% versus 5.8%, p = 0.038).

Conclusion: The multiple number, the large size of the ingested body and the predominance of metallic ones testify the severity of FB ingestion in the inmates. These are characteristics to be considered by the practitioner before extraction and also for better management of a fragile population in order to reduce the recidivism rate.

Disclosure: Nothing to disclose

P1565 "LIGHT BLUE CREST" SIGN FOR DIAGNOSIS OF GASTRIC INTESTINAL METAPLASIA USING MAGNIFYING ENDOSCOPY WITH I-SCAN OPTICAL ENHANCEMENT

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Introduction: Gastric intestinal metaplasia (GIM) is considered as a premalignant condition and associated with a high risk for the development of gastric cancer [1]. However, conventional white light imaging endoscopic features of GIM has a high rate of interobserver variability and correlates poorly with the histology. Uedo et al. first described "light blue crest" (LBC) sign as highly accurate sign of the presence of histological GIM using magnifying endoscopy and narrow band imaging (NBI) system with a monochrome CCD and rotary RGB filter (Lucera, Olympus) [2]. LBC was defined as an optical phenomenon caused by the reflectance of narrowed spectrum light on the ciliated surface of the epithelium that can be seen at the tangential observation of edge of the surface. However the possibility of LBC detection and its efficacy in diagnosis of GIM with other narrowed spectrum technologies were not fully investigated.

Aims & Methods: The aim of this study was to evaluate the diagnostic efficacy of LBC in diagnosis of GIM with magnifying i-scan optical enhancement endoscopy (PENTAX Medical, Japan). 86 gastric lesions in 46 patients (mean age 52.1 years, SD=10.2, 54% male, 46% female) were observed with magnifying i-scan optical enhancement endoscopy (EPK-i7010, endoscope EG-2990Zi, PENTAX Medical). Presence of LBC were assessed by two endoscopists (R.K. and S.K.), cases with low confidence of LBC diagnosis was consulted with developer of the LBC concept (N.U.). LBC was defined as a fine, blue-white line on the crests of the epithelial surface/gyri[2]. Forceps biopsy was performed for a histological evaluation of lesions.

Results: From 86 gastric lesions complete GIM was confirmed in 14 cases, incomplete GIM – in 8 cases, mixed GIM – in 9 cases. LBC was diagnosed in 22 cases (all lesions with confirmed GIM). Sensitivity, specificity, accuracy, positive predictive value, negative predictive value for LBC sign in diagnosis of GIM were 0.71, 1.00, 0.90, 1.00, 0.86, respectively.

Conclusion: Magnifying endoscopy with i-scan optical enhancement technology provides accurate diagnosis of GIM by using LBC sign. Further studies are needed to evaluate the efficacy of different previously described endoscopic features of IM using new optical technologies.

References: 1. Pimentel-Nunes P., Libânio D., Marcos-Pinto R. et al. Management of epithelial precancerous conditions and lesions in the stomach (MAPS II): European Society of Gastrointestinal Endoscopy (ESGE), European Helicobacter and Microbiota Study Group (EHMSG), European Society of Pathology (ESP), and Sociedade Portuguesa de Endoscopia Digestiva (SPED) guideline update 2019. Endoscopy. 2019 Apr;51(4):365-388. 2. Uedo N, Ishihara R, Iishi H et al. A new method of diagnosing gastric intestinal metaplasia: narrow-band imaging with magnifying endoscopy. Endoscopy. 2006 Aug;38(8):819-24.

Disclosure: Nothing to disclose

P1566 ESD WITH DOUBLE CLIP AND RUBBER BAND TRACTION OF NEOPLASTIC LESIONS DEVELOPED IN THE APPENDICEAL ORIFICE IS EFFECTIVE AND SAFE

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Introduction: Endoscopic resection of Superficial Colorectal lesions in close proximity to the Appendiceal Orifice (L-PAO) was shown to be feasible but is still considered impossible in case of deep invasion into the appendix (Toyonaga type 3). We report here a series of Endoscopic Submucosal Dissection with double clip and rubber band traction (DCT-ESD) of L-PAO to determine the outcomes.

Aims & Methods: We reviewed retrospectively all the consecutive DCT-ESD resections of L-PAO in 3 french centers. Toyonaga's classification was described for each lesion and type 0 lesions which are not in contact of appendiceal orifice were excluded. Our primary outcome was En bloc and R0 resection rates for L-PAO. Morbidity (bleeding, perforation and acute appendicitis) and salvage surgery were recorded.

Results: 32 patients underwent DCT-ESD (mean age 67). 11 patients had previous appendectomy (28.6%). Toyonaga's type of lesion was type 3 (enter deeply in appendiceal orifice) for 22 lesions (68.8%) including 11 (34.4%) without history of appendectomy and 11 (34.4%) with previous appendectomy, 7 type 2 (enters orifice, and transition to normal appendiceal mucosa is discernible on inspection of the appendiceal lumen) (21.9%) and 3 type 1 lesions (reaches border of the appendix orifice) (9.4%). Median diameter of the specimen was 35 mm (10-110mm) and median resection duration was 47 min (10-230 min). En bloc resection was achieved in all cases exclusively with DCT-ESD. Histology confirmed R0 resection in 29 cases (90.6%) and R1 in 3 cases but only with lateral contact with low grade dysplasia. Finally, 11 perforations occurred per-procedure and were all immediately closed with clips. In post-operation, 3 patients (10.7%) underwent delayed surgery without stomia for remaining leakage in 2 cases for complications related and in 1 case for incomplete resection. No death occurred.

Conclusion: DCT-ESD is effective and safe for resection of lesion developed into appendiceal orifice. Most procedures allowed En Bloc curative resection by endoscopic means only avoiding surgery in 90.6% of cases.

Disclosure: Nothing to disclose

P1567 LONG-TERM OUTCOMES OF ENDOSCOPIC RESECTION FOR T1 COLORECTAL CANCER

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Introduction: Endoscopic resection allows treating intramucosal colorectal cancer with a low morbidity and no mortality. However, lymph node involvement is found in about 10% of submucosal colorectal carcinomas, indicating additional surgical resection. According to the Japanese (JSCCR) and European (ESGE) guidelines, the presence of a deep submucosal infiltration (beyond 1000µm), poor differentiation, lympho-vascular invasion, or grade 2-3 tumor budding should lead to complementary surgery. The aim of this study was to assess the safety and long-term outcome of endoscopic resection for T1 colorectal carcinoma in a Western population.

Aims & Methods: We conducted a retrospective study, from a prospectively collected database including all patients with endoscopic mucosal resection or endoscopic submucosal dissection performed at a single French tertiary referral center. We included 68 consecutive patients with T1 colorectal cancer between February 2014 and May 2018. All patients were discussed in a dedicated multidisciplinary meeting for superficial gastrointestinal cancers.

We collected demographic data, procedural histological data and follow-up data in order to determine the local and distant recurrence rates and overall, progression free and cancer specific survival.

Results: The mean age of the population was 71.5 +/- 11.8. 44/68 (64.7%) lesions were in the colon and 24/68 (35.3%) in the rectum. 14/68 (20.6%) lesions were pedunculated. 26/68 (38,2%) patients had an endoscopic mucosal resection (EMR), 22/68 (32.4%) an endoscopic submucosal dissection (ESD), 8/68 (11.8%) a hybrid technique, 7/68 (10.3%) a conventional polypectomy and 5/68 (7.4%) a full-thickness resection using a dedicated device (FTRD). En bloc resection rate was 49/68 (72.1%), histologically resection rate was 45/68 (66.2%) and curative resection rate was 11/68 (16.2%). Overall, 49/68 (72.1%) patients had an indication for complementary surgery.

However, only 29/68 (42.6%) actually underwent the surgery: eight were lost to follow-up, seven declined surgery and five were not fit for the surgical procedure. Among the patients who underwent surgery, 6/29 (20.7%) actually had lymph node metastases. The median follow-up was 32 months (15-41 months). Nine patients were lost to follow-up. During follow-up, 3/59 (5.1%) patients had cancer relapse: one patient developed a metachronous colorectal cancer with distant metastases, one patient developed distant metastases after declining complementary surgery, and one patient developed lymph node metastasis although the initial endoscopic resection was thought to be curative, and was ultimately treated with chemoradiotherapy and then surgery. 3/59 (5.1%) patients died, one from a distant metastatic relapse of his colorectal cancer and the two others from non cancer related other causes.

Finally, among the 59 patients followed after endoscopic resection for T1 colorectal cancer, 8 (13.4%) were metastatic: 6 (10.2%) had lymph node metastasis on the surgical specimen and 2 (3.4%) developed distant metastases during follow-up.

Conclusion: Our data support the validity of the JSCCR guidelines in a French monocentric cohort with long-term follow-up: endoscopic resection of T1 colorectal cancer can be considered safe and curative in the vast majority of cases. Given the high proportion of surgical specimens free of lymph node metastases, additional criteria to assess the risk of lymph node involvement associated with early colorectal cancer are needed.

References: 1) Ueno H, Mochizuki H, Hashiguchi Y, Shimazaki H, Aida S, Hase K, Matsukuma S, Kanai T, Kurihara H, Ozawa K, Yoshimura K, Bekku S: Risk factors for an adverse outcome in early invasive colorectal carcinoma. Gastroenterology 2004; 127: 385-394. 2) Watanabe, Toshiaki, Kei Muro, Yoichi Ajioka, Yojiro Hashiguchi, Yoshinori Ito, Yutaka Saito, Tetsuya Hamaguchi, et al. « Japanese Society for Cancer of the Colon and Rectum (JSCCR) Guidelines 2016 for the Treatment of Colorectal Cancer ». International Journal of Clinical Oncology 23, nº 1 (february 2018): 1-34.

Disclosure: Nothing to disclose

P1568 BIOPOTENTIALS FOR CLINICIAN SATISFACTION WITH SEDATION IN COLONOSCOPY

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Introduction: Nurse-administered propofol sedation (NAPS) with intermittent bolus applications has become the standard procedure for colonoscopy in Germany. Although patient satisfaction with this method is high, little about the satisfaction of the examiner and factors that might negatively influence this satisfaction are available.

Aims & Methods: In this ongoing study we hypothesized that the number of movements or paralinguistic noises during sedation correlate with lower overall scores in the Clinician Satisfaction with Sedation Instrument (CSSI). Further we aimed to measure different biopotentials of the patient in order to accurately identify movements and paralinguistic noises that result in administration of sedating drugs.

Consecutive patients scheduled for a colonoscopy or sigmoidoscopy were prospectively enrolled. Biopotentials including electromyography of different facial muscles, skin conductance level and body temperature were obtained during the procedure. Additionally, events like movements, paralinguistic noises, dosages of sedatives were recorded with the corresponding event time. Clinician Satisfaction with Sedation Instrument (CSSI) was filled out by the examiner after the procedure. Correlation between the number of movements and paralinguistic noises and the global values of CSSI were calculated. Additionally, biopotentials were evaluated for their relationship with the recorded events. ClinicalTrials.gov number: NCT03860779.

Results: 94 patients were enrolled. Biopotentials were available for 76 patients. Mean global satisfaction with the sedation was 84 (95% CI; 81-88) of 100 points. Combined events of movements and paralinguistic noises were mean 7 (95% CI; 6-9) per examination. Lower global satisfaction with the sedation values significantly correlated with higher values of movements and paralinguistic noises (p< 0.001). Skin conductance level was available for 71 patients. Changes in the conductance level show a first relationship between body movements, paralinguistic noises and the application of sedatives in 53 (75%) examinations.

Conclusion: In this ongoing trial we were able to present that movements and paralinguistic noises of the patient during colonoscopy are associated with a lower satisfaction with the sedation using the CSSI. Simultaneously measured biopotentials - in combination with machine learning algorithm - might help to overcome this problem by helping to identify the right timing for the application of sedatives.

Disclosure: Nothing to disclose

P1569 IMPROVED BI-MANUAL ENDOSCOPIC RESECTION USING A CUSTOMIZABLE MANIPULATOR SYSTEM DESIGNED AS AN OVERTUBE FOR STANDARD ENDOSCOPES

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Introduction: Endoscopic submucosal dissection (ESD) can be considered for en-bloc resection of early cancers in the gastrointestinal tract. A major drawback of the current technique is its inability to perform bimanual tasks. We have recently designed and evaluated a 3D-printed platform that was successfully tested in the living pig model (Zizer et al., Endoscopy 2015). Nevertheless, we also experienced that complex procedures in an angulated position might be difficult to perform using such a system.

Aims & Methods: On the basis of an automated design process for the flexible manipulator structures as well as additive manufacturing by means of selective laser sintering the overtube manipulator system for ESD was further modified. Several subtypes were printed that included a single- and dual-arm version, as well as a version for pediatric scopes and standard gastroscopes, respectively. Furthermore, manipulators were either small or long.

Focus of the study was to evaluate the feasibility of endoscopic submucosal resection with the new systems. ESD was performed in a porcine ex-vivo model. 30mm lesion in size were resected located in the upper and lower GI tract (corpus, antrum; cecum, rectum).

Results: In total, 24 ESD's were performed (6 antrum, 6 corpus in inversion, 6 cecum, 6 rectum) with one-arm and two-arm manipulators or small (⌀ 5mm) or standard scopes (⌀ 10mm), respectively. ESD was feasible in 13 cases. Mean procedure time (min±SD) for ESD was 17.5(±7.1) for the corpus, 19.2(±8.5) for antral lesions, 20.5(±12.3) for the rectum, and 30.1(±8.5) for the cecum. Pediatric scope manipulators were too frail for sufficient resection working in inversion and for lesions located in the cecum. Resection was also impaired in the corpus and rectum using longer sized manipulator-arm systems. Single-arm manipulator equipped standard endoscopes offered best results in optimal traction-countertraction during ESD for all locations. ESD was feasible in all those 4/4 cases. Mean procedure time was rather short with 16.5(±4.6).

Conclusion: Based on our preliminary date we conlude that ESD is feasible using a customizable manipulator system designed for standard endoscopes with a monolithic design in an ex-vivo model. A single-arm manipulator system attached onto a standard gastroscope appears to offer the optimum utilization of traction and counter traction during endoscopic resection even in difficult locations.

Disclosure: Nothing to disclose

P1570 CONSULTANT TRIAGE ALONE AND COMBINED CONSULTANT AND ENDOSCOPY NURSE TRIAGE SIGNIFICANTLY REDUCE INAPPROPRIATE ENDOSCOPIES ESPECIALLY URGENT P1 REFERRALS

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Introduction: The Irish public endoscopy service is facing unprecedented pressure in terms of a huge increase in endoscopy referrals over the past 10 years with currently over 20,000 patients on the Inpatient/Daycase National GI Endoscopy waiting list. Despite established referral guidelines many patients are referred inappropriately from both primary and secondary care for urgent and non-urgent endoscopies with high non-attendance and cancellation rates. There is a lack of data assessing the impact of consultant triage and endoscopy nurse triage on endoscopy referrals.

Aims & Methods: To prospectively compare the effect of consultant triage alone (which is relatively less labour intensive) with combined consultant and endoscopy nurse triage (which is relatively more labour intensive) on endoscopy referrals to our endoscopy unit.

Methods: All endoscopy referrals including GP letters, direct access and Surgical, Medical and ED referrals received over a 28 day period in February 2019 were included in this prospective study. Referrals were stratified pre-triage into urgent/priority 1 (P1) within 4 weeks, non-urgent/priority 2 (P2) within 3 months and surveillance groups before being triaged by 4 GI consultants based on established HIQA and BSG endoscopy referral guidelines. Any referrals with missing data, alarm symptoms, prior endoscopy/histology data were subsequently validated by telephone triage by our Endoscopy Triage Nurse. Outcomes were compared between pre-triage, consultant triage and combined consultant and endoscopy nurse triage. Statistical analysis was performed using student *Chi Square* test.

Results: Out of 312 endoscopy referrals during the study period, 12 patients were excluded as they had already undergone consultant triage. Of the 300 patients enrolled (median age 50, range 17-88, M:F 150:150). 142 (47%) were directly referred from their GP, 101 (34%) from the Surgical department, 31 (10.4%) from other Medical departments and 26 (8%) from the Emergency Department. Prior to triage 159 patients were referred for urgent P1 endoscopy, 125 for non-urgent P2 endoscopy and 16 for surveillance endoscopy. Consultant triage alone reduced P1 endoscopies by 16% from 159 to 133 (p=0.02) and combined consultant and endoscopy nurse triage reduced P1 endoscopies by a total of 30% to 112 (p=0.0003). Consultant triage increased overall P2 endoscopies marginally from 125 to 129 and subsequently to 124 after endoscopy nurse triage (P=0.5(nonsignificant). Consultant triage alone reduced all endoscopy referrals by 11% (p< 0.05) redirecting referrals to HP testing/OPD/GP follow-up/CT colonography while combined consultant and endoscopy nurse triage reduced all endoscopy referrals by 21% (p=0.01).

Conclusion: Consultant triage alone significantly reduced 16% of urgent endoscopy referrals and 11% of all endoscopy referrals while combined consultant and endoscopy nurse triage significantly reduced 30% of urgent endoscopy referrals and 21% of all endoscopy referrals. Both consultant triage alone and combined consultant and endoscopy nurse triage can achieve significant reductions and cost savings in endoscopy referrals.

Disclosure: Nothing to disclose

P1571 LESION MORPHOLOGY AND TOPOGRAPHY INFLUENCE THE PREDICTION AND MISS RATES OF SUBMUCOSAL INVASIVE CANCER IN COLORECTAL LATERALLY SPREADING LESIONS

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Introduction: The majority of large (≥ 20mm) colorectal laterally spreading lesions (LSLs) are benign and can be effectively managed by piecemeal endoscopic mucosal resection (EMR). However, a subgroup harbor submucosal invasive cancer (SMIC) and require en bloc resection by an alternative resection technique. Accurately predicting SMIC by optical evaluation is critical to inform therapeutic decisions. It is unknown whether LSL morphology, specifically nodular versus flat morphology, and LSL topography influence the performance of SMIC prediction.

Aims & Methods: Colorectal LSLs ≥ 20mm referred for endoscopic resection, within a prospective multi-center observational cohort, were considered for inclusion. As per protocol, optical evaluation was performed prior to endoscopic resection and included lesion morphology (Paris classification), topography (granular, non-granular, mixed), surface pit pattern and surface vascular pattern characterization. SMIC prediction was based on the identification of established surface pit pattern and vascular pattern features consistent with invasive neoplasia. Rigid/fixed/non-lifting lesions and those with a Paris 0-IIc component were excluded, as these features are strongly associated with SMIC and are established predictors of it.

Sensitivity, specificity, accuracy* and miss rates were calculated for SMIC prediction with histology as the reference gold standard. Outcomes were then stratified by nodular (Paris 0-Is and 0-IIa+Is) versus flat (Paris 0-IIa and 0-IIb) morphology and topography

*Accuracy = correctly predicted lesions for histology (including SMIC and non-SMIC) divided by total number of lesions.

Results: From July 2013 - March 2019, 1808 colorectal LSLs were identified. 258 serrated lesions, 39 rigid/fixed/non-lifting lesions, and 79 lesions with a Paris 0-IIc component were excluded from analysis. Of the remaining 1432 LSLs (mean size 37.2m; range 20-120; 665 nodular, 767 flat), SMIC was identified in 92 (6.4%). Overall sensitivity, specificity, and accuracy of SMIC prediction were 43.5% (95% CI 33.7%-53.7%), 98.4 (95% CI 97.6%-98.9%) and 94.8% (95% CI 93.5%-95.8%), respectively.

Sensitivity decreased when comparing nodular LSLs (37.5%; 95% CI 25.9%-50.0%) vs. flat LSLs (57.1%; 95% CI 37.4%-74.9%) and non-granular LSLs (58.6%; 95% CI 40.6%-75.0%) vs. granular LSLs (32.6%; 95% CI 20.4%-46.9%). The overall miss rate was 3.6%. This was significantly higher amongst nodular vs. flat LSLs (6.4% vs. 1.6%; p< 0.001) with flat granular LSLs having the lowest SMIC miss rate (0.7%; 95% CI 0.2-1.9) amongst all LSL sub-populations.

Variable	Nodular Lesions % (95% CI)	Flat Lesions % (95% CI)	P-value
Sensitivity All Lesions	37.5 (25.9-50.0)	57.1 (37.4-74.9)	
Sensitivity Granular	30.0 (17.6-45.2)	50.0 (16.7-83.3)	
Sensitivity Non-Granular	55.6 (25.4-82.7)	60 (38.4-78.9)	
Sensitivity Mixed	46.7 (23.9-70.6)	50 (6.1%-93.9)	
Specificity All Lesions	97.3 (95.6-98.4)	99.0 (97.9-99.5)	
Specificity Granular	98.1 (96.5-99.0)	100	
Specificity Non-Granular	94.3 (88.0-97.8)	97.5 (95.2-98.9)	
Specificity Mixed	95.3 (85.9-99.0)	100	
Accuracy	91.6 (89.3-93.5)	97.5 (96.2-98.5)	< 0.001
SMIC Missed	6.4 (4.4-8.0)	1.6 (0.9%-2.8%)	< 0.001

[Submucosal Invasive Cancer Prediction Performance and Miss Rates]

Conclusion: The sensitivity of predicting SMIC by pit pattern and vascular pattern is limited in large colorectal LSLs, specifically nodular lesions. Given their SMIC miss rate, nodular LSLs, in the absence of concerning features on optical biopsy, require further risk stratification to accurately

identify optimal candidates for en bloc resection techniques. Alternatively, flat granular lesions, in the absence of optical features of SMIC, need only be removed by EMR.

Disclosure: Nothing to disclose

P1572 A DEDICATED 12 MONTH COMPETENCY-BASED TRAINING PROGRAMME IN ENDOSCOPIC MUCOSAL RESECTION ALLOWS SAFE AND EFFECTIVE RESECTION OF COMPLEX LATERALLY SPREADING LESIONS

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Introduction: No formal training pathways for endoscopic mucosal resection (EMR) currently exist and training is often ad-hoc and sporadic. As such many endoscopists practice EMR without formal training. This may contribute to incomplete polyp resection and referral of large benign colorectal neoplasia to surgery. We aimed to investigate the impact of a dedicated 12-month EMR training program on trainee competency.

Aims & Methods: Prospective data, relating to technical aspects of EMR and outcomes, was collected from consecutive directly-supervised procedures commenced by five trainees over a 12-month period at a tertiary endoscopic resection centre. All trainees had achieved appropriate competency in colonoscopy (at least 200 independent procedures prior to their training year of which at least 50 procedures involved diminutive polypectomy) and undertook a four-week observation period prior to starting cases. Data was analysed in two cohorts divided by procedures performed in the first or second six months of their training period.

Results: Five trainees (median age - 31yrs) performed 98 EMRs in 98 patients over 12 months. Median lesion size in the first half was 30mm (interquartile range [IQR] 25-40) and 35mm (IQR 25-50) in the second. The complexity of LSL increased in the second half of the cohort [SMSA 4 LSL 2nd half vs 1st half, 47.2% (26/55) vs. 32.5% (14/43)]. Other important lesion characteristics did not vary between the halves of the cohort.

The ability to competently perform dynamic submucosal injection and specimen retrieval after EMR was significantly more likely in the second six months of training as compared to the first (86.8% vs 54.8%, p=0.001 and 88.9% vs 60.5%, p=0.002 respectively).

Trainees were significantly more likely to independently complete greater than 50% of the EMR procedure in the second six months of their training as compared to first (81.8% vs 51.2%, p= 0.001, OR - 4.3 (1.7-10.7], p= 0.002). The need for consultant intervention was also significantly less likely in the second half of the training period (62.8% vs 40%, p=0.004).

Despite the involvement of a trainee and the complexity of the lesions attempted the overall technical success was 96.9% and not statistically different between the two cohorts. There was also no significant difference in the rate of adverse events including bleeding and deep mural injury (see Table 1).

Table 1	First Half	Second Half	Total	p	OR (95% CI) 1st vs 2nd Half	p
Median Size, mm (IQR)	30 (25-40)	35 (25-50)				
SMSA Level 2/3/4	13/16/14	12/17/26	25/33/40	0.33		
SMSA-EMR Level: Low Risk/ High Risk	15/28	25/30	40/58	0.30		
Dynamic submucosal injection	17 (54.8)	46 (86.8)	63	0.001	5.6 (1.7-18.0)	0.005
Percentage of resection performed independently <50% v. >50%	21 (48.4) vs. 22 (51.2)	10 (18.2) vs. 45 (81.8)	31 vs. 67	0.001	4.3 (1.7-10.7)	0.002
Consultant takeover	27 (62.8)	22 (40)	63	0.04	2.53 (1.1-5.8)	0.03
Technical success (%)	41 (95.3%)	54 (98.2%)	95 (96.9)	0.42		
CSPEB	3	7	10	0.35		
Total	43	55	98			

[Lesion Characteristics, Trainee and Procedure Outcomes; CSPEB - clinically significant endoscopic bleeding, SMSA - size, morphology, site and access]

Conclusion: Endoscopists competent in diminutive polypectomy can be trained to perform EMR of complex colorectal lesions safely and without detriment to overall outcomes. Key aspects of this programme include a focussed, intensive period of training (>6 months) with competency-based teaching and introduction of sequentially more complex lesions (identified using the SMSA score [1]).

This study may provide a foundation for the development of a structured, competency based training program for endoscopists learning advanced tissue resection.

References: [1] Sidhu M, Tate DJ, Desomer L, Brown G, Hourigan LF, Lee EYT, Moss A, Raftopoulos S, Singh R, Williams SJ, Zanati S, Burgess N, Bourke MJ. The size, morphology, site, and access score predicts critical outcomes of endoscopic mucosal resection in the colon. Endoscopy. 2018 Jul;50(7):684-692. doi: 10.1055/s-0043-124081. Epub 2018 Jan 25. Erratum in: Endoscopy. 2018 Jul;50(7):C7. PubMed PMID: 29370584.

Disclosure: Nothing to disclose

P1573 ENDOSCOPIC MUCOSAL RESECTION IS AN EFFECTIVE AND DEFINITIVE THERAPY FOR LATERALLY SPREADING LESIONS AT THE ANORECTAL JUNCTION

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Introduction: Large (≥ 20mm) laterally spreading lesions (LSLs) at the anorectal junction are most commonly referred for surgery due to the unique anatomical, sensory and physiological characteristics of this area. More recently, it has been argued that these lesions, if treated endoscopically, should be managed by endoscopic submucosal dissection (ESD) or transanal endoscopic microsurgery (TEM). Endoscopic mucosal resection (EMR) is well established as a definitive therapy for colorectal LSLs, however, it is unknown whether it is an effective and durable treatment for LSLs at the ARJ (ARJ-LSLs).

Aims & Methods: We evaluated the technical success, short-term and long-term outcomes of EMR for ARJ-LSLs (defined as distal margin either crossing or within 20mm of the dentate line) in comparison to rectal LSLs within a prospective multi-center observational cohort of LSLs ≥ 20mm.

Technical success was defined as complete removal of all neoplastic tissue during index EMR. Safety was evaluated by the frequency of intra-procedural bleeding, deep mural injury, delayed bleeding and perforation. Long-term efficacy was defined by the absence of either endoscopic or histological recurrence at surveillance colonoscopy (SC) at recommended intervals of 6, 12, 36 and 60 months (SC1 - SC4, respectively).

Results: Between July 2008 - April 2019, 109 ARJ-LSLs and 351 rectal LSLs were considered for endoscopic resection. Twenty (5 ARJ, 15 rectal) LSLs had endoscopic features consistent with deep submucosal invasive cancer (SMIC) and were referred directly to surgery.

One rectal lesion had a concomitant sigmoid cancer and went to surgery. Recently, 39 (18 ARJ, 21 rectal) LSLs were enrolled in a selective ESD protocol and were excluded from analysis. The remaining 86 ARJ-LSLs (mean size 48.3mm, range 20 - 100mm) were removed by EMR. Technical success was 97.7%. SMIC was present in 3 (3.5%) lesions.

The frequency of recurrence was 14.9%, 4.7%, 5.3% and 0.0% at SC1-SC4 and surgery was avoided in all. Amongst 24 ARJ-LSLs which underwent margin snare-tip soft coagulation (STSC) to mitigate the risk of recurrence, no recurrence was identified at SC1 (0.0% vs. 23.3%; p=0.01), nor at SC2 - SC4. The frequencies of technical success, adverse events and recurrence were not different between ARJ-LSLs and rectal LSLs.

Conclusion: EMR is a safe, efficient, effective and durable therapy for ARJ-LSLs. EMR should be considered as the primary therapeutic modality for the majority of these lesions.

Disclosure: Nothing to disclose

Variable	ARJ-LSLs n=86(%)	Rectal LSLs n=314(%)	p-value
Mean Age (SD) (years)	64.3 (12.3)	65.7 (12.4)	
Male Sex	46 (54.8%)	170 (54.7%)	
Mean size (range) (mm)	48.3 (20 - 100)	43.3 (20 - 120)	
Cancer	3 (3.5%)	38 (12.1%)	
Successful Resection	84 (97.7%)	305 (97.1%)	0.786
Intra-Procedural Bleeding	10 (11.6%)	18 (5.7%)	0.058
Intra-Procedural Perforation	0 (0%)	2 (0.6%)	0.458
Delayed Bleeding	9 (10.7%)	24 (7.7%)	0.369
Delayed Perforation	0 (0.0%)	1 (0.3%)	0.604
SC1 Completed/Eligible	67/75 (89.3%)	211/246 (85.8%)	
SC1 Recurrence	10 (14.9%)	35 (16.6%)	0.748
SC2 Completed/Eligible	43/66 (65.2%)	149/213 (70.0%)	
SC2 Recurrence	2 (4.7%)	10 (6.7%)	0.623
SC3 Completed/Eligible	19/39 (48.7%)	73/158 (46.2%)	
SC3 Recurrence	1 (5.3%)	1 (1.4%)	0.300
SC4 Completed/Eligible	5/9 (55.6%)	17/35 (48.6%)	
SC4 Recurrence	0 (0.0%)	0 (0.0%)	NA

[Patient/Lesion Characteristics and EMR Outcomes of ARJ-LSLs vs. Rectal LSLs]

P1574 MULTICENTER STUDY OF LINKED COLOR IMAGING FOR IMPROVING THE VISIBILITY OF FLAT COLORECTAL POLYPS BY ENDOSCOPISTS AND COLOR DIFFERENCE VALUES

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Introduction: Linked color imaging (LCI) is one of image-enhanced endoscopies and can visualize gastrointestinal lesions better. We previously reported that LCI improved the visibility of various colorectal lesions including diminutive polyps and sessile serrated adenoma and polyps (SSA/P) using videos and pictures [1,2].
In this study, we analyzed the efficacy of LCI for improving flat polyp's visibility in various situations including fast-withdrawal or large-monitor observation utilizing endoscopist's visibility scoring and color difference (CD) value in a multicenter study.
Aims & Methods: We recorded videos of flat polyps 2-20 mm in white light imaging (WLI), blue laser imaging-bright (BLI-b), and LCI from July 2017 to December 2017 according to inclusion criteria. All videos were evaluated by 8 endoscopists according to a published polyp visibility score from four (excellent) to one (poor). Additionally, 1.5-times-faster videos and 1.7-times-larger-sized videos were also evaluated. Moreover, we calculated color difference (CD) value in three modes between each polyp and surrounding mucosa.
Results: The mean scores of LCI (3.11±0.95) were significantly higher than WLI (2.55±1.04, p< 0.001), and were not significantly higher than BLI-b. With respect to right-sided location, < 10mm size, and serrated lesions, the scores of LCI were significantly higher than WLI. Additionally, the scores of faster videos were significantly lower than normal videos in each mode. The scores of faster videos in LCI (3.0±1.1) were also significantly higher than WLI (2.0±1.0, p< 0.001) and BLI-b (2.8±1.1, p=0.03). The scores of larger-sized videos weren't significantly higher than normal monitor's videos in each mode. The CD value of LCI was significantly higher than WLI (18.0±7.7 vs. 11.7±7.0, p< 0.001) and BLI-b (15.8±9.6, p=0.04).
Conclusion: Our study showed that LCI significantly improved visibility of colorectal polyps in various situations such as faster withdrawal or a larger-sized monitor observation with multicenter study. Moreover, we proved LCI's increase of objective CD value as an objective indicator for polyp vis-

ibility compared to WLI and BLI-b. According to these results, we thought LCI is promising for polyp detection. Prospective randomized control studies are expected in the future for proving this hypothesis.
References: 1. Yoshida N, Naito Y, Murakami T, et al. Linked color imaging improves the visibility of colorectal polyps: a video study. Endosc Int Open 2017; 5: E518-525 2. Yoshida N, Naito Y, Yasuda R, et al. Linked color imaging improves the visibility of various featured colorectal polyps in an endoscopist's visibility and color difference value. Int J Colorectal Dis 2017; 32: 1253-1260
Disclosure: This study was performed by a research fund from Fujifilm (J162001222). Yoshito Itoh is affiliation with a donation-funded department from FUJIFILM Medical Co. Ltd. Naohisa Yoshida received a research grant from Fujifilm Co. The other authors have no conflicts of interest to declare.

P1575 EFFECTIVENESS OF AN INJECTABLE, POLY(AMIDOAMINE) S BASED HYDROGEL AS SUBMUCOSAL LIFTING AGENT IN COLONIC ESD: IN-VIVO ANIMAL STUDY

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Introduction: Endoscopic submucosal dissection (ESD) is a well- established technique that allows for en bloc removal of superficial gastro-intestinal cancer. To improve the efficacy, safety of endoscopic submucosal dissection techniques the quality and duration of the submucosal lift is key. Currently available agents are not satisfactory. The objective of this study is to assess the safety and efficacy of an injectable, poly(amidoamine)s based hydrogel to lift the submucosa in comparison with standard lifting solution for colorectal ESD in an in vivo porcine study.
Aims & Methods: Prior to ESD proper preparation of the colon was carried out.
ESD of similar size (2x2cm) were performed in the colon 20 to 30cm from the anal verge by an experienced endoscopist. Two types of solutions were used for submucosal lifting: saline solution in the control group and hydrogel. Procedure time, dissection speed, and complications were recorded and compared between the two groups.
Results: 22 procedures were performed in the colorectum of thirteen pigs (10 ESDs in control group and 12 ESDs in hydrogel ESD group). Effective procedure times were 2744 seconds in control group and 1496 seconds in hydrogel ESD group. In the hydrogel ESD group the dissection speed improved significantly after the first five cases (26.77 mm²/min in first five cases vs 49.88 mm²/min in later seven cases) and the mean dissection speed in last seven cases was significantly faster than that in control group (49.83 mm²/min vs 29.13 mm²/min, p=0.019). Perforation occurred in 3 cases in the control group and in 1 case in the hydrogel ESD group.
Conclusion: The use of poly(amidoamine)s based hydrogel as a lifting agent significantly improved dissection speed compared to standard saline solution in colorectal ESD. Further randomized studies should confirm the lower rate of perforation observed in the hydrogel group.
Disclosure: Nothing to disclose

P1576 ENDOCYTOSCOPY-LIKE MAXIMUM-MAGNIFYING EVALUATION WITH CMOS LASER ENDOSCOPY FOR COLORECTAL LESIONS IS CLINICALLY USEFUL

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Introduction: As an endoscopic diagnosis of neoplastic lesions of the colon and rectum, an endoscope capable of ultra-magnifying 520 times has been put on the market and is spreading. Developed by Kudo et al., this is

an extremely excellent and epoch-making endoscope system that allows real-time observation similar to microscopic HE staining by contacting a lens of a colonoscope with a lesion after staining the lesion with methylene blue and crystal violet.

However, the endoscope is limited in that it is a little expensive, that it is used by a system made by Olympus, and that it requires a little techniques to be contacted and observed.

Therefore, we examined how close the conventional magnifying endoscope can be to the above-mentioned super-magnifying endoscope Endocytoscope even by non-contact observation, and how much Endocyte-like evaluation can be observed with the widely marketed and widespread endoscope with laser light source, which is equipped with CMOS image center manufactured by FujiFilm Co., optical 135 times, electronic 270 times magnification.

Aims & Methods: From March 2018 to December 2018, we studied 40 cases in which colorectal lesions were observed on Endocyte and CMOS laser source endoscopy at our hospital.

The Endocyte system used Olympus's CF-H 290 ECI endoscope and EVIS Elite 290 light source system.

The CMOS laser source endoscope used the Fujifilm endoscope EC-L 600 ZP and the light source system LASEREO 4450.

When lesions were observed, they were compared by methylene blue-crystal violet staining with 520 fold magnification for CF-H 290 ECI and 270 fold magnification for EC-L 600 ZP.

In addition, the established EC classification at the end site was made the golden standard, and it was examined in comparison with EC1a, EC1b, EC2, EC3a, EC3b, pathology after the lesion cutting.

Observation with a CMOS laser endoscope at a maximum magnification of 270 times is classified into ECL, a classification similar to EC classification. Classified as (Meaning of EC-like classification or EC-Laser classification). As in the EC classification, ECL 1a, ECL 1b, ECL 2, ECL 3a, and ECL 3b were determined according to the shape of the gland lumen and the state of nuclear staining.

Results: The concordance rate between EC classification and ECL classification was 100% for EC1a and ECL 1a, 100% for EC1b and ECL 1b, 95% for EC2 and ECL 2, 95% for EC3a and ECL 3a, and 100% for EC3b and ECL 3b. However, the EC classification was superior in confidence and strength of diagnosis.

Conclusion: Endocytoscopy-like maximum-magnifying evaluation with CMOS laser endoscopy for colorectal lesions is clinically useful.

Endocytoscopy for colorectal neoplastic lesions is currently the highest point of magnification endoscopy, but equipment deployment is still slow. When CMOS LASER endoscopes, which are already in wide use to some extent, are used at the limits of specifications, it has been found that approximate results can be obtained to some extent.

Disclosure: Nothing to disclose

P1577 COMPARISON OF LONG TERM CLINICAL OUTCOMES BETWEEN COLD ENDOSCOPIC MUCOSAL RESECTION (C-EMR) AND COLD SNARE POLYPECTOMY (CSP) FOR COLORECTAL POLYP LESS THAN 15MM IN SIZE

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Introduction: Incomplete resection rate of small polyp was reported as 6.8% in the CARE study. Several methods of cold polypectomy including cold snare polypectomy (CSP) and cold endoscopic mucosal resection without electrocautery (C-EMR) have been used for routine polypectomy practice. The aim of this study was to assess the long-term efficacy and safety of CSP versus C-EMR for colorectal polyps less than 15 mm in size.

Aims & Methods: Total 472 patients underwent polypectomy with cold methods from July 2015 to December 2017. In this retrospective study, 112 patients who underwent surveillance colonoscopy after colon polypectomy with cold methods were included for analysis. Clinical parameters including recurrence, polyp size and shape, complication between two groups were compared.

Results: Total, 331 colorectal polyps were removed with CSP (n=148) or C-EMR (n=183) from 112 patients. Mean age was 60.9 ± 11.1 years old, and mean surveillance interval was 458.3 ± 237.3 days. Regarding polyp shape, pedunculated polyps (65.4% vs. 34.6%) and flat polyps (69.9% vs. 30.1%)

were tended to resected by C-EMR more frequently than CSP (p=0.053). Mean size was larger in C-EMR group (8.46 ± 1.97 mm) than CSP (6.80 ± 1.21 mm) group (p< 0.001). In histology, 92.3% (12/13) of sessile serrated adenoma and two high-grade dysplasias were removed by C-EMR method. Recurrence rates were 6.1% (9/148) in CSP group, and 2.2% (4/183) in C-EMR group, respectively (p=0.070). Regarding complication, immediate bleeding was 4.4% (8/183) in C-EMR group and 2.0% (3/148) in CSP group (p=0.237), and delayed bleeding was occurred in one patient after C-EMR (0.5%).

Conclusion: Both cold methods were feasible in terms of recurrence rate and safety. C-EMR was performed more in the flat or pedunculated polyps, and larger sized polyp than CSP method with relatively lower recurrence rate. Further large-scaled prospective study with long-term surveillance is required.

Disclosure: Nothing to disclose

P1578 BODY MASS INDEX AND THE RISK OF COLONIC POLYPS

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Introduction: Colorectal cancer (CRC) screening is associated with a decreased incidence and mortality from CRC. However, patient adherence to screening is less than desirable and resources are limited even in developed countries. Better identification of individuals at a higher risk could result in improved screening efforts. Some studies suggest that body mass index (BMI) could be associated with higher frequency of colonic polyps and consequently CRC [1]. *The aim* of this study is to assess whether there is a relationship between BMI and the presence of colonic polyps.

Aims & Methods: A retrospective study was performed including 424 patients whom underwent colonoscopy for various reasons between January 2018-December 2018 in a private endoscopy unit. BMI was calculated as weight/height^2 (kg/m^2). Normal weight was defined as BMI 18.5-24.9 kg/m^2, overweight 25 to 29.9 kg/m^2 and obesity > 30 kg/m^2. The frequency of polyps diagnosed at colonoscopy was assessed.

Results: From the 424 patients included in the study, 60%(256/424) female and 40%(168/424) male, mean age 53±12years, mean BMI 26.8±4.8 kg/m^2. Considering BMI, 33.2% (141/424) were normal, 38.6%(164/424) overweight and 28%(119/424) obese. 18% (77/424) patients presented colonic polyps: 13%(18/141) in the normal patients, 18%(29/164) in overweight patients and 25%(30/119) in obese patients, with significat difference between normal and overweight plus obese patients (*p*< 0.0001). Considering BMI>25 kg/m^2 as a threshold for the risk of developing colonic polyps, the risk was significantly higher for overweight and obese patients OR 1.79 CI 95% (1.01-3.18) *p*=0.043.

Conclusion: Subjects with BMI>25 have a significantly higher risk of association with colonic polyps, therefore, BMI as a measure of obesity can be a valuable and easy to use tool for optimizing screening methods.

References: 1.Theodore F. Shapero et al. Obesity Increases Prevalence of Colonic Adenomas at Screening Colonoscopy: A Canadian Community-Based Study. Can J Gastroenterol Hepatol. 2017; 2017: 8750967. Published online 2017 Jul 11. doi: 10.1155/2017/8750967

Disclosure: Nothing to disclose

P1579 DISEASE-FREE SURVIVAL AFTER WESTERN-BASED ENDOSCOPIC SUBMUCOSAL DISSECTION FOR COLORECTAL NEOPLASIA

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Introduction: In Asian countries, the safety and efficacy of endoscopic submucosal dissection (ESD) is well-established for the minimally invasive treatment of early colorectal cancer. Large retrospective studies have shown favorable long-term outcomes with a disease free survival of 94.6% and 92.1% at 3 and 5 years, respectively [1]. On the other hand, the role of ESD for colorectal lesions in Western communities is unclear. This may be attributed to the limited adoption of ESD in Western centers and disappointing technical outcomes in preliminary studies. In addition, the lack of long-term data for Western-based colorectal ESD generates uncertainty as to the clinical relevance of such a procedure.

Aims & Methods: The aim of this study is to assess the long-term outcomes of a large cohort of patients treated with colorectal ESD in a tertiary Western endoscopy centre. Between 2011 and 2018, a retrospective analysis of a prospectively maintained procedure database was conducted on patients treated by ESD for colorectal lesions at Humanitas Research Hospital in Milan, Italy. Both conventional ESD and hybrid-ESD cases were included. Short-term outcomes of interest were en-bloc, R0 and curative resection rates as well as the occurrence of adverse events. Long-term outcomes of interest were adenoma and carcinoma recurrence rates. Uni- and multi-variable logistic regressions were applied to identify factors associated resectional outcomes and adenoma recurrence.

Results: Over the study period, 244 consecutive patients with colorectal neoplasia underwent colorectal ESD. Conventional ESD was performed in 80.3% of cases. Overall, 189 (77.4%) lesions were adenomas and 55 (22.6%) were cancers (52 adenocarcinomas and 2 neuroendocrine and 1 squamous carcinoma). Rates of en bloc and R0 resection were 87.3% and 82.8%, respectively. On multivariate analysis, only hybrid-ESD technique was negatively related to en bloc resection (OR 0.02 vs standard ESD 95% CI: 0.01-0.08) yet for R0 resection only standard ESD technique (vs hybrid-ESD) was predictive (OR 4.61 95% CI: 1.41-18.58).

Nine perforations occurred: 7 (77.8%) were managed endoscopically; 2 (22.2%) required surgery. Intra- and post-procedural bleeding occurred in 9 (3.7%) and 1 (0.4%) patient(s), respectively; all cases were managed endoscopically. No ESD-related deaths occurred. In total, 39 patients underwent surgical consultation and/or subsequent resection due to non-curative ESD (37 patients) or adverse events (perforation in 2 patients). Thus, the follow-up analysis included 205 patients with a median follow-up of 2.9 years (range 0.5-8.0).

Adenoma recurrence was detected in 5 (2.6%) patients (3 at 6 months, 2 at 1 year and none at 3 or 5 years). The risk of recurrence was higher for patients in the piecemeal resection group than for those in the en-bloc resection group (p=0.05). The adenoma recurrence-free probability at 6 and 12 months from resection was 98.5% (95% CI: 97.0%-100.0%) and 97.4% (95% CI: 95.2%-99.7%), respectively. No carcinoma recurrences were observed.

Conclusion: Colorectal ESD is a safe and effective approach for managing advanced colorectal neoplasia. Furthermore, in expert hands, colorectal ESD can be performed in a Western setting with outcomes comparable to published Eastern series.

References: 1. Yamada M, Saito Y, Takamaru H, et al. Long-term clinical outcomes of endoscopic submucosal dissection for colorectal neoplasms in 423 cases: a retrospective study. Endoscopy. 2017 Jan 20. doi: 10.1055/s-0042-124366.

Disclosure: Nothing to disclose

P1580 DRUG DELIVERY THROUGH COLONIC TRANSENDOSCOPIC ENTERAL TUBING: A REAL WORLD STUDY AND MULTIFACTORIAL ANALYSIS

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Introduction: Colonic transendoscopic enteral tubing (TET) as a new colonic interventional method has been frequently used for complete delivery of fecal microbiota transplantations (FMTs) or whole-colon administration of drugs.

Aims & Methods: To evaluate the possible factors affecting methodology, feasibility and safety of colonic TET. We prospectively recorded patients who underwent colonic TET for FMT or medications in our center from October 2014 to November 2018. The success rate, adverse events and patients' satisfaction, as well as the retaining time of TET tube were evaluated.

Results: Totally 224 patients were included for analysis in this real-world study. The success rate of TET procedure was 100% (224/224). The median retaining time of TET tube was 8.5 (IQR 7 - 11) days in 158 patients with the tube falling out naturally. These patients were divided into the short-retaining group (≤ 8.5 days) and the long-retaining group (> 8.5 days). Univariate and multivariate analysis demonstrated that titanium clip type (p = 0.001) was an independent influencing factor for the retaining time of tube. The number of large titanium clips with longer arms significantly affected the retaining time (p = 0.013). No severe adverse event was observed during and after TET.

	Titanium clip number	Frequency	TET retaining time	P-value
Small titanium clip	3	7	6 (4 - 7)	
	4	9	7 (6.5 - 7.5)	
	5	10	7.5 (5 - 10.5)	
	6	9	7 (5.5 - 9.5)	0.498
Large titanium clip	2	14	7.5 (6 - 11)	
	3	72	9 (7 - 11)	
	4	35	11 (8 - 12)	0.013

[Table 1. Correlation between the titanium clip number and TET retaining time.]

Conclusion: Colonic TET is a feasible, practical, and safe technique with a high degree of patients' satisfaction for multiple FMTs or frequent colonic medication administration. Generally, two to four large titanium clips are recommended to ensure the fixation of the TET tube onto the colonic wall and maintain it for 7-10 days.

Disclosure: Nothing to disclose

P1581 IS POOR BOWEL PREP EVER ACCEPTABLE AND WHAT IS THE EFFECT OF INDICATION FOR THE TEST?

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Introduction: Bowel preparation is recognised as a key quality indicator for colonoscopy. It correlates with the adenoma detection rate (ADR) and is used to guide subsequent surveillance period after a normal investigation. It is also a perennial bug bear of endoscopists, leading to prolonged as well as incomplete procedures. The Boston Bowel Preparation Scale (BBPS) is a commonly used metric for assessing bowel cleansing and a score of 6 is generally regarded as adequate. Evidence demonstrates that a score of 6 or higher is associated with a higher ADR and fewer missed polyps. However, few studies have addressed the relationship between a BBPS of less than 6 and the need for repeat colonoscopy by indication.

The aim of this study was to evaluate association between indication for colonoscopy and the perceived need of repeat colonoscopy in the setting of poor bowel preparation.

Aims & Methods: Endoscopists of varying experiences and grades were invited to take part in the study during a regional endoscopy research meeting. All participants were shown videos of approximately 1 minute duration which demonstrated bowel preparation quality in 3 segments of the bowel; right, transverse and left. They were informed that no abnormalities were seen, and were asked to grade the bowel preparation on a dichotomous scale of "adequate for indication" or "inadequate, requiring repeat colonoscopy". All participants also documented their colonoscopy experience and whether they were bowel cancer screening programme (BCSP) accredited.

Indications are detailed in the table. 2 videos were presented per indication in a random order, each with a BBPS of between 3 and 5.

Chi squared tests were used to assess differences.

Results: 19 endoscopists participated. 18 of whom graded 10 videos and 1 who graded 5 videos. 8 were consultants, 7 registrars, 2 fellows and 2 were nurses. 4 of the consultants were BCSP accredited. Overall 42.2% of cases were recorded as inadequate, requiring a rescope. The number of cases which the reviewers felt were inadequate ranged from 0/10 to 7/10 with a median of 4/10 and interquartile range of 3 to 5. 11.1% of the scores for case 1 were graded as inadequate, compared with 49.0% for all the other cases combined (p< 0.0001). No other indication reached statistical significance. The mean number of inadequate cases rated by BCSP accredited endoscopists was 4.75, compared with 3.93 in the non BCSP group (p=0.35). There was no significant difference between consultants, registrars and nurses.

Conclusion: All of the videos were chosen to demonstrate bowel preparation which was inadequate, as defined by the BBPS < 6. However, only 42% of examinations were considered sufficiently poor to require a rescope. Furthermore there is a considerable variation between endoscopists as to whether a patient required a rescope. The indication for colonoscopy, however, had little influence on judgement of the adequacy of bowel preparation, other than a young patient with possible inflammatory bowel disease, whose suboptimal prep was accepted by most.

These results suggest that suboptimal bowel preparation as defined by a BBPS < 6 is often accepted in clinical practice.

Case	Indication
1	18 year old female with a history of diarrhoea and a family history of ulcerative colitis
2	62 year old male patient with positive faecal occult blood in BCSP
3	74 year old female with rectal bleeding mixed with stool
4	60 year old male with 3 small polyps at index colonoscopy 3 years ago
5	80 year old male patient with iron deficiency anaemia

[Indications for cases]

References: 1. Kaminski MF, Wieszczy P, Rupinski M, Wojciechowska U, Didkowska J, Kraszewska E, et al. Increased Rate of Adenoma Detection Associates With Reduced Risk of Colorectal Cancer and Death. Gastroenterology. 2017;153(1):98-105. 2. Lai EJ, Calderwood AH, Doros G, Fix OK, Jacobson BC. The Boston bowel preparation scale: a valid and reliable instrument for colonoscopy-oriented research. Gastrointest Endosc. 2009;69(3 Pt 2):620-5. 3. Sulz MC, Kröger A, Prakash M, Manser CN, Heinrich H, Misselwitz B. Meta-Analysis of the Effect of Bowel Preparation on Adenoma Detection: Early Adenomas Affected Stronger than Advanced Adenomas. PLoS One. 2016;11(6):e0154149. 4. Clark BT, Protiva P, Nagar A, Imaeda A, Ciarleglio MM, Deng Y, et al. Quantification of Adequate Bowel Preparation for Screening or Surveillance Colonoscopy in Men. Gastroenterology. 2016;150(2):396-405; quiz e14-5.

Disclosure: Nothing to disclose

P1582 THE EFFECT OF CASEMIX ON POLYP DETECTION RATE AND CECUM INTUBATION RATE

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Introduction: Established markers of good colonoscopy quality such as the Cecum Intubation Rate (CIR) and the Polyp Detection Rate (PDR) are known by most colonoscopists and performance goals are readily available. Factors such as patient sex, patient age and colonoscopy indication have the potential to affect the CIR or the PDR[1]. Colonoscopists might not perform examinations on an identical casemix. Different casemix could result in performance goals being too easy or nearly impossible to reach.

Aims & Methods: The primary aim was to introduce a benchmark (based on CIR and PDR) that accounted for differences in casemix between colonoscopists. The secondary aim was to see if colonoscopist performed different than the benchmark.

Individual colonoscopist casemix (patient age, patient sex and colonoscopy indication) were registered on all colonoscopies in a 7-week period at Aalborg University Hospital, Denmark (n = 894). Colonoscopists performing >40 colonoscopies were analyzed individually. Colonoscopist performing <20 colonoscopies and 21-40 colonoscopies were grouped in a *very low volume* and a *low volume* group, respectively.

Statistical analysis were conducted using Stata MP 15.1 and R 3.5.1.

Difference in patient age, patient sex and indication were analyzed using univariate analysis.

Predicted CIR and predicted PDR with 95% CI was calculated using bootstraps. A permutations test was performed to identify whether deviation from predicted performance represented low colonoscopy quality or statistical uncertainty.

Results: Univariate casemix analysis:
Mean age, [range 61 - 67], Diff. p = 0.36.
Male sex [range 44% - 72%], Diff. p = 0.25.
Indication (% of screening), [range 1% - 70%], Diff. p < 0.01.

Individual colonoscopists actual and predicted performance:

Colonoscopist	n	Measured CIR%	Predicted CIR%(95% CI)	Measured PDR%	Predicted PDR%(95% CI)
A	123	87.0	85.9 (83-88)	20.3	26.5 (23-29)
B	96	81.3	85.9 (83-88)	26.0	27.9 (25-31)
C	85	74.1	85.8 (83-88)	22.4	32.4 (29-35)
D	83	92.8	85.9 (83-88)	26.5	26.9 (24-30)
E	81	96.3	88.9 (87-91)	45.7	41.9 (38-46)
F	62	87.1	86.6 (84-89)	40.3	27.9 (25-31)
G	49	91.8	86.0 (84-88)	36.7	36.8 (34-40)
H	47	83.0	88.0 (86-90)	44.7	39.9 (36-44)
I	43	86.0	89.8 (87-92)	55.8	49.0 (44-54)
Low vol. (n 20-40)	98	87.8	89.0 (87-91)	37.8	41.6 (38-46)
Very low vol. (n <20)	127	90.6	87.5 (85-90)	37.8	33.0 (30-36)

[Actual and predicted cecum intubation rate (CIR) and poly detection rate (PDR)]

The permutation test did not find evidence to support that overall deviance from the predicted performance were related to inferior performance (PDR: p = 0.11, CIR: p = 0.81).

Conclusion: Predicted performance allow each colonoscopist to see if he/she performs better or worse than the department average performance given his/her unique casemix.

Actual performance deviated from 95 CI of predicted performance among some colonoscopist, but the deviation was not significant.

Our study found little variation in predicted CIR [range 85.8-89.8] and larger variation in predicted PDR [range 26.5-49.0]. The large variation indicates that numeric performance goals should be applied with caution when there is a large variations in casemix among colonoscopists. A low PDR could simply be related to casemix. Casemix analysis could easily be extended too include additional variables available from Electronic Health records for more precise estimates.

References: 1) Harris JK, Froehlich F, Wietlisbach V, Burnand B, Gonvers JJ, Vader JP. Factors associated with the technical performance of colonoscopy: An EPAGE Study. Dig Liver Dis. 2007;39(7):678-689. doi:10.1016/j.dld.2007.02.012

Disclosure: Nothing to disclose

P1583 RESECTION OF COLORECTAL POLYPS WITH CLIP PLACEMENT LEADS TO REDUCED EPISODES OF POST-POLYPECTOMY BLEEDING COMPARED TO POLYPECTOMY WITHOUT CLIP PLACEMENT

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Introduction: Endoscopic polypectomy is the standard of care for most of colorectal polyps and has expanded to include larger and sessile polyps. We compared the role of clip placement after polypectomy of pedunculated or sessile polyps larger than 2 cm in diameter to prevent postpolypectomy bleeding.

Aims & Methods: Patients who underwent polypectomy of sessile or pedunculated polyps larger than 2 cm were randomized to clip versus no clip placement at the base of the polyp. Patients with obvious bleeding or visible vessel after polypectomy were excluded from the study. The patients were followed-up for any signs of postpolypectomy bleeding for one month after the therapeutic procedure.

Results: In total 50 subsequent patients who underwent polypectomy of sessile or pedunculated polyps larger than 2 cm were studied (30 males, median age 67 years, range 28-86 years, 32 with sessile polyps, 18 with pedunculated polyps). Half of the patients were randomly treated with clip placement after the procedure. The aim of the clip was either to strangulate the peduncle of pedunculated polyp or close the open wound left after the resection of the sessile polyp. None of the patients bled in the group of clip placement, while 4 of the 25 patients bled in the group of no clip placement (P< 0.05). All bleeding episodes were managed conservatively with endoscopy, adrenaline solution injection and clip placement.

Conclusion: Clip placement after resection of pedunculated and sessile polyps larger than 2 cm can prevent postpolypectomy bleeding. In cases of bleeding subsequent endoscopic treatment was effective in all cases.

Disclosure: Nothing to disclose

P1584 ROOT CAUSE ANALYSIS OF 424 POTENTIAL POST COLONOSCOPY COLORECTAL CANCERS USING THE WORLD ENDOSCOPY ORGANIZATION ALGORITHM

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Introduction: Root cause analysis of post colonoscopy colorectal cancer (PCCRC) is essential to understand and prevent cases of PCCRC. The World Endoscopy Organization (WEO) has recently proposed a common method when conducting root cause analysis of PCCRC[1]. The aim of this study was to test the feasibility of the WEO algorithm on a large PCCRC dataset and to perform sub analysis in each WEO category to identify factors that could help avoid PCCRC in the future.

Aims & Methods: All colorectal cancers (CRCs) (ICD-10: C.18-C.20) diagnosed in North Region, Denmark from 2010-2018 were included in the root cause analysis. CRCs were cross-referenced with colonoscopies occurring from 6 months until 4 years from CRC diagnosis. A total of 424 colonoscopies on 330 individuals were investigated in journal records and the pathology database. Cause was assigned according to the WEO algorithm with the most plausible explanation.

Currently, the root cause analysis is based on 100 out of the 424 potential PCCRCs. With later inclusion of the remaining PCCRCs in a complete root cause analysis.

Results: Exclusion criteria and the distribution of PCCRC-cases according to the most plausible cause are found below.

Exclusion (n=42)	
Examination cancelled upon scope insertion (solid stool)	4
Metastastic CRC recurrence recurrence ouitside the colon	21
CRC date not registered correctly	13
Incorrect colonoscopy procedure code	3
Appendix tumor	1
Total	42

WEO PCCRC cause (n = 58)	n (%)
Missed lesion, prior examination adequate	25 (43)
Missed lesion, prior examination inadequate	23 (40)
Detected lesion not resected	2 (3)
Incomplete resection of detected lesion	6 (10)
Deviation from planned management pathway	2 (3)

[Exclusion criteria and WEO PCCRC causes of PCCRC cases]

The location of missed lesions (adequate and inadequate examinations) were: Rectum 33%, Sigmoid: 14%, Descending colon: 0%, Splenic flex: 2%, Transversal colon: 2%, Hepatic flex: 10%, Ascending colon: 9% and the Cecum: 31%.

The main reason for inadequate examinations was the lack of documented cecal intubation (18/23).

Conclusion: Missed lesions were predominantly located in the rectum or the cecum. The cecum can be technically challenging to visualize adequately, and previous studies have found higher risk of missed lesions in the cecum.[2,3] The high proportion of missed lesions located in the rectum may be related to local practices. Mandatory looping in the rectum is not required in North Region, Denmark, and rectal looping was only recorded in one case of a missed rectal lesion.

In cases with a previous inadequate examination, lack of evidence for cecal intubation was the dominant factor. In North Region, Denmark photo documentation is not required, but no evidence of terminal ileum intubation nor visualization of the ileocecal valve, the appendix orificium or an ileocolonic anastomosis were documented.

Incomplete resections were usually related to difficult polypectomies with multiple colonoscopies, polypectomies and short surveillance intervals before a final CRC diagnosis. Only one case of unexpected recurrence was identified.

Deviation from the planned pathway was mostly related to insufficient and unclear journal recording.

The WEO algorithm provides a useful framework to categorize PCCRC. In our study 82% of cases are related to missed lesions which are probably avoidable. The WEO algorithm is a valuable tool to identify areas in the colonoscopy service that could be improved in an attempt to avoid PCCRC.

References: 1) Rutter MD, Beintaris I, Valori R, et al. World Endoscopy Organization Consensus Statements on Post-Colonoscopy and Post-Imaging Colorectal Cancer. Gastroenterology. 2018;155(3):909-925.e3. doi:10.1053/j.gastro.2018.05.038. 2) Morris EJA, Rutter MD, Finan PJ, Thomas JD, Valori R. Post-colonoscopy colorectal cancer (PCCRC) rates vary considerably depending on the method used to calculate them: a retrospective observational population-based study of PCCRC in the English National Health Service. Gut. 2015;64(8):1248-1256. doi:10.1136/gutjnl-2014-308362. 3) Samadder NJ, Curtin K, Tuohy TMF, et al. Characteristics of missed or interval colorectal cancer and patient survival: A population-based study. Gastroenterology. 2014;146(4):950-960. doi:10.1053/j.gastro.2014.01.013.

Disclosure: Nothing to disclose

P1585 COLONOSCOPY FREQUENCY IN DIFFERENT SOCIOECONOMIC GROUPS BEFORE AND AFTER IMPLEMENTATION OF COLORECTAL CANCER SCREENING IN STOCKHOLM-GOTLAND REGION: A NATIONWIDE REGISTER-BASED STUDY IN SWEDEN, 2006-2015

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Introduction: Colorectal cancer (CRC) screening programmes are used to prevent CRC by detection of precancerous lesions or CRCs in less advanced stages. From 2008 and onwards, inhabitants aged 60-69 years in the Stockholm-Gotland Region (SGR) have been invited to participate in a faecal occult blood test (FOBT) based screening. Individuals with a positive FOBT were invited to a colonoscopy. In the rest of Sweden, organised CRC screening has not been implemented. We hypothesize the implementation of the screening programme in the SGR has accentuated socioeconomic disparities in colonoscopy frequency.

Aims & Methods: The aim was to study time trends in the colonoscopy frequency in different socioeconomic groups and geographical areas, with special consideration to the implementation of CRC screening in the SGR in 2008, within the age group 60-69 years. All registered colonoscopies in Sweden 2006-2015 were collected from Swedish in- and outpatient registers. In total 576,598 colonoscopies were included. From this cohort we selected colonoscopies performed on persons 60-69 years old. Data about sex, age, marital status, immigrant status and number of school years were collected from Statistics Sweden and linked to each colonoscopy (using unique personal identification numbers). Groups were categorized according to educational level (low, < 9 years in school; intermediate, 10-12 years; and high, >12 years), immigrant status (Swedish- vs. foreign-born) and sex. We compared colonoscopy frequencies in the population aged 60-69 years before (2006-2007) and after (2010-15) implementation of the screening programme.

Results: In the pre-screening period, the absolute frequency per 1000 was slightly higher in the SGR (8.9 for men, 9.9 for women) than in the rest of Sweden (7.5 for men, 8.6 women). In the SGR, the colonoscopy frequency was markedly higher among people with high educational level, 14.0 per 1000 such persons. By contrast, in the rest of Sweden, the frequency was somewhat lower among people with high educational level, 5.9 per 1000. Between the pre- and post-screening periods the absolute frequency increased by 14.6 units for men and 11.5 for women in the SGR. In the rest of Sweden, the corresponding frequency increases were less pronounced; 4.7 and 5.2, respectively. Comparing the frequency increases for different population groups according to educational level revealed the following patterns: 7.5 (low educational level), 7.0 (intermediate) and 10.7 (high) in the SGR; 4.9, 5.1 and 6.7 in the rest of Sweden. Comparing the frequency increases with regard to immigrant status revealed less pronounced disparities: 13.3 (Swedish-born) and 11.3 (foreign-born) in the SGR; 5.0 and 4.6 in the rest of Sweden.

Conclusion: In the pre-screening period, colonoscopy within the population aged 60-69 years in the SGR was more common among women and among people with high educational level. In the rest of Sweden, colonoscopy was not more common among people with high educational level. The frequency of colonoscopy have increased most pronouncedly in men and in highly educated individuals after the implementation of the CRC screening programme in the SGR. The frequency increase was similar in Swedish- and foreign-born individuals. Prerequisites for a screening programme that creates more equal conditions for attendance need to be addressed in further studies.

Disclosure: Nothing to disclose

P1586 MEASURES TO REDUCE POST-POLYPECTOMY BLEEDING IN PEDUNCULATED POLYPS - DOES A CLIP HELP?

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Introduction: Immediate and delayed post-polypectomy bleeding (PPB) is a serious complication after endoscopic removal of large pedunculated polyps. Options to decrease the risk of bleeding include injecting the stalk with adrenaline, placing endoscopic clips across the stalk (before or after the polypectomy) and placement of a nylon loop around the stalk. The principle of closing a defect to reduce complications is well established but the cost effectiveness of prophylactic clipping remains controversial. There are currently no consensus guidelines.

Aims & Methods: We aimed to investigate the use of endoscopic clips during polypectomy of pedunculated polyps >10mm and assess its association with PPB. We performed a large retrospective study across two sites at a tertiary London-based hospital Trust. Endoscopy software (Unisoft GI reporting tool) was used to identify pedunculated polyps >10mm in size during a 5 year period (January 2014 to March 2019). Patients that did not undergo polypectomy were excluded.

Results: 657 polypectomies were performed for pedunculated polyps during the study period (mean age 65.2 (range 22 - 94), Female 240 (36.5%)). Mean pedunculated polyp size 16.4mm (10 - 60mm). 431 (65.6%) in sigmoid colon. 636 (96.8%) hot snare polypectomy; 264 (40.2%) injected with adrenaline. Endoscopic clip used in 191 (29%). Total immediate (< 6hrs) and delayed bleeding (6hrs to 2 weeks) events were 11 (1.7%) and 14 (2.1%), respectively.

	Endoscopic Clip (n =191)	No Endoscopic Clip (n = 466)	p value*
Size (mm)	18.1	15.7	**0.0002**
Hot Snare (%)	183 (95.8)	453 (97.2)	0.35
Adrenaline injection (%)	115 (60.2)	149 (32.0)	**<0.0001**
Immediate bleeding (%)	9 (4.7)	2 (0.4)	**0.0001**
Delayed bleeding (%)	4 (2.1)	10 (2.1)	0.97

[Table 1. Bleeding complications according to use of endoscopic clip]

Conclusion: Endoscopic clip use was associated with more immediate bleeding events suggesting that it is being used as a treatment strategy (not prophylactically) to achieve haemostasis in high risk patients. Endoscopic clips are being deployed more often with larger polyps and in combination with adrenaline injection. Overall PPB rates in our cohort remain low. There remains considerable variation in practice and the type / size of clip to use and the method of clipping remain unanswered questions. Whilst there is clear guidance from national and international bodies on how to remove sessile polyps, the optimal technique for resection of pedunculated polyp is less clear and this may account for the variability in clinical practice.

Disclosure: Nothing to disclose

P1587 POST-COLONOSCOPY COLORECTAL CANCERS - SHOULD WE BE ASPIRING TO BETTER TARGETS?

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Introduction: The British Society of Gastroenterology (BSG), the UK Joint Advisory Group (JAG) on GI Endoscopy and the Association of Coloproctology of Great Britain and Ireland (ACPGBI) have developed quality assurance measures and key performance indicators for the delivery of colonoscopy within the UK. One of these includes aspiring to a target of < 5% post-colonoscopy colorectal cancers (PCCRC) at 3 years.

Aims & Methods: We performed a retrospective study across two sites at a tertiary London-based hospital Trust. Endoscopy software (Unisoft GI reporting tool) was used to identify all new colorectal cancers diagnosed during colonoscopy during a 16 month period (May 2017 to September 2018). Interrogation for a prior colonoscopy within 3 and 5 years of the date of each colorectal cancer diagnosis was then performed. PCCRC rate was defined as the proportion of PCCRC diagnoses amongst all CRC cases within a 3 year period.

We also analysed demographics, time interval (initial to diagnostic colonoscopy) and colonoscopist performing the procedure (physician vs. surgeon). Quality of bowel preparation was scrutinised in the PCCRC cases (excellent, good, fair, inadequate).

Results: We identified 282 cases of colorectal cancer diagnosed during colonoscopy in the study period. There were a total of 8 cases of PCCRC within 3 years giving our Trust a PCCRC rate of 2.8%. Mean age of patients with a PCCRC diagnosis was 75.8 (64 - 88). Mean interval from initial to diagnostic colonoscopy in PCCRC cases was 2.08 years (0.92 - 3). Of the 8 pa-

tients with PCCRC; 1 was Dukes' A, 4 were Dukes' B2, 2 were Dukes' C1 and 1 was Dukes' C2. 7 of the 8 cases (87.5%) were colonoscopies performed by surgeons or external agency endoscopists. 4 of the 8 cases (50%) had less than good bowel preparation. Retroflexion in the rectum was not performed in 6 of the 8 cases (75%). When PCCRC diagnoses were extended to within 5 years the PCCRC rate was 4.3%.

Conclusion: Our study shows that our Trust is within the quality standards set by the relevant governing bodies. Root cause analyses identified caecal, sigmoid and anastomotic lesions as high risk sites for missed cancers as well as omission of retroflexion in the rectum. Accepting less than good bowel preparation is also a factor in half of PCCRC cases. Only 1 patient had an endoscopically resectable lesion at diagnostic colonoscopy but there were no patients with distant metastases.

In view of the advances made in the quality of colonoscopy training and enhanced endoscopic technology, we suggest raising the bar with regards to acceptable PCCRC by either lowering the target or increasing the time frame to 5 years.

Disclosure: Nothing to disclose

P1588 NURSE-LED EDUCATIONAL TELEPHONE INTERVENTION FOR BOWEL PREPARATION FOR REPEAT COLONOSCOPY AFTER BOWEL PREPARATION FAILURE

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Introduction: Up to 20% of bowel preparations for colonoscopy are considered inadequate and the colonoscopy is not valid. The consequences are missed lesions, cancelled procedures, diagnostic delays, and increased risks and costs. The most important predictor of inadequate bowel preparation is a previous failure. There are no standardized recommendations to prepare those patients. An educational intervention through a telephone call has demonstrated to improve the efficacy of bowel preparation in the general population.

Aims & Methods: The aim of this study was to analyze the efficacy of a nurse-led educational intervention by telephone within the 48 hours before the colonoscopy, in patients with previous bowel preparation failure. This was a multicentre randomized clinical trial with parallel groups (control and educational intervention), endoscopist-blind. The study was approved by each of the 11 participant hospitals. Consecutive patients with inadequate bowel preparation were included. A sample size of 650 participants was calculated to show a 10% improvement in bowel preparation adequacy. Both groups received the same bowel prepararation protocol including 4 liters of PEG in split dose regimen. The main outcome was adequate bowel preparation defined as all segments of the Boston Bowel Preparation scale with 2 or 3 points. Participants with no efficacy data were considered bowel preparation failures. Intention to treat (ITT) analysis included all randomized participants and per protocol (PP) analysis included participants that could be contacted by telephone and control cases. Clinicaltrials identifier: NCT03055689

Results: The investigators included, 651 consecutive participants (329 control and 321 intervention) without differences in the baseline characteristics. In the ITT analysis bowel preparation was inadequate in 97 (29.6%) control cases and in 77 (23.9%) intervention cases, risk difference 5.7%. p=0.1. Attendance to colonoscopy was 296 (91.4%) and 297 (92.2%), p=0.68 in control and intervention groups. Adenoma detection rate was 39.2% and 44.4%, p=0.21 in the control and intervention groups respec-

tively. In the intervention group 267 (82.9%) participants could be reached by telephone. In the PP analysis the bowel preparation was inadequate in 45 cases (16.9%) in the intervention group, with a risk difference with the control group of 12.7%, p>0.001.

Conclusion: In patients with previous failure of bowel preparation a nurse-led telephone education in the 48 hours before the colonoscopy is not effective as intention to treat, due to a limited applicability. However that intervention is clearly effective when the patient can be reached by telephone.

Disclosure: Nothing to disclose

P1589 THE ROLE OF KEY PERFORMANCE INDICATORS IN THE SURVEILLANCE OF POST-RESECTION COLORECTAL CANCER PATIENTS

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Introduction: Between 2013 and 2014, 63-66% of all patients with newly diagnosed colorectal cancer (CRC) in the UK underwent a surgical resection for their tumour[1]. Post-resection surveillance colonoscopy for metachronous CRC has become standard practice, as patients with a previous CRC may be at greater risk of a secondary CRC diagnosis than age and sex-matched controls are of a primary CRC diagnosis[2]. However, the protection offered by surveillance colonoscopy may in fact be limited by the quality of the colonoscopy performed, and in particular, the ability of the colonoscopist conducting the procedure. Key performance indicators (KPIs) are markers of colonoscopy quality, and include adenoma detection rate (ADR), caecal intubation rate (CIR) and polyp retrieval rate (PRR). Unfortunately, the utility of KPIs for surveillance colonoscopy in patients who have undergone surgical resection for CRC is not well described.

Aims & Methods: Using KPIs, we aimed to assess the quality of colonoscopy in a cohort of patients with previous CRC who underwent surveillance post-resection at West Middlesex University Hospital (WMUH), and compare these to non-surveillance KPIs by the same colonoscopists to assess the relationships between them. We retrospectively assessed colonoscopy data for post-resection CRC surveillance at WMUH between 2010 and 2019. Patient demographic and colonoscopy data was collected alongside colonoscopist non-surveillance KPI data and analysed using the software SPSS. All flexible-sigmoidoscopies which did not aim to completely intubate the bowel were excluded. We assessed for correlation between surveillance and non-surveillance KPIs from the same colonoscopists at the trust, and tested for any differences in KPIs between the two cohorts.

Results: In total, 641 surveillance colonoscopies for post-resection CRC were performed by over 50 colonoscopsists. The overall ADR in the 1st, 2nd, 3rd and 4th surveillance colonoscopies was 22.0%, 27.0%, 36.8% and 38.5% respectively, with an ADR of 26.0% across all colonoscopies. 7 colonoscopists performed at least 20 surveillance colonoscopies in our cohort. For these 7 colonoscopists, the total ADR was 25.9% (range 13.6%-45.0%), the total CIR was 97.4% (range 95.0%-100%), and the total PRR was 90.3% (range 76.9-100%). Non-surveillance ADRs correlated with surveillance ADRs ($R^2=0.650$, p< 0.05), but non-surveillance CIRs did not correlate with surveillance CIRs ($R^2=0.270$, p=0.232), nor did non-surveillance PRRs correlate with surveillance PRRs ($R^2=0.532$, p=0.153). There were no significant differences between the surveillance and non-surveillance ADRs observed in these colonoscopists (p=0.115).

Conclusion: Even with a relatively small sample size, we found a clear association between surveillance and non-surveillance colonoscopist ADRs (the primary marker of colonoscopy quality) in our cohort. Although other KPIs including CIR and PRR did not correlate between surveillance and non-surveillance cohorts, there may be practical reasons for this, including the presence of short bowels in post-resection CRC patients and the exclusion of flexible-sigmoidoscopies in our study.

References: 1) Cancer research UK. Available at: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/bowel-cancer/diagnosis-and-treatment [Accessed 01/04/2019]. 2) Mulder SA, Kranse R, Damhuis RA, Ouwendijk RJ, Kuipers EJ, van Leerdam ME. The incidence and risk factors of metachronous colorectal cancer: an indication for follow-up. Dis Colon Rectum. 2012;55(5):522-31.

Disclosure: Nothing to disclose

P1590 INDICATORS OF ADEQUATE INSPECTION OF BOWEL MUCOSA: CAN WE USE ONLY POLYP DETECTION RATE (PDR)?

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Introduction: Adenoma detection rate (ADR) and mean adenoma per colonoscopy (APC) are established quality indicators in colonoscopy. Yet they are not generally used in European countries. This may be because it is rather difficult to obtain them in terms of time and personnel. To improve the compliance of endoscopists with quality control, it is essential to simplify the entire monitoring process. Polyp detection rate (PDR) is a user friendly alternative of ADR that can be easily evaluated from administrative data.
Aims & Methods: The aim of our study was to assess whether PDR correlates with ADR and with APC. Our effort was to determine minimal marginal value for APC. Prospective multicenter study included asymptomatic individuals aged 45-75 who underwent preventive colonoscopy in 2012-2016 as part of Czech study monitoring metabolic risk factors of colorectal cancer. Individuals with incomplete colonoscopy and endoscopists with less than 30 colonoscopies and/or no detected adenoma in the observed group were excluded from the study. Spearman's correlation coefficient was used to assess the relation between individual PDR/ADR and PDR/APC resp. The resulting conversion factors to predict ADR (APC) from PDR were obtained by linear regression.
Results: In total, the study included 1,614 preventive colonoscopies performed by 16 endoscopists. Correlation between PDR and both indicators in all preventive colonoscopies was strong and statistically significant (PDR/ADR: Rs 0.82; p < 0.001; PDR/APC: Rs 0.70; p= 0.0027). We used the same methodology to determine gender-specific and indication-specific PDR/ADR and PDR/APC correlations. In all cases, we demonstrated a strong and statistically significant correlation between PDR and ADR (APC resp). We obtained conversion factors for both quality indicators: PDR to ADR 0.7185, resp. PDR to APC 0.0123.
Conclusion: There is a strong correlation between PDR/ADR as well as between PDR/APC. Because of better availability, PDR may replace ADR and APC in colonoscopy quality assessment. Using our conversion factor we obtained minimal marginal value of APC 0.5 based on 40% minimal marginal value of PDR as recommended by ESGE.
PDR has the potential to increase compliance of endoscopists to quality control, at least until data processing is fully automated.
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Disclosure: Nothing to disclose

P1591 FACTORS AFFECTING THE QUALITY OF BOWEL PREPARATION FOR COLONOSCOPY IN THE ELDERLY: A RETROSPECTIVE ANALYSIS OF A PROSPECTIVE COHORT

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Introduction: The effectiveness of bowel cleansing is essential for a quality colonoscopy as it affects diagnostic accuracy and adenoma detection rate. Inadequate cleansing remains a major challenge, with a suboptimal bowel preparation observed in 25% of procedures.
Among all factors contributing to inadequate preparation, age has been shown to be an independent risk factor for poor bowel cleansing. Nevertheless, factors affecting bowel cleansing in the elderly are not fully known, and current guidelines do not provide a specific recommendation for optimisation of preparation in these patients.
Aims & Methods: This study aimed to assess the difference in bowel cleansing in elderly compared to younger patients and to evaluate independent factors associated with a cleansing success.
We retrospectively reviewed a prospective cohort of 1289 in- and out-patients undergoing a colonoscopy after a standard (afternoon-only) or a split (afternoon-morning) preparation with a 1, 2 or 4L PEG-based solution consecutively enrolled from September 2018 to February 2019 in 5 Italian centres. The elderly population was defined by an age ≥65 years. Bowel cleansing was assessed through the Boston Bowel Preparation Scale (BBPS) and a cleansing success was defined as a total BBPS>6 with a partial BBPS≥2 in each segment. Tolerability was evaluated by a semi-quantitative scale with a score ranging from 0 to 10.
Results: All 1289 patients were included in the analysis. Overall 52.8% of subjects were male, the meanage was 60.5±14, and 44.6% of patients were older than 65 years.
Bowel preparation was performed with a 4L, 2L and 1L PEG solution in 38.0%, 43.9% and 18.1% of cases, in the absence of serious adverse events. Bowel cleansing by BBPS was 6.6±1.4 and 6.3±1.6 (p= 0.006) in the groups of patients aged < 65 and ≥65 years and colonoscopy was completed with cecal intubation in 97.5% and 95.5% (p=0.05) of patients, respectively. Compared to patients < 65 years, patients ≥65 years achieved a lower cleansing success: 70.3 vs 77.3% overall, 61.2% vs 69.5% in the subgroup of standard preparation and 84.9% vs 90.2% in the subgroup of split preparation.
At multivariate analysis, split regimen (OR=2.49, 95% CI=1.38-4.48; p=0.002), adequate cleansing at previous colonoscopy (OR=3.28, 95% CI=1.40-7.68; p=0.006) and tolerability score (OR=1.14, 95% CI=1.03-1.26; p=0.006) were independently associated with a cleansing success in the group of patients aged < 65 years. In the group of patients aged ≥65 years, split regimen (OR=2.43, 95% CI=1.34-4.38; p=0.003), adequate cleansing at previous colonoscopy (OR=2.29, 95% CI=1.14-4.73; p=0.02), tolerability score (OR=1.29, 95% CI=1.16-1.44; p< 0.001), low-fiber diet for at least 3 days preceding colonoscopy (OR= 2.45, 95% CI=1.42-4.24; p=0.001) and colonoscopy within 5 hours after preparation (OR= 2.67, 95% CI=1.28-5.56; p=0.008) were independently associated with a bowel cleansing success.
Conclusion: Compared to younger patients, achieving adequate cleansing in the elderly is more challenging, and it is influenced by a higher number of external factors. Among these, split preparation, timing of colonoscopy within 5 hours after preparation, low-fiber diet for at least 3 days preceding colonoscopy, adequate cleansing at previous colonoscopy and tolerability of preparation were independently associated with a cleansing success. These factors play a crucial role in achieving a proper bowel cleansing and need to be properly addressed to optimise the quality of preparation in elderly, thus avoiding the discomfort and the risks deriving from the repetition of the exam.
Disclosure: Nothing to disclose

P1592 SNARE TIP SOFT COAGULATION OF THE MUCOSAL DEFECT MARGIN FOLLOWING COLONIC ENDOSCOPIC MUCOSAL RESECTION (EMR) REDUCES RECURRENCE IN A "REAL LIFE" SETTING

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Introduction: Large (>20 mm) colonic lateral spreading lesions (LSL) while uncommon, are high risk precursors of CRC, and require Endoscopic Mucosal Resection (EMR) for their safe and efficacious removal. EMR is the treatment of choice due to its high success rates, good safety profile and multiple advantages compared with surgery.

A recent randomized study demonstrated that ablation of the post-EMR mucosal defect margin significantly reduced polyp recurrence at surveillance. Also, recently studies have shown that endoscopic assessment of recurrence is very accurate with a NPP of 99%-100%.

We aimed to determine the efficacy of this technique for reducing polyp recurrence in a "real life" setting.

Aims & Methods: Analysis of a prospectively collected database of LSL≥ 20 mm was performed in two hospitals in Israel. Standard EMR technique was used in all cases emphasizing complete snare excision followed by thermal ablation of the entire defect margin. Surveillance colonoscopy was performed 4-6 month after resection. Recurrence was assessed endoscopically with High Definition White Light (HDWL), Narrow Band Imaging (NBI) and magnification. Normal appearing scars were randomly biopsied as were any scars suspicious for recurrence. The primary endpoint was lesion recurrence at first surveillance colonoscopy.

Results: Over 34 months 313 LSL in 303 patients were removed by EMR. 249/313 (81.7%) were removed piecemeal. 233/249 (93.5%) lesions were treated with ablation of the margin. 176/233 (75.5%) completed first surveillance colonoscopy. Recurrence was suspected endoscopically and confirmed histologically in 4/176 cases. One histological recurrence was detected in a biopsy from a normal appearing scar. Overall recurrence occurred in 5/176 (2.8%) cases. Compared to the final histology, endoscopic diagnosis was accurate in 98%. We had 6/249 (2.4%) cases of clinical significant delayed bleeding all treated conservatively and two cases of deep mural injury treated by clips only.

Conclusion: Ablation of the mucosal defect margin following EMR in a "real life" setting results in very low recurrence rates and low rates of complication. STSC should be performed routinely following piecemeal colonic EMR.

References: 1. Moss et al; Endoscopic mucosal resection outcomes and prediction of submucosal cancer from advanced colonic mucosal neoplasia, Gastroenterology 2011 2. Belderbos T.D.G., Leenders M., Moons L. et al; Local recurrence after endoscopic mucosal resection of nonpedunculated colorectal lesions: systematic review and meta-analysis Endoscopy 2014. 3. Klein A, Tate DJ, Bourke MJ et al. Thermal Ablation of Mucosal Defect Margins Reduces Adenoma Recurrence After Colonic Endoscopic Mucosal Resection; Gastroenterology 2019 4. Desomer L et al. Adenoma recurrence after piecemeal colonic EMR is predictable: the Sydney EMR recurrence tool. Gastrointest Endosc. 2017

Disclosure: Nothing to disclose

P1593 QUANTIFYING EMERGENCY ADMISSIONS AFTER DAYCASE ENDOSCOPY USING ROUTINE DATA

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Introduction: Detailed stratified estimates of adverse events after endoscopy would inform clinical decision making about appropriate investigations in those at higher risk. This is important due to the ever increasing proportion of the population undergoing diagnostic endoscopy. This abstract identified the adjusted total and excess risk of cardiovascular, respiratory, gastrointestinal and symptom events in both primary and secondary care following low risk day case diagnostic gastroscopy, colonoscopy, sigmoidoscopy and double upper and lower procedures.

Aims & Methods: Patients undergoing day case diagnostic endoscopy were identified in the English population from the Clinical Practice Research Datalink hospital data using OPCS-4 coding. Each endoscopy procedure was frequency matched with replacement on decade of birth to at 4 controls alive and registered at the time of the endoscopy including those who might have an endoscopy at a later date. Follow up was censored on; 30 days or the earliest diagnosis of cancer, a subsequent gastrointestinal event, a subsequent interventional procedure, after the first emergency hospital admission, any transfer out the study population, or death.

The first acute event was defined as either the primary reason for the first emergency admission after an endoscopy or a primary care consultation. This was coded broadly by their ICD 10 chapter; and more specifically as a cardiac, cerebrovascular, respiratory, gastrointestinal bleeding, perforation or peritonitis event; or as having an episode coding symptoms of nausea, vomiting or abdominal pain without a gastrointestinal diagnosis. Gastrointestinal events or symptoms recorded both prior and post procedure were censored as likely to be the indication for the procedure. Outcomes were identified in the 30 days after the index date, from either linked primary care consultations, the underlying cause from death certificates, or the main diagnosis from emergency hospital admissions.

The age stratified risk of each type of event following each type of day case diagnostic endoscopy was estimated in a Cox regression model adjusted for age, gender. and a previously developed measure of pre-existing co-morbidity[1]. Then the stratified absolute excess risks were calculated, adjusting for censored and competing events, by using the cumulative incidence functions derived from the Cox model.

Results: 277,535 gastroscopies, 172,862 colonoscopies, 22,995 dual procedures and 73.195 flexible sigmoidoscopies were recorded in the linked data between 1998 and 2016. Of the outcome events 118,089 were coded as cardiorespiratory, 1,463 as gastrointestinal , and 4,213 as pain, nausea or vomiting. The absolute excess cardiovascular risk compared to the general population decreased with age for colonoscopy and double procedures, but increased following gastroscopies and flexible sigmoidoscopies, possibly reflecting the different case mix of patients referred for these procedures. There was no reduction in the risk of a post procedure event over the time course of the study after adjusting for age and co-morbidity. The largest annual relative change was for a slight increase in cardiovascular events after diagnostic gastroscopy (HR=1.005 (1.001-1.009)) with an average 30 day risk of 5% for patients over 80 years.

Conclusion: This study showed the potential of linked routine data to provide a comprehensive population based measurement of post endoscopic events in primary and secondary care. Cardiovascular events predominate, and despite improvements in sedation practice there was no observable reduction in post procedure events.

References: Crooks. PLoS One. 2016;11(10):e0165507

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P1594 SAFETY OF NER1006 IN ELDERLY: A POST-HOC ANALYSIS OF A PROSPECTIVE, MULTICENTER COHORT

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Introduction: The effectiveness of bowel cleansing is a key element for a quality colonoscopy as it affects diagnostic accuracy and adenoma detection rate. A very-low-volume 1L PEG solution NER1006 (Plenvu® Norgine, Harefield, UK) has been recently introduced after the publication of three phase 3 randomized controlled trials showing non-inferiority respect to comparators [1-3]. Despite its proven effectiveness, the safety of NER1006 in the elderly has never been assessed in a real-life setting.

Aims & Methods: This study aimed to assess the difference of NER1006 safety profile in elderly compared to younger patients in a real-life setting. We performed a post-hoc analysis of data from a cohort of 1289 patients undergoing a colonoscopy after a standard (afternoon-only) or a split (afternoon-morning) preparation with a 1, 2 or 4L PEG-based solution

consecutively enrolled from September 2018 to February 2019 in 5 Italian centres. The elderly population was defined by an age ≥65 years. Tolerability was evaluated through a semi-quantitative scale with a score ranging from 0 to 10. Safety was monitored through adverse event (AE) reporting.

Results: Among 1289 patients, 233 subjects undergoing a bowel preparation with NER1006 were included in the analysis. The mean age was 59.5±15.9 years, 52.4% of patients were male, and 43.5% were older than 65 years old.

Mean age was 48.6±11.9 years (range 18-64) in the group of patients aged < 65 years, and 73.7±6.3 years (range 65-91) in the group of patients aged ≥65 years, while prevalence of hypertension, diabetes and obesity was 13.7 vs 32.7% (p=0.03), 3.1 vs 9.9% (p=0.001) and 12.2 vs 13.9% (p=0.7) in the two groups, respectively. Overall incidence of adverse events was 19.8% and 10.9% (p=0.06) in the group of patients aged < 65 and ≥65 years. Incidence of nausea, vomit, abdominal pain, dehydration and headache was 3.1 vs 3.0% (p=0.9), 9.9 vs 5.9% (p=0.2), 0.8 vs 0.0% (p=0.3) 2.3 vs 0.0% (p=0.1) and 2.3 vs 0.0% (p=0.1), in the group of patients aged < 65 and ≥65 years, respectively. No serious adverse events or deaths occurred in any of the two groups.

Conclusion: In this post-hoc analysis, we did not find any substantial difference in the safety profile of NER1006 in the elderly compared to younger patients. Given the observational nature of our study, an assessment of blood electrolyte or creatinine was not feasible. Nevertheless, no clinical event attributable to electrolyte imbalance or dehydration was observed in any patient. These results confirm the safety of this product even in the elderly and in a real-life setting.

References: 1) DeMicco MP, Clayton LB, Pilot J, et al. Novel 1 L polyethylene glycol-based bowel preparation NER1006 for overall and right-sided colon cleansing: a randomized controlled phase 3 trial versus trisulfate. GastrointestEndosc. 2018;87:677-687. 2) Bisschops R, Manning J, Clayton LB, et al. Colon cleansing efficacy and safety with 1 L NER1006 versus 2 L polyethylene glycol + ascorbate: a randomized phase 3 trial. Endoscopy. 2019 Jan;51(1):60-72. doi: 10.1055/a-0638-8125. 3) Schreiber S, Baumgart DC, Drenth JPH, et al. Colon cleansing efficacy and safety with 1 L NER1006 versus sodium picosulfate with magnesium citrate: a randomized phase 3 trial. Endoscopy. 2019 Jan;51(1):73-84. doi: 10.1055/a-0639-5070.

Disclosure: Nothing to disclose

P1595 EFFICACY OF ENDOSCOPIC TREATMENT FOR ADENOMA RECURRENCE AFTER PIECEMEAL ENDOSCOPIC MUCOSAL RESECTION OF LESIONS LARGER THAN 20MM

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Introduction: Endoscopic mucosal resection (EMR) is a safe and effective technique for the resection of large colorectal lesions, but is associated with a high risk of local recurrence (LR). Data on the ideal methods and outcomes of endoscopic treatment of LR after EMR are scarce, with no formal recommendations.

Aims & Methods: We intended to evaluate the efficacy, safety and endoscopic clearance rate following treatment of LR after piecemeal EMR (pEMR).

Retrospective unicentric study based on the analysis of LR after pEMR of lesions with ≥20 mm between January/2010 and December/2017, registering its endoscopic, histological, treatment, complications and surveillance features.

Results: A total of 226 pEMR of lesions measuring ≥20mm (Median 25mm, IQR 20-35mm) were evaluated. LR was observed in 71 patients (31.4%). Mean age of 66 ± 10 years, male in 45%, 42.2% located distal to the hepatic flexure.

LR was small (< 5mm) and unifocal in 76% and 86% of cases, respectively. It was objectified in the first 6 months after index pEMR in 60.5% and submitted to en-block resection in 63.1% of the cases. The modalities used to resect recurrence were cold snare (49.3%), hot snare (25.4%), cold snare and cold-forceps avulsion (11.3%), cold-forceps avulsion alone (3%) and endoscopic full-thickness resection (3%). 8.5% (n = 6) of the patients were referred for surgery due to an inability to resect recurrence. Histology: 50.7% displayed tubulovillous adenoma at histopathology and 38.1% high

grade dysplasia. A second LR was observed in 12.3% (n = 8) patients, all of whom underwent piecemeal resection of the first relapse. 1 patient was referred for surgical resection due to nonresectability of the second relapse. An endoscopic clearance of recurrent adenoma of 91.1% was obtained.

Conclusion: LR after pEMR is often small and can be effectively treated using conventional endoscopic techniques with long-term remission rates greater than 90%. More complex endoscopic techniques (endoscopic full-thickness resection/endoscopic submucosal dissection) and surgery are only necessary in a small number of patients.

Disclosure: Nothing to disclose

P1596 MANAGEMENT OF COLORECTAL POLYPS IN A DEVELOPING COUNTRY: IS THERE ANY DIFFERENCE?

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Introduction: Colorectal polyps are very common in general population. Endoscopy allows the diagnosis and characterization of the polyp which is fundamental to determine the modalities of polyp removal.

Aims & Methods: The aim of our study is to determine the incidence of rectocolic polyps in our department and thus their adequate management. This is a retrospective descriptive and analytical study conducted over a period of 19 years from January 2000 to April 2019 in our department of gastroenterology II of the military teaching hospital of Rabat. We included all patients over 18yo whom had less than 4 colorectal polyps of more than 3mm each, discovered during a total colonoscopy with a complete polyp characterization using white light and narrow band imaging, and whom underwent a complete endoscopic removal and retrieval. For all patients, we assessed the endoscopic devices used for polypectomies, and for complications management. We then performed a statistical analysis using SPSS software 24.0.

Results: 3,23% (n=214) of patients who had undergone total colonoscopies performed during the study period (n=6607) underwent one or multiple polypectomies. The mean age of our patients was 55,89+/-14,45years old [18-90], with a sex ratio M/F of 2,17 and a history of operated rectocolic cancer in 13,2% (n=27). The mean number of polyps in each patient was 1,32+/-0,66. Colonoscopies indications were dominated by rectal bleeding which represented 22,9% (n=47), followed by constipation in 12,2% (n=25), iron deficiency anemia in 5% (n=10) and abdominal pain in 5% (n=10).

During the procedure, the major part of polyps were located in left colon in 45,1% (n=93) and rectum in 27,7% (n=57), followed by transverse colon in 17,6% (n=36), right colon in 15,1% (n=31) and coecum in 5,4% (n=11).

All colorectal polyps were staged according to Paris classification with a predominance of sessile polyps (Is) which represented 73,83% (n=158), followed by pedunculated ones (Ip) which represented 37,38% (n=80). stages IIa , IIb and IIc of Paris classification were less frequent with respectively 0,46% (n=1), 7,47% (n=7) and 0,46% (n=1).

42.05% (n = 90), polyps were removed by forceps, 32.24% (n = 69) had polypectomies using cold snare, 22.89% (n = 49) had endoscopic mucosal resection (EMR), and 28.03 % (n = 60) were biopsied and resected later. Early complication rate defined by the occurrence of bleeding after polypectomy was 2% (n = 2), and there was no late complication noted.

Conclusion: Endoscopic resection of recto-colic polyps is currently an alternative to radical surgery, leading to a significantly lower cost and morbidity and allowing a decrease of the incidence and mortality due to recto-colic cancer. The therapeutic choice depends on good endoscopic characterization in real time. Monitoring after polypectomy is necessary and depends mainly on histological findings

Disclosure: Nothing to disclose

P1597 DOES A ONE-DAY QUALITY IMPROVEMENT CONFERENCE ON SCREENING COLONOSCOPY INFLUENCES QUALITY PARAMETERS? – FOLLOW-UP AFTER SECOND CONFERENCE

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Introduction: After investigating the impact of a quality improvement conference on screening colonoscopy in 2016, we wanted to analyze if attending a second conference one year later has an influence on quality parameters. Thus, our aim of the study was to assess differences in quality measures according to the endoscopist's participation in the conference.
Aims & Methods: 69 902 screening colonoscopies from 213 endoscopists performed within the Austrian Certificate of Screening Colonoscopy were evaluated. The second one-day quality improvement conference on screening colonoscopy was also organized within the framework of the certificate on September 9th, 2017. We investigated the following quality parameters: the adenoma detection rate (ADR), advanced adenoma detection rate (AADR) and cecal intubation rate (CIR).
Results: Data from the year before (September 2016 to August 2017) and the year after the conference (October 2017 to September 2018) were compared.
No statistical significance was found in mean ADR, AADR and CIR from the year before and after the conference among participants of the certificate attending the conference for the second time, first time and those who did not participate (table 1).

		Before conference	After conference	p-value
Endoscopists participating for 2nd time; N= 24 (11,27%)	ADR % (SD)	30,49 (9,39)	32,45 (9,85)	0,2022
	AADR % (SD)	7,83 (6,05)	8,33 (5,87)	0,6064
	CIR % (SD)	97,2 (3,15)	97,46 (2,71)	0,4597
Endoscopists participating for 1st time; N=15 (7,04%)	ADR % (SD)	27,37 (12,82)	28,59 (12,59)	0,5056
	AADR % (SD)	5,81 (3,94)	4,39 (3,0)	0,2621
	CIR % (SD)	98,82 (1,53)	97,71 (3,9)	0,2349
Non-participants; N= 174 (81,69%)	ADR % (SD)	24,39 (12,79)	24,38 (12,43)	0,9930
	AADR % (SD)	5,6 (5,02)	5,11 (4,51)	0,1421
	CIR % (SD)	97,51 (3,15)	97,41 (3,19)	0,6520

[Table 1]

Conclusion: This study did not show any change in the investigated quality parameters among endoscopists who attended the quality improvement conference and the ones who did not participate. Endoscopists attending the conference had higher quality parameters than non-participants already before the conference. Therefore, it is important to reach those endoscopists who need more improvement and encourage them to take part in training.
Disclosure: Nothing to disclose

P1598 ENDOSCOPIC SUB MUCOSAL DISSECTION USING SCISSOR TYPE KNIFE (SB KNIFE) FOR BROAD-BASED OR STALKED COLONIC POLYPS: A SINGLE CENTRE CASE SERIES

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Introduction: Intra procedural and post polypectomy bleeding is a recognised complication of large broad -based or pedunculated polyp resection. Several endoscopic techniques have been applied to prevent bleeding with variable success. Furthermore, piecemeal endoscopic mucosal resection could lead to incomplete resection and future recurrences.
Aims & Methods: We report our preliminary experience in achieving a complete en bloc, Endoscopic Sub mucosal Dissection (ESD) using a scissor type SB knife.
A prospective database was analysed including 26 consecutive patients (median age 66 years, range 34-80) with 28 broad-based colorectal neoplasms resected by ESD between 2015 and 2017.
Results: ESD techniqueOnce a broad-based polyp was detected, the surface was scrutinised with white light and NBI. Firstly, the base was injected with submucosal injection of 0.1% hyaluronate and methylene blue and ESD was performed using SB knife junior (monopolar ESD knife, Sumius,Tokyo, Japan). Following an initial mucosal incision, submucosal (SM) dissection was performed. SM blood vessels (BV) were grasped and coagulated to prevent bleeding. A sequence of coagulation and cutting was performed repeatedly until the polyp was resected completely. Polypectomy base was examined and any oozing BV's were treated with SB knife and the base was closed using haemostatic clips. Polyp tissue were retrieved and sent for histology.
The median (IQR) polyp size was 3.25cm (2-6cm). 89% (25/28) of the polyps were in either rectum or sigmoid colon. Histology showed adenoma with low grade dysplasia in 12/28(42.8%), high grade dysplasia in 28.6%(n=8), T1 adenocarcinoma in 10.7%(n=3), hamartomas in 7.1%(n=2), serrated lesions without dysplasia in 7.1% (n=2) and lipoma in 3.6%(n=1) of endoscopically resected lesions. Intra procedural bleeding was treated either with haemostatic function of SB knife or with snare tip soft coagulation. Base of all polyps, following resection were closed with multiple clips. There were no episodes of perforation or delayed post polypectomy bleeding. 3 patients (11.5%) were electively admitted post procedure for overnight observation and discharged on the following day. The en-bloc, histological complete and curative(R0) resection rates were 100%, 89% and 85%. Three patients (11.5%) at risk of lymph node metastasis underwent additional radical surgery. 20/25(80%) of ESD cases had endoscopic follow up data over a median duration of 12 months (range 6-36 months) and none of them had local recurrences.
Conclusion: ESD using scissor type SB knife is efficient and safe in treating broad-based or stalked polyps. Our series highlighted a favourable short and medium-term outcome.
Disclosure: None declared

P1599 WITHDRAWN

P1600 FULL THICKNESS RESECTION VERSUS ENDOSCOPIC SUBMUCOSAL DISSECTION OF RESIDUAL/RECURRENT COLONIC LESIONS ON SCAR: A RETROSPECTIVE ITALIAN AND JAPANESE COMPARATIVE STUDY

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Introduction: Even if the barriers to the adoption of Endoscopic Submucosal Dissection (ESD) in the current practice in Western countries are falling, it remains, especially for colonic lesions, challenging and with a high risk of adverse events. ESD for residual/recurrent colonic lesions on scar is even more technically difficult and it has significant rate of perforations even in Japanese expert hands. Nevertheless, in Japanese tertially referral centers ESD represents the standard of care in such lesions. Full thickness resection (FTR) with a over-the-scope device (FTRD - Ovesco Endoscopy) is a minimally invasive endoscopic technique recently introduced in Western countries. Even if with some limitations (the major limitation is the maximum size of the lesion, 30 mm), it showed to be safe and effective in the resection of residual/recurrent colonic lesions on scar and, being less technically demanding than ESD, it is more applicable among Western endoscopists.

Aims & Methods: This study sought to compare, therefore, outcomes for endoscopic resection of such lesions between a Japanese and an Italian tertially referral centre. From January 2017 to December 2018 a total of 17 and 48 residual/recurrent colorectal lesions on scar were respectively treated by FTR (in the Italian Centre) and ESD (in the Japanese Centre). En-bloc and R0-resection rates were recorded as primary outcomes and retrospectively analysed. Adverse events, median procedure time and residual lesions at 3-months follow-up were assessed as secondary outcomes.

Results: The proportions of R0 resections were 86.7% in the FTR group vs 97.9% in the ESD group. En-bloc resection rate was achieved in 100% in both groups. Adverse events were not reported in the first group. ESD group Intraoperative perforations rate was 20.8%, all managed conservatively; no delayed perforations were reported and 1 case of bleeding occurred, managed endoscopically. There was no significant difference in median procedure time (56 min vs 67.5 min). At 3-months follow-up relapse was evident in one patient of the FTR group, treated with hybrid ESD while no relapse was reported for ESD group. Mean size of specimens was 21 mm for FTR (20;35) vs 37 mm (12-48) for ESD group. Histological analysis revealed: low-risk adenocarcinoma or adenoma (16 FTR, 46 ESD), high-risk adenocarcinoma (1 FTR, 2 ESD group).

Conclusion: Despite the few numbers of preliminary data and clear limitations when comparing two techniques with different advancement in asiatic and non-asiatic endoscopic centres, FTR showed to be a safe and effective procedure in residual/recurrent colonic lesions on scar and could become the standard of care in such lesions in Western Countries.

Disclosure: Nothing to disclose

P1601 FEASIBILITY OF HYBRID ENDOSCOPIC SUBMUCOSAL DISSECTION WITH MULTIFUNCTIONAL SNARE 'SOUTEN'

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Introduction: Colorectal endoscopic submucosal dissection (ESD) provides complete en bloc resection and precise pathological evaluations. However, ESD is still technically difficult and time required. Therefore, as an alternative option, Hybrid ESD may shorten the procedure time and enable to achieve an en bloc resection for relatively large lesions. Recently, a novel multifunctional snare (SOUTEN; Kaneka Medics, Tokyo, Japan) was intro-

duced to enable successful hybrid ESD procedures. Since the knob-shaped tip helps to stabilize the needle-knife, making it less likely to slip during circumferential incision and partial submucosal dissection, all the processes can be completed using 1 device.

Aims & Methods: The aim of this study is to evaluate the safety and efficacy of colorectal hybrid ESD. In this retrospective study, we applied Hybrid ESD using the "SOUTEN" for relatively large (20-30mm), non-pedunculated colorectal tumors. From June 2016 to December 2018, 46 lesions were removed by Hybrid ESD. Lesions involving the ileocecal valve and/or appendiceal orifice were excluded from this study. In addition, lesions with polypoid growth or converging fold and those suspected of exhibiting severe fibrosis were also excluded. The clinical characteristics and outcomes were evaluated. To assess the efficacy and safety of the hybrid ESD, we extracted the clinical data for patients who received conventional ESD randomly from our ESD database performed within the previous year adjusted for tumor size, morphology, and location.

Results: The patient age was 63.9±8.5 years. All the lesions were successfully resected with the hybrid ESD procedure. The tumor locations were 8, 10, and 28 in the rectum, left-sided colon, and right-sided colon, respectively. The mean procedure time was 16.6±4.8 minutes. The mean diameter of the resected specimen was 28.5±4.7mm, and the mean tumor size was 22.3±3.4mm. The histological assessment revealed low-grade dysplasia in 24 lesions, high-grade dysplasia in 20 patients and SM invasion in 2 lesions. En bloc resection was achieved in all the lesions and R0 resection was 89.1%(41/46) . Delayed bleeding occurred in 1(2.2%) patient and Perforation occurred in 1(2.2%) patient. These complications were controlled by endoscopic treatment. No significant differences in the rates of R0 resection, curative resection, or adverse events were seen between ESD and Hybrid ESD. However, the hybrid ESD group had a significantly shorter procedure time than the conventional ESD group (16.6±4.8 minutes vs. 37.5±21.1 minutes, P>0.001).

Conclusion: Hybrid ESD using a multifunctional snare may enable easy and safe resection of relatively large colorectal tumors. In addition, a cutting device and additional snare are usually required for hybrid ESD. But we could perform all the hybrid ESD steps using the "SOUTEN" snare. Therefore, multifunctional snare also may provide cost benefit.

Disclosure: Nothing to disclose

P1602 WITHDRAWN

P1603 USEFULNESS OF NARROW BAND IMAGING FOR COMPLETE ENDOSCOPIC RESECTION OF SESSILE SERRATED ADENOMA/POLYP (SSA/P), NASA STUDY: KASID MULTI-CENTER STUDY

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Introduction: Sessile serrated adenoma/polyp (SSA/P) is known as high risk lesion of incomplete resection. However, there have been very limited evidence about how to immediate detect of remnant lesion of SSA/P right after the endoscopic resection. We compared Narrow band imaging (NBI) and white light endoscopy (WLE) for detection of remnant lesion of SSA/P right after the endoscopic resection of SSA/P.

Aims & Methods: Prospective randomized multi-center study was done. All target lesions were suspicious SSA/P lesions which had 3 or more than 3 scores out of WLE criteria assigned 1 point on each criterion by observing WLE; non-protruding and non-excavated shape, larger than 1 cm in size, right colon location, being covered by mucus cap, and varicose vessels presence on the surface of the lesion after submucosal injection. After endoscopic resection, we performed NBI or WLE inspection by randomization for detection of remnant tissue, if detected, additional resection was performed. Four directional biopsies for checking the incomplete resection were performed on the resection margin after endoscopic resection including additional resection for remnant lesion. Primary aim was comparing the detection rate of remnant lesion, the diagnosis rate of SSA/P in the

remnant lesion after additional resection, and the incomplete resection rate between two groups. Secondary aim was finding accuracy of endoscopic WLE criteria for SSA/P diagnosis.

Results: Total 145 lesions (NBI inspection group, n=69, WLE inspection group, n=76) were removed. The diagnosis rate of SSA/P was 87.6% (127/145) by criteria. There were no significant differences of remnant tissue detection rate (14.5% vs. 13.2%, p>0.05), proportion of SSA/P of remnant tissue after additional resection (10.1% vs. 10.5%, p>0.05), and the incomplete resection rate (5.8% vs. 9.2%, p>0.05) between NBI and WLE groups. The positive predictive value (PPV) of the individual criteria for diagnosis of SSA/P were 95.2% (mucus cap), 92.2% (ascending colon and cecum location), 92.1% (varicose vessel), and 86.6% (non-protruding and non-excavated morphology). In ROC curve analysis, the sensitivity of the endoscopic criteria by WLE was 93.7% at the cut-off of 2.5 with 0.741 (95% confidence interval 0.588~0.895) of the area under the ROC curve.

Conclusion: There was no significant difference for detecting remnant lesion and for checking incomplete resection between NBI and WLE after endoscopic resection of SSA/P. WLE criteria showed moderate performance in diagnosing SSA/P.

Disclosure: Nothing to disclose

P1604 FEASIBILITY AND ACCEPTABILITY OF NOVEL COLONOSCOPY WITH COMPUTER AIDED EARLY DIAGNOSIS OF BOWEL CANCER

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Introduction: Patients with low risk bowel symptoms often triaged to a non-urgent pathway have longer diagnostic intervals and later detection of cancer. Resource and workforce constraints in delivery of secondary care colonoscopy contribute to these delays

Aims & Methods: This study presents preliminary data to investigate the acceptability and feasibility of a novel type of semi-automated robotic colonoscopy (portable with disposable probes not requiring reprocessing or decontamination) to potentially overcome delays between presentation, referral, diagnosis and treatment decision.

Participants referred by their GP for direct colonoscopy underwent the new procedure (semi-automated robotic colonoscopy) and a parallel (back to back design) standard colonoscopy and were later interviewed via telephone to explore their experience and comparison between the two procedures. Comfort scores and colonoscopy quality indicators and outcomes were compared. An online GP survey exploring feasibility of the new procedure in a primary care setting was also conducted. We also analysed the feasibility and accuracy of developing a machine learning tool to interpret findings at both novel and standard colonoscopy.

Results: Participants (6 M, 9 F) perceived the value, usefulness and purpose of the new procedure, with favourable comparisons made to standard colonoscopy, particularly previous experience of pain and recovery. Lack of requirement for sedation was a key benefit of the new procedure. Primary care was endorsed as a location, with proximity and familiarity viewed favourably, particularly in overcoming negative aspects of bowel preparation and recovery (e.g. not wanting to travel far). Those feeling they would not need sedation also viewed primary care positively. Others were indifferent, with feelings that it was such an undesirable procedure that location would not matter. Twenty-nine GPs completed the online survey. Barriers to the new procedure in GP practices included perceived lack of expertise to interpret findings (74% agreement) and not enough space for equipment (59% agreement). Nearly all participants felt the new procedure had the potential to impact quicker diagnosis (97% agreement), and all participants felt it had the potential to achieve early diagnosis in low risk bowel symptoms not meeting 2 week wait criteria (100% agreement).

Conclusion: Target users found the new procedure acceptable and viewed it favourably compared to standard colonoscopy. GPs perceived uses for the new procedure in primary care, particularly for low risk patients, however expertise and space were a concern. These findings are positive as the new procedure has the potential to improve issues with colonoscopy capacity and diagnostic workforce in the NHS, with a larger scale study now need-

ed. We have previously published on the training requirements and learning curve for the novel colonoscopy procedure and will also present data on computer aided analysis and interpretation of findings at colonoscopy.

References: Kopczynska M, Smits S, Hopps R, Ramaraj R, Warren N, Goddard S, Ye X, Dolwani S. Assessment of technical parameters and skills training to inform a simulation-based training program for semi-automated robotic colonoscopy. Endosc Int Open. 2019 Jan;7(1): E9-E14

Disclosure: Nothing to disclose

P1605 ENDOSCOPIC TREATMENT OF LARGE SYMPTOMATIC COLON LIPOMAS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Various techniques have been described for endoscopic resection of large symptomatic colon lipomas. Relying on spontaneous intraluminal expulsion following partial snare resection, lipoma unroofing might provide a safer, more cost effective and easier technique, compared to dissection-based techniques, endoscopic mucosal resection (EMR) or loop-assisted resection.

Aims & Methods: The aim of this systematic review was to compare efficacy and safety of these four endoscopic techniques. A systematic review was performed by AMVB and MB in March 2019, using PubMed, Embase, the Cochrane Library and Clinicaltrials.gov. As most outcomes were binary in nature and several outcomes did not occur in some studies, routine calculation of standard errors in outcome probability was not possible. Therefore, original patient data were extracted, after which complete resolution rate, recurrence rates and adverse events were compared.

Results: Twenty seven studies between 1979-2019 met selection criteria. In total, 119 lesions were identified (45.5% female, mean age 63 years, mean lesion size 47.9mm). In total, 5 retrospective analyses, 21 case reports and 1 prospective study were included. As no higher quality studies were found, possible publication bias should be taken in account. Heterogeneity was not assessed as most studies were not controlled. Ten patients underwent unroofing (8.4%), whereas 27 patients (22.7%), 33 patients (27.7%) and 48 patients (40.3%) underwent dissection-based technique, EMR or loop-assisted-snare resection respectively. Complete resolution rate was 80%, 100%, 100% and 95.8% respectively. A statistically significant increased rate of complete resolution was seen only amongst patients receiving EMR (OR 19.71 (0.86-450.00 95% CI), p=0.0498), compared to unroofing. As expected, no recurrence was detected in all four groups. More importantly, no adverse events were identified in patients receiving endoscopic treatment by unroofing. Amongst patients who underwent dissection-based resection, EMR or loop-assisted techniques, adverse events were identified in 7.4%, 12.1% and 6.3% respectively.

Conclusion: Compared to unroofing, dissection-based techniques and loop-assisted resection did not provide an increased complete resolution rate which was statistically significant. Owing to the superior safety profile, our data suggest that unroofing should be considered as the primary endoscopic technique for resection of giant colonic lipomas, before resorting to EMR, dissection-based or loop-assisted techniques. However, due to the nature of the studies included, possible publication bias should be taken into account

Disclosure: Nothing to disclose

P1606 BARRIERS TO CHROMOENDOSCOPY: EXPERIENCE IN AN IRISH TERTIARY CENTRE

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Introduction: Chromoendoscopy, CE, is the optimal choice of surveillance for dysplasia in the inflammatory bowel, IBD, disease cohort, particularly for primary sclerosing cholangitis, PSC. However, with the pressure of waiting list and busy endoscopy list, CE can be perceived as a cumbersome task.
Aims & Methods: To review the IBD colonoscopy surveillance practice in a tertiary centre of IBD and PSC patients with regard to CE, highlighting obstacles and perceived barriers. We performed a retrospective review of 121 surveillance colonoscopies for inflammatory bowel disease in a teaching tertiary hospital over a 12month period. Patient demographics including age, IBD phenotype and medication were recorded. Endoscopy settings such as bowel preparation, withdrawal time and endoscopist expertise were recorded along with pre-endoscopy faecal calprotectin. Mode of examination by CE, targeted biopsies or quadrantic biopsies every 10cm were noted.
Results: 121 surveillance colonoscopies were performed over 12months. Median cohort age: 48years. Male:71(58.6%). 58, 25, 2 and 36 patients had Crohn's Disease, Ulcerative colitis, IBD undetermined and PSC-IBD respectively. CE, white band light, WBL, targeted biopsies and quadrantic biopsies at 10cm intervals were performed in 30, 74, and 12 patients respectively. 5 patients had no biopsies taken due to failed procedures/ poor preparation. 49/121(40.5%) had active disease at time of assessment, 9/121(7%) having moderate to severe disease. 41 patients had a faecal calprotectin, FCP, within the 12 months prior to endoscopy, 11/41(27%) of which were >200. 69/121(57%) patients had excellent bowel preparation. However, 52/121(42.9%) had reported adequate or poor preparation, not compatible with EC.
Amongst th4 CE cohort, there was no significant predominance in expertise of endoscopist, fellow 17/30, consultant 13/30. Average withdrawal time for consultants for non-chromo v CE was insignificant; 15.4 v 21 minutes (p value- 0.0571). Average withdrawal time for fellows for non-chromo v CE was significant; 19 v 30 minutes (p value 0.0020). 25/30 patient were reported to have excellent bowel preparation. There was a significant difference between the incidence of CE amongst hepatologist and gastroenterologist endoscopists; 1/17 v 29/91 (p value 0.0020).
Amongst the PSC-IBD cohort, 8/36 patients received chromoendoscopy in equal measuring from fellow and consultant endoscopists. 11/36(30%) patients were reported to have poor bowel preparation not compatible with CE. 6/36(17%) patients had active disease not compatible to EC.
Conclusion: The quality of surveillance endoscopy is influenced by the degree of bowel preparation, remission of disease and mode of inspection. Poor bowel preparation was found to be a significant obstacle to CE, particularly in the PSC-IBD cohort. Few patients had a recent FCP to ensure remission prior to colonoscopy. Both these factors can be optimised pre-endoscopy to facilitate EC performance. While it may be perceived to be a longer procedure, no significance in withdrawal time was seen amongst consultant endoscopy performing EC and standard white light colonoscopy suggesting initial delays seen amongst fellow endoscopist reflects a learning curve.
Disclosure: Nothing to disclose

P1607 CORRELATION BETWEEN SURROGATE QUALITY INDICATORS FOR ADENOMA DETECTION RATE (ADR) AND ADENOMA MISS RATE (AMR) IN QUALIFIED COLONOSCOPY, CORE STUDY; KASID MULTI-CENTER STUDY

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Introduction: Adenoma detection rate (ADR) has been known as a key quality indicator of colonoscopy. However, ADR cannot reflect every adenoma detection during colonoscopy and still it is unclear that ADR can properly reflect adenoma missing rate (AMR). We evaluated the correlation between AMR and ADR, and other surrogate quality indicators.
Aims & Methods: We performed a cross-sectional study of asymptomatic examinees aged 50~75 years who underwent back-to-back screening colonoscopies by 8 endoscopists. The polyp detection rate including adenoma (PDR), the total number of adenomas per colonoscopy (APC), the additional adenomas found after the first adenoma per colonoscopy (ADR-Plus), the total number of adenomas per positive participant (APP), and ADR were calculated for prediction of AMR.
Results: Total 371 back-to-back colonoscopies were performed. ADRs were 64.6% in male, and 51.1% in female examinees (p=0.009). Because there was a significant difference in the gender of the examinees by each endoscopist (p< 0.001), and also was a significant difference of ADRs (65.6, 44, 64.3, 75.4, 54, 48, 52, and 60%, p=0.024), ADRs were separately obtained by gender. There were no significant differences of ADRs of each endoscopist obtained separately for male (p=0.335) and female (p=0.218) examinees. AMRs not differed between endoscopists (31.3, 9.1, 21.9, 22.1, 10.9, 12.5, 19.2, 22.9%, p=0.462) for male examinees and for female examinees (27.8, 8.7, 0, 18.2, 46.4, 0, 31.8 and 23%, p=0.052). There was no related quality indicators with AMR in both male and female examinees. Overall, PDR was significantly correlated with ADR (rho 0.826, p=0.011). In female participants, PDR (rho 0.904, p=0.002) and APC (rho=0.838, p=0.009) were significantly correlated with ADR.
Conclusion: High ADRs endoscopists showed varied AMRs. PDR and APC may be surrogate quality indicators for ADR. However, further studies for surrogate quality indicators to discriminate meticulous endoscopists should be performed.
Disclosure: Nothing to disclose

P1608 WHATSAPP REMINDER IMPROVES THE QUALITY OF COLORECTAL CANCER SCREENING. A SINGLE BLINDED RANDOMIZED CONTROLLED STUDY

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Introduction: Bowel preparation is one of the important factors to ensure a high quality colonoscopy. Efforts to improve bowel preparation level through traditional communication routines have proven to be useful. However, the impact of WhatsApp reminder on the bowel preparation level of screening colonoscopy is still unknown.
Aims & Methods: We aimed to investigate the effectiveness of WhatsApp reminder in bowel preparation level of screening colonoscopy.
Subjects recruited and randomized form a population based CRC screening program. All subjects would receive both verbal and written instructions of bowel preparation by a healthcare professional on the day of appointment making. For subjects randomized to the WhatsApp reminder group, they will receive a WhatsApp reminder with same content of the written instruction and a video of detailed bowel preparation instruction 4 days prior colonoscopy. For subjects randomized to usual care group, they will not receive any reminder.

	WhatsApp reminder	Usual Care	p-value
	N = 333	N = 333	
Male Gender (%)	197 (59.2)	195 (58.6)	0.875
Age (SD)	65.4 (3.8)	65.7 (3.9)	0.261
Hypertension (%)	133 (39.9)	125 (37.5)	0.525
Diabetes (%)	47 (14.1)	3 (12.9)	0.65
Ischemic heart disease (%)	25 (7.5)	22 (6.6)	0.65
Chronic obstructive pulmonary disease (%)	4 (1.2)	3 (0.9)	1
Cirrhosis (%)	2 (0.6)	1 (0.3)	1
Renal impairment (%)	2 (0.6)	5 (1.5)	0.451
Fatty liver (%)	8 (2.4)	5 (1.5)	0.401
Caecal intubation (%)	328 (98.5)	327 (98.2)	0.761
	N = 328	N = 327	
Median withdrawal time in minutes (IQR)	11 (7-17)	10 (7-16)	0.399
Median intubation time in minutes (IQR)	6 (4-9)	6 (4-9)	0.579
Satisfactory bowel preparation level (%)	283 (86.3)	257 (78.6)	0.01
Adenoma detection (%)	240 (72.9)	227 (69.4)	0.318

[Demographics and colonoscopy findings between WhatsApp reminder and usual care groups]

Results: From June 2017 to April 2019, 667 subjects scheduled for screening colonoscopy because of positive fecal immunochemical test were recruited. They were randomized to WhatsApp reminder and usual care groups in 1:1 ratio. Demographics between two group was similar. 12 subjects with incomplete colonoscopy were excluded. No difference can be observed in median intubation and withdrawal time between two groups. When compared to usual care group, more subjects significantly achieved satisfactory (excellent or good) bowel preparation level (86.3% vs 78.6%, p=0.01) during screening colonoscopy. However, adenoma detection rate was similar between two groups (72.9% vs 69.4, p=0.318).

Conclusion: WhatsApp reminder shows significant improvement in the bowel preparation level of screening colonoscopy.

Disclosure: Nothing to disclose

P1609 TIME'S UP: FATIGUE NEGATIVELY IMPACTS COLONOSCOPY ADENOMA DETECTION RATE

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Introduction: The quality of colonoscopy is influenced by patient and operator factors. Various studies on timing of colonoscopy and effect of operator fatigue on adenoma detection (ADR) have yielded conflicting results (1-3). This study aims to compare adenoma detection and complication rates between elective colonoscopies performed first and last in the list, across multiple operators (n=12) in a tertiary public hospital.

Aims & Methods: We conducted a case-control study on patients who underwent elective colonoscopies from 2012 to 2017 at the Prince Charles Hospital. Time of endoscopy was used as a surrogate marker for operator fatigue, whereby colonoscopies performed after 11am on the morning list and after 4pm on the afternoon list were identified as cases, and matched with those performed before 9am and at or before 1pm as controls. Clinical, endoscopic and histological databases were analysed for baseline patient characteristics, colonoscopy quality markers, and adverse events from a 30-day follow up survey.

Results: We report on preliminary analysis of 1216 patients who underwent colonoscopies between April and June 2017. The patients were booked in no particular sequence and have similar baseline characteristics. Colonoscopies done later in the list had lower adenoma detection rates (39.7% vs 55.7%, OR 0.5, p=0.007) and lower mean adenoma count (1.2 vs 1.9, p=0.04). No statistically significant difference was found in SSA detection rates, quality of bowel preparation, and complication rates.

Conclusion: Preliminary data suggests a significant deterioration in colonoscopy quality associated with operator fatigue. Further analysis with stratified data for individual operators, and on extended dataset between 2012-2017 will be carried out to confirm these findings.

References: 1.Almadi MA, Sewitch M, Barkun AN, Martel M, Joseph L. Adenoma detection rates decline with increasing procedural hours in an endoscopist's workload. Canadian Journal of Gastroenterology & Hepatology. 2015;29(6):304-308. 2.Subramanian S, Psarelli EE, Collins P, et al. Colonoscopy performance is stable during the course of an extended three-session working day. Endoscopy International Open. 2015;3(5):E494-E500. doi:10.1055/s-0034-1392523. 3.Lee A, Jensen CD, Marks AR, et al. Endoscopist fatigue estimates and colonoscopic adenoma detection in a large community-based setting. Gastrointestinal endoscopy. 2017;85(3):601-610. e2. doi:10.1016/j.gie.2016.09.033.

Disclosure: Nothing to disclose

P1610 ENDOSCOPIC TATTOOING OF COLORECTAL LESIONS AT NOTTINGHAM UNIVERSITY HOSPITALS: ARE WE SPOT ON?

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Introduction: Endoscopic tattooing is a safe technique useful for localisation of small colorectal lesions, especially in the laparoscopic setting. However, many studies have reported variation in tattooing practice, resulting in inaccuracies in diagnosis and management. The aim of this study was to review tattooing practice in all patients with colorectal cancer and high grade dyplastic polyps who were discussed at the colorectal multidisciplinary team meeting (MDT) at Nottingham University Hospitals (NUH) in 2016.

Aims & Methods: Minutes and colonoscopy reports for all new cases discussed at the colorectal MDT in 2016 were analysed. Cases discussed at the MDT were those with colorectal cancer, polyps with cancer, high grade dysplasia, or suspicious for malignancy. Tattooing practice was evaluated against the local NUH colon tattoo protocol. This states that all suspected cancers identified, excluding those located at the caecum and rectum, should be tattooed at 3 radial sites, 3 cm anal to the lesion. Colonic polyps >2 cm (excluding caecum and rectum) and/or suspicious for malignancy, should be tattooed at at least 1 site 3 cm anal to the lesion. Tattoos and their relationship to the lesion should be photo-documented.

Cases discussed at the colorectal MDT were excluded if they had been previously discussed, the endoscopy report was unavailable, the cancer was identified at emergency surgery or on CT only or there was no cancer/polyp at colonoscopy.

Results: The results are shown in table 1.

	n	Tattooed (%, 95% CI)	Tattooed as per protocol (%, 95% CI)
Colonic cancer	133	96 (72.2, 63.7-79.1)	49 (51.0, 40.6-61.4)
Malignant polyp	14	10 (71.4, 41.9-91.6)	23 (52.3, 36.7-67.5) [all polyps]
HGD polyp	55	24 (43.6, 30.3-57.7)	
LGD or other polyp	21	10 (47.6, 25.7-70.2)	
Suspected rectal cancer	116	17 (14.7, 8.8-22.4)	
Suspected caecal cancer	24	7 (29.2, 12.6-51.1)	

[Table 1: Results]

Rates of tattooing were similar across males and females. There was some variation by patient age, location of the cancer and who did the index colonoscopy. For example, only 59.1% of patients had a tattoo if the index colonoscopy was performed by consultant surgeon compared to over 70% by other professionals (p>0.05). With regards to tattooing as per local protocol, the lowest rate (33%) was seen with independent trainee colonoscopists (p>0.05). No variables however were identified to have statistically significant associations with increased rate of tattooing polyps.

Conclusion: How and when to tattoo colonic lesions is becoming increasingly pertinent in the age of minimally invasive surgery. This audit highlights the need for improvement in this area and serves as a reminder for us to align routine clinical practice with local guidelines. Given these findings, we believe there is a role for regular standardised teaching on endoscopic tattooing for endoscopists.

We acknowledge the limitations inherent in our study, including the small sample size of the study. However, we are undergoing a re-audit for year 2019 of similar qualitative study to ascertain improvements. As conclusion, we consider our findings an important first step towards effective clinical management, and prevention of colorectal cancers.

Disclosure: Nothing to disclose

P1611 DO PATIENTS REDEVELOP THE SAME LESIONS AFTER RESECTING THEM?

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Introduction: Colorectal cancer can arise from nonadvanced adenomas or advanced adenomas. Patients with advanced adenomas have higher risk to develop CRC (Brenner et al., Gut. 2007).

Aim of this study was to see if patients redevelop advanced- or nonadvanced lesions by comparing diagnosis of baseline colonoscopy with diagnosis of surveillance colonoscopy.

Aims & Methods: In this retrospective study 5175 patients underwent two colonoscopies within 1-10 years. Data stem from the Austrian certificate of screening colonoscopy. Diagnosis of patients in first screening colonoscopy got compared with diagnosis of surveillance colonoscopy with a Chi-square-test.

Results: Mean surveillance interval was 4 years. 372 patients (7,19%) got diagnosed with advanced adenomas, 1384 (26,74%) had nonadvanced adenomas and 3419 (66,07%) had no pathological findings in first screening colonoscopy. Diagnosis of surveillance colonoscopy per baseline colonoscopy are shown in table 1. (p=0,0001). Most patients who got diagnosed with advanced adenomas in screening colonoscopy had no pathological findings or nonadvanced adenomas in surveillance colonoscopy. Patients who got diagnosed with nonadvanced adenomas in screening colonoscopy had mostly no pathological findings or got diagnosed with nonadvanced adenomas again.

	Advanced adenomas in surveillance colonoscopy	Nonadvanced adenomas in surveillance colonoscopy	No pathological findings in surveillance colonoscopy
Advanced adenomas in screening colonoscopy	77 (20,70%)	135 (36,29%)	160 (43,01%)
Nonadvanced adenomas in screening colonoscopy	93 (6,72%)	580 (41,91%)	711 (51,36%)
No pathological findings in screening colonoscopy	208 (6,08%)	680 (19,89%)	2531 (74,03%)

[Table 1]

Conclusion: Most of the patients who had advanced- or nonadvanced lesions inscreening colonoscopy had no pathological diagnosis in surveillance colonoscopy. Nevertheless, results demonstrate that patients, who got diagnosed with advanced- or nonadvanced adenomas, redeveloped adenomas, which shows the importance of accurate surveillance colonoscopy. Chi-square test was significant (p=0,0001).

Disclosure: Nothing to disclose

P1612 INFLUENCE OF MOON PHASES ON BOWEL PREPARATION QUALITY IN A SCREENING COLONOSCOPY COLLECTIVE

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Introduction: Moon phases, in particular full moon, are often discussed to have an impact on sleep and activity behavior as well as various other functions of the human body.

Aims & Methods: The aim of the present study was to investigate the impact of moon phases on bowel preparation quality. Therefore, we analyzed bowel preparation quality according to a modified Aronchick Score in screening colonoscopies performed between 08/2008 and 12/2018 within a national quality assurance program in Austria. Preparation quality rated as excellent, good or fair were considered sufficient.

Results: 207,593 screening colonoscopies were included in the study. 50,74% of screenees were woman, mean age was 60.9 years (SD 9.1). Bowel preparation quality was sufficient in 95.94% of examinations. Overall bowel preparation quality differed significantly between moon phases (new/waning/waxing/full moon, p=0.014). 3.12% (n=6,480) of colonoscopies were performed the day after a full-moon night. Those patients had a significantly higher rate of inadequate bowel preparation as compared to other moon phases (relative risk 1.18 [95% CI 1.06-1.32], p=0.004). Notably, this effect was only significant in men (5.32% vs. 4.22% insufficient preparation; p=0.003%, women p=0.26%).

Conclusion: If screening colonoscopy is scheduled on a day after a full moon night, patients, particularly male patients, should be intensely instructed to follow bowel preparation guidelines.

Disclosure: Nothing to disclose

P1613 PREVALENCE OF ADENOMAS AMONG DIMINUTIVE UNRESECTED POLYPS IN LEFT COLON

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Introduction: The American Society for Gastrointestinal Endoscopy (ASGE) recommends that diminutive polyps located in the distal colon can be left in place without any resection if they are predicted to be nonadenomatous with a negative predicting value of >90%. However, we know that approximately 30% of adenomas are located in the left colon. Therefore, aim of our study was to assess the prevalence of adenomas among unresected diminutive polyps in the distal colon.

Aims & Methods: 315.822 screening colonoscopies between 2007 and March 2019 performed by 355 endsocopists were analyzed within the Austrian quality assurance program. Histopathologic diagnosis of polyps under 5mm located in the left colon that were not resected but where endoscopists took biopsies to ensure were assessed. Further the negative predictive value for adenomatous lesions among those polyps was analyzed.

Results: Overall In 39,24 % (n= 123.942) polyps were detected. 14,18% (n=17581) were diminutive and located in the left colon. 3,22% (n=566) of those lesions remained unresected but a biopsy was taken.

Among those 566 unresected diminutive polyps 2,83% (n=16) were advanced and 21,91% (n=124) nonadvaned adenomas. In 0,35% (n=2) those lesions were characterized as SSA and in 0,53% (n=3) as TSA. 421 (74,38%) of all unresected left sided diminutive lesions were classified as hyperplastic polyps.

Conclusion: In our study cohort there was a high prevalence of adenomas (24,74%) among unresected diminutive polyps in the left colon were a biopsy was performed. The negative predictive value for adenomas, SSAs, as well as TSAs was 74,38% which is lower than recommended. Therefore left-sided diminutive lesions that macroscopically appear to be hyperplastic but were the endoscopist decided to take a biopsy should be resected. Only in case the endoscopists can characterize the adenomatous lesions with high confidence, predict and leave behind strategy may be used.
Disclosure: Nothing to disclose

P1614 EFFICACY OF ENDOSCOPIC TREATMENT IN LARGE BILE DUCT STONES: A REVIEW OF A TUNISIAN SERIES

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Introduction: Therapeutic endoscopic retrograde cholangiopancretography (ERCP) is the first approach in the management of bile duct stones. It is estimated that bile ducts can be cleared in 90% of the cases with conventional endoscopic methods. Large stones, however, can be sometimes challenging to remove.
Aims & Methods: The aim of our study was to investigate the management and the complications associated with large common bile duct stones.
We realized a retrospective study including all patients that underwent an ERCP between 2013 and January 2018. The patients who had common bile duct stones were divided into two groups:
- First group: those who had large common bile duct stones (>=10mm).
- Second group: patients with smaller common bile duct stones.
Results: During the study period, 424 ERCPs were performed to remove common bile duct stones. The mean age of the patients was 61,3 years old (13-98) with a sex ratio (F/M) of 2. Large stones have been found in 22,16% of the procedures (n=94). In both groups of patients, an acute biliary pancreatitis or cholangitis was associated in 5,3% of the cases. Bile duct clearance was obtained respectively in 95,74% and 90,6% within the first and second group. Nine patients from the first group needed more than one ERCP. When it came to large stones, lithotripsy was performed in 5 patients, we placed a nasobiliary catheter once and a biliary endoprostheses in 12 patients. Among the second group, a biliary endoprostheses was needed 5 times and one patient had a nasobiliary catheter placed. No difference was found in terms of short term ERCP complications between the two groups (p=0,349).
Conclusion: Large common bile duct stones may require additional techniques while ERCP to be removed but do not cause more short term complications than smaller bile duct stones.
Disclosure: Nothing to disclose

P1615 EFFICACY OF INTRAMUSCULAR DICLOFENAC IN THE PREVENTION OF POST-ERCP PANCREATITIS: A PROSPECTIVE, RANDOMIZED, PLACEBO-CONTROLLED STUDY

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Introduction: Rectal nonsteroidal anti-inflammatory drugs (NSAIDs) reduce the risk and the severity of post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis (PEP). However, rectal NSAIDs are not available in some countries including Korea. Recently, two contrary studies about the effect of intramuscular NSAIDs to PEP had been reported. The aim of this study was to evaluate the efficacy of intramuscular NSAIDs in prevention of PEP.
Aims & Methods: This is prospective, randomized, placebo-controlled clinical trial. Patients who underwent ERCP with naïve papilla received single dose of intramuscular diclofenac (75mg) or placebo immediately before

ERCP. The primary outcome was PEP, which was defined as followings; newly developed abdominal pain, elevation of serum amylase or lipase at least three times the upper normal limits 24 hours after ERCP, and prolongation of hospitalization at least 2 days.
Results: Total 171 patients were randomized, and 168 patients were finally enrolled in study. Demographic and clinical factors, comorbidities, ERCP findings, and types of treatment were similar between two groups. The PEP developed in 6 of 73 patients (8.2%) in the diclofenac group and in 5 of 95 patients (5.3%) in placebo group (p=0.443). While most of PEP had mild severity (90.9%), moderate case was only 1 patient of PEP in diclofenac group (p=0.338). There was no case of severe PEP in both groups. In multivariate logistic regression analysis, factor associated with prevention of PEP was endoscopic retrograde pancreatic drainage (odds ratio 0.012; 95% confidence interval 0.001-0.184; p-value=0.002) and not intramuscular diclofenac (odds ratio 0.565; 95% confidence interval 0.114-2.798; p-value=0.565).
Conclusion: Intramuscular diclofenac does not seem to be effective in prevention of PEP.
Disclosure: Nothing to disclose

P1616 WEIGHT-BASED DOSING STRATEGY IN RECTAL DICLOFENAC USE IS FEASIBLE FOR PREVENTION OF POST-ERCP PANCREATITIS IN A REAL-WORLD JAPANESE POPULATION

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Introduction: Acute pancreatitis is a common complication after endoscopic retrograde cholangiopancreatography (ERCP) and called post-ERCP pancreatitis (PEP). It is, however, difficult to completely prevent it. ESGE guideline 2014 says that nonsteroidal anti-inflammatory drugs (NSAIDs) routine rectal administration of 100mg of diclofenac or indomethacin immediately before or after ERCP in all patients without contraindication. 100 mg of diclofenac is higher than the normal single dose used for the Japanese population. However, there are still few evidence of the efficacy of a low dosage of rectal diclofenac in a real-world Japanese population. The aim of this study was to evaluate the efficacy of low-dose diclofenac use based on weight for prevention of PEP.
Aims & Methods: This study was a retrospective single-center cohort study of consecutive patients underwent ERCP or ERCP-related procedures from January 2016 to March 2019. During the study period, procedures were conducted to prevent PEP using either 50mg or 25mg of rectal diclofenac in patients weighing ≥50kg or < 50kg and intensive intravenous fluid administration when post ERCP 2-hour serum amylase level was more than 2 times of upper limit of normal. Before the study period, we conducted the PEP prevention strategy using prophylactic antibiotics and protease inhibitor for 3 days without the use of NSAIDs. The PEP rate was 3.9% (95% CI: 3.02-5.07) in 1403 patients as historical control (World J Gastrointest Endosc. 2016). In the present study, we evaluated the PEP rate of weight-based dosing strategy in rectal diclofenac use. The following conditions were excluded: 1) gallstone pancreatitis, 2) unreachable to papilla, 3) no use of diclofenac.
Results: A total of 1241 patients (median age 76, female 43%) were enrolled. Of them, 181 cases were excluded. Finally, 1060 cases were analyzed (native papilla: 514, 48%, diclofenac 25mg: N=561, 53%, 50mg: N=499, 47%). The median cannulation time was 1 min (range 1-82), and the median procedure time was 30 min (range 3-120min). PEP developed in 26 patients (2.4%, 95%CI: 1.7-3.6) including 4 severe acute pancreatitis, and perforation and bleeding occurred 0 and 2 patients, respectively. PEP rates were similar in both diclofenac 25 mg and 50 mg (2.7% and 2.2%, respectively).
Conclusion: Low dose rectal diclofenac use and intensive intravenous fluid administration strategy is relatively lower PEP rate than our historical control. It seems to be better compared with the strategy using protease inhibitor without the use of NSAIDs.
Disclosure: Nothing to disclose

P1617 MANAGEMENT OF PANCREATICOJEJUNAL ANASTOMOTIC STENOSIS FOLLOWING PANCREATODUODENECTOMY WITH SINGLE-BALLOON ENTEROSCOPY ASSISTED ENDOSCOPIC RETROGRADE PANCREATOGRAPHY (SBE-ERP)

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Introduction: Pancreaticojejunal anastomostic stenosis (PAS) is recognised as one of the long-term complications post pancreatoduodenectomy (PD). PAS can cause acute pancreatitis and associated complications such as stone formation. Balloon-assisted enteroscopy (BAE) has been available since 2003. It's primary use has been for therapy post hepato-biliary surgery. However, data pertaining to efficacy, safety, and long-term outcomes of the optimal enteroscopic approach for PAS is lacking.

Aims & Methods: Our aim is to assess the efficacy, safety, and long-term outcomes of single-balloon enteroscopy for PAS related acute pancreatitis post PD. 8 patients between November 2013 and March 2017 were enrolled from our center.The pancreaticojejunal anastomosis was assessed with a single balloon enteroscope, using a 3/0 prolene suture for identifying the site. We then proceeded to followed by replacing the plastic stent. Follow up stent removal were performed at 3 months. We recorded;
1) the duration of the onset of acute pancreatitis after operation,
2) success rate of endoscopic treatment,
3) procedure time,
4) complication rate, and
5) recurrence rate of pancreatitis.

Results: The median age in these 8 patients are 66 years old, and male/female are 4/4. All 8 patients underwent pylorus-preserving pancreaticoduodenectomy (PPPD) for malignancy. The average total observation period since PD was 94 (41-151) months, while the period since first treatment was 41 (14-61) months.
1) The mean to time of onset of acute pancreatitis after PD was 45 months (8-129) months.
2) 7 out of 8 patients had a successful endoscopic result (88%).
3) The average procedure time was 86 (56-124) minutes.
4) Two patients (25%) who had hyper amylasemia and one patient (13%) experienced the recurrence of acute pancreatitis due to stent migration. However, there were no serious complications in these 8 patients.
5) 3/7 (42%) cases had recurrence of pancreatitis after recurrent PAS.
For these 3 recurrent cases, the average duration of recurrent pancreatitis was 19 (11-35) months. Despite repeated endoscopic treatment, all three patients experienced multiple episodes of acute pancreatitis.

Conclusion: The previous reports have mentioned that the rate of pancreatitis was 3% after PPPD, with surgical management considered as first line therapy. Evidence for BAE-ERP treatments for PAS have been limited to case reports. However, reported issues include difficulty in identification of the pancoreaticojejunal anastomosis and thus success rate varies. In our study, the success rate was as high as 88% due to using 3/0 prolene sutures as an indicator for locating pancreaticojejunal anastomosis. We had shorter procedure times without signficinat adverse events. Therefore, endoscopic treatment is safe, and less invasive technique in this small case series. Further prospective, multi-centre studies are required to validate our findings.

Disclosure: Nothing to disclose

P1618 ENDOSCOPIC MANAGEMENT OF MINOR AMPULLARY TUMORS: A MULTICENTER CASE SERIES

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Introduction: Ampullary and duodenal carcinoma are aggressive cancers with poor 5 year survival rates. Like colorectal cancer, ampullary and duodenal carcinomas are also thought to follow the adenoma-carcinoma sequence. Ampullectomy is a well-established treatment for adenoma and early stage carcinoma of major ampulla. Several studies have established its safety and efficacy in the management of major ampullary adenomas. However, adenomas arising in the minor ampulla are relatively rare and there are no good case series on endoscopic management of these tumors. We report a multicenter case series of endoscopic ampullectomy in the management of minor ampullary tumors.

Aims & Methods: To establish the safety and efficacy of endoscopic ampullectomy in the management of minor ampullary adenomas. Consecutive patients undergoing ampullectomy for minor ampullary tumor at four hospitals were included in this study over a period of 5 years. A total of 6 patients were included in the study and all six patients underwent ERCP for purpose of minor ampullectomy. MRCP and EUS was performed on all patients prior to ERCP to rule out invasion. Pancreatic stents were placed after ampullectomy in 5 patients, 3 F x 8 cm single pigtail stents in 4 patients, and 5 F x 5 cm straight stent in one patient. All stents were removed in approximately 2 weeks.

Results: Ampullectomy was technically successful in all 6 patients. One patient required two ERCPs for complete ampullectomy. The adenomas varied in size from 1 cm to 3 cm. Pathology revealed adenoma in three patients, adenoma with high grade dysplasia in one patient, carcinoma in one patient, and carcinoid tumor in one patient. One patient (16%) developed post ERCP pancreatitis; this patient was kept in the hospital for 2 days. No other major complications were noted. Two patients had abdominal pain for one day post ERCP; this was considered a minor complication. Follow-up for these patients ranged from 2 to 5 years with EGD using duodenoscope at 3 months, one year and yearly thereafter. One patient had recurrence at 2 years which was thought to be recurrent adenoma (4 mm). This patient was treated with repeat ampullectomy. The patient with carcinoma had endoscopies every 3 months for a year followed by yearly endoscopy; no recurrence was noted during the 3 years of follow-up. An EUS, MRI and PET scans were also performed at 1 year per oncology advice; all tests were negative. Two out of six patients (33%) had Familial Adenomatous Polyposis (FAP). Two patients had Pancreas Divisum, one with Type 1, and other with type 3 Divisum.

Conclusion: In our pilot study, endoscopic ampullectomy appears safe and effective in the management of minor ampullary adenomas.

References: 1.Lapp, Robert T, and Grant F Hutchins. Minor Papilla Adenoma Management in Patients with Pancreas Divisum and Familial Adenomatous Polyposis. ACG Case Reports Journal, American College of Gastroenterology, 8 Oct. 2013 2.Han J, Kim M-H. Technical Review: Endoscopic papillectomy for adenomas of the major duodenal papilla (with video). Gastrointestinal Endoscopy. 2006;63:292-301. doi:10.1016/j.gie.2005.07.022. 3.Irani S, Arai A, Ayub K, et al. Papillectomy for ampullary neoplasm: results of a single referral center over a 10-year period. Gastrointest Endosc. 2009;70:923-932. 4.Sugiyama M, Kimura W, Muto T, et al. Endoscopic resection of adenoma of the minor papilla. Hepatogastroenterology. 1999;46(25):189-192. 5.Lucena JF, Alvarez OA, Gross GW. Endoscopic resection of heterotropic pancreas of the minor duodenal papilla: Case report and review of the literature. Gastrointest Endosc. 1997;46(1):69-72.

Disclosure: Nothing to disclose

P1619 COMPARATIVE ADVERSE EVENT ANALYSIS IN ERCP BETWEEN POST LIVER TRANSPLANT AND NATIVE HEPATOBILIARY ANATOMY

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) carries potential for procedure-related adverse events. Several clinical variables have been identified in prior studies that increase risk for such events. We are reporting data from our ERCP experience to compare adverse events post-ERCP between post-orthotopic liver transplant (pOLT) patients and patients with native anatomy (nOLT).

Aims & Methods: A retrospective review was conducted with prospectively maintained patient data at a single, high-capacity ERCP center. ERCP encounters between Dec 2017 and Oct 2018 were identified from endoscopy software. During this time outpatients were contacted within 72 hours of ERCP to assess for adverse events. Individual patient demographics, clini-

cal and endoscopy data, and reported outpatient and inpatient adverse events were recorded from the electronic medical record. Fisher's exact test was utilized to determine significance between rates of adverse events between pOLT patients and nOLT patients.

Results: 312 nOLT patients underwent 415 ERCPs and 43 pOLT patients underwent 66 ERCPs. 75.6% and 62.8% of nOLT and pOLT patients, respectively, underwent only one ERCP during the study time period; 17.6% and 20.9% had two ERCP encounters and 6.7% and 16.3% had three or more ERCP encounters. The average age of nOLT and pOLT patients was 60 and 55 with both groups being mostly male (71.4% and 54%, respectively). 12.1% of nOLT had cirrhosis prior to ERCP. Leading etiologies of liver disease in the transplant group included non-alcoholic steatohepatitis (28.6%), hepatitis C (21.4%), and alcohol-related (19%). Chronic kidney disease ≥ stage III was found in 4.5% (nOLT) and 11.9% (pOLT) of patients. 13.4% nOLT and no pOLT patients had comorbid pancreaticobiliary malignancy. 19.5% and 4.8% of nOLT and pOLT patients reported a history of acute pancreatitis prior to ERCP. The pOLT group had a greater rate of bile duct strictures than the nOLT group (54.5% vs. 28.4%, p = 0.0001) while the rate of choledocholithiasis was similar (30.3% vs 34.4%, p = 0.58). Stent manipulation was performed in a majority of cases (nOLT 69.6% and pOLT 90.9%, p = 0.0002). Rectal indomethacin was used more often in native anatomy (14.7% vs 1.5%, p = 0.0012). Total adverse event rates were similar in both groups (10.1% nOLT and 10.6% pOLT, p = 0.83) and rates of post-ERCP pancreatitis in nOLT was 1.9% and in pOLT was 6.1%, p = 0.068). Additional ERCP data is described in Table 1.

Conclusion: While pOLT status does not appear to independently predict overall increased rate of adverse events after ERCP, we observed in our cohort that pancreatitis occurs nearly three times more frequently. The transplant group also received indomethacin much less often. A larger prospective study with to further analyze these differences is recommended.

Disclosure: Nothing to disclose

P1620 LONG-TERM FOLLOW-UP: TRANSPANCREATIC BILIARY SPHINCTEROTOMY FOR BILIARY ACCESS IS SAFE

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Introduction: Transpancreatic biliary sphincterotomy (TPBS) is an advanced cannulation method for access to common bile duct (CBD) in endoscopic retrograde cholangiopancreatography (ERCP). If CBD cannulation is difficult, endoscopist can open the septum between the pancreatic and the biliary duct with a sphincterotome to gain the access. Long-term results of this procedure are not well-known. We wanted to evaluate the short- and the long-term complications of TPBS on patients with native papilla.

Aims & Methods: ERCPs performed during years 2007 to 2013 in Helsinki University Hospital Endoscopy unit were reviewed. After exclusion of primary sclerosing cholangitis, chronic pancreatitis (CP), biliary or pancreatic malignancies and deceased patients, there were 170 consecutive TPBS patients with native papilla and a benign indication for ERCP. For these TPBS patients we searched 170 consecutive age- and sex matched controls with same inclusion criteria, but with successful biliary access by primary wire-guided cannulation. Of these groups, 143 (84.1%) patients and 140 (82.6%) controls participated the phone survey ≥ 4 years after first ERCP. Data of patient demographics, acute post-ERCP pancreatitis (PEP), recurrent pancreatitis, CP or symptoms related to CP, upper abdominal pain, new ERCP procedures and surgical treatments was collected from patient records.

Results: PEP developed to seven patients (4.9%) in TPBS and one patient (0.7%) in control group (p=0.067). Other acute complications (cholangitis, perforation, bleeding) were not significantly different between the groups (Table 1). ERCP ended with no access to biliary tract in four cases (2.8%) p=0.122 in TPBS group and all ERCPs in control group were successful. Three patients (2.1%) in TPBS and six patients (4.3%) in control group (p=0.238) suffered from acute recurrent non-ERCP related pancreatitis during the follow-up period. Only one (0.7%) patient in control group developed CP and there were no patients with CP in TPBS group. Upper abdominal pain was as common in both groups: 10 patients (6.9%) in TPBS group and 12 patients (8.6%) in control group suffered from abdominal pain daily and six patients (4.2%) in TPBS group and 12 patients (8.6%) in control group weekly.

	TPBS group (n=143)	Control group (n=140)	p-value
Age* at ERCP	59 (18-93)	62 (21-89)	0.418
Female	106 (74.1)	99 (70.7)	0.595
BMI* (kg/m²)	26.0 (16.9-70.3)	27.9 (16.0-74.0)	0.222
Indication for ERCP			
Biliary stones	112 (78.3)	104 (74.3)	0.485
Biliary pancreatitis	18 (12.6)	24 (17.1)	0.318
Bile duct injury after cholecystectomy	15 (10.5)	16 (11.4)	0.851
Biliary stricture (non-malignant)	15 (10.5)	11 (7.9)	0.485
Post-ERCP pancreatitis	7 (4.9)	1 (0.7)	0.067
Cholangitis	1 (0.7)	1 (0.7)	1.000
Perforation	3 (2.1)	1 (0.7)	0.622
Bleeding	2 (1.4)	2 (1.4)	1.000
No acute pancreatitis in follow-up period	140 (97.9)	134 (95.7)	0.238
Chronic pancreatitis	0 (0)	1 (0.7)	0.495
Abdominal pain during previous year	58 (40.5)	50 (35.7)	0.463
daily	10/143 (6.9)	12/140 (8.6)	
weekly	6/143 (4.2)	12/140 (8.6)	
once a month/seldom	42/143 (29.4)	26/140 (18.6)	
Medication for abdominal pain in previous year	30 (21.1)	22 (15.7)	0.283

[Table 1. Patient and procedure characteristics (n=283). Numerical data are presented as median (range) or number of patients (%)]*

Conclusion: TPBS is a useful procedure with acceptable complication rates. There was no significant difference between groups when evaluating the short-term or long-term complications. Additionally, there were no significant difference during the follow-up period in upper abdominal pain, usage of painkillers, recurrent pancreatitis or development of CP.

Disclosure: Nothing to disclose

P1621 WITHDRAWN

P1622 CONSCIOUS SEDATION IN ERCP: A UK PERSPECTIVE FROM A GENERAL HOSPITAL

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Introduction: Despite the fact, it has been more than 8 years since the release of the UK guidelines for the use of propofol for deep sedation of adult patients undergoing Endoscopic Retrograde Cholangiopancreatography (ERCP) (1) ,yet the lionshare of UK based centres consider conscious sedation as the preferred way of sedation.

Aims & Methods: The goal of this project is to evaluate ERCP under conscious sedation and compare quality indicators with the benchmark stated by British society of Gastroenterology (BSG).

In our centre, we retrospectively analysed all ERCP procedures data from hospital-based registry carried out under conscious sedation and general anaesthesia (GA) during the period (2016, 2017, and 2018), and reviewed related complications during the study period.

Total number of cases 602, 579 were done under conscious sedation, while 23 cases were done under GA.

Results: A total 579 patients had ERCP under conscious sedation during these 3 years, Male 42.1% (241) , mean age 71.7 , and range (17-99) , physical health was assessed via ASA score; 76.1% of our cohort were classified as ASA II-III. 100% of the procedure was intended for therapy. Deep cannulation was achieved in 97.4% (564), and procedure was successfully completed in 93.2% (540), incomplete procedure was 4.14% (24), and failed 2.6% (15). Complications; Pancreatitis was 2.9% (17), no patient had serious bleeding requiring blood transfusion , perforation rate 0.34% (2), and mortality related to the procedure 0.17% (1). Sedation wise, mean sedation rate for Midazolam for age below 70 was (3.2 mg), while for age above 70 was (2.3 mg). Regarding Fentanyl for age below 70, the mean rate is (81.8 mg), while above the age of 70, the rate was (57.84 mg), and

mean comfort score was (2.5). Antibiotic for incomplete decompression of bile duct was given in 100%. While the cases that needed ERCP under GA (N=23), 65% of the cases were classified as ASA score 2-3. These cases formed 3.8% of the whole ERCP pool during the period of the study.

Conclusion: In a summery, we concluded that ERCP under conscious sedation is still safe and effective in vast majority of the cases, and on pars with the guidelines (4, 5). However a small number of cases still require GA or propofol, this would need discussion and collaboration between gastroenterologists and anaesthetists base on each case due to the peculiar situation in the UK where propofol should be given only by anaesthetist (1).

References: 1 Guidance for the use of propofol sedation for adult patients undergoing Endoscopic Retrograde Cholangiopancreatography (ERCP) and other complex upper GI endoscopic procedures .April 2011 On behalf of the Joint Royal College of Anaesthetists (RCoA) and British Society of Gastroenterology (BSG) Working Party. 2 Propofol Sedation for ERCP Procedures: A Dilemma? Observations from an Anesthesia Perspective. Hindawi Publishing Corporation, Diagnostic and Therapeutic Endoscopy, Volume 2012, Article ID 639190, 5 pages, doi:10.1155/2012/639190 3 J. Aisenberg, J. V. Brill, U. Ladabaum, and L. B. Cohen, "Sedation for gastrointestinal endoscopy: new practices, new economics," American Journal of Gastroenterology, vol. 100, no. 5, pp. 996-1000, 2005 4 ASGE : Guidelines for sedation and anesthesia in GI endoscopy , GASTROINTESTINAL ENDOSCOPY Volume 87, No. 2 : 2018 5 BSG ERCP - The Way Forward, A Standards Framework ,Mark Wilkinson, (BSG Endoscopy, working party convenor and chairman) et al. June 2014

Disclosure: Nothing to disclose

P1623 PLACE OF ERCP IN HEPATIC HYDATID DISEASE WITH CYSTOBILIARY COMMUNICATION: A 17 YEARS EXPERIENCE

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Introduction: Hydatid disease is an infectious disease caused by Echinococcus Granulosus, it affects most commonly the liver. Intrabiliary fistulisation is one if its rare and severe complications which remains frequently misrecognized.

Aims & Methods: The aim of our study is to evaluate the efficacy and safety of ERCP in management of hepatic hydatid cysts with cystobiliary communication based on our experience.

We conducted a retrospective bi-centric descriptive and analytical study, from january 2002 to march 2019 in both the departments of gastroenterology of military teaching hospital, and Cheikh Zayed Hospital in Rabat, including 50 patients with hepatic hydatid cyst communicating with biliary tract. Endoscopic retrograde cholangiopancreatography with endoscopic sphincterotomy were performed in all our patients. Global success was defined by the final clearance of bile ducts and drying up of biliary fistula. IBM SPSS software 24.0 was used for statistical analysis of our data.

Results: The mean age of our population was 46,2+/-14,9 years old with a sex ratio M/F of 2,06. Of the 50 patients enrolled in the study, ERCP was performed before surgery in 52,2% cases and post-operatively in 47,8% cases. Indications of ERCP included cholangitis due to biliary obstruction in 43,5%, and persistant external biliary fistula in 34% of cases. During ERCP, mean diameter of common bile duct (CBD) was 10,7+/-4,06 millimeters, and median diameter of cyst of 35mm [20-60] measured by leakage of contrast into cyst cavity. CBD was filled by defect of varying size in 82,1%, and we noted a distal stenosis in 28,6%. Endoscopic sphincterotomy was performed in all cases, so that we could empty out hydatid cysts and daughter cysts encountered in bile duct using biliary occlusion balloon and/or dormia basket in 87% of cases. Nevertheless, 21,7% required nasobiliary drainage and 8,7% required biliary stenting due to CBD stricture. Global success defined by the final clearance of bile ducts was obtained in 100%. Regression of jaundice was noted in 5 to 10 days after ERCP and biliary fistula healed in a median of 10 days.

Conclusion: ERCP is a safe, effective and conservative procedure to manage hepatic hydatid disease with cystobiliary communication. Endoscopic sphincterotomy allows the treatment of associated cholangitis and biliary obstruction most frequently, It leads to decrease the duration of hospital stay and to avoid a heavy surgery in some cases.

Disclosure: Nothing to disclose

P1624 RETROSPECTIVE COMPARISON OF EFFICACY AND COST-EFFECTIVENESS OF SELF-EXPANDABLE METAL STENTS AND PLASTIC BILIARY STENTS IN THE MANAGEMENT OF MALIGNANT BILIARY OBSTRUCTION

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Introduction: Self-expandable metal (SEMS) and plastic stents (PS) placement are the two alternative therapeutic option for the palliative endoscopic management of unresectable malignant biliary obstruction. The longer stent patency might compensate for the substantially higher cost of SEMS compared to PS. Current guidelines recommend the use of SEMS if the patient's life expectancy is more than four months. **The aims** of this study were to compare the therapeutic efficacy and cost-effectiveness of SEMS and PS in the treatment of malignant biliary obstruction.

Aims & Methods: 135 consecutive patients were retrospectively enrolled who underwent endoscopic stent placement due to unresectable malignant biliary obstruction between 2011 and 2017 at University of Szeged. Patients were divided into PS (41 patients), primary SEMS (39 patients), and secondary SEMS (55 patients) subgroups. The efficacy and cost-effectiveness of stents were determined on basis of technical and functional success rate, stent patency and cumulative cost of treatment.

Results: The 135 enrolled patients underwent 111 SEMS and 153 PS placement with similarly high technical (100% vs. 98.69%) and functional success rate (90.10% vs. 86.27%) during the study period. The average patency of SEMS was significantly higher compared with PS (22.16 vs. 10.28 weeks; p< 0.001). In the PS subgroup multiple stent implantation and larger stent diameter increased the stent patency compared with the 7 Fr stents (10.88 vs. 10.55 vs. 7.63). The mean survival of patients was substantially higher in the secondary SEMS subgroup (47.07 weeks, range 1-134, med. 40) compared with the primary SEMS (24.46 weeks, range 2-72, med. 17) and PS groups (18.27 weeks, range 3-76, med. 12). There was no difference in the average cost of treatment per month between the PS, primary and secondary SEMS groups (892.12 EUR vs. 939.12 EUR vs. 788.46 EUR). The cumulative cost of first two-months' treatment was substantially lower in the PS group compared with primary and secondary SEMS groups (1645.19 EUR vs. 1937.82 EUR vs. 1755.82 EUR), however, if the patients' survival time was more than two months, the cost-effectiveness of SEMS was better than plastic stents: 4-months cumulative cost was 2325.14 EUR in SP, 1898.96 EUR in primary SEMS and 2009.02 HUF in secondary SEMS group.

Conclusion: Considering the cost of treatment, the burden of patients and health care system we recommend the SEMS implantation if the life expectancy of patients is more than two months. In short survival cases or if the SEMS not available the multiple plastic stent implantation is recommended.

Disclosure: Nothing to disclose

P1625 TREATMENT STRATEGY FOR CHOLEDOCHOLITHIASIS IN VERY ELDERLY (≥85 YEARS) PATIENTS

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Introduction: Endoscopic sphincterotomy with stone extraction is a widely accepted standard therapy for choledocholithiasis. Use of endoscopic therapy in very elderly patients with common bile duct (CBD) stones has increased with the aging society. However, it is sometimes difficult to perform lengthy or frequent procedures in elderly patients because of poor physical status or comorbidities. Several studies have reported that long-term biliary stenting is safe and effective for the elderly.

Aims & Methods: This study aimed to evaluate strategies for endoscopic management of choledocholithiasis in very elderly patients.

This is a retrospective cohort study of very elderly patients (age, ≥85 years) who had undergone endoscopic retrograde cholangiopancreatography (ERCP)-related procedures for CBD stones at Kyoto Second Red Cross Hos-

pital between 1998 and 2018. Patients who failed biliary cannulation or presented with biliary stricture, post Billroth II reconstruction, Roux-en-Y reconstruction, and biliary reconstruction were excluded. 477 very elderly patients were analyzed and divided into two groups according to the management strategy: stone extraction group (n=304), patients who underwent endoscopic CBD stone removal; and stent group (n=173), patients who underwent endoscopic bile duct stenting without stone removal. Patient characteristics, treatment, clinical outcomes, long-term outcomes, and complications were compared between the groups.

Results: There were significant differences between the stone extraction and stent group with regard to age (88.7 vs. 91.1 years, p< 0.001), presence of multiple (≥5) CBD stones (19.7% vs. 37.6%, p< 0.001), and presence of large stone (28.7% vs. 53.3%, p< 0.001). There was no significant difference in presence of comorbidities and antithrombotic therapy between the groups.

Significantly more ERCP sessions were required during hospital stay in the stone extraction group than in stent group (1.7 vs. 1.2, p< 0.001). Total procedure time were significantly longer in the stone extraction group than in the stent group (66.9 vs. 42.2 min, p< 0.001). The rate of complete stone removal was 88.7% in the stone extraction group.

There was no significant difference in the rate of complications during and after ERCP between the groups. Kaplan-Meier analysis showed a significantly lower rate of CBD stone and/or cholangitis recurrence in the stone extraction than in the stent group (p< 0.001).

Conclusion: In terms of long-term outcomes, endoscopic stone extraction is recommended as the first choice even in very elderly patients. For difficult common bile duct stones, long-term biliary stenting is a feasible option and appropriate in patients with short life expectancy due to old age and comorbidities.

Disclosure: Nothing to disclose

P1626 PREVALENCE AND RISK FACTORS FOR ERCP ADVERSE EVENTS

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Introduction: Since its first description, endoscopic retrograde cholangio-pancreatography (ERCP) has evolved into a leading modality in the treatment of the pancreas and biliary tract conditions. Its enormous therapeutic potential also carries the possibility of adverse events (AEs) that may be associated with a significant morbidity and mortality. Numerous studies have helped determine the expected rates of ERCP-related AEs and possible methods for improving the safety of ERCP, but many of them are limited by nonuniformity of definitions, small sample sizes or analyse each AE separately.

Aims & Methods: The aim of our study was to evaluate the AEs' prevalence after ERCP, and risk factors for its occurrence.

Retrospective cohort study of all patients who underwent ERCP between January 2012 and December 2017, in a single tertiary center. Demographic and clinical data, including post-procedural AEs, were analysed. Risk factors for global and individual AEs occurrence were identified using multivariate logistic regression analysis.

Results: During the study period a total of 2002 ERCPs were performed on 1492 consecutive patients, 51.4% male, with a median age of 68 years (IQR 56-79). The main indications for ERCP were choledocolithiasis (37.0%), jaundice (11.1%), biliary stenosis (11.4%) and imaging abnormality of the bile duct (8.6%).

The overall AE rate was 15.3% [Planned bile duct cannulation with naive papilla - 210/1339 (15.7%); Planned bile duct cannulation with previous sphincterotomy - 55/499 (11.0%); Planned pancreatic duct cannulation with naive papilla - 18/83 (21.7%); Planned pancreatic duct cannulation with previous sphincterotomy - 21/70 (30%)]. The main post-ERCP AE was pancreatitis (7.5%), followed by cholangitis (4.9%), hemorrhage (1.3%), perforation (1.0%), cardiopulmonary events (0.9%) and cholecystitis (0.3%). ERCP AE-related mortality rate was 1.0%.

In the multivariate analysis, ERCP difficulty degree (III/IV *vs* I/II: OR 1.842, p< 0.001), difficult biliary cannulation (OR 1.992, p< 0.001), imaging abnormality of the bile duct (OR 1.636, p=0.025), periprocedural haemorrhage (OR 3.656, p< 0.001) and ampulectomy (OR 4.681, p=0.018) were

independently associated with an increased risk of AEs. Naïve papilla (OR 2.170, p=0.008), pancreatic duct cannulation (OR 1.923, p=0.026), imaging abnormality of the bile duct (OR 2.035, p=0.009), choledocholithiasis (OR 0.535, p=0.01), previous post ERCP-pancreatitis (OR 3.434, p=0.003), periprocedural haemorrhage (OR 2.432, p=0.022) were independently associated with pancreatitis.

Periprocedural haemorrhage (OR 9.747, p<0.001), anti-aggregation plus anticoagulant therapy (OR 11.832, p=0.028), sphincteroplasty (OR 3.545, p=0.013) and distal common bile duct stricture (OR 8.767, p=0.003) were independently associated with postprocedural haemorrhage. Hilar stricture was the only independent factor associated with cholangitis (OR 8.685, p=0.006). Altered anatomy (OR 9.391, p=0.014) and peripapillary diverticulum (OR 3.813, p=0.019) were associated with perforation.

Post-ERCP AEs-related mortality was independently associated with difficult biliary cannulation (OR 3.160, p=0.020), jaundice (OR 5.071, p=0.006), anticoagulation with NOACs (OR 26.660, p=0.007) and ASA score (4 *vs* 1-3, OR 5.273, p=0.008).

Conclusion: ERCP AEs' prevalence is significant. Patient-related risk factors assume a non-negligible role for its occurrence. Adequate stratification, considering potentially modifiable risk factors, with identification of high-risk patients and targeted prophylactic management may be important to prevent or minimize their occurrence.

Disclosure: Nothing to disclose

P1627 ERCP IN THE TREATMENT OF IATROGENIC BILIARY INJURIES AFTER CHOLECYSTECTOMY - A LEAP OF FAITH

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Introduction: Post-cholecystectomy iatrogenic biliary injuries, though more uncommon than in the early years of laparoscopic surgery still represents an important burden of morbidity and mortality. When discovered during surgery the injuries can be easily managed, otherwise endoscopic retrograde cholangio-pancreatography (ERCP) represents the first choice of treatment.

Aims & Methods: The aim of this study is to evaluate the role of ERCP in the managment of biliary laparoscopic induced lesions after cholecistectomy. We conducted a retrospective study which enrolled the patients with iatrogenic biliary injuries after laparoscopic cholecystectomy hospitalized in the Clinical Emergency Hospital Bucharest, who underwent ERCP from January 2014 to March 2019.

Results: The study included 48 patients diagnosed with post laparoscopic cholecystectomy iatrogenic injuries or who had a high clinical and imaging suspicion of biliary lesion, and were mainly referred to our tertiary center for ERCP. The mean age was 54,5 years (range 20 to 84).

According to S.M. Strasberg classification 72, 91% of the patients had a type A lesion, which was associated in half of the cases with main bile duct lithiasis. ERCP with plastic stent insertion was used in 22 patients, the stent was extracted on average after 30 days with full recovery, while for 13 patients only sphincterotomy was performed also with full recovery. A type D lesion was described during ERCP for 5 patients, 4 of whom were treated surgically after an initial ERCP with sphinterotomy, while one patient had a full recovery after plastic stent placement.

More complex type E lesions where described in 8 patients (E1-3 patients; E2 - 4 patients; E3- 1 patient), and in all except one patient the first ERCP had failed to treat the lesion.

One patient with type E2 lesion had a plastic stent inserted via ERCP in the surgery room and need it another 6 ERCP's with multiple plastic stent exchange for 18 months until full recovery.

Conclusion: ERCP remains a useful treatment tool for Iatrogenic biliary lesions after laparoscopic cholecystectomy. Therapeutic ERCP can successfully treat low complexity lesions and in some cases can be used in rendezvous procedures in the surgery room for very complex injuries.
Disclosure: Nothing to disclose

P1628 CHOLANGIOSCOPY IN INDETERMINATE BILIARY STRICTURE

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Introduction: Single-operator cholangioscopy (SOC) has been a major advance in indeterminate biliary stricture (IDBS) diagnosis because it has made direct visualization and optically guided biopsy of these lesions. However, SOC-guided biopsies have shown limited sensitivity. In order to overcome this limitation, identifying the cholangioscopic features that most strongly suggest malignancy is an interesting way to improve SOC diagnostic capabilities; however, no systematic analysis of SOC findings has been conducted to date.The aim of our study is to establish endoscopic criteria allowing to distinguish between benign and malignant lesions.
Aims & Methods: 4 referral centers included 98 Spyglass DS cholangioscopy recordings performed for indeterminate biliary strictures (IDBS) whose final diagnosis was known by histology or follow-up for more than 1 year. 7 experts in cholangioscopy participated in the development of a consensual reading grouping 20 semiological criteria. The videos were analyzed individually by each expert after randomization according to the reading grid. A hypothesis diagnosis was issued for each examination. After a statistic analysis a second meeting with the same methodology were held for criteria validation.
Results: 98 IDBS videos from 95 patients of mean age 66 years (13 - 89) were analyzed; there were 38 benign and 60 malignant strictures. The Sensitivity ranged from 68% to 81% and specificity from 55 to 71%. The univariate and multivariate analysis identified 4 significant criteria. One for benign lesions: the presence of endobiliary material odds ratio (OR)= 0.649; 95% confidence interval (CI), 0.427 - 0.988. Three for malignant lesions: villous pattern OR = 1.477; 95% CI, 0.98 - 2.21; irregular vessels OR = 2.042; 95% CI, 1.35 - 3.08; redish aspect OR = 1.67; 95% CI,1.09 - 2.53.
Conclusion: Simple criteria's could assist malignancy diagnosis and enhance The performance of cholangioscopic visual diagnosis of IDBS.
Disclosure: Nothing to disclose

P1629 QUALITY IN ERCP - APPLICATION OF QUALITY INDICATORS TO EVALUATE TECHNICAL OUTCOMES AND ADVERSE EVENTS

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Introduction: ERCP is a technically challenging and high-risk procedure requiring focussed training and experience to maximize technical success and minimize adverse outcomes. Quality indicators in ERCP are useful to evaluate and monitor technical performance and adverse outcomes.
Aims & Methods: The objective of this study was to evaluate the technical performance and the fulfillment of quality indicators in ERCP practice in a tertiary center.

We retrospectively evaluated 941 consecutive ERCPs that were performed at a tertiary hospital between October 2016 and January 2019 and were prospectively registered.
We excluded 92 procedures due to lack of an attempt to cannulate the papilla of Vater (mainly due to duodenal obstruction often due to malignant stricture and altered small intestinal anatomy with Roux en Y anastomosis) and in 13 procedures due to inadequate post procedure follow-up data. Finally, the study cohort included 836 procedures. Intravenous hydration with Ringer's lactate and prophylactic diclofenac suppository were performed in all procedures. Prophylactic post ERCP antibiotic prophylaxis was prescribed when indicated.
The technical performance was compared with the quality indicators for ERCP recommended by the American Society of Gastrointestinal Endoscopy (ASGE) and the European Society of Gastrointestinal Endoscopy (ESGE).
Results: The mean age of the study sample was 71 ± 15.8 years and 51% (426) of the procedures were performed in men.
The indications for ERCP were as follows: Choledocholithiasis 57% (476); malignant biliary stricture 27% (226); benign biliary stricture 6% (48); biliary fistula 4% (30); acute gallstone pancreatitis 2% (17); ampuloma 0.2% (2) and others 4.4% (37).
The overall rate of deep cannulation of the main bile duct was 97.8% (818/836) and in patients with intact papilla of Vater was 97% (543/560). The incidence of post ERCP pancreatitis (PEP) was 2.5% (21), post sphincterotomy haemorrhage 1.1% (9) and perforation 0.2% (2). The technical performance indicators of ERCPs compared to those recommended by ASGE and ESGE are presented in table 1.
The following variables were not documented in the study: the use of prophylactic antibiotic therapy and the success rate of bile duct stent placement.

	ASGE	ESGE	Technical performance
1)Appropriate indication for ERCP	>90%		100%
2)Native papilla deep cannulation rate	>90%	>90% (>95% ideal)	97%
3)Extraction rate of <1cm common bile ducts stones	≥90%	>90%	100%
4)Successful biliary stent placement rate	≥90%	>95%	Not recorded
5)Post-ERCP pancreatitis rate	Yes	<10% (<5% ideal)	2.5%

[Table 1. Evaluation of technical performance when compared to quality indicators of ERCP recommended by ASGE and ESGE]

Conclusion: The awareness and use of a prospective database allowed a detailed analysis of the performance indicators in ERCP as recommended by ASGE and ESGE and may have contributed to the good technical outcomes and low incidence of adverse outcomes.
Disclosure: Nothing to disclose

P1630 INCIDENCE OF POST ERCP ADVERSE EVENTS AND PREDICTORS OF POST-ERCP PANCREATITIS - ANALYSIS OF A PROSPECTIVE DATABASE

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) is one of the endoscopic techniques with the highest rate of adverse events. The expected rate of post-ERCP pancreatitis (PEP) varies between 1% and 7% for most average-risk patients, haemorrhage post endoscopic sphincterot- omy varies between 0.8% to 2% and perforation varies between 0.1% to 0.6%
Aims & Methods: The objective of this study was to evaluate the incidence of adverse events after ERCP and determine risk factors for post-ERCP pancreatitis (PEP).
We retrospectively evaluated 941 consecutive ERCPs that were performed in a tertiary hospital between October 2016 and January 2019. Data related to the procedures was prospectively registered. The indication for ERCP,

incidence and predictors of PEP were evaluated. We excluded 92 procedures wherein cannulation of papilla of Vater was not attempted (mainly because of duodenal obstruction due to neoplastic stricture, altered small intestinal anatomy with Roux en Y anastomosis) and 13 procedures due to inadequate follow-up data. The final study sampled included 836 ERCP procedures. All patients received intravenous Ringer's lactate and rectal diclofenac 100mg suppository for prophylaxis of PEP.

Patients at high risk for PEP were defined by intact papilla of Vater and time to cannulation of the main bile duct > 5mins or ≥2 cannulations of the pancreatic duct. Descriptive statistical analysis, chi square and logistic regression were realized (SPSS° 21).

Results: The average age of the study sample was 71±15.8 years with 51% (426) being men. The main indications for ERCP were: Choledocholithiasis 57% (476); Malignant stenosis 27% (226); Benign stenosis 6% (48). The cannulation rate of intact papilla of Vater was 97% (543/560). Guide wire assisted cannulation was used in 72% (591) and precut papillotomy in 13.3% (111). The time to main bile duct cannulation was < 5mins in 65% (546) patients. The pancreatic duct was cannulated in 24% (202) patients. Contrast was injected into the pancreatic duct in 6.2% (52) and a prophylactic 5Fr stent placed in the pancreatic duct in 9.1% (76) patients. The high-risk group for PEP represented 33% (275) of ERCPs. The overall incidence of complications after ERCP was 4.3% (36) with PEP occurring in 2.5% (21) patients as shown in table 1.

PEP was associated with time until cannulation of main bile duct > 5mins (p = 0.01); ≥1 pancreatic duct cannulations (p <0.01) and pancreatic duct contrast injection (p < 0.01). The only predictor of PEP was ≥2 cannulations of the pancreatic duct (OR: 4.7; 95% CI, 1.29-17.1, p = 0.019).

	Overall study sample (n=836)	Native papilla of Vater (n=560)	Prior sphincterotomy (n=276)
Main bile duct cannulation rate	97.8% (818)	97% (543	99.6% (275)
PEP	2.5% (21)	3.4% (19)	0.7% (2)
Hemorrhage	1.1% (9)	1.4% (8)	0.4% (1)
Cholangitis	0.5% (4)	1.4% (2)	0.4% (1)
Perforation	0.2% (2)	1.4% (2)	0%

[Table 1. Cannulation rate and incidence of post ERCP adverse events]

Conclusion: In our prospective registry, the incidence of ERCP adverse events was low with a PEP rate lower than that usually described in published literature. The only independent predictor of PEP were ≥2 cannulations of the pancreatic duct.

Disclosure: Nothing to disclose

P1631 SERUM AMYLASE LEVEL AT 2 HOURS AFTER ERCP CAN BE A PREDICTIVE FACTOR FOR THE SEVERITY OF POST-ERCP PANCREATITIS; MULTICENTER PROSPECTIVE STUDY, SOSUI

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Introduction: The severity of post-ERCP pancreatitis (PEP) is a major problem because of its occasional lethality. However, no predictor of the severity has been identified. In the present multicenter prospective study, SOSUI, we investigated potential predictive factors for the severity of PEP.

Aims & Methods: We prospectively followed 3,914 patients who underwent ERCP between February 2015 and May 2017 at five high-volume centers in Kyoto or Shiga prefecture in Japan. 3,661 patients were included after 253 those who had been complicated by pancreatitis, undergone biliary tract reconstruction, or had papilla not reached were excluded.

Of the 3,661 patients, we evaluated 263 patients who developed PEP. We compared between the mild and severe cases to examine potential predictors for the severity of PEP. PEP was diagnosed when patients presented with at least two of three following manifestation: (1) serum amylase elevation (above the upper limits of each center) on the following day, (2) abdominal pain lasting for longer than 24 hours and (3) pancreatitis on CT. The severity of PEP was assessed based on the severity criteria of the Japanese Ministry of Health, Labour and Welfare.

Results: 35 (0.9%) and 228 (6.5%) patients developed severe and mild PEP. A significant difference was found between patients with severe and mild PEP with regard to the serum amylase level at 2 hours after ERCP (P =0.0016), abdominal pain immediately and 24 hour after ERCP (P=0.011 and 0.0024) and performing lithotomy (P=0.031). ROC analysis was conducted on the serum amylase level at 2 hours as a predictive factor for severe PEP, demonstrating that the cutoff value was 3.6 times higher than the upper limits of each center (sensitivity: 60%; specificity: 68%; and AUC: 0.63). In multivariate analysis using logistic regression by dividing the amylase level at 2 hours after ERCP into 3.7 times higher or lower than the reference values of each center, abdominal pain immediately after ERCP and AMY values at 2 hours after ERCP were identified as independent factors.

Conclusion: In the present study, abdominal pain immediately after ERCP and serum amylase level at 2 hours were identified as predictive factors for the severity of PEP. They can be useful for facilitating urgent therapeutic intervention. We have to investigate more to identify appropriate treatment for preventing PEP.

Disclosure: Nothing to disclose

P1632 DIAGNOSTIC ACCURACY AND THERAPEUTIC EFFICACY OF DIGITAL SINGLE-OPERATOR CHOLANGIOSCOPY FOR BILIARY LESIONS AND STENOSIS

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Introduction: Digital single-operator cholangioscopy (dSOC) has revolutionized bile duct visualization during endoscopic retrograde cholangiography (ERC). Visual inspection of suspicious areas and targeted biopsies have become possible quick and easy, as well as interventions like electrohydraulic or laser lithotripsy. One main indication for dSOC is the evaluation of indeterminate biliary strictures.

Aims & Methods: In this study 180 dSOCs performed 2016 till 2017 in a high volume tertiary center have been retrospectively analyzed to evaluate sensitivity, specificity as well as positive and negative predictive values for indeterminate strictures and lesions. Furthermore technical success and complications were analyzed.

Results: In 92-97% the region of interest was reached and visualized and in 83-100% successful biopsies were taken in the biliary tract in this study. Only the distal bile duct was less successful with only 84% and 62%, respectively. The procedure was safe with cholangitis as main complication. Regarding the diagnostic accuracy of dSOC of indeterminate biliary lesions and strictures we found a sensitivity of 0.87 and specificity of 0.88. The investigators assessment directly after dSOC had a positive predictive value of 0.63 and a very high negative predictive value of 0.97.

Conclusion: Our study demonstrates that dSOC has a very high diagnostic efficacy as well as a favorable safety profile. Therefore, it should be discussed as standard of care in addition to ERC for indeterminate biliary lesions.

Disclosure: Nothing to disclose

P1633 ENDOSCOPIC TREATMENT OF COMPLICATIONS OF HYDATID CYSTS IN THE LIVER BROKEN IN THE BILE DUCTS: EXPERIENCE OF A MOROCCAN DEPARTMENT

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Introduction: The Hydatid cyst of the liver is a parasitic disease due to the development of the larval form of the Taenia of the dog Echinococcus granulosus. By its clinical latency, the Diagnosis is most often at the stage of complications. Fistulization of the cyst hydatid in the bile ducts is the most common complication. Endoscopy is necessary because of the therapeutic problems and risks associated with surgery.

Aims & Methods: The objective of our study was to evaluate and analyze the effectiveness of ERCP in the diagnosis and treatment of Hydatid cysts of the liver broken in the pathways ducts.

This is a 15-year retrospective and descriptive study, ranging from January 2003 to October 2018, focused on patients with fistulized Hydatid cyst in the pathways bile duct. ERCP and endoscopic biliary sphincterotomy were performed in all patients, 18 times pre-operatively and 21 times post-operatively.

Results: 39 patients with broken Hydatid cyst in the biliary duct, 2.4% of the indications ERCP in our series were included. The average age of patients was 47, with male predominance in 65% of cases. KHF broken in the ways galls were complicated by persistent external biliary fistula post operatively in 34% of cases. Sphincterotomy was performed in all patients allowing removal of Hydatid material by extraction balloon or Dormia basket. The evolution was marked by the disappearance of jaundice after 5 to 12 days in average after endoscopic gesture and dryness of external biliary fistula after 10 to 12 days.

Conclusion: The results of our study confirm the efficacy and safety of ERCP and the endoscopic sphincterotomy in biliary complications of echinococcosis hepatic. It makes it possible to shorten the post-operative stay and to avoid are operation, often difficult and haemorrhagic.

Disclosure: Nothing to disclose

P1634 THE ROLE OF RECTAL EUS BIOPSY IN PRE-SACRAL UNDEFINED LESIONS IN PATIENTS WITH HISTORY OF LOWER GI NEOPLASIA

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Introduction: Colo-rectal neoplasia is one of the most commonly diagnosed malignancies, representing in Italy the second cause of overall malignan-cies in the man, after prostate neoplasia, and in woman, after breast neo-plasia, with 373.000 new diagnosis/years in 2018. Pre-sacral lesions may arise in the follow up after colo-rectal surgery, after adjuvant chemotherapy (CT), or neo-adjuvant chemo-radiotherapy. CTscan and pelvic RM are the two most used diagnostic tool in these patients, but they can be inconclusive in the diagnosis of pre-sacral lesions. PET scan adds more information but, in presence of inflammation, can show false positive results.

Aims & Methods: The aim is to critically evaluate the role and the efficacy of endoscopy ultrasound (EUS) and Fine Needle Aspiration or Biopsy (FNA/FNB) in the multimodal restaging of suspected local recurrence or progression disease in patients with history of rectal cancer. Procedures were performed with linear EUS scope. The number of EUS FNA/FNB passes was decided by the endoscopist based on the gross morphology of the specimen (if core was visible) and or rapid on-site evaluation if available.

Results: From September 2015 to March 2019 we retrospective enrolled eight patients referred to our units for pre-sacral lesions undergoing endoscopy ultrasound (EUS) and Fine Needle Aspiration or Biopsy (FNA/FNB). In all cases the radiological findings (CT scan and or PET/MRI) were inconclusive for a final diagnosis. Table 1 summarizes patients', lesions' and procedures' results. In 6 of 8 patients pathological evaluation confirmed the suspicion of local recurrence and they were referred for onco-logical re-treatment.

In two patients EUS-FNB of lymph-node yielded a diagnosis of inflammation (at histology) with no tumoral cells at cytology. Radiological follow-up for these two patients confirmed benign characteristics. In only two cases both cytology and histology were performed, and in both tissue acquisition by EUS-FNB allowed to reach a diagnosis. All lesions resembling masses resulted in local recurrence. In only one of three cases in which lymph-nodes were targeted, cytology evaluation on an EUS-FNB of 15 mm lymph-node showed tumoral cells. Procedures were performed in out-patient setting. All patients underwent antibiotic prophylaxis with intra-venous cefalosporine one shot before the biopsy. No adverse events or infection were observed.

Conclusion: EUS plus FNA/FNB should be a mandatory diagnostic tool in patients with a history of lower GI neoplasia in case of pre-sacral lesions supposed to be local recurrence. EUS-FNB seems to offer a higher diagnostic power. High diagnostic accuracy allows to redefine oncologic treatment and follow-up strategy. Further and wider retrospective cohort studies are warranted to offer more significative results.

Disclosure: Nothing to disclose

P1635 WITHDRAWN

P1636 WITHDRAWN

SEX/AGE	NEOPLASIA	TNM	TREATMENT	MONTHS FROM DIAGNOSIS	SUSPICION	LESION/SIZE	NEEDLE/ PASSES	CYTOLOGY	HISTOLOGY
M 79	RECTAL ADENOCARCINOMA	T3N1	SX + aCT	80	CT scan + PET	MASS 10 mm	FNB 25GA/2	NA	ADENOCARCINOMA
M 74	RECTAL ADENOCARCINOMA	T3N1	SX + aCT	26	CT scan + PET	MASS 33 mm	FNB 22GA/2	NA	ADENOCARCINOMA
F 62	SIGMOID ADENOCARCINOMA	T3N0	SX	22	CT scan + MRI	MASS 30 mm	FNB 25GA/3	NA	ADENOCARCINOMA
M 78	RECTAL ADENOCARCINOMA	T1N0	SX	36	CT scan	MASS 22 mm	FNB 25GA/3	INADEQUATE	NEOPLASTIC CELLS
M 56	RECTAL ADENOCARCINOMA	ypT0N0	RT + SX	36	CT scan	LN 4 mm	FNB 22GA/3	INADEQUATE	INFLAMMATION
F 48	ANAL SQUAMOUS CELL CARCINOMA	NA	CT + RT	3	CT scan	LN 15 mm	FNA 25GA/3	NEOPLASTIC CELLS	NA
M 58	RECTAL ADENOCARCINOMA	pT3N1a	SX + aCT	19	CT scan + PET	MASS 8 mm	FNB 25GA/2	NEOPLASTIC CELLS	NA
M 72	RECTAL ADENOCARCINOMA	pT3N1b	SX	12	CT scan + PET	LN 6 mm	FNB 25GA/2	NO NEOPLASTIC CELLS	NA

SX: surgery; CT: chemotherapy; aCT: adjuvant chemotherapy; RT: radiotherapy; LN: Lymph-node; NA: not available.

[P1634 Table 1]

P1637 PERFORMANCE OF EUS-GUIDED TISSUE ACQUISITION IN SAMPLING OF GI SUBEPITHELIAL LESIONS

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Introduction: EUS-guided tissue acquisition (EUS-TA) is crucial step in the differential diagnosis and management of patients with gastrointestinal subepithelial lesions (GI-SELs).

Aims & Methods: The aim of the study was to evaluate the adequacy of EUS-TA performed with standard needles (SN) and with fine needle biopsy needles (FNB needles), using a standardized protocol for the management of specimens in the diagnosis of GI-SELs.

This retrospective, single center study enrolled patients who underwent EUS-TA of upper or lower GI-SELs. A macroscopic on-site evaluation (MOSE) was performed by the endoscopist after every needle pass. All specimens obtained using either standard or histology needles were processed in the same way according to the MOSE.

Specimens were defined as "diagnostic" when sufficient material for histologic or cytologic evaluation was present. If the biopsies did not allow a complete evaluation, the specimens were considered as "not adequate". If the patient underwent surgical resection of the SEL, the EUS TA findings were compared with the final pathological diagnosis.

Results: 86 patients were included in the study (45 males, 52.3%), with mean age 64.0 years (SD = 11.6 years). The average size of the lesions was 36.3 mm (SD = 23.2 mm). 61.2% of lesions were detected in stomach, 19.8% in the duodenum, 15.1 % in the esophagus and cardias, and 4.7% in the rectum. FNB was used in 53 patients (61.6%), in the remaining 33 (38.4%) a SN was used. Adequate samples were obtained in in 65 patients (75.6%): 59 had adequate histologic samples, 19 had an adequate cytology and 13 patients had both adequate histology and cytology samples.

In terms of adequacy, no statistically significant difference was found between standard and FNB samples (69.7% versus 80.0%, respectively, p=0.306). (69.7% versus 80.0%, respectively p=0.306). The mean number of needle passes was 2.2 (SD = 0.8 passes, range: 1-4 passes). It did not differ between the standard needle and the FNB groups (2.2±0.9 passes versus 2.3±0.8 passes, respectively, p=0.431), nor the adequacy of the specimens not affected by the mean number of needle passes (2.3±0.8 passes for adequate samples vs 2.1±0.9 passes for inadequate samples p=0.400).

A histological sample was, however, more frequently obtained with FNB needles than with standard needles [74.0% *versus* 60.0%, respectively (p=0.008)]. The adequacy of histological samples was higher than the adequacy of cytological specimens (85.3% *versus* 65.3%, respectively, p=0.015). No early adverse events or technical difficulties were registered in either group.

Fifty-tree patients (61.6%) underwent surgical resection, of which 40 had a diagnostic EUS-TA. In all of them, the final diagnosis confirmed that obtained with EUS-TA. Considering EUS and surgical findings, the final diagnosis was: GIST in 68 patients (79.6%), leiomyoma in 6 (6.9%), schwannoma in 2 (2.3%) and desmoid tumor in 1 (1.2%). Inadequate specimens were obtained, and no subsequent surgery was performed in 8 patients (9.6%): considering the lesion characteristics (< 20 mm, without worrisome features) and/or age >75 years, clinical and imaging follow up alone was proposed to these patients.

Conclusion: using a standardized protocol based on MOSE for the management of specimens from the endoscopy suite to the pathology department in an expert center, EUS-TA had a high rate of diagnostic accuracy and concordance between biopsy and surgical specimens, with no difference between FNBs and SN. FNB needles guaranteed a higher rate of histological specimens for ancillary analysis.
Disclosure: Nothing to disclose

P1638 ENDOSCOPIC ULTRASOUND ELASTOGRAPHY IN DIAGNOSTICS OF GASTROENTEROPANCREATIC NEUROENDOCRINE TUMORS

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Introduction: Endoscopic ultrasound (EUS) is a specific endoscopic examination used to diagnose various types of gastrointestinal tumors. An important role of the EUS was found in the diagnostics of neuroendocrine tumors of the gastrointestinal tract (GEP NETs). In recent years, other modalities have been developed which, in combination with the EUS, improve diagnostics, give detailed description about invasion into surrounding structures, and allow prediction of the tumor's biological behavior. Such methods include elastography (EG). EG is based on demonstrating the difference in tissue stiffness between tumor and reference area. Strain EG measures tissue response to external or internal application of a certain force. It is based on the fact that the stiffer tissue has a lower elasticity and therefore is less deformed upon exposure to pressure. Tissue characteristics are analyzed based on a color qualitative method, or using one of the semi-quantitative methods: strain ratio (SR), strain histogram (SH). SR is the difference in elasticity between two regions in one region of interest (ROI). SH represents the average elasticity value in the defined area.

Aims & Methods: The aim of our study was to find a typical image, SR and SH of GEP NET in endoscopic elastographic measurement using strain qualitative and semi-quantitative methods. In our prospective pilot study, patients with subepithelial tumors of the stomach, duodenum and pancreas were examined. The lesions were displayed on an endoscopic ultrasonography using a convex probe with 7.5-10 MHz. The elastographic image contained the entire tumor in the region of interest and the same amount of comparison region. For the evaluation of the qualitative picture we used the 4-stage EG image rating scale according to WFUMB (World Federation for Ultrasound in Medicine and Biology) 2015. SH and SR were obtained by three different measurements in each case. The selected reference area for SR was chosen non-standard. SR was obtained by comparing subendothelial tumor with the stomach or duodenal wall, pancreatic NETs were compared with the unaffected pancreatic tissue.

Results: 30 patients (20 females and 10 males) with histologically confirmed GEP NET from 2017 to 2019 were included in the study. The mean age of subject was 53.7 years (17 to 74 years). We observed EG qualitative image of GEP NETs homogeneous hard, heterogeneous hard, heterogeneous soft, homogeneous soft 73.3%, 20.0%, 3.3%, 3.3%, respectively. The mean SR observed was 5,17 (95% CI; 5,41 - 10,61) and SH 26,6 (95% CI; 21,35 - 35,02). Sufficient correlation coefficient in the group with qualitative image - homogeneous hard between SR and SH was reached r=-0,613 (95% CI; -0,8 to -0,2585; p=0,0024).

Conclusion: Endoscopic ultrasonography with elastography allows to evaluate changes in tissue elasticity in otherwise poorly accessible locations. Gastroenteropancreatic neuroendocrine tumors exhibit considerable homogeneity in qualitative endoscopic elastographic images. The relatively small range of strain ratio and strain histogram measured between tumor and healthy tissue in our study, indicates the possibility of using these semi-quantitative methods in GEP NETs differential diagnostics.

Disclosure: Nothing to disclose

P1639 ROLE OF ENDOSCOPIC ULTRASOUND IN EVALUATION OF PATIENTS WITH NORMAL LIVER BIOCHEMISTRY AND UNEXPLAINED DILATATION OF COMMON BILE DUCT

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Introduction: The assessment of bile duct dilatation can be carried out using many diagnostic modalities including abdominal ultrasonography (US), computed tomography (CT), and magnetic resonance cholangiopancreatography (MRCP). However, failure to identify the cause of CBD dilatation has been observed in subjects with normal liver function tests and nonspecific abdominal symptoms. EUS has emerged as an important tool for evaluation of biliary disease. Some literatures suggest its impact in detection of a potential biliary pathology, despite a low pre-test clinical suspicion.

Aims & Methods: The aim was to assess the diagnostic value of EUS in patients with normal liver blood tests and unexplained dilatation of common bile duct following other diagnostic modalities including US, CT, and MRCP. Methods: we conducted a retrospective study on 56 patients referred to TBRI (Theodor Bilharz Research Institute) over the period of 2 years. The patients who had dilated CBD, but evaluation with US, and CT or MRCP did not provide a specific cause with normal liver biochemistry {alkaline phosphatase,or AST, or ALT} were included in our study. The patients in whom a diagnosis had been provided by prior imaging (CT/MRCP/US), those with obscure etiology on CT and/ or US alone, and those with previous ERCP or pancreaticobiliary surgery were excluded from this study. There were 11 patients had normal alkaline phosphatase (45-120 IU/L), 21 patients had normal aspartate aminotransferase {AST} (20-40 U/L), and 24 patients had normal alanine aminotransferase {ALT} (20-50 U/L). All patients were enrolled to determine the diagnostic yield of endoscopic ultrasound in this condition.

Results: Our study revealed that among 11 subjects with normal alkaline phosphatase, there were 5 males and 6 females, with a mean (±SD) age of 45.18 (±14.58). The diameter of CBD dilatation by abdominal ultrasound was 9.96 (±1.13). EUS findings were as follows: 6 cases (54.55%) had stone, 2 cases (18.18%) had benign stricture, another 2 cases (18.18%) had prominent CBD no obstruction, and 1 case (9.09%) had malignant stricture. Among 21 subjects with normal AST, there were 12 males and 9 females, with a mean (±SD) age of 50.19 (±11.11). The diameter of CBD dilatation by abdominal ultrasound was 11.55 (±2.53). EUS findings were as follows: 8 cases (38.10%) had stone, another 8 cases (38.10%) had malignant stricture, 3 cases (14.29%) had benign stricture, and 2 cases (9.52%) had prominent CBD no obstruction. Among 24 subjects with normal ALT, there were 11 males and 13 females, with a mean (±SD) age of 50.75 (±13.16). The diameter of CBD dilatation by abdominal ultrasound was 11.79 (±2.59). EUS findings were as follows: 11 cases (45.83%) had stone, 8 cases (33.33%) had malignant stricture, 3 cases (12.50%) had benign stricture, and 2 cases (8.33%) had prominent CBD no obstruction.

		Alkaline phosphatase (45-120 IU/L)	AST (20-40 U/L)	ALT (20-50 U/L)
		N (%)	N (%)	N (%)
	Stone	6 (54.5%)	8 (38.1%)	11 (45.8%)
EUS	Benign stricture	2 (18.1%)	3 (14.2%)	3 (12.5%)
	Malignant stricture	1 (9.09%)	8 (38.1%)	8 (33.3%)
	Prominent CBD dilatation without obstruction	2 (18.1%)	2 (9.5%)	2 (8.3%)
Total		11(100%)	21 (100%)	24 (100%)
CBD diameter	Mean ± SD	9.96 ± 1.13	11.55 ± 2.53	11.79 ± 2.59
Age	Mean ± SD	45.18 ± 14.58	50.19 ± 11.11	50.75 ± 13.16

[Table 1. Descriptive data of the study]

Conclusion: In our study we revealed firstly that CBD dilatation with normal liver chemistry is not always a benign condition. Secondly the importance of EUS as a diagnostic modality in patients with normal liver blood tests and dilated CBD and negative prior imaging tests.

Disclosure: Nothing to disclose

P1640 DIAGNOSTIC YIELD OF A NEW MICRO-BIOPSY FORCEPS IN THE ASSESSMENT WORK OUT OF PERITONEAL CARCINOMATOSIS: A PRELIMINARY EXPERIENCE

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Introduction: Peritoneal carcinomatosis (PC) is the metastatic seeding of malignant cells to peritoneal cavity. It is associated with a dramatic prognosis worsening, with limited therapeutic options. Although cumbersome in diagnosing, due to its presentation variability, it should be ruled out before starting any invasive treatment modality. Recently, a new through-the-needle micro-biopsy forceps (Moray Forceps, US Endoscopy) have been proposed, allowing micro-histology cores.

Aims & Methods: With this novel application, we aimed to evaluate the feasibility of MF in the assessment of PC to complete patient diagnostic work out.

All procedures were conducted under moderate sedation, by 2 expert endosonographers. After a complete EUS evaluation, ascites was punctured, with a 19G FNA needle. Before suction, the MF was introduced through-the-needle, and the suspected carcinomatosis nodule was sampled. Micro-histology specimens were collected in formalin and evaluated by a dedicated pathologist.

Results: 3 consecutive patients (2 F, 1 M; mean age 72 yo), with ascites and suspicion of PC, referred to our center for EUS staging, were sampled with MF. Tissue sampling with MF was feasible in all patients, with a technical success of 100%. Sample quality was medium-high, in all the cases, giving the opportunity for immuno-histochemical staining, when necessary. No adverse events where observed both during and after the procedure in all cases.

Case 1 A 75 yo man underwent investigations for abdominal pain and weight loss. A CT scan showed a 70 mm solid lesion of the pancreas tail. A subsequent EUS confirmed the lesion and showed the presence of ascites, with hypoechoic nodules, suspicious for PC. A FNB of the pancreatic lesions was performed, together with ascites sampling and nodules biopsy with MF. Pathology evaluation reported extended necrotic carcinoma on nodules biopsies, compatible with PC.

Case 2 A 64 yo woman underwent US and CT scan, showing PC, with unknown primary lesion. After negative EGD and colonoscopy, pt underwent EUS, showing ascites with omentum nodules, biopsied with MF. Pathology evaluation reported malignant cells on peritoneal nodules. Supplemental analysis for immunohistochemistry showed CK7, WT1 positivity and CK20 negativity, compatible with ovarian primitivity.

Case 3 A 77 yo woman underwent staging EUS for a focal solid lesion of the pancreatic tail, with abundant peri-hepatic and pelvic fluid. Since the finding of ascites with irregular peritoneal nodular-like lesions, with hypo-enhancement after contrast medium injection, a MF biopsy was performed, for micro-histology. Pathology evaluation of both pancreatic lesion FNA and MF biopsy showed pancreatic ductal adenocarcinoma.

Conclusion: This is the first experience reporting a micro-histology forceps in the ascites work-out to rule out PC. The technique, using this through-the-needle device, is feasible and safe, with technical success rate of 100%. It allowed to sample peritoneal irregularity, with high quality tissue fragments in all the cases, giving the opportunity for additional assessment, as immunoistochemical staining.

Disclosure: Nothing to disclose

P1641 IMPROVING PSEUDOACHALASIA WORKUP: ROLE OF ENDOSCOPIC ULTRASOUND (EUS) IN ADDITION TO HIGH RESOLUTION MANOMETRY (HRM) AND CT IMAGING

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Introduction: Pseudoachalasia is an infrequent secondary form of achalasia which can result from malignant or benign tumors, postoperative complications or paraneoplastic syndromes. Management can be vastly different between achalasia and pseudoachalasia, making it important to exclude the latter condition. Esophago-gastro-duodenoscopy (EGD), high resolution manometry (HRM), barium esophagram, CT scan and EUS play complementary roles to procure a diagnosis of achalasia and exclude pseudoachalasia. This is one of the few studies that aims to evaluate the role of EUS in excluding pseudoachalasia for patients referred for achalasia workup.
Aims & Methods: Data was collected retrospectively from hospital electronic records from 2008 to 2015. Our study group comprised 77 patients (female=44, male=33) with a mean age of 62 years. All cases had a prior EGD and EUS performed. Only cases with a non-diagnostic EGD (including negative esophageal biopsies) were included. Cases with obvious mass seen on EGD were excluded. Work up included the following:(A)classic achalasia symptoms, (B)normal EGD, (C)positive HRM +/-barium for achalasia/gastro-esophageal junction outflow obstruction (GEJ-OO) and (D) had CT scan performed. Yield of excluding pseudoachalasia with addition of EUS was analysed in 4 groups: (1)A+B, (2)A+B+C, (3)A+B+D and (4) A+B+C+D. Cases referred without information on manometry, barium or CT findings were excluded appropriately in the subgroup analysis. Surveillance was performed within 6-12 months to detect any missed cases of pseudoachalasia. Statistical analysis was performed using SPSS V20 using the McNemar Chi-Square and Cochran's Q.
Results: Almost all patients (98.7%) had dysphagia as one of the main symptoms. EGD was non-diagnostic in all cases. EUS was performed in all patients. Number of pseudoachalasia cases detected in Group (1)[n=77], Group (2)[n=53], Group (3)[n=38] and Group (4)[n=26] were 0, 0, 3 and 0 respectively. With addition of EUS (Table 1), incremental detection of pseudoachalasia in these respective cohorts were 7.8% (p=0.031), 1.9% (p=NS), 0% (p=NS) and 0% (p=NS). EUS showed a sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of 85.7%, 100%, 100% and 98.6%. There was only 1 case of pseudoachalasia that was not picked up which manifested 2 years later. Other modalities (B, C and D) complemented each other to give excellent values of sensitivity, specificity and NPV (Table 2).
Conclusion: In excluding pseudoachalasia, additon of EUS to a well complemented workup (typical symptoms, EGD, HRM and/or CT scan) may not yield statistically significant benefit. However, EUS demonstrated good sensitivity and excellent specificity, PPV and NPV for pseudoachalasia detection clinically and should be considered on a case-by-case basis especially in any diagnostic dilemma.
Disclosure: Nothing to disclose

P1642 THE THICKNESS OF THE FNA NEEDLE CONTRIBUTING TO THE PROCEDURES AND HISTOLOGICAL RESULTS BY EUS-FNA

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Introduction: Recently, the newly franseen shaped EUS-FNA needle has been used in worldwide. However, it remains unclear which gauge needles are optimal for the improvement of the diagnostic yield with biopsy specimens.
Aims & Methods: The aim of this study is to whether the thickness of the FNA needle affects procedures of EUS-FNA or histopathological diagnosis. We retrospectively enrolled the patients whose EUS-FNA were performed in our hospital between December 2017 and May 2019. Thirty-two and fifty-one patients underwent EUS-FNA by using 19G and 22G franseen shaped

needle, respectively. We investigated the difference in the success rate of histopathological diagnosis between these two groups. Additionally, we analyzed clinical characteristics (age, sex, clinical diagnosis, target site, puncture tract, the number of punctures, the success rate of string like tissue sampling, the success rate of histopathological diagnosis) to identify the factors contributing to an accurate diagnosis. The Pearson χ test or the Fisher exact test was used for the categorical variables, whereas Student's t-test or Mann-Whitney U test was used for continuous data. Multivariate analysis was performed for the factors which showed p ≦ 0.20 by univariate analysis.
Results: With regard to clinical characteristics, there were no statistical differences in age, sex, clinical diagnosis, and target site (p = 0.55, 0.10, 0.70, 0.06, and 0.06, respectively). In the 19G group, the mean number of punctures was significantly lower than that in the 22G group (1.81 vs 2.21, p = 0.04). The success rate of string like tissue sampling and histopathological diagnosis didn't show significant differences between these two groups (p = 0.94 and 0.21, respectively). We could not identify the significant factors by multivariate analysis, while younger age could contribute to accurate diagnosis by univariate analysis (p = 0.036).
Conclusion: EUS-FNA using 19G franseen shaped needle could have the advantage of achieving the accurate histopathological diagnosis by a significantly smaller number of punctures in comparison with the 22G franseen needle.
Disclosure: Nothing to disclose

P1643 CYTOLOGICAL ANALYSIS BY ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE BIOPSY IN SAMPLING SOLID GASTROINTESTINAL LESIONS: A FEASIBILITY STUDY

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Introduction: Anecdotal results suggest FNB (fine needle biopsy) needles, used for tissue acquisition during endoscopic ultrasound (EUS), yield just as good results when cytological evaluation was performed, as it does with histological analysis.
Aims & Methods: We studied the feasibility of FNB needle (ProCore®, Cook) to obtain samples for cytology analysis. 29 randomly selected patients who underwent EUS-guided FNB of a solid gastrointestinal lesion, with sampling taken for both cytological and histological analysis, between 2016 and 2018, were retrospectively enrolled. Positive cytology was defined as adequate material for interpretation, following either of these cytological techniques: rapid on-site evaluation, sample in fixative or cell block. Data was collected through the medical notes.
Results: 29 patients (59% males, mean age 66) had EUS-FNB of a gastrointestinal lesion (pancreas 80%; others 20%). Positive cytology was obtained in 24/29 cases (83% sensitivity), 23 of which had correct diagnosis (23/24; 96% specificity). Positive histology was obtained in 20/29 cases (69% sensitivity), 19 of which had correct diagnosis (19/20; 95% specificity). Analysing malignant cases only (20), sensitivity was 90% (18/20) and 65% (13/20) for cytology and histology respectively. 5 cases were diagnosed cytologically but not histologically.
Conclusion: This small feasibility study confirms that EUS-FNB needle samples can be sent for cytological analysis. The high sensitivity and specificity of cytology, which in this cohort were even higher than histology, suggests that cytology should be included when EUS-FNB is performed. Sending samples for cytology and histology using 1 needle would increase the yield, while remaining cost-effective. Larger studies are however needed to confirm this.
Disclosure: Nothing to disclose

P1644 FACTORS INFLUENCING DIAGNOSTIC ACCURACY OF ENDOSCOPIC ULTRASOUND WITH FINE NEEDLE ASPIRATION (EUS-FNA) IN PANCREATO-BILIARY TUMORS

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Introduction: Endoscopic ultrasound (EUS) with fine needle aspiration (FNA) is a well-established technique for assessing lesions of the pancreas and biliary tract. Diagnostic yield of EUS-FNA varies according to the expertise of endosonographer raging from 65% to >90%. ESGE guideline suggests to perform a formal training in EUS before starting supervised EUS-FNA. At least 20 to 30 EUS-FNAs with rapid on-site cytopathological examination (ROSE) are recommended to reach a diagnostic accuracy of 80%. Whether the absence of ROSE prolongs the learning period required to achieve a diagnostic accuracy ≥90% has not yet been defined.
Aims & Methods: Aim of the study was to evaluate the factors, including the absence of ROSE, influencing diagnostic accuracy of EUS-FNA in patients with suspected pancreato-biliary tumors in a tertiary center. From 2010 to 2018, 557 consecutive EUS-FNAs were carried out by a single operator under conscious/deep sedation using an echo endoscope (Olympus GFUCT140 or GFUCT180). EUS FNAs were carried out using a needle of different type (Echotip ProCore, Wilson-Cook, Expect TM Boston Scientific, Shark Core TM FNB Medtronic, Acquire Boston Scientific) and with different size (19, 20, 22 Gauge). All samples were fixed in formalin solution for histopathological assessment. In case of absence of clear findings of neoplasm, the sample was deemed as not diagnostic. All clinical data, sex, age, type and size of the needle, site of the lesion, number of passes, and sampling technique (with/without stilet) were prospectively recorded in an electronic database. EUS-FNA performance was defined on the basis of sensitivity, specificity and diagnostic accuracy calculated according to kind and size of the needle, site of the lesion, and progressive experience expressed in the number of procedures grouped in blocks of 50. Variables associated with diagnostic accuracy were evaluated by multivariate logistic regression analysis.
Results: Of 557 EUS-FNA, 308 were carried out for pancreato-biliary neoplasms. The final diagnosis was pancreatic cancer in 253 patients, cystic pancreatic lesion in 8 patients, primary and metastatic liver cancer in 5 patients, and cholangiocarcinoma in 17 patients. Overall sensitivity of EUS-FNA was 66% (95% CI: 60.8 - 71.8), specificity 100%, and diagnostic accuracy 69% (95% CI: 64.0 - 74.4). When tissue sampling was performed using a new fine needle biopsy (FNB) (Acquire/Shark needles), the diagnostic accuracy increased up to 90.5% (95% CI: 80.7 - 99.3). When EUS-FNA was targeted to both primary and metastatic lesions (33 patients) sensitivity raised to 98% (95% CI: 93.9 - 100). Diagnostic accuracy was influenced by the experience of the operator, reaching 87.5% after 250 procedures (95% CI: 78.8 - 96.2). Variables associated with diagnostic accuracy were FNB needle (OR 3.06; 95% CI: 0.94 - 9.94), operator expertise (OR 1.21; 95% CI: 1.02 - 1.43) and EUS-FNA of primary and metastatic sites (OR 9.67; 95% CI: 1.27 - 73.75). No EUS-FNA-related complication occurred during the study period.
Conclusion: EUS-FNA is a safe procedure with high diagnostic accuracy in pancreato-biliary neoplasms. The diagnostic accuracy increases during the learning curve period, being necessary at least 250 EUS-FNAs to achieve a good (>85%) value in the absence of ROSE. The new FNB needles seem to strongly improve EUS performance.
Disclosure: Nothing to disclose

P1645 STUDY ON COMPLICATIONS OF EUS-FNA IN CASES TAKING ANTITHROMBOTIC DRUGS

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Introduction: Endoscopic examinations under antithrombotic medication have been performed with increasing frequency in recent years, and there have been a few reports of bleeding after EUS-FNA[Endoscopic Ultrasound-Fine Needle Aspiration]. We retrospectively examined bleeding and complications after EUS-FNA among users of antithrombotic drugs in our institution.
Aims & Methods: The subjects were 665 consecutive patients (February 2013 to January 2019) who underwent EUS-FNA according to the BSG and ESGE guidelines 2016 for users of antithrombotic drugs.
(1) We divided the patients into two groups according to the preoperative intake condition,(antithrombotic drug group and non-antithrombotic group)and examined the bleeding rate and technique related factors.
(2) The antithrombotic group was further divided into four groups: a continuation group, a withdrawal group (a withdrawal of more than 24 hours before surgery), an aspirin or cilostazol substitution group, and a heparin substitution group.
Direct oral anticoagulants (DOAC) are recommended to be discontinued for more than 48 hours according to the guidelines, and were included in the withdrawal group.

The definition of hemorrhage was a decrease of Hb $\geqq 2$ g/dl within 24 h after the operation according to the guidelines of the International Society for Thrombosis and Hemostasis.
Results: The puncture site of the lesion was pancreas in 474, liver in 7, lymph node in 67, digestive tract in 83, and other organs in 34.
A total of 98 patients in the antithrombotic group, and 567 in the non-antithrombotic group, had a significantly higher proportion of men in the group (p = 0.002), had a significantly higher proportion of the age in the group (p < 0.001). There were no significant differences in the number of punctures, in the puncture sites between the 2 administration groups (P = 0.228, P = 0.248). The overall incidence of FNA complications was 16 cases (2.4%), 4 cases of bleeding, 6 cases of hematoma, 2 cases of pseudocyst, 1 case of pancreatitis, 2 cases of peritonitis, and 1 case of intraabdominal abscess. There were 1 case (1.0%) and 3 cases (0.53%) of bleeding in the antithrombotic and non-antithrombotic groups, and there was no association (P = 0.472).
(2) The antithrombotic drugs consisted of antiplatelet drugs in 69, anticoagulants in 25, and concomitant medication in 4. There were 28 patients in the continuation group, 34 in the drug holiday group, 18 in the aspirin or cilostazol substitution group, and 18 in the heparin substitution group. The bleeding rates in the continuation group, withdrawal group, aspirin or cilostazol substitution group, and heparin substitution group were 0% (0 case), 0% (0 case), 5.6% (1 case), 0% (0 case) being highest in the aspirin or cilostazol substitution group (P = 0.213). No bleeding was observed in patients taking direct oral anticoagulants.
Conclusion: Rates of bleeding and complications after EUS-FNA were similar to those previously reported. Hemorrhaging was more frequent in the aspirin or cilostazol replacement group than in the other groups but improved with conservative treatment. Even in patients taking antithrombotic drugs, the risk of bleeding is low, and it may be possible to safely perform EUS-FNA.
Disclosure: Nothing to disclose

P1646 INCIDENCE AND RISK FACTORS ASSOCIATED WITH BLEEDING POST ENDOSCOPIC ULTRASOUND FINE NEEDLE ASPIRATION/BIOPSY (EUS-FNA/FNB) OF SOLID AND CYSTIC PANCREATIC MASSES

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Introduction: Endoscopic ultrasound fine needle aspiration/biopsy (EUS-FNA/FNB) is an established technique for pancreatic tumor evaluation and considered a high risk bleeding procedure.
Aims & Methods: The aim of this study was to assesses the bleeding rate of EUS-FNA/FNB of solid and cystic pancreatic masses according to use of antithrombotic agents and coagulations parameters (platelet count and prothrombin time).
Our retrospective analysis included EUS-FNA/FNB of solid and cystic pancreatic masses performed between 01/2017-03/2019 in our newly established GI-Department, which features a centralized endoscopy-service in a University affiliated tertiary care teaching hospital.
Bleeding rate was assessed separately for solid pancreatic masses and pancreatic cysts. Parameters analyzed regarding the occurrence of bleeding were: age, use of acetylsalicylic acid (ASA), low molecular heparin (LMWH) or other antithrombotic/anticoagulant agents, platelets count, prothrombin time, and use of EUS-FNB needles.
Results: 115 patients were included into this analysis (76 with solid and 39 with cystic pancreatic masses). Only EUS-FNA was used for pancreatic cysts. EUS-FNA was used in 88.1% of cases with solid pancreatic masses.
No bleeding was observed by EUS-FNA of pancreatic cysts. ASA was present in medication at EUS-FNA in 9/39 (23.1%) of these patients and LMWH in 3/39 (7.7%) cases. Platelets were lower than 100.000/mm^3 in one case (2.5%) and prothrombin time < 60% in 5/39 (12.8%).
Bleeding with hemodynamic instability was not observed in our cohort of EUS-FNA/FNB of solid pancreatic masses. In one case (1.3%) bleeding from a vessel from the duodenal wall was observed with Doppler-US and immediately treated with a hemoclip. In 8/76(10.5%) cases slight intraluminal bleeding with spontaneous termination was registered.
The use of EUS-FNB needles and biopsy in ASA-users trend to increase the bleeding rate in patients with solid pancreatic masses.

Factor	Patients without bleeding (n=67)	Patients with any type of bleeding (n=9)	p value
Age (years)	65.6±14.1	64.8±16.9	0.88
Use of antithrombotics			
- Acetylsalicylic Acid (%)	16.4	44.4	0.12
- LMWH (%)	13.4	11.1	0.73
Platelets (cells/mm3)	260.9±78.7	266.7±76.7	0.83
Prothrombine time (%)	90.1±15.9	81.3±18.9	0.13
Use of FNB needles (%)	8.9	33.3	0.08

[Table: Risk Factors associated with Bleeding post EUS-FNA/FNB of Solid and Cystic Pancreatic Masses]

Conclusion: No bleeding was observed post EUS-FNA of pancreatics cysts. Slight bleeding was observed in 11.8% of EUS biopsies of solid pancreatic masses, but no hemodynamic relavant bleeding occurred. Only in one case a hemoclip was needed to stop bleeding. Use of EUS-FNB needle and ASA trend to increase the bleeding rate.
Disclosure: Nothing to disclose

P1647 GASTROINTESTINAL SUBEPITHELIAL LESIONS (GI SELS): OPTIMIZING UNNECESSARY SURVEILLANCE AND PATIENT CARE WITH ENDOSCOPIC ULTRASOUND (EUS)

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Introduction: Upper GI subepithelial lesions (SELs) are commonly found during oesophagogastroduodenoscopy (OGD) and most are <2cm on average. Management of these small SELs are often variable by different centres. Many patients are routinely brought back for frequent 1-2 yearly surveillance despite being asymptomatic and this significantly escalates health care cost without benefit to patients or actual improvement in clinical management if the SELs are small and stable.
Aims & Methods: We aim to determine the outcome of these small but frequently seen SELs based on a retrospective analysis of a cohort of SEL cases followed prospectively. Patients with SELs < 2cm and no change in GI symptoms from 2007 up to 2016 with OGD and EUS done were analyzed in terms of demographic characteristics and size progression of SEL, lymph node presence and eventual change in management from first detection right up to the last OGD/EUS surveillance. Cases with less than 3 years of follow up were excluded for meaningful analysis. Analysis using paired sample T-test for mean SEL size was done using SPSS.
Results: There was 210 patients ranging from 29-83 years of age, 61% being female. Average follow up range from 3 to 11 years with mean of 6 years. SEL size on index EUS and final EUS range from 3-19mm and 2-20mm respectively. The SEL distribution comprised 72% gastric and 18% esophageal origin.
Of all cases, 62% , 28% and 10% were found on EUS to arise from muscularis propria (MP), muscularis mucosa (MM) and submucosa of the GI tract respectively. About 10% underwent fine needle aspiration (FNA) with none being malignancy. Only 1 case demonstrated an increase in size of more than 50% but less than 100% over 3 years. All other SELs had fluctuations in mean size of < 33% or size regression and was deemed overall stable by endosonographer.
There was no significant difference between the initial mean size of these SELs on index EUS compared to final mean size on the last EUS (p=0.288). There was 0% mortality related to all these SELs.
Conclusion: This study suggests small GI SELs < 2cm can generally adopt a longer interval surveillance from baseline and may not need continuous yearly/biyearly surveillance if the initial repeat EUS is stable compared to the index scope, done within 3 years. A reasonable surveillance sequence proposed include 1 year followed by 3 years and then every 5-10 yearly if SEL remains stable and patient has no new GI symptoms. This has potential to reduce health care cost and growing endoscopy burden without sacrificing important clinical outcomes for patients.
Disclosure: Nothing to disclose

P1648 EFFICACY OF LUMEN APPOSING METAL STENTS VS SELF-EXPANDABLE METAL STENTS FOR ENDOSCOPIC ULTRASOUND-GUIDED CHOLEDOCHO-DUODENOSTOMY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Endoscopic ultrasound (EUS)-guided biliary drainage (BD) is gaining a primary role for endoscopic palliation of malignant common bile duct obstruction. Lumen apposing fully covered metal stents (LAMS) are now replacing self-expandable metal stents (SEMS), commonly used for this procedure in the past.

Aims & Methods: The aim of this systematic review and meta-analysis was to evaluate the efficacy and safety of LAMS vs SEMS for biliary drainage via endoscopic ultrasound- guided choledocho-duodenostomy.

A meta-analysis was performed using the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) protocols. Three databases (PubMed, EMBASE and Google Scholar) were searched for studies containing data on EUS-guided choledocho-duodenostomy. English language articles from inception to 03 February 2019 were checked against our predetermined eligibility criteria. Odds ratios (OR) and mean differences (MD) were pooled using the random effects model with the DerSimonian-Laird estimation and displayed on forest plots.

Results: A total of 29 studies were included containing data on 960 patients. LAMS and SEMS were evaluated in 4 and 25 studies, accounting for 174 and 786 patients, respectively. Overall, the pooled rate of clinical success was 82.1% [95% CI 76.3-86.7], and significantly higher for LAMS than SEMS (91.5% [95% CI 86.2-94.9] vs. 71.4% [95% CI 61.2-79.9, p< 0.001). The overall technical success rate was 78.2% [95% CI 70.8-84.2], and significantly higher for LAMS than SEMS (93.4 % [95% CI 60.5-79.0] vs. 70.6% [95% CI 61.2-79.9], p< 0.001).

Both the procedure-related adverse events (AEs) and re-intervention rates were lower for LAMS than SEMS, although the rate of overall AEs was significantly higher for LAMS than SEMS (18.4% [95% CI 11.3-28.5] vs. 11.2% [95% CI 8.5-14.6], p< 0.001).

Conclusion: LAMS outperformed SEMS in terms of efficacy of EUS-guided choledocho-duodenostomy for biliary drainage. Their use was associated with less procedural AEs and fewer re-interventions when compared to SEMS placement, however, more post-procedure AEs occurred with LAMS when compared to SEMS. This most critical point requires further investigation.

Disclosure: Nothing to disclose

P1649 MULTICENTER, RANDOMIZED COMPARISON OF 19-GAUGE STAINLESS STEEL AND NITINOL-BASED NEEDLES FOR EUS-FNB OF SOLID PANCREATIC MASSES

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Introduction: Endoscopic ultrasound guided fine needle biopsy (EUS-FNB) represents the current standard for obtaining a histological diagnosis of a pancreatic mass. 19G stainless steel needles are relatively rigid and technical difficulties due to the inability to advance the needle out of the endoscope often prevent tissue collection, especially for the transduodenal puncture route. Nitinol-based needles are more flexible and might decrease technical difficulties and thus increase diagnostic accuracy. In this prospective, multicenter, randomized, partially blinded study we compared the diagnostic value of those two needle types in patients with a solid pancreatic lesion.

Aims & Methods: Consecutive patients with a solid pancreatic mass were diagnosed with EUS-FNB using one puncture with each needle in a randomized fashion. Olympus EZ Shot 2 19G were used as steel needles and EZ Shot 3 Plus 19G were used for nitinol-based needles. Final diagnosis was made by histology and diagnostic procedures during follow up. Primary endpoint was diagnostic accuracy of each needle. Secondary endpoints included time for puncture, amount of tumor tissue obtained, and technical failure. Histological specimen were centrally reviewed by a pathologist blinded to the final needle type and final diagnosis. ClinicalTrials.gov Identifier: NCT02909530.

Results: Out of 46 prospectively recruited patients central pathological examination was available for 41. Diagnostic accuracy for the two needles combined was 87.8%. Diagnostic accuracy was 66% and 68% using the stainless steel and nitinol-based needle respectively. Analysis of diagnostic accuracy divided by transduodenal and transgastric route furthermore presented no significant difference. Time spent for puncturing was 137 +/- 61 seconds (mean +/- SD) for the stainless steel and 111 +/- 53 seconds for

the nitinol-based needle (p<0.001). Technical failure occurred in 3 (6.5%) cases using the stainless steel and in none using the nitinol-based needle. Postprocedural self-limited bleeding occurred in 2 (4%) cases.

Conclusion: Usage of a nitinol-based 19G needle failed to present a significant difference regarding diagnostic accuracy compared with a stainless steel needle in EUS-FNB of solid pancreatic lesions. Usage of a nitinol-based needle was faster and resulted in no technical failures.

Disclosure: Nothing to disclose

P1650 ENDOSCOPIC ULTRASOUND GUIDED BIOPSY USING FRANSEEN NEEDLE:COMPARISON WITH EUS GUIDED FINE NEEDLE ASPIRATION

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Introduction: Current guidelines suggest that the EUS-FNB is equivalent to FNA and both tissue acquisition techniques may be utilised for cytopathological analysis.With the FNB technique there is a possibility of assessing tissue adequacy macroscopically obviating the need for ROSE.Possibility of immunohistochemistry in these samples aids classification of the neoplasia particularly in difficult casesReduction in number of passes would lead to fewer complications.

Aims & Methods: We performed a retrospective cohort study of patients with solid masses or lesions needing EUS-guided core biopsy between January 2018 and November 2018. All core biopsies were obtained using an Acquire™Fine Needle Biopsy Device- 22 gauge (Boston Scientific Corporation, Natick MA, USA).This data was compared to the matched population in the previous year using the standard 22-25 gauge needle for FNAC. All patients having EUS-FNAC/FNB were evaluated for the study. Patients with cystic lesions based on EUS and other cross-sectional imaging data were excluded from the study. Details of the location of the lesion, size of the lesion, endoscopic ultrasound findings, type of tissue acquisition (transesophageal, transgastric, trans duodenal), tissue acquisition techniques (slow pull, fanning vs. suction),technical success, operator visual satisfaction on tissue acquisition, pathologist satisfaction, average passes, size of the core in FNB and final cytopathologist or histopathologic diagnosis with or without IHC were recorded.

Results: A total of 207 patients, 134 (64.7%) male and 73 (35.3%) female were included in this study. The mean age of the study population was 54.3±11 years83 of these patients has FNB and 124 had FNAC.148 (71.4%) of the biopsied lesions were located in the pancreas and 59 (28.6%) were extrapancreatic in location.Only 3/83 needed repeat biopsy for diagnosis in the FNB group vs. 17/124 in the FNAC group with average pass of 1 and 2.7 respectively.Notably 2/3 repeat biopsies in the FNB group were gastric wall thickening? Linitus plastica and the third was a retroperitoneal tumour with extensive necrosis.There were no significant complications in either group.

Conclusion: FNB sampling provides intact cores that provide better characterization of malignancy and improve the diagnostic accuracy for benign lesions. With extrapancreatic lesions (especially gastrointestinal stromal tumors, lymphoma, and neuroendocrine tumors), histology is crucial for reaching a diagnosis, as cytology alone cannot uniformly provide adequate architecture and cellular configuration.We encountered no procedure-related complications.In this large, single-center study, EUS-FNB performed with a novel Franseen-type biopsy needle proved to be an effective modality for tissue acquisition from all solid lesions.EUS FNB should replace FNAC in our opinion.

Disclosure: Nothing to disclose

P1651 EUS-GUIDED SAMPLING OF PANCREATIC ADENOCARCINOMA: STANDARD VERSUS CORE NEEDLE WITHOUT ON-SITE CYTOPATHOLOGY

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Introduction: With the development of the new core needles, fine needle biopsy (FNB) has emerged as an alternative to standard fine needle aspiration (FNA) for procurement of larger amounts of tissue. Several studies have been published so far on core needles, most of them coming from expert centers. Our aim was to compare the diagnostic adequacy and yield of a core versus standard needle, in a center without on-site cytopathology.
Aims & Methods: We enrolled all patients with a diagnosis of pancreatic adenocarcinoma admitted in our clinic over a period of 16 months, who underwent endoscopic ultrasound (EUS) guided tissue sampling using either standard EchoTip, or ProCore needle (Cook Medical). EUS examinations were carried out using a Pentax-Hitachi system using a linear probe. Final diagnosis was set by FNA/FNB, repeated FNA/FNB, surgery or long-term outcome. We compared the diagnostic adequacy of samples and the diagnostic yield for malignancy between the two groups - FNA versus FNB needle.
Results: Altogether 58 patients were enrolled, median age 62 years, 63.8% males. FNB using the core needle was done in 19/58 (32.8%) of patients, while the other 67.2% were punctured using FNA needle. Mean tumor size was 33 mm in the FNA group, and 33.9 mm in the FNB group. More pancreatic head tumors were sampled using an FNA needle - 51.3% versus 31.6%. Also, more 22G needles were used in the FNA group (46% vs. 37%). Diagnostic adequacy was achieved in 89% of FNA samples and 94% of FNB. Diagnostic yield for malignancy was slightly better for FNB - 89.5%, compared to FNA - 82.1%.
Conclusion: In our study, high diagnostic performance was achieved with both needles without on-site cytopathology, but the core one proved to be slightly better.
Disclosure: Nothing to disclose

P1652 THE ON- DEMAND NUMBER OF NECROSECTOMY SESSIONS DURING LUMEN APPOSING METAL STENTS DRAINAGE IN WALLED-OFF PANCREATIC NECROSIS CANNOT BE PREDICTED

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Introduction: The fully-covered stents lumen apposing metal stents (LAMS) are designed for one step placement and facilitates the direct endoscopic necrosectomy into the walled-off pancreatic necrosis (WOPN). However, the prediction of the number of necrosectomy sessions in these patients is not known.
Aims & Methods: To assess the possible prediction for the need of necrosectomy according to the amount of necrosis inside the WOPN assessed during endosonography (EUS).

This is a single center prospective analysis at a single tertiary referral center. There were enrolled patients with symptomatic WOPN (pain, infection or gastric or biliary outlet obstruction) with more than 4 weeks after the onset of acute pancreatitis. The amount of necrosis was assessed by EUS in the session of LAMS placement . There were noted the clinical success regarding LAMS placement , the number of necrosectomies, the need for additional drainage (pigtail stents), the complications and the survival rate. The need for necrosectomy was performed on-demand when fever or inflammatory biological markers raised after LAMS placement. The patients were discharged when the inflammatory markers normalized and they were followed-up monthly by abdominal ultrasound and by CT scan at three months.
Results: There were 28 patients included and more than half were infected. The median size of the WOPN was 108mm (IQR: 81-146). LAMS was successfully placed in all patients, without immediate complications following the procedure. Necrosis was present in all patients and one third of them had more than 50% of the WOPN cavity with necrosis. Necrosectomies were performed in 25/28 (89.2%) patients. The median number of endoscopic debridement sessions was 2 (IQR: 1-4). There was no statistically significant association between the size of the WOPN and number of necrosectomies performed (Spearman's r coefficient =153, p=0.427) or between the amount of necrosis and the number of necrosectomies (p>0.05). The median duration until stent removal was 36 days (IQR: 24 - 55 days). Overall, WOPN resolution at 3 months follow up was noted in 24/28 (85.7%) patients. Two patients died, one due to pseudoaneurysm bleeding and another with bleeding from gastric collateral circulation.
Conclusion: The size of WOPN and the amount of necrosis prior LAMS drainage of WOPN cannot predict the need for on-demand necrosectomy sessions.
Disclosure: Nothing to disclose

P1653 OVER THE SCOPE CLIPS FOR EUS DUODENAL PERFORATION

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Introduction: EUS represent nowadays an essential tool the identification, staging sampling and follow-up of benign and malignant bilio-pancreatic lesions. Diagnostic endosonography has traditionally been associated with a very low rate of complications Perforation stay one of the most deemed complication in endoscopy and in EUS, although surgery allows simultaneous treatment of the perforation and of an associated biliary or pancreatic disorder, surgery is an invasive treatment carrying its own morbidity and mortality, especially when undertaken in a context of emergency. We wanted to assess the feasibility, efficacy and safety of the immediate endoscopic repair of EUS-induced duodenal perforations with over-the-scope clips and report our experience to determine whether this procedure can be recommended in such cases.
Aims & Methods: We performed a retrospective study of patients with EUS related iatrogenic perforation observed in our unit from 2011 to 08/2018.
We included all consecutive patients with EUS related perforation with immediate diagnosis, and receiving a conservative endoscopic management. Patients with primary surgical management and conservative, non-interventional management, as well as perforation resulting from an endoscopic intervention (*eg* endoscopic sphicnterotomy, cyst fenestration, etc), were excluded.
Results: 13 perforations in 8504 EUS procedure occurred (0.15%).
Two patients were excluded, one for a large duodenal tear requiring immediate surgery, the other one for misdiagnosing the perforation leading to early discharge and readmission 24h later with peritonitis and emergency surgery.
A total of 11 patients were included, all women. The mean patient age was 75 (range 68-88) years. 8/11 (72.7%) perforations were due to a radial probe. All procedures were performed at a diagnostic end.
Perforations were located in the superior flexure of the duodenum in 9/11 (81%), in the descending part of the duodenum 1/11(9%), and in the inferior duodenal flexure 1/11 (9%). The size of the defect was ranged from 10-15mm. All clipping procedures experienced a technical and clinical success. 3/11(27%) had a stay in intensive care unit for less than 72h, total hospital stay ranged from 3-22 days.

Conclusion: Although bearing a low rate of specific complications, diagnostic EUS is not adverse event-free and observing proper indications is necessary, especially in elderly patients. Duodenal perforation is a potentially serious adverse event, but conservative endoscopic treatment with over-the-scope clips represents a feasible, efficient and safe treatment that can prevent surgery in most instances.
Disclosure: Nothing to disclose

P1654 COMPARISON OF DIAGNOSTIC OUTCOMES OF TWO DIFFERENT CORE NEEDLES FOR EUS GUIDED TISSUE ACQUISITION: 22-GAUGE REVERSE BEVEL VERSUS 22-GAUGE FRANSEEN NEEDLE

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Introduction: Endoscopic Ultrasound (EUS) guided tissue acquisition of lesions adjacent to the gastrointestinal tract has been previously achieved by fine needle aspiration (FNA). Recently, core biopsy from EUS guided approach has been successfully performed with the new tip-modifying needles, known as fine needle biopsy (FNB) needles. The first of these was the reverse bevel needle known as ProCore™ (Cook Medicine). The more recently developed core needles include the franseen-tip needle (Acquire™, Boston Scientific) and fork-like tip needle (Sharkcore, Metronics). Although the use of these core needles obtained more tissue and is associated with a better diagnostic yield than the FNA needles, data on diagnostic outcome between these core needles are lacking.
Aims & Methods: To compare diagnostic outcomes of EUS guided tissue acquisition between the 22-gauge Cook ProCore™ and the 22-gauge Boston Scientific Acquire™ needles.
This is a prospective evaluation of consecutive patients who were referred for EUS tissue acquisition of lesions of at least 1cm adjacent to the upper GI tract. Biopsy was performed without the presence of on-site cytology and two needle passes were taken from each lesion, with one pass from a 22-gauge ProCore needle and one pass from a 22-gauge Acquire needle. The order of the needle was randomized. Macroscopic On-Site Evaluation (MOSE) was performed to examine the adequacy of the acquired tissue and the samples from each needle were sent in separate pots for histology. Core was defined as whitish tissue and the length of the core was measured to be 3 times that of the width. Final diagnosis was based on either surgical specimen or from biopsy specimen with at least 6 months clinical follow up.
Results: A total of 78 needle passes were taken from 39 lesions, including 24 pancreatic lesions, 6 lymph nodes, 4 subepithelial lesions, 3 biliary masses, 2 liver lesions and 1 GB mass. The mean size of the lesions was 27±9mm. Overall, tissue diagnosis was achieved in 38/39 lesions, giving a diagnostic accuracy of 97%, which included 21 pancreatic cancers, 8 metastatic cancers, 2 pancreatic neuroendocrine tumour, 2 GIST, 2 leiomyoma, 1 focal pancreatitis, and 3 reactive nodes. There was no difference in diagnostic yield between the two needles (Procore = 90% (35/39) vs. Acquire = 95% (37/39); P=0.97). In 3 patients, the Acquire needle provided a diagnostic sample whereas the ProCore did not. In one patient, the ProCore needle provided a diagnostic sample whereas the Acquire did not. Both needles were unable to obtain an adequate sample for a retrocardiac lymph node. Based on MOSE, the core length of tissue taken from the Procore needle was longer than that of the Acquire needle (14.6mm vs. 12.8mm, P=0.038). This, however, did not contribute to an increase in diagnostic yield
Conclusion: This tandem EUS guided biopsy study showed that, even in the absence of rapid on-site cytology, the diagnostic accuracy from 2 passes of FNB needles is high (97%), and there is no difference in the diagnostic yield between the reverse bevel and franseen tip needles. These findings support the use of these new FNB needles in routine EUS guided tissue acquisition.
References: 1. Iglesias-Garcia, J. et al. Feasibility and yield of a new EUS histology needle: results from a multicenter, pooled, cohort study. Gastrointest. Endosc. 73, 1189-1196 (2011). 2. Jovani, M., Abidi, W. M. & Lee, L. S. Novel fork-tip needles versus standard needles for EUS-guided tissue acquisition from solid masses of the upper GI tract: a matched cohort study. Scand. J. Gastroenterol. 52, 784-787 (2017). 3. Leung Ki, E.-L. et al.

Macroscopic onsite evaluation using endoscopic ultrasound fine needle biopsy as an alternative to rapid onsite evaluation. Endosc. Int. Open 07, E189-E194 (2019).
Disclosure: Nothing to disclose

P1655 VALIDATION OF THE COMPUTED ASSESSMENT OF SMALL-BOWEL CLEANSING OF THE MIROCAM® MC1600 CAPSULE ENDOSCOPY AND COMPARISON WITH THE OLD VERSION (MC1200)

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Introduction: Currently, a validated scale for grading small-bowel cleansing in capsule endoscopy (CE) is lacking. The computed assessment score of the small-bowel cleansing (CAC) is based on objective measurements of color intensities (red over green) in the Rapid Reader® of the PillCam® CE system. Areas of adequate mucosal visibility should be associated with high values of red intensity and areas of inadequate mucosal visibility associated with low values of green intensity. The CAC score was adapted to Mirocam® MC1200 system by *Ponte et al*, being considered an objective and feasible score in the assessment of small-bowel cleansing. *About Ali et al*, considered a CAC score cut-off of 1.6 to best discriminate adequately from inadequately cleansed frames. Recently, Mirocam® system created a new informatic software (MC1600) which enables capturing around 6 frames per second, comparing with the 3 frames per second in MC1200.
Aims & Methods: This study aimed to adapt the CAC score to the Mirocam® MC1600 system and evaluate the correlation of this computed score with *Brotz* grading scales (Quantitative Index - QI and Qualitative Evaluation - QE) in the old CE MC1200 and in the new CE MC1600. The authors performed a retrospective single-center analysis of CE Mirocam® MC1200 and MC1600. Patients with active bleeding and whose capsule did not reach the cecum were excluded from the study. The first duodenal image and the first cecal image were selected from all CE videos, and all the remaining findings were deleted. Map View function displays a bar circumscribed by a blue line which represents the small bowel images. The histogram function of GIMP® was used to measure the mean intensity value of the green and red channels. Afterwards, these values were entered into a database and the CAC score were determined according to the *Weyenberg et al* formula. The correlation between the CAC scores and the 10 points QI was performed using Spearman's correlation coefficient. The CAC scores and the 4 grades QE were compared using the intra-class correlation coefficient (ICC).
Results: 73 CE videos were analyzed referring to 73 patients, 53.4% were male (n=39), with a mean age of 54.2 (± 18.8) years-old. 58.9% (n=43) of the CE videos were performed with the MC1600, and 41.1% (n=30) with the MC1200. The main indication was OOGIB in 61.6% (n=45), followed by suspected Crohn's disease (CD) in 32.9% (n=24). The sex, age and indication to perform CE did not show to be different between the 2 softwares (p=0.23, p=0.06 and p=0.29, respectively). The QI (New: 8.16 vs. Old: 7.87, p=0.44) and a poor QE (New: 11.6% vs. Old: 6.7%, p=0.89) did not differ between the 2 softwares. On the other hand, the CAC score was higher with the MC1600 version (5.62 vs. 4.95, p=0.03). With the MC1600 version, a poor correlation between QI and CAC score was found with a Spearman's Rho of 0.36 (p< 0.05), and a poor correlation between QE and CAC score was found with an ICC of 0.15 (CI 95% = -0.11 to 0.44, p = 0.01). With the MC1200 version, a fair correlation between QI and CAC score was found with a Spearman's Rho of 0.48 (p< 0.01), and a poor correlation between QE and CAC score was found with an ICC of 0.21 (CI 95% = -0.18 to 0.56, p = 0.03).
Conclusion: The new software (MC1600) presented higher CAC scores, which could be of great importance since this score allows a more objective assessment of small-bowel cleansing. With this new software version, the authors were not able to verify a better correlation between this computed assessment and the *Brotz* grading scales.
Disclosure: Nothing to disclose

P1656 A CONVOLUTIONAL NEURAL NETWORK ALGORITHM WITH CLASS ACTIVATION MAP FOR DETECTION OF VARIOUS LESIONS DURING SMALL BOWEL CAPSULE ENDOSCOPY

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Introduction: Although small bowel capsule endoscopy (SBCE) has become the best diagnostic modality for small bowel lesion, time-consuming and tedious review process leads to low diagnostic yield.

Aims & Methods: The aim of this study was to develop a convolutional neural network (CNN) algorithm for automatic detection of various small bowel lesions. A total of 3,313 still images containing pathology findings were collected from 389 SBCE videos. These were classified into two categories by expert readers: vascular lesion (red spot/angioectasia/active bleeding) and depressed lesion (erosion/ulcer/stricture). A VGG-like CNN [1] (14 convolutional, 7 max-pooling and 2 fully-connected layers) was implemented to extract features which carry principal characteristics of an input image in both categories. Then we combined the two different binary classification models (normal-vascular and normal-depressed) not only to detect two types of lesions from each model, but also to yield conservative negative. Furthermore, we visualized where the detected lesions are, class activation map (CAM), by calculating contributions of each pixel in a feature to the classification result [2].

Results: The algorithm for detection of vascular lesions yielded a sensitivity of 88.3%, a specificity of 97.3%, a positive predictive value of 97.0%, a negative predictive value of 89.3%, and an accuracy of 92.8%. The algorithm for detection of depressed lesions revealed a sensitivity of 88.9%, a specificity of 95.6%, a positive predictive value of 95.2%, a negative predictive value of 89.6%, and an accuracy of 90.0%. We combined these two algorithms in the way that a normal image was defined when it was not classified as a pathology image by either vascular or depressed lesion detection algorithm. As a result, the combined algorithm yielded a sensitivity of 91.4%, a specificity of 93.2%, a positive predictive value of 93.1%, a negative predictive value of 91.6%, and an accuracy of 92.3%. Furthermore, CAM accurately pinpointed lesion parts from the pathology images, which means that it colored the lesion parts red but non-lesion parts blue.

Conclusion: Our CNN algorithm showed high diagnostic performances for detecting various lesions of SBCE. Visualization of the relevant lesions by CAM could help to reduce missed detection with the naked eye.

References: 1. K. Simonyan and A. Zisserman, "Very Deep Convolutional Networks for Large-Scale Image Recognition," arXiv preprint arXiv:1409.15556, 2014. 2. R. R. Selvaraju, A. Das, R. Vedantam, M. Cogswell, D. Parikh, and D. Batra, "Grad-cam: Why did you say that? Visual explanations from deep networks via gradient-based localization," arXiv preprint arXiv:1610.02391, 2016.

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P1657 OPTIMAL PREPARATION FOR SMALL BOWEL CAPSULE ENDOSCOPY

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Introduction: Visualization of the mucosa in Small bowel capsule endoscopy (SBCE) is frequently impaired by intestinal contents (e.g. food residue, air bubbles and unclear turbid intraluminal fluid), more often in the lower small intestine where we tend to encounter more endoscopic and pathological findings. A meta-analysis had shown that small-bowel purgative preparation (polyethylene glycol solution or sodium phosphate) improves the diagnostic yield (Am J Gastroenterol 2009; 104: 219-227). The Canadian Association of Gastroenterology (CAG) and the European Society of Gastro-

intestinal Endoscopy (ESGE) does recommend the use of a bowel preparation (Gastroenterology. 2017 Feb;152(3):497. Endoscopy 2010; 42: 220-227.), but no specific preparation regimen is shown.

Aims & Methods: The aim of this study was to seek an appropriate preparation for SBCE. We reviewed a consecutive 340 patients (201:139/ male:female) who underwent SBCE from Jul. 2009 to Sep. 2017 in Okayama Saiseikai General Hospital and assessed retrospectively from the clinical record. SBCE was performed using the Given Imaging PillCam SB2 and SB3. For each SBCE, two segments of 10 minutes were selected, one at the last 10 minutes of the small intestine transit and one at the start of the last quartile of the small intestine transit time. Visibility of the SBCE image was assessed based on percentage of (or proportion) of 5 elements: (1) visualized mucosa, (2) fluid and debris, (3) bubbles, (4) bile/chyme staining, and (5) brightness.

Among 340 subjects, Group A followed the conventional overnight fast (n=58, 17.1%). Group B received 0.9L of magnesium citrate (MC) solution after the overnight fast, 2 hours prior to the endoscopy (n=84, 24.7%).

Group C received 1~2L of polyethylene glycol (PEG) solution after the overnight fast, 2 hours prior to the endoscopy (n=29, 8.5%).

Group D received 1~2L of PEG solution after the overnight fast before colonoscopy, and SBCE was performed immediately after the negative colonoscopy, but the duration was not assessable (n=117, 34.4%).

Group E received 0.18L of MC solution before the overnight fast (n=24, 7.1%). 28 subjects were excluded, 24 because the visibility was not assessable due to massive bleeding, unreached cecum, recording failure and 4 because of preparation unknown.

Results: The use of 0.9L of MC solutions led to a significant improvement in (4) bile/chyme staining (P=0.0101) and (5) brightness (P=0.0014). Also, (1) visualized mucosa (P=0.0826), (2) fluid and debris (P=0.0515), and (3) bubbles (P=0.0592) seemed to show a trend toward visibility improvement. All the patients in Group B were able to ingest the whole 0.9L solutions before the SBCE.

Conclusion: Comparatively low volume (0.9L) MC solution improves visual quality of SBCE and was feasible.

Disclosure: Nothing to disclose

P1658 CAPSULE ENDOSCOPY FOR SMALL BOWEL CROHN'S DISEASE - SHOULD WE TRUST IN MAGNETIC RESONANCE ENTEROGRAPHY?

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Introduction: Currently, both small bowel capsule endoscopy (SBCE) and magnetic resonance enterography (MRE) can be used to assess small bowel involvement in Crohn's disease (CD). However, SBCE appears to be more sensitive in the detection of mild and proximal lesions.

Aims & Methods: We aimed to compare the diagnostic yield for SBCE and MRE.

Adult patients with either confirmed or suspected Crohn's disease who were submitted to both SBCE and MRE were retrospectively reviewed. Only patients performing SBCE and MRE within 3 months were included and patients with changes in CD therapy during this period were excluded.

Presence of ulcers, villous edema and stenosis were assessed in SBCE, and patients with Lewis Score (LS) ≥135 were considered to have significant inflammation. SB wall thickening, hyperenhancement, edema, comb sign or presence of ulcers were considered signs of active CD in MRE.

Results: Included 30 patients (53.3% suspected and 46.7% confirmed CD) with a median age of 31±11 years, 56.7% of which were females. Comparing SBCE and MRE, SBCE had a significantly higher diagnostic yield (90.0% vs 53.3%, p=0.007), with higher detection of ileal lesions (83.3% vs 53.3%, p=0.022).

Even more importantly, only SBCE identified jejunal inflammatory activity (46.7% vs 0.0%, p< 0.001). Despite the fact that statistical significance was not attained, SBCE identified 2 traversable strictures that were not identified by MRE (6.7% vs 0.0%, p=0.500) and out of 14 patients with suspected Crohn's disease, SBCE identified significant inflammation in 4 patients with negative MRE (85.7% vs 57.1%, p=0.289). MRE was more

likely to detect findings when SBCE showed moderate to severe inflammatory activity (LS ≥790) compared with those with mild inflammatory activity (LS 135-790) (72.7% vs 30.8%, p=0.041).

Conclusion: In our cohort, SBCE showed a significant overall higher diagnostic yield than MRE, with higher detection of distal lesions and, more importantly, SBCE identified proximal lesions in nearly half of examination while MRE was unable to identify any case. MRE diagnostic yield was more heavily influenced by the severity of inflammatory activity, being significantly inferior to SBCE in patients with mild inflammatory activity.

Disclosure: Nothing to disclose

P1659 VIDEO CAPSULE COLONOSCOPY: MAY THERE BE PREDICTORS OF COLORECTAL POLYPS FINDINGS AFTER INCOMPLETE CONVENTIONAL COLONOSCOPY?

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Introduction: Even though conventional colonoscopy remains as the first line approach in colorectal polyps detection, Video Capsule Endoscopy (VCE) may play an important role on further investigation after an incomplete colonoscopy.

Aims & Methods: Our aim was to evaluate the existence of predictive factors for colorectal polyps detection by VCE on patients with previous incomplete conventional colonoscopy.

For that, a retrospective monocentric study of patients who underwent VCE after previous incomplete colonoscopy between April 2015 and January 2019 was carried out. Analyzed variables included age, gender, capsule's transit time in colon, previous hemoglobin, positive fecal occult blood test, personal history of colorectal polyps, familiar history of colorectal cancer, smoking habits, obesity, progression level on the incomplete colonoscopy and existence of previous complete colonoscopy. Mann-Whitney test was used for evaluation of continuous variables and Chi-square test for categorical variables.

Results: 59 patients were included, 49 being females (83.1%), with a median age of 68 (interquartile range of 18). Colorectal polyps were documented in 18 patients (30.5%), with sessile polyps prevailing (88.9% of the patients with positive findings). 17 of these patients (94.4%) presented polyps in locations not previously approached by the incomplete colonoscopy. Smoking habits (former or current) were significantly associated with the detection of colorectal polyps after incomplete colonoscopy (66.7% vs 26.0%; p=.041). Other analyzed variables did not show any statistically significative differences (p>0.05).

Conclusion: VCE is a very useful technique to be used on further investigation of patients with previous incomplete conventional colonoscopy, allowing to detect colorectal polyps in around one-third of the evaluated patients. There was a significant association between smoking habits and colorectal polyps on VCE.

Disclosure: Nothing to disclose

P1660 CLEANLINESS SCORES FOR SMALL BOWEL CAPSULE ENDOSCOPY: AN EXTERNAL (UN)VALIDATION STUDY

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Introduction: Small bowel (SB) capsule endoscopy (CE) is a standard for the examination of the SB in patients with occult gastrointestinal bleeding (OGIB) or suspicion of Crohn's disease. The detection of lesions in CE may be dependent on the quality of the visualization of the SB. Brotz et al. developed 3 different scores to assess the SB cleanliness: one quantitative score named Qualitative Index (QI); and two qualitative scores named Qualitative Evaluation (QE), and Overall Adequacy Assessment (OAA). After internal validation these 3 scores were considered as a reference. However, no external validation of any of these score has been performed to date. The aim of our study was to assess their reproducibility.

Aims & Methods: One hundred and fifty-five complete, third-generation SB-CE videos were analysed. These videos were extracted from a recent, randomized, controlled multicenter trial (PREPINTEST, NCT01267981); which evaluated three different modalities of preparation of SB, in 834 patients with OGIB; by selecting third-generation SB-CE from the 5 largest inclusion centres. All 155 videos were read twice, in a random order, at six-week interval, by three SB-CE expert readers. The 3 scores (QI, QE, OAA) were determined by each expert independently, using the definitions of the initial study:

- QI was based on a 10-point scale, with 2 points allotted to each of five items amongst mucosa visibility, fluid and debris, bubbles, bile/chyme staining, brightness;
- QE based on QI items but simplified, grading the cleansing of the SB as poor, fair, good and excellent;
- OAA was defined by the "adequacy" or "inadequacy" of the preparation. Linear weighted Cohen's Kappa were calculated to assess intra-observer and inter-observer reproducibility for each score.

Results: Intra-observer reproducibility was fair to moderate, with Kappa coefficients varying between 0.37-0.46, 0.41-0.51 and 0.41-0.50 for QI, QE and OAA, respectively.

Inter-observer reproducibility was fair to substantial correlation, with Kappa coefficients between experts varying between 0.40-0.64, 0.29-0.65 and 0.52-0.71 for QI, QE and OAA, respectively (Table 1).

	Qualitative index (QI) Mean (range)	Qualitative evaluation (QE) Mean (range)	Overall Adequacy Assessment (OAA) Mean (range)
First Reading (at week-0, random order)			
Expert 1 vs 2	0.49 (0.41 - 0.58)	0.48 (0.37 - 0.59)	0.52 (0.27 - 0.77)
Expert 1 vs 3	0.57 (0.49 - 0.66)	0.53 (0.42 - 0.64)	0.70 (0.48 - 0.91)
Expert 2 vs 3	0.55 (0.47 - 0.63)	0.65 (0.55 - 0.75)	0.66 (0.45 - 0.88)
Second Reading (at week-6, random order)			
Expert 1 vs 2	0.40 (0.30 - 0.49)	0.29 (0.17 - 0.40)	0.52 (0.34 - 0.71)
Expert 1 vs 3	0.46 (0.37 - 0.54)	0.43 (0.32 - 0.54)	0.67 (0.51 - 0.82)
Expert 2 vs 3	0.64 (0.57 - 0.71)	0.53 (0.42 - 0.65)	0.71 (0.57 - 0.86)

[Table 1: Inter-observer reproducibility of three scores assessing small bowel cleanliness in capsule endoscopy]

Specifically, some of the 5 QI items were poorly reproducible, and particularly the evaluation of the amount of bile and chime, with Kappa coefficient varying from 0.21 to 0.29 and from 0.16 to 0.34, for intra and inter-observer reproducibility, respectively.

Conclusion: One of the main preparation score used in research studies proved to be poorly reproducible wenhever the same or a different reader was used as comparator. There is a major need for improved preparation scores to allow satisfying data analysis in small bowel capsule endoscopy.
References: Brotz C, et al. Gastrointest Endosc. 2009;69:262-70
Disclosure: Nothing to disclose

P1661 ACCURACY OF ARTIFICIAL INTELLIGENCE AIDED REPORTING IN VIDEO CAPSULE ENDOSCOPY

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Introduction: Video Capsule Endoscopy (VCE) is primarily used for diagnostic examination for the area of small bowel, which cannot be assessed by conventional gastroscopy or colonoscopy. VCE offers a variety of advantages like being non-invasive, easily tolerable with small swallowed capsule, painless, sedation free, potentially avoidance of harmful radiation and invasive investigations.
However, the reviewing and examination of each VCE can be a tedious and time-consuming process, potentially taking up to 1-2 hours (depending on experience) of a Gastroenterologist time. A new Artificial Intelligence (AI) algorithm - Docbot CapsuleAI version 1.3, which consists of a multi-class convolutional neural network and pHash post-processing algorithms, was developed to highlight and present the potential clinically significant frames, with the aim to reduce the reviewing time and improve the accuracy of VCE reporting.
Aims & Methods: To examine the accuracy of this new AI aided reporting system (Docbot CapsuleAI version 1.3) in VCE.
50 anonymized VCEs (pre-reported by Gastroenterologists, inclusive of 40 VCEs with abnormal findings and 10 VCEs with normal findings) were selected to test the diagnostic accuracy of the new AI algorithm (Docbot CapsuleAI version 1.3) in aiding the reporting process. All the frames highlighted by AI, will be subsequently reviewed by 2 Gastroenterologists, to determine the sensitivity, specific and accuracy of the AI aided diagnostic system, against the gold standard of human reporting by Gastroenterologist.
Results: Out of the total 50 VCEs, the AI algorithm picked up an average total frame of 190 per VCE (Min=27, Max =417). There were lower number of average total frames picked up by AI for the normal VCEs = 168 Vs abnormal VCEs =195. For the abnormal VCEs, the average number of abnormal frames picked up by AI were 22.
Overall, this AI algorithm has the sensitivity of 95%, specificity of 100% with the accuracy of 96%, in picking up the clinically significant frames, for the final diagnostic reporting of VCE.
The AI algorithm has successfully highlighting clinically significant frames (ranging from normal, vascular lesion, ulcer, erosion, tumour, stricture, and inflammation) in 48 out of 50 VCEs. 2 VCEs with abnormal finding which were not picking up by the AI algorithm were small duodenal polyp and sub-mucosal lipoma.
Conclusion: The new AI algorithm has high sensitivity, specificity and accuracy in highlighting clinically significant frames to clinician, helping to improve time spent and accuracy of VCE reporting.
Disclosure: Nothing to disclose

P1662 WORLD'S LARGEST SERIES WITH CAPSOCAM®. FEASIBILITY, COMPLETION AND DETECTION RATE OF THE NEW GENERATION OF CAPSULE ENDOSCOPE WITH A 360° LATERAL PANORAMIC VIEW - A SINGLE CENTER RETROSPECTIVE STUDY

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Introduction: Capsule endoscopy started in 2000 a revolution in diagnosing small bowel diseases. The first capsule endoscope was M2A® with one camera at one end of the capsule (Given Imaging, Yoqneam, Israel). It was the first time that direct visualization of the entire small bowel was possible. From this year onwards, we can see a rising number of examina-

tions and indications for capsule endoscopy. The drawback of the endview capsule is the limited view - PillCam SB3®(Medtronics, Dublin, Ireland) 156°, MiroCam®(IntroMedic, Seoul, Korea), 170°.
With the introduction of CapsoCam®(CapsoVision, Saratoga, CA, USA) with a lateral panoramic view of 360°, now we have a total view on the mucosa. Because of this 360° lateral panoramic view, we have the chance to get a better detection rate for capsule endoscopy.
Aims & Methods: The aim of this single center retrospective study was to compare the different capsule systems used at the KA Rudolfstiftung, Vienna, Austria (CapsoCam®, PillCam®, MiroCam®), in respect to visibility of the Papilla of Vater, completion rate, detection rate (defined as pathology identified according to the indication), loss of data because of technical problems, image quality, download and reading time of the 360° lateral panoramic view of CapsoCam® and the endview systems including PillCam® and MiroCam®.
Included are examinations from 2012 to 2018 with the CapsoCam® system including the three generations of SV1®, SV2® and CapsoCam Plus®: 852 (CapsoCam Plus®:516), and the PillCam SB2® and SB3®: 803 and MiroCam®: 315 - a total of 1970 examinations.
Results: Visibility of Papilla of Vater: CapsoCam® 81.7%; Endview 9.6%
Complete examination: CapsoCam® 97.4%; Endview 84.8%
Detection rate: CapsoCam® 51.3%; Endview 44.6%; p-value: 0.003901
Loss of data: CapsoCam® 3.1%; Endview 6%
Download time: CapsoCam® 15 min; PillCam SB3® 90 min; MiroCam® 35 min
Reading time: CapsoCam® 15-20 min; PillCam SB3® 30-40 min; MiroCam® 30-40 min
Conclusion: CapsoCam® showed an excellent visibility of the Papilla of Vater at more than 80% and a complete examination of the small bowel at more than 97%. These numbers are the highest published data to this time. In our series, the CapsoCam® is superior in finding relevant pathologies according to the indication with a p-value of 0.0039
The main fear of experts about the loss of data because of the inability to retrieve the excreted CapsoCam® can be rejected. In our study we found twice the data loss in the endview group because of problems with the data recorder, SD-card or the sensor belt. With CapsoCam Plus®we have the same image quality as with the PillCam SB3®. Because of these data, the fastest download and reading time CapsoCam Plus® have a clear benefit compared with the established endview systems.
Disclosure: Consultant for Medtronic, Boston Scientific, CapsoVision

P1663 HIGH-RISK FACTORS FOR GASTRIC RETENTION IN SMALL BOWEL CAPSULE ENDOSCOPY. A SINGLE CENTRE RETROSPECTIVE COMPARATIVE STUDY

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Introduction: Certain conditions and medications have been identified as risk factors for gastric capsule retention (GCR). ESGE guidance recommends the use a real-time viewer to guide appropriate early preventative intervention such as prokinetic administration when delayed gastric emptying occurs.
Aims & Methods: To examine the prevalence and associations of GCR in an Irish cohort and to compare findings against a control group. Patients with video confirmation of gastric retention for the duration of the study were identified from a small bowel capsule endoscopy (SBCE) database of 3078 cases. Using this database, we also retrospectively identified patients who underwent a SBCE immediately after each GCR patient without retention. These patients were used as controls. Demographic and clinical data was extracted from medical records. Cases and controls were compared using a chi[2] test, a p value of < 0.05 was considered significant.
Results: A total of 70 GCR cases were identified giving an occurrence rate of 2.3%. Data was available for 61 GCR and 55 control patients. There were more females than males in both groups; 36/61 (59.1%) GCR group and the 34/55 (61.8%) control group. The mean age was 58 years in both groups. In keeping with standard SBCE practice, the commonest indications for SBCE were iron deficiency anaemia [32/62(52%) GCR group and 20/55(36%) control group] and suspected Crohn's disease [15/61(25%) GCR group and 17/55(31%) control group].

There was significantly more patients with hypothyroidism in the GCR group 12/61 (20%) vs 4/55 (7%) than in the control group [P = 0.0438]. There was no difference in the rate of diabetes [10/61(16%)) GCR group vs 9/55(16%) control group [P =1.000]] nor psychotropic medication use [14/61 (23%) GCR group vs 16 (29%) control group [P = 0.4630]]. While there were over twice as many patients 14/61 (23%) in the GCR group with more than one associated risk factor vs the control group 6/55 11%) this was not statistically significant [P = 0.0894]. Interestingly, there were significantly less current or ex-smokers 18/61 (30%) in the GCR group versus 28/55 (51%) in the control group [P = 0.0217].

Conclusion: GCR was a relatively frequent occurrence in our large capsule population. In our cohort, only hypothyroidism was associated with an increased risk of GCR. Contrary to published data, older age, female gender, smoking, diabetes and use of psychotropic medications were not predictive. Our data suggests current predictive measures of GCR are inadequate and unlikely to accurately select patients for real time monitoring and appropriate early intervention. The role of multiple risk factors for GCR prediction warrants further evaluation.

Disclosure: Nothing to disclose

P1664 EFFECT OF INTRAVENOUS METOCLOPRAMIDE ON SMALL BOWEL TRANSIT TIME DURING MAGNETIC CAPSULE ENDOSCOPY EXAMINATION: A PROSPECTIVE, RANDOMIZED STUDY

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Introduction: Diagnostic yield with capsule endoscopy (CE) is limited by incomplete study due to slow small-bowel transit and poor view quality in the distal bowel. Prokinetics may increase gastric transit time, but currently, there are conflicting results regarding the effect of metoclopramide on small bowel transit time and optimal preparation protocol during CE.

Aims & Methods: aim of our present study was to investigate whether intravenous metoclopramide accelerates small bowel transit time and increases the completion rate of CE examination.

191 patients who underwent magnetic capsule endoscopy (MACE) after 6 hours of fasting period were randomized to receive either 5 mg intravenous metoclopramide (metoclopramide (MC) group: 103 cases) or no prokinetic treatment at all (control (C) group: 88 cases), after the completion of a 30 min automated gastric mucosal surface robotic examination protocol. During the small bowel examination period all patients in each group received 1000 ml PEG solution to improve visibility of the distal small bowel.

Results: PEG administration during CE resulted in an excellent small bowel and distal ileal mucosal visibility which was demonstrated in both patient groups without significant differences. Complete small bowel examination was detected in 100/103 (97%) in the MC group, and 87/88 (98%) of the C group, without significant differences. However, we demonstrated significant differences in the small bowel transit time between the MC and the C group, 3:07:41+1:57:47 vs. 4:03:01+1:52:19 (p=0,00007), respectively.

Conclusion: Intravenous metoclopramide proved to have a significant effect on shortening the small bowel transit time, but it has no effect on the completeness of the entire small bowel visibility, which is due to the fact of long-lasting operation time and possibility of active pyloric passage of MACE. One liter of PEG administration during the small bowel transit period might improve the quality of distal ileal mucosal visibility and have an additive effect on the high success rate to accomplish combined gastric and small bowel MACE examinations.

Disclosure: Nothing to disclose

P1665 PREVALENCE AND RISK FACTORS FOR DUODENAL PERFORATION DUE TO MIGRATED BILIARY PLASTIC STENTS

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Introduction: Transpapillary biliary drainage by stent placement through endoscopic retrograde cholangiography (ERC) is a well-established treatment for bile duct obstruction. Migrated stent-induced perforation of the duodenal wall can be a potentially life-threatening complication. The actual prevalence of this complication is however unknown and risk factors for perforation are unclear.

Aims & Methods: We aimed to analyze the prevalence, risk factors and clinical course of migrated stent-induced duodenal perforation (MSDP). All consecutive patients who underwent an ERC with biliary plastic stent placement during the study period January 1st 2014 till December 31st 2017 in our center were retrospectively analyzed. Data on demographic factors, medical history, indication for ERC, biliary stricture and stent characteristics were systematically collected in all patients. In addition, for patients who were diagnosed with a MSDP, date of perforation, clinical presentation at diagnosis, type of treatment of perforation and outcome of treatment were reviewed.

Results: During the study period, a total number of 2487 ERCs were performed in 1228 patients (mean age 59 years, 59% male). In 630 patients (51%), a biliary plastic stent was placed; in 304 patients (25%), one or more stents were placed for perihilar strictures.

A total of 14 MSDPs were diagnosed in 13 patients (mean age 63 years, 79% male). All perforations occurred in patients with a perihilar stricture. The overall prevalence of MSDP was 1,1% in all patients who underwent an ERC, 2,2% for patients who underwent ERC with biliary stent placement and 4,6% for patients with a biliary stent for a perihilar stricture.

The median length of the stents was 15 cm (IQR 12-15 cm), perforation did not occur with stents shorter than 12 cm. Perforation occurred both with 7 and 10 French stents (21% and 79% resp.), and with either center or duodenal bend type stents (42% and 58% resp.). The stenosis was malignant in 8 patients (57%). The majority of perforated stents were deployed with the proximal tip in the left intrahepatic ducts (57%). Biliary sphincterotomy and stricture balloon dilation were not significantly associated with MSDP. Median time to diagnosis of perforation was 13 days (IQR, 4-66 days). In 71% of the patients (n=10) duodenal perforation was clinically suspected due to presentation with abdominal pain, fever and/or laboratory abnormalities. 4/14 patients were asymptomatic and MSDP was diagnosed at elective stent retrieval. Treatment was either conservative by removal of the stent, endoscopic closure with an over the scope clip (OTSC) or surgery in respectively 36% (n=5), 57% (n=8) and 7% (n=1) of the patients. Two patients died due to ongoing abdominal sepsis (14%), despite repeated endoscopic, percutaneous and surgical interventions.

Conclusion: This is the first study to report on the prevalence of MSDP in patients who undergo ERC. Despite the overall low risk of MSDP, it represents a potentially life threatening complication of ERC after transpapillary drainage for perihilar biliary strictures. The risk of MSDP needs to be acknowledged for this indication and warrants consideration in symptomatic patients after ERC.

Disclosure: Nothing to disclose

P1666 STENT SELECTION FOR PREOPERATIVE DRAINAGE OF A DISTAL MALIGNANT BILIARY OBSTRUCTION

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Introduction: For stent placement in cases of unresectable distal malignant biliary obstruction, self-expandable metallic stents (SEMS) are recommended, as they have a longer patency period than plastic stents (PS). However, there has been no consensus on the types of stents that should be recommended for preoperative drainage. In recent years, preoperative adjuvant therapy has been increasingly adopted in the clinic, and the preoperative waiting periods have lengthened in an increasing number of cases. This study examined the selection of stents for preoperative drainage.

Aims & Methods: For stent placement in cases of unresectable distal malignant biliary obstruction, self-expandable metallic stents (SEMS) are recommended, as they have a longer patency period than plastic stents (PS). However, there has been no consensus on the types of stents that should be recommended for preoperative drainage. In recent years, preoperative adjuvant therapy has been increasingly adopted in the clinic, and the preoperative waiting periods have lengthened in an increasing number of cases. This study examined the selection of stents for preoperative drainage.

Results: The median patient age was 72 years, and the sex breakdown was 37 men and 11 women. The causative diseases included pancreatic cancer in 26 cases, bile duct cancer in 14 cases, papillary cancer in 7 cases, and intraductal papillary-mucinous carcinoma in one case. Stent malfunction was observed in one case in the SEMS group (6.7%) and in eight cases in the PS group (24.2%). The mean estimated patency periods that were obtained through the Kaplan-Meier method were 136 days in the SEMS group and 74 days in the PS group, and the mean period was significantly longer in the SEMS group (p=0.043). The median technical costs were 359,340 JPY in the SEMS group and 170,710 JPY in the PS group, which indicates that the cost was higher in the SEMS group. On the other hand, in patients who received multiple treatments, the median technical cost in the PS group was 331,580 JPY, and there was no significant difference from that in the SEMS group (p=0.220). Procedural accidents included acute pancreatitis in two cases in the SEMS group (13.3%) and acute cholangitis in one case in the PS group (3.0%), and both cases were mild. The mean estimated preoperative waiting periods were 28 days in the non-NA group and 131 days in the NA group.

Conclusion: As preoperative waiting periods were shorter in the non-NA group, the patency period of PS was sufficient for this group. Since the cost that is incurred by the use of PS is low, PS is recommended for patients in the non-NA group. On the other hand, preoperative waiting periods are long in the NA group, and the use of PS for this group would likely require multiple treatments. Therefore, from the perspectives of cost and invasiveness, SEMS is recommended for patients in the NA group.

Disclosure: Nothing to disclose

P1667 CONCOMITANT MALIGNANT DUODENAL AND BILIARY STENOSIS: DUODENAL STENTING AND HEPATICOGASTROSTOMY DURING THE SAME PROCEDURE IS A SAFETY PROCEDURE (SAMETIME STUDY)

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Introduction: The concomitant biliary and duodenal malignant stenosis is a rare event, reflecting a locally advanced neoplastic process. Endoscopic management is usually an association of duodenal and biliary retrograde stenting. EUS biliary drainage is an alternative drainage for these patients with inaccessible papilla. We conducted a single retrospective study to evaluate EUS biliary drainage in association duodenal stenting.

Aims & Methods: Patients were included from 01.01.2011 to 31.12.2017. Patients were included if they had palliative endoscopic management with biliary drainage and duodenal stenting in the same time or within 7 days or less for concomitant bilio-duodenal malignant stenosis. Patients were extracted from our database with ConSore soft.

Patients were divided into several groups for statistical analysis.

First, according to the timing of biliary drainage: in the SAMETIME drainage group if the two procedures were done on the same day and in the DEFFERED drainage group if the two procedures were done in different days (< 7 days).

And secondly, depending on the biliary drainage method used: EUS-HG if hepaticogastrostomy or DUODENALACCESS if the drainage was done by ERCP, radiological or choledoduodenostomy.

Results: From 01.01.2011 to 31.12.2017 31 patients were included (19 women, mean age=66). Stenosis was related to pancreatic cancer for 17 patients (54%), colorectal cancer for 4 (12.9%), breast cancer metastases for 3 (9.7%), vesicular adenocarcinoma for 3 (9,7%), duodenal adenocarcinoma for 1 (3.2%), uterine sarcoma for 1 (3.2%), ovarian cancer metastases for 1 (3.2%) and one gastric adenocarcinoma (3.2%). Patients had an average Karnofsky index of 72%, the average preoperative bilirubin was 143µmol/L.

Sixteen (52%) patients were in the SAMETIME group, 15 in the DEFFERED: 11 (35%) with biliary drainage after duodenal stenting and 4 (13%) with biliary drainage before duodenal stenting.

Biliary drainage was done by EUS-HG for 11 (35%) patients, by DUODENALACCESS for 20 (65%): percutaneous path for 11 (35%) patients, by ERCP for 8 patients (26%) and choledoduodenostomy for 1 patient.

30 of 31 patients died during follow-up. Median survival was 76 days (mean 152 days +/-206).

Patients in the group SAMETIME had significantly shorter hospitalization than the DEFFERED group: 7.47 days vs 12,5 days (p=0.035). The SAMETIME group trended to have a lower rate of significant postoperative complications (27% VS 56%; p=0.0953).

The EUS-HG group trended to have lower rate of significant postoperative complications Dindo-Clavien classification> III (18% VS 55% p=0.065) and less biliary endoscopic revision (9% VS 30% p=0.37).

Conclusion: In case of double biliary and duodenal obstruction, SAMETIME drainage is associated with a halved hospitalization time and probably with less adverse events than a two procedures drainage. In case of double stenosis EUS-HG should be preferred. No more complication were described in our study than others drainage and on the contrary a tendency to better patency, less complication, and in current practice an easier re-intervention for stent obstruction.

Disclosure: Nothing to disclose

P1668 WITHDRAWN

P1669 THE EFFECTIVENESS AND SAFETY OF ENDOSCOPIC TRANSPAPILLARY GALLBLADDER STENTING FOR PATIENTS WITH ACUTE CHOLECYSTITIS

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Introduction: The gold standard definitive therapy for acute cholecystitis is cholecystectomy. However, it is not possible to perform cholecystectomy all the time, especially in poor performance status patients. In those cases, the Endoscopic transpapillary gallbladder stenting (EGBS) is more effective rather than other drainage methods. EGBS is relatively new gallbladder drainage method for acute cholecystitis. Therefore, the effectiveness and safety of EGBS has not been considered enough.

Aims & Methods: We evaluate the effectiveness and safety of EGBS for acute cholecystitis.

This retrospective cohort study included the patients which had diagnosed for acute cholecystitis and underwent EGBS at our institution between September 2012 and January 2018. The primary endpoint of this study was a technical success rate of EGBS. The adverse events of EGBS and recurrence of the cholecystitis after undergoing EGBS were also considered.

Results: A total of 111 patients (77 men and 34 women; median age 66 years) underwent EGBS. The severity assessments of acute cholecystitis were 46 mild, 60 moderate, and 5 severe. The technical success rate for EGBS was 80.0% (89/111). Among them, 36 patients had common bile duct and were performed for endoscopic lithotripsy. The adverse events of EGBS were observed in 6 patients. Of these, 3 patients were penetration of cystic duct, 2 patients were pancreatitis, and 1 patient was bleeding during Endoscopic sphincterotomy. No recurrence of acute cholecystitis was observed during waiting periods for cholecystectomy after EGBS.

Conclusion: The success rate of EGBS was relatively high and recurrence of cholecystitis was not observed. In addition, the adverse event rate was also low. Therefore, we consider that EGBS is effectiveness and safety, and becomes one of the effective treatments for acute cholecystitis.

Disclosure: Nothing to disclose

P1670 CHARACTERISTICS OF MAJOR DUODENAL PAPILLA IN EFFICACY AND SAFETY OF NEEDLE-KNIFE FISTULOTOMY

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Introduction: Needle-knife Fistulotomy (NKF) is a commonly used rescue method for biliary cannulation in challenging ERCP cases. The type of Major Duodenal Papilla (MDP) is suggested to be an effective factor in selection of patients suitable for NKF. However, data from clinical studies is scarce. In this study we aim to compare the success and complication rates of NKF between three types of MDP.
Aims & Methods: The study samples were patients who experienced difficult cannulation during an elective ERCP procedure conducted in an affiliated university hospital between September 2017 and March 2018. The success and complication rates of NKF administered for these patients were compared by the patients' type of MDP. Three categories of MDP (small, bulging, long) were defined based on the anatomical characteristics observed during endoscopy.
Results: A total of 72 patients (35 men, 37 women; mean ± SD age 62.3±15.5 years) underwent NKF and were classified into 3 groups of small (N=24), bulging (N=20) and long (N=28) MDP. The overall success rate of NKF was 70.8%, which was highest in patients in the bulging MDP group (90%), followed by the small (75%), and long (53.6%) MDP groups (P=0.02). The total complication rate was 59.7%, including post ERCP Pancreatitis (13.9%), bleeding (19.4%), perforation (4.2%) and asymptomatic hyperamylasemia (25%). Overall complication rates were lowest among patients in the small MDP (45.8%) followed by budging MDP (55%) groups and highest in the long MDP groups (78.6%) (P=0.03).
Conclusion: Characteristics of MDP is an important factor for selection patients for NKF. The best outcome for NKF (highest success and lowest complication rate) was achieved in patients with bulging MDP and the worst outcome (lowest success and highest complication rate) was observed in patients with long MDP.
Disclosure: Nothing to disclose

P1671 INTRADUCTAL VS. TRANSPAPILLARY FULLY COVERED METAL STENT PLACEMENT FOR MALIGNANT BILIARY STRICTURES

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Introduction: Endoscopic trannspapillary placement of a metal stent (MS) for treatment of a malignant biliary stricture has been widely accepted as a standard palliative biliary drainage technique. A conventional fully covered metal stent is placed across the duodenal papilla. Duodenobiliary reflux though a biliary stent placed across the major duodenal papillary is considered to be a predisposing factor for stent occlusion and cholangitis. Intraductal placement of a biliary stent above the duodenal papilla (inside stent) may be associated with longer stent patency and a lower occlusion rate because of reduced duodenobiliary reflux.
Aims & Methods: The aim of this study was to determine whether intraductal fully covered metal stent placement(IP) or transpapillary fully covered metal stent placement(TP) is a better therapeutic technique for- malignant biliary strictures.
From January 2016 to December 2018, a total of 79 patients with malignant biliary strictures were retrospectively enrolled in this study. The patients were divided into an IP group(n=30) and TP group(n=49). Technical and clinical success, complication, and stent patency were compared between the two groups.
Results: There were no significant differences between the IP and TP groups in the rates of technical success(100% vs. 100%), clinical success(100% vs. 100%), early complications(10.0% vs. 6.1%), late complications(0% vs. 4.1%), or stent occlusion(23.3% vs. 20.6%). The average

patency periods in the IP and TP groups were 150.0 and 103.7 days, respectively. Cumulative stent patency also did not differ significantly between the two groups(P=0.680).
Conclusion: TP for malignant biliary strictures showed a high technical success rate, low complication rate, and no difference in stent patency when compared with IP. Long-term follow-up and prospective comparative studies are needed to evaluate the usefulness of IP.
Disclosure: Nothing to disclose

P1672 COMPLICATIONS OF PERCUTANEOUS TRANSHEPATIC CHOLANGIOGRAPHY AND BILIARY DRAINAGE (PTCD)

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Introduction: Percutaneous transhepatic cholangiography and biliary drainage (PTCD) is used for treatment for biliary obstruction after failed endoscopic biliary cannulation.
Aims & Methods: Our aim was to evaluate complication rates and risk factors for adverse outcome of PTCD in a real-world population. We performed a multicenter (4 Teaching and 1 University hospitals) cohort study in the period 2011-2016.
Our primary outcome was the incidence of infectious (sepsis, cholangitis, abscess or cholecystitis) and non-infectious complications (bile leakage, catheter blockage, severe hemorrhage, etc.) and mortality within 30 days of a PTCD procedure. Intra Class Correlations (ICC) were calculated to determine variance of outcomes between the five hospitals. Multilevel logistic regression analysis was performed to identify risk factors for predefined outcomes.
Results: In total, 331 patients with PTCD were analyzed, 251 of whom had malignant biliary tract obstruction. Two-hundred-twenty-six patients (68.3%) developed a complication after PTCD.
In 224 patients without pre-existent infection, 114 developed one or more infectious complications (40.6%), i.e. cholangitis in 26.3%, sepsis in 24.6%, abscess in 2.7% and cholecystitis in 1.3%. Non-infectious complications were seen in 167 of 331 patients (50.5%). PTCD-related 30-day mortality was 8.5%.
Risk factors for infectious complications were internal drainage (OR 2.12, 95% CI 1.03-3.38) and drain obstruction (OR 2.60, 95% CI 1.39-4.88), while multiple re-interventions were related to non-infectious complications (OR 2.11, 95% CI 1.64-2.71). No risk factors for mortality were identified.
Conclusion: This multicenter study shows that PTCD is associated with a high number of adverse events and substantial mortality. Infectious complications, in particular cholangitis and sepsis, are common and appear to be caused by drain malfunction and internalized drainage. These high complication rates should stimulate the search for alternative strategies for biliary drainage.
Disclosure: Nothing to disclose

P1673 UNCOVERING CLINICAL GAPS IN THE MANAGEMENT OF CHRONIC LIVER DISEASE-ASSOCIATED THROMBOCYTOPENIA IN ADULTS REQUIRING ELECTIVE INVASIVE PROCEDURES: A CLINICAL PRACTICE ASSESSMENT

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Introduction: Optimal implementation of emergent thrombopoetin receptor agonists (TPO-RA) such as lusutrombopag and avatrombopag is anticipated to require significant changes to the treatment paradigm for patients with Chronic Liver Disease (CLD)-associated thrombocytopenia (TCP) requiring elective invasive procedures (EP). In order to provide clini-

cians with optimum education, guidance and support to achieve the best outcomes with these agents in routine practice, it is important to identify current knowledge and clinical gaps that need to be addressed.

Aims & Methods: This study determined the readiness of clinicians to implement TPO-RA in practice by exploring understanding of current patient selection criteria, the limitations of platelet infusions and the scientific rationale and supporting efficacy and safety data for emergent TPO-RA, including considerations related to practical application. A 25-question, online, continuing medical education (CME) survey was developed that included a range of demographic, knowledge and practice-based questions. The activity launched on December 20, 2018 and data collected through February 6, 2019.

Results: 31 gastroenterologists, 47 hematologists, and 30 other physicians completed the survey. All were required to be involved in the management of patients with CLD-associated TCP undergoing EP. 47% of participants were from community hospitals, 30% from teaching hospitals and the remainder from solo/group community practices. Delay to invasive procedures due to TCP was common: 25% of participants reported a delay >40% of the time, 22%, 21-40% of the time, and 41%, 1-20% of the time. Only 13% never experienced delays. Lack of awareness/availability of newer treatment options (45% participants), lack of evidence-based guidelines (20%), and insufficient time to manage TCP before the procedure (12%) were identified as the current most significant barriers to optimal management of patients. Participants were currently only slightly (32%) or moderately (39%) confident in application of TPO-RA in practice. Only 16% were mostly/very confident. Only 49% of participants correctly identified 50,000/mL as the platelet threshold for considering intervention for TCP. Participants were familiar with the role of TPO in the pathophysiology of TCP (79%) and the mechanism of action of TPO-RA (75%). However, participants generally lacked knowledge on a range of questions that explored understanding of the clinical evidence for avatrombopag and lusutrombopag including identification of eligible patients in terms of type of EP and bleeding risk, magnitude and type of efficacy benefit, safety profile, duration of use, and monitoring requirements. 62% failed to identify that portal vein thrombosis occurred at a similarly low level in patients receiving lusutrombopag or placebo in the LPLUS1/2 trials. Only 22% of participants correctly identified that platelet counts should be monitored for 4 weeks after initiating treatment with TPO-RA.

Conclusion: The findings reveal significant current knowledge and clinical gaps amongst clinician specialties involved in the management of CLD-associated TCP in patients undergoing EP. Whilst this highlights some of the key issues and challenges in current practice, and may reflect the current lack of access to and clinical experience with TPO-RA, this strongly points to a need for education to establish a better understanding of the impact of TPO-RA on practice. Clinicians require support with the implementation of the paradigm shift that is needed for effective and safe routine application of TPO-RA to achieve the best patient outcomes.

Disclosure: Markus Peck: Investigator, AbbVie, Arqle-Daiichi, Bayer, BMS, Boehringer-Ingelheim, Imclone, Lilly, MSD, Novartis, Roche, Shionogi; Speaker, Advisor: AbbVie, Bayer, BMS, Boehringer-Ingelheim, Eisai, Ipsen, Lilly, MSD, Roche, Shionogi; Grant Support, AbbVie, Arqle-Daiichi, Bayer, MSD, Roche. No others

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P1674 EMERGING TREATMENTS FOR CHRONIC LIVER DISEASE-ASSOCIATED THROMBOCYTOPENIA IN ADULTS REQUIRING ELECTIVE INVASIVE PROCEDURES: EFFECT OF ONLINE EDUCATION ON CLINICIAN KNOWLEDGE, AND CONFIDENCE

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Introduction: Thrombopoetin Receptor agonists (TPO-RA) such as lusutrombopag and avatrombopag are emerging as alternative treatment options to platelet transfusions for patients with Chronic Liver Disease (CLD)-associated thrombocytopenia requiring elective invasive procedures. Optimal implementation of these agents is anticipated to require significant changes to the treatment paradigm, so education of clinicians on the rationale and supporting data as well as practical application of these agents will be important.

Aims & Methods: This study determined whether online continuing medical education (CME) could improve clinicians' knowledge of the rationale behind the development of TPO-RA and the supporting clinical evidence, and improve clinicianconfidence with application of these agents in practice. A 30-minute online video discussion between 2 experts was launched for countries in Europe in December 2018, with data collected until February 2019. Educational effect was assessed with a repeated-pairs pre-/post-assessment study design, where individual participants served as his/her own control. 3 multiple-choice, knowledge questions and 1 self-efficacy, 5-point Likert scale (confidence) question were analyzed. Chi-squared test assessed pre- to post-assessment change (5% significance level, $P< .05$). Magnitude of change in total number of correct responses overall, and for each question, were determined with Cramer's V (effect size: < 0.05 modest; 0.06-0.15 noticeable, 0.16-0.30 considerable, >0.30 extensive).

Results: 78 gastroenterologist and 72 hematologists completed both pre- and post-assessments. An overall positive extensive education effect was observed for both specialties (V=.306, p< .001 and V=.281, p< .001, respectively).

For both specialties significant improvements were observed between pre- and post-assessment for all 3 questions which covered identification of the complications of platelet infusions, identification of the correct platelet count defining eligibility for the ADAPT-1 and ADAPT-2 Phase 3 trials of avatrombopag and identification of the correct efficacy and safety data from the L-PLUS1 and L-PLUS2 Phase 3 trials of lusutrombopag. Average % of correct responses improved from 28% to 88% pre-and post-assessment for gastroenterologists and from 43% to 68% for haematologists.

Both specialties had only modest baseline knowledge of the key data for both agents (24-47% gastroenterologists and 49-56% hematologists), with significant improvement post-assessment. Improved confidence in the ability to treat thrombocytopenia in patients with CLD requiring an elective invasive procedure was demonstrated post-assessment, with a total average confidence improvement of 35% for gastroenterologists and 25% for haematologists.

Conclusion: This on-demand, online video discussion resulted in a highly positive educational effect with improvements in clinician knowledge and confidence. However, the study revealed that there is currently only a modest baseline understanding of key data supporting the implementation of TPO-RA in practice. In addition, despite the positive educational gains, there are persistent knowledge gaps evident post-assessment for a significant proportion of clinicians.

Further education is merited given the important implications of these agents to the treatment paradigm. Online medical education is valuable in supporting the interpretation of new data and practical application of new agents in practice, as well as identifying areas of continued educational need

Disclosure: Markus Peck: Investigator, AbbVie, Arqle-Daiichi, Bayer, BMS, Boehringer-Ingelheim, Imclone, Lilly, MSD, Novartis, Roche, Shionogi; Speaker, Advisor: AbbVie, Bayer, BMS, Boehringer-Ingelheim, Eisai, Ipsen, Lilly, MSD, Roche, Shionogi; Grant Support, AbbVie, Arqle-Daiichi, Bayer, MSD, Roche. No others

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P1675 WITHDRAWN

P1676 COMBINED ULTRASOUND- AND FLUOROSCOPY GUIDED TRANSHEPATIC BILIARY DRAINAGE IS SUPERIOR TO CONVENTIONAL RADIOGRAPHY GUIDED TECHNIQUE

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Introduction: Difficult biliary cannulation (DBC) is a common condition in endoscopy and often remains challenging. DBC is related to benign, malignant or iatrogenic diseases. In case of unsuccessful ERCP, EUS-guided or percutaneous transhepatic biliary drainage (PTCD) are standard procedures for alternative bile duct access. PTCD is often performed by ultrasound guided puncture (US-PTCD) but also conducted without sonography (non-US-PTCD). However, there is no comparative data showing any supe-

riority for the use of US-PTCD with regard to technical success or complications. Thus, we performed a retrospective two-center study comparing US-PTCD with non-US-PTCD.

Aims & Methods: Data of 269 patients who underwent PTCD between 2002 and 2018 were collected and retrospectively analyzed. Indications, outcome, technical efficacy, comorbidities and procedural characteristics were analyzed. Fisher's exact test, Student's t-test and Chi-Square-test were used to identify dispersions between both groups.

Results: We identified 200 patients, who were treated by US-PTCD and 69 by non-US-PTCD. Mean age was 66.3 (US-PTCD) and 67.4 years (non-US-PTCD) and PTCD was performed mostly in men (64.5% and 66.7%). In both groups, right-sided PTCDs were conducted more often than left sided (78% and 79%). Main indications for PTCD were palliative (63.5% and 62.2%) bile duct drainage due to prior abdominal surgery or unsuccessful ERCP. US-PTCD resulted in technical efficacy of 81% compared to 79.7% in non-US-PTCD (p>0.05). Internal duodenal drainage was achieved in 50.5% (US-PTCD) and 36.2% (non-US-PTCD) patients (p=0.05). Interventions could be performed without sedation in 19% of patients in US-PTCD but only in 3% in non-US-PTCD group (p< 0.001). Minor complications (severe pain, dislocation, bleeding, cholangitis and other) occurred in 18.5% of US-PTCD and 20.3% of non-US-PTCD (p>0.05) but severe complications (pleural or cardiac injuries, perforation and fistula) occurred significantly less in US-PTCD (2% vs. 6.2%, p=0.04).

Conclusion: US-PTCD and non-US-PTCD showed comparable technical efficacy but US-PTCD resulted in improved internal duodenal biliary drainage, less necessity of sedation and less severe complications compared to non-US-PTCD.

Disclosure: Nothing to disclose

Surgery III

09:00-14:00 / Poster Exhibition - Hall 7

P1677 DOES ENDOSCOPIC OBSTRUCTION IN COLORECTAL CANCER REQUIRE URGENT SURGERY AND RESULT IN POOR PROGNOSTIC FACTORS?

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Introduction: Colonoscopy is an endoscopic tool for evaluation of colorectal cancer, and there is no conclusive evidence of a connection between clinical gut obstructions and obstructed seen in endoscopy (obstructed colonoscopy). Unplanned urgent operations in obstructed colorectal cancer by endoscopic processes may increase mortality and the possibility of poor outcome. The suitable waiting time to complete staging and prepare patients before surgery has not been reported.

Aims & Methods: The aim of the study is to determine the suitable waiting times, incidence of emergency surgery during waiting times, and outcomes of obstructed colonoscopy.

Retrospective cohort of obstructed colonoscopies in colorectal cancer was analyzed. Patients who refused surgery or failed to attend follow up appointments were excluded. Data was collected from both emergency and elective operation groups, including incidences of emergency surgery, waiting times, staging, level of obstruction and outcome.

Results: The total of 4,017 colonoscopies were analyzed. There were 211 (5.25%) unsuccessful procedures due to tumor obstruction. Twelve patients (7.3%) had emergency operations during waiting for surgery. The average waiting time was 25 days. No perioperative deaths were reported. 5-year survival rate was lower in stage II and III cancer.

Conclusion: In this study, we found low incidence (7.3%) of emergency surgery in unsuccessful colonoscopy from obstructed colorectal cancer. Patients are able to wait 2-3 weeks after the date of colonoscopy without risk of increased mortality.

Disclosure: Nothing to disclose

P1678 LONG TERM HEALTH RELATED QUALITY OF LIFE FOLLOWING COLORECTAL CANCER SURGERY: PATIENT REPORTED OUTCOMES IN A REMOTE FOLLOW-UP POPULATION

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Introduction: Remote follow-up (RFU) after colorectal cancer (CRC) surgery allows delivery of surveillance tests without the need for regular clinical review. However little is known about long term health related quality of life (HRQoL) in RFU patients.

Aims & Methods: The aim of this cross sectional survey was to investigate HRQoL in this patient group. EQ-5D and QLQ-C30 questionnaires were sent to all CRC enrolled into RFU between 2011-2016. Primary outcomes were HRQoL scores. We analysed HRQoL scores with respect to year of RFU, demographics, operation type and stoma.

Results: In total 428 of 722 patients responded (59.3%) with a median RFU time of 2.6 years. 26.6% of patients reported 'perfect health'. The median EQ-5L index score was 0.785 (IQR: 0.671-1) and QLQ-C30 Global HRQoL score was 75 (IQR: 58.3-83.3). HRQoL scores were similar in different years of follow up. Lower HRQoL score were related to having a stoma (p< 0.003), cancer recurrence (p=0.009), female gender (p=0.009) and right-sided resection (p=0.03). Right-sided resection patients reported higher pain severity compared with those who underwent left-sided resections (p=0.037).

Conclusion: HRQoL is good in remotely followed up CRC patients. Predictors of lower scores will be a useful in service planning and holistic needs assessment. Despite an abundance of literature describing morbidity related to anterior resection, right-sided resection patients in this cohort reported worse HRQoL and symptoms.

Disclosure: Nothing to disclose

P1679 ILEOANAL POUCH CANCER: A CASE SERIES

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Introduction: There are few data detailing management and outcomes of ileoanal pouch cancer.

Aims & Methods: We aimed to determine the clinical presentation, management and outcomes for patients with ileoanal pouch cancer with Familial Adenomatous Polyposis (FAP) and Ulcerative Colitis (UC). Patients were identified by a search of two prospectively maintained institutional databases: UC pouches (2006-2019) and the Polyposis Registry (1978-2019). Endoscopic surveillance and cancer staging and management data were retrieved from hospital records.

Results: Thirteen cases were identified; three=FAP, nine=UC, one both. Two patients were referred to our centre following a diagnosis of pouch cancer locally. Five patients were diagnosed at our centre with pouch cancer following a referral to our centre for other reasons such as fistula, pouch sepsis, and stricture.

Six patients were diagnosed at our centre whilst on annual surveillance; median time to diagnosis of pouch cancer from previous surveillance endoscopy was 11.5 months (range 6- 18 months). 3/6 on surveillance at our centre had UC; none of whom had any adenomatous or dysplastic lesion visible on prior surveillance endoscopy.

Eleven patients had cuff cancer, one pouch body cancer (FAP) and one had an anal canal squamous cell carcinoma (UC). The median time since pouch formation was 12 years (3-30) for UC and 30 years (12-34) for FAP. Seven (58%) patients were undergoing active annual surveillance.

Five UC cases had dysplasia (n=3) or cancer (n=2) in their proctocolectomy specimen. Five UC patients developed anal fistulae before cancer diagnosis. Pre-operative imaging was available for review on 11 patients, all of whom had margin threatening disease at diagnosis.

Ten patients had/will be undergoing pouch excision (seven exenteration, three abdominoperineal excision). Ten underwent neoadjuvant chemoradiotherapy. Two had non-operative management (one complete clinical response after neoadjuvant therapy; one palliative chemotherapy). One patient was lost to follow-up. Kaplan Meier one-year survival: 86% (SE 0.132).

Conclusion: There should be a high index of suspicion for pouch cancer in pouch patients with dysplasia or carcinoma at proctocolectomy or late-developing fistulae in patients who have had a pouch for UC. Surveillance does not abolish the risk of developing pouch cancer and adequate cuff examination can be challenging. Ileoanal pouch cancers usually are diagnosed when they are already locally advanced.

Disclosure: Nothing to disclose

P1680 EVALUATION OF EXTENDED LATERAL PELVIC SIDEWALL EXCISION [ELSIE] FOR LOCALLY ADVANCED & RECURRENT RECTAL CANCER (RCC) INVOLVING THE LATERAL PELVIC SIDEWALL

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Introduction: In the context of locally advanced or recurrent rectal cancer, disease extension to the lateral pelvic sidewall is associated with lower rates of complete resection and poorer survival overall. Adaptions to surgical approach may improve complete resection rates but whether improvement in survival will follow is unclear.

Aims & Methods: We aimed to assess the outcomes following surgery for locally advanced and recurrent rectal cancer with disease extension into the pelvic side wall using a novel surgical approach termed ELSiE (Extended Lateral Pelvic Sidewall Excision)

304 consecutive National Health Service (NHS) patients underwent exenterative surgery in a single UK specialist centre. Where pretreatment MRI indicated pelvis sidewall or sciatic notch extension ELSiE was offered as a component of the pelvic exenteration surgery (n=111). Retrospective analysis of a prospectively maintained database assessed R0 rates, Clavien-Dindo morbidity and overall specific survival (OSS - assessed using Kaplan-Meier analysis).

Results: 304 patients underwent pelvic exenteration surgery, 111 of these were offered and underwent ELSiE. R0 rate in the ELSiE group was 85.3% compared to 82.2% non-ELSiE group. 53% of ELSiE procedures were for recurrent or re-recurrent rectal cancer compared to 36% in the non-ELSiE group. 47% of those who underwent ELSiE had en-bloc Total Perineal Excision whilst 27% did in the non-ELSiE population. En-bloc sacrectomy rate in ELSiE was 32.4% (15.5% non-ELSiE). Major-morbidity in the ELSiE group 41.4% and 30% in the non-ELSiE. Morbidity without sacrectomy in ELSiE was 35% as opposed to 24% in non-ELSiE. 90-day mortality was 4.5% ELSiE and 5.0% non-ELSiE. Survival analysis revealed that 70% of patients were alive at 1000-days post-operatively with no differences in OSS between either group.

Conclusion: ELSiE as an adjunct to exenteration surgery for pelvic sidewall disease extension in locally advanced, recurrent and re-recurrent rectal cancer increased R0 rates with relative improvements in OSS. Morbidity remains high in ELSiE and methods to reduce this are required. External validation of the ELSiE technique is now required.

Disclosure: Nothing to disclose

P1681 DEVELOPMENT OF PATIENT SPECIFIC 3D VIRTUAL MODELS FOR PLANNING BEYOND-TME RESECTIONS IN ADVANCED RECTAL CANCER

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Introduction: Advanced rectal cancer is defined by invasion into surrounding structures. Complete tumour clearance (R0), requires radical resections going beyond the usual TME plane. Operative approaches are bespoke and pre-operative planning essential. Patient specific 3D models may be a useful adjunct and enable a personalised operative "roadmap".

Aims & Methods: The following complex cases were selected; Extended Lateral Side-wall Excision (ELSiE), High Subcortical Sacrectomy (HiSS) and posterior exenteration.

Standard axial and sagittal T2-weighted MRI sequences were obtained. DICOM images were imported into open-source software ITK-SNAP[1] and key anatomical structures were manually segmented and exported into 3D software, Blender for processing.

Results: Segmentation took approximately 60-180 minutes and 20-60 minutes for mesh processing. Advanced rendering techniques were employed enabling ultra-realistic anatomical visualisation. Surgeons can manipulate models in 3D space, hide/reveal or change transparency of different structures of interest. In each case the precise anatomical relationship of the tumour to surrounding structures was clearly visualised.

Conclusion: Surgeons currently use a combination of MRI scans, reports and discussion with radiologists to better understand anatomy. The use of these reconstructions in the MDT, in clinic and in the operating theatre could be useful to better communicate complex rectal anatomy, identify areas of difficulty and aid surgical planning.

References: Yushkevich PA, Piven J, Hazlett HC, et al. User-guided 3D active contour segmentation of anatomical structures: Significantly improved efficiency and reliability. Neuroimage. 2006;31(3):1116-1128. doi:10.1016/j.neuroimage.2006.01.015

Disclosure: Nothing to disclose

P1682 UTILITY OF HIGH SUBCORTICAL SACRAL RESECTION {HISS} FOR LOCALLY ADVANCED & RECURRENT RECTAL CANCER EXTENDING ONTO L5/S1/2

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Introduction: In locally advanced and recurrent rectal cancer disease extension onto the lower lumbar spine and sacrum at L5/S1/2 is regarded as surgically unsalvageable, en-bloc bony cortex excision, High Subcortical Sacral resection [HiSS], may offer the chance of salvage in patients regarded as unsuitable or at high risk of incomplete resection with conventional surgical approaches.

Aims & Methods: We aimed to assess whether this technique improved outcomes in this group of patients who have been thought to have surgically unsalvageable disease.

Consecutive National Health Service (NHS) patients undergoing exenterative surgical procedures at a single centre were assessed and those with disease extension onto L5/S1/2 assessed for suitability for HiSS. Patients suitable for mid-distal S1-S1/2 sacrectomy were preferentially offered this option.

A prospective database of these patients was maintained and retrospective analysis performed. Outcomes including R0 rates, Clavien-Dindo morbidity, length-of-stay and OSS (Kaplan-Meier survival analysis) were assessed.

Results: 304 consecutive exenterations were performed, of these 30 were HiSS procedures and 66 were sacrectomies, 46 classified as high sacrectomies [HS] (above S2/3) and 20 as distal sacrectomies [DS]. 60% of HiSS;

28% HS and 50% DS had the diagnosis of primary rectal cancer extending beyond the TME (PRbTME). R0 rates were HiSS 81%; HS 87%; DS 75% and 83% for the non-sacral resection cohort.

Major-morbidity, classified as Clavien-Dindo grades 3 and 4, occurred in HiSS 36%; HS 48%; DS 45% and 28% in the non-sacrectomy group. Median LOS [IQR] varied significantly between the groups p=0.00005: non-sacral exenteration 19 days [IQR 11-29]; HiSS 24 days [IQR 13-45]; HS 35 days [IQR 23-62]; DS 21 days [IQR 11-42]. Survival analysis confirmed no differences in OSS between groups -p=0.829, the OSS for HiSS was 70% at 1000 days.

Conclusion: HiSS may offer an opportunity for radical treatment and improve outcomes for patients previously regards as unsalvageable. The data presented here demonstrate that options to optimise R0 rates and reduce morbidity are needed these could include 3D reconstruction & image-enhanced surgery.

Disclosure: Nothing to disclose

P1683 SURGICAL REPAIR OF ENDOSCOPY INDUCED COLONIC PERFORATIONS: A CASE-MATCHED STUDY OF SHORT-TERM MORBIDITY AND MORTALITY

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Introduction: Iatrogenic perforation of the gastrointestinal tract is mainly caused by endoscopic procedures. Surgical repair of endoscopy induced colonic perforation have only been evaluated in small case series.

Aims & Methods: To study to the short-term morbidity and mortality associated with surgical repair of endoscopy induced colonic perforations, and to compare these outcomes to those of similar surgeries performed for other indications on elective or emergency basis.

We studied all patients with endoscopic colonic perforation (ICD 9-10 codes) who underwent surgical intervention from the 2014-2017 National Surgery Quality Improvement Program (NSQIP) participant use data specific file. NSQIP data base includes prospective validated outcomes and anonymized data for patients undergoing major surgery in more than 500 hospitals. The primary outcome in this study was short term surgical morbidity (including wound, cardiac, respiratory, urinary, neurological, thromboembolism, and sepsis) and mortality.

Outcomes were compared between 3 groups of surgical interventions: Suturing, open segmental colectomy, and laparoscopic segmental colectomy. Then, based on surgery CPT codes, patients (group 1) were matched with 1:2 ratio to control patients undergoing same surgical interventions for other indications on elective (group 2) or emergency basis (group 3).

We used the chi square test or Fisher's exact to compare categorical variables. We used the independent t-test for continuous variables. We performed multivariate analysis to adjust for confounders of 30-day postoperative outcomes between the 3 matched groups. We included confounders into the models based on both clinical and statistical significance.

Results: Over 4 years, 590 patients underwent surgical intervention to repair endoscopy induced colonic perforation. The average age of the patients was 66.5 ± 13.6 with female gender predominance (381, 64.7%). The majority underwent open colectomy (365, 61.8%) while 85 patients (14.4%) underwent laparoscopic colectomy and 140 patients (23.7%) underwent surgical suturing.

Overall mortality occurred in 25 patients (4.2%). No statistically significant difference in mortality was found between open colectomy, laparoscopic colectomy, and suturing (4.0%, 2.6%, and 5.9% respectively, p=0.48). Composite morbidity occurred in 163 patients (27.6%). It was significantly lower in laparoscopic colectomy (14.1%) compared to 30.2% and 29.4% in open colectomy and suturing approaches (p=0.014).

Group 1 patients were shown to have better 30-day outcomes compared to group 3, regarding mortality (OR=0.66, 95% CI [0.51-0.85], p=0.001), sepsis (OR=0.54, 95%CI[0.66-0.91], p=0.002), and bleeding (OR=0.70, 95% CI [0.58-0.85], p=0.0003). Compared to group 2, group 1 patient showed significantly fewer bleeding complications (OR=0.54, 95% CI [0.35-0.84], p=0.0055).

Conclusion: Open segmental colectomy was the most frequent approach used to repair endoscopy induced colonic perforation in our series. Laparoscopic repair was associated with lower composite morbidity. Post-operative mortality, sepsis and bleeding complications were found to be significantly lower than in controls matched for the same procedures performed for other indications on emergency basis.

Disclosure: Nothing to disclose

P1684 ENDOSCOPIC MUCOSAL RESECTION AND ENDOSCOPIC SUBMUCOSAL DISSECTION OF 161 CASES OF LATERALLY SPREADING TUMORS

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Introduction: Laterally spreading lesions, which are traditionally treated surgically, may be amenable to endoscopic mucosal resection (EMR), often using a piecemeal method and Endoscopic submucosal dissection (ESD). Appropriate selection of lesions and a careful technique may enhance the efficacy of EMR and ESD for polyps more 10 mm in diameter without compromising safety. The aim of this study was to identify the factors that may predict the risk of polyp recurrence.

Aims & Methods: A retrospective analysis was conducted on the outcome of 101 polyps more/20 mm in diameter, treated by piecemeal EMR at a single centre using the ''lift and cut'' technique or ESD. All records were reviewed for polyp size, site, morphology and histology.

Polypectomy technique, patient treatment, polyp recurrence and surgical interventions were also recorded.

Results: Over THE 3-year period, 101 colonic polyps measuring more 10 mm were removed by EMR end ESD. Follow-up data WAS available for 83 cases (82%) with a mean polyp diameter of 42.9 mm; the total success rate of endoscopic polyp removal was 98%.

There was no statistically significant relationship between the site and recurrence.

Two patients (2%) underwent surgical intervention after EMR or ESD because of failed clearance. There were no post-EMR or post-ESD perforations and significant bleeding was revealed amog only six patients (5.9%). Based on clinicopathological analyses of LSTs, the indication for colorectal ESD is an LST non-granular type (LST-NG) >20 mm. LST granular type (LST-G) >30 mm or 40 mm are possible candidates for ESD because they have a higher submucosal (SM) invasion rate and are difficult to treat even by endoscopic piecemeal mucosal resection (EPMR).En bloc ESD reduces the local recurrence rate for large colorectal neoplasias. Piecemeal resection is the most important risk factor for local recurrence regardless of the ER method used.

Conclusion: With careful attention to technique, piecemeal EMR or ESD is a safe option for the resection of most sessile and flat colorectal polyps more/20 mm in size. A stricter treatment may be required for larger lesions because of the higher risk of recurrence.

Disclosure: Nothing to disclose

P1685 RECTAL CANCER IN ADOLESCENTS AND YOUNG ADULTS (AYA): PRESENTATION PATTERN AND OUTCOMES

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Introduction: Rectal cancer in AYA (≤ 39 years) is rare but increasingly diagnosed. The aim of our study was to analyze presentation pattern, and outcomes in AYA operated for RC.
Aims & Methods: Data on rectal cancer resections from 2008 to 2018 were collected from the prospectively maintained databases of 3 European referral centers and compared to a control group of consecutive patients over 40 (n=500).
Results: 87 patients in AYA group (mean age: 33.5, range 18-39; 53% males) were compared to 500 patients in the control group (500). In AYA tumors were significantly more advanced (locally advanced 12% vs 4%; p=0.005; metastatic 37% vs 14.3%; p=< 0.0001). Accordingly, neoadjuvant and adjuvant treatment (69% vs 32%, p< 0.0001; 76.2% vs 48.7%; p< 0.001), more complex and staged surgical procedures (9.3%), open surgery (31.1% vs 4.7%; p< 0.0001) and stomas (68% vs 47.6%; p=0.004) were more commonly performed in AYA patients. No differences in perioperative outcomes were reported. At a mean follow-up of 5 years no difference in overall survival (p=0.651), while a significantly lower cancer free survival was observed in AYA (p< 0.0001).
Conclusion: AYA patients undergoing resection for RC are rare, but more advanced at presentation, resulting in more complex operations, a faster cancer progression and lower cancer free-survival. Our data call for increasing awarenesson rectal cancer in AYA population.
Disclosure: Nothing to disclose

P1686 SURGICAL LAPAROSCOPIC TREATMENT OF DEEP ENDOMETRIOSIS WITH BOWEL INVOLVEMENT. A RETROSPECTIVE COHORT STUDY

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Introduction: Deep infiltrating endometriosis invading the intestine occurs in 8 to 12% of women with endometriosis. Surgery is indicated in patients with pelvic pain that do not respond to medical therapy.
Aims & Methods: To access the results of laparoscopic surgical treatment of bowel endometriosis in a single referral center. A retrospective analysis of medical records of patients with intestinal endometriosis submitted to laparoscopic surgical treatment. Number of surgeries, conversion rates, surgical time, length of hospital stay and complications were evaluated.
Results: One-hundred and thirteen patients were included. The mean age was 34.6 (ranging from 19 to 53), 62.8% of the patients have previous surgeries, the mean body mass index (BMI) was 25.2kg/m2. The main surgical indication was chronic pelvic pain (84.9%), followed by infertility (73.5%) and dyspareunia (54.9%). All procedures were done by laparoscopy. Surgeries performed: retosigmoidectomy (n=49, 43.4%), discoid anterior rectum resection (n=35, 31.0%), rectum shaving (n=26, 23.0%), appendectomy (n=11, 9.7%), and colon and ileal resection or ileal resection (n=8, 7.1%). Hysterectomy was performed in eleven patients (9.7%) and bladder

or ureteral lesions with need of resection in 7 patients (6.2%). Thirty-five patients (31.0%) had more than one resection at the same laparoscopic procedure. The mean surgical time was 122 minutes (retosigmoidectomy: 149minutes, anterior discoid rectum resection 114minutes and shaving 87minutes). When more than one procedure was performed at the same laparoscopy the mean surgical time increased to 161minutes.
The mean hospitalization time was 1.5 days (retosigmoidectomy: 1.8 days; discoid anterior resection: 1.4 days; shaving 1.0 day; more than one procedure at same laparoscopy 2.2 days). The conversion rates was 1.8% (n=2). Three patients needed temporary stoma (2.6%). The postoperative complication rates were 23% including rectal bleeding (n=18, 15.9%; only one case needed blood transfusion), wound infection (n=2, 1.8%), anastomotic leakage (n=0, 0%), nonsurgical site infection (n=3, 2.6%), need for reoperation (n=2, 1.8%, due to thermal injury; these two patients need provisory colostomy), readmission at 30 days (n=3, 2.6%, one due thermal injury and other two patients due to abdominal pain and diarrhea), deep vein thrombosis (n=1, 0.9%), and mortality at one year (n=0, 0%). Surgical recurrence occurred in four patients (3.5%) with need of new intestinal resection.
Conclusion: Laparoscopic surgery is safe and should be offered as the first surgical option in patients with deep endometriosis with intestinal involvement.
References: Abrão MS, Petraglia F, Falcone T, Keckstein J, Osuga Y, Chapron C. Deep endometriosis infiltrating the recto-sigmoid: critical factors to consider before management. Hum Reprod Update. 2015 May-Jun;21(3):329-39. doi: 10.1093/humupd/dmv003. PMID 25618908.
Disclosure: Nothing to disclose

P1687 COMPARATIVE RESULTS OF ENDOSCOPIC OPERATIONS FOR ZENKER'S DIVERTICULUM

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Introduction: The best option of treatment of Zenker's diverticulum is still controversial. Recent data shows that same effectiveness of flexible endoscopy and traditional surgery. The only drawback of endoscopic technique is the limitation of myotomy level, which can result in the relapse of symptoms. Driven by new technologies we started to utilize the tunnel technique in patients with Zenker's diverticulum.
Aims & Methods: To evaluate the effectiveness of endoscopic cryopharingoesophagomyotomy using a different techniques in the treatment of patients with Zenker's diverticulum.
In the period from July 2014 to April 2019, endoscopic surgery in MCSC A.S. Loginov for Zenker's diverticulum was performed in 113 patients. The average age of patients was 65 (from 34 to 86 years). According to the traditional method, 35 patients were operated on (I group). The average operative time was 42 minutes. According to the tunnel technique, 37 patients were operated on (group II). The mean operative intervention time was 50 minutes. According to the combined method, 42 patients were operated on. The average operative time was 32 minutes.
Results: The peculiarity of the patients who underwent surgery using the new combined method was the almost complete absence of the residual cavity of the diverticulum during the X-ray control examination.
Two patients in the group of traditional endoscopic treatment were reoperated because of complaints recurrence; each of them underwent two re-interventions. In two more cases the traditional endoscopic treatment was completed in two stages due to the large size of diverticulum. No recurrence of symptoms was observed after tunnel or combined technique.
Conclusion: Combined and tunneled endoscopic surgery for Zenker's diverticulum allows to successfully expand the scope of surgical intervention by performing an extended myotomy and dissection of the mucous membrane of the septum. This allows you to create conditions for the prevention of recurrence of the disease, thereby providing the best result of treatment.
Disclosure: Nothing to disclose

P1688 MINIMAL INVASIVE TECHNIQUES IN THE MANAGEMENT OF COLORECTAL ANASTOMOTIC LEAK: A RANDOMIZED EXPERIMENTAL STUDY

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Introduction: Anastomotic leak (AL) after low anterior rectal resection represents dreadful complication, which is associated with significant morbidity, morbidity and affects oncological and functional outcomes. Some of recently developed minimal invasive techniques are potentially suitable for the treatment of early diagnosed AL. TAMIS (Transanal Minimally Invasive Surgery) which was primarily introduced for local rectal excisions is one of those. Another option may be to use endoscopic suturing system (Over-Stitch, Apollo Endosurgery, Inc) providing full thickness closure in hollow viscera.

Aims & Methods: The aim of our study was to compare feasibility and efficacy of two different minimal invasive techniques for early repair of anastomotic leak on animal model.

Model of low colorectal anastomotic leak was introduced in 42 male pigs. Laparoscopic low anterior resection was performed with anastomosis created with 28 mm circular stapler after removing half of the staples. Two days later, the animals were randomized for endoscopic closure, TAMIS repair or control group with no treatment.

In endoscopic group a double-channel endoscope was introduced and anastomotic defect closed with 2/0 prolene and secured with original knotless fixation.

In TAMIS group a special port (GelPOINT) was inserted transanally and pneumorectum established. Standard laparoscopic instruments and 5mm camera were then used to close the defect by interrupted 3/0 vicryl suture. Three - grade scale (I - closed completely, II - closed with visible gaps, III - closure not possible) was introduced to assess the completion of closure. The signs of intraabdominal septic complications (IASC) and anastomotic healing including the burst test were evaluated after animals being sacrificed on 9th postoperative day. Chi square and Mann-Whitney tests were used to compare interventional and control groups.

This project was approved by local ethical committee in accordance with the European Convention on Animal Protection and supported by health research grants (AZV 16-31806A, MO 1012)

Results: Closure was technically possible in all 28 cases (grades I/II/III - 11/3/0 in endoscopic and 9/5/0 in TAMIS group; p>0,005). Two animals after endoscopic closure died due to peritonitis on 8th and 9th postoperative day. There was no difference in operating time - 31 (19-70) min in endoscopic and 43 (20-70) min in TAMIS group (p=0,357).

Overall IASC rate was lower after both endoscopic (5/14; p=0,022) and TAMIS (4/14; p=0,0079) repair compared to control (11/14). Healed anastomosis with no visible defect was observed in 10/14 (p=0,0023) and 11/14 (p=0,0068) in endoscopic and TAMIS groups respectively vs. 2/14 in control group. The burst test confirmed sufficient closure with mean pressure of 200 (80-300) mmHg in endoscopic and 235 (25-300) mmHg in TAMIS group (p=0,619).

Conclusion: Evaluated techniques were proved to be suitable for closure of anastomotic defect with similarly high success rates. Both interventions reduced intraabdominal septic complications. Endoscopic closure seems to require more training since initial procedures were associated with peritoneal soiling and peritonitis.

Disclosure: Nothing to disclose

P1689 SURGERY THROUGH STOMA-SITE INCREASES THE RISK OF PARASTOMAL HERNIA IN THE FIRST 6-MONTHS

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Introduction: The overall reported rate of parastomal hernias (PSH) in literature ranges from 44- 56%, and is highest in end colostomies (48%) followed by loop colostomies (30.8%), end ileostomies (28.3%) and lowest in loop ileostomies (6.2%-16%) [1,2]. Although several risk factors contributing to the development of PSH have been identified, manipulation of the stoma site during surgery has not been studied.

Aims & Methods: The primary aim of this study was to identify the influence of manipulation of the marked stoma-site during surgery (e.g. laparoscopic port placement) on the subsequent development of parastomal hernia (PSH).

We analysed data of consecutive patients who underwent colorectal surgery for benign and malignant pathology between January 2017 and December 2018 at a single tertiary care centre.

Results: A total of 408 patients were analysed. Their mean age at surgery was 54.6 (SD-17.9) years. Forty-nine(12.0%) developed PSH after surgery. The median time to developing a hernia was 222(25 and 75 percentile 147 and 363, respectively) days.

Laparotomy was performed in 233 while 127 and 48 had laparoscopy and single-incision surgery, respectively. One-hundred-and-ten (28.7%) had instrumentation placed through the stoma site during surgery.

A log-rank test was run to determine if there were differences in developing a PSH if the stoma site was being used as a port site. When the first 180-days were considered, the PSH formation was significantly different ($\chi2(2)=9,4,p=.002$). When the entire follow-up period was considered, however, there was no statistically significant difference in PSH formation ($\chi2(2)=1.13,p=.28$).

Conclusion: Using the stoma site as a port site increases the risk of early PSH formation, but this does not lead to an increased risk of PSH formation in the long run.

References: 1.Antoniou, S.A., Agresta, F., Garcia Alamino, J.M. et al.European Hernia Society guidelines on prevention and treatment of parastomal hernias. Hernia (2018) 22: 183. https://doi.org/10.1007/s10029-017-1697-5 2. Gillern S, Bleier JI. Parastomal hernia repair and reinforcement: the role of biologic and synthetic materials. Clin Colon Rectal Surg. 2014;27(4):162-71.

Disclosure: Nothing to disclose

P1690 SINGLE-INCISION LAPAROSCOPIC SURGERY DOES NOT INCREASE THE RATE OF PARASTOMAL HERNIA

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Introduction: The overall reported rate of parastomal hernias (PSH) in the literature ranges from 44- 56% and is highest in end colostomies (48%) followed by loop colostomies (30.8%), end ileostomies (28.3%) and lowest in loop ileostomies (6.2%-16%) [1,2]. Single Incision Laparoscopic Surgery (SILS) uses a port that is larger than standard laparoscopic ports (35-50mm) and therefore exerts a much higher radial force at the stoma site compared to other techniques. The short and medium-term effects of this have not been studied.

Aims & Methods: The primary aim of this study was to identify the incidence of PSH in patients who underwent SILS.

We analysed data of consecutive patients who underwent colorectal surgery for benign and malignant pathology between January 2017 and December 2018 at a single tertiary care centre. Patient and procedural data were retrieved from a prospectively maintained database.

Results: A total of 408 patients were analysed. Their mean age at surgery was 54.4 (SD-17.9) years. A total of 45 (11.3%) developed PSH after surgery. The median time to developing a hernia was 220 (25 and 75 percentile 146 and 368, respectively) days.

Two-hundred-and-thirty-three patients underwent laparotomy while 127 and 48 had laparoscopy and SILS, respectively, with 27(11.5%), 19(14.9%) and 3(6.3%) patients developing PSH. Univariate analysis did not identify a statistically significant difference between different surgical techniques (Chi-square 2.59, p=.27).

A log-rank test was run to determine if there were differences in developing a PSH and the different types of surgery. The survival distributions for the surgeries were not statistically significantly different, χ2(2) = 3.06, p=.22, but there was a non-significant reduction in PSH in SILS patients.

Conclusion: Single Incision Laparoscopic Surgery did not increase the risk of PSH. A study with a larger sample size may show a statistically significant risk reduction in SILS compared to other techniques.

References: 1.Antoniou, S.A., Agresta, F., Garcia Alamino, J.M. et al.European Hernia Society guidelines on prevention and treatment of parastomal hernias. Hernia (2018) 22: 183. https://doi.org/10.1007/s10029-017-1697-5 2. Gillern S, Bleier JI. Parastomal hernia repair and reinforcement: the role of biologic and synthetic materials. Clin Colon Rectal Surg. 2014;27(4):162-71.

Disclosure: Nothing to disclose

P1691 LONG-TERM OUTCOMES OF FLEXIBLE ENDOSCOPIC SEPTUM DIVISION FOR ZENKER'S DIVERTICULUM (TREATMENT NAÏVE AND SURGICAL RECURRENCE) WITH THE STAG BEETLE KNIFE

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Introduction: Flexible endoscopic septum division (FESD) is an established treatment for Zenker's diverticulum, however, data on long term outcomes are sparse. In addition,treatment of recurrences after surgery stapling can be technically challengingand little is known about role of FESD of recurrence after surgical recurrence. In this prospective study we aimed to evaluate long-term efficacy data for FESD and identify predictors of sustained symptom remission (treatment naïve and surgical recurrence).

Aims & Methods: Successive patients undergoing FESD for ZD between 2014-2018 were enrolled in this prospective study. Procedures were performed by a single operator under propofol sedation without endotracheal intubation. Symptom severity pre- and post-FESD was recorded using the Dysphagia, Regurgitation, Complications (DRC) scale. Symptom remission was defined as a total DRC score of ≤1 after index FESD or the latest attempt after planned multi-stage procedures. Symptom-free remission was measured using a Kaplan-Meier approach, with univariable analyses performed using Cox-regression models.

Results: 69 patients (mean age 74.4 years, SD 11.8, 61% male) were included for analysis, of which 60% were categorised American Society of Anaesthesiologists (ASA) Grade III or IV. 19 patients (28%) had undergone previous stapling treatment. The median cricopharyngeal muscle length was 24mm (IQR 17-30mm). The median procedure time was 20 minutes (IQR 19-25). The mean number of sessions of FESD therapy per patient was 1.4 (SD 0.7). In total, 75.4% of patients achieved symptom remission after the last planned FESD procedure. Kaplan-Meier estimated rates of symptom recurrence at 12, 24, 36 months were 12.6%, 36.3%, 46.5% respectively. The median time from the latest planned FESD procedure to symptom recurrence was 46.7 months (95% CI 18.4-75.0). On univariable

analysis, factors associated with symptom recurrence included previous stapling (hazard ratio [HR] 2.88; P=0.33) and younger age (HR 0.959 per year, P=0.030), but not significantly by gender (P=0.699), cricopharyngeal muscle length (P=0.059), procedural duration (P=0.241) or combined DRC score (P=0.080).

Conclusion: Using Kaplan-Meier estimates, the majority of patients develop recurrent ZD symptoms beyond 12 months post-FESD. This risk is higher in patients with recurrent ZD and in younger patients. All patients undergoing FESD for ZD should have either regular or open access follow-up arrangements in case symptoms recur.

Disclosure: Nothing to disclose

P1692 WITHDRAWN

Paediatric: Endocsopy, Imaging and Surgery
09:00-14:00 / Poster Exhibition - Hall 7

P1693 ERCP SAFETY AND EFFICACY IN THE PEDIATRIC POPULATION: A SINGLE TERTIARY CARE CENTER EXPERIENCE

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Introduction: Experience with endoscopic retrograde cholangiopancreatography (ERCP) in the pediatric setting is still limited especially in infant population. Wide heterogeneity of reported safety and efficacy profile and lack of systematic and standardized methodologies use exist, thus limiting pediatric ERCP use even in specialized centers.

Aims & Methods: The aim of this study was to evaluate the efficacy and safety of pediatric ERCP and to identify factors associated with procedure-related adverse events. All consecutive ERCPs performed for any indication in patients under the age of 18 from 2005 to 2018 at our single tertiary referral center were included in the study. Demographic characteristics of patients, indications, technical and clinical success, findings and procedure-related adverse events were retrospectively analyzed. The grade of technical complexity of each ERCP and the procedure-related complications were assessed according to the American Society for Gastrointestinal Endoscopy (ASGE) criteria.

Results: A total of 117 ERCPs were performed in 57 children (median age 7.6 (1-17) years; median weight 23.2 kg) by three ERCP expert endoscopists under general anaesthesia. The most frequent indications of ERCP were as follows: recurrent or chronic pancreatitis (33), post-surgical bile duct injury (19), suspected choledocholithiasis (14), and primary sclerosing cholangitis (PSC) (9). Therapeutic techniques performed were biliary sphincterotomy (32/117), biliary stenting (42/117), biliary stone extraction (21/117), pancreatic sphincterotomy (7/117), pancreatic stone extraction (5/117) and pancreatic stenting (10/117). Technical success was achieved in 112/117 (96%) cases and clinical success in 52/57 (92%) patients. ERCP-related complications consisted of seven episodes of mild pancreatitis (6% post-ERCP pancreatitis (PEP) rate) all resolved following conservative treatment. No procedure-related mortality was recorded.

Conclusion: When performed in experienced hands the use of ERCP in newborns, children and adolescents is safe and effective, with complication rates comparable to those reported in adults.

However well designed prospective studies are needed to better define outcomes.

Disclosure: Nothing to disclose

P1694 COHORT ANALYSIS OF PEDIATRIC INTUSSUSCEPTION SCORE TO DIAGNOSE INTUSSUSCEPTION

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Introduction: Intussusception is a serious cause of intestinal obstruction in young children and delayed diagnosis increases morbidity. Ultrasonography (USG) is the gold standard for diagnosis but operator dependence and unavailable worldwide.
Aims & Methods: The aims of the present study are to study the clinical characteristics and treatment outcomes and to evaluate the diagnostic accuracy of abdominal radiography (AR) with and without promising parameters to diagnose intussusception.
Children with suspected intussusception who underwent abdominal USG investigation in our center from 2006 to 2018 were recruited. Clinical and investigation were evaluated and compared between intussusception and non-intussusception groups. AR images were interpreted by a pediatric radiologist. Diagnosis of intussusception is composed of compatible USG and response with reduction.
Results: Ninety-seven children were diagnosed with intussusception (2.06±2.67 years, 62.9% male), 37.1% of whom were referrals and 74% were < 2 years old. The common manifestations of intussusception were irritable or abdominal pain (86.6%), vomiting (58.5%), abdominal distension (39.2%) and bloody stool (36.1%). The classic triad of intussusception (abdominal pain, bloody stool and palpable mass) had specificity of 100% but sensitivity of 11.3%. Children with no clinical fever and no palpable abdominal mass could discriminate intussusception from other mimics (P< 0.05). The referral cases had more clinical lethargy, bilious vomiting, bloody stool and more failure to reduce intussusception than non-referral cases (P< 0.05). In the multivariate model, clinical irritability and abdominal distension were the significant factors for failure to reduce intussusception. The pathologic leading of intussusception were identified in 28.8% including lymphoma, diverticulum, polyp, Crohn's disease, appendicolith, and enlarged intra-abdominal lymph nodes. AR to diagnose intussusception had sensitivity, specificity, PPV, NPV and accuracy of 73%, 63.6%, 67%, 70% and 68.4%, respectively. However, a combination of clinical irritability or abdominal pain, vomiting and age < 2 years with compatible AR (the Pediatric Intussusception Score model) had a high diagnostic value with a specificity of 93.33%
Conclusion: AR had a poor diagnostic value to diagnose intussusception. Apart from the well-known triad, the Pediatric Intussusception Score could increase the diagnosis accuracy leading to timely specific management.
References: 1. Weihmiller SN, Buonomo C, Bachur R. Risk stratification of children being evaluated for intussusception. Pediatrics 2011;127:e296-303. 2. Territo HM, Wrotniak BH, Qiao H, Lillis K. Clinical signs and symptoms associated with intussusception in young children undergoing ultrasound in the emergency room. Pediatr Emerg Care 2014;30:718-22.
Disclosure: Nothing to disclose

P1695 EFFECT OF PORTOSYSTEMIC SHUNT SURGERY ON CHOLANGIOPATHY IN CHILDREN WITH EXTRAHEPATIC PORTAL VENOUS OBSTRUCTION

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Introduction: There is paucity of literature on portal cavernoma cholangiopathy (PCC) in children and there are a number of unanswered questions regarding the outcome of PCC especially after porto-systemic shunt surgery.
Aims & Methods:
Objectives: To assess the effect of portosystemic shunt surgery on PCC in children with EHPVO.
Methods: Children with EHPVO deemed unfit for Meso-Rex shunt with splenomegaly-related issues and presence of PCC (symptomatic or asymptomatic) underwent Magnetic resonance cholangiogram (MRC) and

Magnetic resonance portovenogram (MRPV) just before non-selective portosystemic shunt surgery. PCC was graded as per modified Llop classification.[1] Those with patent shunt were re-evaluated for PCC at least 6 months after surgery with repeat MRC and compared with pre-shunt images. Pre and post shunt assessment of peribiliary collateral density was made on MRPV and correlated with the vascular anatomy.
Results: Twenty five children underwent portosystemic shunt surgery (central end to side splenorenal shunt with splenectomy in 24, mesocaval shunt in 1). Their duration of disease, age at surgery (pre-surgery PCC assessment) and age at re-assessment (post-surgery PCC) were 77 (15-144) months, 156 (72 - 210) months, 192 (78 to 216) months respectively. All showed shunt patency and adequate flow velocity. Pre-surgery MRC showed PCC grade I in 11, grade II in 1 and grade III in 13. MRPV showed SMV block in 20. Re-assessment for PCC 18 (6 to 54) months after surgery showed grade 1 in 6 and grade III in 19. The overall change in grade of PCC pre and post-surgery was significant (p=0.04). Thus, PCC was progressive in 6 and static in 19 children. Regression was seen in none. The density of peribiliary collaterals decreased in 5, increased in 3 and remained unchanged in 17. Decrease in peribiliary collaterals was seen only in those with SMV patency (n=5) and their PCC was static. Splenomegaly-related issues, gastroesophageal varices on endoscopy and other intrabdominal (esophageal, perisplenic and perigastric) collaterals ameliorated in all.

	Pre-surgery (n=25)	Post-surgery (n=25)	p-value
Grade I	11	6	
Grade II	1	0	
Grade III	13	19	
Wavy changes	19	17	0.16
Angulations	10	10	1.0
Indentations	7	9	0.56
Strictures	14	19	0.02
Upstream dilatation (Intrahepatic)	12	18	0.01
Upstream dilatation (Extrahepatic)	8	13	0.06

[Comparison of MRC features pre and post-portosystemic shunt surgery]

Conclusion: Non-selective porto-systemic shunt surgery decompresses the portal hypertension in esophago-gastro-splenic venous circuit effectively but fails to ameliorate the cholangiopathy and peribiliary collaterals. The peristence of cholangiopathy is attributable to SMV block.
References: [1] Llop E, de Juan C, Seijo S, et al. Portal cholangiopathy: radiological classification and natural history. Gut. 2011;60:853-60.
Disclosure: Nothing to disclose

IBD III

09:00-14:00 / Poster Exhibition - Hall 7

P1696 DISTINCTIVE MICROBIOTA TRAITS ALLOW TO DIFFERENTIATE BETWEEN *CLOSTRIDIUM DIFFICILE* INFECTION AND INFLAMMATORY BOWEL DISEASE PATIENTS IN AN AMERICAN POPULATION

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Introduction: *Clostridium difficile* infection (CDI) incidence has increased in recent years and it is the major cause of antibiotic-associated diarrhoea. Its manifestations have many similarities to exacerbations of Inflammatory Bowel Disease (IBD). Dysbiosis, a deviation from the normal microbial composition, has been widely reported in both CDI and IBD patients.
Aims & Methods: The aim of this study was to compare the abundances of different bacterial markers in stool samples of CDI and IBD patients, which might be used to develop bacterial biomarkers for IBD in symptomatic

patients. A cohort consisting of 20 CDI and 22 IBD patients were recruited by the Gastroenterology department from Beth Israel Deaconess Medical Center (Boston, USA). All CDI and IBD patients presented an active clinical represented by the presence of depositional alteration and abdominal pain. The relative abundance of all bacterial markers by qPCR: *Faecalibacterium prausnitzii* (Fpra), *Escherichia coli* (Eco), *F. prausnitzii* phylogroup I (PHG-I), *F. prausnitzii* phylogroup II (PHG-II), *Akkermansia muciniphila* (Akk), *Ruminococcus sp.* (Rum), *Lactobacillus sp* (Lac), Bacteroidetes (Bac) and *Methanobrevibacter smithii* (Msm) was determined on faecal samples.
Results: The relative abundances of Fpra, PHG-I, PHG-II, Rum, Eco and Msm were significantly different between CDI and IBD patients. While Fpra, PHG-I, PHG-II and Rum were significantly lower in CDI patients when compared with IBD patients, the abundance of Eco and Msm were significantly higher in CDI patients. No significant differences were found in Akk, Lac and Bac.
Conclusion: CDI patients exhibit a lower abundance of anaerobic bacterial markers such as *Ruminococcus, F. prausnitzii* and its phylogroups, which are considered to be beneficial maintaining gut homeostasis, Instead, species with inflammatory properties such as *E. coli* were increased in CDI. These results indicate that conditions with similar phenotypes (symptoms, endoscopic appearance) may display significant differences in faecal bacterial.
Disclosure: Prof. Garcia-Gil, Dr. Aldeguer, Dr. Serra-Pagès, Dr. Ramió-Pujol, Mr. Amoedo, are employees from GoodGut, company who has received private and public funding. Prof. Garcia-Gil, Dr. Aldeguer, Dr. Serra-Pagès, Dr. Ramió-Pujol and Mr. Amoedo report grants from CDTI, during the conduct of the study. Prof. Garcia-Gil, Dr. Aldeguer and Dr. Serra-Pagès are also GoodGut shareholders, outside the submitted work. The rest of the authors have nothing to disclose.

P1697 ESTABLISHMENT OF CHRONIC INFLAMMATION MODEL USING HUMAN SMALL INTESTINAL AND COLONIC ORGANOIDS

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Introduction: Patients with inflammatory bowel disease (IBD) mainly present with ulcerative colitis (UC) or Crohn's disease (CD). Recently, it has been recommended that mucosal healing is therapeutic goal of IBD. Furthermore, histological healing is becoming new target to treat IBD, because dysfunction of epithelial cells such as goblet cell depletion and crypt distortion might cause frequent relapse. However, the mechanism for cell transformation of intestinal epithelial cells by chronic inflammation remains unknown.
Aims & Methods: We have previously reported the irreversible transformation of intestinal epithelial cells after long-term chronic inflammation for over a year by using mice colonic organoids[1]. We therefore aimed to establish human in vitro chronic inflammatory model using human small intestinal and colonic organoid because human model might be useful to assess the molecular mechanism of pathogenesis. Human small intestinal and colonic organoids were isolated from non-inflamed lesion of small intestine and colon, respectively. The expression of inflammatory related receptors in both organoids were assessed by RT-PCR. Inflammatory response of the organoids by each inflammatory reagent was assessed by IL-8 expression. The mixture of inflammatory reagents were added into medium every other day for 12 weeks. The expression of NF-kB target genes IL-8, DUOXA2 was assessed every 3 weeks during 12 weeks stimulation. Microarray analysis was performed at 5 weeks of inflammatory stimulation in colonic inflammatory organoids. This study was approved by the ethics committee.
Results: We identified the difference of the inflammatory related receptors expressed in between human small intestinal and colonic organoids. Inflammatory response by each inflammatory reagent was also different between small intestinal and colonic organoids. The mixture of inflammatory reagents for small intestinal and colonic organoids has therefore been decided respectively for suitable inflammatory response. The stimulation by inflammatory reagents showed the significant induction of IL-8 and DUOXA2 in both small intestinal and colonic organoids. IL-8 was immediately downregulated during 12 weeks stimulation following rapid increase at 3 hours stimulation in both small intestinal and colonic organoids. In con-

trast, the expression of DUOXA2 gene was persistently increased form 3 hours to 12 weeks stimulation in both organoids. Microarray analysis in colonic organoids showed that the highest induced gene was claudin-18 (CLDN18), which has been reported to be increased in UC patients. The expression of CLDN18 were gradually increased at the late phase of inflammatory stimulation for 12 weeks in both organoids, indicating that the expression pattern of inflammatory induced genes was classified by 3 types; tentative, persistent and gradual.
Conclusion: Chronic inflammation into the human small intestinal and colonic organoid might mimic the phenotype of IBD. The establishment of in vitro human model for IBD might be useful for the identification of chronic inflammatory specific genes and developing effective therapy targeted mucosal healing. Moreover, the analysis of genes gradually upregulated at the late phase of inflammatory stimulation might be useful for understanding the pathogenesis of epithelial cell transformation during IBD disease duration. Furthermore, the identification of the differences between in vitro small intestinal and colonic organoids might be necessary for the investigation of differences between UC and CD.
References: 1) Hibiya S, Tsuchiya K et al. Long-term inflammation transforms intestinal epithelial cells of colonic organoids. J Crohns Colitis. 11:621-630, 2017.
Disclosure: Nothing to disclose

P1698 SUCCINATE ACTIVATES THE ERK PATHWAY AND THE EXPRESSION OF WNT LIGANDS IN EPITHELIAL CELLS

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Introduction: Crohn's disease (CD) is a chronic inflammatory disorder of the gastrointestinal tract characterized by initial transmural inflammation, commonly associated with complications, such as stenosis, abscesses and fistulas. The development of fistulas has been associated with the epithelial-mesenchymal transition (EMT) which is the process that allows to change the phenotype of the epithelial cells to a fibrotic behavior. Under inflammatory conditions, the metabolite succinate accumulates and its receptor, called SUCNR1, activates EMT.
Aims & Methods: The objective of this study is to analyze the pathway activated by succinate in epithelial cells. Intestinal resections from CD's patients (subdivided in B2 and B3 according Montreal's classification) were obtained. Healthy resections from colon carcinoma patients were used as controls and succinate levels were measured by using a colorimetric kit. HT-29 intestinal epithelial cells were treated with a constant concentration of 1mM succinate during different times (0 min, 15min, 30min, 1h, 6h and 24h). We analyzed the expression of p-ERK with respect to total ERK by means of Western Blot. The expression of the EMT markers (*Snail1, Vimentin and E-Cadherin*) as well as the expression of Wnt ligands and Wnt targets (*Wnt1, Wnt4 and Wnt10a, c-myc, lgr5*) were analyzed by qPCR after treatment with succinate. In some cases cells were treated with an inhibitor of the ERK pathway (V0126 10 µM). Results are expressed by mean ± SEM (n≥3) and as fold induction vs vehicle. Statistical analysis was performed with one-way ANOVA followed by Newman-Keuls test.
Results: The succinate concentration is higher in intestinal resections from B3 (208.9 ± 26.03) than B2 (127.2 ± 21.66) CD patients. In HT-29 cells, succinate induces an increase in the expression of p-ERK at 15 min (195.5% ± 72.83). It also produces an increase in the mRNA expression of *Vimentin* (fold induction of 1.60 ± 0.20), *Snail1* (2.12 ± 0.09), *Wnt1* (4.76 ± 1.05), *Wnt4* (2.32 ± 0.52), Wnt10a (3.69 ± 0.34), *c-myc* (1.14 ± 0.10) and *lgr5* (1.28 ± 0.12) and a decrease in E -cadherin (0.63 ± 0.08). The treatment with V0126 revert these changes to values that do not differ from that obtained in vehicle-treated cells.
Conclusion: Succinate is increased specifically in B3 patients. In addition, succinate induces the activation of the ERK pathway and the expression of Wnt ligands in epithelial cells, which could be involved in the effects of succinate on EMT.
Disclosure: Nothing to disclose

P1699 ASSOCIATION OF CX3CR1 EXPRESSION IN THE PERIPHERAL BLOOD WITH MUCOSAL INFLAMMATION IN IBD: A NATURAL KILLER STORY?

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Introduction: CX3CR1 is a chemokine receptor expressed on various (immune) cell types, and involved in adhesion on and migration of leukocytes through epithelial and endothelial cells (1,2). The proportion of CX3CR1+ cells within the blood CD4 effector T cell population, has been found to be correlated with clinical disease activity in IBD (3). Moreover, blocking CX3CR1 has been shown to reduce colitis in mice. This renders CX3CR1 a promising drug target for IBD and a potential biomarker for disease activity. We assessed expression of CX3CR1 on a variety of cell types in the blood of IBD patients and healthy controls to find potential target cells for CX3CR1-blockade therapy in humans, and questioned whether expression of CX3CR1 is associated with histologically proven disease activity in the gastrointestinal tract in patients with IBD.

Aims & Methods: Peripheral blood from patients with Crohn's disease (CD, n=11), ulcerative colitis (UC, n=11) and healthy controls (HC, n=11) was collected prior to endoscopy. Whole blood was isolated using washing and lysis of red blood cells, stained with a panel containing various antibodies (CD3, CD8, CD19, CD16, CD14, CD15, CX3CR1, CD56) and subsequently analyzed using an LSR II FACS analyzer. Disease activity was assessed through evaluation of biopsies of macroscopically inflamed areas by a pathologist. Using flow cytometry, the proportion of CX3CR1-positive cells as well as the level of CX3CR1 expression in a variety of cell types was evaluated. Differences between CD, UC and HC, as well as between patients with and patients without disease activity in the gastrointestinal tract were assessed.

Results: We noted CX3CR1 expression on blood (NK) T cells, NK cells, monocytes and granulocytes, but not on B cells. Neutrophils constitute the largest proportion of CX3CR1+ cells in the blood (median 3.7% [IQR 3.3]), whereas within the subpopulations, non-classical monocytes (median 98% [IQR 2.6]) and NK cells (median 90.3% [IQR 8.7]) had the highest proportion of CX3CR1 positive cells. In blood derived from patients with histologically active UC, intermediate monocytes showed a significantly higher proportion of CX3CR1+ cells (p=0.036), whereas CD4+ NK T cells showed upregulation of CX3CR1 on the cell surface (p=0.013), compared to patients with UC in remission. In CD, the proportion of CX3CR1+ CD8+ NK T cells was higher in patients with inflammation versus patients without inflammation (p=0.05).

Conclusion: CX3CR1 is expressed on a wide variety of peripheral blood cells. Although the proportion of CX3CR1+ cells within the CD4 T cell population has previously been reported to be associated with *clinical disease activity* in IBD, we do not find an association between the proportion of CX3CR1+ CD4 T cells and *histologically proven disease activity* in IBD. We do find an association between inflammation and CX3CR1+ CD8+ NK T cells in CD and CX3CR1+ intermediate monocytes in UC, which highlights the role of these cells in IBD. These results provide a baseline for follow-up studies on the role of CX3CR1 in IBD.

References: 1. Imai T, Hieshima K, Haskell C, et al. Identification and molecular characterization of fractalkine receptor CX3CR1, which mediates both leukocyte migration and adhesion. Cell 1997;91:521-30. 2. Nishimura M, Umehara H, Nakayama T, et al. Dual functions of fractalkine/CX3C ligand 1 in trafficking of perforin+/granzyme B+ cytotoxic effector lymphocytes that are defined by CX3CR1 expression. J Immunol 2002;168:6173-80. 3. Kobayashi T, Okamoto S, Iwakami Y, et al. Exclusive increase of CX3CR1+CD28-CD4+ T cells in inflammatory bowel disease and their recruitment as intraepithelial lymphocytes. Inflamm Bowel Dis 2007;13:837-46.

Disclosure: Nothing to disclose

P1700 NO DIFFERENCE IN THE DISTRIBUTION OF PATHOGENIC FACTORS FOUND IN *ESCHERICHIA COLI* ISOLATES FROM PATIENTS WITH CROHN'S DISEASE AND HEALTHY INDIVIDUALS

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Introduction: Dysbiosis of the gut microbiome in Crohn's disease (CD) patients is associated with reduced bacterial diversity and higher relative abundance of Proteobacteria phylum, in particular *Escherichia coli*. In recent decades, *E. coli* is thought to be implicated in CD pathogenesis and considered as one of the possible causes of the disease occurrence and progression.

Aims & Methods: The aim of the study was to characterize *E. coli* strains obtained from diagnosed CD patients and individuals (controls), and to evaluate their contribution to the pathogenesis of CD.

E. coli strains were isolated from stool samples of 14 patients and 18 controls. Fecal suspensions were inoculated on selective Endo medium and colonies were identified by MALDI Biotyper and serological test. Based on quadruplex PCR identification according to Clermont *et al.* (2013), the colonies were assigned to phylogenetic groups. Ninety seven selected isolates were sequenced on MiSeq platform. Reads were assembled using SPAdes v.3.11.1 followed by assemblies' annotation using Prokka v.1.9. Serotypes were assigned using SerotypeFinder-2.0 tool. Using MLT ENTEROtest 24N kit, the strains were tested for the production of H_2S and the ability to utilize various sugars, polyhydric alcohols, glycosides, and amino acids.

Results: Out of 97 sequenced isolates, 33 duplicates were revealed using the comparative genome analysis, i.e. isolates sequenced more than once due to varying colony phenotypes. Sixty four strains had unique genomes - 27 isolates from CD patients, and 37 isolates from the control group.

The phylogenetic group distribution did not differ significantly between CD patients and controls. However, *E. coli* strains belonged to phylogroups E/clade 1 and F were identified only in healthy donors. Clinical significance of strains belonging to these groups is not well understood.

The pathogenicity and virulence of *E. coli* strains were explored by searching for 61 previously reported genes of adhesion and invasion system in their genomes. We found no statistically significant difference in these genes distribution when comparing isolates from both CD and control groups. So, there was no evidence for the association between CD status and the presence of pathogenic or virulent genes in *E. coli* strains. According to the classification of *E. coli* serotypes, among isolated strains 3 enteroaggregative types (EAEC: O17/O44:H18, O15:H18, O126:H27), 3 enteropathogenic types (EPEC: O128ac:H12, O88:H25, O154:H9), and 1 enteroinvasive type (O112ac:H16) were found. The distribution of these types did not differ significantly between CD and control groups, either, though strains of these serological subgroups prevailed in fecal samples from individuals with CD and constituted a smaller proportion in healthy ones. Prevalence of these strains in CD patients may be associated with the development of the disease.

Strains from studied cohorts showed no significant difference in ability to catalyze sugars, polyhydric alcohols, glycosides and amino acids. It is of interest to note, 3 different strains from one CD patient showed ability to produce H_2S. It is supposed that hydrogen sulfide involves in IBD development by disrupting the integrity of the intestinal mucosa.

Conclusion: The whole genome analysis of *E. coli* strains in CD patients and healthy controls did not reveal any connection between *E. coli* virulence and pathogenicity and disease status. It may be assumed that the development of the disease is associated with altered interaction between the bacteria with certain serotypes and human immune system and their balance in community.

References: Clermont, O., Christenson, J. K., Denamur, E., Gordon, D. M. (2013). The Clermont Escherichia coli phylo-typing method revisited: improvement of specificity and detection of new phylo-groups. Environmental microbiology reports, 5(1), 58-65.

P1701 A GUT MICROBIOTA-DERIVED METABOLITE REROUTES INTESTINAL EXPANSION OF ANTIGEN PRESENTING CELLS FROM CIRCULATING MONOCYTES FOR ENHANCING ANTI-TUMORAL ACTIVITY AND SURVIVAL IN COLORECTAL CANCER

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Introduction: The intestinal mucosa inhabits the largest pool of phagocytes that fails to be constantly replenished from circulating monocytes in the absence of the gut microbiota and to some extent in response to antibiotics. Understanding this paradigm is of importance as long-term compositional changes in the gut microbiome has been linked to the initiation and progression of either inflammatory or neoplastic lesions even later in life. We herein investigated whether bacterial muramyl dipeptide (MDP), which occurs physiologically in high concentrations within the intestinal lumen, may interfere on the functional specialization of circulating monocytes into either dendritic cells or macrophages for intestinal homeostasis.

Aims & Methods: The *NOD2* gene expression levels of 427 colorectal cancer patients was respectively compared to outcome using the cancer genome atlas database. The transcriptomic data from NOD2hi and NOD2low tumors were further analysed for identifying gene pathways that were differentially enriched. We next performed multiparametric cell cytometry and gene expression analysis by making use of the Azoxymethane (AOM)/Dextran Sulfate Sodium (DSS) model of mouse colorectal cancer. A mouse model of colitis and competitive bone-marrow chimera mice were used for evaluating the anti-inflammatory properties and the long-term autonomy of M-CSF-derived phagocytes from Nod2-deficient mice respectively. This fate mapping of *Nod2*-deficient bone marrow derived precursors was addressed by reconstituting *Nod2*-deficient CD45.2+ animals with an equal mixture of wild-type CD45.1+ and congenic *Nod2*-deficient CD45.2+ cells. After these *in vivo* systems, we used *in vitro* culture approaches to study the impact of MDP on human monocytes differentiation into either dendritic cells or macrophages.

Results: A shorter median survival time of patients was observed for those with the lowest transcript levels of *NOD2*. Such tumors were markedly characterized by a lowered expression of several genes involved in phagocytosis and antigen presentation. Conversely, the intratumoral abundance of monocyte-derived phagocytes (CD11b+ CCR2- Ly6C- MHCII+) was lowered in tumours from *Nod2*-deficient animals. Quantitative RT-PCR analysis further argued for a specific decrease in the accumulation of antigen presenting cells derived from circulating monocytes despite similar abundance of macrophages. The shift towards monocyte-derived dendritic cells was also found when treating human peripheral blood monocytes with MDP. Adoptive transfer of M-CSF-derived phagocytes alleviated the severity of DSS-induced colitis, while the absence of NOD2 gave a lowered advantage on the expansion of such cells as determined by competitive chimera experiment.

Conclusion: Herein, we identified a key role of the major Crohn's disease predisposing *NOD2* gene on the ontogeny of monocyte-derived dendritic cells that may account for the greater survival of colorectal patients with high levels of intratumoral NOD2.

Disclosure: Nothing to disclose

P1702 CIRCULATING VITAMIN D BINDING PROTEIN, TOTAL, FREE AND BIOAVAILABLE 25-HYDROXYVITAMIN D AND THEIR RELATION TO INFLAMMATION IN INFLAMMATORY BOWEL DISEASE

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Introduction: There is mounting evidence to suggest that vitamin D levels are associated with important clinical parameters and outcomes in patients with inflammatory bowel disease (IBD). In recent years, additional IBD cohort studies have emerged that further support an association between vitamin D deficiency and clinical disease activity (1-4). However, the causal relationship remains unclear. To our knowledge, this is the first study in adult patients with IBD to report the influence of vitamin D binding protein (VDBP) on the association between circulating total, free, and bioavailable 25(OH)D and inflammation in IBD.

Aims & Methods: This study aimed to provide a better understanding of this relationship by more closely examining the relation between inflammation and different vitamin D parameters. A comparative, single-centered, cross-sectional study was conducted in 108 adults with IBD. Blood count, transferrin, albumin and CRP were determined by routine assays. CRP levels ≥5mg/dL were considered biochemical evidence of inflammatory activity. 25(OH)D and VDBP levels were determined by ELISA. Free vitamin D and bioavailable vitamin D levels were calculated with the validated formula (5). Statistical analysis was performed using IBM SPSS version 25.0.

Results: 108 subjects with IBD (54 male, 59 female; 68 CD, 45 UC) with a mean age of 41.08 ±12.84 years were recruited to the study. Of these patients, 32/108 had inflammatory activity (14 male, 18 female; 22 CD, 10 UC; 39.69 ±13.89 years) while 76/108 had no inflammation (36 male, 40 female; 44 CD, 32 UC; 41.54 ±12.43 years). The albumin levels were negatively correlated with CRP (-0.303, p=0.002) and significantly lower in the presence of inflammation (p< 0.05). Average serum 25(OH)D levels were found to be similar in inflammatory and non-inflammatory conditions (25.37 ±11.38 and 23.46 ±10.12 ng/mL respectively, p>0.05). However, VDBP levels were significantly higher when inflammation was present (364.26 ±63.26 mg/L in inflammatory vs. 335.27 ±67.51 mg/L in non-inflammatory conditions, p< 0.05) and also showed a positive correlation with CRP levels (0.288, p=0.003). The free/total 25(OH)D ratio was negatively correlated with CRP levels (-0.260, p< 0.05). Neither free 25(OH)D nor bioavailable 25(OH)D levels were correlated with CRP or albumin levels and no significant inflammation-related variance in levels was found for either of these parameters.

Conclusion: Although no association between total, free and bioavailable 25(OH)D and inflammation was observed, high levels of circulating VDBP were associated with increased levels of inflammation. Confirming this association, the free/total 25(OH)D ratio showed an inverse association with inflammation. These findings suggest that VDBP may play a bigger role than previously thought in the modulation of the complex relation between vitamin D and inflammation. Thus, we propose that the simultaneous detection and investigation of total, free and bioavailable 25(OH)D and VDBP levels in plasma can provide valuable information when studying the relationship between vitamin D and IBD-related inflammation.

References: 1. Blanck S, Aberra F. Vitamin d deficiency is associated with ulcerative colitis disease activity. Digestive diseases and sciences. 2013;58(6):1698-702. 2. Ulitsky A, Ananthakrishnan AN, Naik A, Skaros S, Zadvornova Y, Binion DG, et al. Vitamin D deficiency in patients with inflammatory bowel disease: association with disease activity and quality of life. JPEN Journal of parenteral and enteral nutrition. 2011;35(3):308-16. 3. Alrefai D, Jones J, El-Matary W, Whiting SJ, Aljebreen A, Mirhosseini N, et al. The Association of Vitamin D Status with Disease Activity in a Cohort of Crohn's Disease Patients in Canada. Nutrients. 2017;9(10). 4. Scolaro BL, Barretta C, Matos CH, Malluta EF, Almeida IBTd, Braggio LD, et al. Deficiency of vitamin D and its relation with clinical and laboratory activity of inflammatory bowel diseases. Journal of Coloproctology. 2018;38(2):99-104. 5. Bikle DD, Malmstroem S, Schwartz J. Current Controversies: Are Free Vitamin Metabolite Levels a More Accurate Assessment of Vitamin D Status than Total Levels? Endocrinology and metabolism clinics of North America. 2017;46(4):901-18.

P1703 PTPN2 AND IL-10 IN THE DEVELOPMENT OF INFLAMMATORY BOWEL DISEASE

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Introduction: Inflammatory bowel disease (IBD) is caused by a complex interaction among genetic, immunological, bacterial and environmental factors. In this scenario, protein tyrosine phosphatase non-receptor type-2 (PTPN2) has been recognized as a risk factor for the development of IBD and functional studies revealed a major role for this protein in the development of experimental colitis through the regulation of the inflammasome, among other processes. Similar, the immunoregulatory cytokine interleukin-10 (IL-10), which is a master regulator of innate immune cell function and controls excessive inflammatory cytokine release, e.g. that of the inflammasome product IL-1β, has also been considered a relevant player in the control of intestine inflammation.
Aims & Methods: Here we aimed to elucidate the interaction between IL-10 and PTPN2 dysfunction in the development of intestinal inflammation, at cellular and molecular level, in order to contribute to the identification of new and novel prevention and/or therapeutic approaches.
DSS colitis and the IL-10$^{-/-}$ immune cell-driven colitis models were performed in mice lacking PTPN2 in myeloid cells (PTPN2$^{fl/fl}$xLysMCre mice or PTPN2$^{fl/fl}$xCD11cCre mice). After that, histology studies, flow cytometry, expression analysis, ELISA and barrier function experiments were performed. Bone marrow derived macrophages (BMDMs) were used for *ex vivo* studies.
Results: *Ex vivo* experiments using BMDCs showed that recombinant IL-10 was able to ameliorate the expression of IL1β induced by LPS in WT but not in PTPN2^{CD11cCre} BMDCs. The same experiments using BMDMs from WT and PTPN2^{LysMCre} mice revealed no differences in the expression of IL1β. However, IL-10-induced reduction of the production of mature IL1β was impaired in BMDMs from PTPN2^{LysMCre} mice as compared with their WT littermates. Analysis of different well-known signalling pathways involved in the regulation of the inflammasome and IL1β expression revealed that NFκappaB, Erk and Jnk activation were dysregulated in PTPN2^{LysMCre} BMDMs. Colitis models using IL-10$^{-/-}$ and IL-10$^{-/-}$xPTPN2^{LysMcre} mice also revealed differences in prolapse incidence, histology scores and myeloperoxidase activity, being all these parameters increased in the mice lacking PTPN2 in myeloid cells.
Conclusion: PTPN2 contributes to IL-10-related effects on innate immune response and development of colitis. These results unravel a novel molecular mechanism, by which the beneficial effects of IL-10 on intestinal inflammation depends on the genetic host factors.
Disclosure: Nothing to disclose

P1704 GREATER REDUCTIONS OF GUT T LYMPHOCYTES WITH COMBINED BLOCKADE OF α4β7 AND αEβ7 INTEGRINS VERSUS INDIVIDUAL BLOCKADE ALONE

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Introduction: Therapeutic approaches to treating inflammatory bowel diseases (IBD) include targeting integrins that mediate adhesion and migration of inflammatory lymphocytes to the gastrointestinal (GI) tract. In the era of anti-integrin therapies in IBD, it is important to understand the relative contributions of integrin family members to lymphocyte migration and retention in the GI tract.

Aims & Methods: To dissect the role of β7 integrins in lymphocyte trafficking, we used the KikGR transgenic mouse model which ubiquitously expresses a green-to-red photoconvertible protein. After treatment with antibodies against α4β7, αEβ7, β7 (which targets both α4β7 and αEβ7), or a control, mesenteric lymph nodes (MLNs) were surgically exposed to violet light to photo-convert cells from KikG (green fluorescence) to KikR (red fluorescence). Frequency of KikR$^+$ CD8$^+$ T cells in the colon lamina propria was then analysed by flow cytometry. Statistical testing was conducted using Student's unpaired *t* tests.
Results: Individual blockade of either α4β7 or αEβ7 integrin reduced CD8$^+$ T cell localization to the colon lamina propria from mesenteric lymph nodes, whereas blockade of both led to a greater reduction in CD8$^+$ T cells (Table). Further, we demonstrate superior reductions in both polyclonal and antigen-specific effector T cell accumulation in the intestinal mucosa following concurrent inhibition of both β7 integrins as compared with single blockade of either α4β7 or αEβ7. Additional experiments using intra-vital two-photon microscopy to image mucosal CD8$^+$ T cells from the luminal side of the small intestine showed that αEβ7-expressing T cells actively migrate within the epithelium and can travel across the basement membrane between subepithelial regions and lamina propria compartments. Importantly, blockade of αEβ7 or its ligand E-cadherin reduces T cell interactions with the basolateral epithelial surface. Lastly, blockade of αEβ7, but not α4β7, reduces the retention time of activated effector T cells in the intestinal mucosa.

Comparison	Mean ± SEM (% of migration relative to control)
Anti-αEβ7 vs control	54.6%±9.5% vs 100%*
Anti-αEβ7 vs control	52.1%±6.7% vs 100%*
Anti-αEβ7 + anti-α4β7 vs control	29.1%±6.7% vs 100%***
Anti-αEβ7 + anti-α4β7 vs anti-αEβ7	29.1%±6.7% vs 54.6%±9.5%*
Anti-αEβ7 + anti-α4β7 vs anti-α4β7	29.1%±6.7% vs 52.1%±6.7%*
Anti-β7 vs control	26.4%±6.4% vs 100%**
Anti-β7 vs anti-αEβ7	26.4%±6.4% vs 54.6%±9.5%*
Anti-β7 vs anti-α4β7	26.4%±6.4% vs 52.1%±6.7%*

MLN, mesenteric lymph node; SEM, standard error.
Data were calculated as percentage of KikR$^+$ CD8$^+$ cells migrated from MLN relative to that of the control group. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$. Data are representative of five independent experiments.

[Table. Trafficking of CD8$^+$ T Cells from MLNs to the Colon Is Reduced by Dual Blockade of α4β7 and αEβ7]

Conclusion: Taken together, our results suggest a model in which cell migration to the gut mucosa is mediated through α4β7 while activated effector T cells are retained in the lamina propria and intra-epithelial space via αEβ7:E-cadherin interactions. Co-blockade of α4β7 and αEβ7 leads to increased reduction of T cell accumulation in GI tissues through a stepwise inhibition of T cell migration and subsequent tissue retention. Our data also suggest that a therapeutic blockade of both α4β7 and αEβ7 such as that provided by etrolizumab may provide more efficient inhibition of T cell trafficking to the gut and potentially their inflammatory effects on the gut lining, which could alter the pathogenesis of IBD, than blockade of one integrin alone.
Disclosure: All authors are employees of Genentech, Inc.

P1705 INTRACELLULAR SURVIVAL AND REPLICATION OF ADHERENT-INVASIVE *ESCHERICHIA COLI* (AIEC) AND NON-AIEC WITHIN TWO MACROPHAGE CELL LINES

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Introduction: Adherent-invasive *Escherichia coli* (AIEC) have been associated with Crohn's disease pathogenesis. AIEC pathotype is constituted by *E. coli* able to adhere to and invade intestinal epithelial cells, and able to survive and replicate within macrophages without inducing cell death. Identification of AIEC is based on *in vitro* models of infection and lacks standardisation. Besides, scarce data exist about the intramacrophage survival and replication abilities of non-adherent and non-invasive *E. coli* colonizing the gut mucosa (non-AIEC).

Aims & Methods: We aimed to compare the intracellular survival and replication abilities of AIEC and non-AIEC strains in two different cell lines previously used for AIEC identification. We tested 13 AIEC and 29 non-AIEC strains isolated from the intestinal mucosa of Crohn's disease patients and controls using gentamicin protection assays in triplicate. The cell lines tested were the murine macrophages J774 and the human monocytes THP-1, the latter was differentiated to macrophages. The results are expressed as the percentage of intracellular bacteria after 24h of infection. Indices >100% indicate intracellular survival.

Results: In J774, AIEC strains clearly showed higher indices of intracellular survival/replication than non-AIEC (1143±750% *vs* 282±175%, p< 0.001). However, 85% of non-AIEC were indeed able to survive and replicate within this cell line, what can represent an issue in AIEC screening. We suggest a new threshold value that could be of assistance, as 85% of AIEC strains and only 7% of non-AIEC showed indices over 500% (p< 0.001). In THP-1, the indices of survival/replication were lower than in J774 and no differences were found between strains (AIEC: 90±52%, non-AIEC: 119±72%). No correlation was found between the data obtained by the two models.

Conclusion: In conclusion, we suggest that the human cell line THP-1 is not suitable for AIEC screening and that a higher threshold value of intracellular survival/replication in J774 may be of assistance in AIEC screening. Additional studies using more realistic models such as non-tumour human cell lines would be of interest.

Disclosure: Nothing to disclose

P1706 CURDLAN FEEDING CHANGES MICROBIOTA COMPOSITION AND IMPROVES DSS COLITIS IN MICE

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Introduction: β-glucan consumption is known for its beneficial effects in reducing inflammation. Humans lack the required enzymes to digest β-glucans, but certain intestinal microbiota species can digest β-glucans and thus trigger gut microbial changes, improving human health.
Aims & Methods: In this study, we determined curdlan (bacterial β-glucan) induced microbial changes, and followed its influence on the course of intestinal inflammation in the Dextran Sodium Sulfate (DSS) colitis. C57BL/6 mice were pre-treated with vehicle (5% glucose) or curdlan (10 mg/ml) through oral gavage for 14 days. Subsequently, mice were taken off curdlan and colitis was induced by administering 2% fresh DSS daily to the drinking water for 7 days. Control (non-colitis) groups received normal drinking water. To determine inflammation, colon weight and length was measured and histology scoring and gene expression study were performed. Colon content was collected for 16S amplicon (V3-V4) sequencing of microbiota composition. Differences in amplicon sequence variance (USEARCH) composition were visualized based on the Bray-Curtis-Dissimilarity Index. Fold differences were studied using DESeq2.
Results: In colitis condition, disease activity index, weight loss and inflammation score of the curdlan pre-treated group were improved compared to the vehicle treated group. Concomitant with improved colitis, the bacterial populations exhibited a higher alpha diversity of the curdlan fed animals compared to vehicle. Beta diversity analysis indicated large differences (R² = 0.46) in the bacterial community structure (Bray-Curtis) between the colitis and non-colitis condition. While curdlan feeding did not induce any global community changes, specific taxa did show significant differences in relative abundance. Interestingly, a specific *Bifidobacterium* was observed to be 10 to 100-fold more prevalent in the curdlan fed group in both colitis and non-colitis conditions respectively.
Conclusion: Curdlan feeding improved DSS-induced colitis and our data suggests that alterations in the gut microbiome may mediate the observed beneficial effects.
References: 1. Baldassano S, Accardi G, Vasto S. Beta-glucans and cancer: The influence of inflammation and gut peptide. European Journal of Medicinal Chemistry. 2017;142:486-92. 2. Wirtz S, Neurath MF. Mouse models of inflammatory bowel disease. Advanced drug delivery reviews.

2007;59(11):1073-83. 3. Asto E, Mendez I, Audivert S, Farran-Codina A, Espadaler J. The Efficacy of Probiotics, Prebiotic Inulin-Type Fructans, and Synbiotics in Human Ulcerative Colitis: A Systematic Review and Meta-Analysis. Nutrients. 2019;11(2). 4. Schroeder BO, Birchenough GMH, Stahlman M, Arike L, Johansson MEV, Hansson GC, et al. Bifidobacteria or Fiber Protects against Diet-Induced Microbiota-Mediated Colonic Mucus Deterioration. Cell host & microbe. 2018;23(1):27-40.e7.
Disclosure: Nothing to disclose

P1707 DIFFERENTIAL GENE EXPRESSION AND AMINO ACID SUBSTITUTIONS OF OUTER MEMBRANE PROTEINS IN ADHERENT-INVASIVE Escherichia coli

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Introduction: Variations in the expression and/or the sequence of outer membrane proteins (OMPs) may modulate bacterial virulence. Increased OmpC expression and particular mutations in OmpA sequence have been related to a better interaction of adherent-invasive *Escherichia coli* (AIEC) strain LF82 with intestinal epithelial cells (IECs).
Aims & Methods: We aimed to study in a collection of AIEC and non-adherent and non-invasive *E. coli* colonizing the gut mucosa (non-AIEC): i) the variability of OMPs sequence to look for new variants associated with AIEC, and ii) to study the differential gene and protein expression of OMPs between the two groups of strains to gain knowledge about the role of OMPs in AIEC pathogenicity.
Fourteen AIEC and 30 non-AIEC strains were included in the study. The *ompA, ompC* and *ompF* genes were sequenced by Sanger method. Differential expression of OMPs was studied at the protein level by urea-SDS-PAGE in strains growing LB medium, and for the first time, at the gene level during *in vitro* infection of intestine-407 cells by RT-qPCR. Two fractions were analysed: i) the bacteria present in the supernatants of infected cultures and ii) the bacteria interacting with IECs (either the adhered or the intracellular ones).
Results: Sequence variants were mostly associated with the phylogenetic origin of the strains rather than with the AIEC phenotype. Nonetheless, OmpA-A200V, and OmpC-S89N, -V220I and -W231D amino acid substitutions were more frequently found in AIEC than in non-AIEC strains. OMPs protein levels were also similar between AIEC and non-AIEC growing in conventional culture. However, AIEC showed increased expression of *ompA* and *ompF* in comparison with non-AIEC when growing in the supernatants of infected IECs cultures (p< 0.030). Interestingly, reduced OMPs expression was observed in AIEC strains infecting IECs (p< 0.032), whereas non-AIEC strains did not significantly alter OMPs expression under this condition (p>0.577).
Conclusion: In conclusion, despite no particular OMPs sequence variants have been found as a common and distinctive trait in AIEC, a general trend has been observed in terms of OMPs gene expression using *in vitro* infection models. This supports the hypothesis that differential expression of OMPs proteins could play an important role in AIEC virulence.
Disclosure: Nothing to disclose

P1708 ELTANEXOR RAPIDLY DECREASES INFLAMMATION AND IMPROVES OUTCOMES IN A DSS MODEL OF IBD

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Introduction: Crohn's disease and ulcerative colitis are inflammatory bowel diseases (IBD) leading to abdominal pain, severe diarrhea, fatigue and weight loss. Over 1 million Americans and 2.5 million Europeans are estimated to have IBD, with incidence rates rising exponentially in industrialized nations. To date, there is no cure for IBD, making patients dependent on lifelong symptomatic treatment aimed to reduce recurrence of intestinal inflammation. Thus, novel and effective treatments for IBD are an urgent and unmet medical need. Selective Inhibitor of Nuclear Export (SINE) compounds, that inhibit exportin 1 (XPO1)-mediated nuclear export of over 200 cargoes, may represent a novel option to treat inflammation, such as NfKb and PPAR-g. Eltanexor (KPT-8602), an oral SINE compound, has a broad therapeutic window and minimal brain penetration in preclinical species associated with reduced toxicities while maintaining efficacy. The safety, tolerability, and efficacy of eltanexor is currently being evaluated in patients with relapsed/refractory cancer indications (NCT02649790). Our preliminary data indicated that eltanexor also has potent anti-inflammatory and cytoprotective effects both *in vitro* and *in vivo*, providing clear rationale for its utility as a promising therapeutic agent for IBD. This study sought to determine the effects of eltanexor during intestinal inflammation using a dextran sulfate sodium (DSS)-induced colitis mouse model, as well as its impact on cytokine expression in bone marrow-derived (BMD) macrophages (Mφs).

Aims & Methods: Colitis was induced in C57BL6/J mice by 2.5% dextran sodium sulfate (DSS) in drinking water for 5 days. Disease progression was assessed by a standardized disease activity index (DAI) including body weight loss, stool consistency and blood in the faeces. Myeloid cells infiltrating the colonic mucosa were analyzed via flow cytometry. To assess the therapeutic potential of eltanexor *in vivo*, 10 and 15 mg/kg of the SINE compound were orally administered every other day starting at day 5 of DSS colitis. To study the anti-inflammatory effect of eltanexor at gene expression level, BMDMφs were pre-treated with eltanexor before stimulation with LPS (100 ng/ml) and IFNγ (50 ng/ml).

Results: To test the therapeutic potential of eltanexor, mice treatment was started at the peak of intestinal inflammation, namely day 5 after DSS. Oral administration of 15 mg/kg eltanexor resulted in a rapid and potent reduction of DAI within 48 hours of administration. Eltanexor treatment resulted in recovery of body weight loss, reduced blood in the faeces and normalization of stool consistency. This anti-inflammatory effect was accompanied by a decreased infiltration of colonic inflammatory myeloid cells including neutrophils and monocytes, followed by an increase in mature Mφ. *In vitro*, eltanexor pre-treatment suppressed expression of pro-inflammatory cytokines (IL-1b, IL-1a, NOS2, IL-6 and TNFa) in LPS/IFNγ treated BMDMφs. In parallel, eltanexor was able to induce a rapid increase (within 2 hours post dosage) in LPS+IFNγ stimulated BMDMφs of IL-10 compared to the vehicle pointing towards a strong anti-inflammatory effect.

Conclusion: Eltanexor was able to significantly improve the course of murine DSS-induced colitis. Both *in vitro* and *in vivo*, eltanexor demonstrated the ability to rapidly decrease inflammation and prevent myeloid cell activation. These data suggest that blockage of XPO1-mediated nuclear export may be a promising therapeutic strategy to favor a rapid remission in IBD and further research is warranted.

Disclosure: Nothing to disclose

P1709 DECIPHERING COLONIC MUCOSA-ASSOCIATED BACTERIAL TAXA TO ASSIST IN DISCRIMINATING INFLAMMATORY BOWEL DISEASE SUBTYPES WITH COLONIC LOCATION

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Introduction: The dysbiosis displayed by patients with Crohn's Disease (CD) and ulcerative colitis (UC) are different [1]. Although the location of the disease is a parameter relevant to clinical practice [2], few studies have shown the changes in the microbial community among the subtypes of inflammatory bowel disease (IBD) that affect the colon (E1, E2, E3, C-CD and IC-CD).

Aims & Methods: Our aim was to analyse the richness, diversity and composition of the microbiota associated to the colonic mucosa of IBD patients with disease located in the colon in order to identify bacterial markers that allow their discrimination.

Colonic biopsies were obtained from 21 patients with UC (5 E1, 6 E2 and 10 E3) and 22 with CD (12 C-CD and 10 IC-CD). Mucosa-associated microbial community was analysed by sequencing the V4 region of the 16S rRNA gene by the Illumina MiSeq method (depth 23,611 seqs/sample). Differences between IBD subtypes according to location have been sought by analysing alpha diversity (richness and diversity) and the relative abundance of taxa at different taxonomic levels (phylum-genus). The receiver operating characteristic (ROC) curve analysis was performed for the significant taxa, and accuracy to discriminate amongst disease locations was measured by the area under the ROC curve (AUC). Besides, and given the compositional nature of microbiome data [3], a lineal discriminant analysis was performed with *selbal* [4]. The groups of taxa whose relative abundance allowed the best discrimination between diseases was selected to calculate a balance to differentiate conditions, using a k-fold cross-validation algorithm.

Results: Richness (Sobs=55-288) and diversity (InvSimp=1.9-38.9) of the bacterial community were similar among all the disease locations compared. Six indicators, that determine a differential microbiological signature between IBD locations, have been identified (relative abundance=0.16-20.91%). The abundances of sequences corresponding to indicators 36 and 75 were significantly lower in patients with C-CD compared to those with UC of any location (p≤0.040, AUC≥0.726). Besides, indicators 2, 11 and 69 showed significant differences between E3 and C-CD (p≤0.015, AUC≥0.829). Indicators 2 and 11 also showed differences between UC locations (p≤0.017, AUC≥0.861) while the relative abundance of indicators 51 and 19 is higher in C-CD compared to IC-CD (p≤0.007, AUC≥0.846). On the other side, using the compositional approach, a ratio of two indicators resulted in the best balance to discriminate between diseases, which had an apparent AUC=0.857 when measured on the whole dataset (cross-validation AUC=0.665).

Conclusion: Richness and diversity of the microbiota associated to the colonic mucosa of IBD patients with colonic disease location is similar. However, differential bacterial indicators have been identified and a ratio to discriminate between UC and CD with colonic location is proposed. The quantification of these taxa would allow to refine the use of microbiomarkers to

(i) support the diagnosis between IBD that affect the same location and/or

(ii) assess the risk of disease extension.

References: [1]Machiels,K et al.2014.Gut.63(8):1275-83. [2]Satsangi,J et al.2006.Gut.55(6):749-753. [3] Gloor, G. et.al. 2017. Front. Microbiol. (8): 1-6 [4] Rivera-Pinto et al. 2018 mSystems.17;3(4).pii: e00053-18.

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P1710 BENEFICIAL EFFECTS OF 3-OXO-C12:2 N-ACYL HOMOSERINE LACTONE, A NEW *QUORUM SENSING* MOLECULE FROM THE GUT ECOSYSTEM, ON THE INTESTINAL BARRIER FUNCTION

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Introduction: N-acyl homoserine lactones (AHLs) are molecules involved in *quorum sensing*, a bacterial communication network, which can also impact the host's physiology. We recently showed the presence of AHLs in the human gut ecosystem and identified a new AHL, named 3-oxo-C12:2. This molecule was decreased in inflammatory bowel disease subjects during flare and its absence was associated with dysbiosis, thus suggesting a beneficial role if this new AHL. However, 3-oxo-C12:2 is structurally very close of the well-studied AHL 3-oxo-C12, produced by the opportunistic pathogen *P. aeruginosa*, which is known to impair epithelial barriers.

Aims & Methods:
In this context, **we aimed to investigate the effects of the 3-oxo-C12:2 AHL on the intestinal barrier function**, and compare them to those of the 3-oxo-C12.
Human Caco-2/TC7 enterocytic cells were exposed on their apical side to 3-oxo-C12:2 or 3-oxo-C12 AHLs. These treatments were combined or not with pro-inflammatory cytokines Interferon-g and Tumor Necrosis Factor-a, known to have deleterious effects on the barrier function. We assessed paracellular permeability by measuring the passage of FITC-dextran 4 kDa and analyzed tight junctions (TJ) integrity by immunofluorescence and Proximity Ligation assays.

Results: Upon exposure to 3-oxoC12, the paracellular permeability is increased and the signal of Occludin and Tricellulin, bicellular and tricellular TJ proteins respectively, is decreased. In contrast, 3-oxo-C12:2 AHL modifies neither permeability nor tight junctions integrity. While 3-oxo-C12 potentiates the increase in permeability induced by the pro-inflammatory cytokines, 3-oxo-C12:2 does not exacerbate cytokine effects on permeability. Moreover, 3-oxo-C12:2 attenuates the deleterious effects of cytokines on Occludin and Tricellulin, as well as on their interaction at the plasma membrane with their cytoplasmic partner ZO-1. Preliminary results show that Occludin and Tricellulin interact with the E3-ubiquitin ligase Itch and that the increase in ubiquitination levels of Occludin and Tricellulin caused by cytokines is suppressed in the presence of 3-oxo-C12:2, suggesting that it prevents their endocytosis or degradation.

Conclusion: Our results show that 3-oxo-C12:2, a major AHL in the human gut, exerts a protective role on the intestinal barrier function in pro-inflammatory conditions. Given its loss in inflammatory bowel disease patients, the beneficial role of the 3-oxo-C12:2 AHL in the gut ecosystem leads to interesting perspectives to better understand host-microbiota interactions in this digestive tract pathology.

Disclosure: Nothing to disclose

P1711 IS THERE A BETTER WAY TO MONITOR VITAMIN D METABOLISM IN INFLAMMATORY BOWEL DISEASE?

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Introduction: Vitamin D has traditionally been known as a regulatory factor in bone metabolism and homeostasis, but emerging evidence suggests that it also plays an important role in immune regulation, as indicated by the fact that vitamin D deficiency has been associated with the pathogenesis of inflammatory bowel disease (IBD) (1). While it is possible that vitamin D affects the severity of inflammation and the disease course in patients with IBD, the causal relationship remains uncertain due to the complexity of the interrelationship between vitamin D and inflammation (2-4). Most studies have relied on immunoassays measuring 25-hydroxyvitamin D (25(OH)D3), which may be less accurate than the accepted gold standard of liquid chromatography tandem mass spectrometry (LC-MS/MS). Circulating 25(OH)D3 is hydroxylated to the metabolically active 1,25(OH) 2D3 by CYP27A1. The alternative pathway involves hydroxylation to the inactive 24,25(OH)2D3 via the 24-hydroxylase CYP24A1 prior to elimination (5).

Aims & Methods: Based on the hypothesis that the ratio of 25(OH)D to 24,25(OH)2D3 may be a more accurate measure of vitamin D status than 25(OH)D alone, our study aimed to characterise vitamin D metabolism in patients with active and inactive IBD using LC-MS/MS. The study was conducted as a cross-sectional prospective cohort study. Patients with inflammatory disease had definite endoscopic evidence of ulceration, and either CRP >5mg/L or faecal calprotectin >200mg/kg in stool. Patients who had taken medications with corticosteroids or vitamin D supplementation in the preceeding 4 weeks were excluded. Serum was tested for 25(OH)D3, 1,25(OH) 2D3 and 24,25(OH)2D3 using an LC-MS/MS assay. Spearman's correlation coefficient was used to test correlations and unpaired t-tests to test differences between inflammatory and non-inflammatory IBD patient groups.

Results: Up to November 2018, 87 consecutive patients with IBD (39 CD; 48 UC) were recruited; 55% were male. Median age was 36 years (range 23 to 72 yrs). Fewer patients in the active group were on immunomodulators (40% vs. 61%, p=0.05) or TNF inhibitors (25% vs. 49%, p=0.05). There was no difference in serum 25(OH)D3, or 1,25(OH)2D3 between the groups. Serum 24,25(OH)22D3 levels were significantly lower in the active group (mean 1.9 vs. 2.7ng/mL, p<0.001) and thus the ratio of 25(OH)D3: 24,25(OH)2D3 was higher (49.4 vs. 26.1, p<0.001). There was an inverse correlation between active disease and 24,25(OH)2D3 levels (r2=0.39; p=0.01). Dietary vitamin D intake and sunlight exposure did not differ between the groups.

Conclusion: In the context of inflammation, levels of 1,25(OH)2D3 are maintained by shifting the metabolism of 25(OH)D to 1,25(OH)2D3 rather than 24,25(OH)2D3, suggesting a reduction in 24-hydroxylase activity to maintain the active metabolite. The ratio of 25(OH)D3:24,25(OH)2D3 is increased in active disease and may be a more sensitive marker of vitamin D status in patients with CD.

References: 1. Limketkai BN, Bechtold ML, Nguyen DLJCGR. Vitamin D and the Pathogenesis of Inflammatory Bowel Disease. 2016;18(10):52. 2. Mouli VP, Ananthakrishnan AN. Review article: vitamin D and inflammatory bowel diseases. Alimentary pharmacology & therapeutics. 2014;39(2):125-36. 3. Chetcuti Zammit S, Ellul P, Girardin G, Valpiani D, Nielsen KR, Olsen J, et al. Vitamin D deficiency in a European inflammatory bowel disease inception cohort: an Epi-IBD study. European journal of gastroenterology & hepatology. 2018;30(11):1297-303. 4. Pallav K, Riche D, May WL, Sanchez P, Gupta NK. Predictors of vitamin D deficiency in inflammatory bowel disease and health: A Mississippi perspective. World journal of gastroenterology. 2017;23(4):638-45. 5. Christakos S, Dhawan P, Verstuyf A, Verlinden L, Carmeliet G. Vitamin D: Metabolism, Molecular Mechanism of Action, and Pleiotropic Effects. Physiological reviews. 2016;96(1):365-408.

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P1712 WITHDRAWN

P1713 EFFECT OF ETHNICITY ON THE FAECAL WATER METABOLIC PROFILES IN CROHN'S DISEASE

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Introduction: South Asians (SA) with Crohn's disease (CD) display a different disease phenotype and course (1), as well as a different urinary metabolic profile (2). Metabolic profiling of faecal water has distinguished CD from controls previously, but only in Caucasian (Cau) cohorts, characterised by a reduction in short chained fatty acids.

Aims & Methods: The aim of this study was to compare the metabolic profiles of faecal water in CD patients and healthy controls (H) from Caucasian and South Asian backgrounds.

Samples from 28 CD patients (15 Cau and 13 SA) and 44 healthy controls (20 Cau and 24 SA) were analysed by ^{1}H NMR spectroscopy. Data was assessed using orthogonal partial least squares discriminant analysis (OPLSDA). Hypothesis-led univariate analysis was also performed using metabolites that have been previously shown to distinguish CD from controls (2). These metabolites were as follows: acetate, butyrate, propionate, lactate, methylamine, glutamine, alanine, taurine, valine, and 2-hydroxybutyrate (2HIB).

Results: Multivariate analysis (Table 1) demonstrated that the faecal metabolites driving the separation between CD and controls were similar regardless of ethnicity, although statistically significant separation could not be achieved by multivariate analysis in the smallest group (CD v H in Caucasians).

Univariate analysis demonstrated a statistically significant reduction in butyrate, acetate, 2HIB, and methylamine ($p < 0.05$) in Cau CD patients compared to controls consistent with previous studies, but only a reduction in 2HIB and methylamine was seen with statistical significance in SA patients. When directly comparing Cau and SA patients with CD, butyrate and 2HIB were significantly different ($p = 0.034$ and 0.035 respectively) between these ethnic groups.

Model OPLSDA	n	R2X	Q2	P value CV-ANOVA	Metabolites driving separation in CD
CD : HC All	72 (28:44)	0.145	0.197	<0.001	acetate↓ butyrate↓ glutamine↓ alanine↓ creatine↓ tryptophan↓ 2HIB↓ methylamine↓
CD : H Caucasian	35 (15:20)	0.122	0.126	0.117	acetate↓ butyrate↓ glutamine↓ alanine↓ creatine↓ tryptophan↓ 2HIB↓ methylamine↓
CD : H South Asians	37 (13:24)	0.196	0.290	0.024	acetate↓ butyrate↓ glutamine↓ alanine↓ creatine↓ tryptophan↓ 2HIB↓ methylamine↓

[Table 1]

Conclusion: Despite observing consistent changes in the metabolites driving separation between Caucasian and SA patients compared to controls, univariate analysis reveals differences relating to ethnicity, showing that ethnicity influences faecal water metabolic profiles. The effect of ethnicity is likely to be a combination of genetics, diet and environment. Ethnicity therefore must be accounted for as a potential confounder in this type of analysis.

References: (1). Walker, 2011. AJG. (2). Marchesi, 2008. J. Proteome Res.

Disclosure: Nothing to disclose

P1715 TPL2 INHIBITOR TREATMENT REDUCES MULTIPLE INFLAMMATORY ENDPOINTS IN A SCID T CELL TRANSFER MODEL OF COLITIS

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Introduction: Tumor progression locus 2 (TPL2, also known as MAP3K8) is a mitogen-activated protein kinase kinase kinase and the primary regulator of ERK-mediated gene transcription downstream of multiple proinflammatory stimuli.[1] Converging lines of evidence suggest a critical role for TPL2 in IBD. TPL2 RNA is upregulated in IBD patient colon biopsies and a TPL2 gain-of-function single nucleotide polymorphism (SNP) is associated with the development of IBD.[2-4] Furthermore, TPL2 deficiency has been demonstrated to attenuate disease pathology in murine models of IBD, including TNF$^{\Delta ARE}$ and DSS-induced mouse colitis models.[5,6] As such, TPL2 inhibition represents a potential strategy to modulate inflammation in IBD.

Aims & Methods: The objective of this work was to determine the effect of a highly selective TPL2 inhibitor on chronic intestinal inflammation in a severe combined immunodeficient (SCID) T cell transfer model of colitis. A highly selective TPL2 inhibitor (TPL2i) was dosed in a SCID T cell transfer model. In this model, SCID mice develop chronic intestinal inflammation following the transfer of naïve CD4+CD45RBhi T-cells.[7] Animals were randomized into treatment groups at day 21 (N=15 vehicle, N=15 20 mg/kg TP-

L2i, N=15 60 mg/kg TPL2i) and orally dosed BID for 28 days. On day 21, prior to treatment initiation, 5 naïve and 5 T-cell transferred mice were sacrificed to confirm disease initiation. Following 4 weeks of treatment animals were randomized into necropsy groups and sacrificed at 2, 8, or 12h post-last dose. Plasma TPL2i levels were assessed to estimate target coverage. The effect of TPL2 inhibition on colitis was evaluated based on multiple histopathological endpoints at necropsy. Three independent transverse colon sections (proximal, middle and distal) were scored to assess histology sum score (tabulated from independent inflammation, gland loss, erosion and hyperplasia scores), edema (μm), percent PMN, and neutrophil score. To assess the effects of TPL2i treatment on TPL2 signaling and proinflammatory cytokine levels in the colon, flash frozen colon tissue was analyzed by western blot and MesoScale Discovery, respectively. Statistics were performed using a 2-sided Wilcoxon Rank sum test.

Results: Plasma TPL2i levels demonstrated that the 60 mg/kg dose achieved plasma concentrations sufficient to inhibit TPL2 activity by 50% at trough. Treatment with both 20 mg/kg and 60 mg/kg doses of TPL2i improved colitis at day 49 as demonstrated by a significant improvement in colon weight/length. A statistically significant improvement in multiple histopathological endpoints was also observed with 60 mg/kg TPL2i treatment, including an improvement in histology sum, inflammation, gland loss, percent PMN and neutrophil scores. Modulation of TPL2 activation and a reduction in proinflammatory cytokines were demonstrated in the colon of TPL2i treated animals with a significant reduction in phospho-TPL2 levels (a marker of TPL2 kinase activation) and a clear trend towards reduced TNFα, IL-1β, IL-6, KC, IL-12, IFNγ and IL-17 levels in the colon.

Conclusion: This work demonstrates that a highly selective TPL2i improves colitis and reduces multiple inflammatory markers in a SCID T cell transfer model of colitis.

References: 1. Gantke T, Sriskantharajah S, Ley S. Cell Res. 2011;21:131-145. 2. Arijs, I., et al. Plos One. 2009;4(11):1-10. 3. Jostins, L., et al. Nature. 2012;491:119-124. 4. Hedl M and Abraham C. Gut. 2016;65:1799-1811. 5. Kontoyiannis, D., et al. J. Exp. Med. 2002;196:1563-1574. 6. Lawrenz, M., et al. Mucosal Immunol. 2012;5:129-139. 7. Kiesler, P., Fuss, I.J., and W. Strober. Cell. Mol. Gastroenterol. Hepatol. 2015;1(2):154-170.

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P1716 GS-4875, A FIRST-IN-CLASS TPL2 INHIBITOR SUPPRESSES MEK-ERK INFLAMMATORY SIGNALING AND PROINFLAMMATORY CYTOKINE PRODUCTION IN PRIMARY HUMAN MONOCYTES

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Introduction: Tumor progression locus 2 (TPL2, also known as MAP3K8) is a mitogen-activated protein kinase kinase kinase and the primary regulator of ERK-mediated gene transcription downstream of multiple proinflammatory stimuli including bacterial products (eg, LPS and bacterial peptidoglycans), damage-associated molecular patterns (DAMPs), TNFα, and IL-1β.[1] TPL2 regulates the expression of several proinflammatory cytokines, including TNFα, IL-1β, IL-6 and IL-8. As TPL2 acts on both the production of and response to TNFα and IL-1β, it acts to amplify proinflammatory signaling. Dysregulated signaling downstream of these inflammatory signals can drive uncontrolled immune cell activation and inflammation, associated with IBD and other chronic inflammatory and autoimmune diseases. As such, TPL2 inhibition represents a strategy to modulate inflammation in IBD and other disease states.

Aims & Methods: We evaluated the effect of a highly selective TPL2 inhibitor (GS-4875) on inflammatory signaling and cytokine production in LPS and TNFα-stimulated primary human monocytes and monocyte-derived dendritic cells. A rat LPS-TNFα acute inflammation model was used to establish a PK/PD relationship. A TPL2 kinase assay was used to assess GS-4875 biochemical IC$_{50}$. GS-4875 selectivity was screened using a KINOMEscan™ selectivity assay (ScanMAX, DiscoveRx, San Diego, CA) at 1μM GS-4875. Monocytes or monocyte-derived dendritic cells were pre-cultured with a GS-4875 and stimulated with LPS or TNFα, and phospho-signaling and cytokine production was then evaluated at 30 minutes and 4 hours post stimulation. A431 cells (human epidermoid carcinoma cell line) were stimulated with TNFα or EGF and phospho-ERK was evaluated after 30 minutes. In vivo PK/PD relationship was established using a rat LPS-TNFα model of acute inflammation. In this model, female lewis rats

were dosed orally with 3, 10, 30 or 100 mg/kg doses of GS-4875 or 1 mg/kg dexamethasone followed by IV dosing of 0.01 mg/kg LPS 2 hours later. Animals were bled for plasma at multiple time points between 0 and 5h after compound dosing and plasma concentrations of TNFα and GS-4875 were measured.

Results: GS-4875 inhibits the TPL2 kinase with an IC50 = 1.3 nM with no significant off-target binding activity. GS-4875 selectively inhibited LPS and TNFα-stimulated phosphorylation of TPL2, MEK, and ERK, with little to no inhibition of phosphorylated p38, JNK or p65 observed. Both the RNA production and secretion of TNFα, IL-1β, IL-6, and IL-8 following LPS stimulation in primary human monocytes was similarly inhibited with GS-4875. In monocyte-derived dendritic cells GS-4875 inhibited the secretion of TNFα and IL-6 following LPS stimulation. To confirm TPL2 requirement for inflammatory, but not Ras-mediated (growth factor stimulated) ERK signaling, A431 cells were stimulated with either TNFα or EGF. Although TPL2 inhibition reduced TNFα-stimulated pERK, no effect on ERK activation downstream of EGF was observed. In vivo activity and PK/PD relationship was established using a rat LPS-TNFα model of acute inflammation. GS-4875 treatment showed dose and exposure dependent inhibition of LPS-stimulated TNFα production at all time points with an estimated EC50 (±SD) of 667 ±124 nM. Inhibition of TNFα production at the highest dose tested inhibited TNFα levels at levels equivalent to that of dexamethasone.

Conclusion: This work demonstrates the selective effects of TPL2 inhibition on ERK-mediated signaling and proinflammatory cytokine production and highlights the potential for TPL2 inhibition to treat IBD and other chronic inflammatory and autoimmune diseases.

References: 1. Gantke T, Sriskantharajah S, Ley S. Cell Res. 2011;21:131-145.

Disclosure: Warr M., Hammond A., Park G., Cui Z.-H., Wright N., and Taylor J. are employees of Gilead Sciences, Inc.

P1717 PROSTAGLANDIN E₂ PRODUCTION BY ENTERIC GLIAL CELLS REDUCES COLITIS DEVELOPMENT IN FEMALE MICE

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Introduction: Enteric glial cells (EGCs) are involved in the modulation of intestinal motility, permeability and inflammation. We have shown that these regulations involve the production and release of soluble mediators, including omega-3 and -6 derivatives such as prostaglandins. Prostaglandin E₂ (PGE₂) participates in the control of intestinal functions, but studies focusing on the effects of PGE₂ released specifically by EGC are still lacking. We have evaluated *in vivo* the impact of mPGES1 (PGE₂ producing enzyme) deletion induced specifically in EGC, on intestinal functions and intestinal inflammation.

Aims & Methods: mPGES1 deletion was induced in 10 to 20 weeks old male or female S100b^Cre-ERT2-mPGES1^fl-fl by a daily injection of tamoxifen (tamo) for 5 days. Two weeks after the onset of the induction of deletion, we induced, or not, the development of colitis by adding dextran sodium sulfate (DSS 4%) in the drinking water during 4 days. The intestinal functions measured at the end of the protocol are: (i) the paracellular permeability (sulfonic acid flux), (ii) the total transit time (expulsion time of carmine red given in gavage) and (iii) the disease Activity Index (DAI =presence of blood in the stool and weight loss of the animals). An immunohistological analysis enabled us to verify the induction of mPGES1 after inflammation in the EGC of wild type mPGES1 mice (mPGES1^fl-fl mice treated with tamo), and its deletion in mPGES1 Δ^EGC mice (S100b^Cre-ERT2-mPGES1^fl-fl treated with tamo).

Results: The increased expression of mPGES1 in glial cells was observed after exposure to DSS in the myenteric and submucosal ganglia of male and female wild type mPGES1 mice. This induction was absent in mPGES1 Δ^EGC mice. In female, DSS treatment induced increases in permeability and DAI, and reduction of transit time only in mPGES1 Δ^EGC mice. In contrast, mPGES1 deletion has had no impact on intestinal function or inflammation in males that behaved like mPGES1 Δ^EGC female mice.

Conclusion: This work represents the first *in vivo* evidence of a direct involvement of glial-derived PGE₂ in the pathophysiology of the intestine. In addition it suggest that the resistance to colitis development observed in female could be due to an increase PGE₂ production.

Disclosure: nothing to disclose

P1718 MATERNAL EXPOSURE TO GOS/INULIN MIXTURE FOSTERS COLITIS DEVELOPMENT IN OFFSPRING MICE

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Introduction: An alteration of the gut microbiota is involved in the pathogenesis of inflammatory bowel disease (IBD) and several probiotic strains and/or non-digestible food ingredients such as prebiotics are already used as dietary supplements to improve intestinal health. One alternative to prevent or reduce colitis development could consist of modulating maternal immunity and microbiota through prebiotics. For this purpose, we studied the effects of prebiotics given to Balb/c mice during gestation on the development of colitis in their offspring.

Aims & Methods: 8-10 weeks old offspring mice from mothers exposed to the GOS/inulin prebiotics mixture (9/1, 4% w/w) during gestation or fed with a control diet, were submitted or not to 3 cycles of dextran sodium sulfate (DSS) which induces colitis. A cycle consists of 2 days of 4% DSS in drinking water followed by 5 days of water. At day 4, 11 and 18 of the protocol, the total transit time, the fecal pellet output, the intestinal permeability and the disease activity index (stool consistency, weight loss, and gross bleeding) were measured in the 4 groups of mice. At day 18, the offspring mice were sacrificed and further measurements of intestinal segment permeability, tissue remodelling, systemic and intestinal inflammation as well as microbiota sequencing were performed.

Results: Offspring from mothers that received GOS/inulin prebiotics presented no changes in the humidity percentage of feces or total transit time before or after DSS cycles. Nevertheless when treated with DSS, offspring from mothers that received GOS/inulin prebiotics presented an increased disease activity index compared to the DSS group of offspring from mothers with control diet.

Conclusion: The enrichment of pregnant mice with non-digestible GOS/inulin prebiotics promotes a long-term effect in their offspring that is, unexpectedly, not a protective one but a sensitization to colitis development. Molecular mechanisms involved are under investigation, but our results already question about the "health benefit" that GOS/inulin should confer.

Disclosure: Nothing to disclose

P1719 COMPARATIVE ANALYSIS OF FAECAL CALPROTECTIN AND SHORT CHAIN FATTY ACIDS IN PATIENTS WITH ULCERATIVE COLITIS AND CROHN'S DISEASE

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Introduction: Inflammatory bowel disease (IBD) comprises two distinct diseases: Crohn's disease (CD) and ulcerative colitis (UC). Both are chronic diseases with a relapsing course of inflammation in the digestive system. The aetiology of these diseases has not been fully elucidated but is currently presumed to result from a complex interplay among genetic, environmental, microbial and immune factors. Intestinal homeostasis also depends on genetic, environmental, microbial and immune factors, while dysbiosis has been considered an important immunologic aetiology factor in IBD with quantitative and qualitative changes in the microbial composition. Short chain fatty acids (SCFAs) such as acetic, propionic and butyric acids, arise from bacterial fermentation of carbohydrates, proteins, peptides and glycoprotein precursors and its levels differ between healthy subjects and IBD patients as a results from dysbiosis presented by IBD patients. Endoscopy and histopathology are the golden standard methods for detection and assessment of IBD, but a distinct increase of faecal calprotectin level can be a useful marker for the diagnosis of IBD. Calprotectin is a calcium- and zinc-binding protein, which for practical purposes can be considered to be neutrophil-specific. The amount of calprotectin reflects the number of participating neutrophils in this inflammation. This aspect has been widely confirmed in intestinal inflammatory diseases by significant correlation between faecal calprotectin levels and other measures of acute inflammation.

Aims & Methods: Based on this, the aim of this work was to analyse and correlate faecal calprotectin levels with acetic, propionic and butyric acids production in faeces samples from patients with UC (n=55) or CD (n=35). For that, calprotectin levels were measured using Quantum Blue® fCAL Extended kit (Bühlmann Laboratories) and SCFAs were dosed by chromatographic analysis using a GC-MS Thermo Scientific, model FOCUS equipped with an automatic liquid sampler (Thermo – triplus DUO), and coupled to a Thermo – ISQ 230ST mass detector. All results are represented by mean± SEM and statistical significance were considered for p≤0.05

Results: Calprotectin value were 401.1±56.66 µg/ml for UC and 276.6±52.90 µg/ml for CD patients. Acetic, propionic and butiric acid levels were 0.1367±0.006 mg/ml, 0.2345±0.005mg/ml and 0.069±0.003mg/ml respectively, for UC and 0.1338± 0.006 mg/ml, 0.2500±0.006 mg/ml and 0.07±0.003 mg/ml for CD patients. There is no correlation between calprotectin and SCFAs values, but, when compared UC and DC SCFAs levels, we found major levels of propionic acid in DC patients compared with UC ones (p≤0.05). This result could represent the discovery of a new biomarker useful for IBD subtypes differentiation.

Conclusion: Based on this, SCFAs cannot be used as substitute for calprotectin dosage in IBD patient's diagnosis; however, SCFAs can represent a new biomarker for IBD subtypes differentiation. Additional experiments should be performed in order to evaluate SCFAs levels in healthy subjects and compare to IBD patients.

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Disclosure: Nothing to disclose

P1720 ASSOCIATION OF PROINFLAMMATORY CYTOKINES WITH INFLAMMATORY BIOMARKERS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Crohn's disease (CD) and ulcerative colitis (UC) are main clinical forms of inflammatory bowel disease. IBD is a chronic inflammatory disorder of the intestine and its pathogenesis remains unclear.

The cause of IBD is unknown, but it is suggested that an aberrant immune response toward the commensal microbiota is responsible for the disease in genetically predisposed individuals.

Aims & Methods: The purpose of the study is to analyze the serum level of several proinflammatory cytokines and standard inflammatory biomarkers (C reactive protein (CRP) and calprotectin) in patients with CD and UC.A total of 286 patients with IBD (156 with UC and 130 with CD) were included into the study. 67 healthy volunteers were included into the control group. UC patients included 61% females, 39% males, average age was 41,6±12,8; 43,9% had pancolitis, 36,5% was with left-sided colitis and 19,5% presented symptoms of proctitis. CD patients included 52,7 % females, 47,2% males with average age 34,5±11,7; 25% of patients had localized form, 75% – distant form. Serum cytokine levels were analyzed using multiplex immunoassay.CRP was measured in serum by ELISA test. Calprotectin was analyzed in stool samples. Statistical analysis was performed using STATISTICA 6.0 Software Package.

Results: Statistically significant increase of CRP (mg/L) both in UC (8,51±8,17) and CD (15,2±24,55) patients compared to controls (1,23±1,61) was revealed (p < 0,001). The same trend was observed for calprotectin (ɳg/kg) in UC (572,6190±501,0668) and CD (539,80±674,7079) patients compared to controls (34,5±30,98) (p < 0,001).

Besides statistically significant increase of IL1b, IL8, IFNg serum levels was observed in UC patients both in acute stage and remission compared to control group (p < 0,001). Serum level of proinflammatory IL-6 was not increased in UC patients compared to controls (p < 0,001). It was noticed statistically significant increase of IL1b, IL6, IFNg in CD patients both in acute stage and remission compared to controls (p< 0,05). It was also re-

vealed a correlation between CRP & IL6 (RS=-0,4, p=0,007), CRP &IL8 (RS=0,34,p=0,02), calprotectin&IFNg (RS=0,3 ,p=0,04), calprotectin&IL1a (RS=0,35,p=0,02) in UC patients. Analysis of CD patients showed correlation between CRP&IL12p70 (RS=0,3,p=0,04), CRP&IL1b (RS=0,5,p=0,003), calprotectin&IL-4 (RS=0,35, p=0,03), calprotectin & fractalkine (RS=0,5 ,p=0,0009).

Conclusion: Thus, proinflammatory cytokines contribute to chronic inflammation in IBD both in acute stage and remission correlatinfg with inflammatory biomarkers CRP and calprotectin.

Disclosure: Nothing to disclose

P1721 GUT-BRAIN AXIS IN INFLAMMATORY BOWEL DISEASES: EMERGENT ROLE OF INTESTINAL PERMEABILITY

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Introduction: Inflammatory bowel diseases (IBD) are characterized by chronic inflammation of the intestine, malabsorption and loss of protein and micronutrients. The pathogenesis of these disorders is not yet defined, but numerous evidences allow to hypothesize that it is due to a dysregulation of the mucosal immune response to the antigenic components of the intestinal flora. Factors like depression and chronic psychosocial distress seem to represent a risk factor for the arise of disease, as well as showing an influence on the course of the disease.

Stress can increase intestinal permeability, probably as a result of alterations in the cholinergic nervous system and mucosal mast cell functions.

Aims & Methods: The aim of this study is to investigate whether the alterations of the intestinal barrier are associated with psychometric alterations. We enrolled 33 IBD patients: 20 CD and 13 UC, with a mean age of 45 years. Serum samples were collected for determination of the ZO-1, TNF alpha and LPS proteins by ELISA assay to study the alterations of the intestinal barrier. Each patient completed a specific questionnaire for mood disorders: Minnesota Multiphasic Personality Inventory-2 (MMPI-2), State-Trait Anxiety Inventory (STAI Y1 – Y2), Hospital Anxiety and Depression Scale (HADS), Connor-Davidson Resilience Scale (CD-RISC), Barrat Impulsiveness Scale (BIS), Aggression Questionnaire (AQ). All study participants gave written informed consensus before sampling and data collection.

Results: The 61% of patients suffered from anxiety, and 37% from depression. Despite this, patients maintained good resilience: 94% have CD RISC scores > 40. Moreover 88% of patients are positive for some MMPI-2 items, in aprticular Schizophrenia (Sc), Psychastenia (Pt), Paranoia (Pa), hypomania (Ma), depression (D) and hysteria (Hy).Patients were divided by disease activity and no significant psychometric profile differences were found. the levels of ZO-1 and TNF were elevated in patients with high scores in anxiety scales (STAI Y1 and Y2 and HADS) but high LPS levels did not seem to be significantly associated with any of the variables examined.

Conclusion: This study showed that the prevalence of psychometric alterations in patients with IBD is significant, although the possible alterations of behavior are independent of disease activity. Furthermore, the increase of intestinal permeability could have a role in the worsening of anxiety. Further studies and more patients are necessary to better understand the development of mood disorders in course of IBD, and the role of Gut-Brain Axis in the medium-long term reactivation of patients, especially in terms of response and adherence to therapy.

Disclosure: Nothing to disclose

P1722 INCIDENCE AND PREVALENCE OF MICROSCOPIC COLITIS: SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Microscopic colitis (MC), comprising both collagenous colitis (CC) and lymphocytic colitis (LC), currently constitute an emergent cause of chronic watery diarrhea. Previously considered as a rare disease, several epidemiological studies have documented an increasing incidence of MC in Western countries.
However, there seems to be a significant variation in the reported incidence and prevalence rates among countries. Furthermore, a good estimation of the proportion of MC in patients presenting with chronic diarrhea is unclear.
Aims & Methods: To provide accurate estimates on the incidence and prevalence rate of MC and the frequency of MC in patients presenting with chronic diarrhea through a systematic-review and meta-analysis.
MEDLINE and EMBASE databases were searched for studies exploring on the epidemiology of MC up to December 2018. A pre-determined protocol following the PRISMA criteria was used.
The pooled incidence and prevalence rates, the pooled frequency of MC in chronic diarrhea patients and the geographical distribution of MC were calculated with random-effects models. Female/male odds ratios were estimated with a random-effects model. Heterogeneity between studies was assessed with the chi-square test (Cochran Q statistic) and quantified with the I^2 statistic.
Results: Of the 1,446 citations retrieved, 26 population-based studies from North-America and Europe were included for calculating incidence and prevalence rates, showing high heterogeneity and most of them (80%) providing high quality methodologies. The pooled overall incidence and prevalence rates of MC were estimated to be 11.9 (95%CI,9-14.8;I^2=99.73%) new cases per 100,000 person-year (N=21 studies) and 119 (95%CI,73-166;I^2=97.1%) per 100,000 persons (N=5 studies), respectively.
For CC, the pooled overall incidence and prevalence rates were 5.2 (95%CI,4.2-6.2;I^2=98.3%) new cases per 100,000 person-year (n=25 studies) and 50.1 (95%CI,13.7-76.5;I^2=98.4%) cases per 100,000 persons (n=6), respectively. For LC, this was 5.2 (95%CI,4.1-6.4;I^2=97.7%) new cases per 100,000 person-year (n=21 studies) and 61.7 (95%CI,48.2-75.3;I^2=80.6%) per 100,000 persons (n=5), respectively.
There are geographical variations in the incidence of MC (table 1). However, the relative low number of studies from Southern Europe compared to Northern Europe in combination with the different time periods studied, impedes direct comparisons.

Geographic regions	CC(95%CI)	LC(95%CI)	MC(95%CI)
Northern Europe	5.9(4.6-7.4)	4.9(3.5-6.2)	12.1(8.3-15.8)
Southern Europe	2.4(0.6-4.1)	3.1(1.4-4.7)	7.5(5.2-9.8)
North America	5.5(3.4-7.4)	8.0 (5.0-11.0)	14.3(8.9-19.8)

[Table 1]

Subgroup analyses on the incidence of MC by sex was possible in 18 studies and demonstrated that female sex is significantly associated with an increased risk of MC (OR 2.5;95%CI,2.3-2.9;I^2=86.7%) as well as for CC and LC (OR 3.2;95%CI,3-3.5 and OR 2.0;95%CI,1.8-2.3, respectively) independently of the setting, study fashion (retrospective or prospective), level (national, regional or local) and geographical region considered.
The pooled frequency of MC in patients with chronic diarrhea was estimated to be 12.8% (95%CI:9.9-15.9,I^2=93.6%), considering only studies with a moderate/high quality and sample size of ≥100 patients (n=14).
Conclusion: The population-based incidence and prevalence of MC vary widely across individual studies and geographical areas, probably due to differences in background populations, environmental exposure, genetic background and differences in the awareness on the disease. More prospective, large-scale, and population-based studies are needed to better evaluate MC epidemiology.
Disclosure: Nothing to disclose

P1723 A PICTURE PAINTS A THOUSAND WORDS: INVESTIGATING DISABILITY IN INFLAMMATORY BOWEL DISEASE

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Introduction: Inflammatory bowel disease (IBD) impacts on the physical and mental wellbeing of patients. Addressing and quantifying disability in IBD as part of Patient Reported Outcomes (PROs) is a major therapeutic target in IBD.
The IBD-Disk is a visual self- administered, abbreviated version of the IBD Disability Index which gives a rapid over view of disability in patients with IBD.
Aims & Methods: The aim of our study was to assess for correlation between disability reported by patients with IBD, their endoscopy findings and IBD therapy using the IBD Disk. A prospective study was conducted over 3 months between July to September 2018. Patients attending the IBD clinic were invited to complete the 10 item IBD-Disk questionnaire. Patient demographics, endoscopy findings and IBD therapy were also recorded.
Results: 58 patients completed the questionnaire. 59% (34) male, age range 19-85 years. 59% (34) had ulcerative colitis (UC) and 41% (24) crohn's disease. Low energy levels was the commonest disability reported affecting 57% (33), followed by difficulty sleeping at 53% (31). Dissatisfaction with body image, followed by sexual dysfunction accounted for lowest levels of disability at 24% (14) and 22% (13) respectively. 10% (6) of patients had no disability and were receiving either 5- aminosalicylate (5-ASA) monotherapy or combination with an immunomodulator. 40% (23) used 5-ASA alone, 31%(18) used immunomodulators and 26% (15) were receiving biologics. 6% (2) had a Mayo Endoscopic score of 3.
Conclusion: In our study difficulty sleeping and poor energy levels accounted for the greatest disability among our patients. There was no correlation between the degree of disability, endoscopic scores and IBD treatments. Disabilities reported were variable, but the IBD Disk rapidly highlights patient concerns allowing health care professionals adequately address them.
Disclosure: Nothing to disclose

P1724 FAECAL CALPROTECTIN SUGGESTS PRESENCE OF GUT INFLAMMATION IN AXIAL SPONDYLOARTHRITIS WITHOUT IBD

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Introduction: Studies since early 1980s have shown the presence of subclinical gut inflammation in up to 60% of the patients with axial spondyloarthritis, 6% of which proceed to become inflammatory bowel disease (IBD) in 10 years. Here we aim to further explore the presence of gut inflammation using acute inflammatory markers in stool and serum and correlate the results with disease characteristics.
Aims & Methods: A collaborative group comprising of gastroenterologists and rheumatologists was formed between 2 healthcare trusts in UK. Clinic lists and electronic operating systems were interrogated with appropriate ethical approval to identify patients with axSpA with or without IBD (axSpA-IBD and axSpA not-IBD, respectively) and psoriatic arthritis as disease controls. Eligible patients were called prior to their clinic appointments and were sent stool containers. On the day of their clinic appointments,

patients were consulted for 15-30 minutes where their disease was carefully phenotyped, drug history obtained and they were consented in to the study. Stool and blood samples were collected and analysed for faecal calprotectin (FC) and ESR and CRP respectively.

Results: 116 patients with axial spondyloarthritis (79 axSpA-not IBD, 22 axSpA-IBD and 15 psoriatic axSpA [axSpA-PsA]) and 22 patients with psoriatic peripheral spondyloarthritis (pPsA) were recruited.

Total of 81 stool samples were analysed. Faecal calprotectin (FC) was elevated to above 50ug/g in 36 stool samples; 21 out of 44 (48%) patients with axSpA-not IBD (median 72, range 51- 587), 9 out of 18 (50%) patients with axSpA-IBD (median 224.5, range 51->2000), 2 out of 7 (29%) patients with axSpA-PsA (median 69, range 51-87) and 6 out of 14 (43%) patients with pPsA (median 61.5, range 57- 122). Of the elevated FC samples, only one patient with known Crohn's disease had significant GI symptoms.

10 out of 36 (28%) patients with elevated FC were taking daily NSAIDs compared to 4 out of 48 (8%) patients with normal FC. Daily NSAID users did not have higher mean FC.

9 out of 11 (82%) patients who had disease duration of more than 10 years had elevated FC.

13 out of 28 (46%) patients with BASDAI index (axSpA disease activity score) of > 4 had elevated FC and 13 out of 33 (39%) with BASDAI < 4. BASDAI of above 4 reflects active disease.

Patients on biological therapy were equally distributed across all cohorts.

Conclusion: Significant proportion of axSpA-not IBD patients have gut inflammation as evidenced by raised faecal calprotectin however median level in axSpA-not IBD is still lower than axSpA-IBD. NSAIDs have relatively little impact. There is a correlation between gut inflammation and age of symptoms onset, disease duration and serum inflammatory markers. There is no correlation between gut inflammation and joint disease activity. Based on this study, further work is required to delineate at risk population with a view to determining those in whom a colonoscopy would be a helpful tool.

References: Mielants, H et al. Macroscopic and histological changes of the ileum HLA-B27 related diseases: therapeutic consequences. Int J Clin Pharmacol Res. 1984;4(6):409-14. Hamilton, L et al. The prevalence of axial spondyloarthritis in the UK: a cross-sectional cohort study. BMC Musculoskelet Disord. 2015; 16: 392.

Disclosure: Nothing to disclose

P1725 IS AXIAL SPONDYLOARTHRITIS IN IBD DIFFERENT TO AXIAL SPONDYLOARTHRITIS WITHOUT IBD?

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Introduction: Up to 40% of the patients with inflammatory bowel disease (IBD) have MRI evidence of axial spondyloarthritis compared to 1.5% in the non IBD population. Here we aim to distinguish axial spondyloarthritis associated with IBD (axSpA-IBD) from axSpA without IBD (axSpA-not IBD) and psoriatic axSpA (axSpA-PsA).

Aims & Methods: A collaborative group comprising of gastroenterologists and rheumatologists was formed between 2 healthcare trusts in UK. Clinic lists and electronic operating systems were interrogated with appropriate ethical approval to identify patients with axSpA-IBD, axSpA-not IBD and axSpA-PsA. Patients were contacted prior to their clinic appointments and were sent stool containers. On the day of their clinic appointments, they were consulted for 15-30 minutes where their diseases were carefully phenotyped, drug history obtained, and informed consent taken. Stool and blood samples were collected and analysed for faecal calprotectin and acute inflammatory markers.

Results: 62 patients were analysed for this study; 22 patients (10 Crohn's/ 12 UC) with axSpA-IBD, 24 with axSpA-not IBD and 16 patients with axSpA-PsA. Of the patients with IBD, 13 out of 22 (59%) were diagnosed with IBD first. Median duration of IBD before the diagnosis of axSpA was 3.5 years. Remaining 9 patients who were diagnosed with axSpA first, the median duration of disease before the diagnosis IBD was 3.5 years as well. Median age of onset for joint disease in axSpA-IBD is 30 years compared to 27 and 22 in axSpA-not IBD and axSpA-PsA cohorts.

All three cohorts had gender predominance towards the male sex with 82% in axSpA-IBD, 86% in axSpA-not IBD and 94% in axSpA-PsA. There was no ascertainment bias with the male gender when the diagnosis of axSpA was given first.

Association with HLA B*27 is stronger in the axSpA-not IBD group with 76% patients possessing the polymorphism compared to 50% in axSpA-IBD and 40% in axSpA-PsA. Median BASDAI (ankylosing spondylitis disease activity score) for axSpA-IBD, axSpA-not IBD and axSpA-PsA are 4.3, 3.95 and 3.2 respectively. Scores of above 4 indicate active disease.

Mean faecal calprotectin in axSpA-IBD is 233.7ug/g compared to 99.1 and 28.2 in axSpA-not IBD and axSpA-PsA.

Pearson correlation coefficient between faecal calprotectin and BASDAI scores was 0.0451.

Conclusion: In our cohort, we have shown that IBD related axial spondyloarthritis is different to axSpA-not IBD in terms of its weaker association with HLA B*27 antigen, higher degree of gut inflammation and increased age of onset for joint disease. Mean faecal calprotectin in axSpA-not IBD was still significantly higher than axSpA-PsA.

Weaker association with HLA B* 27 antigen in axSpA-IBD points to the possibility of a different genetic loci or mode of aetiopathogenesis.

Contrary to what we had expected, male gender predominance is similar across both axSpA-IBD and axSpA-not IBD group. We've found similar joint disease activity and functional disability across all cohorts. Further work is required to compare this study population with previously studied population.

References: Harbord, M et al. The First European Evidence-based Consensus on Extra-intestinal Manifestations in Inflammatory Bowel Disease. Journal of Crohn's and Colitis, 2016 March; 10 (3): 239-254. Orchard, TR et al. The prevalence, clinical features and association of HLA-B27 in sacroiliitis associated with established Crohn's disease. Aliment Pharmacol Ther. 2009 Jan;29(2):193-7.

Disclosure: Nothing to disclose

P1726 EPIDEMIOLOGICAL AND CLINICAL CHARACTERISTICS, AND RESPONSE TO TREATMENT, IN PATIENTS WITH MICROSCOPIC COLITIS

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Introduction: Microscopic colitis (MC) is a common cause of chronic diarrhea with an increasing incidence. However, its etiology and pathogenesis are not fully understood.

Aims & Methods: i) To describe the main epidemiological and clinical characteristics of the patients with MC; ii) to evaluate the efficacy of the different treatments for MC; and iii) to determine the relapse rate in patients who achieved clinical remission with budesonide. All patients aged over 18, diagnosed with collagenous colitis (CC) or lymphocytic colitis (CL) at the Gastroenterology Department from Hospital Universitario de La Princesa from January 1, 2010 to June 31, 2018, were included. Efficacy and loss of response to budesonide were evaluated by Kaplan-Meier analysis.

Results: 113 patients diagnosed with CC or CL were included (78% female, mean age at diagnosis 65 years, 59% had CC). The median time from symptoms to diagnosis was 4 months (IQR 2-7). The most frequent symptoms were: diarrhea (98%), weight loss (43%), and abdominal pain (31%). 3% had a family history of inflammatory bowel disease, 44% history of smoking, and 19% cancer antecedents. 31% suffered from depression and 48% had at least one autoimmune disease associated, the most frequent being thyroid disease (19%), allergic asthma (10%), type 1 diabetes mellitus (5%) and celiac disease (4%). At diagnosis, 43% of the patients were on proton-pump inhibitors, 34% on statins, 29% on non-steroidal anti-inflammatory drugs, 25% on selective serotonin reuptake inhibitors and 20% on beta blockers. The diagnostic colonoscopy showed mucosal abnormalities in 16% of the patients, the most frequent being: erythema (13%), edema (10%), loss of vascular pattern (5%) and spontaneous bleeding (5%). Only in 12% of all colonoscopies biopsies were taken by colon segments and the mean number of biopsies per colonoscopy was 6. At the onset of the disease, 30% of the patients experienced a spontaneous clinical remission. Of the remaining, 75% received budesonide, 27% 5-aminosalicylic acid (5-ASA), 7% systemic steroids and 3% thiopurines.

93% achieved remission with budesonide, 43% with 5-ASA, 7% with loperamide and 100% with systemic steroids (60% became steroid-dependent). 2 patients received thiopurines due to lack of response to other treatments and both achieved clinical remission. Of the patients treated with budesonide at diagnosis, 19% were unable to discontinue the drug and received maintenance therapy. Of the 51 patients who achieved remission with budesonide at diagnosis, 39% relapsed. Of them, 90% responded again to budesonide. A second relapse after budesonide withdrawal occurred in 28% and all of these patients achieved remission after restart of budesonide. There was no difference in response to budesonide between patients with CC and CL (P>0.05). The cumulative incidence of loss of response after achieving remission with budesonide at diagnosis (median follow-up time of 55 months) was 39% (95% CI 26-54%): 20% at 1 year, 32% at 2 years, and 46% at 3 years of follow-up. The rate of adverse events of the patients treated with budesonide was 4%, leading to drug discontinuation in all cases.

Conclusion: MC is more frequent in elderly women. Diarrhea, weight loss and abdominal pain are the most common symptoms at diagnosis. MC frequently appears in patients with autoimmune disorders, smoking history and under treatment with certain drugs. The vast majority (93%) of the patients treated with budesonide at diagnosis achieved remission, however, almost 40% of them lost response subsequently. Retreatment with budesonide after relapsing was effective in most cases.

Disclosure: Nothing to disclose

P1727 TOP LIST OF MALIGNANCIES OBSERVED IN THE HUNGARIAN POPULATION WITH ULCERATIVE COLITIS

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Introduction: Ulcerative colitis (UC) is associated with an increased risk of colorectal cancer (CRC) and the second most common cause of death among UC patients is CRC. An increased risk for extraintestinal malignancies are also observed among IBD patients.

Aims & Methods: Our aim was to recognize malignancy pattern associated with UC using the National Health Insurance Fund social security databases including inpatient-, outpatient care between 2010 and 2016. This is an epidemiological study based on a Hungarian national database. Hungarian UC patients were enrolled. Patients were classified as having a certain kind of cancer if they have at least two appearances in the in- or outpatient care with the corresponding ICD codes.

Results: 37795 patients with UC were included in the study during the observational period. Investigating all malignant neoplasms of the UC population, colorectal cancer (CRC) was found to be the most frequently observed cancer. 1424 patients, 3.7% of the total UC population were diagnosed with CRC. Colonic localisation (2.16%) was more frequent than rectal localisation (1.7%). The second most common malignancy was non-melanotic skin cancer, in 1.48% of the patients, the third was prostate cancer in 0.99% of the patients. Malignant neoplasm of the urogenital tract and the breast were diagnosed in 0.54-0.46% of the patients. Malignant melanoma of the skin was the fifteenth most common malignancy, 0.21% of the patients were diagnosed with malignant melanoma. Among our patients intestinal non-Hodgkin lymphomas were observed in 0.092% of the patients. Malignancies with the least incidence were malignant neoplasm of the uvula and testis and bone and articular cartilage, 10-10 UC patients were diagnosed with these malignancies.

Conclusion: Our results underly that colorectal carcinoma is still a real danger in UC patients, highlight that surveillance need to be improved in national level. The most common extracolonic malignancies were non-melanotic skin cancer.

Disclosure: Nothing to disclose

P1728 USEFULNESS OF NATURAL LANGUAGE PROCESSING (NLP) COMBINED WITH DEEP MACHINE LEARNING AS A TOOL FOR CLINICAL RESEARCH IN CROHN'S DISEASE. PREMONITION-CD STUDY

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Introduction: Natural Language Processing (NLP) is a technology that uses computer-based linguistics and artificial intelligence to identify and extract information from free-text data sources such as progress notes, procedure and pathology reports, and laboratory and radiologic test results[1]. NLP can accurately and efficiently use the vast data resources that have been relatively unavailable for meaningful clinical or research use until now. However, it is still unknow the full potential and applicability of NLP in clinical practice and research[2]. In this study, we have tried to understand if NLP could become another alternative of generating evidence in Crohn's Disease.

Aims & Methods: This is a data-driven, observational, retrospective, non-interventional, study using secondary data captured in Electronic Medical Records (EMRs). A data-driven system based on Natural Language Processing (NLP) and big data techniques, has been used to conduct the study, using the EHRead technology (Savana). Natural Language was extracted from EMRs and captured as free text. Medical concepts were detected by using computational linguistic techniques and comprehensive clinical contents, scientifically validated (like SNOMED Clinical Terms, CT). This unstructured data has been treated as big data and analysed with artificial intelligence. The results presented here belong to an interim analysis of data from 3 Spanish hospitals participating in PREMONITION-CD study (NCT03668249). The period for extracting the data has been bounded to the last available five years of clinical practice contained in the EMRs available at each site.

Results: Using this innovative technology, we have been able to extract data from 877 EMRs from Crohn's Disease (CD) patients. NLP has allowed us to determine some of the main descriptive characteristics of these patients and Health Care Resources Utilization (HCRU) . Therefore, we have learned that 50.6% of patients were female and, out of those patients with available data about faecal calprotectin, CRP and hemoglobin, mean (SD) were 532 (638.8) µg/g, 460.6 (133.4) mg/L and 12.8 (2.1) g/dL respectively. Regarding previous medical history, the most common conditions were disorders of cardiovascular system (20.3%) and disorder of lipoprotein/lipid metabolism (13.3%).

Additionally, NLP also allowed us to gather information about HCRU. For example, the average (SD) number of visits/year to GI units has been relatively stable along last years, ranging between 1.5 (2.4) and 2.1 (2.9). However, the average number of visits to the hospital day have steadily increased over the last years from 6.4 (7) visits in 2013, to 8.3 (8.9) in 2017; with a similar trend regarding visits to other specialists: from 6.6 (8.6) in 2013 to 8.3 (9.7) in 2017.

Conclusion: NLP seems to be a promising tool that can be used in specific situations to accurately provide meaningful information in patients with Inflammatory Bowel Disease. We anticipate it will become more widely used within clinical, research, and administrative roles. Quality of clinical data contained within EMRs and validation of data extraction process must be taken into consideration in order to let NLP become a key resource to answer questions that otherwise would be too expensive or time consuming to address with a traditional research methodology.

References: 1. Velupillai S, Suominen H, Liakata M, Roberts A, Shah AD, Morley K, Osborn D, Hayes J, Stewart R, Downs J, Chapman W, Dutta R. Using clinical Natural Language Processing for health outcomes research: Overview and actionable suggestions for future advances. J Biomed Inform. 2018 Dec; 88:11-19 2. Hou JK, Imler TD, Imperiale TF. Current and future applications of natural language processing in the field of digestive diseases. Clin Gastroenterol Hepatol. 2014 Aug;12(8):1257-61.

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P1729 EARLY DISEASE ACCELERATION IN PATIENTS WITH NEWLY DIAGNOSED CROHN'S DISEASE IN INDIA AND ISRAEL: INSIGHTS FROM AN EAST-WEST INCEPTION COHORT

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Introduction: Crohn's disease (CD) is a progressive disease with variable rate of acceleration. An increase in the incidence of CD is evident in Asia and specifically in India. Data on clinical presentation and course in the Indian population is lacking.

Aims & Methods: The Indo-Israeli IBD GastroEnterology paRtnership (TiiiGER) aimed to assess patterns of early disease among Indian and Israeli patients with newly diagnosed CD. Prospective observational inception cohorts were recruited in two large referral centers in India and Israel between May 2013 and December 2017. Adults (>18 years) suspected of CD or patients with newly diagnosed CD were included. Disease acceleration was defined by the first CD-related surgery, hospitalization or recommendation to start steroids, immunomodulators or biologic therapy.

Results: Two hundreds sixty patients were included, 104 Indians and 156 Israelis. Indian patients had male predominance compared with the Israeli cohort (65.4% vs. 50.6%, p=0.019). At diagnosis Indian patients were older (37.8±12.8 vs. 31.8±12.8, p< 0.0001) and were less likely to be active smokers (8.7% vs. 22.4%, p< 0.0001). Indian patients had significantly more colonic and upper gastrointestinal disease location (35.6% vs. 19.2%, p=0.003 and 13.5% vs. 5.1%, p=0.018, respectively), more stenotic behavior (36.6% vs. 6.5%, p< 0.0001) and lower rate of perianal disease involvement (5.8% vs. 23.7%, p< 0.0001), compared to Israeli patients. Furthermore, Israeli patients had higher body mass index (23.4±4.5 vs. 19.9±4.3, p< 0.0001) and significantly more family history of CD (22.4% vs. 3.8%, p< 0.0001).

Overall during a follow-up period of up to 43 months, disease acceleration rate was 50% (52/104) in Indian and 66.7% (104/156) in Israeli patients, with median time to disease acceleration of 7.6 (interquartile range [IQR] 1.9-25.6) and 3.4 (IQR 1.3-23) months, p=0.05, respectively. In multivariate cox regression model, Indian compared to Israeli patients were less likely to have disease acceleration or to be treated with steroids, immunomodulators or biologic therapy (hazard ratio [HR] 0.598; 95% CI, 0.4-0.8; p=0.011 and HR 0.563; 95% CI, 0.373-0.851, p=0.006).

Conclusion: In a first indo-Israeli inception cohort of patients with newly diagnosed CD more than half of the patients experienced early disease acceleration. Distinct demographic and phenotype characteristics at CD diagnosis and different rates of disease acceleration were identified. Ethnic variations in disease phenotype may help to identify key genetic, environmental & behavioral factors contributing to the development of IBD.

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P1730 COMPARISON OF DIETARY PATTERNS IN IBD PATIENTS BETWEEN THE NORTHERN AND SOUTHERN PROVINCES OF THE NETHERLANDS

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Introduction: Evidence-based dietary guidelines are not available for patients with Inflammatory Bowel Disease (IBD). Therefore, patients tend to follow their own "unguided" dietary habits, often leading to unbalanced intakes that may further impact disease course. Hence, we aimed to identify dietary patterns in post-diagnosis habitual dietary intake in 2 separate cohorts of Dutch IBD outpatients.

Aims & Methods: 489 IBD patients (286 Crohn's Disease (CD), 203 Ulcerative Colitis (UC)) from Groningen and 236 IBD patients (154 CD, 82 UC) from Maastricht with data on demographics and disease phenotype were included. Dietary intake, including nutrients and 22 food groups, was obtained via semi-validated food frequency questionnaires. Dietary differences in macronutrients and food groups, and baseline characteristics were analysed between the cohorts using a students' t-test or X^2-test when appropriate. A preliminary principal-components analysis (PCA) was conducted on 22 food groups to identify relevant dietary patterns.

Results: Compared to the Maastricht cohort, patients in the Groningen cohort had a lower age at inclusion and diagnosis, disease duration, and less men (all p< 0.05); no differences were observed in phenotype, BMI or smoking. The total energy intake including energy from all separate macronutrients was significantly lower in the Groningen cohort. Moreover, patients in Groningen consumed less legumes, grains, red and processed meat, poultry, fish, confectionery, coffee, oils, alcoholic beverages and condiments, but more potatoes, dairy, non-alcoholic beverages and prepared meals than patients in Maastricht.

First, a PCA was run in the Groningen cohort to identify dietary patterns. This PCA, with an overall Kaiser-Meyer-Olkin (KMO) measure of 0.624 revealed 8 components with eigenvalue >1. Visual inspection of the scree plot (Cattell, 1966) and interpretability criteria, indicated that two components should be retained, explaining 22.0% of the total variance. The interpretation of the data was in line with the western and prudent components as described before (Stricker, 2013). Condiments, grain products, potatoes, oils, processed and red meat, snacks and confectionery contributed to a western component; whereas fruits, vegetables, fish, tea, eggs and nuts loaded positively, and snacks and non-alcoholic beverages loaded negatively on the prudent component. To confirm the above patterns, a PCA was also run on the Maastricht data, with an overall KMO of 0.602 and revealing 9 components with an eigenvalue >1. Here, visual inspection of the scree plot and interpretability criteria also indicated that two components should be retained. These explained 21.8% of the total variance and were also consistent with the western and prudent component. The same food groups loaded on the western component and prudent component, except for snacks and fruits to the prudent component. This might be due to smaller sample size in the Maastricht cohort.

Conclusion: Our study shows that IBD patients in the Groningen cohort mainly use a western or prudent-based diet after diagnosis. These findings were confirmed in the geographical distinct Maastricht cohort; as mainly the same patterns were extracted. Since, adapting a western dietary pattern may contribute to potentially unintended effects on disease course, dietary intervention in these patients might be beneficial.

References: Abstract: V. Peters and C. Spooren are shared first author, D.M. Jonkers and M.J.E. Campmans-Kuijpers are shared last author.
Ref: Cattell, R. B. (1966). The scree test for the number of factors. Multivariate Behavioral Research, 1, 245-276. Stricker, M.D. (2013). Dietary patterns derived from principal component- and k-means cluster analysis: Long-term association with coronary heart disease and stroke. Nutrition, Metabolism & Cardiovascular Diseases, 23, 250e256.

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P1731 INCREASING INCIDENCE OF CROHN'S DISEASE IN EPIRUS, GREECE: A 30-YEAR PROSPECTIVE STUDY FROM A REFERRAL CENTER

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Introduction: The number of individuals affected by inflammatory bowel diseases (IBD) has been globally increasing. We have described a low incidence of Crohn's disease in our area in the past. The aim of this extended study was to investigate and update the incidence and prevalence of IBD and its subtypes (UC, CD, IBD unclassified) in Epirus which is a well-defined geographical area of Greece with a 30-year observation period of these diseases.
Aims & Methods: The epidemiological study was conducted in the region of Epirus, one of the 13 prefectures of Greece, and in the two neighboring islands of the Ionian Sea, Corfu and Lefkada. The study was conducted in two periods, 1982-2002 and 2003-2015 so that we could trace any changes in the incidence and behavior of IBD during time in our area.
Results: The overall incidence of Crohn's disease was 1.16/100,000 inhabitants (95% C.I. 0,62 – 1,60) [1,41 (95% C.I. 0.75 – 2.15) for males vs 1.02 (95% C.I. 0,39 – 1,23) for females] on the first period (1982-2002) and 2,75/100,000 inhabitants (95% C.I. 1,53 – 3,46) [3,67 (95% C.I. 1,96 – 4,71) for males vs 1,85 (95% C.I. 0,77 -2,64) for females] of the second period (2003-2015). These observations showed a significant increase of Crohn's disease in both genders in our area. In addition, the prevalence of ulcerative colitis per age group showed a decrease of the incidence of UC in older ages during the most recent time period compared to the past. This decrease was more prominent to male patients over 70 years of age. Regarding the age distribution of ulcerative colitis, it appears that there is a significantly increasing trend to affect younger ages during the second time period (the recent one). At the same time, as mentioned, a noteworthy decrease in the incidence of ulcerative colitis after the age of 70 years has been documented during the second period of the study.
Conclusion: The results of our study confirm the continuing change of epidemiology of IBD in our area, with increasing incidence of Crohn's disease and decreasing incidence of ulcerative colitis in elderly patients. In addition, based on international multicenter studies, patients with IBD and particularly CD are expected to increase within the next decades. Awareness of the disease, early diagnosis and consistent and prompt monitoring from the time of diagnosis will provide them with a better quality of life and prevent complications.
Disclosure: Nothing to disclose

P1732 PREVALENCE AND PREDICTORS OF SEXUAL AND ERECTILE DYSFUNCTION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Inflammatory Bowel Disease (IBD) has a negative impact on quality of life (QOL), and sexuality is one of its major determinants. The impact of disease characteristics on sexuality and intimacy is one of the main concerns of IBD patients. Despite the obvious relevance of this problem, knowledge of the extent and the determinants of sexual dysfunction in persons with IBD is limited.
Aims & Methods: The main goal of the study was to determine the prevalence of sexual dysfunction (SD), erectile dysfunction and association with quality of life (QOL) and it's components in patients with IBD, and to search for predictors of SD and ED.
In this cross-sectional study patients fulfilled anonymous validated questionnaire on their sexual function. In International Index of Erectile Function (IIEF) for males, five domains were evaluated through questions on erectile function, orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction. In women were six domains assessed, desire, arousal, lubrication, orgasmic function, satisfaction and pain. For both scores, higher scores indicated a better function. Patients also fulfilled IBDQ-32, a validated questionnaire for assessing quality of life in IBD patients. IBDQ-32 score is ranging from 32 to 224 with higher scores representing better quality of life and consists of four main components (social, emotional, systemic and bowel function). Disease activity was defined as Crohn's Disease Activity Index (CDAI) >150 or Partial Mayo Score ≥3 for CD and UC, respectively.
Results: In this study we have enrolled 202 patients who fulfilled the questionnaire (133 CD, 69 UC). Among them 122 were men and 80 women. Average age of included patients was 39.2±11.02. In women, SD rates were 75% (N=60), and were significantly higher than 18% (N=22) in men (p< 0.001). QOL was significantly lower in patients with SD, in which IBDQ-32 score amounted 167.47±30.4 vs. 182.8±31.9, p=0.01. ED was reported by 30% (N=37) of male IBD patients. Patients with ED had lower IBDQ-32 score comparing to patients without ED (161.4±35.4 vs. 186.6±27.5, p< 0.001). In univariate analysis, significant positive predictors for SD in total IBD population were female gender, UC and impaired social, emotional, systemic and bowel function components of IBDQ. Multivariate analysis showed that the significant predictors for SD were female gender (OR=17.5, 95% CI 8.3-37.2) and emotional component of IBDQ (OR=3.5, 95% CI 0.7-17.05). Disease duration, disease activity, history of lower abdominal surgery, presence of stoma, perianal disease and current biological treatment were not significant predictors of SD.
Conclusion: The results show that SD is highly prevalent in IBD patients, with women to man ratio of almost 4 to 1. Erectile dysfunction is present in approximately every third male patient. Patients with both SD and ED have lower QOL. Significant and strong predictors for SD are female gender and emotional component of IBDQ, which consists of questions regarding frustration, depression, tension, worry about surgery, irritation, angriness, fear of not finding a toilet, being tearful or upset, feel lack of understanding and satisfaction with personal life. Improvement of QOL is one of the main goals in treating IBD patients. Because of its strong connection with sexual function and satisfaction, it is important to identify those problems and to provide proper psychological support, medical treatment and educational information.
Disclosure: Nothing to disclose

P1733 ERECTILE DYSFUNCTION IN MEN WITH NEWLY DIAGNOSED INFLAMMATORY BOWEL DISEASE

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Introduction: Crohn's disease (CD) and ulcerative colitis (UC) are chronic inflammatory bowel diseases (IBDs) that often present between the second and fourth decades of life, when sexual identity and relationships are developing. Sexual function is one of the top concerns expressed by patients with IBD yet remains poorly explored by researchers and clinicians.

Aims & Methods: Cross-sectional studies on sexual function in men with inflammatory bowel disease (IBD). Using a prospective incidence cohort, we aimed to describe sexual function at baseline and over time and to identify factors associated with impaired sexual function in men with IBD. 18 years and older enrolled between April 2016 and January 2019 in our centre with a minimum three months of follow-up were eligible for study. Male sexual function was assessed using the International Index of Erectile Function (IIEF), a self-administered questionnaire that assesses 5 dimensions of sexual function over the most recent 4 weeks. To assess changes in the IIEF per various demographic and clinical factors, linear mixed effects models were used.

Results: Fifty two of 73 eligible men (71 %) completed the questionnaire (19 Crohn's disease, 33 ulcerative colitis). The mean age (SD) of the cohort at diagnosis was 29.4 years. At baseline, 28 % of men had global sexual dysfunction, and 85% had erectile dysfunction. Independent factors associated with erectile dysfunction are older age and lower physical and mental component summary scores on the Short Form Health Survey (SF-36).

Conclusion: In an incident cohort of IBD patients, most men had erectile dysfunction. Physicians should be aware of the high prevalence of erectile dysfunction and its associated risk factors among men with newly diagnosed IBD to direct multidisciplinary treatment planning.

Disclosure: Nothing to disclose

P1734 OBESITY AND OSTEOPOROSIS IN INFLAMMATORY BOWEL DISEASE PATIENTS: A NATIONWIDE ANALYSIS

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Introduction: Osteoporosis is a major health problem in patients with inflammatory bowel disease (IBD) with reported prevalence ranging from 30-60% among this population in the United States. Obesity on the other hand has conflicting evidence as it relates to osteoporosis especially among IBD patients with some studies reporting a protective effect while others demonstrate worsening bone mass effect. Given the rising global prevalence of obesity and the poorly understood consequences in IBD patients, we aimed to examine the relationship between obesity and osteoporosis in IBD patients using the largest repository of discharges in the united states. We hypothesize that obesity will be associated with osteoporosis in IBD patients.

Aims & Methods: We performed a retrospective study using the 2014 National Inpatient Sample database. All adult patients with a primary or secondary discharge diagnosis of inflammatory bowel disease were included in this study. Data on patient and hospital level characteristics, sociodemographic factors, and outcomes were obtained. Diagnosis of both obesity and osteoporosis diagnosis were identified using ICD 9 codes. Descriptive and inferential analysis was performed. Patient and outcome characteristics were compared using chi-square and logistic regression. We controlled for sociodemographic factors and patient comorbidities.

Results: A total of 273,905 discharge records with inflammatory bowel disease met our inclusion criteria for this study. The prevalence of obesity was significantly higher in patients with Ulcerative colitis compared to Crohn's disease (10.64% versus 10.03 % p-value < 0.05). Using multivariable analysis to control for patients age, sex and comorbidities, obese patients with Crohn's disease were 43% significantly less likely to have osteoporosis compared to their non-obese counterparts (AOR 0.57, 95% CI 0.46 - 0.71).

Obese patients with Ulcerative colitis were 16% less likely to have osteoporosis compared to non-obese patients (AOR 0.84, 95% CI 0.69 - 1.14), however this relationship was not statistically significant.

Conclusion: Our study demonstrates a protective effect of obesity against osteoporosis in patients with Crohn's disease but not in patients with Ulcerative colitis. Although prior studies have shown conflicting results concerning the role of obesity in IBD, our study further adds to the literature demonstrating different effects of osteoporosis in Crohn's disease versus ulcerative colitis. The mechanism by which obesity may possibly protect against osteoporosis is poorly understood,
more so, in light of studies that associate obesity predominantly with active Crohn's disease, prospective studies are needed to understand these findings better and provide higher level evidence as well as a molecular basis for this interaction.

Disclosure: Nothing to disclose

P1735 THE OMIS (OCULAR MANIFESTATIONS IN IBD SCREENING) QUESTIONNAIRE: A TOOL FOR CLINICIANS FOR EARLY DETECTION OF OCULAR INVOLVEMENT IN INFLAMMATORY BOWEL DISEASE

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Introduction: Extraintestinal manifestations (EIM) are common in Inflammatory Bowel Disease (IBD) being reported in up to 50% of patients. Among EIMs ocular manifestations are less frequent (less than 15%) but may be associated with significant morbidity, including blindness. They may be related to active inflammation or have an independent course or represent adverse events of pharmacological therapies. Ocular complaints are often non specific and are frequently ignored from both physicians and patients. Biological therapies, especially anti-TNFs, have been shown effective on some eye EIMs, probably reducing their prevalence.

Aims & Methods: Our aim was to assess the accuracy of a dedicated questionnaire in patients with IBD treated with biological drugs for the detection of ocular EIMs in a tertiary IBD referral clinic. We developed a questionnaire, OMIS (Ocular Manifestations in IBD Screening), after agreement between gastroenterologists and ophthalmologists. The questionnaire was administered by a non-ophthalmologist physician to 96 IBD patients treated with biological drugs (anti-TNFs) in the Gastroenterology clinic during infusion or in the waiting room.

Results: Out of 96 interviewed patients, EIMs were reported in 55 persons (57%), mainly as joint menifestations (36%). Thirty-five patients (36.5%) tested positive for ocular involvement at screening and were selected for ophthalmologic examination. Red eye (12 patients, 34.28%), ocular pain (10 patients, 28.57%), photophobia (14 patients, 40%) and visual fogging (18 patients, 51.42%). On ophtalmological visit, ocular EIMS were confirmed in 29 of 35 patients (82.85%): 4 cases of uveitis (11.42%), all dated before the beginning of biologics, 12 cases of dry eye (34.28%) and 13 cases of cataracts (37.14%), in progress or already treated with surgery.

Conclusion: The OMIS questionnaire is a useful tool for non-ophthalmologist physician in everyday practice during the outpatient visit, in order to select patient to be addressed to ophthalmological visit, creating a real integrated multidisciplinary clinical equipe, to improve management of IBD, to prevent visual disability and guarantee quality of life.

Disclosure: Nothing to disclose

P1736 UPGRADED DIFFERENTIAL DIAGNOSIS OF MULTIPLE PSEUDOPOLYPS AND PRECANCEROUS POLYPS: 10 YEARS PRACTICE BASED STUDY

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Introduction: It's common knowledge that the risk of colorectal cancer in patients with ulcerative colitis (UC) is greatly increased compared with the general population. Pseudopolyps (PP) are considered as a part of UC manifestation, in the same time, they can mask adenomatous polyps that may become malignant. In case of multiple PP, differential diagnosis with the precancerous is subjective by endoscopist evaluation, besides, biopsy of all PP and is financially and technically difficult process.

Aims & Methods: The aim of the study was to optimize the identifying potential precancerous polyps among the multiple PP.

For a 10 years study, 80 patients with moderate to severe UC with endoscopic and histologic established multiple PP were undergone CT of abdomed, pelvis and enterography on TOSHIBA Aquilion 64 Slice CT Scanner with dual contrast (intravenous and oral). Based on conclusion results, they were divided into two groups. Group 1 included 28 patients with PP that were determined on CT. Other 52 patients were included in Group 2 as they had no evidence of polyps on CT. Then, all patients were received conventional and immunobiological treatment up to achieve clinical and laboratory remission (in general 54 patients: 23 (82.1%) in Group 1 and 31 (59.6%) in Group 2). After that, they were undergone colonoscopy.

Results: 1. Group 1 had before treatment the mean size of polyp 1.7+/-0.4 cm and the affected by PP area 30 +/- 5 % per bowel segment. After treatment, 20 patients (87%) had the same size and affected area (p< 0,05). Other 3 patients (13%) got improvement - mean size of polyp decreased to 1.2+/-0.3 cm (p< 0,05), affected area left the same. After biopsy of the largest PP in each subject, the different type adenoma was found in 10 (43.5%), hyperplastic in 3 (13%) and chronic inflammation in 10 (43.5%) cases.

2. Group 2 had before treatment the mean size of polyp 1.0+/-0.4 cm and the affected by PP area 27% +/- 4 % per bowel segment. After treatment, 24 patients (77.4%) had disappearance of PP (p< 0,05). Other 7 patients (22.6%) got improvement - mean size of polyp decreased to 0.6+/-0.2 cm (p< 0,05), affected area to 23 % +-3%. After biopsy of the largest PP in each subject only chronic inflammation was observed.

Thus, the most polyps that were determined on CT after biopsy (56%) were precancerous, versus polyps that were not (chronic inflammation) (p< 0,05). The using of CT is allowed to decrease number of biopsies and more accurately determine precancerous polyps.

Conclusion: The CT, in the aggregate with standard methods, could be used for verification of precancerous polyps among PP.

Disclosure: Nothing to disclose

P1737 EFFECT OF ANTINUCLEAR ANTIBODIES ON THE PHARMACOKINETICS OF INFLIXIMAB IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: The presence of antinuclear antibodies (ANA) in serum of inflammatory bowel disease (IBD) patients has been associated with a worse response to treatment with anti-TNF agents including infliximab (IFX). An association between ANA and the development of paradoxical cutaneous and rheumatological manifestations in IBD patients under IFX has also been reported. However, there is limited data on the direct correlation of ANA with the pharmacokinetics of IFX.

Aims & Methods: The aim of this study is to investigate the potential association of serum ANA with IFX trough levels (IFX-TLs) and IFX antibodies (ATIs) in IBD patients treated with IFX. We studied IBD patients under maintenance treatment with IFX retrospectively in whom we had at least one IFX-TLs and ATIs measurement and one ANA measurement in the serum. IFX and ATIs as well as clinical disease activity scores (HBI or SCAI), biomarkers (CRP) and development of adverse events were compared between patients with positive and negative ANA.

Results: Fifty IBD patients under maintenance therapy with IFX were enrolled. Of these, 28 had positive ANA [men 15 (54%), median age 46.8 ± 12.1 years, 20 with Crohn's disease (71.4%), median disease time 14.1±11 years, median IFX therapy time 62.5±51 months, 11 smokers and 7 ex-smokers, 15 under combination therapy with an immunomodulator AZA/MTX (53.5%)] and 22 had negative ANA [men 17 (77.2%) mean age 41.8 ± 17.9, 18 Crohn's disease (81.8%), median disease time 12.2±7.9 years, median IFX therapy time 51.9±36.8 months, 7 smokers and 7 ex-smokers, 12 under combination therapy with AZA/MTX]. The median IFX-TLs (IQR) in serum of group 1 was 3.51 μg / ml (1.26-6.74), significantly lower than those of group 2 [7.38 μg / ml (4.85-10.18)], P = 0.017.

In addition, the median ATIs in the 1st group (ANA +) were 2.65 U / mL (2.41-3.21) significantly higher than the median ATIs of the 2nd (ANA-), [2.35 U / mL (2.12-2.81)], P =0.031. No significant differences in regards of clinical activity scores, CRP levels or the development of adverse events between positive and negative ANA patients was found (P>0.05).

Eight patients of the first group also showed positive anti-ds-DNA. Positive anti-ds-DNA patients did not have a statistically significant difference in IFX-TLs versus patients with negative anti-ds-DNA (P>0.05). There was also no difference in ATIs levels between patients with positive or negative anti-ds-DNA (P>0.05).

Conclusion: In IBD patients under maintenance treatment with IFX the presence of positive ANA is associated with lower IFX-TLs and higher ATIs compared to those with negative ANA. Further study is needed in a larger population to evaluate the significance of this finding.

Disclosure: Nothing to disclose

P1738 PREVALENCE AND RISK FACTORS FOR NON-ALCOHOLIC FATTY LIVER DISEASE IN CROHN'S DISEASE

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is responsible for up to 40% of hepatic alterations diagnosed in inflammatory bowel diseases (IBD).

Aims & Methods: We aimed to evaluate the prevalence and risk factors for NAFLD in patients with Crohn's disease (CD).

Methods: This is a comparative retrospective study of 86 cases of CD (42 men and 44 women, sex-ratio of 0.95) with a mean age of 42.47 years (18-88 years). We used as a control group, 50 patients consulting for an intestinal functional disorder (29 women and 21 men) whose average age was 42 years.

In both groups, hepatic steatosis was sought by abdominal ultrasound as well as calculation of the HSI score (Hepatic Steatosis Index). Patients with chronic liver disease whose etiology is different from NAFLD, or daily alcohol consumption greater than 20 g/day for women and 30 g/day for men were excluded.

Results: We collected 86 patients followed for CD, the median duration of follow-up was 54 months; 44.2% (36) of patients were smokers, 12% had a family history of CD, 25.6% (22) were overweight with an average BMI of 22.45 kg/m2 (15-30.47kg/m2), 44.2% (38) had ileal disease, 14% (12) a colonic disease and 38.6% (33) ileocolic localization.

CD was inflammatory in 38.4% of cases, stenotic in 34.9% of cases, fistulizing in 7% of cases and both stenosing and fistulizing in 17.4% of cases. NAFLD based on abdominal ultrasound data and HSI score calculation was observed in 21 (24.7%) patients with CD versus 8 cases in the control group (16%) (p = 0.04).

The prevalence of diabetes and overweight was comparable between the two groups. Among patients with CD, those with NAFLD were more likely to be women (14 women versus 7 men) with an average age greater than 45 years. BMI was higher in patients with hepatic steatosis. Factors associated with the presence of hepatic steatosis during CD were overweight (BMI > 25 kg/m2) (p = 0.026), smoking (p = 0.006), and cortico- steroid therapy (p = 0.032). There was no significant association between history of surgery and the concept of fatty liver.

Conclusion: Hepatic steatosis is the most common hepatobiliary event during CD. Its screening should be systematic in order to introduce preventive measures avoiding its progression towards fibrosis.
Disclosure: Nothing to disclose

P1739 A SCREENING TOOL FOR THE EARLY DIAGNOSIS OF EXTRAINTESTINAL MANIFESTATIONS IN INFLAMMATORY BOWEL DISEASE: THE EMAIL QUESTIONNAIRE

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Introduction: Data on prevalence of extraintestinal manifestations (EIMs) in inflammatory bowel disease (IBD) range from 6% up to 47%. Recently, several red flags and questionnaires have been proposed for early diagnosis of articular manifestations.
Aims & Methods: Our aim was to analyze the prevalence of EIMs in a single center prospective cohort, using a comprehensive questionnaire developed by our group to detect all EIMs (Extraintestinal MAnifestations in Inflammatory boweL disease , EMAIL) . Patients with IBD attending our Clinic from November 2017 to January 2019 were interviewed using a two-part questionnaire, the first part for clinical-demographic data and the second part for EIMs (date of diagnosis, pharmacological therapies at onset and for EIMs, response to therapy, relationship with disease activity). Patients positive to screening were referred for multidisciplinary approach.
Results: 206 IBD patients were interviewed, 114 (55,3%) Crohn's disease (CD) and 92 (44,7%) ulcerative colitis (UC), 52,4% male, mean age 46,7 years (SD± 15,2). Familial predisposition for IBD was reported in 28,2% (47/206). Smokers were 63 (30,6%). 60 (53%) CD patients and 48 (52%) UC patients, in total 108, had history of at least one EIM. 37 patients (18%) had more than one EIM. The maximum number of EIMs was 4. Articular EIMs were found in 49 pts (24%), 36 (31,6%) with CD; peripheral arthritis was found in 14% (29/206), axial arthritis in 9,7% (20/206): 7 pts (3,4%) had ankylosing spondylitis, 13 (6,3%) sacroiliitis. Mucocutaneous EIMs were detected in 39 pts (19%), 27 (23,7%) with CD; erythema nodosum in 15 pts (7,3%), pyoderma gangrenosum in 9 (4,4%), psoriasis in 15 (7,3%), folliculitis in 7 (3,4%). Ocular EIMs were observed in 35 pts (17%), 19 (16,6%) with CD: uveitis in 7 pts (3,4%), conjunctivitis in 8 (3,9%), optic neuritis in 2, glaucoma in 2 pts, cataract in 13 (6,3%), dry eye in 4 (1,9%), central serous chorioretinopathy in 1. Hepatobiliary EIMs were observed in 31 pts (15%), 19 with UC: 26 steatosis (12,6%), 5 (2,4%) primary sclerosing cholangitis. 4 (2%) pts had DVT. There was a significant correlation between CD and articular EIMs (p=0,001) , between axial arthritis and IBD related surgery (p= 0,001) and age at IBD diagnosis between 16 and 40 years (p= 0,042). Skin manifestations were more frequent in female (p=0,002) in CD (p=0,032), in pts without perianal disease (p=0,019). There was a strong correlation between skin manifestations and IBD activity (p< 0,001). Ocular manifestations were more frequent in pts without perianal disease (p=0,042). Hepatobiliary manifestations were more frequent in male (p= 0,017) and in UC (P=0,044). There was a significant correlation between DVT and IBD activity (p= 0,016). 59,6% of patients with EIM (64/108) were treated with biologics, immunomodulators were used in 25/108 patients (23%). Combo Therapy was used in 11/108 pts (10%).
Conclusion: The questionnaire developed by our group proved to be a sensitive screening tool since the prevalence of EIMs in our cohort was higher than that reported in the literature. Articular and cutaneous EIMs are more frequent in CD, hepatobiliary EIMs are more frequent in UC. A gender difference has been found since cutaneous EIMs are more frequent in females, hepatobiliary more in males. Cutaneous EIMs and DVT are related with IBD activity. EIMs require a multidisciplinary approach and the frequent use of biologics and immunomodulators, early diagnosis could improve response to therapy and positively impact on quality of life.
Disclosure: None to declare

P1740 PREDICTORS OF NEGATIVE C-REACTIVE PROTEIN IN ACTIVE CROHN'S DISEASE

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Introduction: Due to its wide accessibility, fast availability and proven correlation with disease activity, C-reactive protein (CRP) remains an essential tool in the management of Crohn's disease (CD). However, the correlation of CRP with CD activity is not per- fect. It is therefore of great importance to identify the group of patients with active dis- ease and negative CRP.
Aims & Methods: We performed a retrospective case-control study, with inclusion of CD patients with proven active disease as demonstrated by endoscopic and/or radiologic examinations. The CRP's cut-off value used to separate patients in two groups (cases and controls) was 1 mg/dl. Demographic, phenotypic and clinical characteristics were collected. Statistical analysis was performed with SPSS 20.0.
Results: We included 77 patients (38 men, 39 women) with a mean age of 40.21 years (18-88 years) and median duration of disease of 58 months (24-310 months). Twenty seven (35%) of these patients had negative CRP. There weren't statistically significant differences in CD activity between cases and controls, as evaluated by Best index. Upon exploratory analysis, there were statistically significant differences regarding gender as 47.36% of men vs. 23.07% of women had a negative CRP (p = 0.04). Even though location was not a significant predictor, all patients with a negative CRP had ileal involvement. On multivariate analysis, gender remained a significant predictor (p = 0.02). There was also a tendency to a higher probability of negative CRP in isolated ileal disease (p = 0.058). There were no differences in age, behaviour, disease duration, previous abdominal surgery or smoking status.
Conclusion: Despite being a useful tool, CRP has some limitations and it can be negative in cases of active disease. In patients with the identified characteristics: men with ileal disease, other methods should be used to exclude with confidence the presence of inflammatory activity.
Disclosure: Nothing to disclose

P1741 DEGRADATION AND FORMATION OF TYPE III, IV AND V COLLAGEN ARE ASSOCIATED WITH DISEASE ACTIVITY, DISEASE SEVERITY AND DISEASE EXTENSION IN PATIENTS WITH ULCERATIVE COLITIS

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Introduction: Ulcerative colitis (UC) is an idiopathic chronic inflammatory bowel disease, where increased matrix metalloproteinases are the major contributor to the intestinal tissue remodelling UC. The intestinal basement membrane (main constituent is type IV collagen) is directly positioned underneath the epithelial cells. The supportive interstitial matrix (main constituent are type I, III and V collagens) is mainly produced by fibroblasts. Both matrices are important for intestinal health and are highly affected in UC.
Aims & Methods: We investigated serum biomarkers of collagen degradation and formation of the respective extracellular matrix (ECM) compartments and their association with disease activity, severity and extension in 29 UC patients and 29 healthy donors (HD) were included as a control group. A combination of the partial mayo score and biochemical activity was used to determine disease activity (pMayo>1 and CRP>5). Disease severity and extension was assessed by Montreal classification. Biomarkers of type III collagen degradation (C3M) and formation (PRO-C3), type IV collagen degradation (C4M) and formation (PRO-C4), type V collagen formation (PRO-C5) and C-reactive protein (CRP) were measured in serum by ELISA. One-way ANOVA (Tukey's multiple comparisons test), and spearman rho correlations were applied for statistical analyses.
Results: C4M was significantly elevated in active UC compared to UC in remission (P< 0.05) and HD (P< 0.001), and PRO-C4 was also significantly elevated in active UC and UC in remission compared to HD (P< 0.01). C3M

was significantly elevated in active UC compared to UC in remission (P< 0.05) and HD (P< 0.05), whereas PRO-C3 was significantly elevated in active UC and UC in remission compared to HD (P< 0.001). PRO-C5 was elevated in active UC compared to HD (P< 0.01) (figure 1). In addition, C3M (r=56,P< 0.01), C4M (r=0.41,P< 0.05), PRO-C4 (r=58,P< 0.001), PRO-C5 (r=49,P< 0.01), and CRP (r=47,P< 0.01) correlated with disease severity, and PRO-C4 (r=48,P< 0.01), PRO-C5 (r=0.38,P< 0.05), and CRP (r=45,P< 0.01) correlated with disease extension.

Conclusion: The biomarkers C3M and C4M were associated with disease activity in UC and disease severity in addition to PRO-C4 and PRO-C5. PRO-C4 and PRO-C5 also correlated with disease extension. These data demonstrated that ECM remodelling of the intestinal basement membrane and interstitial matrix are associated with disease status and progression, which can be used to optimize treatment strategies for UC patients.

Disclosure: JHM, MAK, and TMJ are full time employees at Nordic Bioscience. MAK and TMJ hold stocks in Nordic Bioscience.

P1742 WITHDRAWN

P1743 ELEVATED ECTODOMAIN OF TYPE XXIII COLLAGEN IS A NOVEL BIOMARKER OF THE INTESTINAL EPITHELIUM TO MONITOR DISEASE ACTIVITY IN ULCERATIVE COLITIS AND IN CROHN'S DISEASE

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Introduction: *Crohn's disease* (CD) and ulcerative colitis (UC) is marked by inflammation of the gastrointestinal tract and characterized by intermittent periods of active disease (flares) and inactive disease (remission) resulting in impaired intestinal epithelial barrier and induced tissue damage and remodeling. Methods for assessment of the intestinal permeability can be used to evaluate the disease burden, however, there are only a few non-invasive biomarkers available. The epithelial cells are positioned directly on top of the basement membrane, which is remodeled extensible in IBD. The transmembrane collagens connect the epithelial cells to this extra cellular matrix (ECM).

Aims & Methods: Since transmembrane collagens have an important role in epithelial cell homeostasis, we sought to determine whether type 23 collagen, a transmembrane collagen expressed in epithelial cells as associated with the basement membrane, could serve as surrogate for disease activity in patients with CD and UC active disease.

We developed an enzyme-linked immunosorbent assay (ELISA, named PRO-C23) to detect the ectodomain of type 23 collagen in serum, followed by evaluation of its levels in both rat dextran sulfate sodium (DSS) model and human UC and human CD cohorts. Serum from 44 CD and 29 UC patients with active and inactive disease based on the simple endoscopic score for CD (SES-CD) and on the Mayo score for UC (pMayo), respectively were included in this study.

Results: In patients, serum levels of PRO-C23 were elevated in CD (p< 0.05, Fig. 1A) and UC (p< 0.001, Fig. 1B) patients with active disease compared to healthy donors. In the DSS induced rat colitis model, PRO-C23 level was significantly increased in the rats with active disease (Fig. 1C) and returned to normal level after disease remission.

Conclusion: This is the first study that showed type 23 collagen levels were elevated in IBD, and consequently that transmembrane collagens and the basement membrane axis is important for the pathology of IBD. We demonstrated that biomarker, PRO-C23, was elevated in rats with active colitis (proving accuracy) and in CD and UC patients with active disease. This indicates that PRO-C23 is associated with a compromised interstitial mucosa, and epithelial cell dysfunction. PRO-C23 may potentially be used as non-invasive surrogate of disease activity in CD and UC patients and thus aid in the diagnosis and monitoring patients, in combination with other biomarkers.

Disclosure: JHM, MAK, SS, ML, and TMJ are full time employees at Nordic Bioscience. MAK and TMJ hold stocks in Nordic Bioscience.

P1744 INSIGHTS FROM A MULTIDISCIPLINARY REFERRAL CLINIC FOR DERMATOLOGICAL COMPLICATIONS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES: IBD-DERMA-CLINIC

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Introduction: Dermatological manifestations are common among patients with inflammatory bowel diseases (IBD). They may be driven by the inflammatory process, nutritional deficiencies, or medications. As the diagnosis and treatment of dermatologic manifestations is often challenging, we established a multidisciplinary referral clinic (IBD-DERMA) for joint decision making and patient care.

Aims & Methods: We aimed to estimate the impact of multidisciplinary care in the IBD-DERMA clinic. The clinic functions since 2018. It is conducted by an IBD expert and a dermatologist with expertise in immunological disorders. Consecutive patients with IBD who have developed a dermatological complication and were referred for consultation by either gastroenterologists or dermatologists were included. Joint decision making was driven by the status of the IBD, past medical history, exposure to medications, and the dermatological diagnosis. Mann Whitney or Chi- square tests were employed to compare continuous or categorical variables, accordingly.

Results: Overall 92 patients were included: 50 males (54.3%), median age 34 years (IQR 29-44), and median disease duration of 8 years (IQR 3-13). Crohn's disease - 75 patients, most with small bowel involvement, and a form of bowel damage (L1- 50%, L3-37%, B2 -24%, B3 27%, B2/3-17%), and 43% with perianal involvement. Ulcerative colitis -16 patients, of whom 71% had pancolitis. In 23% of the cohort there was a history of IBD-related surgery, and 48% had at least one extra-intestinal manifestation in addition to IBD and dermatologic manifestations. Only 20% of patients had a history of dermatological condition prior to IBD diagnosis (mostly psoriasis [63%]). Sixty percent of patients were experienced with thiopurines, 12% with methotrexate, and 78.5% with anti-tumor necrosis factor agents (ATNFs). At referral 80% of patients had quiescent IBD, most (92%) controlled with medications. The most prevalent dermatologic diagnosis was skin eruptions induced by ATNFs, complicating 45.6% of the cohort: 28/42 patients with psoriasiform dermatitis (PD), and 14/42 patients with dominant inflammatory alopecia (IA). Characteristics of patients with PD and dominant IA were comparable, however therapeutic strategies differed. Intervention strategies were: (i) topical therapy (steroid ointments/ injections or phototherapy), systemic steroids, combination with methotrexate - without discontinuation of the offending ATNF, (ii) discontinuing the ATNF, (iii) a biologic switch. Altogether 88% significantly improved. Topical treatments were effective in 60.7% of patients with PD but only 21.4% of those with IA (p=0.023). Discontinuation of the offending ATNF was necessary in 93% of the patients with IA compared to 36% of patients with PD (p< 0.001). A switch to a different biologic class was needed in order to control either the skin condition and/or the IBD in 57.1% of the IA patients, compared to only 10.7% of patients with PD (p=0.002).

Conclusion: An IBD-DERMA clinic provides expert care for patients with IBD and dermatological manifestations. Paradoxical skin eruptions were the most prevalent diagnoses. Almost a third of the patients presented with dominant IA secondary to ATNF, a condition that has a distinct course, and may represent a different pathophysiologic process. Joint decision making resulted in improvement in 88% of dermatologic manifestations. The IBD-DERMA clinic is a platform enabling professional and personalized approach to treat patients with IBD and dermatological manifestations.

Disclosure: Nothing to disclose

P1745 MUCOSAL ABNORMALITIES OF THE ESOPHAGEAL IN PATIENTS WITH IBD: AN ENDOSCOPIC STUDY

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Introduction: Crohn's disease (CD) is generally found in the ileum and/or colon, albeit, since the 1960s it has become evident that this chronic inflammatory disorder of unknown etiology can affect the whole gastrointestinal tract from mouth to anus. In 0.5-13% of patients with ileocolonic CD, upper gastrointestinal tract is affected, with 0.2 to 1.8% of cases being mainly located in the lower third of the esophagus, however, should a systematic esophageal biopsy be performed in all patients with IBD?

Aims & Methods: The aim of this study is to evaluate the interest of systematic esophageal biopsy in every IBD patient's case, as well as the prevalence of esophageal Crohn's disease in our series.

We conducted a prospective and descriptive study including 64 patients with IBD supervised within our department , and who have had an upper enodoscopy .Epidemiological, clinical, endoscopic and histological data were collected, These patients systematically underwent biopsy esophageal.

Results: A total of 64 patients were included , 35 men (54 ,68 %) and 29 females (45,32%) , with an average age being 39.32 years (range : 22-76 ans). Among them, 39 patients (60,9%) had crohn's disease , 19 patients (29.6 %) had ulcerative colitis, and 5 patients (7.8 %) had inderterminate colitis .Upper endoscopy was systematically performed on 58 (90.6 %)patients and was indicated to investigate an upper gastro intestinal disorder in 9.3% (6 patients)of cases. It was normal for 55 patients (85.9%) and revealed: Esophagitis in five cases (grade A of Los Angeles (three patients), grade B (one patient), and grade C (one patient), typical manifestations evoking an esophageal localization of crohn's disease were found in 2 patients: superficial ulcerations scattered in the lower third of the esophagus and an oval ulcer of 6 mm. These 2 patients are females whom respective ages are 35 and 31 years old, they have a low localization of Crohn's disease (L2 and L1 according to the Montreal classification), one of them, had an upper gastro intestinal truct symptom: epigastralgia. Histological findings were nonspecific, indicating ulcerative esophagitis for both patients.For the other patients, histological findings showed chronic and hyperplasic esophagitis in 33 cases (51.5%), normal esophageal mucosa in 22 cases (34.3%), congestive mucosa in 3 cases (4.6 %), and reflux oesophagitis in 3 cases (4.6 %).

Conclusion: Our study showed that a systematic esophageal biopsy performed on all IBD patients is far from being profitable, while a systematic upper GI endoscopy might be more useful.

Disclosure: Nothing to disclose

P1746 SEROLOGICAL BIOMARKERS OF TYPE VI COLLAGEN REMODELLING REFLECT ENDOSCOPICALLY AND CLINICALLY ACTIVE CROHN'S DISEASE

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Introduction: The relapsing and transmural inflammation of Crohn's disease (CD) may cause intestinal tissue damage that eventually may result in surgery. Disease activity in CD patients is assessed by clinical symptoms and macroscopic findings of intestinal inflammation at endoscopy. Type VI collagen is positioned in the interface of the interstitial matrix and basement membrane in the intestine. It affects epithelial cell-fibronectin interaction that is important for cell proliferation, adhesion, and migration. Collagens hold signalling potential, and endotrophin that is released from the pro-peptide of type VI collagen during enzymatic processing can itself stimulate fibroblasts to produce more extracellular matrix (ECM).

Aims & Methods: Type VI collagen is more than just a structural protein and we investigated if serum biomarkers of its remodelling could serve as surrogate of disease activity in CD patients.

Serum from 17 CD patients with active (n=10) and inactive (n=7) disease based on the simple endoscopic score for CD (SES-CD) were included in this study. Two competitive ELISAs were used to estimate serum levels of degradation and formation of type VI collagen, respectively. One for a neo-epitope of matrix metalloproteinase (MMP)-9 mediated degradation of type VI collagen α3 chain (C6Ma3) and one for endotrophin; C-terminus of released C5 domain of type VI collagen α3 chain (PRO-C6).

Results: Serum levels of C6Ma3 were elevated in CD patients with a SES-CD above 2 compared to patients with a SES-CD of 0-2. A receiver operating characteristic (ROC) analysis showed an area under the curve of 1 for C6Ma3 with specificity and sensitivity both at 100%. The area under the ROC curve for CRP and Fcal were 0.87 and 0.81, respectively. Serum levels of PRO-C6 were lower in CD patients with active disease compared to patients in remission based on the Harvey-Bradshaw Index (HBI) and serum PRO-C6 demonstrated an inverse correlation to HBI.

Conclusion: Our data show that biomarkers of tissue remodelling reflect endoscopically and clinically active CD. MMP mediated destruction of type VI collagen (C6Ma3) was associated with endoscopically active CD and could separate endoscopically active and inactive patients with 100% sensitivity and specificity. Decreased levels of endotrophin (PRO-C6) was associated with clinically active CD and showed an inverse relationship with HBI. This indicates that remodelling of type VI collagen measured by C6Ma3 and PRO-C6 can be used as surrogate markers of endoscopically and clinically active CD, and fragments and signalling molecules released from type VI collagen are associated with pathological features of CD.

Disclosure: ML, MP, JHM, MAK, and TMJ are full time employees at Nordic Bioscience. MAK and TMJ hold stocks in Nordic Bioscience.

P1747 A SEROLOGICAL BIOMARKER OF TYPE VIII COLLAGEN THAT CONTAINS THE ANTI-ANGIOGENIC SIGNALLING MOLECULE, VASTATIN, IS ASSOCIATED WITH THE EXTENSION OF DISEASE IN ULCERATIVE COLITIS

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Introduction: Ulcerative colitis (UC) is characterized by superficial inflammation that starts in the rectum and can extend proximally to affect the entire colon. Endoscopy is used to diagnose patients in terms of extension of disease, however this is invasive and cannot always be completed e.g. if the colon is too severely inflamed. The epithelial and endothelial basement membrane (BM) is an abundant extracellular matrix (ECM) of the intestine. Type VIII collagen is directly associated with the BM and the C-terminus of this collagen contains the anti-angiogenic signalling molecule, vastatin.

Aims & Methods: Due to the abundant vasculature in the intestine, we investigated if a serum biomarker that targets the vastatin site of type VIII collagen was associated with the degree of inflammation in UC.

Serum was collected from 61 UC patients that were endoscopically recorded for extension of disease: remission, proctitis, left-sided, pancolitis, and unknown. Endoscopy could not be completed in patients with unknown extension of disease, however, five out of six unknown patients had at least left-sided colitis, but most possibly pancolitis. Rat serum from acute (n=10) and chronic dextran sulfate sodium (DSS) colitis (n=39) were included. A competitive ELISA for the C-terminus of type VIII collagen (PRO-C8) was used to estimate serum levels of type VIII collagen/vastatin.

Results: Serum levels were elevated in UC patients with proctitis (P=0.003), left-sided (P=0.008), pancolitis (P=0.002) and unknown (P=0.0003) extension of disease compared to patient in endoscopically remission. In addition, PRO-C8 serum levels were elevated in unknown (P=0.036) and pancolitis (P=0.03) patients compared to proctitis. The levels were also elevated in unknowns (P=0.04) compared to left-sided, for which pancolitis patients had a tendency (P=0.065) of higher PRO-C8 levels. Serum PRO-C8 was confirmed to be increased in both acute and chronic DSS colitis.

Conclusion: PRO-C8, containing the anti-angiogenic signalling molecule vastatin, was associated with extension of disease in UC patients and was elevated in patients for which endoscopy could not be completed. Increased PRO-C8 was shown to originate from intestinal inflammation in DSS colitis in rats. Thus, PRO-C8 may be a serological biomarker that reflects intestinal tissue inflammation based on extension of disease. This

also indicates that UC patients with broad tissue involvement may have an altered collagen signalling and that ECM signals are part of the disease pathology.

P1748 MUCOSAL CAPILLARY PATTERN RECOGNITION BASED ON AUTOMATED IMAGE ANALYSIS DURING ENDOSCOPY ACCURATELY DETECTS HISTOLOGICAL REMISSION IN ULCERATIVE COLITIS

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Introduction: A treat to target strategy in ulcerative colitis (UC) requires an objective evaluation tool to assess remission. The Mayo endoscopic sub-score (MES) and the ulcerative colitis endoscopic index of severity (UCEIS) have important inter-rater variability mainly in evaluating remission. Histological remission is the best predictor for sustained clinical remission in UC. The infiltration of neutrophils is associated with morphological irregularities of the pericryptal capillaries.

Aims & Methods: The aim was to develop a new objective automated tool for a prototype colonoscopic system to assess histological remission based on the evaluation of the morphology of the pericryptal capillaries during endoscopy.

We used a prototype endoscopic system enabling activation of a short wave-length monochromatic light through adaptation of a LED system. This enables to evaluate in real time the mucosal architecture (crypts, pericryptal capillaries, bleeding) up to a depth of around 200μm. In initial observations histological non-remission was associated with bleeding (mucosal/luminal) and capillary congestion. For this, an image analysis algorithm was applied to provide a score that quantifies the specific morphology of the mucosal capillaries. The algorithm included two steps. First, bleeding (mucosal/luminal) was assessed by pattern recognition. Samples with bleedings were automatically classified as non-remission. In case of non-bleeding (mucosal/luminal), the degree of congestion of the capillaries was measured (maximal localized density estimation after morphological hessian based vessel recognition) to assess an ideal cut off value to identify histological remission (Geboes score (GBS) < 2B.1; no neutrophils in the lamina propria). Consecutive UC patients at the University of Leuven were evaluated with the MES, UCEIS, visual capillary evaluation based on short wave-length monochromatic light and the automated image analysis algorithm. To test the reliability of the algorithm and scores, the results were correlated with the GBS. Biopsies were taken in the matching area of the endoscopic evaluation.

Results: Fifty eight patients with UC (53% male, median age 41y IQR 38-56, disease duration 7.1y IQR 2.4-16.4) with 113 evaluable segments (89% rectum or sigmoid) were included. The correlation between GBS and MES, UCEIS and visual short wave-length was good (r= 0.76, 0.75, 0.74, respectively). The automated image analysis algorithm detected histological remission with a high performance (sens 0.79, spec 0.90) compared to UCEIS (sens 0.95, spec 0.69) and MES (sens 0.98, spec 0.61), resulting in a positive predictive value of 0.83, 0.65 and 0.59 for the automated image analysis algorithm, UCEIS and MES respectively. The algorithm detects histological remission with high accuracy (86%). (table 1)

	Mayo endoscopic sub score	Ulcerative colitis endoscopic index of severity	Visual capillary score	Image analysis algorithm
n	113	113	113	113
accuracy	0,743	0,788	0,876	0,858
sensitivity	0,976	0,952	0,810	0,786
specificity	0,606	0,690	0,915	0,901
Positive predictive value	0,594	0,645	0,850	0,825
Negative predictive value	0,977	0,961	0,890	0,877

[Table 1: performance of the different evaluation tools]

Conclusion: Mucosal capillary pattern recognition based on image analysis with short wave-length monochromatic light detected histological remission with high accuracy in UC. This technique provides an objective and quantitative tool to assess histological remission, and excludes inter-reader variability.

Disclosure: Nothing to disclose

P1749 SYSTEMATIC LIVER BIOPSY DURING SURGERY FOR INFLAMMATORY BOWEL DISEASE: WHAT CONTRIBUTION?

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Introduction: Hepatic disorders associated with IBD are frequent and varied according to the type of IBD (Crohn's disease or ulcerative colitis). The abnormalities of biochemical liver tests observed may be transient or lasting. The most specific of these is primary sclerosing cholangitis (PSC) with a risk of degeneration.

Aims & Methods: The objective of our study was to evaluate the prevalence of various hepatic histological lesions, especially PSC in patients operated for ulcerative ulcerative colitis or Crohn's disease, and to discuss the value of systematic perioperative liver biopsy.

Descriptive and analytical prospective study including 14 patients who had surgery for severe acute colitis or complicated Crohn's disease, consent was previously bled by the patients to have their agreement to perform a liver biopsy.

Results: Fourteen patients (6 women, 8 men) were included in the study. 9 patients with Crohn's disease and 5 patients with ulcerative colitis. The various histological lesions discovered are: chronic hepatitis in 6 patients associated with fibrosis in 5 cases, including 4 cases FI and one case F2 according to the Metavir score, nonspecific inflammatory lesions compatible with lesions of small duct cholangitis or chronic portitis in 7 patients, 2 patients had hepatic steatosis and one patient had a hepatic capillary haemangioma. Liver biopsy was normal in only one case. However, no patient presented histological lesions suggestive of primary sclerosing cholangitis.

Conclusion: Our study (preliminary results) proves that performing a systematic perioperative liver biopsy can be cost-effective by allowing the diagnosis of early-stage histological abnormalities such as hepatic steatosis and small channel cholangitis in order to initiate treatment. adequate and regular follow-up to avoid complications.

Disclosure: Nothing to disclose

P1750 THERAPEUTIC DRUG MONITORING IN CROHN'S DISEASE PATIENTS, A COMPARISON BETWEEN HOMOGENEOUS MOBILITY SHIFT ASSAY AND POINT OF CARE METHOD

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Introduction: Therapeutic Drug Monitoring (TDM) is a useful tool to help physicians managing patients with Inflammatory Bowel Disease treated with anti-tumor necrosis factor (TNF) drugs. Different techniques are currently available to evaluate serum drug concentration (TL), and various studies found an association between drug TL, evaluated either with ELISA or HMSA, and IBD activity. However, these techniques are time consuming. Recently, a point-of-care (POC) method has been proposed to evaluate drug TL and overcome the limitations inherent to other methodologies.

Aims & Methods: The aim of our study was to evaluate the capability of POC to discriminate between IBD relapse and remission, and to evaluate the concordance of drug TL measured with POC and HMSA.

We analyzed with Quantum BlueÒ(Buhlmann Laboratories AG, Schonenbuch, Switzerland) (POC) 200 Adalimumab (ADA) and 200 Infliximab serum samples of 46 Crohn's Disease (CD) patients previously assessed with HMSA. Blood samples were drawn at standardized time points during anti-TNF treatment (2, 6, and every 8 weeks), before anti-TNF administration. Disease activity was assessed by the Harvey-Bradshaw Index (HBI, remission defined by HBI< 5).

Results: We evaluated 46 CD patients who responded to anti-TNF induction with ADA (n= 25, 54.3%) and IFX (n= 21, 45.6%), with a median follow-up of 83 weeks (range 16-144 weeks).

At week 16, median ADA TL of patients in remission were significantly higher as compared to patients in disease relapse using both HMSA [12.7 mcg/mL (range, 8.9-23.6 mcg/mL) vs 6.6 mcg/mL (range, 0.7-9.6 mcg/mL), P=0.0001] and POC [17.8 mcg/mL (range 7.6-35.0 mcg/mL) vs 9.8 mcg/mL (range 5.8-11.4 mcg/mL), P=0.0003]. The concordance between the two different techniques has been assessed as 0.76 by Choen Kappa. Considering IFX TL, patients in remission had higher serum drug concentration using both HMSA [7.0 mcg/mL (range, 0.0-21.8 mcg/mL)] and POC [6.2 mcg/mL (range 0.4-14.3 mcg/mL)] as compared to patients who experienced disease relapse [HMSA, 0.1 mcg/mL (range, 0.0-4.1 mcg/mL), P=0.019; POC, 0.45 mcg/mL (range 0.4-3.3 mcg/mL), P=0.0072]. The concordance between the two different test for IFX TL was 0.81.

At the end of follow up, median ADA TL of patients in remission were significantly higher as compared to patients who experienced disease relapse, using both HMSA and POC [respectively, 10.7 mcg/mL (range, 4.6-18.3 mcg/mL) and 16.2 mcg/mL (range 5.7-35.0 mcg/mL) vs 5.6 mcg/mL (range, 3.1-9.9 mcg/mL) and 6.5 mcg/mL (range 1.3-17.1 mcg/mL) P=0.001 and P=0.0012] with a concordance of 0.75.

Lastly, considering IFX TL, patients in remission had numerically higher serum drug concentration [4.7 mcg/mL (range, 0.1-18.6 mcg/mL) and 2.4 mcg/mL (range 0.4-11.1 mcg/mL)] compared to patients who experienced disease relapse [0.2 mcg/mL (range, 0.1-6.7 mcg/mL) and 0.5 mcg/mL (range 0.4-4.8 mcg/mL)] (P=0.13 and P=0.25) using HMSA and POC, respectively. The concordance between the two different test we used to calculate TL was 0.70.

Conclusion: In conclusion, we observed that both POC and HMSA are TL tests able to differentiate relapse and remission in IBD patients. The association between anti-TNF TL and disease status (remission/relapse) was better in ADA-treated patients rather than patients treated with IFX. Lastly, we demonstrated a good concordance between HMSA and POC. Anti-drug antibody concentrations while available on HMSA were not available on POC. This would limit the identification of anti-TNF non-responders on the POC test if a percentage of those were anti-drug antibody positive.

Disclosure: Nothing to disclose

P1751 USEFULNESS OF FECAL CALPROTECTIN IN PRIMARY CARE SETTING: AN EXPERIENCE IN NORTH - EAST ITALY POPULATION

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Introduction: Calprotectin, a calcium and zinc binding protein present in the cytosol of granulocytes neutrophils, monocytes, and macrophages. Fecal calprotectin (FC), a marker of colonic inflammation, can be used as first diagnostic tool and in the follow up of inflammatory Bowel Diseases (IBD). Many studies show that fecal calprotectin is useful in IBD diagnosis and in specialist settings but its benefit in the clinical practice of general practitioners is still not clear.

Aims & Methods: Our aim was to analyze the usefulness of fecal calprotectin indication in a north - east Italy population with lower GI symptoms of mild to moderate severity. A cohort of 2487 laboratory exams of fecal Calprotectin were selected from January 2018 to December 2018. 2388 of these were requested by the General Practitioner (96.0%) and the other 99 exams by a Gastroenterologist (4.0%), which were excluded from the

analysis. The study population was thus composed of 937 men (39.2%) and 1451 women (60.8%), mean age 49.48 years (range 18-96).According to the literature, 3 cut off values were selected for this exam: 0-49 µg/g was considered negative, 50-149 µg/g was considerate indeterminate and ≥150 was considerate positive.

285 of these patients were sent to a Colonoscopy by general practitioners.
Results: The results of 2037 fecal calprotectin was divided into: negative (0-49 µg/g): n. 1735 (72.7%), indeterminate (50-149 µg/g) n. 493 (20.6%) and positive (≥150 µg/g) n. 160 (6.7%).

The patients who underwent colonoscopy after FC testing were 285 (14.0% of the total number of requested FC tests): 155 with negative FC, 81 with indeterminate FC, and 49 with positive FC.

Colonoscopic findings in patients with negative FC were: normal in 89 cases (57.4%), diverticular disease in 33 cases (21.3%), polyps in 10 patients (6.5%), IBD in 16 cases (10.3%), other types of colitis (ischemic and non-specific) in 6 patients (3.9%), and colorectal neoplasia in 1 patient (0.6%). Colonoscopic findings in patients with indeterminate FC were: normal in 37 cases (45.7%), diverticular disease in 27 patients (33.3%), polyps in 6 cases (7.4%), IBD in 3 patients (3.7%), other types of colitis in 7 cases (8.6%) and, colorectal neoplasia in 1 case (1.2%).

Colonoscopic findings in patients with positive FC were: normal in 19 (38.8%) cases, diverticular disease in 4 (8.2%) cases, polyps in 2 patients (4.1%), IBD in 17 patients (34.7%), other types of colitis in 5 cases (10.2%) and neoplasia in 2 patients (4.1%).

Conclusion: Although positive FC values are more frequently associated with organic disease, especially IBD, and should therefore prompt colonoscopic evaluation, the latter, as well as diverticular disease and even colorectal neoplasms can be present with normal FC values. We notice a high rate of indeterminate FC in diverticular disease patients, suggesting that an early treatment and subsequent FC retesting might be an optimal approach.

Considering FC in association to some clinical data (such as age) can increase the usefulness of the test. Despite the high number of false positive cases, Calprotectin alone can be useful in the clinical practice for the general practitioner in the management of patients with low GI symptoms, to avoid diagnostic delay and to restrict unnecessary invasive and expensive exams.

Disclosure: Nothing to disclose

P1752 SERUM BIOMARKERS OF DEGRADATION AND FORMATION OF TYPE III, IV AND V COLLAGEN ARE ASSOCIATED WITH DISEASE ACTIVITY IN PATIENTS WITH CROHN'S DISEASE

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Introduction: Crohn's disease (CD) is characterized by episodes of relapse and remission and therefore requires continuous evaluation of disease activity. Extra Cellular Matrix (ECM) consists of basement membrane (BM) and interstitial matrix (IM). BM is positioned directly underneath the epithelial cells and consists mainly of type IV collagen, while IM consists mainly of type I, III and V collagen, and is produced by fibroblasts. Pathological environment, such as inflammation and fibrosis, leads to impaired remodeling, structure, quality and function of the collagen in the ECM.

Aims & Methods: Our aim was to investigate biomarkers of collagen degradation and formation and their association with disease activity and in patients with CD.

In this cross-sectional study we measured five biomarkers of ECM remodeling in 75 patients with CD (60% males, age 35(IQR 26.5-43.5)), and 29 healthy controls matched by age and gender. Biomarkers of type III collagen degradation (C3M) and formation (PRO-C3), type IV collagen degradation (C4M) and formation (PRO-C4), type V collagen formation (PRO-C5) and C-reactive protein (CRP) were measured in serum by ELISA. Inflammatory activity was defined as combination of clinical or biochemical disease activity (CDAI≥150 or CRP>5). Disease behavior was assessed by Montreal classification. One-way ANOVA (Tukey's multiple comparisons test), and ROC analysis was applied in statistical analysis.

Results: Biomarkers of interstitial matrix remodelling showed that C3M was significantly elevated in active CD compared to inactive CD (P< 0.05) and HD (P< 0.05), whereas PRO-C3 and PRO-C5 were significantly elevated in active CD and inactive CD compared to HD (P< 0.001, P< 0.05). (Figure 1) Turnover type III collagen showed highest diagnostic accuracy for active disease (AUC=0.74). Area under curve was for C3M 0.63, PRO-C3 0.36 and PRO-C5 0.52.

Biomarkers of basement membrane remodelling showed significantly higher C4M in active CD compared inactive (P< 0.05) and HD (P< 0.001), whereas PRO-C4 was significantly elevated in active and inactive CD compared to HD (P< 0.01). Area under curve was for C4M 0.64, C4M/PRO-C4 ratio 0.57 and PRO-C4 0.56.

Conclusion: Both biomarkers of interstitial matrix (C3M) and basement membrane (C4M) were associated with disease activity. PRO-C3, PRO-C5 and PRO-C4 were associated with CD regardless of disease activity. Interstitial matrix biomarkers of turnover type III collagen C3M/PRO-C3 showed highest diagnostic accuracy for disease activity. In conclusion, these biomarkers may be used in monitoring and prediction of disease activity and in differentiation between patients with CD and healthy individuals.

Disclosure: Nothing to disclose

P1753 FAECAL CALPROTECTIN SHOWS POOR CORRELATION WITH ENDOSCOPIC ACTIVITY IN CROHN'S DISEASE PATIENTS WITH AN END-ILEOSTOMY COMPARED TO THOSE POST ILEO-COLONIC RESECTION

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Introduction: Faecal Calprotectin (FCP) has been found to be an accurate surrogate marker for post-operative recurrence in Crohn's disease (CD). However, the use of FCP to monitor disease activity in patients with an ileostomy due to CD has not been established. The aim of this study was to assess the performance characteristics of FCP in patients with CD and an ileostomy and to compare this to patients with CD post ileo-colonic resection.

Aims & Methods: Post-operative patients with CD attending a single academic centre were identified using a prospectively maintained database of >4000 Inflammatory Bowel Disease (IBD) patients. These were cross-referenced with the local hospital endoscopy reporting system to identify patients with small bowel endoscopic assessment from 2014 onwards. Endoscopic CD activity was classified using the Rutgeert's score (RS) and RS≥2 was used to define endoscopic recurrence. A FCP cut-off 150µg/g was used to define disease activity. MRE assessment was used to classify patients as active or inactive CD.

Results: 1,896 surgeries for CD were identified from our IBD database. A total of 80 (ileostomy: n=27, anastomosis: n=53) contemporaneous endoscopic and FCP results in 74 patients were analysed. Median age was 46.9 (IQR 37.0-57.1)) and did not significantly differ between the two groups. Similar numbers of male (n= 30) and female (n=44) were identified in both groups. Patients with an ileostomy had significantly higher rates of negative disease predictors including younger age at diagnosis (p< 0.05), longer disease duration (p=0.001) and a higher proportion of perianal disease (p=0.01). Patient demographics, disease characteristics and baseline biochemistry are outlined in Table 1.

72% had i0-1 disease, and 28% i2-4 disease in the ileostomy group compared to 47.2% and 52.8% respectively in the anastomosis group, with a trend towards more active disease in the anastomosis group (p=0.052). No significant correlation was identified between endoscopic scores and FCP results in patients with an ileostomy (p=0.109, R=0.328). In the anastomosis group, there was a significant correlation between level of FCP and RS≥2 (p=0.012, R=0.343), particularly in patients with FCP >150 (p=0.008, R=0.371).

Conclusion: Our study confirms the strong correlation between FCP and endoscopic activity in post-operative CD and in particular shows a high degree of accuracy when 150µg/g is used as a cut off in these patients.

There was, however, poor correlation in CD patients with an ileostomy. FCP is best used with caution in this patient cohort and in conjunction with other validated objective tools.

Disclosure: Nothing to disclose

P1754 THE SYSTEMIC IMMUNE-INFLAMMATION INDEX PREDICTS DISEASE SEVERITY OF ULCERATIVE COLITIS

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Introduction: Ulcerative colitis (UC) is an intractable chronic inflammatory disease characterized by diffuse inflammation of the colonic mucosa. Current indexes to evaluate the severity of UC include blood routine (BR), ESR and clinical grading system such as Mayo score and Baron endoscopic score[1]. But there is still lack of reliable objective index to assess disease severity. Systemic immune-inflammation index (SII) is a newly developed composite index based on BR, which is defined as platelet×neutrophil/lymphocyte[2]. It has been proved to be both convenient and feasible in predicting treatment effect and prognosis of small cell lung cancer[3], pancreatic cancer[4], colorectal cancer[5] and hepatocellular carcinoma[6]. Hence, we analyze the correlation between SII and severity of UC patients, and estimate its value in UC diagnosis.

Aims & Methods: We retrospectively include patients in our department from January 2013 to December 2018. UC patients were diagnosed according to Third European Evidence-based Consensus on Diagnosis and Management of Ulcerative Colitis. The exclusion criteria include coronary heart disease, diabetes, chronic renal failure, hematopathy, hypersplenism, autoimmune disease, pregnancy, carcinoma, radiotherapy, infection, antiplatelet or NSAID drug intake. The control group was selected from patients who received colorectal polyps ESD. Their medical and family history were clear and pathological results of ESD samples were hypertrophic polyps. Their baseline information, BR, ESR, CRP and Mayo score were recorded. Statistical analyses were performed using Graphpad prism 8.

Results: There were 79 UC patients and 79 age and sex matched controls. The disease duration of UC patients was 45.78±65.31 months. Most patients suffered from pancolitis (n=50), while the number of left sided and distal colitis patients were 17 and 12, respectly. Mesalazine (n=52) was most commonly used in these patients, others were glucocorticoid (n=7), salazosulfapyridine (n=6), azathioprine (n=3), infliximab (n=2) and thalidomide (n=1). There were 18 patients who have never used any anti-immune, anti-inflammatory medicine or have been suspended for over 3 months. According to Mayo scoring system, the patients were classified into remission (n=8), mild (n=8), moderate (n=48) and severe (n=15).

There were significant differences between UC patients and controls in PLR, NLR and SII (p< 0.0001). Notably, SII was significantly lower between remission/mild group and severe group (p=0.012). Moreover, PLR, NLR and SII were associated with Mayo score, ESR and CRP. Among them, SII and Mayo score are most relevant (r=0.505, p< 0.0001). This revealed the outstanding ability of SII in estimating disease severity of UC.

NLR and SII shows excellent ability in UC diagnosis (Table). The AUC of NLR and SII was 0.808 and 0.858, separately, with cut-off values of 2.535 (p< 0.0001, SE=0.034, 95% CI [0.742, 0.874]) and 619.1 (p< 0.0001, SE=0.030, 95% CI [0.800, 0.917]). Similarly, PLR can diagnose UC with a cut-off value of 174.5 (AUC=0.755, p< 0.0001, SE=0.030, 95% CI [0.800, 0.917]).

Conclusion: This is the first report to demonstrate that SII has great potential in evaluating UC severity and diagnosis. Properly designed prospective studies are needed for further investigation.

References: 1. Schoepfer AM, et al. Ulcerative colitis: correlation of the Rachmilewitz endoscopic activity index with fecal calprotectin, clinical activity, C-reactive protein, and blood leukocytes. Inflamm Bowel Dis 2009; 15: 1851-1858 2. Zhong JH, et al. Prognostic role of systemic immune-inflammation index in solid tumors: a systematic review and meta-analysis. Oncotarget 2017; 8: 75381-75388 3. Hong X, et al. Systemic Immune-inflammation Index, Based on Platelet Counts and Neutrophil-Lymphocyte Ratio, Is Useful for Predicting Prognosis in Small Cell Lung Cancer. Tohoku J Exp Med 2015; 236: 297-304 4. Aziz MH, et al. The Systemic-Immune-Inflammation Index Independently Predicts Survival and Recurrence in Resectable Pancreatic Cancer and its Prognostic Value Depends on Bilirubin Levels: A Retrospective Multicenter Cohort Study. Ann Surg 2018, DOI: 10.1097/sla.0000000000002660: 5. Xie QK, et al. The systemic immune-

inflammation index is an independent predictor of survival for metastatic colorectal cancer and its association with the lymphocytic response to the tumor. J Transl Med 2018; 16: 273 6. Hu B, et al. Systemic immune-inflammation index predicts prognosis of patients after curative resection for hepatocellular carcinoma. Clin Cancer Res 2014; 20: 6212-6222
Disclosure: Nothing to disclose

P1755 THE RISK OF COLORECTAL CANCER IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Inflammatory bowel disease (IBD) is associated with a higher risk of colorectal cancer (CRC). However, studies have investigated this risk and reported widely varying rates.
Aims & Methods: This meta-analysis aims to estimate the risk of colorectal cancer in inflammatory bowel disease from multiple aspects.A literature search using Medline and Pubmed was conducted for terms related to colorectal cancer in inflammatory bowel disease from 1988 to 2018. All the full-text articles were searched and studies should meet our inclusion criterias ,in which no country restricted, the number of patients was over 500 and the follow up time was over 5 years. Overall pooled incidence rate , with 95% confidence intervals (CI),of colorectal cancer was obtained using a random-effects model as well as a cumulative risk at 10 years, 20 years, and 30 years of disease.
Results: Of 3620 studies , 46 articles were included and the total number of inflammatory bowel disease patients was 142190 in which 38672 were Crohn's disease(CD) and 103518 were ulcerative colitis(UC). The overall prevalence of CRC in IBD patient was estimated to be 1.17%(95% CI 1.03-1.31%). The CRC incidence of 71.03/100000 person year duration(pyd) in CD patients yielded differently to the incidence of 122.56/100000 pyd in UC patients. The CRC incidence rate in CD patients varied in intestinal site, being 34/100000 pyd in colon, 31.2/100000 pyd in caecum and 25.26/100000 pyd in rectum. The CRC incidence rate in UC also varied in intestinal site,being 60.88/100000 pyd in colon, 44.61/100000 pyd in cecum and 34.61/100000 pyd in rectum. The worldwide CRC incidence rate varied regionally, being 169.03/100000 pyd in North America, 95.05/100000 pyd in Europe, 95.05/100000 pyd in Asian , 235.12/100000 pyd in Australia and 139.78/100000 pyd in South Africa. The risk for CRC was 0.91% (95% CI 0.63-1.20%) at 10 years, 3.66% (95% 2.42-4.90%) at 20 years, and 12.58% (95% CI 5.92-19.23%) at 30 years after IBD diagnosis. Subgroup analysis by stratifying the studies according to data source,study design and gender of the study did not reveal any significant differences.
Conclusion: Using the meta-analysis we determined the incidence of CRC in IBD patients was 1.17% and the higest incidence rate was found in Australia in 5 continents. UC patients had a higher risk of CRC than CD patients. No matter UC or CD, colon had a higer risk of developing CRC. Hence, adherence to colonoscopy is essential. A larger prospective study is needed to obtain a better incidence of CRC.
Disclosure: Nothing to disclose

P1756 NORMALISATION OF FAECAL CALPROTECTIN WITHIN 12 MONTHS OF DIAGNOSIS IS ASSOCIATED WITH REDUCED LONG-TERM DISEASE PROGRESSION IN CROHN'S DISEASE

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Introduction: Faecal calprotectin (FC) is a reliable surrogate marker of mucosal inflammation in Crohn's disease (CD). Recent data suggest a FC-directed treat-to-target approach results in superior mucosal healing compared to a symptom-based treatment approach.[1] However, it is unknown whether normalisation of FC within the first 12 months of diagnosis improves long-term outcomes in CD.

Aims & Methods: We performed a retrospective cohort study to establish if normalisation of FC within 12 months of diagnosis was correlated with disease progression. Inclusion criteria were: (a) diagnosis of CD between 2009-2017; (b) measurement of FC at diagnosis or +/- 2 months and prior to any initiation of treatment; (c) a FC value ≥250 μg/g at diagnosis; (d) at least 1 additional FC within 12 months after diagnosis; (e) >12 months follow up.
The primary endpoint was a composite of progression in Montreal disease behaviour (B1-B2/3, B2-B3 or new perianal disease), resectional IBD surgery or disease related hospitalisation 12 months post-diagnosis onwards.[2] Normalisation of FC was defined as < 250 μg/g. When >1 FC was performed in the 12 month post-diagnosis period, the last FC was used to determine normalisation. Survival analysis was performed using Kaplan Meier curves and groups compared via the log-rank test. Multivariable Cox-regression analysis was used to determine independent factors associated with disease progression.
Results: A total of 200 patients met inclusion criteria with a median follow up of 4.9 years (IQR 2.9-7.3 years). 46% (92/200) of patients normalised FC within 12 months of diagnosis. Normalisation of FC within the first 12 months of diagnosis was associated with a significantly lower rate of the composite endpoint of disease progression (Table 1, log-rank p< 0.001).
There was no difference in disease characteristics at diagnosis (sex, age, Montreal location/behaviour, perianal disease, smoking status, FC) between patients who normalised FC versus those that did not. FC-normalisation was associated with a higher rate of biologic use (37.0% vs 18.5%, p< 0.001). Correcting for age, sex, disease location / behaviour and FC value at diagnosis; smoking (Hazard Ratio 1.8, 95% CI 1.1-3.0, p=0.03), biologic use within 12 months of diagnosis (Hazard Ratio 2.7, 95% CI 1.6-4.6, p< 0.001) as well as normalisation of FC within 12 months of diagnosis (Hazard Ratio 0.2, 95% CI 0.1-0.4, p< 0.001) were independently associated with disease progression.
Conclusion: This study demonstrates that normalisation of mucosal inflammation in the first year of CD will substantially impact long-term outcomes. The data indicate that FC is an excellent surrogate marker for this purpose and are of immediate clinical utility.

Status at 12 months	Cumulative progression rates after first 12 months from diagnosis		
	1-Year	3-Years	5-Years
FC normalised (<250 μg/g)	7.0%	18.7%	24.4%
FC not normalised (≥250 μg/g)	28.1%	43.2%	63.8%

[Table 1. Cumulative progression rates (composite of progression in Montreal disease behaviour or new peri-anal disease/ surgery/ IBD hospitalisation)]

References: 1.Colombel JF, et al. Effect of tight control management on Crohn's disease (CALM): a multicentre, randomised, controlled phase 3 trial. Lancet. 2017; 390: 2779 - 2789 2.C Yzet, et al. OP35 Endoscopic and deep remission at 1 year prevents disease progression in early Crohn's disease: long-term data from CALM, Journal of Crohn's and Colitis, 2019; 13 (Issue Supplement 1): S024-S025

P1757 DOES CRP LEVEL CAN PREDICT MUCOSAL REMISSION?

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Introduction: Ulcerative colitis is a mucosal inflammatory disease of the colon. Depending on the extent and degree of mucosal involvement there may not be signs of systemic inflammation like high CRP values. Although fecal calprotectin can predict mucosal remission in ulcerative colitis, data about CRP level in this context is insufficient

Aims & Methods: The aim of this study is to define a CRP level to predict mucosal remission in ulcerative colitis. We retrospectively reviewed colonoscopy reports of ulcerative colitis patients (who are not on any steroid treatment) between December 2016 and March 2019 and also their CRP levels which were obtained at the same week of the colonoscopy examination. Mucosal remission was defined as Mayo score 0 or 1 at colonoscopy. The best CRP level for mucosal remission prediction was assesed by ROC curve analysis and also by positive and negative predictive values

Results: A total of 289 patients were involved. CRP levels which predicts mucosal remission is shown at the table. At the ROC curve analysis we found that CRP levels between 2.69-2.78 mg/dl can predict mucosal remission with a 80% sensitivity and specificity. For subgroups with Montreal E2 and E3 ROC curve analysis suggested 2,1 mg/dl (sen. 80%, spe. 80%) and 2,95 mg/dl (sen. 83% , spe. 85%) CRP levels can be used for prediction of mucosal remission respectively

Crp Level mg/dl	Mayo 0-1 group	Mayo 2-3 group
<5	131	61
>5	7	89
Sens: 0,94; Spec: 0,59; PPV: 0,68; NPV: 0,92		
<3	117	30
>3	21	120
Sens: 0,84; Spec: 0,80; PPV: 0,79; NPV: 0,85		
<2	94	20
>2	44	130
Sens: 0,68; Spec: 0,86; PPV: 0,82; NPV: 0,74		

[Table 1. Sensitivity and specificity values for predicting mucosal remission.]

Conclusion: CRP cutoff level of approximately 2.7 mg/dl can predict mucosal remission in ulcerative colitis better than standard cutoff of 5 mg /dl
Disclosure: Nothing to disclose

P1758 FECAL EOSINOPHIL-DERIVED NEUROTOXIN/EOSINOPHIL PROTEIN X (EDN/EPX) SHOWED HIGH SPECIFICITY AND POSITIVE PREDICTIVE VALUE AS A BIOMARKER FOR DETECTING DISEASE ACTIVITY IN INFLAMMATORY BOWEL DISEASE COMPARE TO FAECAL CALPROTECTIN

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Introduction: Colonoscopy with histological analysis with multiple biopsies represents the accepted procedure used to find the diagnosis of patients with chronic diarrhea and to assess disease activity and severity. However, it is invasive and costly. Fecal calprotectin (FC) is used as a biomarker for intestinal inflammation in inflammatory bowel disease (IBD) but there is always a search for new biomarker for microscopic colitis (MC). Moreover, the best biomarker for distinguishing functional from organic intestinal disorders is elucidated. In some studies is demonstrated that, mucosal inflammation in IBD and MC is done by eosinophil activation and this need to be evaluated in future bigger studies.

Aims & Methods: The AIM is to evaluate the diagnostic accuracy of faecal eosinophil-derived neurotoxin/eosinophil protein x (EDN/EPX) and to compare it to FC in patients with chronic diarrhoea. In this prospective study, we enrolled 109 adult patients with chronic diarrhoea who underwent standard laboratory test, CRP, colonoscopy, faecal EDN/EPX and FC at 'Tsaritsa Yoanna - ISUL' University Hospital, Sofia, Bulgaria. We divided the patients into six groups: 30 patients with active IBD, 21 patients with IBD in remission, 21 patients with IBD after surgery (IBD-IL), 23 patients with IBS-D, 14 patients with MC and 11 healthy control subjects. We used ELISA to detect EDN/EPX and quantitative immunochromatographic to evaluate FC.

Results: Of these 109 (90,9%) patients with chronic diarrhea included in the analysis, elevated levels of EDN/EPX above 366 ng/ml was confirmed in 51 patients (46,8%) and lower levels of 58 patients (53,2%) as using cut-off level of disease activity compare to 11 (9,1%) healthy controls (p=0,002). We found a EDN/EPX cut-off level of 366 ng/ml for IBD active group with sensitivity of 80% (95% CI 61.43% to 92.29%), specificity 90,9 % (95% CI 58.72% to 99.77%), negative predictive value 62,5% (95% CI 44,3% to 77,74%) and positive predictive value (PPV) of 96% (78.6% to 99.37%) (p=0,001), compare to FC with sensitivity 78% and specific 72,2%. Mean FC levels among the 6 groups were IBD Active (750 μg/g) vs IBD in remission (81 μg/g) vs IBD after surgery (375 μg/g) vs IBS-D (47 μg/g) vs MC (221 μg/g) vs healthy controls (43 μg/g), respectively (p= 0,002). Mean EDN/EPX levels among the 6 groups were IBD Active (2777 ng/ml) vs IBD in remission (412 μg/g) vs IBD after surgery (1425 μg/g) vs IBS-D (524 μg/g) vs MC (187 μg/g) vs healthy controls (179 μg/g), respectively (p= 0,002). We found correlation between EDN/EPX and FC to be moderate (Pearson's r=0,6, p-value < 0,01). We estimate higher median levels of EPX/EDN in IBD patients with active disease, IBD patients after surgery and lower levels of EPX/EDN in MC group and no difference between IBD in remission and IBS-D group.

Conclusion: EPX/EDN fecal biomarker could be used as surrogate markers for assessing disease activity in IBD patients with active disease and provided additional discrimination from IBD in remission. EDN/EPX showed higher specificity and PPV for detecting disease activity in IBD patients compared with FC. Combination of EDN/EPX and FC should be used for identifying patients with active IBD and they could possibly be used as biomarkers for differentiating IBD and MC from IBS-D or healthy subjects with high diagnostic accuracy. Both EDN/EPX and FC can be used as a screening and monitoring surrogate markers for non-invasive disease activity. Furthermore, bigger studies are needed to establish the efficacy of EDN/EPX.

References: 1. Wagner M, Sjöberg K, Vigren L, Olesen M, Benoni C, Toth E, et al. Elevated fecal levels of eosinophil granule proteins predict collagenous colitis in patients referred to colonoscopy due to chronic non-bloody diarrhea. Scand J Gastroenterol . 2016 Jul 2;51(7):835-41. \ 2. Pisani LF, Tontini GE, Marinoni B, Villanacci V, Bruni B, Vecchi M, et al. Biomark-

ers and Microscopic Colitis: An Unmet Need in Clinical Practice. Front Med. 2017 May 10;4(May):54. 3. Wagner M, Peterson CGB, Stolt I, Sangfelt P, Agnarsdottir M, Lampinen M, et al. Fecal eosinophil cationic protein as a marker of active disease and treatment outcome in collagenous colitis: A pilot study. Scand J Gastroenterol . 2011 Jul 11;46(7-8):849-54. 4. von Arnim U, Wex T, Ganzert C, Malfertheiner P, Schulz C. Fecal calprotectin: a marker for clinical differentiation of microscopic colitis and irritable bowel syndrome. Clin Exp Gastroenterol . 2016 Apr;9(1):97.

Disclosure: Nothing to disclose

P1759 BONE MINERAL METABOLISM IN INFLAMMATORY BOWEL DISEASE: A CROSS-SECTIONAL STUDY

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Introduction: Crohn's disease (CD) and ulcerative colitis (UC) are the main forms of inflammatory bowel disease (IBD), chronic relapsing-remitting inflammatory conditions of uncertain origin affecting the gastrointestinal tract. Vitamin D plays a key role in gut immunity and maintenance of the mucosal barrier and also may be a predictive factor of bone mineralisation.
Aims & Methods: The objective of our study was to determine the prevalence of vitamin D deficiency and the levels of biochemical markers of bone mineral metabolism in patients with IBD. A total of 87 patients with IBD were included. Serum calcium, albumin, phosphorus, parathyroid hormone, 25-hydroxyvitamin D (25-OHD), Beta-crosslaps (CTX), osteocalcine and urine phosphorus levels were evaluated.
Results: 57 patients with CD (32% were women) and 30 patients with UC (55% women) were enrolled in the study. The mean calcium level was 2,32 ±0,13 mmol/L in CD patients and 2,31±0,34 mmol/L in UC patients. Albumin level was 4,14±0,52 g/dL in CD and 4,26±0,45 in UC group. Interestingly 21% of UC patients and 5% of CD had hypophosphatemia (p< 0,05). Mean phosphorus in urine was 59,6±48,1mg/dL in CD and 44,6±36,1 mg/dL in UC patients (p=0,179). Deficiency of 25-OHD was very high, with a prevalence of 86% in patients with UC and 83% in patients with CD. Hyperparathyroidism, defined as a parathyroid hormone level >56,9 pg/mL was present in 18% of patients with CD and 14% of patients with UC. Whatmore CTX was elevated in 22% of CD patients and 40% of UC. Mean osteocalcin level in CD was 23,12±9,8 and 20,74±11 in UC patients. No significant differences were observed between CD and UC (p=0,865 for PTH; p=0,140 for CTX and p=0,891 osteocalcin).
Conclusion: Bone mineral metabolism disorders were common in UC and CD patients. Hypophosphatemia and bone turnover markers were more frequent in CU group. Vitamin D deficiency was likely to occur in IBD patients, therefore it should be monitored and supplemented to avoid bone damage.
Disclosure: Nothing to disclose

P1760 VITAMIN D DEFICIENCY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE IS ASSOCIATED WITH INCREASED DISEASE ACTIVITY

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Introduction: Vitamin D has an inhibitory role in the inflammatory signaling pathways and supports the integrity of the intestinal barrier. Due to its immunomodulatory effect, vitamin D appears to play a role in the course of chronic inflammatory bowel disease (IBD) and a corresponding deficiency is associated with an increased risk of a flare.
Aims & Methods: The aim of this study was to investigate to what extent the 25(OH)D3 level correlates with clinical and laboratory parameters of disease activity and whether a cut-off value for prediction of remission could be defined.Patients with IBD treated in the outpatient department of the University Hospital Frankfurt were included and analyzed retrospectively. The 25(OH)D3 levels were measured and correlated with clinical and laboratory chemical activity parameters. Vitamin D deficiency was defined as 25(OH)D3 levels < 30 ng/ml.

Results: A total of 481 (218 male,45.5%) patients with IBD were included, 274 (58.1%) with Crohn's disease (CD), 198 (41.9%) with ulcerative colitis (UC). The median age of the patients was 41.65 (17-84). In 294 patients (61%) a vitamin D deficiency was detected. CD patients had significantly more vitamin D deficiency than UC patients (p= 0.04). 217 (46.6%) patients received oral vitamin D substitution. However,165 of these patients (76%) still had a relevant vitamin D deficiency. In the logistic regression analysis of the HBI (Harvey Bradshaw Index) in CD patients was inversely associated with the 25(OH)D3 serum concentration. A 25(OH)D3 serum concentration of 27.5 ng/mL seems to be the optimal cut-off value to predict remission in our cohort.
Conclusion: In our study, vitamin D levels were inversely associated with disease activity. Thus, especially in high-risk patients, close monitoring should be established in clinical routine and, if necessary, optimized substitution should be considered.
Disclosure: Nothing to disclose

P1761 MMP-2 AND -8 DEGRADED AND CITRULLINATED-VIMENTIN (VICM) CORRELATES TO DISEASE ACTIVITY IN INFLAMMATORY BOWEL DISEASES

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Introduction: Vimentin is a type III intermediate filament protein that stabilises cell architecture, but might be more active involved in intestinal inflammation during Crohn's disease (CD) and ulcerative colitis (UC). In lamina propria vimentin is found in mesenchymal cells like fibroblast and myofibroblasts, but are also produced by activated macrophages in inflammatory diseases. Protein fragments from vimentin turnover can be measured by competitive enzyme-linked immunosorbent assay (ELISA) targeting MMP-2 and -8 degraded and citrullinated-vimentin (VICM) and thereby maybe act as aserological biomarker of intestinal inflammation.
Aims & Methods: The aim of this study is to evaluate how VICM correlates to clinical and endoscopic disease activity in CD and UC.We included 63 CD patients, 107 UC patients and 20 healthy controls in a prospective study aimed at biomarker evaluation. 35% (n=24) of CD patients and 49% (n=52) of UC patients with active disease. We recorded Harvey-Bradshaw Index (HBI) or Simple Clinical Colitis Activity Index (SCCAI), and measured VICM, C-reactive protein (CRP) and faecal calprotectin (FC). 17 CD and 63 UC patients were evaluated with sigmoidoscopy or colonoscopy from where we recorded Simple Endoscopic Score for Crohn's disease (SES-CD) or Endoscopic Mayo Score.
Results: VICM was significantly elevated in CD and UC patients compared to healthy controls (p=0.0001). VICM correlated positively to SES-CD, SCCAI and Endoscopic Mayo Score and, and had a tendency to correlate to HBI VICM had a stronger correlation to the endoscopic scores than CRP but not as strong a correlation as FC.
Conclusion: VICM is significantly elevated in IBD patients in remission and IBD patients with active disease compared to healthy controls. Furthermore, VICM correlates significantly to endoscopic disease activity in CD, to clinical and endoscopic activity in UC, and have a tendency to correlate to clinical disease activity in CD. VICM correlates more to the endoscopic scores compared to CRP This might reflect the fact that VICM is produced locally in the inflamed gut, whereas CRP is a systemic inflammation marker produced in the liver. VICM might act as a serological biomarker of inflammation in the intestinal wall in IBD.
Disclosure: ML, JHM, MAK, and TMJ are full time employees at Nordic Bioscience. MAK and TMJ hold stocks in Nordic Bioscience.

P1762 FECAL SHORT-CHAIN FATTY ACIDS IN INFLAMMATORY BOWEL DISEASES PATIENTS

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Introduction: Short-chain fatty acids (SCFA) play an important role in maintaining colon homeostasis, provide optimal levels of acidity and are probably involved in the pathogenesis of various bowel diseases.

Aims & Methods: The aim of the study was to determine the level of fecal SCFA in patients with ulcerative colitis (UC) and Crohn's disease (CD). Seventy seven IBD patients, including 42 UC and 35 CD patients were included into the study. The control group consisted of 42 healthy volunteers. Determination of fecal SCFA in IBD patients and control group volunteers was carried out by gas-liquid chromatographic analysis.

Results: In our study, the ratio of major SCFA was as follows: in the control group - C2 (68.5%), C3 (11.8%), C4 (19.7%), in the group of CD patients - C2 (62.2%), C3 (17.4%), C4 (20.4%), in UC patients - C2 (63%), C3 (18%), C4 (19%). The C2-C4 profile showed an increase of the relative content of propionic acid in CD - (0.16±0.07 units) and UC patients - (0.16±0.07 units), compared to the control group - (0.13±0.03 units), p=0.0188, p=0.0079, respectively, with the unchanged relative content of acetic and butyric acids. However, UC and CD patients showed a decrease in the absolute content of acetic acid - (3.07±2.02 and 3.65±2.75 mg/g) and butyric acid - (0.93±0.81 and 1.20±1.15 mg/g) compared to the control group - (6.32±4.81 and 1.82±1.56 mg/g, respectively), p< 0.05. Besides we found that CD and UC patients had reduced absolute content of isobutyric (IC4) - (0.20±0.23) mg/g, (0.18±0.18) mg/g and isovaleric (IC5) acids - (0.25±0.23) mg/g, (0.23±0.26) mg/g, as well as isocaproic acid (IC6) level was decreased in UC patients- (0.011±0.016) mg/g compared to the control group - (0.33±0.34) , mg/g for IC4, (0.41±0.39) mg/g for IC5, (0.006±0.018) mg/g for IC6, p< 0.05. The sum of all SCFA (C2+C3+C4+C5+C6+IC4+IC5+IC6) was lower in UC - (5.51±3.89) mg/g and CD patients - (6.58±5.08) mg/g compared to the control group - (10.35±7.7) mg/g, p=0.0018, p=0.0194. There was also a tendency to the shift of the anaerobic index to a more negative side in UC (-0.56±0.24) u. and CD patients - (-0.55±0.26) u , compared to the control group - (-0.47±0.18) u.

Conclusion: Reduced absolute content of butyric acid in IBD patients allows to suppose the presence of the link between decreased butyrate level and gut inflammation. A shift in the anaerobic index to a more negative side indicates the activation of opportunistic bacteria in IBD patients. A decrease in the absolute content of particular SCFA and their total number in IBD patients may indicate the inhibition of functional activity and the number of anaerobic microbiota and/or an increase of the SCFA utilization by colonocytes.

Disclosure: Nothing to disclose

P1763 FECAL EOSINOPHIL CATIONIC PROTEIN IS A DIAGNOSTIC AND PREDICTIVE BIOMARKER IN YOUNG ADULTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Fecal biomarkers are important non-invasive means for the diagnosis, measurement of disease activity and evaluation of treatment efficiency in inflammatory bowel disease (IBD), but endoscopy remains the gold standard for the diagnosis and determination of state of inflammation and disease activity in inflammatory bowel disease (IBD).

Aims & Methods: Here, we evaluate the significance of fecal Eosinophil Cationic Protein (fECP) and compare it to the most studied fecal biomarker calprotectin (fCal). fECP and fCal were analyzed in fecal samples of patients with Crohn's disease (CD, n = 144), Ulcerative colitis (UC, n = 70), clostridium difficile infection (CDI, n = 9), primary food allergy (PFA, n = 11), secondary pollen-associated food allergy (SFA, n = 25) and non-inflammatory controls (total n = 78; healthy controls n = 37; disease controls n = 13; irritable bowel syndrome n = 28). In IBD patients, results were correlated with serum CRP and both clinical and endoscopic activity scores. Endoscopy was performed in 83 IBD patients (CD n = 42; UC n = 41).

Results: Compared to controls, fECP was significantly elevated in CD, UC, CDI and PFA. fCal was increased in CD, UC and CDI, but not PFA. fECP correlated with disease activity markers in IBD patients; however, ROC analyses shows a lower diagnostic accuracy to differentiate between endoscopically active and inactive IBD patients (AUC = 0.77) than for fCal (AUC = 0.88). In contrast to fCal, fECP correlated negatively with age. fECP elevation in IBD patients below the age of 45 years was independent of clinical and endoscopic activity (endoscopically inactive IBD vs controls; AUC for fECP = 0.86; AUC for fCal = 0.62). Furthermore, in IBD patients < 45 years and low inflammatory activity (fCal < 250 mg/kg), fECP is a prognostic marker indicating the necessity of change of treatment or surgery (fECP < 200 μg/kg = 22 %; 200 - 600 μg/kg = 44 %; > 600 μg/kg = 82 % at month 48 of follow-up).

Conclusion: fECP could serve as a diagnostic marker and indicates disease progression in young IBD patients in remission.

Disclosure: Nothing to disclose

P1764 IL-33/ST2 LEVELS AND GUT MICROBIOTA CHARACTERIZATION CAN PREDICT MUCOSAL RESPONSE TO ANTI-TNF THERAPY IN ULCERATIVE COLITIS

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Introduction: It is now well-established that IL-33/ST2 axis and gut microbiota are important factors in the pathogenesis of IBD with a potential reciprocal influence. Recent evidence has shown that tumor necrosis factor

(TNF) inhibitors (anti-TNF) are able to modulate the IL-33/ST2 axis as well as gut microbiota in inflammatory conditions. Anti-TNF are considered to be effective in inducing mucosal healing in patients with moderate-to-severe Ulcerative Colitis (UC).

Aims & Methods: The aim of our study was to explore the potential role of the IL-33/ST2 axis and gut microbiota in the mucosal healing process mediated by anti-TNF therapy in UC. Endoscopic MAYO score was calculated before the first anti-TNF infusion (T0) and after 6 weeks (T2). 26 UC patients (MAYO score at T0 ≥ 2), grouped into 14 responders with mucosal healing (MAYO score ≤ 1) and 12 non-responders to anti-TNF at T2 (MAYO score ≥ 2) were enrolled. 10 healthy controls undergoing routine colonoscopy for tumor screening were also enrolled. At each time point, serum and fecal samples were collected. ELISA and western blot were performed to assess IL-33/ST2 protein levels and to evaluate protein isoforms, respectively. Intestinal biopsies were also taken from the rectum and IHC was done to evaluate mucosal IL-33/ST2 expression and localization. Genomic DNA was extracted from fecal samples and V3-V4 regions of the 16S rRNA gene were sequenced by MiSeq Illumina platform for microbiota characterization.

Results: IL-33 protein levels were significantly increased in responders *vs.* non-responders, both at T0 and T2. Among responders, IL-33 protein was slightly reduced at T2 vs. T0, while unchanged in non-responders. Interestingly, significantly higher levels of ST2 were found in responders *vs.* non-responders at T0, while no differences between groups were found at T2. Among responders, ST2 levels were dramatically reduced at T2 *vs.* T0. No significant differences were found in non-responders at both time points. Healthy controls showed significantly lower levels of both IL-33 and ST2 compared with other groups. Full-length, bioactive IL33 (31 kDa), ST2L (76 kDa) and sST2 (52 kDa) were expressed in all experimental groups; the cleaved, less active form of IL33 (24 kDa) was increased in only non-responders vs. responders and healthy controls.

IHC confirmed these observations. In particular, IL-33 and ST2 staining was more intense within the inflamed and ulcerated mucosa of responders compared to non-responders at T0. After 6 weeks, ST2 staining was even more evident in responders, notably localized to the healed mucosa and in close proximity to areas of re-epithelialization. Little to no staining for both IL-33 and ST2 was present in healthy controls. Microbiota analysis showed an increased biodiversity at T0 in responders vs. non-responders. At T0, non responders showed lower levels of Verrucomicrobia (Akkermansia municiphila) and Firmicutes, with an increased abundance of Bacteroidetes vs. responders.

Conclusion: Our results suggest a possible role for IL-33/ST2 and gut microbiota in predicting gut mucosal wound healing in patients with moderate-to-severe UC treated with anti-TNF. IL-33/ST2 axis and gut microbiota could thus represent a useful diagnostic tool to evaluate therapeutical options in IBD patients. Further studies are underway to determine mechanisms of action that support these findings.

Disclosure: Nothing to disclose

P1765 IMMUNOMODULATOR AND BIOLOGICAL THERAPY ARE INCREASED IN INFLAMATORY BOWEL DISEASE PATIENTS WITH ASSOCIATED IMMUNO-MEDIATED INFLAMMATORY DISEASES

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Introduction: Immune mediated diseases (IMIDs) include a heterogenous group of chronic diseases that are characterized by the loss of the immune system tolerance causing inflammation and tissue damage in different organs. Inflammatory bowel diseases (IBD) belong to IMIDs group together with other autoimme diseases. Literature data showed a IMIDs prevalence of 9-15% in IBD, depending of the region studied.

Aims & Methods: The aim of our study is to describe the prevalence and influence of IMIDs in IBD.

A retrospective and descriptive study was designed to evaluate the influence of IMIDs in IBD. 1448 IBD patients were studied to evaluate the different clinical characteristics and evolution course of the disease depending on the associated IMIDs.

Results: We included 1448 patients of whom 46.96% (n=680) were diagnosed with Crohn's Disease, 48.34% (n=700) with Ulcerative Colitis and 4.7% (n=68) with IBD Unclassified. A IMIDs prevalence of 25.69% was present in IBD patients compared to 74.31% (n=1076) of IBD patients without IMIDs. The most prevalent IMIDs were intrinsic ashma and skin psoriasis following rheumatoid conditions. An increased risk of IMIDs was observed in IBD women (OR 1.48 (IC 95%: 1.17 - 1.87) p=0.001). Furthemore, more proportion of IMIDs patients was observed in Crohn's Disease compared to Ulcerative Colitis (OR 1.35 (IC 95%1.07-1.70) p=0.02). It is important to highligh that IMIDs required more immunomodulator (OR 1.61 (IC 95%: 1.27 -2.03) p=< 0,01) and biological therapy (OR 1.89 (IC 95%: 1.47 -2.43) p= < 0,01).

Conclusion:
1. There is an increased IMIDs prevalence in IBD patients.
2. Crohn's Disease patients and women have a higher risk of associated IMIDs to their IBD.
3. IBD patients with associated IMIDs require more immunomodulator therapy or biological therapy to control their disease , probably caused by a more aggressive course of IBD.
4. More studies are necessary to increase the knowledge in IBD patients with associated IMIDs.

	IBD with IMIDs associated (%, n)	IBD without IMIDs (%, n)	OR (IC)	p
Gender: men	44.64% (168)	52.34%	1.48 (1.17 - 1.87)	0.001*
Type of Disease: Crohn's Disease	52.21% (201)	45.06% (478)	1.35 (1.07-1.70)	0.026*
Immunomodulator Therapy: yes	48.31% (186)	36.78% (391)	1.61 (1.27 - 2.03)	<0.000*
Biological Therapy: yes	36.36 % (140)	23.24% (247)	0.89 (1.47 - 2.43)	<0.000*
Surgery: yes	21.04%(81)	19.59% (208)	1.1 (0.82 - 1.46)	0.536

[Odss ratio of clinical characteristics and therapy.]

Disclosure: MJG; MP, CDP, LR and BC have no conflict of interest to declare. MR has served as a speaker and advisory member for Abbvie, MSD and Janssen. JC is a consultant of Abbvie, Gilead, MSD and Intercept. Also JC obtained grants of aforementioned companies.

P1766 NUTRITIONAL HABITS AND INFLUENCE OF BODY MASS INDEX IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Prevalence of overweight and obesity is increasing worldwide, as well as of Inflammatory Bowel Disease (IBD). However, there is lack of evidence about the nutritional habits of patients with IBD and also about the relationship between the course of the disease and the body mass index (BMI).

Aims & Methods:
1) To determine the healthy and nutritional habits of patients with IBD and their adherence to Mediterranean diet (MD).
2) To analyze the course of the disease, regimens of treatment and quality of life depending on body mass index (BMI).

We performed a prospective cohort study that included consecutive patients with IBD attending our adult IBD clinic in a one-month period. Demographic characteristics and disease related factors were obtained from Spanish ENEIDA database. Health-related quality of life was measured using the disease-specific Inflammatory Bowel Disease Questionnaire (IBDQ-9)[1] and anxiety and depression were estimated by the Goldberg Anxiety and Depression Scale (GADS). Adherence to MD was evaluated using the 14-point Mediterranean Diet Adherence Screener from PREDIMED study[2]. The variables were analyzed depending on the BMI (underweight ≤ 18.4, normal 18.5-24.9, overweight 25-29.9, obesity ≥ 30). Statistical analysis was performed using SPSS version 22.0.

Results: A total of 104 patients were included in our study. Mean age was 47.0±14.4 years and 56.7% of patients (59/ 104) were females); 53.8% (56/104) of patients had ulcerative colitis and 46.2% (48/104) Crohn's disease. More than half of patients were diagnosed of overweight (41.3% (43/104)) or obesity (15.4% (16/104)) with a significantly increase in BMI as age does (mean age 41.6±14.7 years in normal-underweight, 49.7±12.3 years in overweight and, 55.1±13.2 years in obesity; p=0.001). There were more former smokers in the group of obese and overweight patients than in normal-underweight ones (62.5% (10/16), 55.8% (24/43), 33.3% (15/45), respectively, p=0.034). Since IBD diagnosis, 42.3% (44/104) of patients have modified their diet with weight changes in 61.4% (27/44) of them (55.6% (15/27) of patients lost weight and 44.4% (12/27) gained weight). No statistically significant differences were observed between the physical activity and the BMI (p=0.269).

47.1% (49/104) of patients had a good adherence to MD, decreasing adherence as the BMI increases, but without reaching statistical significance (55.6% (25/45), 41.9% 18/43) and 37.5%(6/16) in normal-underweight, overweight and obese; respectively, p=0.308).

There were no significant differences neither in the disease related factors (type, location, extension, activity of the disease, extraintestinal manifestations or complications) nor in the IBD treatments depending on BMI.

Concerning quality of life, the mean mark in the IBDQ-9 questionnaire was 44.8±10 (equivalent to 61.5 in the 0-100 scale) without significantly differences between BMI groups. More than half percent of patients (59.6% (62/104)) had probably depression based on Golberg questionnaire.

Conclusion: Nearly 50% of patients modify their diet after the diagnosis of IBD and there is a low adherence to MD, specially in those with obesity. No differences were shown in the course of IBD, treatment and outcomes depending on BMI. A high number of patients have probably depression and quality of life could be improved.

References: (1): Alcala MJ, Casellas F, Fontanet G, Prieto L, Malagelada JR. Shortened questionnaire on quality of life for inflammatory bowel disease. Inflamm Bowel Dis 2004;10:383-91. (2): Estruch R, Ros E, Salas-Salvadó J, Covas MI, Corella D, Arós F et al. Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. N Engl J Med. 2018 Jun 21;378(25)

Disclosure: Nothing to disclose

P1767 CROHN'S DISEASE, ARTHRITIS AND INFLAMMATORY BACK PAIN ARE ASSOCIATED WITH A HIGHER CHANCE OF AXIAL SPONDYLOARTHRITIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Spondyloarthritis (SpA) is one of the most common extraintestinal manifestations (EIM) of Inflammatory bowel diseases (IBD). The diagnosis of SpA in patients with IBD is challenging, treatment strategy should be often revised when IBD and SpA coexist.

Aims & Methods: The aim of the study is to evaluate factors associated with higher risk of axial SpA in patients with IBD. The single-center observational cross-sectional study included patients with a definite diagnosis of IBD and chronic back pain (duration > 3 months). Inflammatory Back Pain (IBP) was determined according to ASAS criteria (2009). If suspected with SpA, patients underwent X-ray and/or MRI of sacroiliac joints. SpA was diagnosed according to ECCO recommendations. All patients diagnosed with SpA also fulfilled ASAS criteria for axial SpA. Univariate and multivariate logistic regression analysis was performed to assess the factors associated with higher risk of being diagnosed with axial SpA.

Results: The study included 91 patients (males – 47 (51.6%), mean age – 40.2±11.7 years, duration of IBD – 7.7±7.6 years) with IBD: 52 (57.1%) with ulcerative colitis (UC), 39 (42.9%) with Crohn's disease (CD). IBP was present in 39 (42.9%) patients with IBD, 26 (28.6%) patients were diagnosed with axial SpA, among them 14 (15.4%) patients with radiographic axial SpA. In the univariate logistic regression model, 4 factors were associated with a higher chance of SpA diagnosis: presence of arthritis, arthralgia, CD and IBP. The associations remained statistically significant when mul-

tivariate logistic regression model was constructed (Table 1). In particular, patients with CD had higher chance of being diagnosed with axial SpA compared with UC 3.51 (1.04-11.82).

Parameter	Univariate analysis, OR (95% CI)	Multivariate analysis; OR (95% CI)
Male sex	0.57 (0.23-1.44)	
HLA-B27	4.00 (0.55-29.17)	
Smoking	0.91 (0.26-3.25)	
Arthritis	10.77 (2.26-44.2)	20.03 (3.05-131.69)
Crohn's Disease	2.92 (1.14-7.48)	3.51 (1.04-11.82)
Arthralgia	4.12 (1.55-10.95)	
Inflammatory back pain	8.07 (2.8-23.23)	16.41 (3.99-67.34)

[Table 1. Factors associated with a higher chance of axial spondyloarthritis]

Conclusion: Presence of CD was associated with higher chance of being diagnosed with axial SpA compared to UC. Arthritis, arthralgia and IBP were also associated with a higher chance of axial SpA diagnosis.

Disclosure: Nothing to disclose

P1768 DOES HISTOLOGICAL REMISSION (NANCY INDEX) PREDICT RELAPSE-FREE SURVIVAL IN PATIENTS WITH ULCERATIVE COLITIS IN ENDOSCOPIC REMISSION?

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Introduction: During the last decades, treatment goals in patients with ulcerative colitis (UC) have shifted from clinical remission only to clinical remission combined with mucosal healing. However, yet, the value of achieving histological remission remains unclear.

Aims & Methods:

Aim: To examine whether histological healing could be a predictor of sustained remission in UC patients with mucosal healing and to investigate risk factors for relapse.

Methods: This was a retrospective monocentric study conducted in the Departments of Gastroenterology and Pathology of Mohamed Taher Maamouri Hospital , between January 2012 to December 2018. Patients diagnosed with UC who had been in clinical remission for at least 6 months were evaluated for endoscopic remission. Those in endoscopic remission (Mayo score ≤1) underwent colonic biopsies. Histological findings were analyzed according to Nancy index. Histological remission was defined as a Nancy index of 0 or 1. Clinical demographics including age, sex, smoking status, history of appendectomy, disease extent and use of medications were collected.

Results: Sixty one patients had a sustained clinical remission with a duration ranged from 9 months to 25 years. Of these 61 patients, 28 were in endoscopic remission, 18 were female with a median age of 50.82 years. Medical therapy included 5-aminosalicylic acid (78.6%) and immunosuppressive treatments(21.4%). According to the affected areas, proctitis type accounted for 21.4% of the patients , left-sided type for 21.4% , and pancolitis type for 57.1% . Histological remission was noted in 60.7% (17/28) of the patients, while 11 (39.1%) patients still had histologically active disease. The remission maintenance rate was higher in the histological healing group, without reaching statistical significance (88,3% VS 45,5% ,p=0.2). Histological remission did not depend on the disease duration (p=0.5) . Endoscopic findings were graded as Mayo score 0 in 57.1% of the patients (n=16) and 1 in 33, 9% (n=12).The remission maintenance rate was higher in the Mayo score 0 group (p=0.04). Others factors as :age, gender, and duration of clinical remission were not found to be statistically significant in predicting relapse.

Conclusion: In our study histological remission failed to reach statistical significance to predict relapse but it showed that patients with Mayo score 1 may need examination of histological inflammation to improve UC patients outcomes.

Disclosure: Nothing to disclose

P1769 COST-UTILITY ANALYSIS OF MRI AND CT IN RADIATION-INDUCED NEOPLASMS IN INFLAMMATORY BOWEL DISEASE

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Introduction: Given the chronic nature of IBD, frequent imaging with CT and MRI is often used to assess disease activity and complications. The advantages of CT scans include greater accessibility, lower cost and better spatial resolution. However, its major disadvantage is ionizing radiation. On the other hand, MRIs do not contain ionizing radiation and have improved soft tissue resolution, but are costlier, more time-intensive and are less accessible. Currently, CT scans are used more commonly in the management of IBD, despite recent studies demonstrating similar sensitivity and specificity in the two imaging modalities. This is of importance, given that the lifetime attributable risk of neoplasm and mortality related to radiation is directly related to the cumulative radiation exposure. As a result, a Markov model was created to ascertain the cost utility of utilizing MRI rather than CT in preventing radiation-induced neoplasms in patients with inflammatory bowel disease.

Aims & Methods: A provincial (Ontario) database of 72 933 IBD patients from 1999-2016 was examined. Quarterly rates of CT/MRI utilization were extrapolated from this database. The lifetime attributable risk of malignancy related to radiation was taken from the BEIR VII study from the National Academies Press (2006). Cost considerations for MRI/CT were taken from the American College of Radiology and mortality rates were taken from Statistics Canada. A hypothetical population of patients aged 40 was examined over a 30 year period. An analysis was conducted with Markov modeling to examine whether use of MRIs rather than CTs was cost effective with regards to increased health utility from reduced rates of malignancy and malignancy-related death in IBD patients.

Results: In the female group, the aggregate cost of CT and MRI scans was $7291.05 and $11023.88, respectively. This represents a $3732.84 cost difference. The total QALY in the MRI group compared to the CT group was 29.32 and 29.27, respectively. This represents a difference of 0.049 QALY, and an ICER of $75782.53/QALY. A sensitivity analysis was conducted in this group and demonstrated that the ICER was < $100000/QALY after 26 years, and < $50000/QALY after 35 years. In the male group, the total cost of CT and MRI scans was $7257.22 and $10971.06, respectively. There was a cost difference of $3713.84. The total QALY in the MRI group compared to the CT group was 29.11 and 29.08, respectively. This represents a 0.036 QALY difference, and an ICER of $102473.35/QALY. A sensitivity analysis demonstrated that the ICER was < $100000/QALY after 31 years and < $50000/QALY after 39 years.

Conclusion: A hypothetical Markov model was constructed to evaluate the cost-effectiveness of using MRIs rather than CTs in IBD patients, given the increased health utility from reduced rates of malignancy and malignancy-related death. In our analyses, use of MRIs was cost-effective to CTs in females and males after 26 and 31 years of imaging, respectively, starting at the age of 40. As a result, there may be a role in using MRIs over CT scans in patient populations requiring frequent imaging given the cost-effectiveness of the intervention.

Disclosure: Nothing to disclose

P1770 FECAL CALPROTECTIN AND FECAL IMMUNOCHEMICAL TEST HAVE DIFFERENT VALUES DEPENDING ON MUCOSAL STATUS IN PATIENTS WITH ULCERATIVE COLITIS

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Introduction: Although fecal calprotectin (Fcal) and fecal immunochemical test (FIT) have been to be associated with endoscopic disease activity in ulcerative colitis (UC), the values of each marker depending on the mucosal status are not well known.

Aims & Methods: This study evaluated the differences between two fecal markers depending on the mucosal status in UC. A total of 174 results, obtained in simultaneous examination with endoscopy and fecal tests, were retrospectively evaluated for 127 UC patients from March 2015 to February 2018. The usefulness of fecal markers as a surrogate marker of endoscopic disease activity and the difference between fecal markers depending on the mucosal status was statistically evaluated. Endoscopic disease activity was divided into Mayo endoscopic subscore (MES) and ulcerative colitis endoscopic index of severity (UCEIS).

Results: Both fecal markers showed statistically significant correlation with MES (r = 0.678 for Fcal ($p < 0.001$) and r = 0.635 for FIT ($p < 0.001$)) and UCEIS (r = 0.711 for Fcal ($p < 0.001$) and r = 0.657 for FIT ($p < 0.001$)). Fcal was significantly superior to FIT in predictive accuracy for endoscopic disease activity (AUC; 0.863 versus 0.765 in MES ($p < 0.001$) and AUC; 0.847 versus 0.757 in UCEIS ($p < 0.001$). FIT was significantly superior to Fcal in sensitivity for complete mucosal healing (98.0% versus 78.4% in MES, 94.9% versus 74.6% in UCEIS).

Conclusion: Both Fcal and FIT were well correlated with endoscopic disease activity in UC patients. Fcal was more accurate correlation with endoscopic disease activity in patients with active inflammation, while FIT was more sensitive in predicting the achievement of complete mucosal healing.

Disclosure: Nothing to disclose

P1771 THE VARIATION OF FAECAL CALPROTECTIN LEVEL WITHIN THE FIRST MONTHS AFTER BOWEL RESECTION IS PREDICTIVE OF ENDOSCOPIC POSTOPERATIVE RECURRENCE IN PATIENTS WITH CROHN'S DISEASE

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Introduction: Early detection of postoperative recurrence (POR) remains a major concern in patients with Crohn disease (CD).

Aims & Methods: We aimed to assess the performances of serial faecal calprotectin monitoring within the three first months following ileocolonic resection to predict CD endoscopic POR at 6 months.

In this multicenter prospective study, all the patients with CD who underwent ileocolonic resection were consecutively enrolled. Stools samples were collected at baseline, at one month (M1) and M3 to measure faecal calprotectin level. The stools samples were collected in the morning the day before the endoscopy to reduce intraindividual variation, and immediately stored at 4 °C. Faecal calprotectin was measured using quantitative immunoassay . Ileocolonoscopy was performed at M6. The endoscopic severity was graded independently according to the Rutgeerts' index by two experienced central readers, blinded from clinical or biological data. Endoscopic POR was defined as Rutgeerts' index ≥ i2b.

Results: Overall, 48 patients were included. Among them, 18 patients (36%) presented with endoscopic POR (Rutgeerts score ≥ i2b) 6 months after surgery. We did not observe any significant difference between patients with or without early endoscopic POR (M6), respectively, regarding the level of faecal calprotectin at baseline (100[50-190] vs 166 [89-312] µg/g; p=0.15), at M1 (93 [48-104] vs 100 [50-180] µg/g; p=0.44) and at M3 (100 [68-328] vs 99 [50-100] µg/g; p=0.28). Faecal calprotectin kinetics during the first three months after surgery was significantly different between the patients with or without POR at M6 (p=0.021). The relative variation (median) between the level of faecal calprotectin at baseline and M3 (ΔFcal M3-M0) was significantly higher in patients with endoscopic POR +60% IQR[- 47%; + 217%] compared to those without POR - 38% IQR[- 64%; 0%] (p=0.01). ΔFcal M3-M0 > +10 % demonstrated the best performances to predict endoscopic POR at M6 (AUC=0.73, sensitivity = 64.7% CI[41.1-82.7], specificity = 87.5% CI[68.0-96.3], negative predictive value = 77.8% CI[57.5-91.4] and positive predictive value = 78.6% CI[49.2-95.3]).

Conclusion: Faecal calprotectin variation within the first months after ileocolonic resection is an accurate predictor of early endoscopic POR in CD patients.

Disclosure: Nothing to disclose

P1772 CUTTING EDGE TECHNOLOGIES PIMS MOLECULAR FINGERPRINT AND NPOT MOLECULAR NETWORK IN DETERMINATION OF RESPONSE TO VEDOLIZUMAB IN A PROSPECTIVE TREATMENT OF ULCERATIVE COLITIS (UC) AND CROHN`S DISEASE (CD)

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Introduction: The complexity of underlying pathophysiology of IBD and the difficulty to understand the relevance of, "-omics" have prompted us to asses alternative approaches and technologies. Physiological intermolecular modulation spectroscopy (PIMS), and nematic protein organization technic (NPOT) two cutting edge label free technologies that have been used to reconcile these "omics" with the clinical relevance. PIMS, stratifies patients to responder and non-responder in regard to a treatment. NPOT identifies the functional molecular network in responder patients, thus paving the way to identify success biomarkers.

We have therefore in a prospective study used PIMS and NPOT to predict responder IBD patients prone to be treated with Vedolizumab and isolated their underling functional molecular network.

Aims & Methods: In a prospective clinical study, protein extracts of peripheral blood mononuclear cells (PBMC) of 31 outpatients (female = 17, mean age= 55.6 years and men=14, mean age=41.7) diagnosed with UC or CD (UC=13, CD= 18) prone to be treated with Vedolizumab were subjected to PIMS analysis.

PIMS analysis were performed blinded on isolated PBMCs from 4 different treatment period (week 0, 2, 6 and 14). Patient's data were blinded. One microgram of total protein from each patient's PBMC was challenged with 1μM of Vedolizumab.

After determination of base line, the samples were frozen at -17°C. Dynamic changes in macromolecular interaction were registered from -17 to 5°C. After deblinding IBD patients from each group of responder (n=3) and non-responder (n=3) were subjected to Nematic protein Organization technique (NPOT) in order to identify the signaling pathways in both group respectively.

Results: PIMS predictions were in accordance with clinical response to Vedolizumab from treatment on set (week 0) to last treatment (week 14) as follow 14 CD 77-92% and UC, 78-100% respectively. NPOT revealed the presence of proteins ITGB7, ITGAV, ITG3, PF-4 and ASGH in Vedolizumab responder patients whereas no distinct signaling pathway was observed in non-responder patients.

Conclusion: PIMS could predict responder from non-responder and NPOT highlighted the signaling pathway required for positive clinical response to Vedolizumab. The combination of these two technologies can pave the way in identification of success and resistance biomarkers.

Disclosure: Nothing to disclose

P1773 INCREASED ADALIMUMAB LEVELS ARE ASSOCIATED WITH CLINICAL, BIOLOGICAL AND ENDOSCOPIC REMISSION, AND LOWER DISEASE-RELATED COMPLICATIONS RATE IN PATIENTS WITH IBD

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Introduction: Retrospective and prospective treat-to-target studies have shown biological and endoscopic remission are superior to clinical remission in achieving improved long-term clinical outcomes in patients with inflammatory bowel diseases (IBD). Stricter, more rigorous therapeutic targets may require higher drug levels.

Aims & Methods: We aimed to study whether higher maintenance adalimumab drug levels are associated with clinical, biological and endoscopic remission. Demographic, clinical, laboratory and endoscopic data were collected retrospectively from 66 consecutive IBD patients treated with adalimumab who had a C-reactive protein (CRP) and/or stool calprotectin measured and endoscopic evaluation within 12 weeks of adalimumab serum trough levels. We defined clinical remission as HBI< 5 or MAYO < 2 for Crohn's disease (CD) and ulcerative colitis (UC), respectively; biologic remission as CRP < 0.5 mg/dL and/or calprotectin < 250; endoscopic remission as SESCD ≤3 (for ileal disease) or SESCD ≤4 for a more extensive CD or endoscopic Mayo ≤1 for UC. Data was analyzed using STATA statistical analysis software. This study was approved by the local IRB.

Results: Sixty-six consecutive patients were included in our study. Median age was 37 years (range 20 to 79), 50% were male, most patients (86%) had CD. Patients who achieved clinical, biologic and endoscopic remission had higher serum trough adalimumab levels (ug/mL±StdErr, 8.9±0.9 Vs. 5.7±1, p=0.016; 8.2±0.8 Vs. 6.6 ±1.1, p=0.023; 9.2±1.0 Vs. 6.1±0.7, p=0.019, respectively) .

Increased levels of adalimumab were required to reach deeper levels of remission, reaching significance comparing clinical and deep (clinical, biologic and endoscopic) remission (ug/mL±StdErr, 5.9±1 Vs. 11.7±1.5, p=0.04).

Patients who achieved remission had lower odds ratio of developing disease-related complications (OR=0.4, p=0.04). Lower complications rate was also associated with higher maintenance adalimumab serum trough levels (8.4±0.8 Vs. 5.7±0.9, p=0.04).

Conclusion: Higher adalimumab trough levels may be required to achieve better disease control. This study provides additional data to guide therapeutic drug monitoring with adalimumab.

Disclosure: Nothing to disclose

P1774 ULCERATIVE COLITIS PATIENTS WITH LOW SERUM LEVELS AFTER THE INDUCTION OF ANTI-TNF DRUGS DO NOT ACHIEVE MUCOSAL HEALING AT ONE YEAR. A PROSPECTIVE STUDY

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Introduction: Anti-Tumor Necrosis Factors (TNF) are currently the most commonly used drugs for moderate to severe ulcerative colitis (UC). Therapeutic drug monitoring (TDM) is a promising strategy to optimize the health care resources in case of loss of response during antiTNF treatment, but a proactive management of TDM is being debated.

Aims & Methods: The aim of this prospective study was to evaluate the use of Trough Levels (TL) of Infliximab (IFX), Adalimumab (ADA) or Golimumab (GOL) at the end of the induction phase as predictors of mucosal healing (MH) in patients with UC.

All the patients who started anti-TNF treatment with IFX, ADA or GOL in monotherapy at Pisa University Hospital since November 2017 were prospectively enrolled. At the end of the induction (week 6 for IFX or GOL, week 8 for ADA) TL were evaluated on serum samples drawn before drug administration, by using an ELISA test (Promonitor®, Grifols, Spain). At week 54, MH (defined as Mayo Endoscopic Score< 2) and clinical remission (CR, defined as a Partial Mayo Score< 2) were evaluated. Statistical correlation between TL and MH or CR was performed using Wilcoxon signed-rank test and ROC curves.

Results: At present, 61 patients were enrolled: 32 treated with IFX, 15 with ADA, 14 with GOL. MH was reached in 30 patients (14 with IFX, 9 with ADA, 7 with GOL). A collective correlation between TL and MH was found (p < 0.01), which was confirmed when the 3 drugs were considered separately: in particular, patients with low TL were less likely to achieve MH. ROC curve analysis, currently performed for IFX, identified a cut-off of 5.4μg/ml (AUC 0.885, p< 0.001) in predicting the probability of non-achieving MH.

Conclusion: TL in UC patients after the induction of anti-TNF treatment were predictors of endoscopic response. For all the drugs evaluated, high TL showed a correlation with MH. For IFX, TL less then 5.4μg/ml predicted with good accuracy the lack of MH at one year.

Disclosure: Nothing to disclose

P1775 SAFETY OF USTEKINUMAB IN INFLAMMATORY BOWEL DISEASES: INTEGRATED SAFETY ANALYSIS OF RESULTS FROM PHASE 2 AND 3 STUDIES IN CROHN'S DISEASE AND ULCERATIVE COLITIS

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Introduction: Ustekinumab (UST) is a well-established therapy in Crohn's disease (CD) and psoriatic diseases. Recently presented phase 3 data showed that UST was safe and effective in ulcerative colitis (UC). Phase 3 induction and maintenance studies of UST in CD (UNITI, IMUNITI) and UC (UNIFI) had similar designs, which allows for integrated analysis across both inflammatory bowel disease (IBD) indications.

Aims & Methods: We present an analysis of integrated safety data of UST in IBD. Data from 6 phase 2/3 CD and UC studies were pooled, and safety was evaluated through 1 year of follow-up. In phase 3, CD and UC pts received a single IV placebo (PBO) or UST (130mg or ~6mg/kg) induction dose followed by SC maintenance doses of PBO or UST (90mg q8 or q12 wks). Concomitant immunomodulators (IMM) and corticosteroids were permitted. All pts who received ≥1 dose of UST were included. Safety outcomes through 1 year are presented as the number of pts with events per 100 pt-years (PY) of follow-up

Results: At induction baseline (2370 pts in pooled phase 3 IBD studies), median age was 38.0 years, 46.9% were receiving corticosteroids, 30.8% were receiving IMM, 53.0% had failed biologics, and 37.1% were naïve to biologics.

In phase 3 IBD studies, through Wk8 of PBO-controlled induction, 1582 pts were treated with UST. Pts with ≥1 event (PBO vs UST) were 55.8% vs 53.9% with AEs, 6.2% vs 4.4% with SAEs, 19.9% vs 19.3% with infections, and 1.3% vs 1.1% with serious infections.

Through 1 year in pooled phase 2/3 IBD studies, 2574 pts were treated with UST with 1733 PY. The number of patients per 100 PY with AEs (PBO 165.99 vs UST 118.32), SAEs (27.50 vs 21.23), infections (80.31 vs 64.32), serious infections (5.53 vs 5.02), malignancies including non-melanoma skin cancer (NMSC) (0.50 vs 0.81), and discontinuations of study agent because of an AE (13.41 vs 7.73) were similar between UST and PBO. The most frequently occurring AEs (excluding diseases under study) were arthralgia (PBO 16.93 vs UST 16.56), headache (16.43 vs 16.50), nausea (13.25 vs 11.94), and abdominal pain (14.59 vs 11.54), and infections were nasopharyngitis (16.26 vs 18.11) and upper respiratory tract infection (11.40 vs 11.36). Results were similar for the CD and UC studies separately (Table shows key safety events).

	CD Studies[a]		UC studies[b]	
	PBO[c] (n=943)	UST[d] (n=1749)	PBO[c] (n=446)	UST[d] (n=825)
Total PY of follow-up	347	1106	250	627
Adverse events	197.97 (686)	131.52 (1455)	121.65 (304)	95.03 (596)
Serious adverse events	34.05 (118)	25.94 (287)	18.41 (46)	12.91 (81)
Infections	95.52 (331)	72.59 (803)	59.23 (148)	49.75 (312)
Serious infections	6.64 (23)	6.06 (67)	4.00 (10)	3.19 (20)
Discontinuation of study agent because of an adverse event	13.56 (47)	9.76 (108)	13.21 (33)	4.15 (26)
Malignancies (including NMSC)[e]	0.58 (2)	0.63 (7)	0.40 (1)	1.12 (7)

a. NCT00265122, NCT00771667, NCT01369329, NCT01369342, and NCT01369355
b. NCT02407236
c. The PBO group includes data up to the first UST dose for patients who were initially treated with PBO and data at or after 16 wks from the first UST dose for patients who were randomized to placebo maintenance.
d. The UST group includes data up to 16 wks from the first UST dose for patients who were randomized to placebo maintenance.
e. Malignancies that occurred in patients receiving UST included colon cancer, papillary renal cell carcinoma, squamous cell carcinoma, basal cell carcinoma, prostate cancer, small intestine adenocarcinoma and incidental carcinoid tumor, and rectal adenocarcinoma.

[Number of pts with key safety events through 1 year of treatment per 100 PY of follow-up (number of patients with events) in phase 2/3 CD & UC studies]

Regarding serious infections, the CD-specific manifestation of anal abscess occurred in PBO 2.02 and UST 0.90 pts per 100 PY in CD pts. When CD-specific events were excluded, overall rates of serious infections were similar between UC and CD populations.

In pooled phase 2/3 studies, the only malignancy (excluding NMSC) reported in >1 UST-treated pt was prostate cancer; no lymphomas were reported through 1 year. Two pts receiving UST (0.12 per 100 PY; both had UC) died from events that investigators considered to be unrelated to study agent (esophageal varices hemorrhage and acute respiratory failure during thyroid surgery).

Conclusion: The safety profile of UST in pts with UC and across integrated IBD indications through 1 year was favorable and consistent with the established safety profile in pts with CD and psoriatic disease.

Disclosure: Drs. Ghosh, Sands, Sandborn, and Danese were investigators in clinical trials sponsored by Janssen. Drs. O'Brien, Tikhonov, Zhou, Volger, Marano, Ott, and Gasink are employees of Janssen.

P1776 DOES ANTI-TNF MAKES DIFFERENCE IN OSTEOARTICULAR MANIFESTATIONS ASSOCIATED TO INFLAMMATORY BOWEL DISEASE?

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Introduction: Among the extraintestinal manifestations (EIM) related to inflammatory bowel disease (IBD), which occur in 15-40% of patients, the most prominent are those of osteoarticular spectrum, due to their high prevalence (30%) and impact in quality of life.

Aims & Methods: With this study, the authors intended to evaluate the prevalence of osteoarticular manifestations (OAM) in patients undergoing biological therapy and the main factors associated with their development. Retrospective and unicentric study, with inclusion of patients followed in referral outpatient care of IBD, under anti-TNF at time of the study. Demographic characterization with determination of OAM [mechanical complaints (MC), OAM secondary to therapy and IBD-related arthropathy (AD)] and the predictor factors related to their development.

Results: A total of 422 patients were included [337 with Crohn's disease (CD) and 85 with ulcerative colitis (UC)], with median age of 40 years (IQR 29-50), 54% of female gender. The OAM prevalence was 23% (89% in DC). A higher prevalence of OAM was associated, with statistic significance, to female gender in ulcerative colitis (p=0.045) and to age higher than 40 years in DC (p=0.018). MC were identified in 20% of cases and OAM secondary to therapy in 18% (15 osteopenia/osteoporosis and 2 cases of arthritis caused by IFX). Among AD's patients, 56% presented manifestations of axial predominance (30% of ankylosing spondylitis, 21% of axial spondylarthritis related to IBD and 15% sacroileitis), 35% of peripheral spondylarthritis and 7% with a enthesopathic component. In 21%, the OAM occurred before IBD's diagnosis.

The absence of therapy with anti-TNF was risk factor for AD manifestations (p<0.001) and, in cases of DC, the higher rate of AD was associated, with statistic significance, to a clinical active disease when it appeared (p=0.001). The presence of OAM led to therapeutic changes in 86% of patients, the most leading to the initiation or dose optimization of anti-TNF.

Conclusion: The OAM present higher prevalence in CD patients conditioning, frequently, changes in therapeutic strategy. The absence of anti-TNF therapeutic and, in CD, absence of clinical remission, was related to AD.

Disclosure: Nothing to disclose

P1777 ELEMENTAL DIET THERAPY PLAYS A SIGNIFICANT ROLE IN AVOIDING POSTOPERATIVE SURGICAL RECURRENCE IN PATIENTS WITH CROHN'S DISEASE IN THE ERA OF BIOLOGICS

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Introduction: Postoperative recurrence affects most patients with Crohn's disease. Novel therapies have been introduced, including anti-tumour necrosis factor-alpha agents, integrin antagonists, and endoscopic balloon dilatation. However, little is known about their efficacy in the long term.
Aims & Methods: We aimed to clarify which therapies could decrease postoperative surgical recurrence in patients with Crohn's disease. Seventy operations in 46 patients with Crohn's disease were included in this retrospective study. Survival curves were created, and univariate and multivariate analyses were performed.
Results: Smokers were significantly more likely to develop recurrences (p=0.023). Patients who were administered anti-tumour necrosis factor-alpha therapy had significantly better prognoses than those who did not receive it (p=0.028). Patients who underwent endoscopic balloon dilatation procedures had significantly better prognoses (p=0.017). Immunomodulators were significantly more effective at preventing surgical recurrences (p=0.046). Patients who maintained an elemental diet (greater than 900 kcal/day) had significantly better prognoses than those who did not or those whose diets were lower in quantity (p< 0.001). However, multivariate analysis indicated that the only significant factor for controlling postoperative surgical recurrence was nutritional therapy (p=0.0058).
Conclusion: Univariate analyses showed that smoking, anti-tumour necrosis factor-alpha therapy, immunomodulator therapy, endoscopic balloon dilatation therapy, and elemental diet therapy exerted significant effects on postoperative recurrence in patients with Crohn's disease. However, the multivariate analysis revealed that only elemental diet therapy was significantly associated with surgical recurrence rates. Elemental diet therapy can play a significant role in the management of Crohn's disease even in the era of biological therapies.
Disclosure: The author received grant support from Mitsubishi Tanabe Pharma Co. Ltd

P1778 METHOTREXATE AFTER ANTI-TNF-α FAILURE IN CROHN'S DISEASE: A RETROSPECTIVE SERIES FROM THE ENEIDA REGISTRY. TEACHING AN OLD DOG NEW TRICKS?

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Introduction: Methotrexate (MTX) is an inmmunomodulator that has shown efficacy in Crohn's disease (CD). Its use is mainly recommended to maintain remission in patients with steroid-dependency and failure of, or intolerance to, thiopurines. Data on its use as monotherapy in patients with failure of anti-TNF-α drugs are limited.
Aims & Methods:
(1) To determine the short and long term efficacy of MTX monotherapy in CD patients with previous failure and/or intolerance to anti-TNF-α.
(2) To evaluate the safety profile in this scenario.
(3) To identify factors associated to short- and long-term efficacy.
Multicentre, observational, and retrospective study on the Spanish National IBD Registry ENEIDA. Patients with CD who were treated with MTX for active disease, defined by Harvey-Bradshaw index (HB) ≥3, with previous failure and/or intolerance to at least one anti-TNF-α were included. Patients with MTX as part of a combined therapy regimen were excluded. Short-term results were evaluated between 12 and 16 weeks of therapy. Remission was defined as HB< 3, and response as a decrease of 3 points, at least, in the HB score, without achieving remission. Long-term success was defined as continuation on steroid-free monotherapy at the maximum follow-up. Adverse events were specifically registered.
Results: 110 patients were included. Demographic and disease-related characterics are reflected in Table 1. A 77.2% had been exposed to thiopurines. All patients had received at least one anti-TNF-α, infliximab (IFX) in 73.6% and adalimumab (ADA) in 26.4%, 44.5% had received two anti-TNF-α (ADA and IFX), and 1.8% three anti-TNF-α (IFX, ADA, and certolizumab). Induction of MTX therapy was done with 25 mg in 80.9% of cases, and with SC injection in 93.6%. On induction, mean HB score was 6.6±3, and C-reactive protein (CRP) 12.2 ± 10 mg/L. Steroids were associated in 42.6%

Monday, October 21, 2019

Tuesday, October 22, 2019

Wednesday, October 23, 2019

of cases. In the short term analysis (week 12-16), percentages of remission, response, and failure, were 33.0, 31.1%, and 35.9%, respectively. Mean CRP at this point was 7.7 ± 6mg/L. Partial or complete steroid withdrawal was achieved in 96.3% at week 12-16. Long-term succes was 36.4% with a median therapy duration of 36 months (range 4-300). Long-term MTX withdrawal was necessary in 73.6%, due to failure (44.5%), adverse events (29.1%), or both. Adverse events were registered in 41.2% of cases, mainly digestive intolerance (15.5%), weakness/malaise (10.9%), and liver injury (7.3%). In 22.7%, these adverse events resulted in drug withdrawal. In the multivariate analysis non-smoking status (OR 1.56, CI 1.05-2.33), and the use of only one anti-TNF-α before MTX therapy (OR 1.25, CI 1,01-6,08) were factors significantly associated to short term remission/response. No predictors of long-term response could be identified.

Gender (M/F)	43/67 (39,1/60,9%)
Age (years)	47±14
Tobacco use (No/Yes/Former)	53/30/27 (48,1/27,2/24,5%)
Obesity (No/Yes)*	99/11 (90/10%)
Liver disease (No/Yes)**	103/7 (93,6/6,4%)
Duration of disease (years)	16±10
Disease localization (L1/L2/L3/+L4)	41/22/47/29 (37,2/20/42,7/26,4%)
Disease behaviour (B1/B2/B3)	55/30/25 (50/27,3/22,7%)
Perianal disease (No/Yes)	62/48 (55,4/44,6%)
Previous surgery (No/Yes)	39/71 (35,5/64,5%)

[Table 1. Demographic and disease-related characteristics. *BMI>30, ** viral hepatitis/steatosis/cirrhosis]

Conclusion: MTX has an acceptable short-term efficacy and safety profile in a group of CD patients with previous anti-TNF-α failure or intolerance. Although treatment discontinuation due to lack of efficacy and/or side effects is frequent, a long-term therapeutic benefit is obtained in one third of patients.

Disclosure: Nothing to disclose

P1779 BIOLOGIC USE IN ADULT PATIENTS NEWLY DIAGNOSED WITH ULCERATIVE COLITIS IN THE UNITED STATES, 2010-2013 AND 2014-2016

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Introduction: The objective of this research was to characterize treatment patterns and sequences of biologic initiation in adult patients newly diagnosed with Ulcerative Colitis (UC) in the United States in 2010-2013 and 2014-2016.

Aims & Methods: Adult (18+ years) patients with ≥2 UC diagnosis codes (ICD-9: 556.x; ICD-10:K51.x) from October 1, 2010 to September 30, 2016 were included in this retrospective analysis of medical and pharmacy claims data from the IBM Marketscan Commercial, Medicaid, and Medicare-Supplemental Claims database. Patients were excluded if they were < 18 years old, had a Crohn's disease (CD) diagnosis two years pre- or post-index, had a dual UC and CD diagnosis, or did not have treatment throughout the study period. Pathway visualization techniques and subgroups analyses were conducted for the 2 years post diagnosis to compare biologic use following first diagnosis during 2010-2013 and 2014-2016. Two-sample t-tests were conducted to compare continuous variables and two-sample proportion tests were used to compare categorical variables in two time periods of diagnosis.

Results: A cohort of 7,794 UC patients were identified with 4,637 (59.5%) diagnosed with UC during 2010-13 and 3,157 (40.5%) diagnosed during 2014-16. Overall, during both periods of diagnosis, patients were more likely to be female (55%). Patients diagnosed during 2014-16 tended to be younger when compared to 2010-13 (mean age at diagnosis: 49.2 vs. 46.2 years; p< .00001). In general, the majority of patients initiated conventional treatment (aminosalicylates, immunomodulators, and/or corticosteroids)

at the time of diagnosis (99%). 231 (5.0%) diagnosed 2010-13 and 304 (9.6%) diagnosed 2014-16 initiated at least one biologic treatment during the 2 year follow-up. The median time to biologic treatment in the 2 years post diagnosis was 289 days for those diagnosed 2010-13 versus 223 days for those diagnosed during 2014-16 (p< 0.00001). On average, patients initiated biologic treatment 66 days earlier when receiving a UC diagnosis during 2014-16. Infliximab was more frequently identified as the first-line biologic in the 2 years post diagnosis for those diagnosed 2010-13, while adalimumab was the first-line biologic for those diagnosed 2014-16. However, pathway visualization Sankey diagrams illustrated limited switching from one biologic to another after initiation of biologic therapy during the 2 years post diagnosis for 2010-13, with no predominant sequence identified. This trend remained for the 2014-16 cohort (data not shown).

Characteristic:	Diagnosis in 2010-2013 (N=4,637)	Diagnosis in 2014-2016 (N=3,157)	P-value
Gender			
Male; n (%)	2,064 (44.5%)	1,434 (45.4%)	0.427
Female; n (%)	2,573 (55.5%)	1,723 (54.6%)	0.427
Age (years); mean (standard deviation)	49.2 (15.8)	46.2 (16.5)	<.00001
Treatment at Diagnosis			
Conventional Treatment; n (%)	4,620 (99.8%)	3,137 (99.6%)	0.92
Biologic Treatment; n (%)	9 (0.2%)	14 (0.4%)	0.046
Time to Biologic Treatment (days)*			
Median* (Q1, Q3)	289 (132, 495)	223 (89.5, 389)	<.00001
Min-Max	0-715	0-727	

*Wilcoxon rank test, Q1=first quartile, Q3=third quartile, Min=Minimum; Max=Maximum

[Patient Demographics and Clinical Characteristics]

Conclusion: Despite recent authorization of safe and effective biologic treatments for UC, updated clinical guidelines, and initiatives to treat patients more aggressively to delay disease progression, conventional treatment is still more common at the time of diagnosis. Biologic use in UC remains limited; however, the time to biologic initiation after diagnosis is decreasing.

Disclosure: Drs Naegeli, Mahoui, Morton, Dong, Hunter, Farrar, and Stefani-Hunyadi are employees and stock holders of Eli Lilly and Company.

P1780 BIOLOGIC USE IN ADULT PATIENTS NEWLY DIAGNOSED WITH CROHN'S DISEASE IN THE UNITED STATES, 2010-2013 AND 2014-2016

D'Haens G.R.[1], Naegeli A.[2], Mahoui M.[3], Morton S.[3], Dong Y.[3], Hunter T.[2], Farrar M.[2], Canavan J.[3], Stefani-Hunyady D.[4]
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Introduction: The objective of this research was to characterize treatment patterns and sequences of biologic initiation in adult patients newly diagnosed with Crohn's disease (CD) in the United States in 2010-2013 and 2014-2016.

Aims & Methods: Adult (18+ years) patients with ≥2 CD diagnosis codes (ICD-9: 555.x; ICD-10:K50.x) from October 1, 2010 to September 30, 2016 were included in this retrospective analysis of medical and pharmacy claims data from the IBM Marketscan Commercial, Medicaid, and Medicare-Supplemental Claims database. Patients were excluded if they were < 18 years old, had an Ulcerative Colitis (UC) diagnosis two years pre- or post-index, had a dual CD and UC diagnosis, or did not have treatment throughout the study period. Pathway visualization techniques and subgroups analyses were conducted for the 2 years post diagnosis to compare biologic use following first diagnosis during 2010-2013 and 2014-2016. Two-sample t-tests were conducted to compare continuous variables and two-sample proportion tests were used to compare categorical variables between two time periods of diagnosis.

Results: A cohort of 5,460 CD patients were identified with 3,219 (59.0%) diagnosed with CD during 2010-13 and 2,241 (41.0%) diagnosed during 2014-16. Overall, during both periods of diagnosis, patients were more likely to be female (55%). Patients diagnosed during 2014-16 tended to be younger when compared to 2010-13 (mean age at diagnosis: 44.8 vs. 42.1 years; p< .00001). In general, the majority of patients initiated conventional treatment (aminosalicylates, immunomodulators, and/or corticosteroids) at the time of diagnosis (97%). 468 (14.6%) diagnosed 2010-13 and 553 (24.7%) diagnosed 2014-16 initiated at least one biologic treatment during the 2 year follow-up. The median time to biologic treatment in the 2 years post diagnosis was 139 days during 2010-13 versus 91 days during 2014-16 (p< .00001). On average, patients initiated biologic treatment 48 days earlier when receiving a CD diagnosis during 2014-16. Adalimumab was more frequently identified as the first-line biologic in the 2 years post diagnosis for those diagnosed 2010-13 and 2014-16. Pathway visualization Sankey diagrams illustrated limited switching from one biologic to another after initiation of biologic therapy during the 2 years post diagnosis for 2010-13, with no predominant sequence identified. This trend remained for the 2014-16 cohort (data not shown).

Characteristic:	Diagnosis in 2010-2013 (N=3,219)	Diagnosis in 2014-2016 (N=2,241)	P-value
Gender			
Male; n (%)	1,397 (43.4%)	1,048 (46.8%)	0.014
Female; n (%)	1,822 (56.6%)	1,193 (53.2%)	0.014
Age (years); mean (standard deviation)	44.8 (16.3)	42.1 (16.2)	<.0001
Treatment at Diagnosis			
Conventional Treatment; n (%)	3,128 (97.5%)	2,134 (95.4%)	.0002
Biologic Treatment; n (%)	79 (2.5%)	103 (4.6%)	.00001
Time to Biologic Treatment (days)			
Median* (Q1, Q3)	139 (57, 316.2)	91 (42, 243)	<.00001
Min-Max	0-728	0-723	

*Wilcoxon rank test, Q1=first quartile, Q3=third quartile, Min=Minimum; Max=Maximum

[Patient Demographics and Clinical Characteristics]

Conclusion: Despite recent authorization of safe and effective biologic treatments for CD, updated clinical guidelines, and initiatives to treat patients more aggressively to delay disease progression, conventional treatment is still more common at the time of diagnosis. Biologic use in CD remains limited; however, the time to biologic initiation after diagnosis is decreasing.

Disclosure: Drs Naegeli, Mahoui, Morton, Dong, Hunter, Farrar, and Stefani-Hunyadi are employees and stock holders of Eli Lilly and Company.

P1781 TREATMENT WITH THIOPURINES IN PATIENTS WITH ULCERATIVE COLITIS. IS ADHERENCE A SIGNIFICANT FACTOR?

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Introduction: Thiopurines are drugs used as maintenance therapy in patients with ulcerative colitis (UC). There are dissimilar results regarding the relationship between adherence to treatment and risk of relapse.
Aims & Methods: To evaluate the percentage of adherence to thiopurines, its repercussion in the evolution of the disease and the factors related to it. Analytical, observational and retrospective study of patients with UC followed at University Clinic Hospital of Valencia under treatment with thiopurines from October 2017 to October 2018. Adult patients registered in the ENEIDA database in clinical remission at the beginning of the study were included. The adherence was evaluated with an electronic pharmaceutical prescription system (GAIA), considering adherence to the dispensation of

≥80% of the prescribed medication. The study analyzed, according to the degree of adherence, clinical variables (age, gender, comorbidity, smoking habit, disease extent, time of evolution, extraintestinal manifestations, number and severity of relapses) and therapeutic variables (number of tablets, dose, concomitant treatment).
Results: Forty-six patients with UC (67.4% males) were included with a median of 43 (IQR 32-55) years old. The adherence was of 74% and no correlation with fewer disease relapses was found. A lower dose of thiopurines was considered as a predictor of non-adherence. A tendency to higher risk of relapse was observed in the non-adherent group after the 30th week of follow-up in the Kaplan-Meier curve. Mesalazine and biologic therapy was prescribed in 74% and 24% of patients, respectively. The adherence to mesalazine correlates with the adherence to thiopurines.

Variables	NO adherence	YES adherence	p-value
Gender, n (%): Males // Females	6 (19,4) // 6 (40)	25 (80,6) // 9 (60)	0,135
Extraintestinal manifestations, n (%)	5 (31,2)	11 (68,8)	0,560
Adverse reaction to thiopurines, n (%)	5 (38,5)	8 (61,5)	0,230
Concomitant treatment related to IBD, n (%)	9 (25,7)	26 (74,3)	0,918
Concomitant treatment not related to IBD, n (%)	5 (26,3)	14 (73,7)	0,976
Comorbility, n (%)	6 (28,6)	15 (71,4)	0,725
Relapse, n (%) // Mild relapse, n (%) // Moderate/severe relapse, n (%)	5 (38,5) // 2 (28,6) // 3 (50)	8 (61,5) // 5 (71,4) // 3 (50)	0,230 // 0,871 // 0,153
Dose/day (mg), x (sd) // No of tablets/day, x (sd)	90 (49) // 2 (1)	132 (51) // 3 (1)	0,015 // 0,050
Adherence to mesalazine, n (%)	0 (0)	20 (76,9)	<0.001

[Results]

Conclusion: The adherence to thiopurines evaluated by the electronic prescription system was of 74%. No relation between adherence and number and severity of disease relapse was observed during one year follow-up. Dose and adherence to mesalazine were factors related to adherence to thiopurines. It may be necessary to extend the follow-up period.
Disclosure: This abstract has been previously presented as a poster at a national scientific meeting, in the 22th anual meeting of the Spanish Gastroenterology Group (AEG).

P1782 SEVERE FATIGUE IS COMMON AND ASSOCIATED WITH LOW QUALITY OF LIFE AND WORK PRODUCTIVITY LOSS IN IBD: THE WORK-IBD STUDY

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Introduction: More than 40% of inflammatory bowel disease (IBD) patients suffer from fatigue, even during quiescent disease. Associations have been reported between anti-TNF use and severe fatigue in IBD,[1] which can be related to the mode of action, side-effect profile or indirectly to more severe disease.
Aims & Methods: One of the aims of the prospective WORK-IBD study was to determine the prevalence and burden of severe fatigue and identify predictors for severe fatigue in IBD. All Crohn's disease (CD) and ulcerative colitis (UC) patients that attended the outpatient clinic of two non-academic and two academic hospitals between May 1st and August 31st 2017 were invited. Only (self-) employed patients were eligible to participate. Fatigue, quality of life, work productivity and disease activity were measured using the Multidimensional Fatigue Inventory (range 0-100), Short Inflammatory Bowel Disease Questionnaire (range 10-70), Work Productivity and Activity

Impairment questionnaire, patient-reported Harvey Bradshaw Index and Simple Clinical Colitis Activity Index, respectively. Severe fatigue was defined as a general fatigue score above the 95th percentile of the general population adjusted for gender and age.[2] Factors with p-value below 0.1 in univariable analysis, or that were considered clinically relevant, were entered into multivariable logistic regression analysis using backward elimination (likelihood ratio).

Results: In total, 1590 IBD patients were invited out of which 768 (48%) responded (119 not eligible, 86 declined participation), and 536 were included (58% female, 53% CD) with a median (IQR) age of 45 (33-53) years, respectively (table 1). Severe fatigue was reported in 252 patients (47%). Considering type of treatment, severe fatigue was reported in 42/113 (37%) of patients receiving mesalamine (5-ASA), 51/112 (56%) receiving immunomodulators (thiopurines, methotrexate), 45/86 (52%) on anti-TNF monotherapy, 23/42 (55%) on anti-TNF combination therapy, 15/29 (52%) using vedolizumab, 12/16 (75%) using ustekinumab and in 64/138 (46%) of patients without maintenance treatment. Patients from academic centers were more likely to report severe fatigue compared to non-academic patients (53% vs 38%, p=0.001). Clinical disease activity (OR 3.6, 95% CI 1.9-6.8) and arthralgia (OR 1.8, 95% CI 1.0-3.3) were independent risk factors for severe fatigue and patients treated with 5-ASA had a significant lower risk to report severe fatigue (OR 0.3, 95% CI 0.1-0.8). Patients suffering from severe fatigue reported significantly lower quality of life (median (IQR) 50 (43-55) vs 60 (55-64), p<0.001) and significantly higher percentages work productivity loss (median (IQR) 30% (0-60) vs 0% (0-10), p<0.001).

	Total (n=536)	No treatment (n=138)	5-ASA (n=113)	Immuno-modulator (n=112)	Anti-TNF (n=128)	Vedoli-zumab (n=29)	Usteki-numab (n=16)
Crohn's disease, n (%)	286 (53)	83 (60)	12 (11)	66 (59)	91 (71)	19 (66)	15 (94)
Disease duration, median years (IQR)	11 (5-20)	12 (6-21)	10 (4-20)	11 (5-20)	12 (6-20)	14 (5-20)	11 (7-15)
Prior bowel resection, n (%)	143 (27)	57 (41)	3 (3)	26 (23)	40 (31)	7 (24)	10 (63)
Disease activity, n (%)	122 (23)	28 (20)	17 (15)	28 (25)	32 (25)	7 (24)	10 (63)
Arthralgia, n (%)	179 (34)	42 (30)	37 (33)	40 (36)	43 (34)	10 (35)	7 (44)
Severe fatigue, n (%)	252 (47)	64 (46)	42 (37)	51 (46)	68 (53)	15 (52)	12 (75)

[Table 1. Baseline characteristics]

Conclusion: In this large IBD cohort, 47% of patients reported severe fatigue. Clinical disease activity and arthralgia were significantly associated with severe fatigue, whereas 5-ASA treatment was associated with a lower incidence. The latter may be due to the favorable safety profile or a mild disease course. In contrast to prior studies, no higher risk for severe fatigue was found for patients treated with anti-TNF. Severe fatigue was associated with reduced quality of life and higher percentage of work productivity loss.

References: 1. Williet N, Sarter H, Gower-Rousseau C, et al. Patient-reported Outcomes in a French Nationwide Survey of Inflammatory Bowel Disease Patients. J Crohns Colitis. 2017;11(2):165-174. doi:10.1093/ecco-jcc/jjw145. 2. Schwarz R, Krauss O, Hinz A. Fatigue in the general population. Onkologie. 2003;26(2):140-144. doi:10.1159/000069834.

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P1783 FECAL CONCENTRATION OF VEDOLIZUMAB CORRELATES WITH TISSUE DRUG LEVELS AND ENDOSCOPIC ACTIVITY IN INFLAMMATORY BOWEL DISEASE PATIENTS

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Introduction: Therapeutic drug monitoring is being incorporated into everyday clinical management with anti-TNF therapy; however, measurement of serum drug and antibody levels of vedolizumab (VDZ) is less clear to guide drug dosing in the clinical practice. According to all available data, serum trough levels alone seem to be inadequate to predict clinical response with VDZ therapy. At present, no data is available on the potential correlation between mucosal or fecal VDZ concentration and therapeutic response to VDZ.

Aims & Methods: The aim of this study is to assess the correlation between serum, mucosal and fecal VDZ concentrations to get a better view on the pharmacokinetic-pharmacodynamic relationships of the drug in inflammatory bowel disease (IBD-Crohn's disease [CD], ulcerative colitis [UC]) patients receiving maintenance therapy.

Patients and methods: Patients with luminal CD and UC receiving maintenance VDZ therapy were enrolled in the study. Clinical disease activity was assessed, blood samples and fecal specimens were collected and colonoscopy with biopsy samples was performed in every patient. Biopsy samples were obtained from inflamed and uninflamed tissue from the colon. Serum, mucosal and fecal VDZ levels were determined by ELISA assay.

Results: Data of 26 patients (8 CD, 18 UC) have been available so far. The mean duration of VDZ therapy was 5.8 months. Seven patients were naive to biological therapy at induction. Twenty patients had endoscopic activity during colonoscopy. Mucosal drug level did not show difference between either samples obtained from the inactive vs. active part of the bowel (0.54 vs. 0.39 µg/g, p=0,28), or between samples obtained from patients with endoscopic activity vs. mucosal healing (0.44 vs. 0.86 µg/g, p=0.11). Similarly, median serum trough level did not differ significantly between patients with endoscopic activity and remission (31.96 µg/ml vs. 28.99 µg/ml, p=0.3). However, median fecal concentration of VDZ was significantly lower in patients with endoscopic activity compared to those showing mucosal healing (0.22 µg/ml vs. 0.55 µg/ml, p< 0.001). Fecal drug level showed significant correlation with tissue drug levels obtained from both inflamed and uninflamed region of the colon (r=0.80, p=0.001 and r=0.78, p=0.0003), however no correlation was shown between serum and fecal and between serum and tissue drug levels.

Conclusion: Our study would be the first that simultaneously examine serum, mucosal and fecal concentrations of VDZ comparing with endoscopic activities. Our data suggest that determination of fecal drug concentration may be promising in the evaluation of endoscopic response to VDZ therapy and may help to identify a useful surrogate marker of tissue drug concentration.

Disclosure: Nothing to disclose

P1784 SAFETY AND EFFICACY OF ENDOSCOPIC DILATATION OF SMALL BOWEL CROHN'S DISEASE STRICTURES BY BALLOON-ASSISTED ENTEROSCOPY: A POOLED ANALYSIS OF INDIVIDUAL DATA FROM 219 PATIENTS

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Introduction: Strictures are a common complication of Crohn's disease (CD). While colonoscopy has been proven suitable and effective for dilation therapy of CD-associated strictures of the ileocecum, the published evidence on safety and efficacy of balloon-assisted enteroscopy (BAE) for balloon dilation therapy of CD strictures of the small intestine is scarce.

Aims & Methods: In the present study we performed a pooled safety and efficacy analysis based on individual patient data. Therefore, a systematic literature review was performed to assess all relevant citations found in Embase, Medline and the Cochrane library regarding BAE used for EBD of small intestinal CD strictures. In addition, conference proceedings including DDW, ECCO, UEGW, A-IBD, AGA and German Gastroenterology Congress were screened for additional data. Study authors were contacted to provide individual patient data. Descriptive statistics were used to summarize patients' characteristics. Univariate cox proportional hazards regression model was applied to find out possible risk factors for need for re-dilation and surgery. Backward model selection procedure was used and multi-variate cox model were built.

Results: 19 publications with a total of 468 CD patients and 1194 performed dilation procedures were included. 25.1% of strictures were anastomotic strictures (74.9% de novo, respectively). Technical success rate was 88.1%, resulting in clinical efficacy in 78% of patients. Major complications defined as perforation, bleeding or dilation-related surgery occurred in 3.7% of all procedures. During a mean follow-up period of 16 months, 45.7% of patients reported symptomatic recurrence, while 38.1% of patients needed to undergo re-dilation and 27.5% required surgical intervention.

Multivariate analysis of 219 individual patients identified a 73% higher hazard of re-dilation in CD patients with clinical symptoms compared to asymptomatic patients and a 40% lower hazard in patients with prestenotic dilation compared with patients with no prestenotic dilation. Additionally, increased CRP values at dilation (elevation of CRP per 0.1 increased the hazard for surgery by 8.6%) and inflamed mucosa at dilation (2.8 times increased hazard as compared with non-inflamed mucosa) were identified as risk factors for the need for surgery.

Conclusion: Balloon-assisted enteroscopy for dilatation therapy of CD-associated strictures of the small intestine possesses a high rate of short-term technical and clinical success with acceptable complication rates. Main predictors for intermediate therapeutic failure are clinical symptoms, non-stenotic dilation, increased CRP values and mucosal inflammation at the time of dilation. Endoscopic dilation by BAE is a valuable alternative to surgery in selected patients with small bowel CD associated strictures.

Disclosure: Nothing to disclose

P1785 COMPARATIVE ASSESSMENT OF FECAL MICROBIOTA TRANSPLANTATION AND CURRENT THERAPIES AS INDUCTION TREATMENT FOR ACTIVE REFRACTORY ULCERATIVE COLITIS: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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Introduction: For patients with non-responding or refractory to standard treatment ulcerative colitis (UC), tofacitinib and biologic agents pose an additional alternative. Emerging evidence suggest that fecal microbiota transplantation (FMT) can also induce remission of UC.

Aims & Methods: We performed a systematic review and network meta-analysis to compare FMT to current therapies with regard to safety and efficacy in induction of remission of UC. We searched Medline, Embase, CENTRAL and grey literature sources up to November 2018. We included randomized controlled trials (RCTs) in patients with active UC that compared FMT, infliximab, adalimumab, golimumab, vedolizumab and tofacitinib to each other or placebo as induction therapies. Efficacy outcomes included clinical remission, clinical response and endoscopic remission. Safety was assessed with the incidence of any adverse event (AE), serious AEs and infections. We conducted random-effects network meta-analysis and ranked treatments based on the surface under the cumulative ranking (SUCRA) probabilities. We estimated Predictive intervals (PrIs), which indicate the interval within which the relative effect of a future study is expected to be, to facilitate interpretation of the results in the light of the magnitude of heterogeneity.

Results: Twenty placebo-controlled trials (FMT 5 trials) with 4634 patients were included in the network meta-analysis. FMT was superior to placebo in clinical remission (OR 2.80; 95% CI 1.46-5.36) and response (OR 2.53; 95% CI 1.52-4.23), however there was no difference in terms of endoscopic remission (OR 1.91; 95% CI 0.62-5.86). No indirect comparisons between FMT and licensed treatments reached statistical significance in any efficacy outcome. Results remained stable when PrIs were applied. On SUCRA analysis, infliximab (SUCRA 0.94, 0.73 and 0.87) and tofacitinib (SUCRA 0.79, 0.86 and 0.87) were ranked highest while adalimumab (SUCRA 0.28, 0.25 and 0.28) was ranked lowest in terms of response, clinical and endoscopic remission, respectively. FMT (SUCRA 0.64, 0.60 and 0.53) had comparable SUCRA values with golimumab (SUCRA 0.45, 0.56 0.46) and vedolizumab (SUCRA 0.40, 0.49 and 0.46). Regarding safety, there was no increase in the rates of any AEs for FMT and licensed therapies (data on infliximab were not available) and no differences in indirect comparisons. Vedolizumab (SUCRA 0.78) was the safest option, followed by tofacitinib (SUCRA 0.57). FMT (SUCRA 0.38) had comparable SUCRA values with adalimumab (SUCRA 0.38) and golimumab (SUCRA 0.49). Only tofacitinib increased the incidence of infections compared to placebo (OR 1.51; 95%CI 1.05-2.19, SUCRA 0.06), but the risk was not retained when PrIs were included in the analysis. Based on SUCRAs, FMT (SUCRA 0.85) was safest in terms of infections followed by golimumab (SUCRA 0.55), adalimumab (SUCRA 0.52) and vedolizumab (SUCRA 0.49). There was no difference between treatments regarding incidence of serious AEs, however FMT was ranked lowest (SUCRA 0.10). Lack of efficacy data in FMT trials based on prior anti-TNF exposure precluded evidence synthesis separately for anti-TNF naïve and anti-TNF experienced patients.

Conclusion: Preliminary evidence suggest that FMT could be an alternative induction therapy for ulcerative colitis with comparable efficacy and safety to licensed pharmacological treatments. Nevertheless, due to the absence of head-to-head trials, the short duration of studies and the limited size of FMT trials (277 patients) conclusions must be interpreted with caution.

Disclosure: Nothing to disclose

P1786 THE ECONOMIC BURDEN OF CROHN'S DISEASE IN EUROPE: FINDINGS FROM A SYSTEMATIC LITERATURE REVIEW

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Introduction: Crohn's disease (CD) is an inflammatory bowel disease characterized by chronic inflammation of the gut. As new treatments become available, analyses of the cost to healthcare systems, patients, and their caregivers incurred by CD are increasingly important. The aim of this systematic literature review (SLR) was to identify and summarize the costs and healthcare resource utilization associated with CD in Europe from a societal perspective.
Aims & Methods: An SLR was conducted to identify studies reporting healthcare resource use and direct and indirect costs associated with CD, published in English from 1 January 2012 to 22 June 2018. Literature searches were conducted using MEDLINE, Embase, EconLit, and the Cochrane library databases. Conference abstracts from the past 2 years were reviewed, and bibliographic lists of relevant SLRs were interrogated. Study selection was guided by prespecified inclusion and exclusion criteria. Currency values were adjusted using purchase price parity values and inflation data using EU28 values (OECD, 2019).
Results: A total of 40 studies presenting resource use, productivity and/or cost data were identified. Twenty-seven studies reported healthcare resource use data, 23 studies assessed direct costs, and 15 studies estimated indirect costs/lost productivity, 3 of which specifically assessed caregiver economic burden.
Various methodologies including prospective questionnaires, database claims analysis, surveys, observational studies, and randomized controlled trials were used to estimate the direct cost of CD. Medication use (n = 20) and hospitalizations (n = 15) were the most frequently reported resources. The proportion of patients hospitalized ranged from 9.3% in patients on a biologic to 66% in patients with perianal disease. In addition, the mean hospital length of stay ranged from 2 days reported for a patient population in which only 14% of patients presented with active disease to 23 days in a study of patients with perianal disease. Total annual direct costs per patient varied widely across Europe, ranging from €4639 for a newly diagnosed patient population in Italy to €24 374 for a Spanish patient population receiving 12 months of biologic treatment.
Before the introduction of biologics, the main components of the direct cost of CD across European healthcare systems were related to surgery and hospitalizations: after the introduction of biologics, the main cost driver was that associated with anti-tumor necrosis factor (TNF) therapies. Indirect costs such as productivity loss, sick leave, travel expenses, and out of pocket expenses contributed between €665 and €7591 per patient per year to the economic burden of CD.
Conclusion: This systematic review indicates that the direct costs and healthcare resource use associated with CD present a considerable economic burden in Europe. Although surgery and hospitalizations can have a substantial impact on costs, more recent studies show that the cost of biologics is now the main cost driver in CD patients across Europe.
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P1787 IMPROVEMENT OF SYMPTOMS AND QUALITY OF LIFE AFTER REPEATED FAECAL MICROBIOTA TRANSPLANTATION FOR TREATMENT OF CHRONIC POUCHITIS

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Introduction: Pouchitis is a common long-term complication after restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA) in the surgical treatment of Ulcerative Colitis (UC) (1). Many theories have been proposed, but the exact disease mechanism of pouchitis is still uncertain. Current evidence suggest that the gut microbiota could be a significant factor in the aetiology of pouchitis (2). During the last decades, interest in faecal microbiota transplantation (FMT) has grown rapidly.
This intervention as a new 'ecological' therapy for several diseases including chronic pouchitis. Studies have shown that FMT may restore the intestinal microbial balance in treated patients - re-establishing an almost normal intestinal microbial environment (3-4). However, evidence to use repeated FMT for treatment of chronic pouchitis is still lacking.
Aims & Methods: To investigate the clinical effect of FMT in treatment of patients with chronic pouchitis, we performed a 2-week FMT treatment pilot study. The study was designed as an open-label cohort study with a 2-week intervention period and a 6-month follow-up period. Patients diagnosed with chronic pouchitis were included in the study. All patients were allocated to treatment with FMT delivered by enema daily for two consecutive weeks. FMT material was obtained from healthy faecal donors recruited from the Blood Bank and screened according to international guidelines (5).
Disease severity was accessed before and after FMT using the Pouchitis Disease Activity Index (PDAI) score. A PDAI score < 7 was considered equivalent to clinical remission. The clinical PDAI score (cPDAI) was used in the 6-month follow-up period. Quality of life was measured using the Short Inflammatory Bowel Disease Questionnaire (SIBDQ) before and after FMT.
Results: Ten patients were included of whom one was excluded before the FMT intervention. Nine patients completed the 2-week FMT treatment period. At 30-day follow-up, 44% of the patients had clinical remission with a PDAI score < 7. A non-significant improvement of the PDAI score was found between inclusion and 30-day follow-up, mean 7.0 (SD 3.13) before FMT and mean 5.2 (SD 4.02) after FMT, p=0.81. The clinical effect lasted to end of follow-up at 6 months in 33% of the patients. The cPDAI score improved from mean 2.7 (SD 1.25) at inclusion to mean 0.7 (SD 0.47) at 6-month follow-up, p=0.07. The SIBDQ score showed a non-significant improvement between inclusion (mean 43.0 (SD 13.43)) and 30-day follow-up (mean 48.0 (SD 8.37)), p=0.29.
Conclusion: In this study, we found that FMT induced clinical remission in 44% of patients with chronic pouchitis with improvement of symptoms and quality of life. Although our study showed no significant clinical remission of pouchitis symptoms after FMT, we still believe that FMT can be a new treatment of chronic pouchitis. Several factors might influence the effect of FMT, such as the route used for FMT administration and duration of FMT treatment. Approaches in FMT treatment of chronic pouchitis need to be explored. This includes length of treatment, use of maintenance treatment, FMT donor-mix versus single donor, and if antimicrobial therapy should be administered prior to FMT treatment. Finally, a randomized controlled study is required to examine the true role of FMT in treating chronic pouchitis.
References: (1) Hata K, Ishihara S, Nozawa H et al. Pouchitis after ileal pouch-anal anastomosis in ulcerative colitis: Diagnosis, management, risk factors, and incidence. Dig Endosc. 2017 Jan;29(1):26-34. doi: 10.1111/den.12744. (2) Segal JP, Oke S, Hold GL et al. Systematic review: ileoanal pouch microbiota in health and disease. Aliment Pharmacol Ther. 2018 Feb;47(4):466-477. doi: 10.1111/apt.14454. (3) Fang S, Kraft CS, Dhere T et al. Successful treatment of chronic Pouchitis utilizing fecal microbiota transplantation (FMT): a case report. Int J Colorectal Dis. 2016 May;31(5):1093-1094. doi: 10.1007/s00384-015-2428-y. (4) Stallmach A, Lange K, Buening J et al. Fecal Microbiota Transfer in Patients With Chronic Antibiotic-Refractory Pouchitis. Am J Gastroenterol. 2016 Mar;111(3):441-3. doi: 10.1038/ajg.2015.436. (5) Cammarota G, Ianiro G, Tilg H et al.; European FMT Work-

ing Group. European consensus conference on faecal microbiota transplantation in clinical practice. Gut. 2017 Apr;66(4):569-580. doi: 10.1136/gutjnl-2016-313017.
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P1788 ECONOMIC EVALUATIONS OF BIOLOGICAL TREATMENTS FOR MODERATE-TO-SEVERE CROHN'S DISEASE: FINDINGS FROM A SYSTEMATIC LITERATURE REVIEW

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Introduction: Moderate-to-severe Crohn's disease (CD) is a chronic, progressive disease characterized by inflammation of the lining of the gut. Treatment options include targeted biological therapies such as tumor necrosis factor (TNF)-alpha inhibitors (e.g. infliximab, adalimumab) and anti-integrin and anti-IL-23 treatments (vedolizumab, ustekinumab). With increasing treatment options, understanding economic evaluations of different therapies is crucial to inform clinical practice. The aim of this systematic literature review (SLR) was to summarize published economic evaluation models of biologic treatments for CD in Europe.
Aims & Methods: An SLR was conducted to identify studies (economic analyses, systematic literature reviews, meta-analyses, and health technology assessments [HTAs]) of biological therapies in patients with moderate-to-severe CD, published in English from 1 January 2012 to 22 June 2018. Literature searches were performed in MEDLINE, Embase, EconLit, and the Cochrane library databases. Conference abstracts from the past 2 years were reviewed, along with key HTA websites. Bibliographic lists of relevant SLRs were also interrogated. Study selection was guided by prespecified inclusion and exclusion criteria.
Results: Thirteen economic analyses were identified, of which 10 compared biological treatment with biological and/or conventional therapy, 1 compared biological treatment with surgery and 2 focused on clinical management of CD. Biologics considered included infliximab, infliximab biosimilar, adalimumab, vedolizumab, and ustekinumab. Ten analyses were performed from a health systems perspective while three studies presented data from a societal perspective. Economic models utilized in the studies included decision tree models, Markov models, or hybrid decision tree-Markov approaches. The models were built around key endpoints of response and remission. Efficacy of first- and second-generation biologics when compared with one another was estimated primarily using network meta-analyses. The time horizon of analyses ranged from 48 weeks to lifetime. Key health states considered include remission, mild disease, moderate/severe disease, surgery, and death. The value of second-generation biologics (vedolizumab and ustekinumab) was examined separately in anti-TNF naïve and anti-TNF failure patient populations in five studies. These biologics were more cost effective in the anti-TNF failure population than the anti-TNF naïve group. Sequencing of biologics was considered in two analyses.
Conclusion: Several modelling structures have been used to model CD using various time horizons. As treatment options for CD increase in Europe, economic evaluations comparing biologics to each other has become increasingly important. In addition, as more treatments are approved, the impact of sequencing of biologics may need to be considered and may in turn dictate analyses of longer time horizons.
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P1789 CIRCULATING CD8 α4β7+ MEMORY T CELLS AS EARLY BIOMARKERS OF REMISSION TO VEDOLIZUMAB IN ULCERATIVE COLITIS

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Introduction: Vedolizumab (VDZ) is a humanized monoclonal antibody targeting the $\alpha_4\beta_7$ integrin us in ulcerative colitis (UC). So far, no VDZ response biomarker has been identified.
Aims & Methods: Aim: to assess whether baseline circulating CD4+ and CD8+ memory T lymphocytes subpopulations could be biomarkers of response to VDZ treatment in patients with UC.Prospective study, n=15 patients with active UC defined as Ulcerative Colitis Disease Activity Index (UCDAI) >3, Mayo endoscopic subscore >1 and fecal calprotectin >250 mcg/g. Treatment with VDZ (300mg iv) was scheduled as standard induction regime.
Peripheral blood samples were obtained before the first dose of VDZ. Purification of circulating memory T cells (CD45RO+) and simultaneous analysis of CD4+ and CD8+ lymphocytic subpopulations ($\alpha_4\beta_7$+/-, HLA-DR+/-, IL23R+/-, CCR9+/-, IL17A+/-, IL-23R+/-, IL-9+/-, β_7 +/-) by flow cytometry were performed.
Clinical response and remission, faecal calprotectin levels and Mayo endoscopic subscore were evaluated at week 14.
Results: 8 females, median of age was 45 (IQR=32) years, disease extent (Montreal – E1: 2 patients, E2: 8 patients, E3: 5 patients), 7 severe colitis (UCDAI > 9). Most patients (14) had prior failure to antiTNF-α: primary non-response in 8 patients and loss of response in 6.
Washout period were: 1 month for infliximab, 2 weeks for adalimumab. Vedolizumab treatment combined with steroids (prednisone 1 mg/kg/day PO) was started in 13 patients.
At week 14: 10 patients achieved steroid-free clinical remission, 9 patients had fecal calprotectin levels < 250mcg/g and 9 patients achieved biochemical and/or endoscopic remission (calprotectin levels < 250 mcg/g and/or Mayo endoscopic subscore < 1).
Patients with steroid-free clinical remission presented baseline absolute account of CD8 α4β7+ memory T cells significantly higher when compared with patients with no VDZ response (table 1). Patients with biochemical and/or endoscopic remission at week 14 presented baseline absolute account of CD8 α4β7+ T cells significantly higher and CD8 CCR9+ T cells significantly lower than non-responders.
No differences were identified according to flare severity, the extent of disease or the type of antiTNF-α failure. No statistical differences were found in the other lymphocyte subpopulations included in the study.

Baseline lymphocytes (absolute account/ml)	CLINICAL REMISSION 14Wk	NON CLINICAL REMISSION 14Wk	p value
CD4	394,47	327,66	0,026
CD8 α4β7+	19,265	11,4	0,026
Baseline lymphocytes (absolute account/ml)	BIOCHEMICAL AND/OR ENDOSCOPIC REMISSION 14W	NON BIOCHEMICAL AND/OR ENDOSCOPIC REMISSION 14W	p value
CD8CCR9+	0,33	1,12	0,041
CD8 α4β7+	24,1	10,57	0,007

[Analysis of baseline T cells subpopulations]

Conclusion: The absolute account of CD8 α4β7+ memory T cells before starting VDZ therapy could be an early biomarker of remission and therefore help us to select a subset of responders.
Disclosure: Investigator Initiated Sponsored Research by Takeda

P1790 COMBINATION OF BIOMARKERS REFLECTING TYPE IV COLLAGEN DEGRADATION AND CITRULLINATED VIMENTIN PREDICTS RESPONSE TO ADALIMUMAB WITH HIGH DIAGNOSTIC ACCURACY, IN PATIENTS WITH CROHN'S DISEASE

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Introduction: In inflammatory bowel diseases (IBD), up to 40% of patients do not respond to biologic treatment, e.g. anti-TNFα antibodies. A personalized medicine approach may facilitate the best possible treatment option for IBD patients. Currently, no biomarkers have sufficient sensitivity to separate responders from non-responders within the first weeks of anti-TNFα therapy, which limits the personalized medicine approach for IBD patients.

Aims & Methods: We investigated serum biomarkers that reflect basement membrane degradation (C4M: MMP mediated degradation of type IV collagen) and citrullinated vimentin (VICM: activated macrophages), and their ability to predict response to anti-TNFα treatment in Crohn's disease. This was a single-centre cohort study. We measured clinical responses to adalimumab at week 8 after treatment induction in 22 patients with Crohn's disease, using the Harvey Bradshaw Index (HBI). Response was defined as clinical remission (HBI< 5) at week 8. ELISA was applied to quantify the degradation of type IV collagen (C4M) and macrophages activity (VICM). Inflammation was estimated by C-reactive protein (CRP). The biomarkers were combined in a backwards multivariate regression model to increase the prediction value for non-response to anti-TNF.

Results: At baseline, C4M serum levels was significantly higher in non-responders compared with responders (AUC: 0.81 [CI: 0.58-1.00], p=0.027). VICM serum levels were not significantly different at baseline between responders and non-responders but was modulated in patients who responded to anti-TNF and was significantly lower at week 1 compared with non-responders (AUC=0.89 [CI: 0.69-1.00], p=0.007). CRP did not demonstrate any predictive value at baseline (AUC=0.65 [CI:0.42-0.89], p=0.301) or week 1 (AUC=0.66 [CI: 0.38-0.94], p=0.282). C4M and VICM were included in the final model. The combination of C4M and VICM increased the predicted value to identify patients that do not respond to anti-TNF treatment (AUC=0.94 [CI: 0.75-1.00], p=0.005), with an odds ratio of 22 (CI: 2.70-313).

Conclusion: The combination of baseline serum levels of C4M and week 1 serum levels of VICM demonstrated high accuracy to predict who will respond to anti-TNFα treatment in Crohn's disease, and was superior to CRP. Thus, baseline levels of C4M in combination with week 1 levels of VICM may be used to predict response to anti-TNF and may therefore aid in a more personalized treatment approach.

Disclosure: JHM, MAK, and TMJ are full time employees at Nordic Bioscience. MAK and TMJ hold stocks in Nordic Bioscience.

P1791 DIFFERENCE IN CLINICAL EFFICACY AND SAFETY IN CROHN'S DISEASE PATIENTS TREATED WITH INFLIXIMAB ACCORDING TO TIMING FOR ADDITION OF THIOPURINE

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Introduction: Although clinical efficacy of combination therapy with infliximab (IFX) and thiopurine has been demonstrated in Crohn's disease (CD), it remains uncertain when to add thiopurine in CD patients treated with IFX. The present study aimed to clarify appropriate timing for the addition of thiopurine in CD patients treated with IFX.

Aims & Methods: We performed a retrospective analysis of CD patients treated with IFX as the first-line biologic during the period between June 2002 and July 2018 at our institution. Patients were classified into early combination (EC) group and late combination (LC) group; EC group includes patients who were initiated thiopurine prior to IFX or simultaneously. LC group includes patients who were initiated IFX monotherapy or those who were added thiopurine after losing response to IFX. We then compared continuation rate of IFX between EC and LC groups using the Kaplan-Meier method and the log-rank test. We also compared adverse events (AEs) rates between the two groups.

Results: A total of 176 patients were included in the present study [64% men, median age, 23 (10-75) years], and the mean observation period was 76.8 months [range; 1-182 months]. 49 patients were classified into EC group and 127 patients were into LC group. The mean observation period and CRP level at the start of IFX were not significantly different between the two groups (64 months vs. 71 months; p=0.61, 0.55 mg/dl vs. 0.47 mg/dl; p=0.77). The mean period of taking thiopurine were significantly longer in EC group than LC group (53 months vs. 0 months; p< 0.0001). The cumulative IFX continuation rates showed no significant difference between the two groups (p= 0.25). 19 patients (38.7%) in the EC group and 28 patients (22%) in the LC group experienced AEs, and the rate was significantly higher in the EC group compared to LC group (p= 0.03). Serious AEs including pneumonia and pancreatitis requiring hospitalization were identified in 4 cases (8.2%) in the EC group, and 6 cases (4.7%) in the LC group, whereas the rate was not different between the two groups (p= 0.36).

Conclusion: The addition of thiopurine after loss of response to IFX monotherapy might be an alternative to the early combination therapy in CD when considering safety profile during treatments, whereas more precise analysis with regard to disease control should be necessary.

Disclosure: Nothing to disclose

P1792 EOTAXIN-1 AND MUCOSAL EOSINOPHIL ABUNDANCE PREDICT TREATMENT RESPONSE TO VEDOLIZUMAB IN INFLAMMATORY BOWEL DISEASE

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Introduction: Vedolizumab, an antibody against α4β7-integrin capable of blocking immune cell migration across intestinal endothelia expressing MADCAM-1, is a second-line biological treatment for moderate-to-severe inflammatory bowel disease (IBD). Because of moderate response rates to this drug, there is an urgent need for predictive markers to identify patients who are likely to benefit from vedolizumab. Our aim was to explore the predictive value of selected serum inflammatory biomarkers regarding response to vedolizumab induction therapy.

Aims & Methods: 76 IBD patients (Crohn's disease (CD), n=33, ulcerative colitis (UC), n=43) completed vedolizumab induction therapy and 10 serum inflammatory biomarkers were quantified prior to vedolizumab treatment (CRP, SAA, TNF-α, IFN-γ, IL-6, IL-8, IL-10, IL-17A, eotaxin-1 and eotaxin-3). Eosinophils were quantified in serum and in non-inflamed colon tissue (numbers per High Power Field (HPF 0.24 mm²)) prior to treatment. Eosinophil numbers were quantified up to 60/HPF and when ≥60 were set at 60. Clinical response was defined as a decrease of at least 3 points in the Harvey Bradshaw Index (HBI) for CD or Simple Clinical Colitis Activity Index (SCCAI) for UC.

Results: Baseline serum eotaxin-1 levels were significantly higher in vedolizumab responders, compared to primary non-responders (0.31 [0.22-0.46] vs. 0.20 [0.16-0.29] ng/mL, P< 0.05). Doubling of baseline serum eotaxin-1 levels was significantly associated with increased odds of attaining clinical response or remission at week 14 (adjusted OR: 3.28, P< 0.05). The final prediction model based on serum eotaxin-1 levels showed an adjusted area under the receiver operating characteristics curve (AuROC) of 0.81, with an optimally balanced cut-off value for serum eotaxin-1 >0.49 ng/mL with a sensitivity of 75.0% and specificity of 76.7% (Youden's index 0.52). A significant inverse correlation was observed between serum eotaxin-1 levels and serum eosinophil count (P< 0.01). As eotaxin-1 regulates the migration of eosinophilic granulocytes into the intestinal mucosa, we also analyzed mucosal eosinophilic granulocyte abundance in a subset of 24 IBD patients (10 CD and 14 UC) prior to treatment. Baseline median eosinophil numbers in non-inflamed tissue were significantly higher in responders compared to non-responders (60 ± 12 vs. 25 ± 7.5 eosinophils/HPF, P< 0.001). Patients with >30 eosinophils/HPF achieved clinical response in 83.3% of cases (n=12), whereas only 8.3% of patients with

< 30 eosinophils showed therapy response (n=12). Preliminary analyses (in 15 patients) revealed a positive correlation between serum eotaxin-1 and mucosal eosinophil abundance, though this was not significant yet in this small sub cohort. None of the other tested serum biomarkers showed significant predictive value for response or non-response to vedolizumab in this patient cohort.

Conclusion: Serum eotaxin-1 and mucosal eosinophil abundance in non-inflamed colon tissue are reliable predictors for vedolizumab response in IBD patients. Our findings await further validation in an independent patient cohort.

Disclosure: Nothing to disclose

P1793 AZATHIOPRINE CO-MEDICATION HAS NO IMPACT ON VEDOLIZUMAB PHARMACOKINETICS

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Introduction: It is now well established that response to anti-tumor necrosis factor (antiTNF) biologics in inflammatory bowel disease (IBD) is dependent on their pharmacokinetics. Azathioprine (AZA) co-medication has been associated with higher rate of therapeutic levels of antiTNF biologics. Vedolizumab (VDZ) has recently enriched the therapeutic options for IBD and the data on its pharmacokinetics, especially in the setting of AZA co-medication are scarce.

Aims & Methods: Therefore, the aims of this study were first, to determine the association of vedolizumab trough levels with clinical response to vedolizumab. Second, to analyze the impact of azathioprine co-medication on vedolizumab pharmacokinetics.

All IBD patients treated with vedolizumab for at least 6 months in two referral IBD centra between September 2015 and October 2019 were included. Sera were collected in a prospective manner from each patient prior the first maintenance infusion. VDZ levels were determined by ELISA (Ridascreen®, Biopharm) and the differences in VDZ levels between responders and non-responders as well as between patients with AZA co-medication vs. patients on VDZ monotherapy were analyzed statistically.

Results: In total, 42 IBD patients (28 with Crohn`s disease and 14 with ulcerative colitis) were included. There were 25 (59.5%) responders at 6 months of the treatment. Responders had significantly higher VDZ levels compared with non-responders (respective means±SEM – 15.08±2.475 µg/ml vs. 6.853±0.982 µg/ml; p=0.0118). The clinical response rate did not significantly differ between patients with AZA co-medication and patients on VDZ monotherapy (67% vs. 55%, p=n.s.). There was no difference in VDZ levels between these two groups of patients (13.2±2.859 µmol/l among AZA users vs. 11±2.26 µmol/l in VDZ monotherapy group; p=n.s.).

Conclusion: Clinical response to vedolizumab is associated with higher trough levels of vedolizumab during the maintenance phase of treatment. In contrast to antiTNF biologics, vedolizumab pharmacokinetics do not seem to be influenced by azathioprine co-medication.

Disclosure: This study has been supported by a grant from Slovak Research Agency

P1794 A FRENCH NATIONWIDE PROSPECTIVE STUDY OF INFLIXIMAB BIOSIMILAR CT-P13 USE IN REAL LIFE (REFLECT): A TWO-YEAR FOLLOW-UP

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Introduction: Reflect study has been carried out to assess in real life the use of CT-P13, the first monoclonal antibody biosimilar to infliximab (IFX) approved in France. Long-term real-life data on CT-P13 use are limited in patients (pts) suffering from Inflammatory bowel diseases and rheumatic diseases.

Aims & Methods: Reflect is a multicenter, prospective, observational study conducted in France which aims to describe characteristics of pts' receiving CT-P13 and to assess safety and effectiveness in real-life conditions. Pts (age ≥ 6 years) with Crohn's disease (CD), ulcerative colitis (UC) and rheumatic diseases treated with CT-P13 were eligible for enrolment, including IFX naive pts (IFXn) or those having switched from IFX originator to CT-P13 (IFXs). Complementary data after a two-year follow-up period in pts suffering from CD and UC using descriptive statistical analyses are presented here.

Results: From 3rd October 2018 to 31st January 2019, of the 1321 included pts, 680 pts with inflammatory bowel disease were analyzed in the present sub analysis [480 CD pts (48.3% males; mean age: 37.1 ± 14.1 years; median disease duration: 6.9 years) and 200 UC pts (54.5%; 41.2 ± 17.5 years; 5.4 years)]. Previous biologics other than IFX were taken by 40,3% of CD and 41,8% of UC pts. At baseline, a minority of pts (21.8% of CD and 18.5% of UC) have been switched from the IFX originator to CT-P13; more pts have an active disease in IFXn 79,5% for UC and 52,2% of CD comparing to IFXs pts 37.5% and 15,4% respectively (p=0.002 and p< 0.001). In UC pts, median Mayo score were 7.5 and 1.5 in IFXn and IFXs pts at baseline and, it decreased by 3 and 5 points at 12 and 24 months in IFXn pts. In CD pts, median Harvey-Bradshaw Index (HBI) were 4 and 1 in IFXn and IFXs pts respectively and, it decreased by 2 and 1 points in at 12 and 24 months IFXn pts. In IFXs pts, there was no change in both UC and CD median disease activity scores at 12 and 24 months except for the HBI which increased slightly at 24 months by 1 point. The treatment with CT-P13 has been withdrawn due to treatment failure or safety reason in 5,6 % of CD pts and 12,7 % UC pts in IFXn pts and in 2,1% and 2,9% of IFXs pts.

Conclusion: The two years follow-up data suggest that CT-P13 was effective in inducing and maintaining remission in CD and UC in both naive and switched patients. This real-life study did not identify new safety concerns.

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P1795 REAL LIFE EXPERIENCE OF FIRST LINE ANTI-TNF IN CROHN'S DISEASE PATIENTS IN SPAIN: DO WE HAVE DATA TO CHOOSE BETWEEN INFLIXIMAB AND ADALIMUMAB?

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Introduction: Anti-TNFs represent a key treatment strategy for the management of IBD. However, it would be important to have more data about their use with the aim of facilitating the right choice in clinical practice. One of the aims of this study was to learn about the patterns of use of two anti-TNFs, adalimumab and infliximab, when used in biologic-naïve patients for the treatment of Crohn's disease (CD).

Aims & Methods: This was a retrospective, observational study, conducted in 24 hospitals in Spain. IBD patients who started first anti-TNF treatment between June 2011 and June 2013 were included consecutively in the participating centres. Data about anti-TNF management were collected. Kaplan Meier analyses were used to evaluate time to treatment intensification and time to discontinuation in CD with adalimumab and infliximab. Data are presented descriptively

Results: One hundred and ninety-four CD patients were included (n=85 treated with infliximab and n=109 treated with adalimumab). Median age was 43.0 years (range: 20.0-74.0) and most patients presented ileum and colon (L3=44.6%) or terminal ileum location (L1=37.3%). The most common disease behaviour was inflammatory (B1=44.6%). Median follow up time (from treatment initiation until informed consent signed) was 59.7 (range: 43.5 - 76.2) and 60.2 (range: 45.3 - 74.9) months for adalimumab and infliximab respectively.

Dose intensification was recorded in 29.4% of patients treated with adalimumab and 28.2% of patients treated with infliximab. Median time to first dose intensification was similar with adalimumab, 15.1 months (range 1.3-61.8) and infliximab, 14.1 months (range 0.2-59.5).

Regarding treatment discontinuation, it occurred in 56.0% of patients treated with adalimumab, and in 63.5% with infliximab. Median time to treatment discontinuation was 27.4 months (range 0.9-66.9) with adalimumab, and 23.0 months with infliximab (range 0.0-58.9).

Concomitant use of corticosteroids at any time during maintenance was similar with adalimumab (31.2%) compared with infliximab (28.2%) being the mean number of cycles needed was similar (adalimumab 1.5, SD 0.8 vs infliximab 1.2, SD 0.5). The use of immunosuppressants at any time during maintenance was similar among the two products (adalimumab: 60.5% vs infliximab: 76.5%) being the mean number of required cycles was also comparable (adalimumab 1.3, SD 0.9 vs infliximab 2.2, SD 8.4).

Conclusion: Similar proportions of patients with CD received dose intensification with infliximab and adalimumab, and the discontinuation rates with both anti-TNFs were also similar.

Dose intensification with both anti-TNFs was required in around one in every three patients, and after a similar median time (slightly longer than 1 year).

More than half of patients treated with adalimumab and infliximab discontinued treatment during the follow-up, and this occurred after a comparable median time (slightly longer than 2 years).

Although a significant proportion of patients required concomitant use of corticosteroids and/or immunosuppressants, the average number of required cycles was low.

Despite the common use of anti-TNFs as the first biologic in CD, we have not found any major difference between adalimumab and infliximab that could lead to a preferred treatment option.

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P1796 TOFACITINIB INDUCTION EFFICIENCY AND INTRACELLULAR CYTOKINE DYNAMICS IN ULCERATIVE COLITIS: RESULTS FROM CLINICAL PRACTICE

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Introduction: Tofacitinib is an oral JAK inhibitor with intracellular mechanism of action, approved for the treatment of ulcerative colitis (UC). Its efficiency was proven in registration trials, however data from clinical practice are insufficient. Our aim was to evaluate response to tofacitinib after 8 weeks in UC patients, and to assess potential predictors of response including early cytokine production shifts.

Aims & Methods: Data from consecutive UC patients who started tofacitinib 10 mg b.i.d. between January and April 2019 were evaluated. Disease activity was assessed by Mayo score including endoscopic Mayo at baseline and week 8 together with C-reactive protein (CRP) and fecal calprotectin (FC). Production of IL-4, IL-10, IL-17, TNFα and IFNγ in T-helper cells was determined at baseline and week 4 by flow cytometry after lymphocyte activation.

At week 8, patients with total Mayo 0-5 with endoscopic subscore 0-1 (corresponding to mucosal healing) were considered responders. Adverse events were registered at every visit (weeks 2, 4 and 8).

Results: 24 patients (41.7% males, 58.3% females), mean age 35.3±11.8 years were included. Mean disease duration was 8.3±5.2 years. In median, the patients were previously treated with 2 biologic agents, however, 25% of the patients were naive to any biologic therapy. Systemic corticosteroids were present in 41.7% patients at baseline and no patient had concomitant biologic or other immunosuppressive therapy. At week 8, 52.9% of patients responded to therapy. Total Mayo decreased in responders from mean 5.9±3.5 to 1.1±1.3 (p=0.01), while in nonresponders it changed from 8.0±2.5 to 8.9±2.1 (p=0.86). Endoscopic subscore decreased from 2.0±1.0 to 0.6±0.7 (p=0.02) in responders, however remained stationary in nonresponders (2.9). CRP and FC dropped significantly in responders (6.7±6.2 vs. 2.0±2.2 mg/L, p=0.04; 1195±1189 vs. 578±654 μg/g, p=0.05), but not in nonresponders. The responding and nonresponding groups differed significantly in baseline triglycerides, which were higher in nonresponders. Other baseline parameters were comparable including corticotherapy, previous biologic therapy, disease duration and laboratory values, however, nonresponders tended to have more active disease at baseline and there were more females in the responding group (62.5% vs. 18.2%, p=0.07). Significant difference was observed in shifts of production of cytokines IL-4 and IL-10 in T-helper cells. In responders, there was a significant decrease in IL-4 and no change in IL-10, while in nonresponders, there was no change in IL-4 and significant decrease in IL-10. Interestingly, there was also a significant increase of intracellular TNFα in all patients. Tofacitinib was stopped in 23.5% of patients at week 8 due to insufficient response. Two patients reported headaches after treatment initiation and single events of CMV colitis, *C. diff.* colitis and oral candidiasis occurred.

Conclusion: Tofacitinib was efficient in inducing clinical response with mucosal healing in about 50% of UC patients after 8 weeks of therapy in clinical practice. There was no clear baseline predictor of response, however, considering limited sample, there was also no indication of even multiple biologics failure negatively affecting response. Tofacitinib might thus be an option in respective patients. Preliminary results of cytokine dynamics suggest early IL-4 decrease as a potential biomarker of response, warranting further investigation.

Disclosure: Nothing to disclose

P1797 MADCAM1 EXPRESSION IS STABLE OVERTIME AND IS NOT INFLUENCED BY IMMUNE SUPPRESSIVE MEDICATION

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Introduction: Approximately one third of inflammatory bowel disease (IBD) patients are primary non-responders to vedolizumab, a monoclonal antibody against α4β7 integrin receptor. Activated lymphocytes are homing to the gut mucosa through binding to mucosal vascular adressin cell adhesion molecule 1 (MAdCAM1) localised on the intestinal endothelial cells. MAdCAM1 expression is subject to great interindividual variability which may impact the efficacy of vedolizumab. If stable overtime decreased or absent MAdCAM1 expression might be one of the determinants of primary non-response to vedolizumab.

Aims & Methods: The aim of this study was thus to determine the stability of MAdCAM1 expression on intestinal endothelial cells of IBD patients overtime and the influence of immune suppressive therapy on this expression.

From all IBD patients who underwent bowel resection in one referral center between January 2016 and March 2019 the resection specimens were randomly selected for assessment of MAdCAM1 expression in lamina propria endothelial vessels. The expression was determined by immunohistochemistry and was arbitrarily assigned into three categories: negative, low and high (0%, up to 30% and above 30% of MAdCAM1 positive lamina propria vessels, respectively). For patients with serial specimens, resection or biopsies, the changes in MAdCAM1 expression overtime were assessed. The medication used in the last 30 days before resection was noted and the differences between the respective groups according to MAdCAM1 expression were analyzed.

Results: There were in total 112 resections performed, out of which 52 resection specimens (38, 73% with Crohn`s disease, 14, 27% with ulcerative colitis; 48% of males) were randomly selected for MAdCAM1 expression

assessment. There were 6 pts (12%) with negative MAdCAM1 expression, 10 (19%) had low and 36 (69%) had high MAdCAM1 expression. There were no differences in rates of respective immune suppressive therapies used preceding the surgery; the systemic steroids, azathioprine and biologics were equally distributed among all three groups.

For fifteen patients, serial specimens were available. Among these patients, there were 11 patients with high MAdCAM1 expression and 4 with low expression. All patients with high MAdCAM1 expression had concordant levels of expression overtime. From four patients with low MAdCAM1 expression, one patient had negative expression in one and low expression in a second specimen, other three had low MAdCAM1 expression in all serial specimens.

Conclusion: One fifth of IBD patients do not express or have low expression of MAdCAM1. The expression of MAdCAM1 is stable overtime and is not influenced by immune suppressive medication. Further studies are needed to determine whether this low MAdCAM1 expression might underly the primary non-response to vedolizumab.

Disclosure: ZZ received lecture fees from Takeda.

P1798 MANAGEMENT OF ANTI-TNF ANTIBODY THERAPY FOR LONG-TERM REMISSION OF CROHN'S DISEASE

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Introduction: To maintain the long-term remission of Crohn's disease, it is important to sustain the effects of anti-tumor necrosis factor (TNF) antibody therapy. Here we examined risk factors related to primary or secondary failure of anti-TNF therapy.

Aims & Methods: We analyzed 127 patients with Crohn's disease who treated with anti-TNF antibody as maintenance therapy at our hospital, and the frequency of primary as well as secondary failure of anti-TNF antibody therapy was determined. In addition, factors related to primary or secondary failure during the treatment were examined retrospectively.

Results: Among subjects, 100 patients were treated with infliximab (IFX) and 27 patients were treated with adalimumab (ADA) as first biologics. Primary failure was observed in 6 patients (6%) treated with IFX and 3 patients (11%) treated with ADA, with no differences among the drugs. We further examined 118 patients excluding primary failure, secondary failure was observed in 53 patients (56%) treated with IFX and 3 patients (13%) treated with ADA. Thiopurines were administered in 62 patients (66%) treated with IFX and 15 patients (63%) treated with ADA. The cumulative rate of secondary failure was 5% for 1 year, 28% for 3 years, and 47% for 5 years. We next examined risk factors related to secondary failure by Kaplan-Meier method and log-rank test. Thiopurine administration prior to anti-TNF antibody (p = 0.01) and C-reactive protein (CRP) less than 0.3 mg/dl at the start of treatment (p = 0.02) showed significantly longer prognosis of primary therapy. In multivariate analysis by proportional hazards model, the time to secondary failure was significantly longer in the cases with prior administration of thiopurine (p = 0.03), whose hazard ratio was 3.3. Finally, 55 cases were examined whether the single nucleotide polymorphism of Fcγ receptor could be a predictor of primary or secondary failure of anti-TNF therapy. The frequency of primary failure of IFX was significantly higher in the cases with single nucleotide polymorphisms of *FCGR2A* and *FCGR3A* (p = 0.006).

Conclusion: Continuation of primary treatment is important for maintaining long-term remission of Crohn's disease, and prior administration of thiopurine was considered to be useful to avoid secondary failure of anti-TNF therapy. In addition, it has been suggested that single nucleotide polymorphism of Fcγ receptor may be a predictor to IFX primary failure.

Disclosure: Nothing to disclose

P1799 THE METHODOLOGY, FEASIBILITY AND SAFETY OF COLONIC TRANSENDOSCOPIC ENTERAL TUBING: A MULTICENTER, RANDOMIZED CONTROLLED TRIAL

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Introduction: Colonic transendoscopic enteral tubing (TET) is a novel, safe and quick technology for microbiota transplantation (MT) and whole colon administration. During the TET procedure, this technique needs insert colonoscope twice, the first time is for inserting the TET tube, the second time is for affixing the TET tube to the intestinal wall using titanium clips. However, it is difficult to find the cavity during the second time after inserted tube for some patients because of the gather of colonic folds and acute angle of colonic cavity caused by the TET tube pulling. It is well known that cap assisted colonoscope is easier to flatten the haustral folds and improve mucosal exposure. Here we establish the hypothesis that using cap assisted colonoscope can decrease the second cecal intubation time which not only improve work efficiency, but also save procedure time.

Aims & Methods: We designed a prospective multicenter, randomized controlled trial to compare the effect of with or without cap assisted colonoscopy for the second insertion on colonic TET procedure in order to perform the colonic TET faster and more convenient. All subjects who underwent colonic TET were included at three centers in China from August 2018 to March 2019. Subjects were randomly assigned to cap assisted group (n=105) and non-cap assisted group (n=106). The primary outcome was the second cecal intubation time. Secondary outcomes included TET procedure time, success rate, single titanium clip fixation time, retaining time of TET tube, maximum insertion pain score and all related adverse events (AEs).

Results: Baseline characteristics were comparable between the two groups (P>0.05). The TET tubes were used in 50 patients for MT and whole colon administration, 127 patients for MT, and 6 healthy volunteers for sampling. The success rate of TET procedure was 100% in two groups. The median second cecal intubation time in the cap assisted group was shorter in comparison with non-cap assisted group (2.6 (IQR: 1.7-3.4) min vs 3.0 (IQR: 2.0-4.1) min, P=0.019). The difference of mean second cecal intubation time was more obvious in two groups among patients with constipation (cap vs non-cap: 2.9±1.2 min vs 4.0±2.0 min, P=0.017). The mean second cecal intubation time in cap assisted group was shorter than that of non-cap assisted group among patients with ulcerative colitis, however, there was no statistical difference (2.5±1.2 min vs 3.2±2.1 min, P= 0.137). The median TET procedure time was shorter in cap assisted group, but there was no significant difference between the groups (8.9 (IQR 7.5-11.9) min vs 9.1 (IQR 7.0-10.9) min, P=0.352). The median single titanium clip fixation time was also no significant difference between the groups (1.2 (IQR 0.9-1.5) min vs 1.2 (IQR 1.0-1.4) min, P=0.777). Their maximum insertion pain scores were lower in cap assisted group, but there was no significant difference (4.6±2.6 vs 5.2±1.9, P=0.573). 3 subjects had anal discomfort and 1 subject had anal pain in cap assisted group, and 1 subject had anal pain in non-cap assisted group after TET. AEs were no significant difference between the groups (4.5% vs 1.0%, P=0.201). No severe AEs was observed during and after TET.

Conclusion: This study confirms that cap assisted colonoscopy for TET procedure can shorten the second cecal intubation time, and is a safe and effective method. Therefore, it is recommended to insert colonoscope in the second time with cap assisted in TET procedure to improve work efficiency and reduce procedure time, especially for patients with constipation.

References: [1]Peng Z, Xiang J, He Z, et al. Colonic transendoscopic enteral tubing: A novel way of transplanting fecal microbiota[J]. Endosc Int Open, 2016, 4(6): E610-3. [2]Zhang F, Zhang T, Zhu H, et al. Evolution of Fecal Microbiota Transplantation in Methodology and Ethical Issues[J]. Curr Opin Pharmacol, 2019. DOI: 10.1016/j.coph.2019.04.004. [3]Ding X, Li Q, Li P, et al. Long-Term Safety and Efficacy of Fecal Microbiota Transplant in Active Ulcerative Colitis[J]. Drug Saf, 2019.

Disclosure: Nothing to disclose

P1800 PATIENT SATISFACTION AND ADHERENCE TO FECAL MICROBIOTA TRANSPLANT ON LONG-TERM CLINICAL OUTCOME OF ULCERATIVE COLITIS

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Introduction: Ulcerative colitis (UC), a phenol type of inflammatory bowel disease (IBD), is a chronic relapsing and remitting inflammatory disorder of the gastrointestinal tract. Although the pathophysiology of UC remains unknown, growing evidence suggests that the changes in gut microbiota composition may be a key element in gut inflammatory processes[1]. Fecal microbiota transplantation (FMT), which involves the infusion of fecal microbiota from a healthy donor into a patient's intestine for reconstructing gut microbiota, has become an option for the treatment of UC.The way to improve the long-term efficacy of FMT remains unclear.

Aims & Methods: This study aimed to evaluate the UC patients' satisfaction with FMT and the role of adherence to scheduled FMT for long-term clinical outcomes.Patients with UC who underwent FMT at our center from November 2012 to September 2018 were evaluated. We assessed patient satisfaction with post-FMT outcomes, adherence to the second course of FMT, and attitude towards delivering ways of FMT.

Results: 176 patients were included into the final analysis. At one week, one month, three months, and six months after FMT, the clinical response rate was 48.9%, 69.3%, 49.4%, and 32.7%, respectively. Patients' quality of life was significantly higher one year after FMT than that before FMT (P < 0.001). Partial Mayo score at one month post-FMT (P < 0.001) was an independent factor of patients' satisfaction. The laboratory preparation process was related to the incidence of adverse events (P < 0.05). 76.2% (93/122) of patients exhibited poor adherence to the treatment of sequential FMTs while 23.8% (29/122) of patients followed our recommendation for the second course of FMT. Patients achieved longer clinical response in the good adherence group as compared with the poor adherence group (P < 0.001). Patients preferred to choose colonic transendoscopic enteral tubing (TET) as the FMT delivery route.

Conclusion: Patients' good adherence to scheduled FMT is an important factor to maintain long-term clinical benefits achieved from FMT.

Disclosure: Dr. Faming Zhang invented the concept of GenFMTer and transendoscopic enteral tubing and devices related to it.

P1801 A PROPENSITY SCORE-WEIGHTED COMPARISON OF VEDOLIZUMAB, ADALIMUMAB, AND GOLIMUMAB IN PATIENTS WITH ULCERATIVE COLITIS: REAL-LIFE DATA FROM THE SICILIAN NETWORK FOR INFLAMMATORY BOWEL DISEASE (SN-IBD)

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Introduction: The recent VARSITY trial showed that Vedolizumab (VDZ) was superior to Adalimumab (ADA) in achieving clinical remission and mucosal healing in patients with ulcerative colitis (UC). Conversely, no real-life data on the comparative effectiveness of VDZ, ADA, and Golimumab (GOL) in UC have been published yet.

Aims & Methods: Data of consecutive patients with UC treated with VDZ, ADA, and GOL from June 2015 to December 2018 were extracted from the cohort of the Sicilian Network for Inflammatory Bowel Disease (SN-IBD). A three-arms propensity score-adjusted analysis was performed to reduce

bias caused by imbalanced covariates at baseline, including the proportion of TNF-α inhibitor naïve and non-naïve patients, using the Inverse Probability of Treatment Weighting (IPTW) approach. The effectiveness was evaluated at 8 weeks, 52 weeks, and as treatment persistence at the end of follow up. The clinical endpoints were steroid-free clinical remission (partial Mayo score < 2 without steroid use) and clinical response (reduction of the partial Mayo Score ≥2 points with a concomitant decrease of steroid dosage compared with baseline). The sum of the two outcomes was defined as clinical benefit. The achievement of mucosal healing (endoscopic Mayo score 0-1) was assessed after at least 6 months of biological treatment.

Results: A total of 463 treatments (187 VDZ; 168 ADA; 108 GOL) were included, with a median follow-up of 47.6 weeks (IQR 20.0-85.9). At 8 weeks, a clinical benefit was achieved in 70.6% patients treated with VDZ, in 68.5% patients treated with ADA, and in 67.6% patients treated with GOL (p = n.s. for all comparisons); at 52 weeks, VDZ showed better rates of clinical benefit compared with both ADA (71.6% vs. 47.5; OR: 2.79, 95% CI 1.63-4.79, p< 0.001) and GOL (71.6% vs. 40.2%; OR: 3.77, 95% CI 2.08-6.80, p< 0.001), while the difference between ADA and GOL was not significant. Cox survival analysis demonstrated that patients treated with VDZ had a reduced probability of treatment discontinuation compared to those treated with ADA (HR: 0.42, 95% CI 0.28-0.64, p< 0.001) and GOL (HR: 0.30, 95% CI 0.19-0.46, p< 0.001), while patients treated with ADA had a significantly reduced risk of treatment discontinuation compared to those treated with GOL (HR: 0.71, 95% CI 0.50-1.00, p=0.048). Post-treatment mucosal healing rates showed a numerical but non-significant difference in favour of VDZ (48.1%) compared with ADA and GOL (38.0% and 34.6%, respectively).

Conclusion: In the first study comparing at the same time the clinical effectiveness of VDZ, ADA, and GOL in UC patients via propensity score-adjusted analysis, VDZ was superior to both subcutaneous agents at 52 weeks and as treatment persistence, while ADA showed a superior treatment persistence compared to GOL.

Disclosure: Fabio Salvatore Macaluso served as an advisory board member for MSD and Biogen, and received lecture grants from MSD, AbbVie, and Takeda Pharmaceuticals. Maria Cappello served as an advisory board member for AbbVie, MSD, Takeda Pharmaceuticals, and received lecture grants from AbbVie, MSD, Chiesi, and Takeda Pharmaceuticals. Filippo Mocciaro served as an advisory board member for AbbVie and MSD Pharmaceuticals, and received lecture grants from AbbVie, MSD and Takeda Pharmaceuticals. Sara Renna served as an advisory board member for AbbVie and MSD Pharmaceuticals, and received lecture grants from AbbVie, MSD and Takeda Pharmaceuticals Ambrogio Orlando served as an advisory board member for AbbVie, MSD, Takeda Pharmaceuticals, and received lecture grants from AbbVie, MSD, Sofar, Chiesi, and Takeda Pharmaceuticals.

P1802 THE FREQUENCY OF FECAL MICROBIOTA TRANSPLANTATION FOR MAINTENANCE OF LONG-TERM EFFICACY IN PATIENTS WITH ULCERATIVE COLITIS: A PILOT STUDY

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Introduction: Ulcerative colitis (UC), a phenol type of inflammatory bowel disease (IBD), is a chronic relapsing and remitting inflammatory disorder of the gastrointestinal tract. Although the pathophysiology of UC remains unknown, growing evidence suggests that the changes in gut microbiota composition may be a key element in gut inflammatory processes[1]. Fecal microbiota transplantation (FMT), which involves the infusion of fecal microbiota from a healthy donor into a patient's intestine for reconstructing gut microbiota, has become an option for the treatment of UC.Increasing evidence has shown that fecal microbiota transplantation (FMT) is emerging as a novel therapy for ulcerative colitis (UC).

Aims & Methods: To study the frequency of fecal microbiota transplantation for maintenance of long-term efficacy in patients with ulcerative colitis.Patients were recruited from November 2012 to September 2018. 122 patients who achieved clinical response at one month after first course of FMT were included into the final analysis. The risk factors of the efficacy maintenance time and readmission for FMT were assessed by Chi-square test or non-parametric test.

Results: The median time of maintaining clinical response to the first course of FMT in total 77 patients was 90 days (IQR, 30-150). The time of maintaining clinical response to the second course of FMT in 25 of 77 patients was 180 days (IQR, 97.5-297.5). Compared with the time of maintaining clinical response to the first course FMT, the second course of FMT achieved prominently longer maintenance time in the 25 patients (p <0.05). No severe adverse event related to the FMT was observed during and after the FMT procedure, as well as during the long-term follow-up. The volume of fecal microbiota did not affect the clinical response maintenance time (p = 0.562). The patients with readmission attained remarkably longer time of maintaining efficacy than those without readmission (p <0.0001) and they had significantly better efficacy at 3 months after the first course of FMT comparing with the patients who were not readmission (p <0.0001).

Conclusion: This study demonstrated that patients with UC could be administered the second course of FMT less than 3 months after the first FMT and they were advised to get the third course of FMT less than 6 months after the second one for maintaining the long-term clinical benefits from the FMT. Readmission for next course of FMT was valuable to maintain long-term efficacy.

Disclosure: Dr. Faming Zhang invented the concept of GenFMTer and transendoscopic enteral tubing and devices related to it.

P1803 ASSOCIATION OF USTEKINUMAB SERUM CONCENTRATIONS AND PERIANAL FISTULA RESOLUTION IN THE CROHN'S DISEASE UNITI PROGRAM

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Introduction: Previous studies have demonstrated the efficacy and safety of ustekinumab (UST) IV induction and SC maintenance in Crohn's disease. Analysis from the Phase 2 and 3 UST trials also demonstrated possible benefit in fistula resolution at week 8 [14.1% (10/71) PBO vs 24.7% (37/150) all UST doses combined] despite a small proportion (10.8 to 15.5% across the studies) of patients with active perianal fistulas at baseline (Sands et al DDW 2017). Here we examine the relationship between perianal fistula resolution at induction week 8 (maintenance week 0) and maintenance week 44 based on serum UST levels at maintenance weeks 0 and 24 in patients receiving IV UST induction and SC UST maintenance.

Aims & Methods: Patients in UNITI-1 and 2 induction studies were randomized to IV PBO or UST (130mg or ~6mg/kg). Patients with open, draining perianal fistulas at baseline had their fistulas assessed by physical exam (including gentle compression). Patients were analyzed for complete fistula resolution (100% reduction) at subsequent study visits. Fistula resolution at induction week 8 was also analyzed based on week 8 UST serum concentration quartiles, while fistula resolution at maintenance week 44 was analyzed based on maintenance week 24 UST serum concentration quartiles (incorporating non-randomized and randomized groups). Patients who started a prohibited medication (e.g. another biologic) were considered not to be in fistula resolution.

Results: In observed data, among randomized patients with open, draining perianal fistulas at baseline of UNITI-1/2 27.5% (11/40) receiving 130mg, 23.7% (9/38) receiving ~6mg/kg UST and 25.6% (20/78) combined UST had fistula resolution induction week 8 compared to 9.3% (4/43) in the PBO group (p=0.03, 0.08, and 0.03, respectively). At week 44, 85.7% (6/7) and 71.4% (5/7) patients randomized to UST maintenance (90mg Q8W or Q12W) had perianal fistula resolution, compared to 44.4% (4/9) of patients randomized to PBO (p=0.15 and 0.36, respectively). Incorporating all patients (randomized and non-randomized) treated with UST maintenance, perianal fistula resolution occurred in 42% (21/50) of patients. In the induction week 8 quartile analysis, perianal fistula resolution was 38.9% (7/18) in Q1, 11.8% (2/17) in Q2, 27.8% (5/18) in Q3, and 29.4% (5/17) in Q4 for all UST treated patients (Table 1). Fistula resolution at maintenance week 44 based on week 24 concentration quartiles also did not show any exposure response relationship (Table 1).

Fistula Resolution at Week 8 Post Induction (Week 0 Maintenance) by Serum Concentrations at Week 8 Post Induction (Week 0 Maintenance)

UST Concentration Quartiles WK 0[a]	130mg UST[b]	~6mg/kg[c]	Combined
Q1	33.3% (3/9)	44.4% (4/9)	38.9% (7/18)
Q2	11.1% (1/9)	12.5% (1/8)	11.8% (2/17)
Q3	44.4% (4/9)	11.1% (1/9)	27.8% (5/18)
Q4	33.3% (3/9)	25.0% (2/8)	29.4% (5/17)

Fistula Resolution at Week 44 Post Maintenance by UST Serum concentrations at Week 24 Post Maintenance

UST Concentration Quartiles WK 24[a]	90 mg Q8W[d]	90mg Q8W or Q12W[e]	-
Q1	85.7% (6/7)	75% (9/12)	-
Q2	57.1% (4/7)	50% (6/12)	-
Q3	28.6 (2/7)	25% (3/12)	-
Q4	14.3% (1/7)	27.3% (3/11)	-

a Patients in fistula resolution with missing PK data were excluded from this analysis
b Q1: <1.18 µg/ml; Q2 >1.18 µg/ml <1.62 µg/ml; Q3: >1.62 µg/ml <2.84 µg/ml; Q4 >2.84 µg/ml
c Q1 <3.40 µg/ml; Q2 >3.40 µg/ml <5.04 µg/ml; Q3 >5.04 µg/ml <9.30 µg/ml; Q4 >9.30 µg/ml
d Q1: <1.34 µg/ml; Q2: >1.34 µg <1.99 µg/ml; Q3: >1.99 µg/ml< 3.01 µg/ml; Q4 > 3.01 µg/mL
e Q1: <1.25 µg/ml; Q2: >1.25 µg <2.31 µg/ml; Q3: >2.31 µg/ml< 3.47 µg/ml; Q4 > 3.47 µg/mL

[Table 1: Fistulation Resolution at Induction Week 8 and Maintenance Week 44]

Conclusion: Some evidence of efficacy in perianal fistula resolution is present with UST in both induction and maintenance, despite a relatively small number of patients with perianal fistulas. However, perianal fistula resolution did not appear to be associated with higher UST serum concentrations.

Disclosure: Bruce E Sands, Jean-Frederic Colombel, David Schwartz are all investigators for Janssen Research & Development, LLC Brian C. Kramer Christopher Gasink are employees of Janssen Scientific Affairs, LLC Douglas Jacobstein, Long-Long Gao, Tony Ma, and Omoniyi J Adedokun are all employees of Janssen Research & Development, LLC

P1804 LOWER TNF-A INHIBITOR DRUG SURVIVAL IN FEMALE PATIENTS WITH INFLAMMATORY BOWEL DISEASE IS REALTED TO A GREATER RISK OF SIDE EFFECTS

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Introduction: Approximately 11% of patients fail to respond to induction therapy with anti-tumour necrosis factor-α (TNF-α) (primary non-responders) and 25-40% of primary responders discontinue treatment because of loss of response or side effects over time. Identification of patient-specific factors related to drug discontinuation is therefore important to aid physicians in clinical decision making. In rheumatoid arthritis and psoriasis female sex has been shown to be associated with discontinuation of anti-tumour necrosis factor-α (TNF-α) therapy. We assessed the association between sex and TNF-α drug survival in patients with inflammatory bowel disease (IBD).

Aims & Methods: All IBD patients treated with infliximab (IFX), adalimumab (ADA) or golimumab (GOL) between January 2011 and December 2017 were retrospectively identified in the hospital's pharmacy's record. Patients with a follow-up time of less than 12 months at our hospital were excluded. Patient and treatment characteristics and reasons for anti-TNF-α discontinuation (primary non-response, secondary loss of response, side effects and 'other' discontinuation reasons) were recorded.

The primary analyses were done by multilevel Cox proportional hazards regression models with random intercepts per patient. Univariable hazard ratios for overall discontinuation were estimated. Subsequently the association between sex and overall anti-TNF-α discontinuation was multivariable assessed. Competing risks Cox proportional hazards models were fitted to assess uni- and multivariable hazard ratios for the discontinuation reasons separately.

Results: In total 529 patients were included (50.1% female, 631 treatment episodes - 357 IFX, 240 ADA, 34 GOL - and 2280 TNF-α inhibitor treatment years). Female sex (adjusted hazard ratio [aHR] 1.42, 95% CI 1.16 - 1.74), higher age at start of therapy per decade (aHR 1.15, 95% CI 1.04

Variable	Total cohort all discontinuations Univariable	Total cohort all discontinuations Multivariable	Total cohort loss of response Univariable	Total cohort loss of response Multivariable	Total cohort side effects Univariable	Total cohort side effects Multivariable	Total cohort 'other' discontinuations Univariable	Total cohort 'other' discontinuations Multivariable
Female sex (male reference)	1.37 (1.10-1.70)	1.42 (1.16-1.74)	1.13 (0.87-1.46)	1.17 (0.91-1.51)	4.01 (2.35-6.85)	4.05 (2.36-6.98)	1.03 (0.67-1.58)	1.00 (0.64-1.55)
Age at start per decade	1.15 (1.05-1.27)	1.15 (1.04-1.27)	1.06 (0.95-1.19)	1.10 (0.97-1.26)	1.24 (1.06-1.45)	1.23 (1.00-1.52)	1.25 (1.04-1.50)	1.20 (0.96-1.52)
Second and later treatment episode	1.08 (0.81-1.45)	0.97 (0.70-1.36)	1.41 (0.98-2.02)	0.86 (0.56-1.33)	1.34 (0.77-2.34)	1.36 (0.70-2.67)	1.55 (0.81-2.97)	1.38 (0.64-2.95)
Adalimumab therapy (infliximab reference)	0.98 (0.74-1.29)	1.08 (0.78-1.49)	1.24 (0.87-1.77)	1.70 (1.11-2.60)	0.94 (0.54-1.63)	0.61 (0.32-1.16)	1.26 (0.67-2.37)	1.03 (0.50-2.12)
Golimumab therapy (infliximab reference)	2.25 (1.27-3.99)	1.95 (1.06-3.61)	3.64 (1.88-7.03)	4.97 (2.30-10.74)	2.05 (0.68-6.20)	1.05 (0.29-3.77)	3.64 (0.99-13.38)	2.01 (0.47-8.50)
Duration of disease (yrs)	1.01 (1.00-1.03)	1.00 (0.98-1.02)	1.00 (0.98-1.02)	0.99 (0.97-1.02)	1.03 (1.00-1.06)	1.01 (0.98-1.04)	1.03 (1.00-1.06)	1.01 (0.97-1.05)
Current smoker	0.94 (0.61-1.44)	0.93 (0.62-1.40)	0.92 (0.55-1.55)	0.87 (0.52-1.47)	1.20 (0.60-2.41)	0.94 (0.45-1.95)	0.94 (0.38-2.33)	Removed from model
Dose escalation	3.54 (2.64-4.76)	3.74 (2.78-5.02)	6.88 (4.77-9.92)	7.71 (5.28-11.26)	1.22 (0.61-2.44)	1.39 (0.67-2.87)	0.60 (0.27-1.35)	Removed from model
Concomitant immunomodulator use	0.95 (0.72-1.27)	0.94 (0.71-1.24)	0.98 (0.69-1.41)	0.89 (0.62-1.28)	0.72 (0.42-1.22)	0.76 (0.44-1.34)	1.14 (0.61-2.12)	Removed from model

[P1804 Table. Total cohort & total cohort cause-specific analysis]

- 1.27) and dose escalation (aHR 3.74, 95% CI 2.78 - 5.02) were associated with anti-TNF-α therapy discontinuation in both primary and sensitivity analyses. Total cohort cause-specific analysis identified female sex to be associated with side-effects but not with other reasons for discontinuation (aHR 4.05, 95% CI 2.36 - 6.98). Adalimumab (aHR 1.70, 95% CI 1.11 - 2.60) and golimumab (aHR 4.97, 95% CI 2.30 - 10.74) use and dose-escalation (aHR 7.71, 95% CI 5.28 - 11.26) were associated with secondary loss of response.

Conclusion: Drug survival of anti-TNF-α therapy is lower in females as compared to males, mainly because of higher rates of discontinuation for side effects in females. Understanding the sex-specific differences in effectiveness and safety of anti-TNF-α compounds can aid physicians in clinical decision-making.

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P1805 EARLY VEDOLIZUMAB TROUGH LEVELS PREDICT TREATMENT PERSISTENCE OVER THE FIRST YEAR IN INFLAMMATORY BOWEL DISEASE

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Introduction: The role of Therapeutic Drug Monitoring widely validated for anti TNF-α drugs, especially in case of loss of response, remains debated with Vedolizumab.

Aims & Methods: We investigated the utility of early serum Vedolizumab trough levels for predicting the first-year Vedolizumab therapy outcome and identifying patients at higher risk of therapy failure. We included consecutive patients affected by Crohn's disease and Ulcerative Colitis, who started Vedolizumab therapy at two hospitals in Italy. Vedolizumab trough levels and anti-Vedolizumab antibodies were assayed by ELISA at week 6

and 14. Clinical remission (according to Harvey Bradshaw Index and Partial Mayo Score, as appropriate) was assessed at week 6, 14, 22 and 54. The primary endpoint was to explore the correlation between early Vedolizumab trough levels and Vedolizumab persistence over the first year of treatment, defined as the maintenance of therapy because of sustained clinical benefit.

Results: 101 patients (82% exposed to anti TNF-α drugs) were included. Median VTL were 28.3 µg/mL (IQR 16.9-39.8) at week 6 and 18.4 µg/mL (IQR 11.8-25) at week 14 after the first infusion of vedolizumab. A cut-off TL of 16.55 µg/ml at week 14 predicted Vedolizumab persistence within the first year of therapy with a sensitivity of 73.3 % and a specificity of 59.4% (p =0.0009, AUROC 0.686, 95% CI 0.581-0.779).

Week 14 Vedolizumab trough levels were significantly higher in patients with clinical remission at week 14, 22, 54, as well as in those patients achieving mucosal healing within 54 weeks. Early Vedolizumab trough levels were significantly correlated with serum albumin levels (Spearman's rho=0.204, p=0.0107).

Conclusion: High VTL at week 14 were associated with a higher probability of maintaining Vedolizumab therapy over the first year because of a sustained clinical benefit.

Disclosure: Nothing to disclose

P1806 IMPACT OF THE SWITCH FROM ORIGINAL ADALIMUMAB TO BIOSIMILAR ADALIMUMAB SB5 ON SERUM DRUG TROUGH LEVELS, CLINICAL AND BIOLOGICAL DISEASE ACTIVITY IN PATIENTS WITH IBD

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Introduction: Biosimilar adalimumab SB5 is a biosimilar monoclonal antibody for the treatment of patients with autoimmune diseases such as inflammatory bowel disease (IBD). Generally, biosimilars are biological products showing high resemblance to the reference biological products, and they exhibit no clinically meaningful differences in terms of safety and effectiveness.

Since monitoring of adalimumab serum trough levels hold an important significance in treatment modalities, insufficient data about monitoring of drug serum trough levels in IBD patients treated with SB5 are present to date.

Aims & Methods: In this study, we applied original adalimumab-validated ELISA based on TNFa as a target antigen to determine drug serum levels of SB5. The primary objective of current study was to compare serum trough levels of original adalimumab and SB5 before and after switching from the original to the biosimilar drug. Secondary aims were to assess clinical effectiveness of biological treatment after the switching from original adalimumab to SB5 by symptom activity indexes (Harvey-Bradshaw index (HBI) in Crohn's disease, and partial Mayo score (pMayo) in ulcerative colitis and response as assessed by systemic and local inflammatory markers (C-reactive protein, CRP; and fecal calprotectin, FC).

Eighty-seven IBD patients, responders in maintenance adalimumab treatment period, after the switching from original adalimumab to SB5, with known previous three measurements of the original adalimumab trough levels, were included. Sera form IBD Blood Bank established according to the Ethics Committee of *ISCARE* (Nr 2015/Ia) were used, and patient data were anonymously processed according to the latest version of the Helsinki Declaration of Human Research Ethics.

Biosimilar adalimumab trough levels at W10 after the switching were measured by enzyme immunoassay (ADALIMUMAB ELISA ImmunoGuide, REF: IG-AA103). CRP serum concentrations measured by immunonephelometry and fecal calprotectin levels measured by fluoroimmunoassay on switching day were compared with W10 values after the switching.

Results: Of 87 patients, 47 were women and 40 were men; 77 with Crohn's disease and 10 with ulcerative colitis; median age 39.5 (23 to 70) years. No differences in CRP and FC values before and after the switching were observed (Spearman's rank correlation coefficients r = 0.320 (p = 0.0048) and r = 0.833 (p < 0.0001), respectively). Similarly, no significant differences were found in HBI and pMayo values: Kruskal-Wallis H-test have shown p = 0.824 for HBI and p = 0.855 for pMayo indexes. Moreover, excellent quantitative agreement was observed between mean adalimumab trough levels before and after the switching from the original drug to SB5: Spearman's rank coefficient values were r = 0.756 and p < 0.0001.

Conclusion: TNFa-based ELISA kit for measuring adalimumab trough levels showed similar overall performance in the detection of original and biosimilar adalimumab-containing sera. Clinical effectiveness of adalimumab treatment after the switching from the original to the biosimilar adalimumab SB5 assessed by symptom activity indexes and by systemic and local inflammatory markers remained identical after the switching.

Disclosure: Supported by the IBD-Comfort Endowment Fund.

P1807 CLINICAL DECISION SUPPORT TOOL PREDICTS RISK OF INFECTION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE TREATED WITH VEDOLIZUMAB

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Introduction: Disease activity is an independent predictor of infections while patients are receiving biologic therapy; however, prior studies have not taken into consideration the persistence of disease activity due to ineffectiveness of therapy when attempting to identify predictors of infectious complication. We hypothesized that a clinical decision support tool (CDST) that predicts treatment effectiveness would also predict the risk of developing an infection while on therapy.

Aims & Methods: Two previously built and externally validated CDSTs that predict the treatment effectiveness of vedolizumab in ulcerative colitis (UC) and Crohn's disease (CD) were used in combination with the phase 3 clinical trial data sets (GEMINI). UC and CD patients were stratified by baseline variables using the CDSTs into low, intermediate, or high probability of response to vedolizumab. Time-to-event with Cox proportional hazard models was used to compare the risk of infection across groups and to identify independent predictors of infections among subgroups.

Results: A total of 618 UC and 1,023 CD patients were included. Among both UC and CD patients, those categorized as having a low-intermediate probability of response (n=479 UC, n=814 CD) to vedolizumab were more likely to develop infectious complications while on therapy than those categorized as having a high probability (n=139 UC, n=209 CD) of response to vedolizumab (UC: hazard ratio [HR] 1.383, 95% confidence interval [CI] 1.024-1.868; CD: HR 1.458, 95% CI 1.124-1.893). The proportion of patients developing a serious infection was 1% of UC and 3% of CD patients in the high-probability groups versus 2% of UC and 5% of CD patients in the low-

intermediate probability of response groups. Among the low-intermediate probability of response UC group, independent predictors of developing an infection were baseline extraintestinal manifestation (no versus yes; HR 0.755, 95% CI 0.569-1.001), previous tumour necrosis factor (TNF) antagonist exposure (no versus yes; HR 0.671, 95% CI 0.497-0.906), and baseline faecal calprotectin (log transformed; HR 1.135, 95% CI 1.016-1.268). Among the low-intermediate probability of response CD group, an independent predictor of developing an infection was previous TNF antagonist exposure (no versus yes; HR 0.727, 95% CI 0.553-0.957).

Conclusion: Vedolizumab is an overall safe and well-tolerated biologic therapy in both UC and CD. We observed that patients with a low-intermediate probability of response to vedolizumab have an increased risk for developing infectious complications. These data suggest that persistence of disease activity due to lack of efficacy may be a primary determinant of safety, as opposed to drug-related mechanisms.

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P1808 SORBICILLIN FRACTION OF *PENICILLIUM FLAVIGENUM* FOR THE TREATMENT OF INFLAMMATORY BOWEL DISEASE: *IN VITRO* AND *IN VIVO* STUDIES

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Introduction: Inflammatory bowel diseases (IBD) are chronic relapsing intestinal inflammation that often require to treat patients over years and to adapt the therapy repeatedly with respect to side effects or loss of previous medication effect. By so, we constantly need to search for a new non-toxic compound to better optimize the current IBD treatment.

Aims & Methods: The aim of the present study is to test the effects of secondary metabolite sorbicillin of *Penicillium flavigenum in vitro* and *in vivo* model of IBD.

1) Aqueous fraction of sorbicillin was extracted from *Penicillium flavigenum* isolated from Lake Salt (Konya, Turkey) and analysed on LC-MS.

2) The cytotoxicity, cell proliferation and apoptotic effects of sorbicillin and mesalazine (positive control) (500, 250, 125, 62.5 and 31.25 µg/mL) were investigated on Caco2 colorectal adenocarcinoma cells after 24 h incubation by WST-1 assay, *xCELLigence* RTCA-*DP Real Time Cell Analyzer* and AnnexinV-PI assay, respectively. IL-1β production by LPS (1 µg/mL)-stimulated THP-1 human monocyte cells was analysied by *flow cytometry*.

3) Ulcerative colitis (UC) was induced in unfasted Wistar rats by 6% iodoacetamide (IA) in 1% methylcellulose or vehicle - control (0.1 ml/rat, given intracolonically).

Sorbicillin (50, 100 and 200 mg/kg) dissolved in H_2O or placebo (sterile H_2O) were gavaged daily for 5 days after IA enema, followed by autopsy on the 7th day. Body weight, lethargy and diarrhea were recorded daily. Damage score of colonic lesions; MPO activity by H_2O_2-dependent oxidation of *o*-dianisidine hydrochloride; colonic vascular permeability by the extravasation of Evans blue injected intravenously 15 min prior euthanasia; glycoproteins levels in colonic mucus by PAS staining on PVDF membrane; and cecum weight were recorded.

Results: Sorbicillin and mesalazine did not show cytotoxic and apoptotic effects at all studied concentrations on Caco2 cells. Whereas treatment of LPS-stimulated THP-1 cells with 500 µg/mL of Sorbicillin or mesalazine for 24 h reduced the levels of IL-1β from 28.4% in control to 6.6 and 6.7 %, respectively. Sorbicillin in dose 50 and 100 mg/kg did not induce significat effect on clinical and morphological signs of IA-UC. While, rats treated with sorbicillin 200 mg/kg had the same pattern of body weight gain as the control rats (15% IA+sorbicillin *vs* 4% in IA+placebo). Sorbicillin in dose 200 mg/kg significantly (p< 0.05) reduced lesioned area, loss of rugae, dilatation, weight of colon/100 g, ceacum weight/100 g and colonic MPO activity *vs.* IA+placebo group. Moreover, sorbicillin (200 mg/kg) reduced 2-fold (p< 0.05) the colonic vascular permeability and increased 1.5-fold (p< 0.05) glycoproteins levels in colonic mucus in rats with IA-UC *vs.* IA+placebo group.

Conclusion: Sorbicillin-containing aqueous fraction of *Penicillium flavigenum* does not have cytotoxic and apoptotic effects on Caco-2 cell, but has anti-inflammatory effect by reducing IL-1β levels in LPS-stimulated THP1 cells. Sorbicillin ameliorates iodoacetamide-induced UC in rats. The restoration of mucosal barrier and resolving inflammation are the potential mechanism of sorbicillin beneficial effect. *Acknowledgement: This study was supported by Mevlana Project Based International Exchange Programme (Project number: D26-MEVLANA-01).*

Disclosure: Nothing to disclose

P1809 REVERSE SWITCHING TO ORIGINATOR INFLIXIMAB MAY BE CONSIDERED IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES EXPERIENCING NEW SIDE EFFECTS OR LOSS OF RESPONSE AFTER SWITCHING TO A CT-P13 BIOSIMILAR

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Introduction: In current clinical practice, patients with inflammatory bowel disease (IBD) treated with originator infliximab (IFX) have been or are being switched to biosimilar infliximab because of lower costs and seemingly similar effectiveness of biosimilars. Over a one-year follow-up 7%-26% of the patients discontinued biosimilar IFX treatment, which is comparable to originator IFX. Common reasons for discontinuation of biosimilar IFX treatment are (subjective) loss of response or side effects. As a result of newly experienced side effects or loss of response while using biosimilar infliximab, patients are occasionally switched back to treatment with originator IFX. However, not much is currently known regarding reverse switching to originator IFX.

Aims & Methods: Our aim was to assess the prevalence of and the specific reasons for reverse switching to originator infliximab within 52-weeks after an initial conversion from originator infliximab to a CT-P13 biosimilar in patients with IBD. Additionally, we evaluated whether reinitiating originator infliximab led to the desired favorable effect.

In this retrospective, observational, multi-centre cohort study, data of IBD patients from two tertiary care centres and two large general hospitals in the Netherlands were collected. Adult patients with IBD were eligible for inclusion if they had been switched from infliximab originator to the CT-P13 biosimilar and had a follow up time of at least 52 weeks after initial conversion. Reasons for re-switching were categorised into side effects or loss of response to the biosimilar.

Results: A total of 254 patients with IBD were switched (165 Crohn's disease, 52 Ulcerative colitis and 2 IBD-Unclassified). Reverse switching occurred in 35/254 (13.8%) of the patients after a mean of 23.6 weeks. Reverse switchers were more often female (48.9% versus 68.6%, *p* = 0.02) than those who stayed on biosimilar treatment.

Thirty-two patients (91.4%) switched back to the originator because of newly experienced side effects and only three (8.6%) because of loss of response on biosimilar IFX. Most frequently reported side effects were skin reactions in 37.1% of patients (13/35), an increase in IBD related symptoms 37.1% (13/35) of patients and fatigue in 25.7% (9/35) of patients. Three patients had by calprotectin (>250 mg/L) objectified loss of response on infliximab biosimilar. In 75% (24/32) of the patients experiencing side effects and 100% (3/3) of the patients with loss of response, reverse switching to originator IFX led to the desired effect of improvement of the side effect or regaining of response to IFX therapy.

Conclusion: Switching back to originator infliximab seems effective in patients with IBD, who experience side effects or loss of response after switching from originator to biosimilar infliximab. Switching patients back to originator infliximab may therefore be justified in case patients experience new side effects or loss of response after switching to a biosimilar IFX.

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Demographics	Patients remaining on biosimilar (n=219)	Patients switched back to originator (n=35)	p-value
Sex			
- Female, n (%)	107 (48.9%)	24 (68.6%)	0.02
- Male, n (%)	112 (51.1%)	11 (31.4%)	
Age at diagnosis (years), mean (SD) [ζ]	27.5 (±13.9)	27.7 (±13.7)	N.S. ∞
Age at initial switch (years), mean (SD) [ζ]	40.7 (±15.8)	40.2 (±16.9)	N.S. ∞
Months on originator infliximab, mean (SD) [ζ]	62.2 (±35.5)	59.0 (±39.5)	N.S. ∞
Type of IBD, n (%)			
- Crohn's Disease	165 (75.3)	28 (80)	N.S. ∞
- Ulcerative Colitis	52 (23.7)	7 (20.0)	
- IBD-Unclassified	2 (0.9)	0 (0)	
Smoking, n (%)			
- Missing	12 (5.5)	1 (2.9)	N.S. ∞
- Never	128 (58.4)	18 (51.4)	
- In the past	27 (12.3)	8 (22.9)	
- Currently	52 (23.7)	8 (22.9)	
Hospital, n (%)*			
- UMCU	86 (39.3)	15 (42.9)	N.S. ∞
- AZN	94 (42.9)	13 (37.1)	
- CWZ	25 (11.4)	3 (8.6)	
- UMCG	14 (6.4)	4 (11.4)	

[ζ]: standard deviation; *UMCU: University Medical Centre Utrecht; AZN: St. Antonius Hospital Nieuwegein; CWZ: Canisius Wilhelmina Hospital; UMCG: University Medical Centre Groningen; ∞: Not significant

[Comparison of demographics between patients who did and did not switch back to originator infliximab]

P1810 SHORT- AND LONG-TERM EFFICACY OF VEDOLIZUMAB THERAPY ON CLINICAL AND ENDOSCOPIC ACTIVITY IN PATIENTS WITH ANTI-TUMOR NECROSIS FACTOR ALPHA RESISTANT INFLAMMATORY BOWEL DISEASE

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Introduction: Vedolizumab (VDZ) therapy as alternative option in the management of moderate and severe IBD has been registered since 2016 in Hungary, however all newly initiated VDZ therapy was individualized, it should be approved by the steering committee of five Hungarian IBD-specialist up to 2019. This situation resulted that only those patients could be received VDZ treatment whose longstanding disease showed inadequate response to the conventional anti-TNF-alpha and/or immunosuppressant therapy. The aim of our observational study was to assess the efficacy of short- and long-term VDZ therapy on clinical and endoscopic activity in moderate and severe active IBD in real-life setting.

Aims & Methods: Our non-interventional multicenter cohort study enrolled all adult IBD patients with moderate and severe activity who received VDZ therapy between July 2016 and December 2018 in our entire country. The therapeutic response was assessed based on the changes of clinical (Crohn's Disease Activity Index [CDAI], Mayo score) and endoscopic (Simple Endoscopic Score for Crohn Disease [SES-CD], endoscopic Mayo score) scores. Clinical response was defined as >3 points decrease in the total Mayo score or >100 decrease in CDAI score from baseline. Remission was defined as Mayo score ≤2, with no individual subscores >1, or as CDAI score ≤150. Mucosal healing was defined as Mayo endoscopic subscore ≤1 or as SES CD score ≤4.

Results: 83 Crohn's disease (CD) and 121 ulcerative colitis (UC) patients completed VDZ induction therapy. The mean age was 39.9 years (range 18-78; median 36) and the average disease duration was 9.6 years (range 1-36; median 8). Extraintestinal manifestations occurred in 57 patients (27.9%), and in 11 cases (5.4%) IBD was associated with primary sclerosing cholangitis (PSC). The mean value of activity scores significantly decreased by the end of short-term treatment period both in CD (SES-CD: 20.93 vs. 13.55; p< 0.00001; CDAI: 303.58 vs. 167.66; p< 0.00001) and UC (Mayo: 9.74 vs. 4.33; p< 0.00001; eMayo: 2.80 vs. 1.41;su p< 0.00001) subgroups. The rate of clinical response during the short-term VDZ therapy was substantially higher in the UC group compared with CD group (84.3% vs. 61.5%; p< 0.0001). No significant difference in terms of the proportion of clinical remission and steroid-free remission was observed between the UC and CD subgroups (49.6% vs. 51.8%, p=0.777; and 27.3% vs. 37.4%, p=0.169). In 124 cases (72 UC and 52 CD) the first-year VDZ treatment could have been completed during the study period, however in 32 cases (25.8%) primary non-response for induction therapy was observed. 92 patients (60 UC and 32 CD) received maintenance VDZ therapy. The rate of response, clinical remission and steroid-free remission were substantially higher in UC (65.3%, 47.2% and 44.4%) compared with CD (42.3%, 32.7% and 30.8%) by the end of first-year therapy (p< 0.001). Significant difference was observed between UC and CD subgroups in terms of mucosal healing both by the end of induction and by the end of first-year therapy (52.9% and 21.7%, p< 0.0001vs. 51.4%and 21.2%, p=0.015).

Conclusion: Our results suggest that both the short-term and the one-year long maintenance VDZ therapy is effective and safe therapeutic option in anti-TNF-alpha failure or intolerant IBD patients with moderate or severe disease activity, however significant difference was observed between the UC and CD subgroups. Mucosal healing was achievable in every second UC and in only every fifth CD patients both by the end of the induction and by the end of first-year treatment in this difficult-to-treat population.

Disclosure: Nothing to disclose

P1811 EFFICACY AND SAFETY OF THIOGUANINE AS RESCUE TREATMENT FOR INFLAMMATORY BOWEL DISEASE: A MULTI-CENTRE STUDY

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Introduction: Thioguanine (TG) is an alternative thiopurine therapy which has been used for patients with inflammatory bowel disease (IBD) who have failed azathioprine or 6-mercaptopurine due to side effects or suboptimal response. Its widespread use has been hampered from concerns about safety of TG due to reports of liver toxicity, especially nodular regenerative hyperplasia (NRH), when TG was used in higher doses.

Aims & Methods: The aim of this study was to investigate the long-term efficacy and safety of low-dose TG in IBD after failure of prior conventional therapy in an English cohort.

A retrospective multicentre chart study was performed on IBD patients who were treated with TG from 2006 to 2019 in three hospitals in the United Kingdom. Both patients' characteristics and drug history as well as the efficacy and safety profile of TG therapy were reviewed in the patients' medical records. Clinical, radiological and laboratory parameters were collected; to assess NRH liver biopsies and MRI results were assessed. Clinical remission was defined as: no (re)initiation of corticosteroids, no initiation of biological therapy and no surgical intervention.

Results: In total 193 patients (57% female and Crohn's disease in 64%) were included, with a median daily TG dose of 20 mg (range: 20-40 mg), a median treatment duration of 23 months (range: 0-155 months) and a median follow-up of 36 months (range: 1-155 months). 71% of the patients showed clinical remission to TG within 6 months and 54% of the patients were still using TG at final follow-up. Forty-three patients (22%) stopped TG due to intolerance(s) and 15 patients (8%) stopped due to resistance. Intolerances to TG occurred in 28% of the patients (n = 54), primarily consisting of elevated liver enzymes (n = 9, 5%), myelotoxicity (n = 9, 5%) and rash (n = 9, 5%). Pancreatitis only occurred in one patient with a history of thiopurine-induced pancreatitis. NRH was diagnosed in two patients (1%).

Conclusion: Long-term follow-up shows that thioguanine was effective and well-tolerated in 54% patients who had failed conventional therapy. The occurrence of pancreatitis and NRH was very little in this study.

Disclosure: Nothing to disclose

P1812 THE OUTCOME OF RESECTED CROHN'S DISEASE PATIENTS WITH NO POSTOPERATIVE TREATMENT BUT UNDER CLOSE ENDOSCOPIC FOLLOW UP AND ACCELERATED STEP UP TREATMENT IN CASE OF ENDOSCOPIC RELAPSE: A TERTIARY REFERRAL CENTER PILOT STUDY

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Introduction: According to POCER study, postop. endoscopic follow up at 6 mo. and relevant treatment (tx) escalation of resected CD patients might decrease endoscopic relapse rates at 18 mo. compared to those getting the best postop. tx according to their risk stratification without endoscopic follow up. However after minimizing the inflammatory load in the postop. setting there might be still a group of unnecessaryly overtreated patients. So our aim was to determine the outcome of resected CD patients with no initial postop. tx independent of risk status.

Aims & Methods: Starting in 2012 we closely followed up each CD patient after their first ileocecal resection with colonoscopy at 3-6-12-18-24 mo. and then annually. Active smoking, resection for penetrating disease were accepted as risk factors for relapse but both high or low risk groups were followed up without any initial tx. If relapse was detected at any colonoscopy an accelerated step up tx. was applied starting with 5-ASA+ budesonide, continuing with AZA and ending up with biologics in an add on fashion.

All patients' demographic features like age, age at onset, operation, sex, disease duration, location, behaviour, reason for resection, smoking status, Rutgeerts score at each colonoscopy were noted. Patients with active perianal disease and upper GI involvement were excluded.

Results: A total of 45 patients [mean age 40.40±10.66 yr, 24 being female, 29 (65%) with high risk] were enrolled into the study. Mean follow up time was 54.46±18.83 mo. The overall endoscopic relapse rate during whole follow up was 36/45 (80%), median time to relapse being 3 mo. Relapse rate showed no relation with parameters like age, age at onset, and operation, sex, disease location, and established risk factors for postop. relapse (active smoking, penetrating disease). After starting the step up tx the percentage of relapsers decreased to 23 out of 36 at the very last visit. Nine out of 45(20%) never had a relapse although six of them actually having risk factors.

Conclusion: In light of previous POCER study the relapse rate at 18 mo. was 50% when the best tx immidiately was started and managed according to postop. colonoscopy at 6 mo. In the present study the endoscopic relapse rate was the same despite a longer follow up time of 54 mo., although none of them had an immidiate postop. tx. but received the appropriate tx. in an accelerated step up manner. These results make us question the defined postop. risk factors and we think that our approach could help tailoring individual tx. and avoiding unnecessary tx. at least in a subgroup of patients.

Disclosure: Nothing to disclose

P1813 METAANALYSIS OF EARLY SURGERY VERSUS INITIAL MEDICAL THERAPY WITH OR WITHOUT DELAYED SURGERY IN PATIENTS WITH ILEOCOLONIC CROHN'S DISEASE

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Introduction: Previous studies have demonstrated that early bowel resection (EBR) in ileocolonic Crohn's disease (CD) can result in an improved clinical course compared to initial medical treatment (IMT), including escalation to biologic therapy
Aims & Methods: We sought to compare the safety and efficacy of EBR versus IMT for the management of patients with ileocolonic CD. A systematic search was performed to identify studies that compared EBR (performed < 1yr from initial diagnosis) or IMT for the management of ileocolonic CD. Log hazard ratios (lnHR) for recurrence free survival (RFS) and their standard errors were calculated from Kaplan-Meier plots and pooled using the inverse variance method. Dichotomous variables were pooled as odds ratios (OR). Quality assessment of the included studies was performed using the Newcastle-Ottawa (NOS) and Jadad scales
Results: 7 studies of 1863 CD patients (EBR n= 581, 31.2%; IMT n= 1282, 68.8%) were eligible for inclusion. The studies had a moderate to high risk of bias. The median NOS was 8 (range 7-9). There was a reduced likelihood of overall (OR 0.53 95% Confidence interval [95% CI]: 0.34, 0.83, p=0.005) and surgical (OR 0.47, 95% CI 0.24, 0.91, p=0.03) recurrence with EBR than with IMT. There was also a less requirement for maintenance biologic therapy (OR 0.24, 95% CI 0.14, 0.42, p< 0.0001).
Patients who underwent EBR had a significantly improved RFS than those who underwent IMT (HR, 0.62 95% CI 0.52, 0.73, p< 0.001). There was no difference in morbidity (OR 1.67, 95% CI 0.44, 6.36, p=0.45) between the groups.
Conclusion: Surgery is associated with reduced recurrence and need for maintenance biologic therapy in CD. It is critical that both a surgeon and a gastroenterologist review patients early, at the time of diagnosis, to facilitate informed management decisions.
Disclosure: Nothing to disclose

P1814 HOME-DELIVERED INFLIXAMAB INFUSION: SAFETY DATA FROM 373 HOME INFUSIONS OVER 4 YEARS

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Introduction: Treatment with infliximab for patients with Inflammatory Bowel Disease (IBD) in the UK consists of intravenous infusions usually delivered in hospital via a nurse-led service. Several studies have proven the safety of infliximab infusions at home which also eases the capacity for hospital infusions. However, the uptake in clinical practice has been slow in the UK. We aim to evaluate the safety and patient satisfaction of home infliximab infusions in a district general hospital 4 years after its introduction.
Aims & Methods: This is a retrospective audit of all IBD patients enrolled in a home infliximab infusion programme from July 2014 to July 2018. Data were collected from the electronic database and case notes. Data collected included serious adverse reactions requiring hospital admission and number of times home infusions were put on hold/stopped because of safety concerns. Patients currently on the home infliximab infusion programmed were interviewed by telephone by 2 Gastroenterology specialist trainees. Satisfaction rate (out of 10) were collected for adequate communication, delivery times, customer service, driver assistance/attitude, nurse support service, clinical waste collection and overall satisfaction.

Results: A total of 41 patients were included in the analysis (3 excluded due to insufficient follow up data): median age was 42 years, 19 (46.3%) were women, 9 (22%) had ulcerative colitis and 32 (78%) had crohn's disease. Three hundred and seventy three (373) infliximab infusions were given at home: there were no deaths and no adverse reactions requiring hospital admission. There were 3 (0.8%) instances where home infliximab infusions were put on hold or stopped as shown in table 1. Patients were given a median number of 7 doses of infliximab in hospital before moving to the home infliximab infusion. The median follow up time on home infliximab was 14 months and the median number of doses given at home was 7. Eighteen (69.2%) out of 26 patients on home infliximab in July 2018 responded to a telephone interview. Mean and median satisfaction rates were 9.7 and 10 (out of 10).
Conclusion: A home infliximab infusion programme for patients with IBD is safe with all adverse reactions being minor and managed in the community. Patient satisfaction rate is high.
Disclosure: Nothing to disclose

P1815 THE DUBLIN INFLAMMATORY BURDEN SCORE PREDICTS EARLY CLINICAL AND BIOCHEMICAL RESPONSE TO GOLIMUMAB TREATMENT IN UC; EARLY RESULTS OF THE GOAL-ARC STUDY

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Introduction: Golimumab (GLM) is an anti-TNF monoclonal antibody licensed for the treatment of Ulcerative Colitis. Higher trough levels are associated with enhanced response to therapy. (GOAL-ARC) is a randomized multi-centered trial of the impact of personalized dosing of Golimumab based on inflammatory burden (assessed by FCP - faecal calprotectin) and therapeutic drug monitoring versus standard of care (with dosing according to label). We aimed to evaluate the impact of inflammatory burden in UC on drug levels and early response to GLM treatment.
Aims & Methods: All study participants had a diagnosis of UC, with moderate to severe disease activity (Mayo 6-12), with an endoscopic sub-score of ≥2. Clinical response was defined as a decrease in baseline modified partial mayo score of 2 points or a decrease of ≥30% from baseline. GLM was administered at 200mg at week 0, 100mg at week 2 in all patients in advance of week 6 assessment.
Induction data was analyzed to week 6 including baseline inflammatory burden (DUBLIN Score - Rowan et al, JCC 2019), FCP and modified partial mayo scores and week 6 trough GLM levels.
Results: 70 patients have been recruited to GOAL-ARC. 90% have completed the induction phase to week 6. Moderate disease activity was present in 79% with a Mayo endoscopic sub-score of 2 at screening. 56% had a weight < 80Kg.
Pre and post induction data was available on 51 patients,. Clinical response was achieved in 57% at week 6. The median modified partial mayo score decreased from 4(IQR 3-5) at baseline to 2(IQR 1-3) at week 6 (p< 0.001). Median FCP reduced from 1380 (IQR 685-3000) at baseline to 180 (IQR 15-1122) at week 6 (p=0.001). A lower baseline DUBLIN score was associated with clinical response at week 6 (p=0.048).
Median GLM level at week 6 was 3.97 (IQR 2.3-5.8). Higher week 6 drug levels were associated with clinical response. (p=0.012). Week 6 GLM level was inversely proportional to week 6 FCP(p=0.001). Baseline DUBLIN score was inversely proportional to week 6 drug levels (p=0.021).
Conclusion: Early results of GOAL-ARC demonstrate the majority (57%) of UC patients treated with GLM show early clinical response (by week 6). Significant improvements are observed in modified partial Mayo scores and FCP by week 6, with higher drug levels being significantly associated with achieving clinical response and reductions in faecal calprotectin. Lower baseline DUBLIN (inflammatory burden) scores are associated with higher trough drug levels and clinical response at week 6 indicating that a higher inflammatory burden is associated with poorer outcomes.

	Baseline	Week 6	p value
Faecal Calprotectin µg/g Median (IQR)	1380 (685-3000)	179.5 (15-1122)	0.001
Modified Partial Mayo score median (IQR)	4 (3-5)	2 (1-3)	<0.001

[Table 1. Comparison of baseline and week 6 median faecal calprotectin and modified partial mayo scores following induction with Golimumab]

References: 1. Rowan CR, Cullen G, Mulcahy HE, Sheridan J, Moss AC, Ryan EJ, et al. DUBLIN (Degree of Ulcerative colitis Burden of Luminal INflammation) score, a simple method to quantify inflammatory burden in Ulcerative Colitis. J Crohns Colitis 2019 Mar.
Disclosure: GD has received research and/or unrestricted educational funding from; Abbvie, MSD, Pfizer, Janssen, Takeda, Tillott's, Shire GD has received speaker fees or participated in advisory boards for; Abbvie, MSD, Pfizer, Janssen, Amgen, Mylan, Shire, Dr Falk

P1816 EARLY 'REAL WORLD' EXPERIENCE WITH TOFACITINIB FOR MODERATE TO SEVERE ULCERATIVE COLITIS

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Introduction: Tofacitinib is an oral, small molecule Janus kinase inhibitor, which received NICE approval for the treatment of moderate to severe treatment-refractory ulcerative colitis in late 2018. We present early clinical and biomarker outcome data for a cohort of new starters in a tertiary IBD referral centre.
Aims & Methods: A retrospective cohort analysis of patients was undertaken using prospectively maintained records. Patients commenced on tofacitinib between October 2018 to April 2019 were included. Clinical disease activity was measured at baseline and at four and eight weeks using the Simple Clinical Colitis Activity Index (SCCAI). Faecal calprotectin (FCAL) and C-reactive protein (CRP) were measured at baseline and eight weeks. Descriptive statistics and Wilcoxon signed rank test were calculated using GraphPad Prism version 8.0.
Results: Twenty five patients commenced tofacitinib, median age 32 (range 19-74) and median disease duration of 7 years (range 0.4-20). All patients had previously failed biologic therapy (24 anti-TNF, 1 vedolizumab and 13 both). Paired outcome data was available for n=20 at week 4 and n=15 at week 8. Median baseline SCCAI fell from 8 (range 2-14) to 3 (1-7) after four weeks (n=20), further decreasing to 2 (0-6) at week 8 (n=15) (p< 0.0001). Median baseline FCAL (n=15) fell from 451(63-6020) to 95(5-1420) (p< 0.0001). There was no significant change in CRP following induction therapy. One patient discontinued due to non-response. Tofacitinib was well tolerated in our cohort with only one patient ceasing therapy after two weeks due to headaches. No significant haematological or biochemical abnormalities were noted.
Conclusion: Our early experience with tofacitinib for those with disease refractory to one or more biologic agents, is encouraging. Real life effectiveness appears to be at least as good as the efficacy demonstrated in the trial programme and tolerance is also reassuring, albeit in a small cohort with limited follow up.
Disclosure: SH: Lecture fees: Janssen. Financial support for education/training: Janssen, Vifor Pharma, Falk. PMI: Lecture fees: Abbvie, Warner Chilcott, Ferring, Falk Pharma, Takeda, MSD, Johnson and Johnson, Shire. Financial support for research: MSD, Takeda Advisory fees: Abbvie, Warner Chilcott, Takeda, MSD, Vifor Pharma, Pharmacosmos, Topivert, Genentech, Hospira, Samsung Bioepis

P1817 PREDICTIVE FACTORS FOR THE RESPONSE TO INTRAVENOUS CORTICOSTEROID THERAPY IN SEVERE ACUTE COLITIS

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Introduction: Acute severe colitis can be a revelation or occur in the course of a known chronic inflammatory bowel disease, especially ulcerative colitis. Intravenous corticosteroid therapy (IVC) is the first-line medical treatment of acute severe colitis. The aim of our work is to evaluate the predictors of the response to intravenous corticosteroid therapy in severe acute colitis
Aims & Methods: This is a two-year observational study of 27 cases of acute colitis collected in our department. acute severe colitis was defined by a Lichtiger score greater than 10. Clinical, biological, endoscopic and radiological data were collected and analyzed by SPSS20 software.
Results: The average age of our patients is 37.9 ± 17.1 years with a clear female predominance (21/27). 6 patients (22.2%) had known IBD. The average Lichtiger score was 13 ± 1.45. 9 patients (33.3%) were naive steroids. 9 patients (33.3%) had endoscopic severity criteria. 19/20 of the patients in failure with the CO received the IFX, a patient was operated for colectasie. In univariate analysis, the factors significantly associated with the failure of CO IV were: CRP elevated on D3 (>45mg / l), presence of blood on D3, pancreatic involvement, non-naive status with corticosteroids . In multivariate analysis and adjusting to the above factors, only CRP >45mg / l to J3 is significantly associated with CO IV failure (OR = 1.3, p = 0.02).
Conclusion: Our study confirms the data in the literature on the importance of the CRP assay at D3 to evaluate the response or failure to intravenous corticosteroid therapy in the initial management of severe acute colitis.
Disclosure: Nothing to disclose

P1818 THE EFFICACY AND THE SAFETY OF VEDOLIZUMAB IN A GROUP OF ANTI-TNF EXPERIENCED PATIENTS WITH IBD; A REAL-LIFE DATA FROM TURKEY

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Introduction: Vedolizumab is a new agent acting as an anti-Integrin which has been started to be use in treatment of Crohn's disease (CD) and Ulcerative Colitis (UC). In this retrospective study we aimed to examine the safety and effectiveness of vedolizumab treatment in anti-TNF experienced patients with CD and UC. In addition we aimed to show whether there is a role for thiopurines in vedolizumab treatment.
Aims & Methods: : Chart review was performed retrospectively in patients with UC and CD in Cerrahpasa University, Ankara University and Acıbadem University IBD outpatient clinics. Clinical response and clinical remission rates were calculated by using Harvey-Bradshaw Index and Partial Mayo score.
Results: Total of 101 patients [mean age 39,4±12,7 yr, 51 Male, 57 CD (56%)] were enrolled into the study. The clinical response rates were 66%, 62% and 44% in 3, 6 and 12 months of vedolizumab treatment in CD patients. The Clinical remission rates were 22%,34% and 36% in the same intervals in CD patients. The clinical response rates were 59%, 62% and 36% in 3, 6 and 12 months of vedolizumab treatment in UC patients. The Clinical remission rates were 25%,39% and 33% in the same intervals in UC patients. There was no correlation found between thiopurin use, disease duration, clinical response and clinical remission rates in either diseases. No serious side effects were recorded during vedolizumab treatment.
Conclusion: Vedolizumab treatment is effective and safe in patients who were previously treated with anti-TNF agents. Thiopurins did not show any beneficiary effect over Vedolizumab treatment.
Disclosure: Nothing to disclose

P1819 5-AMINOSALICYLATE INTOLERANCE IS ASSOCIATED WITH A POOR PROGNOSIS IN PATIENTS WITH ULCERATIVE COLITIS

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Introduction: 5-aminosalicylates(5-ASA) are the key drugs in induction and maintenance therapy in ulcerative colitis (UC). Some UC patients are involved in 5-ASA intolerance after induction of oral 5-ASA compounds. There are no evidence of the prognosis including the risk of colectomy in 5-ASA intolerant UC patients.

Aims & Methods: The aim of this study is to establish the prognosis of 5-ASA intolerant UC patients in multicenter cohort study.A retrospective review of a prospective multicenter database (2014-2018) of 1,208 UC patients was carried out and a total of 1,064 patients treated with oral 5-ASA compounds were enrolled. We compared the risk of colectomy and biologics induction between patients (i) tolerant to first 5-ASA compound (880), (ii) intolerant to first 5-ASA compound but tolerant to other 5-ASA compound (96) and (iii) intolerant to 5-ASA compound and withdrawal of 5-ASA (88).

Results: We identified 1,064 patients with UC, of which 32 patients (3%) resulted in colectomy and 211 patients (20%) treated with biologics. Colectomy rate in patients (iii)intolerant to 5-ASA and withdrawal of 5-ASA were higher than (i) tolerant to first 5-ASA and (ii) intolerant to first 5-ASA but tolerant to other 5-ASA (6.1%, 3.1%, 2.1%, respectively). (iii) Patients withdrawal of 5-ASA showed higher risk of colectomy compared with (i) tolerant to first 5-ASA (Hazard ratio (HR) 3.02, 95% Concidence interval (CI): 1.08-8.45). The risk of colectomy among (ii) patients intolerant to first 5-ASA but tolerant to other 5-ASA showed no significant difference compared with (i) tolerant to first 5-ASA (HR 0.72, 95% CI: 0.16-3.10). The biologics induction rate in (iii) patients withdrawal of 5-ASA was significantly higher than (i) tolerant to first 5-ASA and (ii) intolerant to first 5-ASA but tolerant to other 5-ASA (39%, 21%, 17%, respectively). Also (iii) patients withdrawal of 5-ASA showed higher risk of induction with biologics compared with (i) tolerant to first 5-ASA (HR 2.10, 95% CI: 1.28-3.45). Those risk among (ii) patients intolerant to first 5-ASA but tolerant to other 5-ASA showed no significant difference compared with (i) tolerant to first 5-ASA (HR 0.72, 95% CI: 0.40-3.45).

Conclusion: Patients with UC who had 5-ASA intolerance and withdrew from 5-ASA showed poor prognosis. We should consider trying other 5-ASA compounds even if the patients had intolerance to one 5-ASA compound.

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P1820 AUDIT OF STEROID EXCESS IN INFLAMMATORY BOWEL DISEASE IN THE ERA OF BIOLOGICS

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Introduction: Currently systemic corticosteroids are key treatments in the induction of remission of inflammatory bowel disease (IBD). Steroid excess can cause significant adverse side effects. Steroid dependency, excess and appropriateness have each been defined within ECCO guidelines, but currently there is no agreed benchmark on what is an acceptable rate of steroid use in IBD(1-2). A large study from the United Kingdom (UK) found a steroid use of 30% and excess in 14.9% in patients seen in IBD clinics(3). The aim of this study is to evaluate the rates of steroid use/excess in patients attending a large tertiary IBD clinic in the era of increasing biologics usage.

Aims & Methods: Data was collected over 16 weeks from unselected patients seen in our IBD clinic in Wales, UK, where over 4000 patients attend. A steroid assessment tool was used to determine patients' steroid use. Oral steroid (Prednisolone/Budesonide) data was collected from the patients at clinic and cross referenced with the hospital patient records, hospital pharmacy database and primary care records. Each set of results were evaluated against ECCO guidelines, steroid excess or dependency was defined as a patient requiring >2 courses of steroids in the past 12 months or a disease flare with tapering of a steroid course or a relapse within 3 months of stopping steroids. Prescriptions were evaluated to determine their appropriateness. Current and prior drug usage including all immunosuppressants (IS) were collected.

Results: 258 patients were analysed in total, 60.9% of these had Crohn's disease(CD), 33.7% Ulcerative Colitis(UC) and 5.4% Inflammatory bowel disease unclassified (IBDU). Mean age 45 years, Male 50% Female 50%. Disease severity was assessed and 58.9% of patients had inactive disease, 26.0% mild, 14.0% moderate and 1.1% severe. Drug usage:

	5ASA		Thiopurine		Other IS		Anti-TNF		Anti-integrin		Anit-IL23	
	Current	Past	Current	Past	Current	Past	Current	Past	Current	Past	Current	Past
UC	21.3%	9.7%	7.0%	7.4%	0.8%	1.2%	3.1%	2.3%	0.8%	0.8%	0%	0%
Crohn's	5.0%	19.4%	13.1%	29.5%	2.7%	10.8%	13.6%	10.9%	1.2%	2.7%	4.3%	0.4%
IBD-U	2.3%	2.7%	0.4%	1.6%	0.4%	0.4%	0.4%	1.2%	0%	0.8%	0%	0%
Total	28.6%	31.8%	20.5%	38.5%	3.9%	12.4%	17.1%	14.4%	2.0%	4.3%	4.3%	0.4%

In the preceding 12 months 34.1% of patients had received at least 1 course of oral corticosteroids, 16.7% patients were in steroid excess/dependency. The dependency/excess occurred more frequently in Crohn's patients (CD 17.8%, UC 14.9%). Of the people in steroid excess the percentage on each drug were 5ASA 14.0%, Thiopurine 14.0%, Other IS 4.7%, Anti-TNF 14.0%, Anti -integrin 2.3%, Anti -IL23 9.3%

Conclusion: High proportion of IBD patients seen in clinic were exposed to steroids in the preceding year. In comparison to previous study(3) the use of steroids seems higher despite increasing use of biologics. When evaluating steroid excess it is essential to include primary care and hospital pharmacy records. Future studies should evaluate steroid use in all IBD service set up including patient directed self management service.

References: 1. Magro F, Gionchetti P, Eliakim R, Ardizzone S, Armuzzi A, Barreiro-de Acosta M et al.Third European evidence based consensus on diagnosis and management of ulcerative colitis. Part 1: definitions, diagnosis, extra-intestinal manifestations, pregnancy, cancer surveillance, surgery, and ileo-anal pouch disorders. Journal of Crohn's and Colitis 2017;11:649-670. 2. Gomollon F, Dignass A, Annese V, Tilg H, Van Assche G, Lindsay JO et al.3rd European evidence based consensus on the diagnosis and management of Crohn's disease 2016: part 1: diagnosis and medical management. Journal of Crohn's and Colitis. 2017;11:3-25. 3. Selinger CP, Parkes GC, Bassi A, Fogden E, Hayee B, Limdi JK, et al. A multi-centre audit of excess steroid use in 1176 patients with inflammatory bowel disease. Alimentary pharmacology & therapeutics. 2017;46(10):964-73.

Disclosure: Nothing to disclose

P1821 VEDOLIZUMAB IN THE TREATMENT OF CHRONIC REFRACTORY POUCHITIS - A SYSTEMATIC REVIEW

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Introduction: Approximately 50% of patients with ileal pouch anal anastomosis (IPAA) develop pouchitis, with 10-15% of acute pouchitis developing chronic pouchitis(CP). Whilst the majority responds to antibiotic therapy, treatment options for chronic antibiotic refractory pouchitis(CARP) include combination antibiotic therapy, budesonide, immunomodulators(IM) or anti-tumour necrosis factor (TNF) antibodies. There is limited data on the role of vedolizumab(VZB), an a4b7 integrin antagonist, in the treatment of CP. We performed a systematic review of the literature to explore the efficacy of VZB in CP

Aims & Methods: A systematic literature search in MEDLINE (1966-November 2018), Cochrane Central Register of Clinical Trials, and abstracts from recent major gastroenterology meetings (Digestive Disease Week, United European Gastroenterology Week and Congress of European Crohn's and Colitis Organisation) was performed using the following terms: "integrin", "vedolizumab", "pouchitis". Only English language publications and abstracts on the efficacy of VZB for CP in ulcerative colitis patients with

IPAA were included; Crohn's disease of the pouch was excluded. Additional trials were identified through review of reference list of included articles

Results: 6 case reports (n=6)[1-6] and 3 retrospective case series[8-10] (2 in abstract form, n=51) were included; 1 case series (Philpott J 2017)[7] was excluded (duplicate). Only 1 ongoing randomised-controlled phase IV study (NCT02790138) was found whose data has yet to be reported.

All patients (n=57) had chronic antibiotic refractory/ dependent pouchitis and received VZB after failing prior therapy, including IM and anti-TNF. In the case reports, 6 patients (mean age 36yrs, M:F 1:1) with CARP received induction/maintenance VZB; symptom improvement was seen as early as 6 wks and pouchoscopy at 14-33 wks reported near/complete resolution of pouchitis.

In the 3 retrospective case series, 64-75% achieved improvement/clinical remission(CR) at 12-14 wks, with 58.3% still in CR at 46 wks:(a) 14 of 19 (73.7%) with CARP who received at least 1 dose of VZB had improvement of modified Pouchitis Disease Activity Index (mPDAI) at 12 wks (median decrease 2 units, p=0.031) ;(b) 9 of 12 (75%) who received induction/maintenance VZB achieved CR (mPDAI< 5 + decrease of >=2) at 14 wks, with 7 (58.3%) still in CR at median 46(14-105) wks ;(c) after 3-4 doses of VZB, 64% with CARP/antibiotic dependent pouchitis achieved CR (PDAI< 7) at 14 wks. Minor adverse events were reported in 10-16%

Conclusion: From uncontrolled studies and case reports, VZB appears to be efficacious and safe for the treatment of CP refractory to antibiotics and other therapy including anti-TNF. Controlled data is needed to confirm its efficacy in this group of patients.

References: 1. Martins D, Ministro P, Silva A. Port J Gastroenterol 2018;25:340-341. 2. Orfanoudaki E, Foteinogiannopoulou K, Koutroubakis LE. Annals of Gastroenterology 2018;31(3):379. 3. Coletta M, Paroni M, Caprioli F. J Crohns Colitis 2017;11:1507-1508 4. Mir F, Yousef MH, Partyka EK, Tahan V. Int J Colorectal Dis 2017;32(10):1517-1518. 5. Bethege J, Meffert S, Ellrichmann M, Conrad C, Nikolaus S, Schreiber S. BMJ Open Gastroenterol 2017;4(1): e000127 6. Schmid M, Frick JS, Malek N, Goetz M. Int J Colorectal Dis 2017;32(4):597-598. 7. Philpott J, Ashburn J, Shen B. Inflamm Bowel Dis. 2017 Jan;23(1):E5-E6. doi: 10.1097/MIB.0000000000000992. PubMed PMID: 27930413 8. Bar F, Kuhbacher T, Dietrich NA et al. Aliment Pharmacol Ther 2018;47(5):581-587. 9. Amandeep Singh, Freeha Khan, Rocio Lopez, Bo Shen, Jessica Philpott. Gastroenterology 2018; 154 (6) Supplement 1: S-411, Sa1829. 10.Verstockt B, Claeys C, Van Assche G, D'Hoore A, Wolthuis A, Vermeire S, Ferrante M. J Crohns Colitis 2018;12(supplement 1): S425 11.Phase 4 Study to Evaluate the Efficacy and Safety of Vedolizumab in the Treatment of Chronic Pouchitis. Https://clinicaltrials.gov/show/nct0279013

Disclosure: Nothing to disclose

P1822 SYSTEMATIC REVIEW OF CALCINEURIN INHIBITORS (CNI) AND VEDOLIZUMAB (VDZ) COMBINATION THERAPY IN ACUTE SEVERE ULCERATIVE COLITIS (ASUC)

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Introduction: Patients with acute severe ulcerative colitis (ASUC) may be refractory to treatment with steroids and anti-tumour necrosis factor agents (anti-TNF). Ciclosporin inhibitors (CNI) have been used effectively as a fast-acting bridge to slower-onset immunomodulators in thiopurine-naïve patients; however concerns over toxicity limit prolonged use of CNI as maintenance therapy. Patients who are azathioprine-exposed or anti-TNF-refractory have limited medical treatment options, often resulting in colectomy.

Combination of CNI as induction therapy, together with slower-acting but potentially safer vedolizumab (VDZ) has recently been used in patients with severe inflammatory bowel disease (IBD). We aim to review the utility of this combination treatment in ASUC.

Aims & Methods: A systematic bibliographic review was conducted on PubMed using the keywords "vedolizumab", "calcineurin inhibitors", "inflammatory bowel disease", and "severe ulcerative colitis". Additional studies were identified by manual search of reference lists.

6 articles were identified within the period 2013 to March 2019. Only English language publications and abstracts on use of combination CNI+VDZ in adult ASUC patients were included. 1 paediatric study [1], 1 case report[6] and 1 abstract [2] (ASUC data not reported) were excluded.

Results: There were 2 prospective observational studies[3,4] [N= 30] and 1 retrospective study [5] [N=39]. Patients were refractory to conventional treatment with steroids [1 study, N=17] and/or anti-TNF therapy [N=48]. CNI (ciclosporin or tacrolimus) was used for induction of remission in majority of cases, or as rescue agent in those failing induction with Vedolizumab [subgroup of 1 study, N=7].

In 2 studies, IV cyclosporine 2 mg/kg titrated to goal trough level 300-400 or Tacrolimus 0.05mg-0.1mg/kg/d with target levels 10-14ng/mL was started; a week later, CNI-responsive patients were given vedolizumab (IV 300mg at week 0,2,6 then maintenance 8-weekly) and CNIs were stopped after 8-12 weeks per protocol. In another study, VDZ was initiated on average 30days after CNI, with average combination CNI+VDZ of 64 days.

Combination CNI+VDZ showed good short-term efficacy (1 study: 14/15 in remission). At 1 year, there was a respectable colectomy-free rate of 75% (2 studies, N=39/52), comparable to other studies with infliximab/ciclosporin combined with azathioprine. In those receiving steroids at baseline, Steroid-free remission was achieved in 18/36 = 50% at week 14. Serious adverse events (N=7) were attributed to CNIs; there were no deaths.

Conclusion: Preliminary studies of combination CNI and VDZ in patients with ASUC appear promising. However, the methodology in these limited studies was heterogenous. Further prospective trials are needed for the confirmation of the utility and efficacy of this treatment strategy in the management of ASUC.

References: [1] Hamel B et al. , (2018), Outcome of tacrolimus and vedolizumab after corticosteroid and antiTNF failure in paediatric severe colitis [2] M. Rutka, (2017), Efficacy of combination therapy with cyclosporin and vedolizumab in inflammatory bowel diseases refractory to antiTNF agents [3] D. Tarabar , (2017), Combination therapy of cyclosporine and vedolizumab is effective and safe for severe, steroid resistant ulcerative colitis patients: A prospective study [4] B. Christensen, (2019), Safety and Efficacy of Combination Treatment With Calcineurin Inhibitors and Vedolizumab in Patients With Refractory Inflammatory Bowel Disease [5] Pellet G, (2019), Efficacy and Safety of Induction Therapy With Calcineurin Inhibitors in Combination with Vedolizumab in Patients With Refractory Ulcerative Colitis [6] W. Alana, (2014), Novel Use of Cyclosporine Induction Therapy as a Bridge to Vedolizumab in Severe Ulcerative Colitis [7] Laharie D, (2018), Longterm outcome of patients with steroid refractory acute severe UC treated with ciclosporin or infliximab.

Disclosure: Nothing to disclose

P1823 ORAL CURCUMIN IS NOT MORE EFFECTIVE THAN PLACEBO TO PREVENT ENDOSCOPIC POSTOPERATIVE RECURRENCE IN PATIENTS WITH CROHN'S DISEASE TREATED WITH CONCOMITANT THIOPURINES

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Introduction: Postoperative recurrence is a major concern in patients with Crohn's disease (CD). Curcumin exhibited antiinflammatory and antioxidative properties in cellular and rodent models. Recently, a randomized controlled trial demonstrated that oral curcumin was more effective than placebo to induce clinical and endoscopic remission in patients with ulcerative colitis failing to mesalamine [1].

Aims & Methods: We aimed to assess the efficacy of oral curcumin compared to placebo to prevent endoscopic POR in patients with CD receiving concomitant thiopurines therapy. We conducted a double-blind, randomized, placebo-controlled trial in eight IBD centers. All patients with CD (> 18 years-old) undergoing bowel resection were consecutively enrolled within

15 days after the surgery or the closure of diverting stoma. All macroscopic lesions had to be removed and the anastomosis had to be reached by colonoscopy. The patients were randomized to be treated with azathioprine 2.5mg/kg, and either placebo (placebo group) or oral curcumin (3g/day) (curcumin group).

The primary endpoint was endoscopic POR at 6 months (M6), defined as Rutgeerts' index ≥ i2a.

Secondary endpoints were severe endoscopic POR (≥ i3), clinical POR (CDAI > 150), quality of life (IBDQ) and safety. An intermediary analysis was planned after the enrollment of 50% of the patients (n=62 patients).

Results: Overall, 62 patients were enrolled (mean age 36.3 ± 12.0 years, mean CD duration 8.1 ans ± 8.0 years, 67.2 % female genders, 37.8% smokers, 8.2 % with perianal lesions, 45.9 % with structuring CD, 36.1 % with fistulizing CD, 45.9 % with prior bowel resection, 18.0 % of anti-TNF naïve patients). In intermediary analysis (intent-to-treat), curcumin was not more effective than placebo to prevent endoscopic POR at M6: 67.7 % (21/31) vs 58.1 % (18/31) (p=0.60), in curcumin and placebo groups, respectively (Figure 1). The rate of severe endoscopic POR was significantly higher in patients treated with curcumin (17/31, 54.8%) compared to placebo (8/31, 25.8 %) (p= 0.02). The rate of clinical POR was not different between the two groups: 38.7 % (12/31) in curcumin group vs 45.2 % (14/31) in placebo group (p = 0.80). IBDQ was similar between the two groups (178.5 in the curcumin group vs 181.5 in the placebo group; p=0.63). The rate of adverse events was not different between the two groups.

Conclusion: Oral curcumin was not more effective than placebo to prevent endoscopic postoperative recurrence (POR) in patients with CD receiving concomitant thiopurines therapy.

References: [1] Lang A et al. Clin Gastroenterol Hepatol 2015.

Disclosure: Nothing to disclose

P1824 IMPACT OF PATIENT EDUCATION ON SWITCH ACCEPTANCE IN IBD PATIENTS IN REMISSION, WITH INFLIXIMAB ORIGINATOR SWITCHED FOR AN INFLIXIMAB BIOSIMILAR: A PROSPECTIVE STUDY

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Introduction: CT-P13, the first biosimilar to infliximab (IFX), has an efficacy and tolerance profile comparable to IFX originator, at a lower cost. Physicians are thus strongly encouraged to propose a biosimilar. However, for patients, the switch from IFX originator to a biosimilar is not always accepted.

Aims & Methods: The aim of this study was to evaluate the impact of patient education (PE) on the acceptance of a switch from IFX originator to biosimilar in IBD patients treated with IFX originator. In a monocentric prospective study, all IBD adult patients treated with IFX originator between June 2017 and June 2018, in clinical remission for at least 6 months, were asked to complete a questionnaire specifically designed for this study, to assess their knowledge on biosimilars and their acceptance of a switching strategy. Patients had the choice whether or not to accept the switch, with or without PE. The primary endpoint was the percentage of patients who accepted the switch, after receiving a PE session due to an initial refusal. Secondary endpoints were the evaluation of patient knowledge and feeling regarding biosimilar treatment; clinical remission, based on the Harvey-Bradshaw Index (score < 4) for CD and the partial Mayo score (< 2) for UC; biological remission: C reactive protein (N< 5 mg/l) and faecal calprotectin (N< 150 µg/g stool) and immunogenicity after the switch, trough levels of IFX (TLI) and anti- IFX antibodies (ATI).

Results: 86 patients (median age: 44 years [19-79]) were included (36% UC and 64% CD). The switch was initially refused by 47% of patients. In this subgroup, 78% agreed to participate in an educational interview with the PE nurse; 68% finally accepted the switch.

At Week 16, the persistence on biosimilar was 91%. At weeks 0, 8 and 16, respectively, Mayo score was 0.68 ± 0.69, 0.81 ± 0.95 and 0.57 ± 0.76 (p = 0.733) and Harvey-Bradshaw score was 0.88 ± 1.70, 1.95 ± 2.27 and 2.14 ± 2.36 (p = 0.134); CRP was 2.92 ± 4.52, 3.48 ± 5.99 and 4.33 ± 10.82 (p = 0.724); faecal calprotectin was 291 ± 402, 418 ± 596 and 427 ± 459 (p = 0.745); TLI was 5.00 ± 3.98, 4.81 ± 3.97 and 4.44 ± 3.34 (p = 0.642); no

patients had immunisation after the switch; IBDQ was 182.61 ± 28 at W0 and 175 ± 34 for at W16 (p = 0.494). The evaluation on the knowledge of biosimilars at W0 showed that 77% of patients had never heard about it, 85% were in favour of the switch and 61% expressed fears about their use. At Week 16, the same evaluation showed that 84% of patients said they knew about biosimilars, 93% were in favour of the switch and 39% were still concerned about their use.

Conclusion: This study confirms the safety of switching infliximab by CT-P13 and demonstrates for the first time that PE plays a key role in switch acceptance by patients.

Disclosure: The study was funded by Pfizer, France

P1825 PERSISTENT OBESITY AFTER TREATMENT WITH WEIGHT LOSS MEDICATIONS OR BARIATRIC SURGERY IS A RISK FACTOR FOR DEVELOPMENT OF INFLAMMATORY BOWEL DISEASE

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Introduction: An association between bariatric surgery and risk of new-onset inflammatory bowel disease (IBD) has been suggested, however, the epidemiology of this association is not well characterized.

Aims & Methods: Using IBD Explorys, a HIPPA-enabled web platform that includes clinical data from over 62 million unique individuals with accompanying lab data, we aimed to quantify the risk for new-onset IBD among patients undergoing bariatric surgery (roux-en-y gastrojejunostomy, sleeve gastrectomy or resection, stomach stapling, gastric banding), versus patients being treated with weight loss medications (orlistat, phentermine + topiramate, lorcaserin, naltrexone + bupropion, liraglutide), and the general population (without prior bariatric surgery, weight loss medication exposure, or IBD diagnosis upon entry into Explorys). We further explored the association between persistence of obesity, defined as a BMI > 30 up to 6 months after exposure to bariatric surgery or weight loss medication, and the risk of new-onset IBD. IBD was diagnosed based on a combination of ICD-9 codes + at least 1 prescription for an IBD specific medication (5-ASA,immunomodulator, biologic). Relative risks (RR) with 95% Confidence Intervals (CI) are reported.

Results: A total of 59,630 and 198,270 patients were exposed to bariatric surgery and weight loss medications respectively, with 640 and 2,240 developing new-onset IBD after exposure. The prevalence of new-onset IBD after exposure to bariatric surgery (1,073/100,000 persons) was comparable with exposure to weight loss medications (1,130/100,000 persons, p=0.222), and both were significantly higher than the prevalence of new-onset IBD in the general population (512/100,000, {RR 2.14, [95% CI 1.98, 2.31] p<0.001}and weight loss medication {RR 2.40, [95% CI 2.30, 2.49] p<0.001}). Among patients who developed new-onset IBD after exposure to bariatric surgery or weight loss medications, >80% of them had a BMI >30 up to 6 months after treatment of obesity (p<0.001). None of the new-onset IBD post bariatric surgery had zinc or selenium deficiency.

Characteristic	All IBD [N = 319,610]	Post-BS IBD [N = 640]	Relative Risk	p
Age, n(%) 18-65 years	203,920 (64)	520(81)	2.67 [2.45, 2.91]	< 0.0001
Race: Caucasian African american Hispanic	263,140 [82] 3 2,660 [10] 4,610 [1]	560(88) 80(13)	2.23 [1.05, 2.42] 2.56 [2.06, 3.19]	< 0.0001
Subtypes, n(%) CD US	135,080 [42] 110,850 [35]	300 [47 220 [34]	2.32 [2.08, 2.60] 2.08 [1.82, 2.37]	< 0.0001
IBD associated surgery: Colectomy Proctocolectomy Ileostomy	39,000 [12] 2,890 [1] 17,030 [5]	100 [16] - 50 [8]	2.68 [2.21, 3.26] - 3.07 [2.33, 4.05]	< 0.0001
All cause mortality	16,780 [5]	30 [5]	1.87 [1.31, 2.68]	0.0006

[Demographics and surgical outcomes]

Conclusion: Exposure to bariatric surgery and weight loss medications is associated with an increased risk for new-onset IBD compared to the general population, and this is predominately seen among those who fail to normalize their BMI up to 6 months after treatment.
Disclosure: Nothing to disclose

P1826 SURGERY AND BIOLOGIC PRESCRIPTION RATES FOR CROHN'S DISEASE IN LOTHIAN, SCOTLAND 2000-2017; A POPULATION BASED COHORT

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Introduction: Recent years have seen a shift in Crohn's disease (CD) management to earlier initiation of biologic therapy using a treat to target strategy. However, the effect on long-term outcomes, in particular surgical resection, remains unclear.
Aims & Methods: The aim of this study was to describe trends in rates of surgery and biologic prescription in CD over time in a population-based cohort. All incident CD cases (adult and paediatric) diagnosed between 01/01/00 and 31/12/17 were identified from the Lothian IBD registry (Jones G, ECCO 2019). Abdominal surgeries were identified from Scottish coding data. All data were manually validated using the EHR and pathology records. Kaplan-Meier methods were used to generate incidence curves for first IBD surgery, repeat surgery, permanent stoma formation and first biologic prescription. To compare surgical resection rates over time the cohort was divided into quartiles by date of diagnosis: 00-04, 05-08, 09-13 and 14-17; analysis was performed using the log rank test.
Results: 532/1753 (30.3%) incident CD cases underwent surgery during the study period. 170/532 (32.0%) patients had surgery at diagnosis and were excluded from survival analysis. The overall cumulative incidence rates of first surgery at 1, 5, and 10 years were 7.6% (95% CI, 4.5%-11.7%), 16.9% (13.3%-20.9%), and 25.7% (21.7%- 29.9%) respectively. When comparing temporal trends there was a significant reduction in surgical rates by date of diagnosis (logrank p < 0.001; see table).
A total of 601/1753 patients (34.3%) were prescribed biologics. The rates of first biologic prescription at 1, 5, and 10 years were 8.8% (CI:, 5.9%-12.3%), 20.3% (17.2%-23.7%), and 29.5% (26.4%-32.8%), respectively. When comparing temporal trends there was a significant increase in biologic prescription rates by date of diagnosis (logrank p < 0.001; see table). Biologic prescription in the first year after diagnosis rose significantly over time from 1.0% in the first cohort to 19.0% in the latest.

Date of Diagnosis	Cumulative incidence of surgery			Cumulative incidence of biologic prescription		
	1 year	5 years	10 years	1 year	5 years	10 years
2000-2004	10.0%	22.0%	32.7%	1.0%	5.7%	14.9%
2005-2008	6.4%	18.3%	27.2%	2.8%	12.2%	25.8%
2009-2013	7.7%	15.5%	21.1%	6.1%	22.0%	43.0%
2014-2017	5.2%	13.7%*	-	19.0%	44.9%*	-

*[Table 1. Cumulative incidence of first surgery and first biologic prescription (Kaplan Meier analysis, *censored).]*

Conclusion: In our population based cohort the earlier use of biologics in CD has been paralleled by a significant reduction in surgical rate and time to first operation.
References: Jones G et al, ECCO 2019, DOP87. Multi-parameter datasets are required to identify the true prevalence of IBD: The Lothian IBD Registry (LIBDR) [Internet]. [cited 2019 Mar 20]. Available from: https://www.ecco-ibd.eu/publications/congress-abstract-s/abstracts-2019/item/dop87-multi-parameter-datasets-are-required-to-identify-the-true-prevalence-of-ibd-the-lothian-ibd-

P1827 INVESTIGATIONS PRIOR TO STOMA REVERSAL IN CROHN'S DISEASE: WHAT IS OUR CURRENT PRACTICE AND DOES IT AFFECT OUTCOMES?

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Introduction: Temporary stomas are commonly used during surgery for Crohn's disease to reduce the risk of anastomotic leaks. There is limited data on pre-operative evaluation prior to reversal and whether this predicts adverse outcomes.
Aims & Methods: We performed a retrospective review of patients with Crohn's disease being considered for stoma reversal between January 2012 and July 2018 in a tertiary inflammatory bowel disease centre. Investigations and results prior to stoma reversal were evaluated. Notes review clarified whether investigations altered management. We also collected data on pre- and post-operative medical management and time to first flare.
Results: 48 patients (age range 15-78y, 21 females:27 males) were evaluated. Montreal classification was; 19% L1 (n=9, 89% B2, 11% B3), 4% L2 disease (n=2 B3), 77% L3 (n=37, 27% B2, 73% B3). 23% also had perianal disease. Investigations performed prior to stoma reversal included faecal calprotectin (2%, n=1), rigid sigmoidoscopy (2%, n=1), endoscopy (27%, n=13), cross-sectional imaging 33% (23%, n=10 MR Enterography, and 10%, n=5 CT enterography), contrast studies 83% (54%, n=26 loopogram, and 30%, n=14 water soluble enema) and examination under anaesthesia (5%, n=2). 19% (n=9) investigation findings changed management; expedited closure n=3, delayed closure n=1, intraoperative endoscopy n=2, reversal indefinitely postponed due to active disease n=3. Time with stoma ranged from 32-1806 (median 192) days. Time with stoma was similar for elective and emergency stoma-forming operations.
Of the patients whose stomas were reversed (n=45), 9 patients had flares within a year of reversal and 28 did not. Contrast studies were requested in 78% (flare) and 79% (no flare) of cases whereas disease activity was assessed in 33% and 54% of cases respectively. The characteristics of each group (those that flared under a year and those that did not flare) differed in terms of disease phenotype (67% vs 36% B2 and 33% vs 64% B3 respectively). There was no significant differences between historical treatments and post-reversal therapy (33% vs 29% no therapy, 56% vs 40% thiopurine monotherapy and 11% vs 32% biologic therapy). Three patients were not reversed; one had obvious symptoms of active disease and supporting investigations, two had abnormal investigation findings (in the absence of obvious symptoms of active disease) resulting in a decision against surgery.
Conclusion: There are no current guidelines to advise how patients with Crohn's disease should be assessed prior to stoma reversal. Practice is variable and investigations focus on anatomical abnormalities (exclusion of strictures) rather than objective measures of disease activity. As clinical symptoms do not always mirror disease activity, failure to assess disease activity may have an association with adverse outcomes post-operatively and deserves further research.
Disclosure: Nothing to disclose

P1828 OPTIMAL TIMING OF ILEOCECAL RESECTION IN CROHN'S DISEASE: NO DIFFERENCE IN CLINICAL OUTCOME AFTER EARLY AND LATE SURGERY

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Introduction: Early ileocecal resection (ICR) in Crohn's disease (CD) may prolong clinical remission and reduce the risk of complications. Optimal timing of ICR is yet unknown as long-term data comparing the clinical outcome after ICR at different CD stages are lacking. In this study, we aim to compare the disease course in CD patients following acute, early and late ICR.
Aims & Methods: CD patients aged 16 years and older who underwent primary ICR between 2000 and 2018 in 4 academic and 2 teaching hospitals were included. Patients were identified in a local pathology database and demographic, clinical and surgical data were collected from medical charts. The study population was divided in 3 groups according to the timing of resection: ICR at first CD manifestation or within 1 month after diagnosis (surgery at diagnosis), within 1 year after diagnosis (early surgery) or more than 1 year after diagnosis (late surgery). The primary outcome was clinical recurrence, defined as the start or switch of CD medication for symptomatic disease. Secondary outcomes were endoscopic recurrence (Rutgeerts score ≥i2b) and/or radiologic recurrence (echo, CT and MRI), surgical recurrence (re-resection) and hospitalization. Early surgery and late surgery cohorts were matched using propensity score matching (1:1) accounting for sex, disease localization, disease behaviour, peri-anal fistulas, smoking, calendar year of ICR, and the use of prophylactic postoperative biologicals or thiopurines. Kaplan Meier survival analysis and Cox proportional hazard analysis were performed.
Results: A total of 513 CD patients (320 females (62%), median age 30.8 (IQR 23.5 - 42.3)) were included. ICR was performed at first CD manifestation or within 1 month after CD diagnosis in 48 patients (9%), early surgery was performed in 103 patients (20%, after median 5.1 months, range 1.1 - 11.9) and late surgery in 361 patients (70%, after median 62.3 months, range 12.5 - 562.6). The cumulative probability of clinical recurrence after surgery at diagnosis was 18.8%, 33.4% and 47.7% after 1, 5 and 10 years respectively, which was significantly lower as compared to 25.6%, 57.1% and 77.6% after early surgery (p =0.005) and 28.4%, 63.6% and 80.6% after late surgery (p=0.001). Endoscopic and/or radiologic recurrence rates were also significantly lower in patients with an acute resection at diagnosis as compared to early and late surgery (p=0.023). No significant differences were observed between groups regarding hospitalization (p = 0.578) and re-resection (p=0.327).
After propensity score matching, clinical recurrence rates for the matched early surgery group (n=99) were 25.5%, 56.9% and 77.6% after 1, 5 and 10 years and 24.0%, 63.1% and 74.8% after 1, 5 and 10 years (p=0.849) in the late surgery group (n=99). No significant differences were found in endoscopic and/or radiologic recurrence, hospitalization or re-resection.
Conclusion: The long-term outcome of acute ICR at CD diagnosis is characterized by lower rates of clinical recurrence as compared to early and late surgery. When accounting for known risk factors for postoperative recurrence and prophylactic postoperative medication use, no differences were observed in clinical, endoscopic or surgical recurrence rates in early versus late ICR in CD.
Disclosure: Nothing to disclose

P1829 FACTORS ASSOCIATED WITH CONVERSION TO OPEN SURGERY IN CROHN'S DISEASE

Wickramasinghe D.[1,2], Adegbola S.[3], Sahnan K.[4], Morar P.[4], Carvello M.[5], Di Candido F.[5], Maroli A.[5], Zafar N.[6], Spinelli A.[7], Warusavitarne J.[8]
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Introduction: Crohn's disease (CD) is a relapsing and remitting disorder with an annual incidence of 3 to 20 per 100,000. Ileocecal involvement is the commonest disease pattern in Crohn's disease (CD) and is seen in over half of the patients [1]. Surgery is required when medical management fails or when secondary complications develop. The probability of requiring surgery for CD is 78% and 90% after 20 and 30 years of disease, respectively [2].
Aims & Methods: The primary aim of this study was to identify factors associated with laparoscopic procedures requiring conversion to open surgery in patients undergoing minimally invasive ileocolic resection (MIICR) for Crohn's disease (CD).
We analysed data of consecutive patients who underwent MIICR between January 2005 and May 2018 for CD at 2 European tertiary care centres.
A Logistic regression analysis was performed to identify statistically significant factors associated with conversion to an open approach.
Results: Three hundred and ninety-two patients (M:F 185:207) underwent MIICR. Their mean age at surgery was 48.3 (SD-14.5) years. Seventy-two (18.4%) patients required conversion to an open approach.
The regression model was statistically significant (p< 0.0001) and classified 84.5% of the cases accurately. The multivariate analysis identified age at surgery (odds ratio 1.03), males (OR 2.8), prior resection (OR 2.9), diversion of stool (OR 4.3) and simultaneous colon resection (OR 2.5) to be associated with a higher risk of conversion to open surgery.
Ethnicity, ASA grade, smoking, diabetes, use of biologics, albumin level, perianal disease, stricturoplasty, or duration of disease did not affect conversion.
Conclusion: Males, older patients, prior resection and stool diversion were associated with a higher chance of conversion to open approach. This finding should be considered during the preoperative informed consent process.
References: 1. Y., L., et al., A laparoscopic approach reduces short-term complications and length of stay following ileocolic resection in Crohn's disease: an analysis of outcomes from the NSQIP database. Colorectal Disease, 2012. 14(5): p. 572-577. 2. Coffey, J.C., et al., Inclusion of the mesentery in ileocolic resection for Crohn's disease is associated with reduced surgical recurrence. J Crohns Colitis, 2018.
Disclosure: Nothing to disclose

P1830 FACTORS ASSOCIATED WITH PROLONGED LENGTH OF STAY AFTER ILEOCOLIC RESECTION FOR CROHN'S DISEASE

Wickramasinghe D.[1,2], Carvello M.[3], Di Candido F.[3], Maroli A.[3], Sahnan K.[4], Adegbola S.[5], Morar P.[6], Warusavitarne J.[7], Spinelli A.[8], Zafar N.[9]
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Contact E-Mail Address: marmaduke007@hotmail.com
Introduction: Crohn's disease (CD) is a relapsing and remitting disorder with an annual incidence of 3 to 20 per 100,000. Ileocecal involvement is the commonest disease pattern in Crohn's disease (CD) and is seen in over half of the patients [1]. Surgery is required when medical management fails or when secondary complications develop. The probability of requiring surgery for CD is 78% and 90% after 20 and 30 years of disease, respectively [2]. A prolonged hospital stay after surgery has health, economical and social implications. Enhanced recovery pathways aim to optimise the hospital stay.
Aims & Methods: The primary aim of this study was to identify pre- and perioperative factors associated with a prolonged length of stay (LOS) after ileocolic resection in CD.
We analysed data of consecutive patients who underwent surgery for CD between January 2005 and May 2018 at 2 European tertiary care centres. A logistic regression analysis was performed to identify statistically significant factors associated with a prolonged hospital stay.
Results: A total of 628 patients (M: F 326:302) were included in the analysis. Their mean age at surgery was 44.1(SD-15.0) years. The median length of stay was 6-days (interquartile range 5-9).
The regression model was statistically significant (p< 0.0001) and classified 66.3% of the cases accurately. The multivariate analysis identified open surgery (Odds ratio 2.2), strictureplasty (OR 2.5), longer disease duration (OR 1.03) and Asian ethnicity (OR 3.1) to be significantly associated with a hospital stay of ≥7 days.
Age at surgery, sex, ASA grade, smoking, diabetes, use of biologics, albumin level, perianal disease, prior bowel resections, simultaneous bowel resection or laparoscopic conversion did not increase the LOS.
Conclusion: Patients undergoing open surgery, strictureplasty and longer disease duration were more likely to require a hospital stay greater than seven days. Such factors should be taken into consideration in any enhanced recovery pathway in order to tailor the patient journey.

References: 1. Y., L., et al., A laparoscopic approach reduces short-term complications and length of stay following ileocolic resection in Crohn's disease: an analysis of outcomes from the NSQIP database. Colorectal Disease, 2012. 14(5): p. 572-577. 2. Coffey, J.C., et al., Inclusion of the mesentery in ileocolic resection for Crohn's disease is associated with reduced surgical recurrence. J Crohns Colitis, 2018.
Disclosure: Nothing to disclose

P1831 FACTORS ASSOCIATED WITH STOMA FORMATION AFTER ILEOCOLIC RESECTION FOR CROHN'S DISEASE

Wickramasinghe D.[1,2], Di Candido F.[3], Carvello M.[3], Maroli A.[3], Sahnan K.[4], Adegbola S.[5], Morar P.[4], Zafar N.[6], Warusavitarne J.[7], Spinelli A.[8]
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Introduction: Crohn's disease (CD) is a relapsing and remitting disorder with an annual incidence of 3 to 20 per 100,000. Ileocecal involvement is the commonest disease pattern in Crohn's disease (CD) and is seen in over half of the patients [1]. Surgery is required when medical management fails or when secondary complications develop. The probability of requiring surgery for CD is 78% and 90% after 20 and 30 years of disease, respectively [2]. Although most patients do not require a stoma at the primary operation, there is no way to predict the likelihood of a stoma. This ambiguity affects pre-operative informed consent. Injudicious avoidance of a stoma can increase the risk of anastomotic complications and need for additional interventions.
Aims & Methods: The primary aim of this study was to identify factors leading to primary stoma formation after ileocolic resection for Crohn's disease (CD).
We analysed data of consecutive patients who underwent surgery for CD between January 2005 and May 2018 in 2 European tertiary care centres.
A Logistic regression analysis was performed to identify statistically significant factors associated with stoma formation in patients undergoing ileocolic resection for CD.
Results: A total of 628 patients (M: F 326:302) underwent surgery. Their mean age at surgery was 44.1(SD-15.0) years. Eighty-one patients (12.8%) had stomas created at the primary operation. Forty-three(53.1%) were end-ileostomies the rest were defunctioning stomas.
The regression model was statistically significant (p< 0.0001) and classified 86.3% of the cases accurately. The multivariate analysis identified lower pre-op albumin (odds ratio 0.89), males (OR 2), simultaneous colonic (OR 7.3) resection and prior resection (OR 2.8 per previous surgery) to be significantly associated with stoma formation.
Age at surgery, ethnicity, use of biologics, smoking, perianal disease, emergency surgery or simultaneous strictureplasty or small bowel resection were not associated with a higher chance of stoma formation.
Of the patients who did not have a stoma at the primary operation, 11 (2%) needed subsequent surgery for anastomotic leaks in the post-operative course. Fifty-five (67.9%) had their stomas reversed.
Conclusion: Low albumin, previous resections, males and simultaneous colonic resection were associated with a higher chance of primary stoma formation. Preoperative strategy planning including the approach to primary-stoma might reduce the need for reintervention.

References: 1. Y., L., et al., A laparoscopic approach reduces short-term complications and length of stay following ileocolic resection in Crohn's disease: an analysis of outcomes from the NSQIP database. Colorectal Disease, 2012. 14(5): p. 572-577. 2. Coffey, J.C., et al., Inclusion of the mesentery in ileocolic resection for Crohn's disease is associated with reduced surgical recurrence. J Crohns Colitis, 2018.
Disclosure: Nothing to disclose

P1832 HOW TO OPTIMIZE THE MEDICO-SURGICAL MANAGEMENT OF PERIANAL FISTULIZING CROHN'S DISEASE TO INCREASE THE RATE OF FISTULA CLOSURE?

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Introduction: Perianal fistulizing Crohn's disease (PCD) remains a challenge to treat, despite the use of TNF antagonists. Several guidelines agreed to recommend a medico-surgical management but half of patients with PCD would still suffer from persistent disease. The aim of the study was to assess the best medico-surgical strategy for treating PCD.
Aims & Methods: The medical records of all patients with fistulizing perianal Crohn's disease treated with TNF antagonists in two referral centers between 1998 and 2018 were reviewed. The therapeutic persistence was performed to compare infliximab and adalimumab treatment using a Kaplan-Meier method. The cumulative incidences of complete fistula closure were estimated using the Kaplan-Meier method. Medical and surgical predictors of long-term outcomes were identified using a Cox proportional hazards model and used to propose the optimal medico-surgical management.
Results: A total of 200 patients were included. At PCD diagnosis, 19% of patients were B3 and 44.5% were L3 according to the Montreal classification. A total of 41% of patients had associated proctitis. The overall cumulative probabilities of fistula closure were 26.8% and 69.8% at 1 and 5 years, respectively. Infliximab were more likely to be used compared to adalimumab (73.5% vs 26.5%, respectively). The therapeutic persistence of TNF antagonist was of 138.73 weeks without difference between adalimumab and infliximab. Of note patients treated with ADA were more likely to experience treatment optimization (60.4% vs 30.6% in IFX group).
Regarding the medical treatment, the combination of TNF antagonist with an immunosuppressant (HR=1.55, p=0.03) and the presence of a proctitis (HR=1.74, p=0.0086) were independently associated with fistula closure. B1 phenotype was associated with lower rate of fistula closure. When considering the perianal surgery, the initial drainage of the fistula with a seton and an additional surgery during the follow-up were also associated with an increase of fistulas closure. No difference was observed between the type of additional surgery (seton insertion, fistulotomy, rectal advancement flap and others). However, this effect was only observed when the complementary surgery was performed within the first year of TNF antagonist treatment.
Finally, the best management of the PCD was the association of a combination therapy following a first drainage with a seton and then a complementary surgery within the first year. The cumulative probabilities of fistula closure in this setting were 44% and 98% at 1 and 5 years, respectively.
Conclusion: The combination of medical and surgical treatment is required for the management of patients with PCD. Both part of the treatment should be early and proactively optimized to increase the rate of fistula closure.
Disclosure: Nothing to disclose

Other Lower GI Disorders III
09:00-17:00 / Poster Exhibition - Hall 7

P1833 THE DEVELOPMENT OF RESISTANCE TO CLARITHROMYCIN AND AMOXICILLIN IN *LACTOBACILLUS PLANTARUM* IS ACCOMPANIED BY MUTATIONS NOT ONLY IN TARGET GENES

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Introduction: In light of the global growth in the spread of antibiotic-resistance in microorganisms, commensal bacteria require serious attention, particularly the key representatives of the human intestinal microbiota in view of their genome plasticity, reservoirs of antibiotic resistance, resistance mechanisms *in vivo* and *in vitro*, as well as the ability to transfer resistance modules. Bacteria of the genus *Lactobacillus*, including *L. plantarum*, are important residents of human gut, oral cavity, and urogenital tract, and are widely used for correction of the intestinal microbiota composition. However, the information of the antibiotics effects on genomic profile and drug sensitivity of these microorganisms is rare and contradictory.
Aims & Methods: The aim of our research was to elucidate the effects of clarithromycin (Clr) and amoxicillin (Amx) used for the eradication therapy of *Helicobacter pylori* on the *L. plantarum* genomic profile and sensitivity to these antibiotics. The object of the study was the strain *L. plantarum* 8P-A3, isolated from the probiotic supplement "Lactobacterin dry" (Biomed Perm Research and Manufacturing Association, Russia), and the clinical strain *L. plantarum* HP227-5, isolated from the intestinal microbiota of a patient who underwent *H. pylori* eradication treatment according to the Maastricht Protocol (amoxicillin 1000 mg bid, clarithromycin 500 mg bid, proton pump inhibitor and bismuthate tripotassium dicitrate 240 mg bid for 14 days). Both strains were cultivated at 37°C on Man-Rogosa-Sharpe (MRS) medium. In order to obtain the resistant strain, sequential cultivation of the initial *L. plantarum* 8P-A3 with an increasing antibiotics concentration to clinically significant levels was performed. Total DNA extracted from strains was sequenced on the MiSeq platform (Illumina). The reads were assembled using SPAdes v.3.11.1, the SNP calling was performed using SNPEff v.3.6.
Results: As a result of selection of the initial laboratory strain *L. plantarum* 8P-A3 (MIC of Clr and Amx was 0.04 µg/ml and 0.01 µg/ml, respectively) the strain *L. plantarum* 8P-A3[Clr+Amx] with high resistance to both clarithromycin and amoxicillin (Clr concentration of 5.5 µg/ml and Amx concentration of 14.5 µg/ml) was obtained. Ten mutations were found in the genome of *L. plantarum* 8P-A3[Clr+Amx], including 4 mutations in antibiotics target genes (rplD, rplV, penA, pbpB) and 6 novel mutations in genes which were not mentioned earlier as determinants of clarithromycin and amoxicillin resistance in bacteria: transcriptional termination factor Rho (rho), PhoH-like protein, teichoic acid ribitol-phosphate polymerase (tarL), GDP-mannose 4,6-dehydratase (gdpP), transcriptional regulatory protein (walR) and one hypothetical protein. However, mutations identified in *L. plantarum* 8P-A3[Clr+Amx] were not detected in the genome of *L.plantarum* HP227-5, and no resistance to clarithromycin and amoxicillin was revealed in the clinical isolate.
Conclusion: Our data suggests that the antibiotic therapy used in the Maastricht Protocol for *H. pylori* eradication does not cause the development of antibiotic resistance in clinical isolate *L.plantarum*, and the mechanisms for adapting to antimicrobials *in vitro* and *in vivo* may vary significantly in these bacteria. To confirm this assumption, it is necessary to conduct a study with a large cohort of patients. The ability of *L. plantarum* str. 8P-A3[Clr+Amx] to transfer clarithromycin and amoxicillin resistance genes to other bacteria also requires further research.
Disclosure: Nothing to disclose

P1834 *FUSOBACTERIUM NUCLEATUM* PROMOTES COLORECTAL TUMOR DEVELOPMENT IN MICE THROUGH DISTURBING THE COLORECTAL MICROBIOTA STRUCTURE

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Introduction: *Fusobacterium nucleatum* has long been found to cause opportunistic infections and has recently been implicated in colorectal cancer (CRC), which brings great attentions widely. However, the mechanism is still largely unknown. We found that the relative abundance of *F. nucleatum* in fecal microbiota was significantly increased in colorectal cancer patients in our previous study. To explore the causative role it may have in CRC development, we inoculated C57BL/6 mice with one clinical *F. nucleatum* strain isolated from a CRC patient's fecal sample, and then evaluated the structure of colon microbiota, colon pathology and gut barrier function after *F. nucleatum* infection.

Aims & Methods: We isolated one clinical strain (FN16) enriched in relative abundance 3% of the CRC patient's gut mucosa bacteria, and identified it as *F. nucleatum* by biochemical tests and 16S ribosomal RNA gene sequencing. Four groups of mice were then compared to reveal difference, i.e., control group, *F. nucleatum* infection group (FUSO), Azoxymethane-induced CRC group (AOM) and AOM+FUSO infection group. To establish infection, we infused 10^8 cells of FN16 every day for two weeks into C57BL/6J mice by gastric gavage. Body weight, length of colon, colorectal tumor formation ratio, colorectal barrier function and gut microbiota structure were assessed to explore the potential role of FN16 in the development of CRC.

Results: The body weight, colon length and colorectal tumor formation ratio profiles exhibited significant differences among the four groups. FUSO group showed significantly reduced body weight and shorter colon length compared with the control group. And AOM+FUSO showed the highest tumor formation ratio and the worst body weight among the four groups. What's more, colon pathology was the most serious in the AOM+FUSO group, which was confirmed by hematoxylin-eosin staining. The colon mucosa of FUSO mice developed obvious inflammation phenotype with the higher level of IL-6 (P< 0.01) and TNF-α(P< 0.01) by the RT-PCR results. The AOM+FUSO group showed the same pattern compared with the AOM group, and the mRNA expression of IL-6 (P< 0.05) and TNF-α(P< 0.01) in colon tissue of AOM+FUSO group were significantly higher. In addition, the mRNA expression of ZO-1 (P< 0.05) and Claudin-1 (P< 0.01) in colon mucosa of FUSO group were reduced, indicating the dysfunction of gut barrier. To explore the reason of *F. nucleatum*-caused colon inflammation and gut barrier damage, we profiled the structure of mucosa microbiota of the four groups. We found that the structure of colon microbiota changed a lot after *F. nucleatum* infection; striking differences in fecal microbial population patterns were observed between FUSO and control group, AOM+FUSO and AOM group. Inflammation-inducing genus *Bacteroides* was enriched in the mucosa microbiota of FUSO and AOM+FUSO group, whereas the genera *Lactobacollus* and *Ruminococcus* were significantly less abundant. The dysbiosis of colon mucosa microbiota, characterized by the enrichment of inflammation-inducing pathogens and the decreased in probiotics members, therefore represent a specific microbial signature of *F. nucleatum* infection, which may provide new sights into the role of this bacteria in promoting colorectal cancer.

Conclusion: The CRC mice with infection of *F. nucleatum* FN16 isolated from the CRC patient shows aggravated intestinal inflammatory conditions and dysbiosis of colon microbiota, suggesting that the *F. nucleatum* may be a contributing factor to CRC, rather than a bystander.

References: Dysbiosis Signature of Fecal Microbiota in Colorectal Cancer Patients. Na Wu, Xi Yang, Ruifen Zhang, Jun Li, Xue Xiao, Yongfei Hu, Yanfei Chen, Fengling Yang, Na Lu, Zhiyun Wang, Chunguang Luan, Yulan Liu, Baohong Wang, Charlie Xiang, Yuezhu Wang, Fangqing Zhao, George F. Gao, Shengyue Wang, Lanjuan Li, Haizeng Zhang, Baoli Zhu. August 2013, Volume 66, Issue 2, pp 462-470

Disclosure: Nothing to disclose

P1835 *HELICOBACTER PYLORI* ERADICATION THERAPY RESULTS IN ALTERATION OF THE HUMAN GUT MICROBIOTA METABOLIC POTENTIAL

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Introduction: Obviously *H.pylori* eradication therapy can lead to changes of gut microbiota composition. However, there is limited data concerning the influence of eradication therapy on functional potential of the human gut microbiota that is probably more important in maintaining human health.

Aims & Methods: The aim of the study was to evaluated influence of *H.pylori* eradication therapy on gut microbiota metabolic potential.

Stool samples from 102 *H.pylori*-positive patients before and immediately after eradication therapy (proton pump inhibitor, amoxicillin 1000 mg, clarithromycin 500 mg and bismuthate tripotassium dicitrate 240 mg bid for 14 days) and 29 samples 1 month after therapy from the same patients were collected. Stool samples total DNA was sequenced on SOLiD 5500xl-W. Reads were mapped to ChocoPhlAn using the HUMAnN2 algorithm for functional profiling. Relative abundances of metabolic pathways (MP) were calculated as "cpm" - a number of reads mapped to pathway divided by a total number of mapped reads, p< 0.05 was considered as significant. MP were categorized by MetaCyc database.

Results: Serious alterations of the gut micriobiota functional potential were observed due to *H.pylori* eradication therapy: significant differences were found in the relative abundance of 180 MP. Most of the changes were observed for biosynthesis pathways: immediately after the therapy 97 MP [biosynthesis of amino acids (6), carbohydrates (9), cell structures (4), cofactors, prosthetic groups, electron carriers (45), fatty acids and lipids (23), nucleosides and nucleotides (7), metabolic regulators (2), siderophores (1)] and 1 tRNA processing MP were more represented in the gut microbiota than initially. However, 8 biosynthesis MP [amino acids (2), cofactors, prosthetic groups and electron carriers (2), fatty acids and lipids (1), nucleosides and nucleotides (1)] became less represented compared to baseline. Changes in abundance of Degradation/Utilization/Assimilation pathways were observed immediately after the therapy, including increased representation of 43 MP [alcohols (2), aldehydes (1), amines and polyamines (4), amino acids (4), aromatic compounds (8), carboxylates (3), secondary metabolites (4), carbohydrates (8), inorganic nutrients (5), nucleosides and nucleotides (1), fatty acids and lipids (3)] while 4 pathways [degradation of pyrimidine nucleotides (1), carbohydrates (2) and formaldehyde assimilation (1)] became less represented after eradication than before therapy.

Similar changes were noted for Generation of Precursor Metabolite and Energy processes: abundance of 6 MP decreased, however, abundance of 21 MP increased immediately after the therapy compared to initial level, including fermentation processes, acetyl-CoA biosynthesis, pentose phosphate pathway, TCA cycle, aerobic respiration, glycolysis.

By the end of the month after eradication therapy a tendency to return to the initial level was observed for most of functional potential changes. However, changes in abundance of 28 MP: Biosynthesis (22), Degradation/Utilization/Assimilation (4) and Generation of Precursor Metabolites and Energy (2) still persisted. Most of these pathways were more represented in the gut microbiota one month after the end of therapy than initially.

Conclusion: So *H.pylori* eradication therapy caused significant changes in the gut microbiota metabolic potential, some of which persisted even one month after the end of therapy. An increased abundance of most pathways could be associated with stress response of the gut microbiota on the background of antibacterial therapy.

Disclosure: Nothing to disclose

P1836 THE ABUNDANCE OF SHORT-CHAIN FATTY ACIDS METABOLIC PATHWAYS IN THE HUMAN GUT MICROBIOTA AFTER *HELICOBACTER PYLORI* ERADICATION THERAPY

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Introduction: Butyrate is a major energy source for colonocytes and plays an important role in maintaining the stability of the gut microbiota, prevention of inflammation and gene expression regulation. Current data suggest a wide spectrum of positive effects of butyrate with a high potential for a therapeutic use. Antibacterial therapy is known to alter composition and functional potential of the gut microbiota.

Aims & Methods: The aim of the study was to assess the influence of *H.pylori* eradication therapy on the gut microbiota functional state with respect to short-chain fatty acids production.

Stool samples were collected from 102 *H.pylori*-positive patients before (the baseline) and immediately after eradication therapy (amoxicillin (1000 mg), clarithromycin (500 mg), proton pump inhibitor, bismuthate tripotassium dicitrate (240 mg) bid for 14 days), as well as 29 stool samples were collected one month after the end of treatment from the same patients. Total DNA extracted from stool samples was sequenced on SOLiD 5500xl-W platform (whole genome sequencing). For metabolic profiling reads were aligned to ChocoPhlAn database using the HUMAnN2 algorithm. Relative abundances of pathway were calculated as "cpm" - a number of reads mapped to pathway divided by a total number of mapped reads. Differences were assessed using Wilcoxon signed-rank test (p-value< 0.05 was considered statistically significant). Metabolic pathways were classified according to MetaCyc database.

Results: The pronounced functional changes of the gut microbiota, including metabolic pathways of fermentation to short-chain fatty acids were revealed immediately after the eradication therapy. Abundance of following pathways - fermentation to lactate (ANAEROFRUCAT-PWY: homolactic fermentation; P122-PWY: heterolactic fermentation), to acetate (P161-PWY: acetylene degradation), to propionate (PWY-7013: L-1,2-propanediol degradation) was increased comparing with baseline - 83.58±46.16 cpm vs. 61.87±33.04 cpm, 12.52±25.28 cpm vs. 4.24±9.02 cpm, 19.80±35.60 cpm vs. 7.99±10.58 cpm and 16.95±63.10 cpm vs. 2.88±8.09 cpm, respectively.

However the abundance of metabolic pathways related to butyrate production - CENTFERM-PWY: pyruvate fermentation to butanoate and PWY-5676: acetyl-CoA fermentation to butanoate II - was decreased in the gut microbiota after therapy compared to initial level: 1.92±2.18 cpm vs. 3.12±3.62 cpm and 15.39±13.18 cpm vs. 17.88±9.72 cpm, respectively. Abundance of following metabolic pathways - PWY-7288 fatty acid β-oxidation, PWY66-391: fatty acid β-oxidation VI, where butyrate could be consumed as the initial agent of the reaction was increased after therapy comparing to baseline, 0.04±0.09 cpm vs. 0.03±0.17 cpm and 0.07±0.17 cpm vs. 0.05±0.25 cpm, respectively. Representation of PWY-6803: phosphatidylcholine acyl editing pathway, in which butyrate derivatives could be produced was increased immediately after the eradication treatment compared to initial level, 22.00±42.54 cpm vs. 6.45±16.12 cpm.

No significant changes were observed in the relative abundance of metabolic pathways involved in butyrate formation in the gut microbiota one month after eradication therapy compared to the baseline level that may be due to the compensatory possibilities of the gut microbiota.

Conclusion: So *H.pylori* eradication therapy leads to alteration of butyrate-producing metabolic pathways in the human gut microbiota, changes return to the initial level one month after the treatment.

Disclosure: Nothing to disclose

P1837 VARIATION OF THE MUCOSA ASSOCIATED MICROBIOME ALONG THE HUMAN GASTROINTESTINAL TRACT IN HEALTH AND DISEASE

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Introduction: Very little is known about the variation in the mucosa-associated microbiota (MAM) along the human gastrointestinal (GI) tract.

Aims & Methods: We aimed to determine the bacterial communities in different parts of the GI tract and compare patients without gastrointestinal disease with patients with Crohn's disease (CD) and Ulcerative colitis (UC). We recruited 72 patients undergoing upper GI endoscopy and colonoscopy for the assessment of a positive FOBT with normal results of the endoscopic investigations (other than small adenoma) and no symptoms reported utilising a standardised assessment of gastrointestinal symptoms (SAGIS). In addition, we recruited 44 patients with CD and 50 patients with UC. Utilising the Brisbane Aseptic Biopsy Device, we obtained biopsies from the proximal small intestine, terminal ileum, ascending colon and rectum without cross contamination from luminal contents or other regions of the GI tract. Biopsy samples were immediately placed under aseptic conditions into a sterile tube containing RNA later (Qiagen). Samples were allowed to incubate at room temperature for 30 minutes, then frozen and stored at -80°C. Total DNA was extracted from biopsies, and sample free reagent controls, using a repeated bead-beating based method. Samples were profiled by high-throughput amplicon sequencing with dual-index barcoding using the Illumina MiSeq platform, targeting the V6-V8 region of the gene encoding 16S ribosomal RNA. The libraries were sequenced on an Illumina MiSeq platform and the data were quality assessed, trimmed and filtered, then processed using the Quantitative Insights into Microbial Ecology version 2 (QIIME2) software. Microbiota and statistical analyses were performed in QIIME2 and R. Significant differences in Shannon and Chao1 alpha diversity metrics between sample types, and between disease states for each sample type, were calculated using Kruskal-Wallis and unpaired Wilcox rank sum tests. Differentially abundant taxa were identified with DESeq2 using a likelihood ratio test while correcting for age, BMI and gender.

Results: Across all patient groups, the three most abundant genera in the duodenum were *Streptococcus, Pseudomonas* and *Prevotella*. However, in the terminal ileum, right colon and rectum, *Faecalibacterium, Bacteroides*, and *Escherichia-Shigella* were the three most abundant bacterial taxa. There were significant differences in the Shannon and Chao1 diversity scores of the mucosa-associated microbiota (MAM) present in the duodenum and terminal ileum (P< 0.001-0.05) between UC and CD, and UC and controls, with greater diversity found for the control subjects. In the right colon and rectum, significantly lower Shannon diversities were observed in UC and CD vs controls (P< 0.05).

Conclusion: There are marked differences in the three most abundant bacteria in the upper and lower gut. Similarly, MAM from different parts of the human GI tract reveal distinct characteristics in the relation to the most prevalent bacterial taxa and the alpha diversity observed at these sites. Interestingly, both UC and CD patients have different MAM profiles in both proximal and distal sites of the GI, and these are different from those observed for healthy asymptomatic controls.

Disclosure: Nothing to disclose

P1838 MULTIDONOR FMT CAPSULES INCREASES FECAL MICROBIOTA DIVERSITY IN PATIENTS WITH IBS FOR AT LEAST THREE MONTHS

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Introduction: Decreased microbial diversity of the fecal microbiota is recognized as a part of gut dysbiosis[1] and hence treatments increasing microbial diversity, such as fecal microbiota transplantation (FMT) have attracted much attention within recent years.
FMT has, in many studies, improved the fecal alpha-diversity which has also been correlated with improved clinical effects [2].
FMT treatment by capsules has emerged as a possible way to continuously transfer fecal material giving lower doses of fecal material, delivered on a daily basis.
Aims & Methods: The aim of our research was to investigate if, and potentially when, FMT delivered through capsules changes the fecal microbiota diversity in patients with Irritable Bowel Syndrome (IBS), and to investigate if the effects diminish over time.
To investigate this we analysed samples from a previously published placebo-controlled randomized clinical trial investigating the effects of 12 days of 25 daily multidonor FMT capsules treating 52 patients with IBS [3]. We tested fecal samples from baseline, and at 15 days, 1, 3 and 6 months following the commencement of treatment using 16S RNA sequencing. Wilcoxon signed-rank tests (p≤0.05) were used to compare alpha-diversity levels at each time-point after baseline with the levels at baseline.
Results: From a median fecal alpha-diversity (Chao1 index) of 306,5 at baseline the median diversity increased at all the following timepoints. The increase was significant after 15 days (404,3, $p=0,005$), 1 month (433,4 $p=0,005$) and 3 months (421,3 $p=0,0002$), but was no longer statistically significant after 6 months (379,1, $p=0,08$). The placebo group did not significantly change their median fecal alpha-diversity at any timepoint. From a baseline level of 342,1 the median fecal alpha diversity was between 324,6 and 376,9 at the following timepoints.
The increases in fecal alpha-diversity was significant when compared to the changes in the placebo group after 15 days ($p=0,03$) and 3 months ($p=0,004$).
Conclusion: Twelve days of daily FMT treatment given by capsules significantly increases the fecal microbiological alpha-diversity of patients with IBS and this persists for at least three months.
However, the increased alpha-diversity was in general not associated with a beneficial clinical effect in the FMT group when compared to the placebo group. Future studies must assess if FMT might improve symptoms in some patients with IBS and in particular in patients with low fecal microbial diversity.
References: 1. Kriss M, Hazleton KZ, Nusbacher NM, et al. Low diversity gut microbiota dysbiosis: drivers, functional implications and recovery. Current opinion in microbiology. 2018 Aug;44:34-40. 2. Rossen NG, Fuentes S, van der Spek MJ, et al. Findings From a Randomized Controlled Trial of Fecal Transplantation for Patients With Ulcerative Colitis. Gastroenterology. 2015 Jul;149(1):110-118. 3. Halkjær SI, Christensen AH, Lo BZS, et al. Faecal microbiota transplantation alters gut microbiota in patients with irritable bowel syndrome: Results from a randomised, double-blind placebo-controlled study. Gut. 2018;67(12):2107-2115.
Disclosure: Nothing to disclose

P1839 EFFECTS OF FECAL SUPERNATANT FROM AUTISM SPECTRUM DISORDER PATIENTS ON INTESTINAL EPITHELIAL BARRIER PERMEABILITY AND ENTERIC NERVOUS SYSTEM PHENOTYPE

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Introduction: Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder in which dysfunctions of the microbiota-gut-brain axis are increasingly recognized. In particular, alterations in gut microbiota or their metabolites, such as secondary biliary acids, have been suggested to contribute to ASD pathology. In order to study how dysbiosis could affect gut functions and enteric nervous system (ENS) homeostasis, we used fecal supernatant (FS) prepared from ASD patients and healthy controls (HC). Specifically, we studied the impact of FS on intestinal epithelial barrier functions and ENS phenotype.
Aims & Methods: Antibiotic-treated mice received enema of FS from ASD patients (n=16) and from healthy controls (n=10). Paracellular and transcellular gut permeability were measured *in vivo* and *ex vivo* in proximal colon. Gene and protein expression for glial (S100b, GFAP), neuronal (GAP43, synapsin1) and inflammatory molecules (IL-1β, TNFα) were analyzed in proximal colon, brain and primary culture of ENS treated with FS from ASD patients or HC. Finally, concentrations of several bacterial metabolites (short chain fatty acids and biliary acids) were measured in FS by mass spectrometry. 16S metasequencing of the intestinal microbiota was performed for ASD patients and HC.
Results: No change of *in vivo* permeability was observed in mice treated with FS from ASD patients while *ex vivo* transcellular and paracellular permeability of proximal colon was decreased as compared to HC. FS from ASD patients induced a decrease of mRNA expression of TNFα, IL-1β, and an increase for S100β and GAP43 in the colon. This latter result was reproduced in primary cultures of ENS. In addition, the protein expression of the synaptic marker synapsin1 was decreased in the colon and showed a trend of reduction in the brain (amygdala) of mice treated with FS from ASD patients compared to controls. The concentration of the secondary bile acid deoxycholic acid was higher in the FS from ASD patients as compared to HC. Changes in bacterial proportion are observed in ASD patients as compared to HC, with a relative increase of Bacteroidetes and decrease of Firmicutes.
Conclusion: FS from ASD patients alter intestinal permeability and expression of inflammatory and ENS molecules. The factors in FS from ASD patients responsible for these changes remain to be identified.
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Disclosure: Nothing to disclose

P1840 ESTABLISHMENT OF A STOOL BANK IN A COUNTRY WITH LOWER HUMAN DEVELOPMENT INDEX

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Introduction: Fecal Microbiota transplantation (FMT) is a novel therapy, with proven efficacy against recurrent Clostridium difficile infection (CDI). For safe implementation and broader application of FMT, quality controlled stool banking is a must. Establishing a stool bank is a complex, time-consuming and expensive process, making it a real challenge in a country with lower Human Development Index (HDI)

Aims & Methods: We aimed to establish the first stool bank in an Eastern European country - Bulgaria. A multidisciplinary team of gastroenterologists, medical microbiologists, infectious diseases specialist and geneticists was set up. We used a questionnaire based on the First European FMT Consensus (1) in order to recruit possible stool donors. Microbiota analysis was performed on all selected donors.

Results: Between October 2018 and April 2019, 112 donor volunteers completed a questionnaire; 70 (62.5%) were excluded, mainly because age above 50, an unhealthy BMI and risk behavior. Fourty-two (37.5%) donor candidates were invited for laboratory testing of blood and feces of which 12 (28.6%) passed this screening. Presence of Helicobacter pylori fecal antigen and Multi Drug Resistant Organisms were the most observed exclusion criteria. Of 12 donors, 4 (33%) failed at a following screening test, which is performed every three months. Finally, 8 (7.14%) active donors were enrolled.

Conclusion: Even though we found many healthy volunteers, only a low percentage (7.14%) of them are suitable to become feces donors. Establishing of a stool bank in a country with lower HDI is important for making FMT saver and more popular as a treatment method, finding further implementation and regulation of FMT and supporting physicians offering this treatment to their patients.

References: 1. Cammarota G, Ianiro G, Tilg H, et al. European consensus conference on faecal microbiota transplantation in clinical practice. Gut. 2017 Apr;66(4):569-580.

Disclosure: Nothing to disclose

P1841 DYNAMIC CHANGES OF OXALATE-DEGRADING ACTIVITY OF FECAL MICROBIOTA IN RATS AFTER CEFTRIAXONE TREATMENT

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Introduction: An urgent problem of modern urology is the increase in the number and rejuvenation of the age of patients suffering from urolithiasis. It has been established that from 70 to 80% of stones excreted during urolithiasis are calcium oxalate, and the level of oxaluria depends in a certain way on the composition and functional activity of intestinal microbiota, in particular on the ability to degrade oxalates. Except for *Oxalabacter formigenes*, a number of normobiote representatives are capable to metabolize oxalate salts (e.g. *Lactobacillus spp., Bifidobacterium spp., Eubacterium lentum, Bacillus spp, Enterococcus faecalis,)*. The anbibiotics decreased the quantity of oxalate-degrading bacteria (ODB) but there is no available data and approaches to evaluate the total oxalate-degrading activity (ODA) of fecal microbiota (without isolation of pure culture).

Aims & Methods: The aim of the present study was to develop approach for evaluation of total ODA of fecal microbiota and to assess the dynamics changes in the ODA of fecal microbiota after broad-spectrum antibiotic ceftriaxone treatment in rats. The object of the study was fecal microbiota of male Wistar rats (200-300 g, n = 6). Ceftriaxone (300 mg/kg, CJSC "Darnitsa", Ukraine) was injected intramuscularly for 7 days. Faeces were collected before antibiotic treatment and on the 1st, 14th and 56th days after antibiotic withdrawal. The quantity of ODB was determined by culture method on a highly selective *Oxalate Medium* (g/L): K_2HPO_4 - 0.25; KH_2PO_4 - 0.25; $(NH_4)_2SO_4$ - 0.5; $MgSO_4 \cdot 7H_2O$ - 0.025; CH_3COON - 0.82; yeast extract - 1.0; rezazurin - 0,001; Na_2CO_3 - 4; L-cysteine-HCl - 0.5; *Trace element solution SL-10* - 1 ml with the following composition per L: HCl (25%; 7.7 M) - 10.00 ml, $FeCl_2$ x $4H_2O$ - 1.50 g, $ZnCl_2$ - 70.00 mg, $MnCl_2$ x $4H_2O$ - 100.00 mg, H_3BO_3 - 6.00 mg, $CoCl_2$ x $6H_2O$ - 190.00 mg, $CuCl_2$ x $2H_2O$ - 2.00 mg, $NiCl_2$ x $6H_2O$ - 24.00 mg, Na_2MoO_4 x $2H_2O$ - 36.00 mg; та $Na_2C_2O_4$ - 5 mg (cultivated anaerobically at 37°C for 48 hours). The redoximetric titration (with KMnO4) was adopted to evaluate the total ODA of faecal microbiota. The results were expressed in % degradation of oxalate for 0.01 g of feces.

Results: At the 1st day after ceftriaxone withdrawal, we observed increase a number of ODB from lg 8.02±0.25 CFU/g to lg 9.47±0.17 CFU/g (p< 0.05) and fecal microbiota ODA from 9.50±1.78 % to 11.67±2.99 %. At the 14th day there was a significant decrease a number of ODB by more than 2 orders of magnitude (from lg 8.02±0.25 CFU/g to lg 5.72±0.48 CFU/g, p< 0.05), that was accompanied diminish the fecal ODA - from 9.50±1.78 % to 6.3±1.46

%. By the 56th day, a number of ODB was almost unchanged *vs.* 14th day of experiment (lg 5,28±0,45 CFU/g, p< 0.05), but fecal ODA continued decrease (from 9.50±1.78 % to 4.67 ± 1.87%, p< 0.05).

Conclusion: 1) The redoximetric titration (with KMnO4) is the reliable method for evaluation of total ODA of the fecal microbiota without isolation of pure culture and might have clinical application. 2) Ceftriaxone treatment reduced the total oxalate-degrading activity of fecal microbiota independently on number of ODB.

Disclosure: Nothing to disclose

P1842 THE DYNAMICS OF MUCOSA-ASSOCIATE BACTERIA IN IRRITABLE BOWEL DISEASE

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Introduction: The gut microbiota between individuals varies greatly, while the composition of gut microbiota within individual slightly changes over time. Fecal samples can be easily collected and are often used to analyzing gut microbiota.

On the other hand, the composition of mucosal bacteria differs from that of luminal bacteria. Though mucosal bacteria are considered to be important in the pathophysiology of intestinal disease including irritable bowel disease (IBS), there are small numbers of study investigating the dynamic analysis of mucosa-associated bacteria because of the difficulty of collecting the sample comparing to fecal samples.

Aims & Methods: The purpose of this study is to analysis the dynamics of mucosa-associated bacteria over time in patient with IBS. The mucus samples including mucosal bacteria were collected from terminal ileum, cecum, transverse colon, sigmoid colon and rectum in same patient with IBS three times at the examination with lower endoscopy using cytology blush. After extracting DNA from mucus samples, 16S metagenome were performed by Miseq platform(Illumina). Sequence data were quality filtered and microbial composition, alpha and beta diversities were analyzed using QIIME open-source software.

Results: The microbial composition of mucosal samples collected by blush were comparable to that of mucosal samples collected by mucosal biopsy and microbial DNA amount in the mucus samples collected by blush were more than 1000 times larger than that of from biopsy samples. Though the microbial composition of mucosal bacteria were different from that of fecal samples, there were not big different change when comparing between each mucosal samples collected from terminal ileum, cecum, transverse colon, sigmoid colon and rectum.

Compared to luminal bacteria, the proportion of Sutterella, Enterobacteriaceae, Delftia and Pseudomonas were increased in the mucus samples on the other hands Phascolarctobacterium, Blautia, Lachnospiraceae, Parabacteroides were decreased. Interestingly PCoA analysis revealed that the microbial composition of mucosa-associate bacteria had slightly changed over time as with the fecal microbial composition.

Conclusion: In this study there are small dynamic changes of mucosa-associate bacteria as with luminal bacteria within the individuals in IBS patient over time and may constantly contribute to the pathophysiology of IBS.

Disclosure: Nothing to disclose

P1843 PEOPLE'S MOTIVATION THROUGH SOCIAL NETWORKS COULD INCREASE PARTICIPATION IN COLORECTAL CANCER SCREENING CAMPAIGNS

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Introduction: Colorectal cancer (CRC) screening using fecal occult blood testing results in reduced CRC mortality. However participation rates in organized campaign remains low and rarely exceed 50% in most French departments. The Colorectal Cancer Screening Association in Seine-Saint-

Denis considered outreach via social networks to people aged 50-74 living in deprived target areas with a high proportion of NPAI (mail invitation campaign not distributed).

Aims & Methods: The purpose of this analysis was to describe the procedure and initial results of the pilot study.

67,000 people aged 50 to 74 years from six municipalities with low socio-economic background and a proportion of NPAI over 10% were considered. Accounting to the biannual frequency of departmental screening campaigns, the average participation rate in these area was only 25% in 2017 with a 19% exclusion rate due to medical reasons (previous colonoscopy, high risk patients...) and 11% NPAI. A pilot Facebook campaign ran for 2 months. Facebook presented the ads as defined by the scientific committee to the target population. The team operated using a simple web-based healthcare engagement platform designed to increase participation developed by Medorion©, Israel. No special computer skills are required and training is a simple 2-hour web seminar. The Facebook campaign does not require names, Emails or any predefined contact information. The rate of engagement can be adjusted to the capacity of the team as well as the project budget. In this campaign, 33,000 Facebook users living in this area were targeted. All data collected is stored outside of Facebook in a HIPAA and GDPR compliant platform according to European legislation.

Results: Over a two-month engagement period, 4317 people click on the CRC screening advertising and 298 people applied for a test kit. Overall, 84% of requests were made outside working hours (9 a.m-5 p.m) and 100% provided an email, postal address, and a phone number (100% mobile). Of these, 160 (53.7%) were eligible for CRC screening after verification on a dedicated regional eligibility site (www.neonetidf.org). Ineligible population included 38 people who resided outside Seine-Saint-Denis, 16 people who were outside the age range, 48 people that could not be verified because to inaccurate information provided, 30 people who had recent CRC screening, and 6 who had recent or ongoing colon disease. The average age of the 160 eligible people was 54 yrs and among them 64 (40%) carried out the screening test to date, higher than the 25% best effort so far. For the other 96 at 60 days after the Facebook campaign closure, a weekly email reminder is still sent to increase this participation.

Conclusion: Extrapolating to a possible year-long project, this method can easily reach a 3 to 5% increase in CRC screening within this target population, which has a history of non-compliance and have not been responsive to previous attempts. It is important to note that the results are based on modest pilot settings, small budget, no specific creative, and not backed by a state trusted entity promoting the screening, making these results even more significant.

Disclosure: Nothing to disclose

P1844 CHANGES IN COLORECTAL CANCER INCIDENCE IN YOUNG ADULTS IN ENGLAND: A POPULATION BASED STUDY 1974 – 2015

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Introduction: Colorectal cancer (CRC) remains a major cause of cancer-related mortality worldwide. Recent reports from the United States[1,2], Canada[3] & Australia[4] have suggested that the incidence of CRC in young adults is rising. Using a novel dataset from the English population we aimed to determine the temporal changes in CRC incidence trends by age group and cohort.

Aims & Methods: This was a retrospective, population-based cohort study of all patients aged 20 years and above diagnosed with CRC between 1974 and 2015 in England. Data were obtained from the National Cancer Registration and Analysis Service operated by Public Health England using ICD-9 and -10 codes for CRC. Mid-year population estimates were obtained from the Office for National Statistics and used to calculate age-specific incidence rates for ten age groups that were age-adjusted to the 2013 European Standard Population. Join-point regression analysis was performed to analyse the magnitude and direction of temporal changes in age-specific incidence rates. Age-period-cohort modelling was used to assess the independent effects of age, period and cohort on CRC incidence rates.

Results: Between 1974 and 2015 a total of 1,145,639 diagnosis of CRC were made (726887 colon, 418752 rectum). Since 1966 there has been a marked rise in the incidence rate ratio (IRR) for both colon and rectal cancer: compared with the reference year 1926, the IRR has doubled (1.92, 95% CI 1.08-3.43) for colon and tripled (3.07, 95% CI 1.79-5.26) for rectal cancer. Strikingly, since 2001 the incidence rate among 20-29 year olds has risen by 20.7% per year and by 12.7% per year among 30 – 39 year olds. CRC incidence initially rose following the introduction of the Bowel Cancer Screening Programme in 2006 but this has subsequently plateaued. The incidence rates of CRC among other age groups has remained largely unchanged.

Conclusion: This novel data from England mirrors the recently described trends in reported in other economically developed countries of rising incidence of CRC in young adults. Work is required to elucidate the underlying causes to allow public health measures required to slow or reverse the current trend which is likely to place further strain on already stretched healthcare resources in England.

Furthermore, understanding the mechanisms underpinning the trends described herein may allow risk stratification for screening tests in younger adults who would not otherwise qualify for testing. Any such expansion of screening practices is likely to have a significant impact on the cost and service provision requirement within the confines of the English National Health System.

References: [1] Siegel, R.L., et al., Colorectal Cancer Incidence Patterns in the United States, 1974-2013. J Natl Cancer Inst, 2017. 109(8). [2] Patel, P. and P. De, Trends in colorectal cancer incidence and related lifestyle risk factors in 15-49-year-olds in Canada, 1969-2010. Cancer Epidemiol, 2016. 42: p. 90-100. [3] Brenner, D.R., et al., Increasing colorectal cancer incidence trends among younger adults in Canada. Prev Med, 2017. 105: p. 345-349. [4] Boyce, S., et al., Young-onset colorectal cancer in New South Wales: a population-based study. Med J Aust, 2016. 205(10): p. 465-470.

Disclosure: Nothing to disclose

P1845 WITHDRAWN

P1846 COLORECTAL CANCER POPULATION-BASED SCREENING PROGRAM IN A PORTUGUESE DISTRICT – PRELIMINARY RESULTS

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Introduction: Colorectal cancer (CCR) is a leading cause of death worldwide. Since there is a strong correlation between mortality and the disease stage, focus on the preclinical phase to recognize and treat precursor lesions is the main priority. Organized screening programs for CCR are emerging in Europe to face the overall growing incidence.

Aims & Methods: The aim of this study was to evaluate the diagnostic performance of the program and to define potential adjustments to the strategy adopted.

Observational study from a pilot population-based screening program for CCR in a Portuguese district based on fecal immunochemical test (FIT) with a cut-off level of 100 ng/mL. Colonoscopy was the standard diagnostic follow-up test. Preliminary data were collected from January 2018 to March 2019 to analyze screening measures and quality indicators according with national advices adapted from the European Union guidelines. Advanced adenoma (AA) was defined as any adenoma with at least one of the following features: ≥10 mm in size, villous or tubulo-villous component, high grade dysplasia.

Results: The tested population consisted of 6636 individuals and the positivity rate was 4% (n=257). Of all those who tested positive, 55% (n=142) underwent colonoscopy. In total, 153 colonoscopies were performed, including 11 repeated for diagnostic/therapeutic purposes, with an overall adequate bowel preparation of 91%. The cecal intubation rate was 92%. The polyp and adenoma detection rates were 57% and 43%, respectively. The AA detection rate was 22% matching 51% of all detected adenomas with a true-positive rate of 24% and a false-positive rate of 32%. Neoplasia was diagnosed in 6 cases.

Conclusion: The AA detection rate was substantially high when compared with data published in literature alongside with an unexpected low positivity rate. These findings could justify lowering the FIT cut-off level, in order to increase the diagnostic yield, and carrying out actions to improve the colonoscopy participation rate.

Disclosure: Nothing to disclose

P1847 PATTERN OF DISTANT METASTASES IN RIGHT VERSUS LEFT COLORECTAL CANCER: A SEER BASED STUDY

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Introduction: Colorectal carcinoma (CRC) is one of the common malignancies with escalating incidence and mortality. Today, it is considered a double-faced disease; each face has a unique pathology, management, and prognosis. Immense efforts are applied to explore the behavior of CRC in both sides of the colon; therefore, in this study we focus on the metastatic pattern of CRC in right and left sides.

Aims & Methods: We identified 10714 patients who have been diagnosed with stage 4 CRC from 2010 to 2013 through Surveillance, Epidemiology and End Results (SEER) database. Metastatic pattern for liver, peritoneum, lung, bone and brain was analyzed.

Results: We found 6805 and 3909 patients had left and right CRC, respectively. Right CRC had higher incidence rate of liver and peritoneum metastases than left CRC (92.9 % vs. 89.7 % and 30% % vs. 27.3 % respectively, P= 0.003). While, on the other hand, left CRC had a higher incidence rate of lung metastases (31.5% vs. 25.6%) than right CRC. No statistical significance difference was found regarding pattern of bone or brain metastases between both colon sides. Males with right CRC were more susceptible to the five sites of metastases than females. Albeit males with left CRC were the least to develop peritoneum, lung and brain metastases compared to females. Concerning the survival rates, patients with tumors arising from left colon had better 1-year survival rates in comparison to those with tumors from right colon (64.7% and 49% respectively, p < 0.001).

Conclusion: Right CRC patients are more vulnerable to liver and peritoneum metastases; however, those with left CRC have higher probability to develop lung metastases, furthermore, they have better survival rates.

Disclosure: Nothing to disclose

P1848 ARE GI CANCERS BEING DIAGNOSED FROM OUTSIDE THE 'URGENT CANCER' REFERRAL PATHWAY?

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Introduction: The UK lags behind Europe in the diagnosis, treatment and survival rates of cancer. To improve on this and diagnose cancer early, patients with alarm symptoms from primary care are referred on a 'Two week wait' (2WW) urgent pathway. Previous data indicates that the majority of cancers diagnosed in the UK are from outside the 2WW pathway. However, demand for upper and lower GI endoscopy via the 2WW has risen dramatically above and beyond the steady increase in overall GI cancer incidence.

Aims & Methods: We aimed to study the diagnostic pathways via which GI cancers are diagnosed. We reviewed the common luminal upper and lower GI cancers diagnosed at endoscopy at a single centre between February 2017 and September 2018 via Unisoft GI Reporting Tool. Known malignancies and diagnoses made at other Trusts were excluded (n= 72). Retrospective analysis of 317 patients with 332 GI cancers was performed.

Results: 332 GI cancers (oesophagus 44 (13.9%), stomach 21 (6.6%), duodenum 6 (1.9%), colon 174 (54.9%), rectum 87 (27.4%)). Mean age 71.1 (range 24 - 97), Female 133 (42.0%). Median time to diagnosis (i.e. presentation to endoscopy) was 22 days (IQR 14 to 34).

Referral pathways included: 202 (63.7%) GP Target 2WW, 45 (14.2%) In-patient, 30 (9.5%) Urgent 2WW from clinic/hospital discharge, 21 (6.6%) Abnormal imaging, 17 (5.4%) Routine clinic, 2 (0.6%) Surveillance.

Only 48 (15.1%) GI cancer patients went 'Straight To Test' (STT) whereas 198 (62.5%) were seen in clinic first. The mean time to diagnosis in those referred via the GP Target 2WW was 25.4 days (STT) versus 32.2 days (clinic review), (p = 0.05).

Conclusion: In this study, we conclude that two thirds of GI cancers were diagnosed following referral via the 2WW pathway but only one third of gastric cancers. Of the 2WW patients, two thirds had a clinic review prior to endoscopy which resulted in a 7 day delay in cancer diagnosis compared to STT patients. We conclude that more patients with cancer are diagnosed on the 2WW pathway than previously documented and triaging patients STT speeds up the diagnosis further by 7 days. We recommend that the majority of 2WW patients be triaged STT so that earlier diagnosis of cancer may result in improved survival and reduce the gap compared to our European counterparts.

Disclosure: Nothing to disclose

	All GI Cancers (n=332)	Oesopha-gus n=44	Gastric n=21	Colon n=174	Rectum n=87	p value
Age (mean, s.d)	71.1 (13.5)	73.8 (11.6)	71.8 (17.8)	71.5 (13.2)	68.0 (13.7)	0.10
Time to diagnosis (median, IQR)	22 (14-34)	19 (7-28)	11 (5-28)	24.5 (17-38.75)	23 (16-33)	0.27
GP ,2WW' Pathway (%)	202 (63.7)	25 (56.8)	7 (33.3)	109 (62.6)	69 (79.3)	**0.0003**
STT (%)	48 (15.1)	9 (20.5)	2 (9.5)	24 (13.8)	13 (14.9)	0.63
Curative Treatment (%)	204 (64.4)	13 (29.5)	2 (9.5)	129 (74.1)	65 (74.7)	<0.00001

[Table 1. Pathways to diagnosis for individual GI cancers (+ STT/clinic/A&E)]

P1849 TEN-YEAR COLORECTAL CANCER MORTALITY AFTER ADENOMA REMOVAL

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Introduction: Patients who have had adenomas removed are believed to be at increased risk for colorectal cancer (CRC). Dependent on adenoma characteristics, these patients are recommended surveillance colonoscopy at regular intervals. Previously, we did not find increased risk for CRC among patients with previous adenoma 7.7 years after polypectomy (1). We have updated the results with more than 10 years follow-up, in accordance with the time horizon of current surveillance guidelines.

Aims & Methods: We identified all patients without a prior diagnosis of CRC who had adenomas removed in Norway from 1993 to 2007 through the Cancer Registry of Norway (1). Norwegian guidelines recommended colonoscopy surveillance after 10 years after removal of high-risk adenomas, and no surveillance after removal of low-risk adenomas. We calculated standardised incidence-based mortality ratios (SMRs) using age-, sex- and period-specific rates for the Norwegian population as comparison. High-risk adenomas were defined as multiple adenomas (two or more) and adenomas with either villous growth-pattern or high-grade dysplasia.

Results: We included 40,824 patients who had colorectal adenomas removed. During a median follow-up of 10.7 years (maximum 23.0 years), 1820 patients were diagnosed with and 520 died of CRC. Overall, adenoma patients had a similar risk of CRC death to the general population (SMR 0.98; 95 % confidence interval (CI) 0.90-1.07). Patients with high-risk adenomas had increased risk of CRC death (SMR 1.23; 95 % CI 1.09-1.39), while patients with low-risk adenomas had reduced risk (SMR 0.82; 95 % CI 0.72-0.92). The absolute risk of CRC death for patients with low-risk adenomas was 1.1 %, and 1.6 % for those with high-risk adenomas.

Conclusion: Patients with low-risk adenomas have a lower risk of CRC death than the general population and do not need surveillance. The risk for patients with high-risk adenomas is only marginally increased and surveillance should be discussed.

References: 1. Loberg M, Kalager M, Holme O, Hoff G, Adami HO, Bretthauer M. Long-term colorectal-cancer mortality after adenoma removal. N Engl J Med. 2014;371(9):799-807.

Disclosure: Nothing to disclose

P1850 SHOULD YOUNG PATIENTS WITH INCIDENTALLY DETECTED ADENOMAS FOLLOW CURRENT COLONOSCOPY SURVEILLANCE RECOMMENDATIONS? RISK OF METACHRONOUS NEOPLASIA AND REAL SURVEILLANCE PRACTICES

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Introduction: The current guidelines for colonoscopy surveillance after screening and polypectomy are for patients aged 50 and older. It is not well known whether post-polypectomy surveillance recommendations are appropriate for young patients less than age 40 years with incidentally detected adenomas.

Aims & Methods: The aims of the study were to identify the occurrence of metachronous advanced neoplasia in young patients < 40 years and to investigate whether surveillance recommendations by endoscopists complied with the current national guidelines. We retrospectively analyzed the medical record obtained from the Catholic University of Korea Seoul St.Mary's Hospital and health screening center. Patients under the age of 40 with ≥1 adenoma removed on colonoscopy between January 2010 and December 2017 were eligible.

Results: Among a total of 8,168 subjects who underwent colonoscopy during the study period, 723 were eligible after excluding those with no neoplastic lesion (n=7,414), familial adenomatous polyposis (n=10), colorectal cancer (n=10), and neuroendocrine tumor (n=11). Of these 723 patients, 140 (19.4%) had high risk adenoma, which consisted of 3 or more adenomas (n=25), any adenoma larger than 10 mm (n=35), any tubulovillous or villous adenoma (n=7), any adenoma with high-grade dysplasia (n=52), and any serrated polyps larger than 10 mm (n=21). The high risk patients were younger (32 vs. 34 years, *P* = 0.015), more female (42.9% vs. 31.7%, *P* = 0.016) and had lower BMI (22.8 vs. 24.2, *P* = 0.001) compared to the low risk patients. Surveillance colonoscopy was performed in 22.3% (130/583) of the low risk patients and 35.7% (50/140) of the high risk patients (*P* = 0.001). Metachronous advanced neoplasia was identified in 1.5% (2/130) of the low risk patients and 12.0% (6/50) of the high risk patients (*P* = 0.002). Furthermore, we could confirm the record of endoscopist surveillance recommendation in 142 patients. The compliance rates with the national guidelines were 25.0% for the low risk neoplasia and 55.0% for high risk neoplasia. Almost all noncompliant patients underwent follow up colonoscopy earlier than recommended.

Conclusion: Even in young patients less than age 40 years, a shorter interval of surveillance colonoscopy should be applied to the patients with high risk adenoma to detect the metachronous advanced neoplasia. Most noncompliant patients were observed to undergo surveillance colonoscopy earlier than recommended.

Disclosure: Nothing to disclose

P1851 SHOULD COLORECTAL CANCER SCREENING IN PORTUGAL START AT AGE 45 YEARS-OLD?

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Introduction: Colorectal cancer (CRC) is one of the most common cancers in Europe. Recently the American Cancer Society published a qualified recommendation advocating the start of CRC screening at 45 years, based on the increase in the incidence of CRC in individuals with <55 years (45-49 years: 31/100,000; 50-54 years: 58/100.000), in contrast to a reduction in individuals with >65 years. Mortality rate (MR) was stable in patients <55 years (45-49 years: 8/100,000; 50-54 years: 13/100,000) and decreased after 55 years.

Aims & Methods: We intended to evaluate if the changes in the CRC incidence/mortality observed in the USA also occur in Portugal and perform a cost-effectiveness analysis of CRC screening starting at 45 years of age. We evaluated the incidence of CRC by age group using data from the National Cancer Registry and MR according to the National Statistics Institute between 1993-2010 and 2003-2016, respectively. Cost-effectiveness analysis performed with a decision tree from a societal perspective comparing biennial faecal immunochemical test (FIT) or one single colonoscopy screening versus non-screening at the age of 45 years-old in Portugal. Efficacy was measured in quality-adjusted life years (QALY). For the base-case scenario, the incidence rate used for the age of 45-50 years-old was 30/100,000, the FIT cost was €3 with a 50% acceptance rate and the colonoscopy cost was €397 with a 38% acceptance rate. The threshold was set at €39,760/QALY and the primary outcome was the incremental cost-effectiveness ratio (ICER).

Results: In Portugal, between 1993 and 2010, there was an increase in CRC incidence of 17% (25/100,000 vs. 30/100,000), 35% (39/100,000 vs. 54/100,000) and 71% (52/100,000 vs. 97/100,000) in patients with 45-49 years, 50-54 years and 55-59 years, respectively. The MR of patients with 45-54 years remained stable between 2003 and 2016 (12/100,000) as a counterpoint to a moderate decrease in individuals with 55-64 (38/100,000 vs. 35/100,000) and a sharp reduction in 65-75 (93/100,000 vs. 75/100,000). Screening for CRC at the age of 45 was not cost-effective with the present incidence. FIT screening provided an ICER of €57,995/QALY while colonoscopy provided an ICER of €2,117,564/QALY. In one-way sensitivity analysis FIT screening would be cost-effective at the present cost and acceptance rates if the incidence rate rises above 38/100,000 (current rates for people aged ≥50 years-old); colonoscopy at this age was never cost-effective despite changes in costs and/or incidence rates.

Conclusion: In Portugal the incidence of CRC in patients aged 45-55 years has been increasing, with stable MR, contrary to the decrease in MR in the age groups covered by CRC screening programs. This scenario is similar to what has been described in the United States of America. However, CRC screening in Portugal, at the age of 45 years-old at present is not cost-effective and will only be cost-effective if the incidence rates rises to 38/100,000. The current CRC screening strategy, starting at the age of 50 years-old, by biennial FIT, is clearly cost-effective as the incidence rate is already 55/100,000.

Disclosure: Nothing to disclose

P1852 SCREENING FOR COLORECTAL CANCER. DIFFERENCES BETWEEN MALES AND FEMALES IN OUR HOSPITAL. RESULTS IN 84559 SUBJECTS

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Introduction: Worldy, Colorectal Cancer (CRC) is the thirth cancer more frequent in males and the second in women. Screening programmes have demonstrated the detection of CRC in early stages allowing a more effective treatment.
Aims & Methods:
- To describe the findings and the differences in neoplastic findings between sexes in the asymptomatic participants.
- Screening programme for CRC was introduced in our hospital in october 2014. We collected data until March 2019. Men and women between 50 and 69 years old were invited to undergo a Faecal Occult Blood Test (FOBT). Those who obtained a positive result were offered to perform a colonoscopy.
The following results have been calculated from the data base CRC Screening Programme of Junta de Castilla y León in Burgos.
Results: In total, 84559 subjects were invited to take part in the program. Of these, 32871 provided a faecal sample resulting in a 38.9% participation rate (52,2% females). FOBT was positive in 3228 individuals (9.8%), 58.1% of them were males; 2649 (82.1%) of them underwent a colonoscopy.
Of those 2649, colonoscopies were negative or had non neoplasic findings in 422 (27.6%) males and 572 (51.1%) females. We detected low-risk adenomas (LRA) in 393 (25.7%) males and in 270 (24.1%) females, p < 0.01; medium-risk adenoma (MRA) in 383 (25%) males and 177 (15.8%) females, p = 0.1; and high-risk adenomas (HRA) in 186 (12.2%) males and 52 (4.6%) females, p = 0,0001. Adenoma detection rate (ADR) resulted in 55.2%. 194 invasive CRC were found (9.4% of males and 4.4% of females). The probability of being diagnosed of adenoma (RR 1.35, 95% IC 1.26 - 1.45; p < 0.0001) and CRC (RR 2.16, 95% IC 1.59 - 2.94; p < 0.0001) was higher in males.
Conclusion: Participation rate of the screening programme in our hospital is very low, remaining below 45%, established as the acceptable rate in European Guidelines. On the other hand, colonoscopy acceptance rate was 82,1%. However, there are an unknown percentage of people, who decide to perform FOBT and/or colonoscopies in private centres.
FOBT positivity rate was 9.8%, slightly higher than in the rest of Spain (6.8%).
ADR was 55.2%, more than 25% required by European quality guidelines. In more than half of participants, neoplasic adenomas were resected avoiding their progression to advanced neoplasia. CRC, LRA and HRA were more frequent in males with similar rates described in bibliography.
Disclosure: Nothing to disclose

P1853 OCCULT BLOOD TEST TRIGGERED COLONOSCOPY VERSUS SCREENING COLONOSCOPY FOR THE DETECTION OF COLORECTAL CANCER

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Introduction: Colorectal cancer (CRC) screening is important because survival mainly depends on the stage at diagnosis.
Aims & Methods: We aimed to analyze the impact of annual fecal immunochemical test-triggered colonoscopy (FIT-C) compared to screening colonoscopy (SCR-C) on the detection rates of low-risk adenomas (LRA), high-risk adenoma (HRA) and CRC among individuals with average CRC risk.

Two prospective population based CRC screening strategies, annual FIT screening vs. SCR-C were compared within a province of Austria. All asymptomatic individuals, who underwent FIT-C or SCR-C between 01/2003 and 12/2014, were included in this population-based screening study. We excluded individuals with a history of inflammatory bowel disease or hereditary CRC syndromes. The lesions were classified in three groups: CRC, HRA and LRA including tubular adenoma ≤ 1cm.
Results: Fourteen thousand four hundred thirteen individuals (median age 62; 53% males) with FIT-C were compared to 10.083 individuals (median age 60; 52% males) with SCR-C.
The CRC detection rates were 1.26% (confidence interval (CI): 1.05; 1.48) in FIT-C compared to 0.54% (CI: 0.39; 0.68) SCR-C (p<0.001). The HRA detection rates were 14.22% (CI: 13.65; 14.79) in FIT-C compared to 6.84% (CI: 6.43; 7.25) in SCR-C (p<0.001). The LRA detection rates were 16.98% (CI: 16.25; 17.72) in FIT-C compared to 12.95% (CI: 12.3; 13.61) in SCR-C (p<0.001).
Conclusion: FIT-C presents an effective CRC-screening method in subjects with average CRC-risk as this population-based study demonstrated that FIT-C doubles detection rate of HRA and CRC in head-to-head comparison with SCR-C.
Disclosure: Nothing to disclose

P1854 DIAGNOSTIC YIELD OF GERMLINE GENETIC TESTING IN NON-POLYPOSIS COLORECTAL CANCER IN YOUNG ADULTS

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Introduction: Non-polyposis colorectal cancer (CRC) in young adults (aged ≤ 50 years) represents 10-15% of all CRC. Current clinical guidelines recommend performing tumour mismatch repair deficiency testing in all CRC patients (by immunohistochemistry (IHC) for MLH1, MSH2, MSH6 and PMS2), as a screening for Lynch syndrome (so-called universal strategy). When IHC reveals loss of protein expression, guidelines recommend performing germline genetic analyses to confirm Lynch syndrome [1]. However, recent studies in early-onset CRC cases suggest the existence of germline mutations in MMR or other genes in which IHC study may not be altered [2].
Aims & Methods: To describe the diagnostic yield of performing universal germline genetic testing in patients with non-polyposis CRC aged 50 years or less in order to improve the identification of hereditary CRC syndromes.
A total of 253 patients, corresponding to all patients aged ≤ 50 years with non-polyposis CRC patients visited in the High-Risk CRC Clinic of Hospital Clinic de Barcelona between 2008 and 2018, were included., Until June 2016, 182 patients were included and studied by IHC.
If the study showed loss of protein expression or was inconclusive, mutations in MMR genes (MLH1, MSH2, MSH6, PMS2) were analysed by Sanger Sequencing and MLPA, while if IHC was normal MUTYH gene was evaluated (prevalent mutations in Caucasian population).
From July 2016 until the end of the study, 70 patients were included and performed multigene panel by Next Generation Sequencing, including MLH1, MSH2, MSH6, PMS2, BRCA1, BRCA2 and MUTYH, regardless of the IHC result.
Results: IHC for MMR proteins was performed in 235 cases, showing loss of expression in 56 (23.8%) of which 35 (62%) patients were diagnosed of Lynch syndrome:16 (46%) had mutation in MLH1, 13 (37%) in MSH2, 3 (8.5%) in MSH6 and 3 (8.5%) in PMS2. Of the remaining 197 patients with normal IHC study (n = 179) or without IHC study (n = 18), in 7 (3.6%) a germline mutation was found: 4 biallelic mutations in MUTYH and 3 diagnoses of Lynch syndrome with normal IHC (2 mutations in MSH6 and 1 in MSH2). Of the 42 patients with Lynch syndrome, 7 (16.7%) were diagnosed by a genetic study not directed by IHC.
Conclusion: Up to 17% of young patients with CRC carry germinal mutations in mismatch repair genes or MUTYH gene. In almost 20% of these patients, the mutation would not have been diagnosed with the standard strategy based on universal IHC. These results support the use of multigene panel testing in all patients with CRC ≤50 years.

Disclosure: Nothing to disclose

P1855 ATG16L1 COORDINATES DNA DAMAGE RESPONSE IN THE INTESTINAL EPITHELIUM

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Introduction: Autophagy is a key pathway involved in cellular homeostasis by orchestrating the degradation of cytoplasmic macromolecular constituents elicited by various stress stimuli (e.g. starvation). It has been suggested that proficient autophagy is involved in mounting an appropriate DNA damage response (DDR). The IBD risk gene ATG16L1is a critical component of the autophagic machinery and absence of ATG16L1 has severe consequences for intestinal epithelial cell survival and function, however a potential role of the protein for DDR is unknown. We have previously shown that deficiency in the enzyme RNase H2b leads to impaired ribonucleotide excision repair and induces spontaneous DNA damage with subsequent p53-dependent suppression of stem cell proliferation. Absence of p53 and RNAseH2b in the intestinal epithelium leads to accumulation of somatic mutations and spontaneous intestinal carcinogenesis. The aim of our study was to test the role of Atg16l1 in coordinating DNA repair and epithelial cell fate decisions in this newly established DNA damage model.
Aims & Methods: Murine intestinal epithelial ModeK cells were gene silenced using siRNA (Atg16l1, Ctrl.) stimulated with the DNA-damaging agent Cytarabin A (AraC) and subjected to gene expression analyses, FACS cell death assays and immunoblot analyses. A conditional intestinal epithelial knockout of Atg16l1, Rnaseh2b and the combined DKO was established by crossing VillinCre mice with mice floxed for Atg16l1, Rnaseh2bor both. Intestinal organoids of WT, Atg16l1$^{\Delta IEC}$, Rnaseh2b$^{\Delta IEC}$and Rnaseh2b/Atg16l1$^{\Delta IEC}$mice were derived by culturing small intestinal crypt cells in a collagen matrix and then used for immunoblot analyses, colony formation assays, RNA sequencing and transcriptome analysis. WT, Atg16l1$^{\Delta IEC}$, Rnaseh2b$^{\Delta IEC}$and Rnaseh2b/Atg16l1$^{\Delta IEC}$mice simultaneously delivered convenient in-vivomodels for basal phenotyping, aging experiments and acute or chronic DSS-colitis models. Post mortemanalyses included fluorescence or IHC stainings, western blot analyses and gene expression analyses.
Results: AraC stimulation let to profound induction of autophagy in IECs, which was dependent on Atg16l1. Vice versa knockdown of Atg16l1 led to increased AraC induced cell death, as shown by propidium idodide staining. In-vivo we observed that co-deletion of Atg16l1 in Atg16l1/H2b^{dIEC}mice led to increased epithelial cell death and consecutive increase of histopathological inflammation. Likewise DSS induced colitis led to a strong manifestation of particular small intestinal inflammation, which was associated with increased cell death and DNA damage. Importantly, Atg16l1-deficiency completely impaired DNA damage induced suppression of stem cell proliferation, as small intestinal crypts in Atg16l1/H2b^{dIEC}mice presented with increased numbers of Ki67 and BrdU+ cells, compared to H2b^{dIEC}mice. In-vitro this finding was validated as intestinal organoids from Atg16l1/H2b^{dIEC}mice showed significantly increased colony forming ability, compared to H2b^{dIEC}. Mechanistically RNA sequencing reveals that Atg16l1 governs a distinct transcriptional programme involved with rescued epithelial proliferation.
Conclusion: We show that Atg16l1is a critical component of physiological DDR and is involved in fate decisions of epithelial cells towards DNA damage-induced dell death. Importantly, we show that Atg16l1-deficiency impairs DNA damage-induced suppression of stem cell proliferation despite ongoing epithelial cell death. Hence, Atg16l1 licenses an essential step of genome surveillance, which might point towards a novel role of the gene in intestinal carcinogenesis.
Disclosure: Nothing to disclose

P1856 KNOCKOUT OF SLC39A7 SUPPRESSES CELL PROLIFERATION, MIGRATION AND INVASION IN HUMAN COLORECTAL CANCER

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Introduction: Colorectal cancer (CRC) is the third most common type of cancer in the world, and its incidence continues to rise. SLC39A7 (ZIP7) is a zinc transporter that plays a key role in intestinal epithelial self-renewal. However, whether or not SLC39A7 is involved in human colorectal cancer remains unclear.
Aims & Methods: To assess the biological function of SLC39A7 in colorectal cancer, we constructed CRISPR/Cas9-based gene knockout. The SW620 and HCT116 cell lines were infected with the constructed virus, then cell proliferation, cell apoptosis and migration assays were detected to de the inhibition efficiency of the adenovirus on hepatoma cells. Immunohistochemical analysis was performed to determine SLC39A7 protein expression levels in the cancer tissues.
Results: Our results showed that the SLC39A7 protein expression levels in the CRC tissues were significantly higher than those in the adjacent normal mucosa, and was positively correlated with the lymph node metastasis. Knockout of SLC39A7 exhibited a significant decrease in cell viability and proliferation of colorectal cancer cells. It was also shown that knockout of SLC39A7 boosted apoptosis in colorectal cancer cells. Furthermore, downregulation of SLC39A7 suppressed Nrf2 expression. In addition, migration assays further demonstrated that knockdown of Zn^{2+} significantly reduced the migration and invasion ability in both SW620 and HCT116 cells.
Conclusion: In conclusion, our results suggest that SLC39A7 plays a crucial role in the proliferation and invasion of colorectal cancer cells, which provides evidence that SLC39A7 might be as a potential therapeutic target for colorectal cancer treatment.
References: [1]Baltaci A K, Yuce K. Zinc Transporter Proteins.[J]. Neurochemical Research, 2017, 43(3):1-14. [2]Wei Y , Dong J , Li F , et al. Knockdown of SLC39A7 suppresses cell proliferation, migration and invasion in cervical cancer[J]. EXCLI J. 2017, 16:1165-1176. [3]Taylor K, Vichova P N, Hiscox S, et al. ZIP7-mediated intracellular zinc transport contributes to aberrant growth factor signaling in antihormone-resistant breast cancer Cells.[J]. Endocrinology, 2008, 149(10):4912-4920. [4]Ohashi W, Kimura S, Iwanaga T, et al. Zinc Transporter SLC39A7/ZIP7 Promotes Intestinal Epithelial Self-Renewal by Resolving ER Stress:[J]. Plos Genetics, 2016, 12(10):e1006349.
Disclosure: Nothing to disclose

P1857 INCREASED RISK OF SESSILE SERRATED ADENOMAS ON INITIAL SCREENING COLONOSCOPY IN POST-BARIATRIC SURGERY PATIENTS

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Introduction: Bariatric surgery effectively induces weight loss in obese patients, decreasing obesity-related co-morbidities and overall cancer risk.[1] While a recent meta-analysis demonstrated a 27% decrease in CRC risk following bariatric surgery, a large cohort study showed an increase in the standardized incidence ratio of CRC with longer follow-up intervals after bariatric surgery.[2,3] By preferentially modulating epigenetic modifications versus de novo chromosomal mutations, the complex physiologic changes

following bariatric surgery may in fact drive CRC via the sessile serrated adenomas (SSA) pathway or conventional adenoma-carcinoma sequence, respectively.[4-7]

Aims & Methods: Our aim was to examine the risk of CRC precursors in post-bariatric surgery patients as compared to the general population. We conducted a single center retrospective case-control study using 2007-2019 data from the electronic medical record. Cases were defined as patients age 40 to 50 at time of bariatric surgery, with subsequent documented initial screening colonoscopy and pathology. Cases were excluded if they underwent a diagnostic colonoscopy or had a family history of CRC (1st-degree relative age< 60 years, or two 1st-degree relatives at any age). 88 patients met both inclusion and exclusion criteria. Cases were matched 1:1 by age ± 2 years and gender to controls with BMI ≥ 25 undergoing average-risk screening colonoscopy during the same time period. Chi-square and t-tests were performed to compare anatomic and histologic distribution of adenomas between groups.

Results: Among cases, bariatric procedures consisted of Roux-en-Y (51%), laparoscopic gastric band placement (28%), and vertical sleeve gastrectomy (20%). Mean BMI pre-surgery was 42 kg/m², compared to 33 kg/m² at initial screening colonoscopy (Table 1). Average time from surgery to colonoscopy was 4.5 years (SD 2.5 years), with 45% undergoing colonoscopy ≥ 5 years post-surgery.

There was no significant difference in adenoma detection rate (ADR) between surgical and control groups (35% vs. 40%, p=0.34). SSA detection rate was significantly higher in post-surgery patients (9.1%) compared to controls (3.9%, p< 0.01). Of all detected adenomas, SSA proportion was significantly higher in surgical (15%) vs. control patients (8.2%, p=0.03). Rectal adenomas were more common in the surgical vs. control groups (12.3% vs 3.0%, p< 0.01), but otherwise we observed no difference in the proportion of adenomas by anatomic location or advanced adenomas. Neither group had high-grade dysplasia or CRC.

Conclusion: SSAs are more common among average-risk obese patients after bariatric surgery compared to non-surgical controls. By anatomic location, adenomas are more common in the rectum compared to non-surgical controls, but the overall distribution of adenomas was similar. Mucosal, metabolic, and microbiome-related changes associated with bariatric surgery may alter profile of CRC precursors. Further studies are needed to understand the risk of CRC following bariatric surgery.

	Bariatric Surgery (n=88)	Control (n=102)	P-value
Female	67 (76%)	70 (67%)	p=0.13
Mean Age at Colonoscopy	51.5 +/- 2.2	52.2 +/- 2.4	p=0.07
Mean BMI at Colonoscopy	33 +/- 6	31 +/- 6	p=0.07
Adenoma detection rate	35.2%	40.2%	p=0.34
Percent SSA	15.1%	8.2%	**p=0.03**
Percent Tubular Adenoma	84.9%	91.8%	**p=0.03**
SSA detection rate	9.1%	3.9%	**p=<0.01**
Adenomatous polyps by location			
Percent adenomas right-sided	63.0%	62.0%	p=0.81
Percent adenomas left-sided	37.0%	38.4%	p=0.81
Percent adenomas rectal	12.3%	3.0%	**p=<0.01**

[Population Demographics and Adenoma Characteristics]

References: 1. Shah M, Simha V, Garg A. Long-Term Impact of Bariatric Surgery on Body Weight, Comorbidities, and Nutritional Status. J Clin Endocrinol Metab. 2006;91(11):4223-4231. doi:10.1210/jc.2006-0557 2. Derogar M, Hull MA, Kant P, Ostlund M, Lu Y, Lagergren J. Increased Risk of Colorectal Cancer After Obesity Surgery. 2013. doi:10.1097/SLA.0b013e318288463a 3. Afshar S, Kelly SB, Seymour K, Lara J, Woodcock S, Mathers JC. The Effects of Bariatric Surgery on Colorectal Cancer Rsik: Systematic Review and Meta-analysis. Obes Surg. 2014;24(10):1793-1799. doi:10.1007/s11695-014-1359-y 4. Strum WB. Colorectal Adenomas. N Engl J Med. 2016;375(4):387-390. doi:10.1056/NEJMc1604867 5. Rex DK, Ahnen DJ, Baron JA, et al. Serrated lesions of the colorectum: review and recommendations from an expert panel. Am J Gastroenterol. 2012;107(9):1315-29; quiz 1314, 1330. doi:10.1038/ajg.2012.161 6. Sainsbury A, Goodlad RA, Perry SL, Pollard SG, Robins GG, Hull MA. Increased Colorectal Epithelial Cell Proliferation and Crypt Fission Associated with Obesity and Roux-en-Y Gastric Bypass. 2008. doi:10.1158/1055-9965.EPI-07-2874 7. Furet J-P, Kong L-C, Tap J, et al. Differential Adaptation of Human Gut Microbiota to Bariatric Surgery-Induced Weight Loss Links With Metabolic and Low-Grade Inflammation Markers. 2010. doi:10.2337/db10-0253
Disclosure: Nothing to disclose

P1858 ASPIRIN TREATMENT CHANGES OXYLIPIN LEVELS IN MURINE AND HUMAN COLON TISSUE

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Introduction: Although prevention and treatment of colorectal cancer (CRC) have improved during recent years due to screening colonoscopies, new chemotherapeutic and antibody approaches, CRC still ranks second in cancer mortality in 2018 worldwide. Therefore, research needs to focus on the prevention of neoplastic colonic lesions. Epidemiological studies showed that regular use of acetylsalicylic acid (ASA) is associated with a preventive effect on the development of CRC [1]. The mechanisms underlying this chemopreventive effect are still unclear, however ASA-mediated inhibition of cyclooxygenase (COX)-1 and COX-2, leading to suppression of prostaglandin biosynthesis, is the primary focus of interest. Recently, we detected significantly lower tissue eicosanoid levels of most COX derived metabolites in ASA treated individuals in healthy colonic mucosal tissue samples obtained during routine colonoscopy. Furthermore, we observed that LOX- and CYP-pathway product concentrations remained unaffected by ASA treatment [2]. Following the hypothesis that ASA could inhibit CRC development via lipid mediator modification, we now aim to investigate the effect of ASA chemoprevention on colon tumorigenesis.

Aims & Methods: Using liquid chromatography-tandem mass spectrometry (LC-MS/MS), we quantified a broad spectrum of omega-6 and omega-3 polyunsaturated fatty acid (PUFA)-derived lipid mediators in normal colonic mucosa and colon tumor tissue. The murine AOM/DSS-induced model of colitis-associated colorectal cancer (CAC) was employed to investigate lipid mediator changes in healthy versus neoplastic mucosa in ASA-naive mice. We then analyzed the effect of ASA treatment on colon tumorigenesis and lipid mediator formation in mice. In order to assess the relevance of these findings in humans, lipid metabolite changes were also analyzed in colorectal adenoma and carcinoma tissues procured during routine colonoscopy examination.

Results: In murine colon tumors we confirmed increases of a variety of COX-metabolites such as PGE_2 and 11-HETE in tumor tissue as compared to normal mucosa and these increases were dampened by aspirin treatment in the murine AOM/DSS model. Aspirin led to a significant reduction of tumor incidence but not size in the AOM/DSS model. Furthermore, we detected strongly elevated levels of 5-LOX and 12-LOX pathway products in murine tumor tissues. A trend showing similar changes of lipid mediator profiles due to aspirin treatment were also found in human colorectal adenoma and carcinoma biopsy samples.

Conclusion: The data presented here provides insight into lipid metabolite profile changes in murine colonic tumorigenesis. Furthermore, these data confirm a chemopreventive anti-tumor effect of ASA treatment which is accompanied by specific changes particularly of COX-1 derived lipid mediators. Pointing towards the relevance of these animal data in humans, we were able to show similar lipid mediator changes in biopsies from patients with colon adenomas and colon carcinoma.

References: 1. Giovannucci, E., et al., Aspirin and the risk of colorectal cancer in women. N Engl J Med, 1995. 333(10): p. 609-614. 2. Gottschall, H., et al., Aspirin alone and combined with a statin suppresses eicosanoid formation in human colon tissue. J Lipid Res, 2018. 59(5): p. 864-871.
Disclosure: Nothing to disclose

P1859 DNA REMETHYLATION, REPAIR AND ALTERATION OF EPITHELIAL-MESENCHYMAL TRANSITION IN COLORECTAL CANCER CELL LINES BY S-ADENOSYLMETHIONINE TREATMENT

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Introduction: Global DNA hypomethylation can be observed along aging of normal cells, and it is also related to genomic instability and the activation of proto-oncogenes during tumor development. S-adenosylmethionine (SAM) is a universal methyl donor molecule, used as a dietary supplement. SAM is involved in DNA methylation processes, thereby it may have a favorable effect on DNA remethylation, repair and remodeling.

Aims & Methods: Our aim was to analyze the effect of SAM treatment on global DNA methylation level, gene expression, DNA integrity and cell cycle of two different colorectal cancer cell lines (HT-29, SW480). HT-29 and SW480 cells were treated with SAM in different concentrations (0, 0.5, 1 mmol/l) for 48 hours. The global DNA methylation status was analyzed by immunohistochemistry and bisulfite pyrosequencing of long interspersed nuclear element-1 (LINE-1) retrotransposons. The gene expression changes were detected using Human Transcriptome Array 2.0 (HTA 2.0). Double-strand DNA break analysis was performed with γH2AX ELISA and immunostaining. Cell-free DNA level of the medium collected at the end of the treatments was quantified following DNA isolation. Flow cytometry measurements were assessed for cell cycle and apoptosis determination.

Results: DNA remethylation, elevated expression ($p<0.05$) of DNA-repair-related genes and decreased expression ($p<0.05$) of genes, that are involved in epithelial-mesenchymal transition were observed after SAM treatment. Increased phosphorylation of H2AX (74.9, 166.5, 200.6 pM) resulted by different SAM concentrations was also referred to the activation of reparative processes. Moreover, elevation of apoptotic cell number and cell-free DNA level (0.23, 0.26, 0.63 ng/ul) were also detected. Proportion of cells was decreased in both G0/G1 (48.4, 28.5, 20.4%) and G2/M (6.0, 10.7, 12.5%) phases by SAM; however, it was increased in S (45.7, 61.7, 67.0%) phase, where the double-strand DNA break checkpoint is located.

Conclusion: SAM can induce DNA methylation and activation of DNA repair processes, while inhibiting epithelial-mesenchymal transition. According to the results of our study, we suppose that DNA can be released from treated cells and apoptosis is also induced by initiating DNA repair. Tumor cells could be targeted by SAM through different pathways; therefore, it might be a potential agent in cancer treatment.

Disclosure: Nothing to disclose

P1860 β6-INTEGRIN ACCELERATES TUMOR GROWTH AND DECREASES T-CELL INFILTRATION IN A CECUM INJECTION MODEL OF COLON CANCER

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Introduction: Integrins are receptors for extracellular matrix proteins and are involved in many critical cellular processes such as cell adhesion, migration, proliferation, differentiation and cell death. The β6-integrin subunit (ITGB6) is hardly ever detectable in normal epithelial tissues, whereas it is highly induced in epithelial cells during embryogenesis, wound repair as well as during tumorigenesis of many epithelial tumors such as colorectal cancer (CRC).

In CRC, patients with high ITGB6 expression in the tumor present with a more aggressive disease and reduced survival rates. ITGB6 is upregulated during epithelial-to-mesenchymal transition (EMT) and activates latent TGFβ that is present in the extracellular matrix. Since TGFβ has been shown to drive immune evasion in mouse colon tumors, TGFβ activation through ITGB6 might lead to a reduced immune response to the tumor,

explaining the reduced survival of patients with ITGB6 expressing tumors. In this study, we aimed at investigating the effect of ITGB6 overexpression on colon cancer growth in vivo.

Aims & Methods: To assess the effect of ITGB6 on tumor growth in vivo, we overexpressed ITGB6 in two mouse colon cancer cell lines, namely CT-26 and MC-38, derived from Balb/c (CT-26) or C57/Bl6 mice (MC-38) using lentiviral vectors. Control cells were transduced with the empty control vector. These cell lines were injected into the cecum wall of Balb/c or C57/Bl6 mice and the mice were sacrificed after 2-3 weeks. Tumors were cut out of the cecum and weighted to determine tumor mass. Cytokine and cytolytic enzyme expression in the tumor was measured by RT-qPCR. T-Cell infiltration was determined by immunohistochemical (IHC) stainings for CD3, CD4 and CD8.

Results: In both cell lines ITGB6 overexpression accelerated tumor growth in vivo, resulting in significantly larger tumors than in control cell tumors at day of sacrifice. RT-qPCR analysis of RNA isolated from the tumors showed decreased IFNγ, TNFα, Granzyme B and Perforin expression upon ITGB6 overexpression, indicating an effect on the tumor immune response. IHC staining of the tumors showed a significant decrease in the number of CD3, CD4 and CD8 positive T-cells in the ITGB6 overexpressing tumors. Ki67 expression was not altered by ITGB6 overexpression, demonstrating that the difference in tumor growth was not caused by enhanced cell proliferation. Therefore, the differences in tumor size are likely to be a consequence of an altered immune response and less tumor cell killing through cytotoxic CD8+ T-cells.

Conclusion: ITGB6 promotes tumor growth in vivo and reduces T-cell infiltration into the tumor. Because of its exclusive expression in epithelial tumors, the tumor growth promoting ITGB6 is an excellent drug target. Therefore, inhibiting ITGB6 alone or as part of a combination therapy might be a promising therapy approach for CRC patients.

Disclosure: Nothing to disclose

P1861 HYPOXIC TUMOR MICROENVIRONMENT REGULATES GRHL2 VIA REDUCING CELL ADHESION AND INCREASING EPITHELIAL-MESENCHYMAL-TRANSITION (EMT) TO PROMOTE COLON CANCER CELL INVASION AND MIGRATION

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Introduction: Grainyhead-like 2 (GRHL2) was reported to maintain the epidermal barrier by directly regulating expression of Cdh1 and Cldn4. Hypoxic microenvironment was important in promoting drug resistance of tumor stem cells. While colorectal cancer (CRC) originates from dysplasia in the epithelial stem cells and forms hypoxic microenvironment when expanding.

Aims & Methods: We aimed in this study to demonstrate the roles of GRHL2 in colorectal cancer in hypoxic environment. To create hypoxic microenvironment, cells were incubated in hypoxic incubator with 1% O_2 and 5% CO_2. Then to investigate functional significance of GRHL2, human HCT116 cell lines with steady decreased GRHL2 expression was generated by lentiviral transfection, meanwhile, overexpressed GRHL2 expression was generated in SW620 cell lines by TrueORF cDNA transfection followed by monoclonal collection. CCK8, colony-formation and transwell assays were applied to evaluate the proliferation and metastasis of colon cancer cell lines. Real-time qPCR and western blotting were used to determine the expression level of EMT markers. Dual Luciferase Reporter Assay was used to examine transcription activity of given sequences in vitro. Chromatin Immunoprecipitation (ChIP) assay was applied to determine whether Hif-1α can functionally bind to promoter region of GRHL2 to inhibit its transcription. For in vivo study, cells were transplanted into wild-type mice through orthotopic or tail vein injection in order to test the function of GRHL2 in two major tumor-associated scenarios: primary tumor growth and remote metastasis.

Results: HCT116, HT29 and SW480 (all initiated from primary tumors) showed relatively higher GRHL2 expression, while SW620 (derived from metastasis lymph node) had a low GRHL2 level. All cell lines exhibited a decrease in GRHL2 expression under hypoxic environment (1% O_2, 24h). Functional knockdown of GRHL2 in HCT116 demonstrated mesenchymal morphology, increased migration, but reduced colony formation ability.

While overexpressed GRHL2 in SW620 showed increased proliferation, but lower migration ability. Western Blot also indicated EMT in shGRHL2 HCT116 (lower E-cadherin and higher Vimentin expression). Also *in vivo*, lower GRHL2 expression led to reduced orthotopic implantations proliferation, but higher metastasis intendancy. To understand the mechanism of down-regulation of GRHL2 in hypoxia, using Jaspar database, we predicted a Hif-1α binding site within the promoter region of GRHL2 after excluding methylation in GRHL2 promoter. Luciferase results also showed decreased transcription activity of this region, possibly leading to down-regulation of GRHL2. Further CHIP assay validated that Hif-1α can directly bind to the promoter region (-533~-523bp) of GRHL2.

Conclusion: Collectively, our findings identify that hypoxia promotes colon cancer metastasis via regulating GRHL2 expression, which may represent a rational therapeutic target in CRC.

Disclosure: Nothing to disclose

P1862 PATIENTS WITH MULTIPLE ADENOMAS IN UNITED KINGDOM BOWEL CANCER SCREENING PROGRAMS ARE NOT REFERRED FOR GENETIC TESTING

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Introduction: Approximately one in twenty cases of colorectal cancer (CRC) are associated with germline mutations that confer higher susceptibility to the disease. Guidelines recommend that patients with ten or more adenomas be referred for genetic testing[1], with evidence that suggests >9% of these patients with 10-19 adenomas have a highly penetrant CRC predisposition syndrome[2].

Aims & Methods: The primary aim of this study was to quantify patients with ten or more adenomas in the West London (WL) and North Central London (NCL) Bowel Cancer Screening program (BCSP) centres. The secondary aim was to determine what proportion of these multiple adenoma patients were referred for genetic screening.

A retrospective cross-sectional study was performed of patients who underwent colonoscopy following a positive faecal occult blood test (FOBt) as part of the WL and NCL BCSPs between May 2007 & June 2018. All polyps were examined histologically and only confirmed adenomas were included. Clinicopathological data including age and gender was recorded from BCSP patient records. Referrals to regional clinical genetics services were ascertained. Statistical analysis was performed in Graphpad Prism.

Results: 11,337 patients underwent colonoscopy following positive FOBt and 5,650 (49.8%) had 1 or more adenomas. 107 patients (0.94%) had 10 or more adenomas. The proportion of patients with 10 or more adenomas was higher in NCL BCSP (1.1%) than in WL BCSP (0.7%) (p=0.02; $\chi 2$ test). 42 patients presented with 10 or more metachronous adenomas at the index colonoscopy or following an early follow up procedure; the remaining 65 patients undergoing excision of a total of 10 or more metachronous adenomas after subsequent surveillance colonoscopy. An accurate family history was not routinely collected in this population. Of the 107 patients with 10 or more adenomas, only 3 (2.8%) were referred to a clinical genetics service.

Conclusion: In two London BCSP centres, patients with ten or more metachronous adenomas are an uncommon finding. Despite guidelines advising genetic testing in this group, referral rates are low. A referral pathway and management strategies should be established to address this patient population.

References: 1. Hampel H, Bennett RL, Buchanan A, et al. A practice guideline from the American College of Medical Genetics and Genomics and the National Society of Genetic Counselors: referral indications for cancer predisposition assessment. Genet Med 2015;17:70-87. 2. Grover S, Kastrinos F, Steyerberg EW, et al. Prevalence and phenotypes of APC and MUTYH mutations in patients with multiple colorectal adenomas. Jama 2012;308:485-492.

Disclosure: Nothing to disclose

P1863 PERFORMANCE EVALUATION OF A BLOOD TEST ASSAYING FOR CTDNA METHYLATED IN IRF4, BCAT1 AND IKZF1 FOR DETECTION OF COLORECTAL CANCER

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Introduction: Participation rates for colorectal cancer (CRC) screening using faecal occult blood tests are suboptimal in many countries. There is therefore a need for the development of other test types that may improve screening uptake. The aim of this study was to evaluate the performance of a blood test for methylation-specific detection of circulating tumor DNA (ctDNA) in a study population with the full range of neoplastic and non-neoplastic pathologies encountered in the colon and rectum.

Aims & Methods: Study participants (n=1,621) had blood collected prior to colonoscopy or colonic surgery (median age, 64.2y (18-88yo), 56% males). Circulating cell-free DNA was extracted from plasma, bisulphite converted and assayed for the presence of methylated ctDNA using a multiplex, methylation-specific real-time PCR assay for detection of methylation in the genes BCAT1, IKZF1 and IRF4. Detection of methylation for any of the three genes deemed a specimen positive for ctDNA. Adenomas were classified as High- (HRA), Medium- (MRA) or Low-Risk Adenoma (LRA) as previously described (1). CRC was staged according to AJCC 7th Edition. The ctDNA blood test performance estimates were calculated from true- and false-positive rates for cancer.

Results: The 3-gene methylation ctDNA blood test had an overall sensitivity for CRC of 73.9% (136/184, 95%CI: 67.1-79.1) with a better detection of later, 81.0%, (68/84; 71.3-87.9) versus earlier stage cancer, 67.3% (66/98; 57.6-75.8; p=0.0375). The ctDNA test sensitivity for stage II, III and IV were 87.7% (50/57; 76.8-93.9), 78.4% (40/51; 60.8-89.5) and 84.8% (28/33; 69.1-93.3), respectively, and were not significantly different. However, the test had a reduced sensitivity for stage I (16/41, 39.0%; 25.7-54.3, p< 0.0001). To determine whether the apparent lower sensitivity for Stage I CRC was a biologically-determined issue, we examined the relationship between test positivity and tumor depth of invasion. Including only cases with no disseminated disease, a significant linear trend (p< 0.0001) was observed between assay positivity and T stage determined at surgery: T1N0M0, 25% (6/24, 12.0-44.9); T2N0M0, 58.8% (10/17, 36.0-78.4); T3N0M0, 85.7% (42/49, 73.3-92.9); T4N0M0, 100% (8/8, 67.6-100). Lesion location of cancer did not influence assay positivity rates (proximal, 38/50; distal, 89/117, p = 0.9920). The estimated specificity for cancer was 90.1% (81/820, 88.0-92.0), of which 82.7% (67/81) were methylation positive in a single gene only. Gender, smoking, family history and age were not significant predictors of test positivity. The sensitivity of the ctDNA blood test for adenoma detection was low (LRA, 9.3%, (26/280, 6.4-13.3); MRA 15.0% (27/180, 10.5-20.9); HRA, 16.6% (26/157, 11.6-23.2)), although a positive trend was observed with the HRA having the highest positivity rate of all the adenoma subtypes (p=0.0290).

Conclusion: With a specificity of 90.1%, the 3-gene methylation ctDNA blood test had an overall sensitivity for CRC of 73.9% and was positive for 67.3% of early stage cancer (stage I and II). The overall cancer positivity rate appears to be a function of tumor invasiveness. Based on the data reported herein, it is justified to proceed to validation of this ctDNA assay in true screening populations.

References: 1. Vieth M et al. Endoscopy 2012;44:Suppl 3:131-9. 2. Pedersen S et al. BMC Cancer 2015; 15: 654.

Disclosure: Nothing to disclose

P1864 VOLATILE ORGANIC COMPOUNDS IN BREATH CAN SERVE AS NON-INVASIVE DIAGNOSTIC BIOMARKERS FOR THE DETECTION OF ADVANCED ADENOMAS AND COLORECTAL CANCER: PROOF-OF-PRINCIPLE STUDY

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Introduction: Colorectal cancer (CRC) is the third most common cancer diagnosis in the Western world. Unfortunately, a non-invasive screening tool with the ability to accurately detect (pre-)malignant colon lesions is still lacking.

The aim of this study was to evaluate if exhaled volatile organic compounds (VOCs) can serve as non-invasive biomarkers for the detection of CRC and its precursor lesions using an electronic nose (e-nose).

Aims & Methods: This multicenter study was conducted in two hospitals in the Netherlands. All consecutive colonoscopy patients aged ≥18 years old, without inflammatory bowel disease or (previous) malignancy, were invited for breath testing. A random sample of two-thirds of the breath samples was used to train the artificial neural network to recognize disease-specific mixtures of VOCs. These training models for CRC and advanced adenomas (AAs) were then used to blindly predict the diagnosis of the remaining patients. Lastly, final disease-specific models were developed using all available data to further improve the discriminatory power of the algorithms.

Results: Breath samples of 511 patients were collected. Sixty-four patients were excluded due to an inadequate breath test (n=51), incomplete colonoscopy (n=8), or colitis (n=5). Classification was based on the most advanced lesion detected. Seventy patients were diagnosed with CRC, 117 had ≥1 AA, and 128 patients had normal colonoscopy. The training model for CRC had a sensitivity and specificity of 83% and 60%, respectively, and predicted the blinded data with similar accuracy. The final disease-specific model for CRC had an AUC of 0.84, with a sensitivity of 95% and specificity of 64%. The final disease-specific model for AAs had an AUC of 0.73, with a sensitivity of 79% and specificity of 59%.

Conclusion: This study suggests that exhaled VOCs could potentially serve as non-invasive biomarkers for the detection of CRC and AA using e-nose technology. Future studies including more patients could further improve the discriminatory potential of VOCs for the detection of premalignant and malignant colorectal lesions.

Disclosure: The eNose company supplied the eNoses for free

P1865 BLOOD COLLECTION AND CELL-FREE DNA ISOLATION METHODS INFLUENCE DNA METHYLATION LEVEL DETECTION IN COLORECTAL CANCER PATIENTS

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Introduction: Cell-free DNA (cfDNA) level increases in several pathological processes including colorectal cancer (CRC). In addition, genetic (e.g. mutations) and epigenetic (e.g. DNA methylation) modifications of cfDNA molecules can be also observed; as DNA can originate from tumorous cells hence it carries cancer-specific DNA alterations. Identification of these quantitative and qualitative changes in peripheral blood - especially with the usage of automated methods - offers a promising tool for CRC screening or detection, however, differing results were reported in the case of several markers.

Aims & Methods: Our aim was to test different blood collection tubes, manual and automated cfDNA extraction methods in order to assess whether these factors influence the cfDNA yield and the methylation pattern of four previously described methylation markers in plasma samples of normal, adenoma and CRC patients.

Besides standard K3EDTA tubes (n=30), Streck Cell-Free DNA BCT® (n=10) and Roche Cell-Free DNA (n=30) collection tubes were tested. In addition

to manual cfDNA isolation (n=121), the MagNA Pure 96 (Roche) (n=30) and InviGenius (STRATEC Biomedical AG) (n=69) systems were used for automated cfDNA extraction from plasma specimens. After cfDNA quantification and bisulfite conversion steps, methylation pattern of *SFRP1*, *SFRP2*, *SDC2* and *PRIMA1* genes was determined using MethyLight PCR containing multiplex preamplification.

Results: Slightly higher cfDNA levels were noticed in case of both automated cfDNA extraction method compared to manual isolation. However, no significant difference was observed in the cfDNA amount after using different blood collection tubes. The methylation level of *SFRP1*, *SFRP2*, *SDC2* and *PRIMA1* showed continuous increase along normal - adenoma - carcinoma sequence after manual cfDNA preparation with methylation percentage values of 22%, 7%, 12% and 14% in CRC samples, respectively. Based on the methylation pattern of the 4 genes, CRC and AD specimens could be distinguished from normal controls with 91.5% and 89.2% sensitivity, and 97.3% and 86.5% specificity values. Interestingly, lower methylation frequencies and levels were observed in the case of all biomarkers using the automated instruments, however, methylation differences have been found between the clinical groups.

Conclusion: Automated isolation techniques may contribute to widespread, screening applications of methylation markers; however, further developments are needed in order to make the results comparable with manual extraction in respect to cfDNA yield and methylation analysis.

Disclosure: Nothing to disclose

P1866 GLOBAL DNA HYPOMETHYLATION IN TISSUE AND LIQUID BIOPSY SAMPLES IN COLORECTAL CANCER PROGRESSION IS CAUSED BY DECREASED METHYL-DONORS

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Introduction: In cancerous diseases global DNA hypomethylation is characteristic, which can lead to genetic instability through the active mobile genetic elements. Alterations of DNA methyltransferase (DNMT) expression and level of methyl-donor molecules (folic acid (FA), S-adenosylmethionine (SAM)) can lead to aberrant global DNA hypomethylation.

Aims & Methods: Our aim was to examine global DNA methylation changes along aging and colorectal normal-adenoma-carcinoma sequence and in inflammatory bowel disease in tissue and liquid biopsy samples for diagnostic purposes. Moreover, we aimed to explore the reasons of global hypomethylation on gene expression level and methyl-donor molecule content.

Bisulfite treatment was performed on DNA isolated from 30 normal (N), 10 adenoma (Ad), 10 colorectal carcinoma (CRC), 10 colitis ulcerosa (UC) tissue samples and on 11 N, 10 Ad, 15 CRC, 12 UC plasma specimens. 30 N samples contained different age groups derived from under 20 to 70 years old healthy controls for examination of aging process. LINE-1 PCR product was generated and pyrosequenced. Whole genome expression level of 60 biopsy samples was evaluated by HTA 2.0 RNA microarraychip (Affymetrix). *In situ* tissue appearance of 5-methylcytosine, FA, SAM and expression of DNMTs were analysed by immunohistochemistry staining (IHC).

Results: According to LINE-1 bisulfite sequencing results, DNA methylation was 72,6±1% in samples of healthy controls under 50 years old and 71,6±1,8% in specimens of patients over 50 years old.

Significant DNA hypomethylation was found in CRC (62,9±8,7%; p< 0,001), Ad (66,7±5,1%; p< 0,001) tissue samples in comparison with N samples (72±1,4%). Significant decrease of DNA methylation was observed in CRC (78,8±1,7%; p< 0,02), Ad (80,1±1,7%; p< 0,02) plasma samples compared to N specimens (82,2±1,8%). Global DNA hypomethylation was not detected in UC samples.

Significantly elevated RNA expression of enzymes connected to nucleotide synthesis was observed in Ad and CRC samples compared to N (p< 0,05), while no changes were detected in the RNA levels of DNA methylation-related proteins. RNA expression of enzymes in DNA repair was found up-regulated in Ad and CRC specimens. The intensity of 5-mC labelling of CRC and Ad samples was lower than in N tissue samples. Decreased FA and SAM levels were detected in CRC compared to N specimens and no expression changes of DNMT enzymes.

Conclusion: Significant decrease in DNA methylation level was found in tissue and liquid biopsy samples of colorectal normal-adenoma-carcinoma sequence, but not in UC specimens. Our results suggest that determination of global DNA hypomethylation could have prognostic and diagnostic value as well, and reduction of DNA methylation level could be linked to decreased FA and SAM availability and not to methylation related activity.
Disclosure: Nothing to disclose

P1867 THE ASSOCIATION OF TOLL-LIKE RECEPTOR (TLR) PATHWAY POLYMORPHISMS AND COLORECTAL CANCER RISK: A META-ANALYSIS

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Introduction: Colorectal cancer (CRC) is the third commonest cancer worldwide. Approximately 35% of CRC risk is due to heritable factors but 5% attributed to associated with known syndromes. Single Nucleotide Polymorphisms (SNPs) are common, low penetrance gene variants that may contribute to the remaining heritable risk. The toll-like receptor (TLR) signalling pathway is a key mediator of inflammation and has unique roles in the gut due to the presence of commensal microbiota. It is also suggested to have a significant role in colorectal carcinogenesis. This systematic review and meta-analysis aims to investigate the association of polymorphisms in the TLR signalling pathway with CRC.
Aims & Methods: A systematic literature review of Pubmed, Ovid MEDLINE and HuGENet databases was conducted. Specific inclusion and exclusion criteria were used to select relevant papers. A per-allele, pooled odds ratio was used to assess the risk of each variant. Heterogeneity was investigated using Cochrane's Q test and I2. Publication bias was assessed through funnel plot asymmetry. Statistical analysis was conducted using the Metafor package in R.
Results: Sixty-seven SNPs were identified in published literature in 14 TLR pathway genes associated with CRC risk, of which 12 SNPs in five genes were eligible for meta-analysis. Two SNPs showed a significant association with CRC risk: TLR4 rs7873784 (Odds ratio = 1.356, p=0.011, 95% C.I. 1.07-1.71) and TLR4 rs5030728 (Odds ratio = 0.916, p=0.025, 95% C.I. 0.86-0.99). Funnel plots demonstrated no evidence of publication bias.
Conclusion: The TLR pathway is an potential target for CRC therapy and risk assessment. This study identifies two SNPs in the TLR4 gene associated with CRC risk. In order that conclusions might be made about the role of this pathway in colorectal carcinogenesis, adequately powered studies of greatly increased population size must be conducted.
Disclosure: Nothing to disclose

P1868 CELL-FREE DNA QUANTITY AND QUALITY ALTERATIONS IN DIFFERENT PHYSIOLOGICAL AND PATHOLOGICAL CONDITIONS

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Introduction: Elevation of cell-free DNA (cfDNA) level in peripheral blood was observed in certain physiological conditions, such as pregnancy, aging or high physical activity. Furthermore, altered cfDNA concentration can also be detected in some pathological processes, as autoimmune or inflammatory diseases, and different cancer types including colorectal cancer (CRC). However, to date, studies about quality changes of cfDNA molecules aimed to analysing the fragment profile and global methylation pattern of cfDNA are lacking.
Aims & Methods: Our aim was to define the quantity and quality changes of cfDNA, including concentration, fragment length and global DNA methylation level during high physical exercise, and in neoplastic and inflammatory colorectal diseases. Moreover, we aimed to monitor treatment response in metastatic CRC patients analysing the above-mentioned parameters during therapy.

Plasma fraction was separated from blood samples of 6 healthy athletes before, during and after physical training, and from healthy (n=16), adenoma (n=13), IBD (n=19), and CRC (n=16) patients. Moreover, plasma longitudinal assessment was performed in the case of 10 metastatic CRC patients treated with chemotherapy. After cfDNA isolation, it was quantified using Qubit 1.0 fluorimeter (Thermo Fisher Scientific), and fragment length distribution was examined with Bioanalyzer 2100 (Agilent). Global DNA methylation analysis was performed by bisulfite pyrosequencing of long interspersed nuclear element-1 (LINE-1) (Qiagen).
Results: Elevated cfDNA levels have been found in plasma of adenoma (72,1±37,5ng), IBD (78,0±50,9ng) and CRC (84,5±70,1ng) patients, compared to controls (36,2±11,3ng). Moreover, high increase of cfDNA amount was observed during physical exercise (198,5±90ng), in comparison with control phase (86,3±40,6ng), and then in restitution period significantly lower cfDNA level (155,6±119,3ng) was detected. CfDNA fragment length distribution showed different pattern in each sample group. Slightly decreasing tendency of global DNA methylation was noticed along normal-colorectal adenoma-carcinoma sequence. Interestingly, the amount and global methylation level alteration of cfDNA revealed negative correlation in CRC patients during therapy and progression.
Conclusion: Characteristic cfDNA level, fragment length and global DNA methylation level were identified in the different sample groups that might contribute to the diagnosis and therapy response analysis of colorectal disorders.
Disclosure: Nothing to disclose

P1869 SEQUENTIAL USE OF FECAL IMMUNOCHEMICAL TEST FOR HEMOGLOBIN AND FECAL CALPROTECTIN IN COLORECTAL CANCER SCREENING

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Introduction: Fecal immunochemical test for hemoglobin (FIT) is widely used in colorectal cancer (CRC) screening, in order to select screening participants more likely to have advanced adenoma (AA) or CRC. Fecal calprotectin (FC) or its subunits have been reported to show high sensitivity and negative predictive value for CRC. We developed an FC reagent adapted to sampling device designated for FIT, in order consecutively analyze FIT and FC from the same samples.
Aims & Methods: To better identify participants with CRC and AA in a screening program by combining FIT and FC in order to lower the need for colonoscopy.
We selected 801 out of 6,000 fecal samples collected with sampling devices for FIT, OC-Auto Sampling Bottle 3, in the SCREESCO study. They had all FIT > 10 ug/g and had been subjected to colonoscopy. The samples had been stored at -80 ºC. We determined fecal hemoglobin and calprotectin concentrations, in the same sample consecutively by OC-SENSOR PLEDIA. Of 801 analyzed, 13 were not possible to analyze because of sample shortage. Sensitivity (Se), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) of FC test were analysed at different FIT cut-offs.
Results: 54 participants had CRC (6.9%) and 152 had AA (19.3%) in the 788 subjects, the other had a normal colonoscopy or one adenoma < 5 mm.. In the participants with CRC the data for Se, Sp, PPV and NPV at FIT >15 ug/g FIT cut-off were 94.1%, 87.4%, 7.1%, 96.8%.. At FIT > 20 ug/g the values were 88.5%, 85.3%, 7.0%, 94.6%, and at FIT > 40ug/g 73.1%, 73.5%, 6.8%, 93.1%, on consecutive FC test.
For participants with AA, the same values at FIT > 15ug/g Hb were 83.1%, 89.0%, 18.3%, 73.1%, At FIT > 20 ug/g: 81.1%, 86.6%, 18.3%, 74.8% and at FIT > 40 μg/g, 64.9%, 75.6%, 17.1%, 74.4%, on consecutive FC test.
For the group CRC and AA, the values at FIT > 15ug/g were 85.4%, 88.6%, 23.5%, 71.0%, respectively, at FIT >20ug/g: 82.2%, 86.6%, 23.2%, 70.3% and at FIT > 40ug/g: 65.4%, 76.1%, 21.5%, 68.5%.
In cases with cut-off values of FIT between 10 and 20 μg/g, FC test following FIT had more than 90% of negative predictive value for CRC at cut-off values between 15 to 100 μg/g FC.

Conclusion: FC test following FIT positivity had more than 90 % of NPV with any cut-off values, and around 90% of sensitivity at 15 or 20 μg/g of FC cut-off. Our data suggest that FC test following FIT positivity have good sensitivity for CRC among average-risk population. For AA, the sequential FIT and FC test possibly has better performance than FIT alone with higher cut-off levels. Thus the combination of FIT and FC may be of use in reducing the number of colonoscopies needed in CRC screening.
Disclosure: The study was sponsored by Eiken Chemical.

P1870 DIAGNOSTIC YIELD USING ARTIFICIAL INTELLIGENCE ASSISTED ENDOCYTOSCOPY FOR SESSILE SERRATED ADENOMA/POLYP

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Introduction: Sessile serrated adenoma/polyps (SSA/Ps) are known to be precursors of CRCs.
Therefore, accurate endoscopic criteria to differentiate SSA/Ps from hyperplastic polyps (HPs) are needed. However endoscopic differentiation with endoscopists' eyes is considered difficult.
Aims & Methods: In this study, we evaluated the performance of the artificial intelligence (AI) combined with endocytoscopy in endoscopic identification of SSA/Ps. We developed the AI system based on the previously proposed model.
The AI system was combined with endocytoscopy (CF-H290ECI from Olympus Co.). which enables in vivo observation of cellular images at 500-fold magnification. The diagnostic algorithm of the AI consisted of the sequence of image acquisition, extraction of 312 visual features from nuclear images and contrast difference of the whole image, and classification into the two pathological groups (SSA/P and Non-neoplastic). We designed this retrospective study to assess the performance of the AI system for prediction of SSA/Ps by using 30 SSA/Ps (822 images) and 69 Non-neoplastic lesions (Total 1574 images) including 66 HPs (1524 images), 1 juvenile polyps (17 images) and 2 inflammatory polyps (33 images) resected between Jul. 2018 and Feb. 2019. Machine learning for the AI was performed by using 14222 images which were acquired and selected from Jan. 2016 to Jun. 2018. The main outcome measures were diagnostic sensitivity specificity, accuracy of the AI system in identifying SSA/P in the image-based analysis and the lesion-based analysis. In the lesion-based analysis, diagnosis of the target lesion was defined as SSA/P when the AI system shown at least one SSA/P output.
Results: The AI system automatically output the pathological prediction of 1667 images (SSA/P 510 images, HP 1157 images) out of total 2396 images immediately with high confidence (probability>=80%).
In the image-based analysis, the AI system showed sensitivity of 19.0% (97/510), specificity of 98.7% (1143/1157) and accuracy 74.4%(1240/1667).
However, in the lesion-based analysis AI system showed sensitivity of 66.6% (20/30), specificity of 89.9% (62/69) and accuracy 82.8% (82/99).
Conclusion: This study revealed AI system diagnosed SSA/P with high specificity.
However further accumulation of endoscopic images for machine learning is required to make more robust model for diagnosing SSA/Ps.
References: Mori Y, Kudo SE, Chiu PW et al. Impact of an automated system for endocytoscopic diagnosis of small colorectal lesions: an international web-based study. Endoscopy 2016; 48: 1110－1118
Disclosure: Nothing to disclose

P1871 NON-INVASIVE DETECTION OF COLORECTAL CANCER AND ADVANCED ADENOMA USING CANCER-SPECIFIC METHYLATION SIGNATURES IN PLASMA CTDNA

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Introduction: Colorectal cancer (CRC) is a common malignant tumor of the digestive tract and one of the leading causes of cancerdeath worldwide. The five-year survival rate of CRC drops from above 90% at stage I to less than 10% at stage IV. Therefore, colonoscopy is recommended as a screening method, but patient compliance can be low due to its invasiveness. Non-invasive biomarker tests have also been developed for years, but are limited in sensitivity and specificity, especially for early-stage CRC and precancerous adenomas. We have established a highly accurate, next generation sequencing (NGS)-based, machine-learning guided screening assay (ColonES) detecting ctDNA methylation signatures in plasma.
Aims & Methods: In this study, we organized a multi-center prospective study to evaluate the clinical performance and utility of ColonES.
Blood samples were collected in EDTA tubes and centrifuged within 4 hrs to separate plasma. ColonES, an NGS based bisulfite sequencing assay covering approximately 2,181 genomic regionswas employed to identify pre-cancerous lesion and CRC. Patient samples were separated into three groups based on colonoscopy results. The high risk group includes CRC, advanced adenoma (AA), and cases with more than three adenomas; the low risk group include healthy individuals or patients with non-malignant diseases; the indeterminate group include non-AA with a sizes under 1cm. Before this study, a separate cohort of 400 samples was used to train the classification model, and a cohort of 514 samples was used to validate the model. This study will enroll approximately 2000 patients covering a full spectrum of clinical conditions to evaluate the accuracy and reproducibility of the assay.
Results: The enrolled 2000 patients are divided equally between different categories. The first phase of the study, which is comprised of 259 patients, hasbeen completed.Sensitivity and specificity of different categories were determined using this group of samples.The sensitivities of stage 0/1 CRC, AA and multi-adenoma are 91.7%, 81.6% and 80.0%, respectively. Symptomatic patients free of neoplasm were divided into two groups: group with no findings in colonoscopy, and the group with pathologically benign condition(s) including inflammation, polypus, or ulcus. The specificities of these groups are 82.9% and 80.8%, respectively. Interestingly, 52.6% of non-AA patients were called positive, suggesting that cfDNA from these patients may contain cancer-specific methylation signals. In-depth analysis of the data revealed that the methylation scores, which are used to categorize the patients, are different in CRC patients of different stages and in CRC patients with different lesion sizes. In AA patients, methylation scores vary depending on sizes in tubular adenoma sub-category, but not in other AA sub-categories.
Conclusion: We demonstrated that cancer-specific methylation signatures can be used for CRC and AA detection in plasma samples with high sensitivity and specificity. This will provide a valuable tool for CRC and AA diagnosis and screening, especially in populations who cannot or are unwilling to undergo colonoscopy.
Disclosure: Hui Wang, Athurva Gore, Hai-Biao Gong and Rui Liu are employees of Singlera Genomics Inc., the product of which was used in this study. No other conflict of interest is declared.

P1872 AGE AND COLONOSCOPY INTERVAL AFTER TRANSPLANTATION IS THE RISK OF ADVANCED COLONIC NEOPLASIA IN RENAL TRANSPLANT RECIPIENTS

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Introduction: Organ transplantation has a higher risk for malignancies compared to general subjects.
Aims & Methods: The purpose of this study was to investigate the incidence of colorectal neoplasms in renal transplant recipients and to find risk factors for the development of advanced colonic neoplasias in renal transplant recipients.
Between 1992 and 2015, colorectal neoplasm screening was performed in renal transplant recipients with colonoscopic evaluation. The incidence of colorectal cancer was compared with that of the general population registered in the National Cancer Registration Statistics. To determine the risk factors for the development of advanced colonic neoplasia, we investigated demographics, body mass index, types of main immunosuppressive agents, and the interval of the first endoscopic evaluation from the transplantation.
Results: Among 1,828 renal transplant recipients, 748 patients underwent colonoscopic evaluation between 1992 and 2017. Colorectal neoplasms occurred in 191 patients (25.5%): non-advanced adenoma in 105 (14.0%), advanced adenoma in 70 (9.4%), cancer in 16 patients (2.1%). The incidence of colorectal cancer in 2016 Korean National Cancer Statistics was 0.06%, showing a higher incidence of colorectal cancer in renal transplant recipients. In multivariate analysis, age over 40 and more than five years interval between transplant and the first colonoscopy were independent risk factors for advanced colonic neoplasia. The risk of advanced neoplasia development in age over 40 was increased compared to under 40 (OR 8.7, 95% CI 2.01-34.33; P=.003). The risk of advanced neoplasia was high if colonoscopy is performed more than 5 years after transplantation (OR 1.1, 95% CI 1.02-1.16; P=.016).

Variables	Univariate analysis		Multivariate analysis	
	Odd ratio (95% CI)	p value	Odd ratio (95% CI)	p value
Age (≥40 years)	8.7 (2.12-36.03)	0.003	8.3 (2.01-34.33)	0.003
Male sex	1.4 (0.88-2.27)	0.151	-	-
Obesity	1.5 (0.87-2.65)	0.139	-	-
DDKT/LDKT*	1.1 (0.94-1.20)	0.313	-	-
CyS/TAC**	1.4 (0.86-2.21)	0.182	-	-
Colonoscopy interval (≥5yrs)	1.1 (1.02-1.17)	0.008	1.1 (1.02-1.16)	0.016

* DDKT: Deceased donor at kidney transplantation, LDKT: Living donor at kidney transplantation ** CyS: Cyclosporine, TAC: Tacrolimus

[Risk factors for Advanced colonic neoplasia after renal transplantation]

Conclusion: Renal transplant recipients had a higher incidence of colorectal neoplasms. Colon cancer screening should be recommended before 40 years in these patients.
Disclosure: Nothing to disclose

P1873 WITHDRAWN

P1874 STUDYING TRADITIONAL SERRATED ADENOMAS - ENDOSCOPIC AND PATHOLOGICAL SIGNS OF NONSERRATED TYPES OF COLON LESIONS

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Introduction: Exact endoscopic and morphological criteria of traditional serrated adenomas (TSAs) of the colon are still not indicated. We examined features of TSAs in patients of our population.
Aims & Methods: To characterize the endoscopic and histological features of traditional serrated adenomas and compare with nonserrated colorectal polyps.
Of the 500 epithelial lesions, removed via colonoscope in 265 patients, 14/500 (2.8%) TSAs with different degrees of dysplasia and focus of adenocarcinoma in 1/14 (7.1%) were histologically identified. The key endoscopic and pathological features of TSAs and immunohistochemical studies with CD44, Ki67, Msi-1 and 1-and 3 - claudins antibodies were evaluated.
Results: Polyps were located in the both parts of the colon, but most of them were located in the left colon (9/14; 64.3%), exactly in the rectum (7/14; 50%). Drew attention to their red color (13/14; 92.9%). The polyps size was 0.5-4.5 cm, while 2 (14.3%) polyps did not exceed 0.5 cm and 3 (21.6%) polyps were more than 2.5 cm. Macroscopically, 5/14 (35.7%) lesions were flat-elevated Type 0-IIa; 9/14 (64.3%) polyps were protruding Type 0-Is, 0-Isp, 0-I. Two (14,3%) polyps were covered with a mucus cap. Three (21.4%) flat-elevated TSAs had pit-pattern II and only one of them presented as dark-green colors on auto fluorescence imaging (AFI) colonoscopy that are similar to the normal surrounding mucosa. This polyps type difficult to differentiate from hyperplastic polyps (HP) and sessile serrated adenomas (SSA); 11/14 (78.6%) had pit-pattern IV and presented as magenta color tone on AFI colonoscopy. This endoscopic features are more typical for adenoma tubular-villous (ATV) and adenoma villous (AV). Immunohistochemically TSA is close to AT/ATV and fundamentally different from HP/ SSA, despite the fact that in current classification they belong to the group of serrated lesions. Statistically significant differences are:
· similar distribution of CD44 (surface) of the AT, ATV and TSA;
· similar levels of Msi-1 cytoplasmic response in AT, ATV and TSA;
· similar levels of Claudine-1 and -3 expression in ATV and TSA.
Conclusion: Often TSA are located in the rectum and corresponds to red protruding type lesions with pit-pattern IV. The TSA diagnosis based on AFI based on changes in magenta color tone. These endoscopic futures are the classical for nonserrated polyps with villous structure. The presence of characteristic ectopic crypts is almost impossible to distinguish from the branching of crypts in any ATV or AV, and there is no consensus on the number of ectopic crypts required for TSA verification. Given the low incidence of TSA, the similarity of endoscopic features and the absence of immunohistochemical differences between TSA and AT/ATV, the feasibility of TSA allocation in a separate classification group is debated and requires further study.
Disclosure: Nothing to disclose

P1875 COMPLICATIONS AFTER ENDOSCOPIC RESECTION OF T1 COLORECTAL CARCINOMAS

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Introduction: In contrast to the complication risk of endoscopic resection (ER) of adenomas, the intra-procedural and post-procedural complication risk of ER of T1 colorectal cancer (CRC) is scarcely reported in literature. One might hypothesize that ER of these early CRCs is associated with an increased complication risk, as these tumors grow into the submucosal layer and sometimes show incomplete lifting.

Aims & Methods: We aimed to identify the complication rate after primary ER of T1 CRCs and to identify risk factors associated with these complications. Medical records were reviewed of all patients diagnosed with T1 CRC between January 2000 and December 2014 within 15 hospitals in the Netherlands. Patients that underwent ER (with or without adjuvant surgery) were selected. Primary outcome was the occurrence of endoscopy related complications (i.e., bleeding, perforation, polypectomy electrocoagulation syndrome (PPES)) requiring re-colonoscopy, surgery, prolonged hospital stay, readmission, or other interventions such as antibiotic therapy or blood transfusion. Secondary outcome was the identification of independent risk factors associated with these complications. Additional information on treatment of complications, and intra-procedural hemoclip placement for prophylaxis was collected of all patients with complications and random controls (sub-cohort) from our total cohort in a 1:3 ratio. For the analysis of possible risk factors, the sub-cohort was used. Multivariate logistic regression was performed.

Results: From a retrospective cohort of 1879 T1 CRC patients, 1069 patients with ER of T1 CRC were selected. Endoscopic complications occurred in 59/1069 (5.5%) of patients, among which 37.3% of complications was classified as mild, 59.3% as moderate, and 3.4% as severe. These complications were delayed bleeding (N=40, 3.7%), perforation (N=13, 1.2%) and PPES (N=6, 0.6%). No fatal complications were observed. Independent predictors for complications were; age > 70 years (OR=2.111; 95% confidence interval (CI)=1.124-3.964), and tumor size >20mm (OR=2.224, 95% CI=1.054-4.694). Age > 70 years was also associated with an increased risk for delayed bleeding (OR=2.616; 95% CI=1.236-5.537).

Conclusion: In this large multicenter retrospective cohort study, complication rate of ER of T1 CRC (5.5%) was comparable with reported complication rates of ER of adenomas in current literature. These data supporting the relative safety of ER for T1 CRCs. More caution is warranted for ER of T1 CRC in patients older than 70 years, and large lesions (>20mm).

Disclosure: Nothing to disclose

P1876 LOW DOSE 5-AMINOSALICYLIC ACID (5-ASA) SUPPRESSES GROWTH OF HUMAN COLORECTAL ADENOMA DERIVED CELLS IN 3-DIMENSIONAL CULTURE: IMPLICATIONS FOR PREVENTION

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Introduction: 5-aminosalicylic acid (5-ASA) is a well-tolerated and inexpensive salicylate used in the treatment of ulcerative colitis and epidemiological data suggests that regular use reduces the risk of colitis-associated cancer[1]. Although aspirin (acetylsalicylic acid) has shown promise as a chemoprophylactic agent in patients with high colorectal polyp burden[2, 3] it is unknown if 5-ASA has the same benefit. Interestingly 5-ASA has been shown to suppress Wnt/b-catenin signalling, deregulation of which is a key event in the initiation of colorectal cancer (CRC) tumorigenesis. Here we demonstrate that 5-ASA can repress the stem potential of human adenoma cells in a 3D organoid culture system and suggest this drug has potential as a chemoprophylactic agent in patients with a high polyp burden.

Aims & Methods: The human colonic adenoma cell line PC/AA/C1 was seeded as a single-cell suspension into Matrigel®(Corning Life Sciences, USA) extracellular matrix and incubated with advanced DMEM/F12 (Sigma-Aldrich, UK) media supplemented with 0.1% bovine serum albumin (Sigma-Aldrich), 2mM glutamine (Gibco), 10mM HEPES (Sigma-Aldrich), penicillin & streptomycin (Life Technologies, UK), 1% N2 (Gibco, UK), 2% B27 (Gibco, UK), 0.2% N-acetylcysteine (Gibco, UK) and EGF (Peprotech, UK). 5-ASA (Sigma-Aldrich) was dissolved in this culture medium and pH balanced to 7.35 - 7.45.

Clinically achievable colonic luminal 5-ASA concentrations using oral preparations is 12 - 25mM[4]; we tested efficacy of lower doses in this 3D system. Serial images through the Matrigel hemispheres were acquired as a Z-stack using a DMI6000 widefield microscope (Leica, Germany) & LAS-X software (Leica) and analysed using a custom in-house MatLab programme to estimate spheroid number and size.

In parallel, cells were grown in T25 flasks (Corning, USA) and treated with 5-ASA before protein lysates were taken for SDS-PAGE and Western blotting for the stem cell marker and Wnt target leucine-rich G protein coupled receptor 5 (LGR5, Abcam, UK).

Results: Adenoma cells exposed to low doses of 5-ASA once seeded into Matrigel established fewer viable organoids than control cells: control mean 95 organoids (95% confidence intervals 49 - 141)), 2mM 5-ASA mean 84 organoids (95% CI 36 - 131) & 5mM 5-ASA mean 30 organoids (95% CI 16 - 43; p < 0.005). After 21 days in culture, adenoma-derived organoids were significantly smaller than control: Control median 58800μm (inter-quartile range 4692 - 171560μm), 2mM median 1951μm (IQR 1207 - 3331μm), 5mM median 1540μm (IQR 1139 - 2304μm)). Cells exposed to 5mM 5-ASA at the time of seeding did not grow over 21 days of culture, but did form organoids if 5-ASA was removed from culture medium by day 11. Where 5-ASA treatment was delayed to day 7 of culture, 5-ASA slowed but did not abrogate growth. Western blots of cell lysates demonstrated downregulation of LGR5 at higher (but clinically achievable) doses but LGR5 expression returned to normal within 8 hours of removing 5-ASA from culture medium.

Conclusion: In these experiments we demonstrate that at low dose 5-ASA reduces the colony forming efficiency and growth of human colonic adenoma cells in 3-dimensional culture system, implying that 5-ASA suppresses stemness, further supported by observed downregulation of the putative cancer stem cell marker LGR5.

This data suggests that 5-ASA would be able to prevent formation and/or growth of adenomas in predisposed individuals. Clinical trials are required to establish if this affordable and well-tolerated drug could reduce polyp burden and cancer risk.

References: [1] Qiu, X., et al., Chemopreventive effects of 5-aminosalicylic acid on inflammatory bowel disease-associated colorectal cancer and dysplasia: a systematic review with meta-analysis. Oncotarget, 2016. [2] Hull, M.A., et al., Eicosapentaenoic acid and aspirin, alone and in combination, for the prevention of colorectal adenomas (seAFOod Polyp Prevention trial): a multicentre, randomised, double-blind, placebo-controlled, 2 x 2 factorial trial. Lancet, 2018. 392(10164): p. 2583-2594. [3] Burn, J., et al., A randomized placebo-controlled prevention trial of aspirin and/or resistant starch in young people with familial adenomatous polyposis. Cancer Prev

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Res (Phila), 2011. 4(5): p. 655-65. [4] Desreumaux, P. and S. Ghosh, Review article: mode of action and delivery of 5-aminosalicylic acid – new evidence. Aliment Pharmacol Ther, 2006. 24 Suppl 1: p. 2-9.
Disclosure: Nothing to disclose

P1877 PROGNOSTIC IMPACT OF NEUTROPHIL-TO-LYMPHOCYTE RATIO AND TRANSFORMING GROWTH FACTOR β RECEPTOR ON COLORECTAL CANCER SURVIVAL IN A LEBANESE POPULATION

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Introduction: Colorectal cancer (CRC) is the third cancer in prevalence and in mortality worldwide. Inflammatory and genetic factors appear to play a role in the prognosis of CRC. A high neutrophil-to-lymphocyte ratio (NLR) is thought to be a predictor of poor prognosis in colorectal cancer. In addition, some authors consider that Transforming Growth Factor Beta Receptor (TGFβR) polymorphism may have prognostic significance in colorectal cancer.
Aims & Methods: Our primary objective is to assess the prognostic impact of NLR and TGFβR polymorphism, independently, on the 3-years and 5-years overall survival rates and on disease-free survival rates in colorectal cancer. Our secondary objective is to assess the prognostic impact of NLR, depending on the TGFβR polymorphism, on the 3-years and 5-years overall survival rates and on disease-free survival rates in colorectal cancer.
This is a retrospective cross-sectional multivariate study conducted in two hospitals in Lebanon. A total of 91 patients diagnosed with colorectal adenocarcinoma prior to 2011, positive for either polymorphism TGFβR*6A/9A or TGFβR*9A/9A by genetic analysis DNA on blood samples and having a complete blood count at diagnosis prior to any treatment, were included in this study.
Results: The impact of NLR on the survival of CRC was statistically significant with a p-Value < 0.05: low NLR was associated with better 3-years and 5-years overall survival rates and with better disease-free survival rates compared to high NLR. The impact of TGFβR polymorphism was not significant: TGFβR*9A/6A polymorphism was not associated with neither decreased overall survival rates nor decreased disease-free survival rates. To our knowledge, this is the first multivariate study to evaluate the impact of NLR and TGFβR polymorphism at the same time.
Conclusion: NLR is a simple, non-invasive and unexpansive tool which can be easily used to classify patients and adapt disease management and follow up in order to optimize outcomes.
It would be interesting, in future studies, to evaluate the exact mechanism of the immunological response in CRC and the elaborate the role of cytokines of lymphocytes.
References: Kuipers EJ, Grady WM, Lieberman D, et al. COLORECTAL CANCER. Nat Rev Dis Primer. 2015;1:15065. doi:10.1038/nrdp.2015.65 2. Marley AR, Nan H. Epidemiology of colorectal cancer. Int J Mol Epidemiol Genet. 2016;7(3):105-114. 3. Bhurgri H, Samiullah S. Colon Cancer Screening - Is It Time Yet? J Coll Physicians Surg--Pak JCPSP. 2017;27(6):327-328. doi:2629
Disclosure: Nothing to disclose

P1878 PREVALENCE AND IMPACT OF ANAEMIA FOLLOWING THERAPEUTIC INTERVENTION FOR COLORECTAL CANCER

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Introduction: Anaemia is common in patients with colorectal cancer and can be worsened by surgical blood loss. Preoperative optimisation aims to correct preoperative anaemia with comparably little attention given to the prevalence and consequences of postoperative anaemia.
Aims & Methods: The aim of this study was to investigate the frequency of postoperative anaemia and any associated short and long-term impacts of anaemia at discharge following laparoscopic colorectal cancer resection.

A dedicated, prospectively populated database of elective laparoscopic colorectal cancer procedures with curative intent within a fully implemented ERAS protocol was utilised. Patient demographics, tumour characteristics, and operative details were captured. The primary endpoint was anaemia at discharge. Anaemia was defined as haemoglobin (Hb) level of < 120g/L for women and < 135g/L for men. Secondary endpoints were anaemia at time of hospital admission, length of stay (LoS), postoperative complications, and overall survival. Median follow up was 61 months with overall survival calculated with the Kaplan-Meier log rank method stratifying for tumour stage. Data was analysed using the IBM SPSS® statistical tool.
Results: Complete data of 532 patients were included with median age of 72 years and BMI 26. 389 were male while 161(24.1%) were ASA III. 46.4% were anaemic preoperatively. Median operative time was 180min (interquartile range 150-250) with 100ml (0-200) median estimated blood loss. At discharge most patients were anaemic (76.6%, Hb 115 g/L (106-125), p< 0.001). 16.7% experienced postoperative complication(s) with a lower discharge Hb seen in this group (110g/L (105-120) vs. 116g/L (107-127), p=0.001). Anaemia at discharge was significantly associated with a longer stay (7 (5-11) vs. 6 (5-8), p=0.037) while preoperative anaemia was not (7 (5-10) vs. 7 (5-9), p=0.063). Admission and discharge anaemia were independently associated with worse overall survival (p=0.027 and p=0.018 respectively) and remained significant after adjusting for tumour stage.
Conclusion: Anaemia at time of discharge following elective laparoscopic colorectal cancer surgery is commonplace with associated negative impacts upon short-term outcomes and overall survival.
Disclosure: Nothing to disclose

P1879 THE VERIFICATION OF THE VALIDITY OF AMBULATORY HOT SNARE EMR AND POLYPECTOMY FOR COLONIC NEOPLASIA

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Introduction: Hot snare endoscopic mucosal resection (EMR) and polypectomy is an efficacious endoscopic therapy for colorectal neoplasia. Due to the complication such as delayed bleeding and perforation, these procedures generally need hospitalization. Ambulatory EMR and polypectomy are easier to manage and can be performed earlier compared to those with hospitalization. However, the curability and safety of ambulatory treatment is not clarified. Thus the aim of this study was to verify the validity of ambulatory hot snare EMR and polypectomy for colonic neoplasia.
Aims & Methods: From January 2007 to November 2018, 97 patients who underwent ambulatory hot snare EMR and polypectomy for colonic neoplasia (ambulatory group. male:female, 67:30; age, 64.3 ± 12.5; 173 lesions), and 1184 patients who underwent those procedure for colonic neoplasia with hospitalization (hospitalization group. male:female, 813:371; age 66.2 ± 10.8 ; 2752 lesions) in Chiba university hospital were included in this study. The curative resection rate, procedure-related complications were compared between the ambulatory group and hospitalization group retrospectively.
Results: Median tumor size (mm) was 7 (range 3-30) in the ambulatory group and 7 (range 2-50) in the hospitalization group. There was no significant difference. The breakdown of SSA/P / low grade intra-mucosal neoplasia/ high grade intra-mucosal dysplasia/ cancer was 10/ 105/ 57/ 1 and 109/ 1774/ 822/ 47 respectively. The curative resection rate was 82.1% in the ambulatory group and 75.5% in the hospitalization group (p=0.051 chi-square test). The number of the patients with the history of use of anticoagulants and/or antiplatelet drugs was 11 (11.3 %) and 226 (19.1%) respectively, and the difference was not significant.
Mean period of hospital stay in hospitalization group was 4.1 ± 2.9 days. Perforation occurred in 0 (0%) patient and 2 (0.2%) patients respectively. Delayed bleeding occurred in 1 (1.0%) patient and 32 (2.7%) patients respectively, and the differences were not significant.

One patient with delayed bleeding in ambulatory group underwent endoscopic hemostasis without hospitalization 2 days after EMR.

Conclusion: Ambulatory hot snare EMR and polypectomy for colonic neoplasia can be performed safely with equivalent curability to those with hospitalization even if the patients had the history of use of anticoagulants and/or antiplatelet drugs.

Disclosure: Nothing to disclose

P1880 MRI COMBINED WITH A STRUCTURED REPORT TEMPLATE AS A PRE-SELECTION TOOL PRIOR TO ENDOSCOPY TO IDENTIFY PATIENTS FOR ORGAN-PRESERVATION AFTER CHEMORADIOTHERAPY IN RECTAL CANCER

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Introduction: MRI and endoscopy are currently the main tools used to assess response and identify potential candidates for organ preserving treatments after chemoradiotherapy (CRT) for rectal cancer. For logistical reasons and when there is limited expertise in endoscopic imaging for restaging, MRI could play a role as a pre-selection tool to identify patients who would benefit from additional endoscopy to differentiate between potential complete responders who may be candidates for organ preservation and poor responders in whom surgery is unavoidable.

Aims & Methods: Aim of this study was to evaluate the performance of MRI (for readers with varying expertise levels) using a simplified structured report template in this specific setting.

Seven independent readers with varying expertise levels retrospectively evaluated 63 patients who routinely underwent a restaging MRI with Diffusion-Weighted Imaging (MRI-DWI). Using a simplified structured report template taking into account the morphologic response on T2W-MRI and the signal pattern on DWI, patients were categorized as:

[1] good - potential complete responders (i.e., would benefit from endoscopy to identify complete responders),

[2] intermediate responders - residual tumour most likely (i.e., endoscopy potentially useful to confirm residual tumour), and

[3] poor responders - highly suspicious of tumour (i.e., endoscopy not required, surgery unavoidable).

The final response outcome of all patients was determined by histopathology in the operated patients or by long term follow-up (local recurrence free follow up of ≥ 1 year) in the patients with a sustained complete response undergoing watch-and-wait.

Results: The median number of patients categorized into the "poor responders" group by the 7 readers was 13(21%) (range 8-24). The vast majority of these patients had confirmed residual tumour at histopathology, with a low rate of "missed complete responders" varying from 0-4% for the different readers. The median number of patients categorized into the "intermediate responders" group was 31 (49%) (range 14-36). The rate of missed complete responders in this group ranged from 0-24% for the different readers. In the group categorized as the "good - potential complete responders" (median 18 (29%), range 14-26 per reader), the majority of patients (44-67%) were confirmed complete responders. When combining the MR poor-intermediate response group together, the risk of missing complete responders ranged from 3-12% for the 7 readers.

Conclusion: MRI using a simplified structured report template can aid in pre-selecting patients for immediate surgery, regardless of radiologists' experience level:

- When applying a stringent pre-selection (MR-poor responders only), the risk for missing complete responders is almost negligible (0-4%) and approximately 21% of patients can be safely referred for direct surgery.

- With a more conservative approach (including both MR-poor and -intermediate responders), around 71% of patients may be referred for direct surgery without endoscopic evaluation, at the cost of missing 3-12% of complete responders.

Using MRI in such a way, can thus facilitate a more selective use of endoscopy to identify the good responding patients and further select candidates for organ preservation.

Disclosure: Nothing to disclose

P1881 THREE EUROPEAN CENTERS EXPERIENCE OF ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) FOR TREATMENT OF GASTROINTESTINAL NEUROENDOCRINE TUMORS (NETS)

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Introduction: Although endoscopic submucosal dissection (ESD) of gastrointestinal (GI) neuroendocrine tumor (NETs) is an increasingly performed minimally invasive technique allowing complete en-bloc resection of mucosal and submucosal lesions, data on efficacy and safety outcome is limited. The aim of this study is to review three European centers experience of endoscopic treatment of superficial GI NET by ESD.

Aims & Methods: Clinical and technical data of patients treated by ESD from three tertiary European centers were prospectively collected from October 2014 to March 2019. Complete resection (R0) was defined as clear lateral and vertical margins.

Results: Thirty ESDs of NETs were performed in 28 patients (females 60.7%), median age of 61 years. Twenty-one NETs (70%) were removed from the stomach, 6 from the rectum (20%), 2 from the duodenum (6.6%) and 1 from the esophagus (3.33%). Seventeen out of 21 (80.9%) gastric NETs were associated with atrophic gastritis, 15 (88.2%) of which of autoimmune etiology. Moreover, 8 out of 21 patients (38.1%) with gastric NET had history of multiples NETs. Among them, 6 patients had been diagnosed with autoimmune atrophic gastritis (75%), 1 patient with helicobacter pylori related gastritis (12.5%) and 1 patient with gastritis of unknown origin (12.5%). En-bloc resection was achieved in all patients (100%). R0 resection rate was 80% (93.3% clear lateral and 80% clear vertical margins). Lymphovascular infiltration was diagnosed in three cases (10%).

Median ESD duration time, recorded in 21 procedures, was 60 min (range 20-240). One case of rectal and one case of duodenal NET removal, presented small perforations, treated conservatively by antibiotics and clip closure. The median specimen size was of 26 mm (range 12-65). Pathological examination showed 17 (56.6%) grade 1, 12 (40%) grade 2 and 1 (3.3%) grade 3 NETs. Sixty-nine percent of lesions were characterized as pT1 and 30.4% as pT2. Three patients were candidates for additional treatment: one had endoscopic mucosal resection for additional known lesions, one underwent surgery with oncological lymph node resection (finally pT2N1) and one refused systemic therapy. Follow up was performed in 21 patients. At the end of a median follow-up of 554 days, two cases of recurrence were identified: one was managed endoscopically, the second refused treatment.

Conclusion: Our series of ESD for selected GI NETs showed favorable results in term of efficacy and safety. However, further studies are needed to determine the role of ESD compared to other resection modalities.

Disclosure: Dr Despott and Dr Murino receive research/ education support from Aquilant Medical, Fujifilm, Olympus, Pentax Medical, Boston scientific and GI supply. All others authors have no conflicts of interest to disclosure.

P1882 ENDOSCOPIC SUBMUCOSAL DISSECTION IN DYSPLASTIC LESIONS IN LONG-STANDING ULCERATIVE COLITIS: RESULTS OF A TERTIARY ENDOSCOPIC REFERRAL CENTER

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Introduction: Endoscopic resection of superficial polypoid lesions in ulcerative colitis (UC) patients is appropriate if a complete resection can be achieved. However, endoscopic mucosal resection (EMR) is ineffective for large, nonpolypoid neoplasms (NPL) in UC, due to submucosal fibrosis and poor data are available on the efficacy of endoscopic submucosal dissection (ESD).
Aims & Methods: The aim of this study is to assess ESD feasibility and efficacy for large, NPL in UC patients in two tertiary endoscopic referral center.From April 2009 to October 2017 superficial NPL >20 mm within the colonic mucosa of ulcerative colitic patients, were retrospectively evaluated, in a tertiary italian endoscopic referral center. Pre resection staging of NPLs was achieved by WLE+cromoendoscopy + NBI (Olympus Comp.) or I-scan System (Pentax Comp.). ESD was performed according to the standard technique, by using CO2 insufflation. Dual knife and Hook knife were used as ablation tools. A hyperosmotic solution (plasma expander + epinephrine + indigo carminio) was used to obtained the lifting of lesion. All endoscopic procedures were performd under conscious sedation (fentanyl + midazolam).
Results: Twenty-three patients (15M and 8F) were considered in the study; median age at time of resection was 62 (30-81). The colonic disease duration was 18 years (1-44) and 87% of the patients had extensive colitis (E3); 13% left side colitis (E2). Twelve of the 23 patients were under 5-aminosalicylic acid, 10 under biologics and 1 patient under azathioprine therapy. Mean lesion size was 38.6 ±22.1 (20-50) mm. En bloc resection was achieved in n=22 patients (95.6%), in 1 patients piecemeal was performed and there were no severe complications. All lesions removed were non polypoid with distinct margins, and no ulceration was observed. In all resected lesions low-grade dysplasia was diagnosticated histopathologically. No patient was referred for colectomy.
Conclusion: In this study, ESD of large non polypoid lesions associated with UC seems to be feasible, safe and curative option. These data support the potential role of advanced endoscopic therapeutic tecnique for a management of dyspalsia associated colitis in selected patients.
Disclosure: Nothing to disclose

P1883 LYNCH SYNDROME - UNIVERSAL SCREENING STRATEGY IMPLEMENTATION

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Introduction: Revised Bethesda Criteria (BC) are used to select patients with colorectal cancer (CRC) for Lynch Syndrome (LS) screening - **selective strategy.**
Given the low sensitivity of these criteria, screening for loss of expression of DNA repair proteins (DRP) / microsatellite instability (MSI) in all patients with CRC diagnosis, or in those < 70 years is currently recommended - **universal strategy.**
Aims & Methods: Our aim was to evaluate the benefits of applying the universal strategy in the identification of patients with LS.

Single-center cohort study. All patients < 70 years with an initial diagnosis of CRC discussed in a multidisciplinary appointment (07/2016 - 12/2017) and submitted to surgery were evaluated.
Clinical data, tumor features (including DRP expression), and genetic / epigenetic studies results were analysed (descriptive statistics).
Results: 105 patients were evaluated [57.1% males, mean age at diagnosis: 58.5 years (15-69)]. 7.7% of the tumours were mucinous or had signet ring cells. In 30% lymphocytic infiltrate was observed.
2.9% met the Amsterdam Criteria and 27.6% BC.
There was loss of DRP expression in 8.6% of tumours (7/9 MLH1 / PMS2; 1/9 MSH2 / MSH6; 1/9 MSH2). In the subgroup of patients with loss of DRP expression, one had a positive genetic diagnosis -LS (patient with MSH2 / MSH6 loss), 5 have ongoing studies (hipermethylation or genetic diagnosis), 2 died before being tested and one refused genetic diagnosis (patient with loss of MSH2). The patient with LS diagnosis fulfilled BC (age < 50 years). Of the remaining 8 patients,3 did not fulfil BC and would not have been investigated by the selective strategy.
Conclusion: The preliminary results of our study demonstrate the importance of the universal strategy widespread implementation for screening of loss of DRP expression/ MSI in CRC.
Disclosure: Nothing to disclose

P1884 LONG TERM FOLLOW-UP OF RECTAL CANCER PATIENTS WITH A COMPLETE RESPONSE FOLLOWED IN A WAIT-AND-SEE APPROACH, IS THERE AN INCREASED RISK FOR METASTASIS?

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Introduction: Patients with a regrowth in a wait-and-see-program are reported to have a higher risk for metastases. This is probably related to an inherent higher risk of incomplete responders, but it cannot be excluded that metastases can arise from the regrowth.
Aims & Methods: The aim of this study was to evaluate the risk of distant metastasis in wait-and-see patients with a clinical(near)complete response (cCR) after neoadjuvant chemoradiation (CRT) for rectal cancer, according to local regrowth and timing of inclusion.
Patients were included in a wait and see program between 2004 and 2019 when a three modality approach with digital rectal examination, endoscopy and MRI showed a (near) cCR. Patients were followed with frequent endoscopy and MRI every 3 months during the first year, and every 6 months thereafter. Oncological outcomes were assessed with Kaplan-Meier curves and a log rank test.
Results: We analyzed 313 patients with a median FU of 39 months (range 2-158) of which the majority (n=191) were prospectively analyzed. 52% (n=161) patients had an immediate cCR at restaging and 47%(n=147)patients had a near cCR during restaging with a cCR after reassessment of 3 months. 19% of the patients developed a local regrowth within 3 years (n=57, 49 luminal, 3 nodal, 5 both luminal and nodal). 9 patients with local regrowth developed distant metastasis (20%, 95%CI 62-90) within 3 years compared to 11 patients with distant metastasis without LR (5%, 95%CI:92-98) (p < 0,001). 7/9 patients developed a local regrowth first before detection of metastasis, 1 patient developed local regrowth and metastasis simultaneously and 1 patient developed metastasis 6 months prior to detection of local regrowth. Patients with a near CR and local regrowth tend to develop more metastasis compared to immediate complete responders who had a local regrowth. 3-year overall survival in patients with local regrowth was 93%(95%CI:80-98) vs. 97%(95%CI:94-99) in patients without local regrowth (p=0.25).
Conclusion: Rectal cancer patients selected for a wait-and-see-program who develop a regrowth have a higher risk of developing distant metastasis, especially in near CR. It is hypothesized that this is related to tumour biology but it remains unsure if metastasis arise from a regrowth. Overall survival outcomes in patients with and without regrowth did not differ significantly.
Disclosure: Nothing to disclose

P1885 OUTCOMES FOLLOWING SURGERY FOR COMPLETELY REMOVED COLONIC LATERAL SPREADING LESIONS CONTAINING SUB-MUCOSAL INVASIVE CANCER

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Introduction: Management of malignant colorectal polyps can be endoscopic or surgical and the best approach has yet to be defined since prospective data is lacking. Endoscopic mucosal resection (EMR) is the treatment of choice for large (>20 mm) lateral spreading colonic polyps (LSL) with high success rates, good safety profile and clinical and economic advantages compared with surgery. There is no data on the outcome and management of malignant LSL (M-LSL) following complete removal by piecemeal EMR.

Aims & Methods: We aimed to determine if salvage surgery for M-LSL following complete EMR resection is necessary. We analyzed data from a prospectively collected database of patients who underwent EMR at three hospitals In Israel. Patients with M-LSL were identified and their surgical and pathological data was reviewed for the presence of residual neoplastic tissue and complication. The primary end-point was the presence of residual localo-regional cancer.

Results: Over 34 months 313 LSL in 303 patients were removed by EMR. 249/313 (81.7%) were removed piecemeal. Complete endoscopic resection was achieved in 249/249 (100%) which endoscopically were not suspicious for containing deep submucosal invasive cancer. The final EMR pathology showed invasive cancer in 23/249 (9.2%).

After multidisciplinary meeting (MDT), 5 cases were not sent to surgery (curative resection or high operative risk). 18 cases were referred for surgery following MDT because EMR was considered non-curative (presence of LVI/tumor budding/submucosal invasion>1mm/poor tumor differentiation/absence of clear margins or a combination thereof). In all cases, 18/18 (100%) patients underwent laparoscopic oncological resection with no major complications. There was no evidence of residual cancer in the resected colons or lymph nodes in all patients.

Conclusion: Colonic LSL removed by piecemeal EMR, may not require surgery even when submucosal invasive cancer is present in the resected EMR specimen. Further research may define specific criteria for avoiding surgery.

Disclosure: Nothing to disclose

P1886 THE IMPORTANCE OF INTRODUCING COLONOSCOPY SCREENING IN THE ADULT CYSTIC FIBROSIS PATIENTS: A SINGLE TERTIARY REFERRAL CENTRE ANALYSIS

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Introduction: The risk of colorectal cancer (CRC) in patients with cystic fibrosis (PWCF) is 10times greater than the general population and 30times greater post-transplant. Due to this increased risk new screening guidelines were published in Gastroenterology by the CF Colorectal Cancer Screening Task Force in 2018.

Aims & Methods: Our aim was to benchmark current practise at our centre against current guidelines. Our endoscopy database was interrogated from 2012 to present to identify PWCF who received a previous colonoscopy.
Results:
Group 1: PWCF non-transplant cohort;
161 patients were included. 26 were >40years. 4 patients had a previous colonoscopy (total number colonoscopies = 4). No colonoscopies were done for screening, all as patients were symptomatic. One patient had a polyp at colonoscopy. Adenoma detection rate (ADR) was 25%.
21 patients >40 have no previous colonoscopy. Surveillance for CRC in this cohort has yet to be implemented with 0% compliance to date.
Group 2: PWCF post solid-organ transplant;
16 patients were included. 13 were >30 years. 11 patients had a previous colonoscopy (total number colonoscopies = 20).

Reasons for index colonoscopy: 5 screening, 3 symptomatic, 3 no indication on report.
10 colonoscopies in total were done for screening.
3 patients had polyps found at index colonoscopy (2 adenomas high grade dysplasia, 4 adenomas low grade dysplasia) and surveillance colonoscopies were arranged subsequently. ADR was 27.27%. Current practise in the post transplant cohort is close to new recommendations with 84% compliance, however only 45.45% of index colonoscopies were done initially for screening.

Conclusion: Current guidelines are only in existence just over 12months. Our analysis suggests there is an awareness of the need for CRC screening in the post-transplant cohort but there is need for improvement. In PWCF with no previous transplant screening has not been a priority and needs to be implemented. Currently we are implementing a screening programme in keeping with current guidelines.

Disclosure: Nothing to disclose

P1887 INAPPROPRIATE NON-INVASIVE COLORECTAL CANCER REFERRAL TO SURGERY: A SCREENING POPULATION-BASED OBSERVATIONAL STUDY

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Introduction: Performance key measures of endoscopic resection and surgery referral are indefinite but heterogeneous operative skills can have a heavy impact on organized colorectal cancer screening programs.

Aims & Methods: Retrospective, observational 2-year study. Consecutive patients referred to surgery for colorectal neoplasms diagnosed in an organized screening program. Primary outcome: non-invasive neoplasm rates stratified on endoscopic staging (superficial vs. deep) and resection attempt. Invasive cancer was defined as cancer invading the submucosa (SM) or beyond on endoscopic and/or surgical specimens. Data were retrieved both from the county registry and cross-checked with date prospectively collected in endoscopy databases.

Results: A total of 468 patients were referred to surgery from 13 centers. Mean age was 64 (range 56-74); males 256 (58%); 213 (47%) from rural areas.

According to endoscopic morphology and approach before surgery, neoplasms were stratified in three groups: superficial underwent endoscopic resection (n.92, Sup-ER); superficial underwent biopsies (n.96, Sup-B); deep underwent biopsies (n.280, Deep-B). Sup-ER were significantly smaller (< 0.0001), more frequently pedunculated (< 0.0001) and in the left colon (< 0.0001) than Sup-B. Sup-ER underwent complete resection were significantly smaller (0.0059) and more frequently pedunculated (0.0433) than incomplete resections.

The non-invasive cancer rate was 11% for Sup-ER, 40% for Sub-B, and 9% for Deep-B. However, non-invasive cancer rate for mass ulcer-negative Deep-B (20%) was significantly higher than thos in stricturing and ulcer-positive (3% and 5%, respectively: P=0.0002).

Centers showed significantly different rates of Sup-ER underwent complete resection (57% to 100%, P=0.0001), quite significantly different overall non-invasive rates (P=0.0549), and significantly different non-invasive rates in Sup-B (P=0.0187). Overall non-invasive cancer rates in the 13 centers ranged from 0% to 30% (P=0.0581), being < 10% and >20% in 5 (29%) centers, respectively.

Non-invasive cancer rate of sup-B was significantly different ranging from 0% (in 5 centers) to >60% in 3 centers.

Conclusion: The rate of noninvasive cancers referred to surgery in screening programs should be measured because rates can be high and center performances widely heterogeneous. Most of noninvasive cancer referred to surgery can be related to suboptimal resection skill or unavailability of advanced techniques that would guarantee an en bloc resection and

accurate histology. Corrective actions should consider: improvement in endoscopic characterization in all centers; expert 2nd-look in endoscopic referral centers in which hybrid EMR and/or ESD can be performed. Rate of noninvasive cancers referred to surgery should be a quality measure both for endoscopic and surgical screening centers.

Disclosure: Nothing to disclose

P1888 IMPACT OF AN EARLY ACTIVE DIETARY COUNSELING ON GRADE ≥ 3 TOXICITY IN PATIENTS RECEIVING FIRST-LINE CHEMOTHERAPY FOR METASTATIC COLORECTAL CANCER

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Introduction: Malnutrition is frequent and negative in cancer patients. In particular, protein-energy malnutrition is associated with increased complications of chemotherapy.

Aims & Methods: This study aimed at assessing the benefits of an early and active individualized dietary counseling (DC) in patients receiving 1st-line chemotherapy for metastatic colorectal cancer (CRC). In a prospective multicentre study, non-malnourished patients were randomised to benefit (G1) or not (G2) from individualised DC by a dietician at treatment initiation and every 2 wk thereafter. ONS or EN/PN were prescribed based on guidelines. The primary endpoint was grade ≥3 toxicity over a 1-y follow-up. To show a 20% difference with a power of 80% and α=0.05, 80 patients per group were needed. Statistics were performed with logistic regressions and Chi-2 tests.

Results: 173 patients were analysed in ITT: G1 (n=85, F/M:31/54, 64±13 y); G2 (n=88, F/M:34/54; 63±12 y). The number of metastatic sites, PS, BMI (25±4 vs 26±4), and treatment protocols were similar. A grade ≥3 toxicity was seen in 49.4% of G1 and 67.0% of G2 patients (RR=0.367; 95%CI: 0.186-0.722; p= 0.0037) with a median delay of 359 (182- ...) vs 169 d (118-252). 9.4% of G1 and 19.3% of G2 patients died (p=0.065). Energy and protein intake of G1 patients exceeded those of G2 patients by 222±76 kcal/d and 11.4±4.8 g/d (p=0.004). Weight variations favoured G1 (p=0.007): at M3, G1 patients had a stable weight and G2 patients had lost 1,2 ± 0,6 kg. At M6, 14.8% of G1 and 30.8% of G2 patients (p=0.03) were malnourished. ONS were prescribed in 48.2% of G1 and 61.4% of G2 patients (p=0.08) and EN/PN in 7.1% of G1 and 14.8% of G2 patients (p=0,105).

Conclusion: An early and active DC reduces the risk of developing a grade ≥3 toxicity during the first-line chemotherapy of metastatic CRC. Even if further studies are needed in order to allow extrapolations, this work advocates a systematic dietary counselling in cancer patients receiving chemotherapy.

Disclosure: Nothing to disclose

P1889 EVALUATION OF THE ENTERIC NERVOUS SYSTEM BY THREE-DIMENSIONAL HOLOGRAPHIC IMAGING IN X-RAY PHASE NANOTOMOGRAPHY

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Introduction: The enteric nervous system (ENS) in dysmotility has been studied by classical light microscopy including immunohistochemistry. However, the procedure is rather time-consuming and only small components of the ENS in two dimensions can be analyzed. Novel x-ray imaging techniques, employed in this study, allow to obtain high-resolution three-dimensional scans of soft biological tissue over a longer segment with an overview of interganglionar neural connections, and different intraganglionar cell types, which would normally show no contrast with standard x-ray absorption microtomography.

Aims & Methods: The aim of the present study was to evaluate the ENS in a three-dimensional manner, to get a more complete architecture of the neural tissue in sickness and health. Full-thickness biopsies of ileum from a patient with Ehlers-Danlos syndrome and secondary severe gastrointestinal dysmotility and from a healthy resection border of proximal colon due to resection of the colonic carcinoma were embedded in paraffin and sectioned. Representative areas of the ENS with presence of myenteric ganglia and submucosal ganglia were identified in Hematoxylin & Eosin stained microscopic sections. By a 1-mm punch, a biopsy was extracted from the paraffin block and put into a plastic tube.

The samples were scanned, without any further preparation, in two different tomography instruments developed at the Institute for X-ray Physics of Georg-August-Universität, Göttingen [1]. The first instrument, a laboratory setup, allowed to image the whole 1-mm sample with a ~1mm effective voxel size during 8 hours with a microscope coupled sCMOS, enabling an identification of the neural tissue structure. Phase retrieval suitable for low coherence sources was performed using the Bronnikov Aided Correction scheme, and cone beam tomographic reconstruction were implemented based on the ASTRA toolbox. Selected regions of interest were then scanned in the second instrument, a synchrotron-based instrument (GINI-X, P10, DESY, Hamburg), which allows to image regions of 320x320x320 mm³ with an effective voxel size of 176 nm. At this resolution, individual cells inside the ganglia can be distinguished.

From the coarser-resolution tomographic scans, the neural tissue structure has been extracted with semi-automatic segmentation methods. Preliminary digital quantification of the volume of the neural tissue over total biopsy volume, were performed from the segmented volumes. A more-in-depth digital analysis, currently in progress, will allow to measure parameters such as the length and average diameter of the ganglia.

Results: The myenteric ganglia from the control were normal regarding both size and cellularity. Neurons and glia cells could be recognized. Between the ganglia, the nerve-bundles were thick and sharply demarcated. In contrast, the ganglia from the patient were smaller and the interganglional nerves were uneven/irregular with alternating thin and "small nodular" regions. Preliminary digital quantification showed that the ratio of neural tissue volume over total biopsy volume in the patient (0.9%) was significantly diminished compared to the control (7.3%).

Conclusion: Three-dimensional nanotomography may be a useful tool and can give valuable information on the changes of the size and interganglionar neural connections of the ENS in dysmotility diseases which cannot be obtained/received by classical methods.

References: [1] Töpperwien, M., van der Meer, F., Stadelmann, C. and Salditt, T., 2018. Three-dimensional virtual histology of human cerebellum by X-ray phase-contrast tomography. Proceedings of the National Academy of Sciences, 115(27), pp.6940-6945.

Disclosure: Nothing to disclose

P1890 THE SIGNIFICANCE OF ILEUS IN THE POST-KIDNEY TRANSPLANT SETTING: A HEALTHCARE UTILIZATION PERSPECTIVE

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Introduction: Ileus is a known early complication following kidney transplant (KTx). Approximately 16,000 KTx surgeries are performed each year in the US, thus it is imperative to study and find solutions to potential hospital complications post-transplant. There is limited data largely from case reports documenting the occurrence of ileus in KTx patients. Potential risk factors include post-operative setting, steroid withdrawal, or even peritoneal sclerosis in patients with a history of peritoneal dialysis (PD).

Aims & Methods: The aim of this study is to assess inpatient prevalence and outcomes of ileus in the same admission as the KTx occurred. Case-control study using the NIS 2012-2016, the largest publically available inpatient database in the US. The ICD9-10CM procedural codes for kidney transplant were used to identify all patients that underwent KTx during the same admission. None were excluded. Patients with associated ileus were identified using ICD9-10CM diagnostic codes. The primary outcome was determining the odds of ileus in post-KTx patients. Secondary outcomes were inpatient mortality, postoperative complications, measured by shock, ICU stay, resource utilization, length of hospital stay (LOS), total hospitalization charges and costs. Propensity score matching was used to create a matching population for gender, age and Charlson Comorbidity Index. Multivariate regression analyses were used to adjust for income in patients' zip code, hospital region, location, size and teaching status.

Results: A total of 89,065 KTx patients were identified, of which 16,880 were propensity score matched for the selected covariates. The mean patient age was 50 years, and 40% were female. On multivariate analysis, the odds of ileus in the KTx cohort was 3.90 (p< 0.01) compared to patients who did not undergo KTx surgery. When patients that underwent KTx and developed ileus during the admission, they had greater adjusted odds of shock 6.22 (p< 0.01), TPN 11.24 (p< 0.01), AKI 1.97 (p< 0.01), multi-organ failure 1.85 (p< 0.01), post-op infection 17.7 (p< 0.01), Deep Vein Thrombosis 2.3 (p=0.02), Pulmonary Embolism 2.79 (p=0.02), and bleeding 2.44 (p=0.04) compared to patients with no KTx. In addition, those who developed ileus had greater hospitals costs, charges, and length of stay (LOS) (Table 1).

Variable	aOR	95%CI	p-value
Ileus in patients with KTx	3.90	3.41-4.46	<0.01
Inpatient Mortality	2.94	0.67-12.83	0.15
ICU	1.60	0.68-3.73	0.27
TPN	11.24	2.43-52.10	<0.01
AKI	1.97	1.28-3.03	<0.01
Post-op infection	17.70	4.12-75.98	<0.01
DVT	2.30	1.12-4.75	0.02
PE	2.79	1.16-6.74	0.02
Post op Shock	2.96	0.69-12.68	0.14
Variable	Adjusted Means	95%CI	p-value
Additional Adjusted Costs	$40,182	21216-59147	<0.01
Additional Adjusted Charges	$129,933	52424-207441	<0.01
Additional Adjusted LOS (days)	13.1	5.1-21.1	<0.01

[Table 1 - Adjusted odds ratio and additional means to the evaluated variables in patients with kidney transplant surgery that develop ileus]

Conclusion: Patients undergoing kidney transplant are more likely to develop ileus than patients who did not have kidney transplant surgery, confirming known reports documenting ileus in the early post-operative period. This cohort of patients who developed ileus following transplant have greater odds of post-operative complications, as well as increased morbidity, resource utilization and economic burden. Future studies should focus on elucidating the etiology of ileus following kidney transplant, as well as associated factors, and creating strategies to address it.

Disclosure: Nothing to disclose

P1891 THE PREVALENCE AND BURDEN OF ROME IV FUNCTIONAL COLORECTAL DISORDERS IN ULCERATIVE COLITIS

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Introduction: Despite advances in Ulcerative Colitis (UC) therapies, many patients suffer refractory symptoms in the absence of active inflammation. For this group, treatment remains challenging, with a paucity of therapeutic options. In this prospective, ongoing study, we aim to determine the prevalence and burden of functional colorectal disorders inpatients with quiescent UC using validated questionnaires.

Aims & Methods: In a cross-sectional study, consecutive patients with UC attending Inflammatory Bowel Disease (IBD) clinics were invited to participate. Patients completed a series of validated questionnaires; including Hospital Anxiety and Depression Scale (HADS), the Rome IV diagnostic questionnaire for functional gastrointestinal disorders (FGIDs), an IBD-QoL score and the IBD-control questionnaire. Participants were requested to return a Faecal Calprotectin (FCP) within 2 weeks of completing questionnaires. Quiescent UC was defined as IBD-control 8 score ≥13 and IBD-control-VAS ≥85, and/or FCP levels ≤250 (where available, FCP data were used in preference to IBD-control to classify UC activity). Based on Rome IV diagnosis and UC disease activity (active or quiescent), patients were divided into groups and data compared using non-parametric tests.

Results: Overall, n=97 UC patients (n=50 males, mean age 48 (range 18-82)) participated. 41/97, (42%) UC patients met the Rome IV diagnostic criteria for ≥1 FGIDs (irritable bowel syndrome n=26, functional constipation n=6 and faecal incontinence (FI) n=22). Disease activity data (IBD-control and/or FCP) were available for all patients, and based on these 61/97, 63% had quiescent UC. Within the quiescent UC group, 25/61 (41%) met the Rome IV diagnostic criteria for ≥1 FGIDs (irritable bowel syndrome n=14, functional constipation n=3 and FI n=13). Within the active UC group, those with co-existing FGIDs, compared to those without FGIDs, had significantly worse median QoL scores (P=0.02), higher HADS-depression (P=0.005) and HADS-anxiety (P=0.05). By contrast, in those with quiescent UC, those with an FGID did not have different median HADS scores (depression P=0.15, anxiety P=0.62) or IBD-QoL scores (P=0.20), compared those without FGIDs.

Conclusion: This study is one of the first to use Rome IV criteria in UC and confirms that the prevalence of FGIDs is high. Patients with active disease and overlapping functional symptoms appear to have worse QoL and more psychological distress compared to those with quiescent disease. Clinicians should therefore be vigilant to this functional overlap and treat both functional and inflammatory driven symptoms.

Disclosure: Nothing to disclose

P1892 TRANSANAL IRRIGATION SIGNIFICANTLY IMPROVES SATISFACTION WITH BOWEL MANAGEMENT IN PATIENTS SUFFERING FROM FUNCTIONAL INCONTINENCE, FUNCTIONAL CONSTIPATION OR LOW ANTERIOR RESECTION SYNDROME: A MULTICENTRIC RETROSPECTIVE STUDY

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Introduction: Transanal irrigation (TAI) is a safe technique designed to assist the evacuation of faeces from the bowel in a controlled manner by introducing water via the anus. This is a widely accepted alternative to

conventional management strategies and is intended to allow people with bowel dysfunction to flush out the distal colon as part of their bowel management strategy, promoting the rehabilitation of bowel function. This also enables the users to choose the time and place of evacuation and to develop a consistent bowel routine.

Aims & Methods:

Aim: To assess how TAI modifies Quality of Life (QoL) of patients with functional constipation (FC), fecal incontinence (FI) and low anterior resection syndrome (LARS).

Methods: Between 1/2016 and 12/2018 patients suffering from FC, FI or LARS were treated with TAI in 11 Italian centers. The primary endpoint was QoL, measured through VAS (all patients) and through validated questionnaires such as Pac-QoL (FC), FI-QoL (FI), Wexner score (FC, FI) and LARS score (LARS); secondary endpoint included patient's compliance analysing dropout rate.

Results: Results concern 195 patients (FI, N=14; FC, N=101; LARS, N=80). The Wexner score after 6 months dropped from 13±5 to 1±2 in FI patients (p< 0.001) and, after 12 months, from 16.6±6.5 to 11.2±3.1 in FC ones (p< .001). The VAS score increased significantly after 1 month (5.6±3.3 vs. 7.8±2.1 for FI patients; 3.8±2.7 vs. 6.8±1.9 for FC patients and 2.3±1.4 vs. 6.8±2.1 for LARS patients, p< .001 in all cases) and further improved over time. LARS patients experienced a drop in the LARS score from 33.7±10.4 to 11.3±12.5 (p< .001) on the first month and at 24 months their LARS score was 0.5±3.1. The average dropout rate at the last follow up was 20.4%.

Conclusion: Patients suffering from IF, FC or LARS were compliant to TAI and experienced significant QoL improvement.

References: 1.Role of transanal irrigation in the treatment of anterior resection syndrome. Tech Coloproctol. 2018 Jul;22(7):519-527. 2.Trans-anal irrigation should be offered to patients with severe bowel dysfunction. Br J Gen Pract. 2019 Mar;69(680):136 3.American College of Gastroenterology Chronic Constipation Task Force An evidence-based approach to the management of chronic constipation in north america. Am J Gastroenterol. 2005;100:1-4. 4.Trans-anal irrigation therapy to treat adult chronic functional constipation: systematic review and meta-analysis. BMC Gastroenterol. 2015

Disclosure: Nothing to disclose

P1893 RELEVANCE OF CENTRAL SENSITIZATION FOR GASTROINTESTINAL SYMPTOMS

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Introduction: Central sensitization (CS) has been proposed to be an important mechanism for symptom generation in functional gastrointestinal disorders (FGID). In this study, we explore the association between symptoms and CS in patients with FGID, and in volunteers with no or mild GI symptoms.

Aims & Methods: Patients with FGID according to Rome IV and volunteers completed questionnaires assessing central sensitization (CSI), sensory processing sensitivity (HSP), GI symptoms (GSRS-IBS), psychological distress (HAD) and non-GI symptoms (PHQ-12). The validated cut-off of CSI (≥40) distinguished between persons with and without reported CS.

Results: We included 77 FGID patients and 79 volunteers (median age 30 [26-39] vs. 25 [22-32] years (p< 0.001); females 57 (74%) vs. 41 (52%) (p=0.007)).

Thirty-three (43%) patients and one (1%) volunteer reported CS. Patients with CS were older (36 [27-47] years vs. 28 [24-33] years, p=0.02), had more severe overall GI symptoms (4.0 [3.8-4.5] vs. 3.7 [3.2-4.2], p=0.03) and non-GI symptoms (9 [8-10] vs. 6 [4-8], p< 0.001) than patients without CS, but with no significant differences in psychological distress or sensory processing sensitivity. Linear trend analyses in all study subjects (divided into CS quintiles) demonstrated gradual increase of GI symptom severity with increasing severity of CS with large effect sizes (Table 1). Furthermore, moderate to strong correlations were seen between CS and GI symptoms (total: rho=0.68; abdominal pain: rho=0.64; bloating: rho=0.65; constipation: rho=0.56; diarrhoea: rho=0.58; satiety: rho=0.55, all p< 0.001).

GSRS-IBS domain	p-value	Partial η^2
Total score	<0.001	0.44
Pain syndrome	<0.001	0.40
Bloating syndrome	<0.001	0.40
Constipation syndrome	<0.001	0.26
Diarrhoea syndrome	<0.001	0.29
Satiety syndrome	<0.001	0.27

[Table 1: Linear relationships between increasing level of central sensitization and gastrointestinal symptoms.]

Conclusion: Central sensitization is common in patients with functional gastrointestinal disorders, and clearly associated with GI symptom severity, indicating that it seems to be an important factor for GI symptom generation.

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P1894 FUNCTIONAL CONSTIPATION IN DIFFERENT PHENOTYPES OF ELDERLY PEOPLE. PREVALENCE OF CLINICAL SYMPTOMS, RISK FACTORS, PATHOPHYSIOLOGY AND IMPACT ON QUALITY OF LIFE

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Introduction: Functional constipation (FC) is a prevalent disorder in elderly people. It impacts on healthcare and quality of life (QoL). The frail phenotype is associated to poor health outcomes including disability, hospitalization, and mortality.

Aims & Methods: To determine the prevalence, pathophysiology and symptoms of FC among older people, and its association with frailty.

This was an epidemiological study of individuals over 70 years of age, stratified into robust, pre-frail and frail (Fried criteria (2)), and recruited from the community, an acute hospital and a nursing-home. Variables collected were sociodemographic data, frailty, Rome III symptoms (1), Brsitol scale for faecal consistency, dependence, cognitive status, and QoL. Anorectal manometry and CTT were performed on a second sample of 56 community-living patients with FC, and 25 hospitalized patients underwent a balloon expulsion test (BET).

Results: The study included 416 patients, 50.2% men, with a mean age of 79.64±6.8. Prevalence of FC was 26.8% (32.4% women, 21.8% men; p=0.019). Excessive strain (89.3%) and hard stools (75.7%) were the most prevalent symptoms in FC, 20.4% showed < 3 bowel movements/week. Patients with FC showed poorer results in QoL. Prevalence of FC was higher in the frail group (41.7%) than pre-frail (33.9%) or robust (24.2%) (p< 0.001).

Obstructive defecation symptoms were very prevalent in frail and pre-frail (53.5% and 48.6%, respectively). In robust the most prevalent subtype was mixed.

Regarding pathophysiology, All robust patients showed dyssynergic defecation, and delayed CCT in 40%. Only 17.3% of the pre-frail had normal BET.

Conclusion: The prevalence of FC in older people, especially women, is very high, and is associated with frailty and poor QoL. Its pathophysiology is mainly associated with dyssynergic defecation and hard stools.

FC differs between gender, age and functional status. Management should be tailored to patient characteristics and underlying pathophysiology.

References: 1. Drossman DA, Douglas A. The Functional Gastrointestinal Disorders and the Rome III Process. Gastroenterology 2006; 130:1377-1390. 2. Xue QL, Bandera Roche K, Varadhan R, Zhou J, Fried L. Initial Manifestation of Frailty Criteria and the Development of Frailty Phenotype in the Women 's Health and Aging Study II. Journal of Gerontology 2008;63: 984-99

Disclosure: Nothing to disclose

P1895 NALOXEGOL PARTLY RESTORES CHANGES IN THE POSTPRANDIAL CYCLIC MEAL RESPONSE OF THE COLON IN A RANDOMIZED THREE-WAY CROSSOVER HIGH-RESOLUTION COLON MANOMETRY STUDY IN HEALTHY VOLUNTEERS

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Introduction: Opioid induced constipation (OIC) is a prevalent condition amongst patients treated with opioids for chronic pain. Constipation and other side effects can be as prevalent as 40-90% resulting in non-compliance and quality of life reduction. The effects of opioids on colonic motor function and their reversal by opioid antagonists have been poorly studied. We therefore conducted a crossover trial to study effects of codeine and the peripheral μ-opioid receptor antagonist naloxegol on colonic manometry patterns in healthy volunteers (HV).

Aims & Methods: On each of three study visits, participants underwent a colonoscopy (conscious sedation with midazolam 2-5mg IV) after half-standard PEG preparation for colonic manometry catheter (40-sensor high-resolution manometry catheter 2.5 cm spacing, Laborie, Mississauga, Canada) placement. Colonic motility was evaluated during 2 hours after a standardized bread meal (645 kcal). After waking up, HV received naloxegol (25mg)/placebo, placebo/codeine (60mg followed by 30mg one hour after the meal) or naloxegol/codeine by oral administration in a randomized, double-blind crossover fashion. Symptom registration for abdominal pain, discomfort, bloating, gas, desire to defecate and urge was performed every 15 minutes during the entire measurement on a visual analogue scale (VAS). A total symptom score was calculated for each symptom by adding the scores for the entire measurement. The data were analysed using mixed-models analysis in SAS with post-hoc analysis after correction for multiple testing.

Results: Ten HV [3 male, aged 26.5 (range 20 - 63) years] finalized all three study visits.

Data on motor pattern prevalence are presented in Table 1 [data are reported as median (interquartile range). (a) p< 0.01 vs. placebo/codeine, (b) p< 0.05 vs. placebo/codeine, (c) p< 0.05 vs. naloxegol/placebo]. Long anterograde propagating waves (PW) were significantly decreased in the codeine/placebo compared to codeine/naloxegol condition. No significant differences were found for short anterograde PW or short retrograde PW. The postprandial cyclic patterns were significantly altered by the treatment condition. First, the cyclic anterograde PW were lower in the placebo/codeine compared to the naloxegol/placebo and naloxegol/codeine treatment. Second, the cyclic retrograde were significantly more frequent in placebo/codeine compared to the two other treatment groups. Finally, significantly less cyclic simultaneous PW were present in the naloxegol/placebo vs. placebo/codeine condition.

The total score for abdominal discomfort was significantly less in the placebo/codeine condition compared to the naloxegol/codeine condition (p=0.046). No significant differences were found for bloating, gas, desire to defecate, urge or abdominal pain.

	Naloxegol/Placebo	Placebo/Codeine	Naloxegol/Codeine	p-value main effect
Short anterograde PW	3.0 (2.00-5.50)	2.5 (1.00-4.50)	4.0 (2.00-7.00)	0.307
Short retrograde PW	6.0 (2.75-15.00)	3.5 (2.00-4.00)	4.0 (3.25-7.75)	0.544
Long anterograde PW	2.0 (0.75-7.00)	1.5 (0-3.00)	3.5 (2.00-12.00)a	0.005
Cyclic anterograde PW	14.5 (7.25-21.75)b	7.0 (3.75-13.50)	15.0 (5.25-23.00)b	0.013
Cyclic retrograde PW	43.5 (20.75-65.00)b	78.0 (43.50-84.50)	37.5 (17.75-52.75)a,c	0.003
Cyclic simultaneous PW	7.0 (2.25-16.25)a	17.5 (6.25-50)	10.0 (5.25-13.00)	0.006
Simultaneous PW	3.0 (0.75-6.50)	2.0 (0.75-3.25)	2.5 (2.00-7.25)	0.361

[Overview of colonic motor pattern prevalence in the postprandial period after codeine and naloxegol administration. (PW: Pressure wave)]

Conclusion: Codeine administration increased cyclic retrograde activity and decreased cyclic anterograde activity in the postprandial period and this effect was reversed by naloxegol. These observations enhance our understanding of the mechanism of OIC and its treatment with peripheral μ-opioid receptor antagonists.
Disclosure: Nothing to disclose

P1896 PREDICTING SUCCESSFUL OUTCOMES OF ANORECTAL BIOFEEDBACK FOR CONSTIPATION: RESULTS OF EXTENSIVE PSYCHOLOGICAL EVALUATION BEFORE TREATMENT AND CORRELATIONS WITH TREATMENT OUTCOMES

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Introduction: Anorectal biofeedback (BF) is a well-established treatment for patients with constipation and functional defaecation disorders, however demand greatly exceeds supply. There is some evidence that pre-treatment clinical or physiological factors may predict success of treatment[1]. As biofeedback is a form of behavioural therapy, we hypothesised that psychological traits could help predict response to BF in constipation

Aims & Methods: To describe pre-BF treatment psychological traits of constipated patients and to evaluate these as predictors of favourable response to treatment.

77 consecutive constipated patients undergoing anorectal BF completed a pre-treatment computer-based questionnaire of multiple emotional state and cognitive psychology measures, in addition to baseline clinical and anorectal physiology testing. Patients underwent weekly BF visits over 6 weeks. The main outcome measure was physician-assessed response to BF (moderately-greatly improved), blinded to baseline psychological evaluation results. Secondary outcome measures included change in patient-rated visual analog scales of impact of bowel dysfunction on quality of life (VAS QOL), feeling of control (VAS control) and satisfaction with bowel motions (VAS satisfaction).

Results: 69 (90%) patients completed BF (mean age 51+-17 yrs, 62 female). Patients with paradoxical anal contraction on push were more likely to respond to BF (OR 5.3, 95% CI 1.2-24, p=0.3), as well as patients with higher self-efficacy scores (OR 1.2, 95% CI 1.1-1.4, p=0.002), higher treatment efficacy expectancy (OR 1.1, 95% CI 1.1-1.2, p=0.03), higher internal health locus of control (OR 2.2, 95% CI 1.2-4.1, p=0.01), and lower perceived stress sub-score of worries (OR 0.4, 95% CI 0.2-0.9, p=0.03). On multivariate analysis incorporating all baseline physiology and psychological predictors, internal health locus of control was the only predictor of a favourable response to BF.

Psychological and cognitive measures also predicted all VAS secondary outcomes. For example, lower scores on perceived stress sub-scores of worries again predicted more improvement in VAS QOL (coef -2.7,, 95% CI -4.4 - (-1.1), p< 0.01) and VAS control (coef. -2.7, 95% CI -4.4 - (-0.9)), while higher treatment efficacy expectancy predicted more improvement in VAS satisfaction (coef. +0.3, 95% CI 0.2-0.4, p< 0.001) and VAS control (coef. +0.2, 95% CI 0.1-0.3, p=0.03).

Conclusion: Success of anorectal biofeedback therapy for constipated patients is dependent on patients' psychological and coping strategies. Addressing potential psychological barriers prior to BF might optimise future patient outcomes

References: 1. Shim L, Jones M, Prott G, Morris L, Kellow J, Malcolm A. Predictors of outcome of anorectal biofeedback therapy in patients with constipation. Aliment Pharmacol Ther. 2011 Jun;33(11):1245-51.
Disclosure: Nothing to disclose

P1897 VOLUMETRIC RECTAL SENSATION TESTING: IS IT CLINICALLY RELEVANT? RESULTS FROM A LARGE PATIENT COHORT

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Introduction: Research based rectal sensory testing using a barostat and infinitely compliant balloon, has previously revealed correlations between disease states and both rectal hypo- and hyper- sensitivity[1]. Similar data for the volumetric only sensation testing methods employed in clinical practice (using a compliant balloon) are lacking, and differences between the commonly measured thresholds for first sensation, urge and maximal tolerated volume (MTV) are unknown.

Aims & Methods: Our aims were, therefore, to determine: (1) Does volumetric rectal balloon sensation testing correlate with disease states? (2) Which, if any, of the three sensory thresholds tested is most relevant for each disease state?

1251 patients (mean age 53+-18, 92% female) referred for volumetric rectal balloon sensation testing as part of anorectal manometry were included in the study. All patients completed the Rome and hospital anxiety and depression (HAD) questionnaires. Data regarding possible factors associated with alterations in rectal sensation were prospectively collected, including relevant surgical, medical and obstetric history. Univariate analysis of all factors was followed by multivariate analysis of positive variables, with sensation thresholds used as continuous outcome measures. Next, volumetric rectal sensitivity values were categorised into low, normal or high using data derived from 44 healthy female volunteers, and distribution of disease states across the categories was compared in a subgroup of female patients (n=1107).

Results: Presenting symptoms of constipation, older age and longer balloon expulsion time (BET) were associated with higher thresholds for all sensations (p< 0.05 for all comparisons). Presenting symptoms of faecal incontinence (FI) was associated with lower thresholds for all sensations (p< 0.001 for all comparisons). The presence of connective tissue disease was associated with lower urge to defecate and lower MTV, while previous pelvic radiation therapy and irritable bowel syndrome (IBS) were associated with lower values on MTV only (p< 0.05 for all).

Using normal values for reference in the female subgroup, older age was associated with hyposensitivity (higher than normal values) on first (OR 1.03, 95% CI 1.02-1.04), urge (OR 1.03, 95% CI 1.02-1.04), and MTV thresholds (OR 1.03, 95% CI 1.01-1.03, respectively) (p< 0.01 for all). Patients presenting with constipation were more likely to be hyposensitive on MTV (OR 2.6, 95% CI 1.8-3.7, p< 0.001), while FI were hypersensitive (lower than normal values) on urge (OR 0.3, 95% CI 0.2-0.5, p< 0.001). Hypersensitivity on first sensation was associated with inflammatory bowel disease (OR 0.3, 95% CI 0.1-0.9, p=0.03), and hypersensitivity on urge sensation with connective tissue disease (OR 0.4, 95% CI 0.2-0.9, p=0.04).

Conclusion: Volumetric sensory testing as commonly practiced is correlated with some disease states known to affect rectal sensation, and thus has clinical relevance. Several conditions, such as IBS, inflammatory bowel disease and connective tissue disease, were correlated with only two or even a single abnormal threshold, suggesting the three sensation thresholds may measure different pathophysiological pathways and should continue to be used in clinical practice.

References: 1. Remes-Troche J, Rao S. Neurophysiological testing in anorectal disorders. Expert Rev Gastroenterol Hepatol. 2008 June ; 2(3): 323-335.

Disclosure: Nothing to disclose

P1898 EFFECT OF DEVICE ASSISTED -AUTOMATIC ABDOMINAL MASSAGE ON THE BOWEL MOVEMENTS IN PATIENTS WITH FUNCTIONAL CONSTIPATION: A PROSPECTIVE STUDY

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Introduction: Manual abdominal massage has been shown to be effective in treating slow transit constipation even burdensome. To improve care efficacy, Bamk-001, a device for automatic abdominal massage, was newly developed.

Aims & Methods: The purpose of this study was to assess the effect of Bamk-001 on symptom profiles and the colonic transit time (CTT) in patients with chronic constipation.

Thirty seven patients with functional constipation diagnosed by Rome IV criteria were enrolled prospectively from December 2018 to Feburary 2019. All of the patients received device assisted-automatic abdominal massage for 15minutes twice a day once in the morning before breakfast and once at night in 14days. CTT was done before and end of the study periods. Symptom profile including spontaneous bowel movements, straining, stool form, feeling of incomplete emptying, anorectal blockage, abdominal discomfort, overall defecation satisfaction, and device related adverse events were analyzed.

Results: Thirty seven patients were finally enrolled. Bamk-001 statistically significantly improved CTT from 54.0[33.6-75.6] hour to 28.8[18.0-52.8] (p=0.001). Both of left sided and rectosigmoid segmental CTT also significantly improved from 21.6[12.6-41.7] to 13.2[3.3-26.7] and from 15.0[6.9-26.7] to 3.6[0.0-13.2], respectively. Moreover, all of the patients' symptom profiles were alleviated after treating. No serious adverse events were reported.

Conclusion: Bamk-001, newly developed device for automatic abdominal massage, showed excellent care efficacies including improved CTTs and symptom profiles in patients with functional constipations. Device assisted-automatic abdominal massage, as an adjunct to management of constipation, offers an acceptable and potentially beneficial intervention to patients with chronic constipation.

References: 1. Sommers T, Mitsuhashi S, Singh P, et al. Prevalence of Chronic Constipation and Chronic Diarrhea in Diabetic Individuals in the United States. Am J Gastroenterol 2018. 2. Choung RS, Branda ME, Chitkara D, et al. Longitudinal direct medical costs associated with constipation in women. Aliment Pharmacol Ther 2011;33:251-60. 3. Almario CV, Ballal ML, Chey WD, et al. Burden of Gastrointestinal Symptoms in the United States: Results of a Nationally Representative Survey of Over 71,000 Americans. Am J Gastroenterol 2018;113:1701-1710. 4. Heidelbaugh JJ, Stelwagon M, Miller SA, et al. The spectrum of constipation-predominant irritable bowel syndrome and chronic idiopathic constipation: US survey assessing

Disclosure: Nothing to disclose

P1899 UTILITY OF CT COLONOGRAPHY AS A DIAGNOSTIC PROCEDURE FOR IRRITABLE BOWEL SYNDROME

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Introduction: Computed tomography colonography (CTC) has been developed as a less invasive alternative method to colonoscopy for colorectal cancer screening. Some subjects who underwent CTC reported abdominal pain induced by carbon dioxide gas injection during examination. We speculated that pain perception during CTC might reflect visceral hypersensitivity related to irritable bowel syndrome (IBS).

Aims & Methods: A prospective study of consecutively registered patients who underwent CTC for colorectal cancer screening between April 2018 and March 2019 in a single medical center was conducted. IBS was diagnosed using the Rome IV criteria, and patients with IBS were classified into IBS subgroups according to the predominant stool pattern experienced by the patient. In addition, all subjects completed the IBS Severity Scale (IBS-SS) and IBS-QOL questionnaire. Pain perception during CTC

was quantified using the visual analog scale (VAS) at six time points during the CTC as follows: (1) before CTC, (2) immediately after carbon dioxide gas injection, (3) until the injection pressure reached a plateau (18 mmHg), (4) in the prone position after carbon dioxide gas injection, (5) in the supine position after carbon dioxide gas injection, and (6) after CTC. We also evaluated the association between the VAS and IBS-SS scores.In this study, we investigated whether pain perception induced by carbon dioxide gas injection during CTC is different between patients with IBS and healthy controls. Furthermore, we evaluated the correlation between the pain score during CTC and the severity of the IBS symptom or the quality of life of patients with IBS.

Results: One hundred twenty-three subjects who underwent CTC were enrolled in this study. Thirteen subjects were excluded because of incomplete questionnaires (n = 10) or a diagnosis of colorectal cancer with CTC (n = 3). Fifteen patients were diagnosed as having IBS on the basis of the Rome IV criteria for IBS. Patients with IBS were classified into the following groups: IBS with diarrhea (IBS-D, n = 1), IBS with constipation (IBS-C, n = 3), mixed IBS (IBS-M, n = 3), and unspecified IBS (IBS-U, n = 8).

No significant differences in background characteristics, including age, sex, alcohol consumption, and smoking habit, were found between the IBS and control groups. The volume of carbon dioxide gas injected during CTC did not show a significant difference between the two groups. The total colon length was not significantly different between the two groups. The VAS score of the IBS groups was significantly higher than that of the control group at two time points, (2) immediately after carbon dioxide gas injection (p < 0.01) and (3) until the injection pressure reached a plateau (18 mmHg; p < 0.01). The maximum VAS score during CTC was also significantly higher in the IBS groups than in the control group (p < 0.05). Although the IBS-SS score was significantly higher in the IBS groups than in the control group, we found no significant correlation between the VAS and IBS-SS scores in the IBS groups. The IBS-QOL score also did not show any significant correlation with the VAS score.

Conclusion: Our study indicates that pain perception evaluated using the VAS during CT colonography might be a potential diagnostic method for IBS. Further study is necessary to clarify the association between pain perception induced by CT colonography and IBS severity.

Disclosure: Nothing to disclose

P1900 SERUM DIAMINE OXIDASE LEVELS IN IBS AND HEALTHY VOLUNTEERS

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Introduction: Diamine Oxidase (DAO) is the extracellular enzyme for histamine degradation pathway. It was recently reported that DAO is an accurate marker of intestinal mucosal integrity in intestinal diseases (Garcia Martin 2007) and after chemotherapy (Motoori 2017) and it was shown in rats that duodenal lipid infusion increases intestinal DAO activity (Ji 2013), suggesting its use to detect intestinal permeability alterations.

Aims & Methods: The aims of the study was the measurement of serum DAO levels in patients with IBS, IBD and HV to ascertain whether it could suggest intetsinal barrier defects. We enrolled 31 IBS patients (12 F, mean age 28±4 yrs; 22 IBS-D and 9 IBS-D) and 21 HV (12 F, mean age 27±5 yrs). Moreover, as pathologic control group, 10 IBD patients in remission were also enrolled (4 F, mean age 31±4 yrs, 5 CD and 5 RCU). Serum samples were collected after an overnight fast and serum DAO was measured (DAO ELISA Listarfish, Italy). In all the subjects, intestinal permeability was detected with lactulose/mannitol test. Lactulose/mannitol % dose urinary recovery was determined after oral administration of 1g of mannitol and 5 g of lactulose.

Results: In HV, serum DAO was significantly higher than in IBS and IBD patients (9.5±1.7, 5.7±2.9, and 4.1±1.8 U ml, respectively, p< 0.01). In IBS, the subgroup of patients with postprandial symptoms showed lower DAO levels than the subgroup without postprandial symptoms (2.3±1.0 vs 6.3±4.6 U ml, respectively, p< 0.01). In IBS patients, serum DAO was slightly correlated with %LMER (r=0.41). Serum DAO levels did not correlate with gender, age, severity of symptoms, duration of disease.

Conclusion: Serum DAO is reduced in both IBS and IBD patients, suggesting a role in the detection of intestinal permeability defects. Moreover, the reduced levels in IBS patients with postprandial symptoms may suggest a role of meal ingestion also in the pathophysiology of IBS symptoms.
Disclosure: Nothing to disclose

P1901 PHENOTYPIC CLASSIFICATION OF ADULT PATIENTS WITH FUNCTIONAL BOWEL DISORDERS OR FUNCTIONAL ABDOMINAL PAIN

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Introduction: Patients with functional bowel disorders (FBD) are classified using the Rome criteria. However, this classification does not take account the intensity of symptoms and bloating.
Aims & Methods:
The purpose of this study is to evaluate whether the intensity of the cardinal signs of FBD (constipation, diarrhea, bloating, abdominal pain) could be used to identify homogeneous groups of patients regardless the Rome criteria.
In this observational study, 1729 consecutive ambulatory FBD patients (73% females) completed the Rome III questionnaire and 10-point Likert scales for the intensity of constipation, diarrhea, bloating and abdominal pain during the week preceding the consultation.
A Gaussian mixture model was used to aggregate patients according to the cardinal signs of FBD without prior information. A classification tree using the intensity of the cardinal signs of FBD was proposed. The comparison of these two classifications were analyzed using ANOVA and logistic regression.

Results: According to the Rome criteria, 707 patients (41%) were classified as having irritable bowel syndrome (IBS) (234 (14%) IBS-Constipation, 225 (13%) IBD-Diarrhea, 126 (7%) SII-Mixed, 122 (7%) IBS-Nonspecific), 374 (22%) functional constipation, 215 (12%) functional diarrhea, 101 (6%) bloating and 194 (11%) non-specific.
According to the intensity of cardinal signs of FBD, patients were divided into 8 clusters named according to their main symptomatology: "painful constipation" (285, 16%), "mild pain constipation" (236, 14%), "painful diarrhea" (166, 10%), "mild-pain diarrhea" (178, 10%), "mixed transit" (126, 7%), "bloating" (255, 15%), "abdominal pain" (89, 5%) and "non-specific"(394, 23%).
The study of the relationship between the Rome III classification and this new classification showed that IBS-Constipation is associated with "painful constipation" (P < 0.01), SII-Diarrhea with "painful diarrhea" (P < 0.01) and "mild pain diarrhea"(P < 0.01), SII-Mixed with" mixed transit "(P < 0.01), SII-nonspecific with "bloating" (P < 0.01), functional constipation with "painful constipation"(P < 0.01) and" mild pain constipation "(P < 0.01), functional diarrhea with "mild pain diarrhea" (P < 0.01) and "nonspecific" (P < 0.01), bloating with "bloating" (P < 0.01) and nonspecific (P < 0.01), non-specific FBD with "non-specific" (P < 0.01) and functional abdominal pain with "bloating" (P < 0.01) and "abdominal pain" (P < 0.01).
Conclusion: This study conducted in a large FBD population shows that the symptomatic phenotype is partially associated with the Rome III criteria. This new classification can be used in addition with the Rome criteria to specify these criteria in clinical or therapeutic studies.
Disclosure: Nothing to disclose

P1902 PROSPECTIVELY RECORDED GASTROINTESTINAL SYMPTOM LEVELS DISCRIMINATE GASTROINTESTINAL DISORDERS FROM HEALTH AND ARE SUPERIOR TO A VALIDATED WIDELY APPLIED SYMPTOM BURDEN MEASURE

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Introduction: Accurate measurement of gastrointestinal symptoms is essential for understanding the severity of disease. Traditionally, gastrointestinal symptoms have been recorded through patient recall of symptoms elicited through standardized instruments, such as the widely used gastrointestinal symptom rating scale[1] (GSRS). Recently our group has shown that symptoms as recalled differ substantially from those elicited prospectively through a diary[2]. Recall questionnaires also attempt to elicit average level of symptoms but generally make no attempt at capturing within-subject variation in symptom levels. Since it is known that functional gastrointestinal disorders (FGIDs) are relapsing and remitting disorders it would be clinically appropriate to also measure the variation in symptoms over time within patients.

Aims & Methods: This study set out to understand the relationship between gastrointestinal symptom burden as measured through the GSRS and as measured prospectively via a smart phone app using a method known as ecological momentary assessment[3] (EMA) in which individuals are asked symptom and other questions once per day over a 14-day period. We also sought to understand the incremental utility of EMA in differentiating gastrointestinal health from disorder versus the GSRS. EMA measures included current mood, gastrointestinal and non-gastrointestinal pain and interference in daily activities, all measured on a 7-point scale, where higher is better mood or worse symptoms. Average level of each measure was calculated across the week along with the within-person variance. Explained variance in GSRS was by calculated through multiple linear regression (Table 1) with bootstrapped statistical inference due to violation of the Normality assumption. Discrimination of GI disorder from health utilised unconditional logistic regression.

Results: 28 GI symptomatic and 27 asymptomatic individuals were recruited from the community. Symptomatic individuals reported higher average symptom scores and greater temporal variability in scores than asymptomatic individuals (Table 1). They also reported higher (better) average mood scores but did not differ in mood variability. The EMA-derived measures of average symptom and mood scores together with within-individual temporal variation in scores accounts for 64% of the variance in GSRS scores. The same EMA-derived measures provided good discrimination between GI symptomatic and asymptomatic groups with an AUC of 0.90. Adding GSRS score to the model increased the AUC to 0.92, indicating little incremental value over and above the EMA-derived measures. GSRS score alone yields an AUC of 0.84.

Measure	Symptomatic mean (SD)	Asymptomatic mean (SD)	Regression b (SE) p
GI pain mean	2.52 (1.30)	0.82 (1.35)	1.70 (0.37) <.001
GI pain SD	2.04 (0.83)	0.90 (0.95)	1.14 (0.23) <.001
GI pain interference mean	1.35 (1.15)	0.36 (0.61)	0.99 (0.25) <.001
GI pain interference SD	1.60 (0.82)	0.55 (0.72)	1.05 (0.20) <.001
Non-GI pain mean	2.56 (1.43)	0.90 (1.36)	1.66 (0.37) <.001
Non-GI pain SD	1.91 (0.78)	0.93 (1.10)	0.98 (0.25) <.001
Non-GI pain interference mean	1.39 (1.19)	0.47 (0.85)	0.93 (0.27) .001
Non-GI pain interference SD	1.56 (0.88)	0.66 (1.07)	0.90 (0.27) .001
Current mood mean	5.20 (1.14)	6.35 (1.59)	-1.16 (0.37) .002
Current mood SD	1.73 (0.68)	1.67 (0.88)	0.07 (0.21) 0.7
GSRS	3.30 (1.12)	1.90 (0.96)	1.39 (0.26) <.001

[Table 1. Discrimination of GI symptomatic from asymptomatic individuals]

Conclusion: EMA-derived measures of symptoms and mood provide superior discrimination of GI disorder from health compared with a widely used validated recall questionnaire, and add useful quantification of the variation that patients experience over time while avoiding potential recall bias. This makes EMA a useful tool worth considering in research and clinical practice.

References: 1. Svedlund J, Sjodin I, Dotevall G. GSRS--a clinical rating scale for gastrointestinal symptoms in patients with irritable bowel syndrome and peptic ulcer disease. Digestive diseases and sciences. 1988;33(2):129-134. 2. Jones MP, Walter S, Faresjo A, et al. Gastrointestinal recall questionnaires compare poorly with prospective patient diaries for gastrointestinal symptoms: data from population and primary health centre samples. Eur J Gastroenterol Hepatol. 2019;31(2):163-169. 3. Mujagic Z, Leue C, Vork L, et al. The Experience Sampling Method--a new digital tool for momentary symptom assessment in IBS: an exploratory study. Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society. 2015;27(9):1295-1302.

Disclosure: Nothing to disclose

P1903 MAINTAINING WORK LIFE UNDER THREAT OF SYMPTOMS: A GROUNDED THEORY STUDY OF WORKING AND LIVING WITH IRRITABLE BOWEL SYNDROME

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Introduction: Irritable Bowel Syndrome (IBS) is a highly prevalent functional gastrointestinal disorder. Earlier studies have shown that IBS can affect work life, limiting ability to perform at work and leading to absenteeism. However, there are few studies focusing on work experiences based on patients' narratives. Further, factors that influence performance have not yet been fully explored.

Aims & Methods: The aim of this study was to construct a theory for how persons with IBS maintain their work life. A qualitative study was conducted using constructivist grounded theory. Semi-structured interviews with 15 women and 8 men with IBS were conducted. The participants were recruited at an outpatient clinic specialized in functional gastrointestinal disorders and were between 26 and 64 years of age. Of the participants, 5 had mild IBS, 10 had moderate IBS and 8 had severe IBS. Fourteen worked full-time, 6 worked part-time and 3 were currently on sick leave. In accordance with grounded theory, the data collection and analysis were conducted simultaneously. The interviews were transcribed verbatim and coded line-by-line, incident-by-incident and thereafter focused coding was done. From the data and codes, categories were generated. Finally, a core category was constructed.

Results: A core category, *balancing work life and living with IBS*, was developed and interpreted as being constituted of four categories illustrating the process of maintaining work life while constantly *being under threat of symptoms*. Persons with IBS coped with being under threat of symptoms by *restricting impact* of IBS on work by using strategies and upholding daily routines; *being ahead* by exerting control over work life; and *reconciling* IBS with work life, which was understood as a successful outcome from being ahead and restricting impact, but also influenced by the individual's outlook on life. These were ongoing processes that took place both during and outside of work hours, and that served to limit the influence of IBS on work by symptoms being milder, perceived as less frequent, or not as bothersome. *Adjusting* to other people in work life interfered with the strategies of being ahead, restricting impact and reconciling, that aimed to limit influence of IBS on work, leaving persons with IBS more susceptible to symptoms.

Conclusion: This study deepens the understanding of the work situation of persons with IBS, and the impact of IBS on work. Health care professionals can use the results of this study in the patient meeting when discussing IBS in regard to work ability and sick leave. The results imply that although balancing work life with living with IBS can be a struggle, there are ways for persons with IBS to reduce impact on work on several different levels.

Disclosure: Nothing to disclose

P1905 DETERMINATION OF SYMPTOM SEVERITY, QUALITY OF LIFE, AND WORK PRODUCTIVITY IN PRIMARY CARE IBS PATIENTS

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Introduction: Irritable bowel syndrome (IBS) is highly prevalent in primary care, although characteristics of patients diagnosed with IBS by general practitioners, still remain to be studied. Therefore, the objective of this study was to evaluate IBS symptom severity, quality of life, and work productivity in IBS patients diagnosed by general practitioners.

Aims & Methods: IBS patients, included by 62 general practitioners, completed questionnaires evaluating demographics, stool types, Rome IV criteria, IBS symptom severity (IBS-SSS), quality of life (IBS-QoL), anxiety (GAD), depression (PHQ9), somatization (PHQ15), and work productivity and activity impairment (WPAI). Patients were subdivided into severity categories based on their IBS-SSS scores: normal < 75, mild 75-175, moderate 175-300, severe ≥300.

Results: 299 primary care IBS patients (75% females, mean age 42±0.9 years, mean BMI 24±0.3) were included and characterized by the following stool types: constipation (22%), diarrhea (26%), mixed stool type (40%), and normal (11%). Normal, mild, moderate, and severe IBS-SSS were represented in 3, 17, 40, and 40% of all patients respectively. Patients with severe IBS-SSS differed significantly from the other IBS-SSS subgroups in QoL, GAD, PHQ9, PHQ15, and WPAI with all p-values lower than 0.05. Symptom severity scores were positively correlated with IBS-QoL (R=0.55), GAD (R=0.35), PHQ9 (R=0.38), PHQ15 (R=0.60), and WPAI (R=0.46).
The Rome IV criteria were fulfilled by 70 percent of all patients (Rome+). Rome+ patients were characterized by a significantly higher IBS-SSS score (290±6 vs. 194±10, p< 0.0001), IBS-QoL (35±1.2 vs. 23±1.5, p< 0.0001), GAD (7±0.4 vs. 5±0.4, p=0.0002), PHQ9 (7±0.3 vs. 5±0.5, p=0.005), and PHQ15 (13±0.3 vs. 10±0.5, p< 0.0001) compared to Rome-. In addition, the work productivity was more affected in the Rome+ group (3.1±0.2) compared to Rome- (1.7±0.3, p=0.0004).

Conclusion: In IBS patients, diagnosed by general practitioners, more than two thirds fulfill the Rome IV criteria. Symptom severity, quality of life, anxiety, depression, somatization, and work productivity were significantly different between the Rome + and Rome - group and the group with severe IBS-SSS compared to normal, mild, and moderate IBS-SSS.

Disclosure: Nothing to disclose

P1906 USEFULNESS OF DIRECT CLIPPING OF THE BLEEDING SOURCE OF COLONIC DIVERTICULAR HEMORRHAGE

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Introduction: The current standard treatment for diverticular hemorrhage is endoscopic hemostasis by clipping, endoscopic band ligation (EBL), or injection therapy. EBL has been used more frequently than clipping because the early recurrent bleeding rate after EBL is lower than that after clipping. However, adverse events, such as diverticulitis and perforation, after EBL have been reported, albeit rarely. On the other hand, the endoclip approach offers the theoretical advantage of causing less injury to adjacent tissues. However, the efficacy of endoclips for diverticular hemorrhage is unclear.

Aims & Methods: To retrospectively evaluate the safety and efficacy of endoclips versus EBL for the treatment of colonic diverticular hemorrhage.
Study population: At Nara City Hospital, 93 patients with colonic diverticular hemorrhage with stigmata of recent hemorrhage (SRH) were treated using endoclips or EBL between January 2013 and December 2018. SRH was defined as a densely adherent clot despite vigorous irrigation, a non-bleeding visible vessel, or active hemorrhage visualized on colonoscopy.
Colonoscopic examinations: All patients received standard supportive medical care for lower gastrointestinal bleeding, including hemodynamic monitoring and fluid resuscitation. Packed red blood cells were transfused to correct severe anemia if necessary. Bowel preparation with polyethylene glycol or glycerin enema was performed before colonoscopic examinations. All patients underwent colonoscopy using water-jet scopes with a tip hood (PCF-Q260AZI or GIF-Q260 J: Olympus Optical Company Ltd, Tokyo, Japan), and a water-jet system was used for vigorous irrigation. To improve endoscopic visualization of colonic diverticula, we observed the colonic diverticulum under full water immersion (Digestive Endoscopy 2018; 30: 121-122) since 2016.
Endoscopic hemostasis with endoclips: We classified the patients treated by endoclips into the direct clipping group and indirect clipping group. Endoclips were placed directly onto the vessel if technically feasible (direct clipping group). When direct placement of endoclips onto the vessel was not possible, the diverticulum was closed in a zipper fashion (indirect clipping group).
Endoscopic hemostasis with endoscopic band ligation: At our institution, we introduced EBL for colonic diverticular hemorrhage in February 2016. After the site of bleeding had been marked with endoclips, the colonoscope was removed and subsequently reinserted after attachment of a band-ligator device. The diverticulum was pulled via suction into the cup of the endoscopic ligator, and the elastic O-ring was released.
Evaluation items: Rate of early rebleeding within 30 days after initial treatment, and complications were retrospectively evaluated.

Results: Of the 93 patients, 34, 28, and 31 were in the direct clipping group, indirect clipping group, and EBL group, respectively. The rate of early rebleeding in the direct clipping, indirect clipping, and EBL groups was 5.9% (2/34), 35.7% (10/28), and 6.5% (2/31), respectively (p=0.001: direct clipping group vs indirect clipping group, p=1: direct clipping group vs EBL group, Chi-squared test). No complications occurred in all groups. All early rebleeding cases in the direct clipping group stopped with EBL.

Conclusion: Direct clip placement is acceptable as the first treatment choice for colonic diverticular hemorrhage. When direct placement of endoclips is not possible, EBL should be performed instead of indirect clipping.

Disclosure: Nothing to disclose

P1907 RISING PREVALENCE OF COLONIC DIVERTICULOSIS IN A MULTI-ETHNIC ASIAN COUNTRY

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Introduction: Singapore is a multi-ethnic country that has undergone rapid development over the last few decades, with increasing influence of western culture, and also faces a rapidly aging population. However, recent data on the prevalence of colonic diverticulosis is lacking.

Aims & Methods: This study aims to evaluate the prevalence of colonic diverticulosis in Singapore and determine its risk factors and association with common gastrointestinal symptoms. We also aim to evaluate any racial differences amongst the three main races in Singapore - the Chinese, Malays and Indians.
We retrospectively reviewed data obtained from the endoscopy database for colonoscopies performed between 2006 to 2016 in National University Hospital Singapore. Colonoscopies were included if they had at least one of the following indications: screening, diarrhea, abdominal pain and constipation. Patients below the age of 21, or with a history of colorectal cancer, colonic surgery, inflammatory bowel disease and Lynch syndrome were excluded. Patients with incomplete or repeated colonoscopies done during the study period were also excluded.

Results: We reviewed 55,679 colonoscopies from 2006 to 2016. After excluding 35,284 colonoscopies, a total of 20,395 were included. The overall prevalence of diverticulosis was 19.6%, and its prevalence has progressively increased from 2006 to 2016 (14.9% vs 23.9%, adjusted trend< 0.001). Patients with diverticulosis were older and had higher BMI. Diverticulosis was significantly more prevalent in Chinese compared to Malay and Indian races (20.5% vs 18.9% vs 15.5%, p<0.05), and in males compared to females (21.5% vs 17.6%, p<0.05). There was no significant trend difference in terms of age, ethnicity and gender distribution of colonic diverticulosis patients recruited from 2006 to 2016. Right-sided diverticulosis was more common than left-sided or pan-diverticulosis (16.2% vs 8.3% vs 4.8%, p<0.05). Multivariate regression analysis revealed age (odds ratio [OR],

1.054; 95% confidence interval [CI], 1.048-1.059), BMI (OR, 1.049; 95% CI, 1.035-1.063), male gender (OR, 1.269; 95% CI, 1.135-1.419), Chinese ethnicity (OR, 1.307; 95% CI, 1.080-1.582), alcohol consumption (OR, 1.227; 95% CI, 1.012-1.487), presence of adenoma (OR, 1.168; 95% CI, 1.032-1.322) and abdominal pain symptom (OR, 1.218; 95% CI, 1.055-1.408) as independent risk factors for colonic diverticulosis. Constipation was negatively associated with diverticulosis (OR, 0.698; 95% CI, 0.573-0.852).

Variable	Odds Ratio (OR)	95% Confidence Interval (CI)	P-value
Age	1.054	1.048-1.059	<0.001
BMI	1.049	1.035-1.063	<0.001
Male Gender	1.269	1.135-1.419	<0.001
Ethnicity (Chinese)	1.307	1.080-1.582	0.006
Alcohol consumption	1.227	1.012-1.487	0.037
Presence of adenoma	1.168	1.032-1.322	0.014
Diarrhea symptom	1.096	0.899-1.336	0.366
Constipation symptom	0.698	0.573-0.852	<0.001
Abdominal pain symptom	1.218	1.055-1.408	0.007

[Multivariate logistic regression for association between colonic diverticulosis and risk factors]

Conclusion: The overall prevalence of colonic diverticulosis in Singapore was 19.6% with a significant increase of 9.0% from 2006 to 2016. There were no significant differences in age, gender and ethnicity distribution of patients with diverticulosis over the years suggesting that there may be other risk factors that contribute to the increasing prevalence of diverticulosis. The most common form of diverticulosis in our Singaporean cohort remained predominantly right-sided. Age, male gender, Chinese ethnicity, elevated BMI, alcohol consumption, colonic adenoma and abdominal pain symptom are associated with diverticulosis.
Disclosure: Nothing to disclose

P1908 PREDICTIVE VALUE OF THE "DICA" ENDOSCOPIC CLASSIFICATION ON THE OUTCOME OF DIVERTICULAR DISEASE OF THE COLON: AN ANALYSIS FROM THE INTERNATIONAL, MULTICENTER, PROSPECTIVE STUDY

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Introduction: Diverticulosis of the colon is the most frequent anatomical alteration detected during colonoscopy. The endoscopic classification called "DICA" (Diverticular Inflammation and Complication Assessment)

has been recently developed in order to have an objective endoscopic description of the colon harbouring diverticula. Retrospective study found a significant relationship between severity of DICA score and clinical and demographic characteristics of people having diverticulosis/diverticular disease.

Aims & Methods: Aim of this multicentre, international, prospective study was to assess the predictive value of this classification in term of acute diverticulitis and surgery occurrence on a 1-year observational follow-up period.

2215 prospective patients at the first diagnosis of diverticular disease were enrolled after exclusion of radiological signs of acute diverticulitis; inflammatory bowel diseases; ischemic colitis; prior colonic resection; patients with severe liver failure (Child-Pugh C) or severe kidney failure; pregnant women; patients who are currently using or who have received any laxative agents or mesalazine or probiotics or antibiotics < 2 weeks prior to the enrollment; inability to comply with study protocol and to give informed consensus to the procedure; patients with or history of cancer, of any origin, within 5 years before enrollment; history of alcohol, drug, or chemical abuse. All patients were classified according to DICA classification.

Results: 1377 (62.15%) patients were classified as DICA 1, 599 (27,04%) as DICA 2, and 239 (10.80%) as DICA 3.

The risk of acute diverticulitis occurrence/recurrence, as well as the risk of surgery, were significantly linked to the severity of DICA score at entry. Overall, acute diverticulitis occurred in 79 (3,6%) patients: it occurred in 17 (1.38%) DICA 1, 30 (5.11%) DICA 2 and 30 (12.82%) DICA 3 patients respectively (p< 0,0001).

Overall, surgery occurred in 29 (1,3%) patients: it occurred in 2 (0.14%) DICA1, 11 (1.87%) DICA 2 and 16 (6.83%) DICA 3 patients respectively (p< 0,0001).

Conclusion: The 1-year results of this prospective study seems to confirm that DICA endoscopic classification has a significant prognostic role on the risk of acute diverticulitis occurrence/recurrence and on the risk of surgery in people having colonic diverticulosis detected at colonoscopy.

Disclosure: Nothing to disclose

P1909 COLORECTAL CANCER IN DIVERTICULOSIS PATIENTS: LOCATION AND DIAGNOSIS RATE AS COMPARED TO A MATCHED CONTROL GROUP

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Introduction: Diverticulosis is considered one of the most common and burdensome GI disorders. Several observations hold that certain epidemiological and etiological characteristics are shared between colonic diverticulosis and colorectal cancer (CRC), suggesting a possible association between these two conditions. This connection is of paramount clinical relevance, as several reports demonstrated that patients with diverticular disease have a higher risk of harboring CRC as well as adenomas. However, data are still controversial and inconclusive, as other recent studies failed to confirm this association. Uunraveling the dilemma appears to be clinically relevant, as tailored screening or surveillance intervals for CRC and polyp follow up could be of benefit in patients with diverticular disease.

Aims & Methods: The present study aims to compare the CRC detection rate and location as well as polyp detection rate between patients with diverticular disease and a matched group. In this retrospective single center study, patients diagnosed with diverticulosis on colonoscopy over a 10-year period were included. Each diverticulosis patient was matched with 1 control by age, gender, setting (inpatient/outpatient) and procedure's indication. CRC and polyp detection rates were recorded and compared between the groups before and after adjustment for bowel preparation quality and exam completion (cecal intubation).

Results: A cohort of 13680 patients (6840 patients with diverticulosis and 6840 matched controls) were included. Diverticulosis was located mainly to the sigmoid and left colon (88.5%). The CRC diagnosis rate was lower in the diverticulosis group (2% vs. 4.5%, odds ratio=0.472, p< 0.001 and 95%CI=0.382-0.584). Moreover, location of CRC was unrelated to diverticulosis location, as more CRCs in the diverticulosis group were located proximal to the splenic flexure as compared to control group (42.5% vs 29.5% respectively; P=0.03). Diverticulosis, however, was associated with increased polyp detection rate compared to controls (30.5% vs. 25.5%; odds ratio=1.2, P< 0.001 and 95%CI=1.11-1.299). These trends were kept also after multivariate analysis.

Conclusion: Diverticulosis was not linked with increased risk for CRC, nor was its location correlated with CRC location.

Disclosure: Nothing to disclose

P1910 CLINICAL FEATURES AND DRUG USE ASSOCIATED TO DIVERTICULAR DISEASE COMPLICATIONS: RESULTS FROM THE REMAD REGISTRY

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Introduction: A variety of drugs have been suggested to act as potential risk factors or protective against complications in diverticular disease (DD).

Aims & Methods: Aim of this study was to assess the role of clinical features and drug use potentially predisposing to [non-steroidal anti-inflammatory drugs (NSAIDs), antiplatelets, anticoagulants] or protective against [statins] the development of complications such as acute diverticulitis (AD) or diverticular bleeding (DB) in a cohort of patients with DD.

The REMAD Registry (Diverticular Disease Registry) is an ongoing 5-year prospective, observational, cohort study, involving 47 centres (Trials.gov: NCT03325829).

For the purpose of this analysis, patients were categorized in: a) patients without history of DD complications; b) patient with past AD (without diverticular bleeding); c) patients with past DB.

Demographic, clinical features and use of drugs assumed before the DD diagnosis [frequent use of NSAIDs (at least once a week: aspirin, NSAIDs, COX-2 inhibitors), antiplatelets (aspirin, ticlopidine, clopidogrel), anticoagulants (heparin, warfarin, factor X and thrombin inhibitors), and statins] were collected in order to identify factors associated with DD complications.

Results: Out of 1217 patients (45.7% female; 75.4% age≥60yrs; 15.9%BMI≥30 kg/m^2; 14.4% Charlson index≥3; 21% family history for DD), 998 (82%) had no history of DD complications, 194 (15.9%) had a past episode of AD and 25 (2.1%) had a past DB.

Compared to patients with no history of DD complications, age ≥60yrs was inversely (OR=0.48; 95%CI:0.34-0.67) whereas first degree family history for DD was positively (OR=1.68;95%CI:1.17-2.41) associated to patients with past AD. On the other hand, age ≥60yrs (OR=4.30; 95%CI:1.16-15.94) and Charlson index ≥3 (OR=2.58; 95%CI:1.07-6.23) were associated to history of past DB.

Regarding drugs potentially predisposing to DD complications, no significant differences were found regarding assumption of frequent NSAIDs and chronic antiplatelets in mono or dual therapy [5.3%, 2.6%, 8.3% (NSAIDs: P>0.05) and 8.7%, 15.8%, 29.2% (antiplatelets: P>0.05) in patients without DD complications, past AD and past DB, respectively]. By considering only ticlopidine assumption, it was significantly associated with past history of AD (3.2%) compared with patient without DD complications (0.9%) (OR 4.0; 95%CI:1.25-12.85).

Anticoagulants were more frequently taken in patients with past DB (12.5%) compared to patients with past AD (2.1%) (P=0.035); particularly warfarin use, was associated to patients with past DB (12.5%) compared to both patients without history of DD complications (2.4%; OR 4.86;95%CI:1.32-17.87) and patients with past AD (1%; OR 9.53; 95%CI: 1.1-79.10). Regarding drugs potentially protective against DD complications, no significant differences were found regarding use of statins (15.2%, 13.5%, 20.8% in patients without DD complication, past AD and past DB respectively; P>0.05).

Conclusion: This Registry study showed that some distinctive clinical features distinguish patients with two different kinds of DD complications: younger age and first degree family history for DD were associated to AD

whereas older age and higher Charlson index were associated to DB. Regarding drugs, since ticlopidine use was associated with past AD whereas use of anticoagulants (particularly warfarin) was associated with past DB, clinicians should pay particular attention at complications in using drugs in DD patients.

Disclosure: Nothing to disclose

P1911 DEVELOPMENT AND VALIDATION OF DICS (DIVERTICULAR CLINICAL SCORE) FOR SYMPTOMATIC UNCOMPLICATED DIVERTICULAR DISEASE IN A PROSPECTIVE PATIENTS COHORT

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Introduction: Following an attack of acute diverticulitis (AD) many patients suffer from persistent symptoms and impaired quality of life. These patients are diagnosed as suffering from symptomatic uncomplicated diverticular disease (SUDD). Few treatment strategies exist in order to improve patients' symptoms. However, there is no validated clinical score for standardized patients' assessment.

Aims & Methods: Our aim was to develop and validate a simplified easy to use diverdticular clinical score. Data from long term prospective study of 261 patients AD was reviewed. Patients' most relevant clinical symptoms were recorded and processed. A simplified questionnaire based on these clinical symptoms and relevant validated questionnaires for pain assessment (VAS) and inflammatory bowel disease activity (IBD control) was designed. Validation was performed using a pilot study focus group containing 20 patients suffering from SUDD after a documented attack of (AD). Personal interview with all patients was conducted using structured cognitive interview questions. Thereafter, a validation cohort consists of 48 patients suffering from SUDD post AD attack was established. Questionnaire's results were compared to physicians' global assessment for disease severity obtained during the visit and to inflammatory markers. questionnaire consists of 9 basic questions, assessing frequency, duration and severity of the abdominal pain, additional symptoms, missed plans activities, mood disturbances and desire for treatment.

Results: A total of 52 questionnaires were filled by 48 patients. Correlation between single questions and total score to disease severity and inflammatory markers is shown in table 1. Correlation matrix demonstrates a very strong correlation between the total score of the questionnaire and the elevation of inflammatory markers (ρ= 0.84).

Cronbach's alpha for measuring internal consistency was 0.91. The area under a ROC curve examining the overall ability of the test to discriminate between patients with/without active disease produced AUC = 0.989.

	Abdominal pain-frequency	Abdominal pain-duration	Abdominal pain-severity	Additional symptoms	Missed activities	Total score	Disease activity	Inflammatory markers
Abdominal pain-frequency	1	0.77	0.93	0.74	0.88	0.94	0.9	0.85
Abdominal pain-duration	0.77	1	0.82	0.56	0.68	0.8	0.74	0.7
Abdominal pain-severity	0.93	0.82	1	0.7	0.85	0.95	0.9	0.86
Additional symptoms	0.74	0.56	0.7	1	0.67	0.82	0.57	0.53
Missed activities	0.88	0.68	0.85	0.67	1	0.85	0.92	0.88
Total score	0.94	0.8	0.95	0.82	0.85	1	0.86	0.84
Disease activity	0.9	0.74	0.9	0.57	0.92	0.86	1	0.96
Inflammatory markers	0.85	0.7	0.86	0.53	0.88	0.84	0.96	1

[Correlation between single questions and total score to disease severity and inflammatory markers]

Conclusion: Patients suffering from SUDD post AD express a wide range of symptoms. Following further research the new DICS questionnaire may help in monitoring those symptoms, facilitate patients' stratification and support therapeutic decisions.

Disclosure: Nothing to disclose

P1912 THE PROGNOSTIC VALUE OF A NEW ENDOSCOPIC CLASSIFICATION FOR DIVERTICULAR DISEASE: DICA (DIVERTICULAR INFLAMMATION AND COMPLICATION ASSESSMENT)

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Introduction: .Colonic Diverticulosis is one of the most common anatomic alterations found in the clinical practice. This condition has 60% incidence in the population over 60 years old. About 20% of patients with this condition will develop Diverticular Disease, and 5% of them will evolve into Diverticulitis. Recently the first endoscopic classification of Diverticular Disease, useful for the clinical management of those patients, has been proposed: DICA.

Aims & Methods: The aim of the study is to analyze the distribution of the severity according to DICA score amongst patients with diagnosis of colonic Diverticulosis in relation to age, gender, the occurrence-recurrence of diverticulitis, other associated complications, and the necessity of surgical procedures, as well as the duration and the economic cost of the hospitalization. We analysed and classified 5635 cases identified at colonoscopy according to the DICA score, in the period between January 2012 and April 2018. Hospital discharge forms for all patients with hospital admitions for diverticular disease or its complications during the same time interval were retrieved.

Results: 69.9% of patients had a DICA score of 1, while 21% and 9.1% of patients have a DICA 2 or DICA 3 score, respectively. Aging increased the frequency and severity of diverticular disease (mean ages for each DICA score being 65.8 years, 67.0 years, and 69.6 years for DICA 1, 2, and 3, respectively). Higher severity scores were found in female patients (DICA1=44.6%, DICA2=50.8%, DICA3=57.8%). The occurrence of overall complications was 5.4%, being 3.5%, 7.7% and 14.2% for DICA scores 1, 2, and 3, respectively. Diverticular disease was not complicated diverticular disease (DICA1=1%, DICA2=1.8%, DICA3=3.5%); not complicated diverticulitis (DICA1=2.1%, DICA2=4.7%, DICA3=6.4%); bleeding in diverticulitis (DICA1=0.4%, DICA2=1.2%, DICA3=4.5%); diverticular perforation (DICA1=0.0%, DICA2=0.1%, DICA3=0.4%). The complications that needed a surgical procedure were for DICA1 about 0.2%, for DICA2 0.8% and for DICA3 2.5%. As well, the average of the occupant days in the hospital and the cost, respectively, was for DICA1, 8.5 days and 2300 Euro, for DICA2, 9.5 days and 3080 Euro, for DICA 3, 13 days and 4090 Euro.

Conclusion: In conclusion, the majority of the patients with Diverticular Disease belonged to the severity score DICA1 and the patients classified with DICA3 were mainly female and older than 69 years old. The study confirmed the prognostic value of the endoscopic classification DICA since the occurrence of complication resulted in a statistically significant relation with the score DICA3. DICA classification was able to discriminate, based on endoscopic records, the patients that could develop complications for Diverticular Disease.

Disclosure: Nothing to disclose

P1913 EVALUATION OF RISK FACTORS FOR COLONIC DIVERTICULOSIS IN EASTERN AND CENTRAL EUROPEAN POPULATION

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Introduction: Colonic diverticulosis (CD) is a frequent condition of the large intestine and an important cause of hospital admissions in Western and industrialized nations [1, 2, 3]. Several factors have been associated with increased risk of CD and its related complications including advanced age, obesity, physical inactivity, and a low-fiber diet [4-8]. Nevertheless, reported data are conflicting and high-powered comprehensive analysis on different dietary and lifestyle factors linked with CD is lacking [1, 4]. Therefore,we set out to investigate the association between potential risk factors and the prevalence of CD using inclusive data from a colonoscopy-based cross-sectional study in eastern and central European population.

Aims & Methods: Study cohort was conducted at two tertiary referral centers in Germany and Lithuania (the Saarland University Medical Center in Homburg and the University Hospital of Kaunas). The local Ethics Committee and National Data Protection Committee approved the study. Adult participants underwent routine colonoscopy and completed a detailed questionnaire on diet, bowel habits and various lifestyle aspects. We considered multiple risk factors for diverticulosis including diet (portion size, amount of meals per day, amount of fluids, amount of fish and red meat per week etc.), frequency of bowel movements, various symptoms of constipation, tobacco use, alcohol use, nonsteroidal anti-inflammatory drug (NSAID) use, education, obesity and gender. Link between risk factors and CD was assessed using logistic regression and standard hypothesis testing methods where pertinent.

Results: The study included 1333 patients, 634 (47,6%) males with a mean age of 61,89 years and 698 females with a mean age of 62,95 years. CD was diagnosed in 858 (64,4%) of patients. Univariate analysis revealed that age (OR 1,073, 95% CI, 1,062-1,085, p< 0,05) and obesity (OR 1,529, 95% CI, 1,155-2,025, p=0,003) were associated with colonic diverticulosis in accordance with prior findings. Our analysis also revealed new risk factors related with CD including frequency of bowel movements (OR 0,131, 95% CI, 0,040-0,426, p=0,001) and rectal tenesmus (OR 1,922, 95% CI, 1,19-3,104, p=0,008). We used a multivariate analysis to re-affirm obtained results. Univariate analysis also showed a significant association between CD and education (p=0,004), working night shifts (p<0,05), amount of meals per day (p=0,006) and previous abdominal surgery (p=0,028); however, these associations were not significant in the multivariate logistic regression. Likewise, we did not find a significant association between CD and gender, NSAID use, alcohol and tobacco use, various symptoms of constipation, education and different dietary aspects.

Conclusion: Our analysis using large population cohort establish older age, obesity, frequency of bowel movements and rectal tenesmus as the main risk factors associated with CD.

References: 1. Tursi A. Diverticulosis today: unfashionable and still under-researched. Therap Adv Gastroenterol. 2016;9(2):213-228. 2. Delvaux M. Diverticular disease of the colon in Europe: Epidemiology, impact on citizen health and prevention. Aliment Pharmacol Ther 2003;18:71-4. DOI: 10.1046/j.0953-0673.2003.01720.x 3. Manousos N, Truelove S, Lumsden K. Prevalence of colonic diverticulosis in general population of Oxford area. Br Med J 1967;3:762-3. 4. Kruis W, Spiller RC, Papagrigoriadis S, et al. Diverticular disease: a fresh approach to a neglected disease. Dig Dis 2012;30:5-5. 5. Strate LL, Liu YL, Aldoori WH, et al. Obesity increases the risks of diverticulitis and diverticular bleeding. Gastroenterology 2009; 136:115-122. 6. Rosemar A, Angeras U, Rosengren A. Body mass index and diverticular disease: a 28-year follow-up study in men. Dis Colon Rectum 2008;51:450-455. 7. Peery AF, Sandler RS, Ahnen DJ, et al. Constipation and a low-fiber diet are not associated with diverticulosis. Clin Gastroenterol Hepatol 2013;11:1622-7. 8. Kopylov U, Gen-Horin S, Lahat A, et al. Obesity, metabolic syndrome and the risk of development of colonic diverticulosis. Digestion 2012;86:201-5. DOI: 10.1159/000339881.

Disclosure: Nothing to disclose

P1914 NUTRITIONAL CHARACTERISTICS OF PATIENTS WITH DIVERTICULAR DISEASE: RESULTS FROM THE REMAD REGISTRY

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Introduction: Several evidences suggest that diet has a critical role in the pathophysiology of diverticular disease (DD). However, no data are available regarding nutritional status of patients with DD and diverticulosis.

Aims & Methods: The aim of this study was to investigate the nutritional characteristics of patients with DD and diverticulosis.

Diverticular Disease Registry (REMAD) is an ongoing 5-years prospective, observational, multicentre, cohort study, involving 47 Centers (Trials.gov:NCT03325829). Patients were categorized according to the following criteria: i) Diverticulosis: presence of diverticula in the absence of abdominal symptoms; ii) Symptomatic uncomplicated diverticular disease (SUDD): recurrent abdominal symptoms as abdominal pain and/or changes in bowel habit, attributed to diverticula in the absence of overt inflammation; iii) Previous diverticulitis (PD): patients who experienced at least 1 episode of diverticulitis in the past.

At the baseline, 1217 [45.7% female, age 66±10 y] patients were enrolled. 705 (58%), 300 (24.7%) and 212 (17.3%) patients fulfilled criteria for diverticulosis, SUDD and PD, respectively.

All patients who were asked to fill in a food frequency questionnaire to assess energy and nutritional intake. In order to compare results, 100 heathy subjects (HS) were asked fill in food frequency questionnaire. WinFood software was used for the estimation of nutrient and caloric intake.

Results: 332 patients with diverticulosis, 147 with SUDD and 83 with PD accepted to fill in self-administered nutritional questionnaire. In order to reduce age-related differences, 205 patients with diverticulosis, 100 patients with SUDD, 73 with PD and 82 HS were included in the analysis (62.6±8.1, 62.5±8.9, 62.2±9.5 and 62.1±7.5 years, respectively; p=0.965).

Patients with PD and SUDD showed a lower calorie intake compared to patients with diverticulosis and HS (1416±405 and 1582±519 vs 1642±554 and 1778±439 kCal; p< 0.001).

Consumption of fat was lower in PD group compared to diverticulosis, SUDD and HS groups (53±18 vs. 60±23, 63±27 and 75±22 g/die; p< 0.001), whereas protein consumption was lower in PD group only compared to diverticulosis group (71±22 vs. 83±27 g/die; p=0.007). No differences were observed in terms of carbohydrate consumption among the four groups. Compared to diverticulosis, SUDD and HS groups, patients with PD reported a lower intake of total fiber (18±7, 18±7 and 20±6 vs. 15±6 g/die; p< 0.001), soluble fibers (4.4±1.7, 4.5±1.9 and 4.9±1.7 vs. 3.7±1.6 g/die; p< 0.001) and insoluble fibers (12±5 12±5 14±4 vs. 10±4 g/die; p< 0.001). Lastly, patients with PD also reported a reduced intake of Vitamin A, Vitamin C, Vitamin D, Vitamin E and Polyphenols (data not shown).

Conclusion: Our data showed that patients with diverticular disease, in particular patients with PD, have a modified intake of calories, fiber and some macronutrients compared to other groups included HS. Moreover, these patients also showed nutritional deficiencies of molecules with anti-oxidant effects, predisposing to recurrence of diverticulitis. If these changes are the consequence of diet modifications after acute diverticulitis needs to be clarified. These data rise attention on dietary interventions in the management of DD.

Disclosure: Nothing to disclose

Paediatric: Lower GI III

09:00-14:00 / Poster Exhibition - Hall 7

P1915 UPPER GASTROINTESTINAL TRACT FINDINGS IN PEDIATRIC IBD: PREVALENCE AND ASSOCIATION WITH OTHER DISEASE FEATURES

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Introduction: During the past few decades, prevalence of pediatric inflammatory bowel diseases (IBD) has increased and diagnostic methods improved. However, data on the frequency and significance of upper gastrointestinal tract (UGT) findings remain limited.

Aims & Methods: Comprehensive medical data of 2395 consecutive children who had undergone gastrointestinal endoscopy with systematic biopsy sampling were collected. Next, IBD patients (n=129) were divided to those with and without histological UGT findings in esophagogastroduodenoscopy for comparisons of the disease features and treatment response. Control group comprised corresponding children who did not receive any diagnosis in endoscopic and other investigations (n=178).

Results: UGT findings were more common in IBD patients than in controls (70% vs 32%, p< 0.001). Of IBD patients, 19% had findings in esophagus, 63% in ventricle and 11% in duodenum, while corresponding figures for controls were 18%, 17% and 5%. Fifty-five percent of IBD patients had ulcerative colitis (UC), 34% Crohn's disease (CD) and 11% IBD unclassified (IBD-U). The findings were more common in CD (84%) than in UC (62%) and IBD-U (64%) (p=0.038). Four CD patients had UGT granulomas, while the other histological findings did not affect to the IBD diagnostics. IBD patients with and without UGT findings did not differ in gender or age distribution, family history, or laboratory results other than albumin at diagnosis (Table 1). The groups were also comparable in the distribution of colonic involvement and clinical presentation at diagnosis, but children with UGT findings showed more often primary treatment response (83% vs. 64%, p=0.024).

	UGT findings N=90		No UGT findings N=39		P value
	N	%	N	%	
Girls	41	45.6	14	35.9	0.308
IBD in relatives	13	14.4	8	20.5	0.391
Positive calprotectin (1)	55	90.2	24	88.9	0.856
	N:o of data	Median (Q1,Q3)	N:o of data	Median (Q1,Q3)	
Age, years	90	13 (11, 14)	39	12 (8, 14)	0.150
ESR, mm	85	18 (12, 34)	37	20 (9, 34)	0.956
Albumin, g/l	56	36 (31, 40)	27	39 (36, 41)	0.020

(1) Data available for 61 patients with and 27 patients without UGT findings.

[Table 1. Baseline characteristics and diagnoses of 129 IBD children with and without upper gastrointestinal tract (UGT) findings.]

Conclusion: UGT findings are common in pediatric IBD, especially in CD patients and in ventricle and, in some cases, may affect the diagnosis. However, they do not seem to associate with more severe disease presentation or poorer initial treatment response.

Disclosure: Nothing to disclose

P1916 HEALTH LITERACY, QUALITY OF LIFE, WORK PRODUCTIVITY AND ACTIVITY IMPAIRMENT IN YOUNG ADULTS WITH CROHN'S DISEASE COMPARED TO DIABETES MELLITUS PATIENTS: LONG-TERM FOLLOW-UP FROM THE BELGIAN CROHN'S DISEASE REGISTRY

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Introduction: Crohn's disease (CD) is a chronic disease often originating in childhood and requiring daily attention. We aimed to assess the health literacy (HL), quality of life (QoL) and related outcomes in CD patients prospectively followed in the Belgian Crohn's disease registry (BELCRO), compared to young type 1 diabetes mellitus (DM) patients.

Aims & Methods: Demographics, clinical data (including Crohn's Disease Activity Index (CDAI) for CD) and validated HL and QoL questionnaires (HLS-EU-Q16, EQ-5D-5L and WPAI) were obtained from young adult CD and DM patients diagnosed in childhood and followed in the BELCRO or Diabetes Clinic UZ Brussel. HL was scored as inadequate (0-8), problematic (9-12) or sufficient (13-16). QoL was dichotomized into 'problems' (EQ-5D levels 2 to 5) or 'no problems' (level 1). Work productivity and activity impairment (WPAI) were scored as percentages. Univariate non-parametric (Mann-Whitney U and chi-squared test) and correlation (Spearman) analyses were performed.

Results: In total, 46 CD (median (IQR) age 25 (24-27) years, 63% male) and 50 DM (age 20 (19-22) years, 50% male) patients were included. Median CDAI-score in CD patients was 67 (30-138). Median HL was the same in CD and DM patients (both 14 (11-15), p=0.81) with similar proportions of inadequate, problematic and sufficient HL (all p>0.05) in CD vs. DM patients. Median QoL was similar in CD and DM patients (both 75 (65-80), p=0.47) with similar proportions of problems with mobility, self-care, usual activities and anxiety/depression but a significance for higher pain/discomfort in CD vs. DM patients (53 vs. 32%, p=0.04). Median work (10 (0-30) vs. 20 (10-40)%, p=0.45) and activity impairment (20 (0-40) vs. 20 (10-40)%, p=0.95) was similar in CD and DM. HL correlated positively with QoL in CD and DM (both r=0.6, p< 0.01) and negatively with work impairment in CD (r=-0.4, p=0.02) but not DM patients. Work impairment for CD correlated with the CDAI (r=0.5, p=0.01) and number of hospitalizations and surgeries in the last 3 years (r=0.4, p=0.03). CD patients with recent hospitalization and surgery (22%) had a trend for higher CDAI (107 (58-252) vs. 41 (20-114), p=0.07) with lower HL (11.5 (10-12) vs. 14 (11-16), p=0.06) and QoL (68 (60-75) vs. 80 (70-85), p=0.02) compared to those without.

Conclusion: In the studied populations, HL is sufficient in the majority of cases. Despite a comparable QoL and WPAI to DM patients, young CD patients with recent hospitalizations and surgeries have lower QoL and HL than those without. Interventions and programs aimed at improving HL and QoL in children and adolescents with CD should be installed to increase health-related outcomes in early adult life.

Disclosure: This study was supported by a grant from MSD to BESPGHAN.

P1917 LATENT TUBERCULOSIS TESTING IN PAEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE TREATED WITH ANTI-TUMOUR NECROSIS FACTOR AGENTS: DO WE NEED NEW TESTING RECOMMENDATIONS?

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Introduction: Anti-tumour necrosis factor (anti-TNF) agents are one of the therapeutic cornerstones in inflammatory bowel disease (IBD). These agents increase the risk of reactivation of latent infections. Latent tuberculosis (LT) testing is recommended prior to anti-TNF therapy in paediatric patients with IBD. In the European Union, Portugal is one of the countries with the highest prevalence of tuberculosis, and the country's northern region has the third highest national notification rate registered in 2017: 20,6 cases per 100.000 inhabitants. Our department is Portugal's northern region paediatric gastroenterology reference centre.

Aims & Methods: We performed a retrospective and descriptive analysis of paediatric patients with IBD eligible for anti-TNF therapy followed at our department during the last 2 years. This study aimed to evaluate the prevalence of LT and active tuberculosis in this group of patients.

Results: Clinical data from 273 paediatric patients with IBD was analysed. 120 of these patients were eligible for anti-TNF therapy (77,5% Crohn's disease, 21,7% Ulcerative Colitis, 0,8% IBD unclassified). The median age was 13 years. LT prevalence was 7,3% (n=9): positive Tuberculin skin test (TST) in 5 cases and positive Interferon-gamma release arrays (IGRA) in 4. In 2 cases initial IGRA testing was negative. A single patient had contact with a case of active tuberculosis. All patients diagnosed with LT were treated with isoniazid. Follow up after treatment of LT varied between 28 and 1496 days. We had no cases of complications or development of active tuberculosis.

Conclusion: Testing for LT prior to anti-TNF therapy is mandatory. Repeating this testing process while under anti-TNF therapy is dependent on a case-by-case analysis. Even in the absence of contact with active tuberculosis its important to test and treat LT. We believe that further studies are needed to formulate new recommendations for LT testing / testing repetition.

Disclosure: Nothing to disclose

P1918 GASTROINTESTINAL GRAFT-VERSUS-HOST DISEASE IN PAEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Introduction: Graft-versus-host disease (GVHD) is a life-threatening multisystemic complication of allogeneic hematopoietic cell transplantation.

Aims & Methods: The aim of this retrospective study was to describe the features of the hematopoietic stem cell transplanted (HSCT) patients diagnosed with Gastrointestinal (GI) GVHD. Paediatric patients (< 18y of age) that had received an HSCT from January 2014 to November 2018 were included. Diagnosis, epidemiological and clinical data were compared between patients who developed GVHD and the rest of patients with HSCT.

Results: A total of 177 patients received HSCT and 28 (14.2%) of them developed GVHD, 50% were women. At the moment of the HSCT, the average age was 8.85 years old (±5.9 y) and GVHD was diagnosed at the age of 9.4 y (±5.8 y). The type of HSCT and the underlying conditions for which HSCT was indicated in patients who developed GVHD (n=28), versus those who did not develop GVHD (n=149) are shown in Table 1.

The most common symptoms of GI GVHD were vomiting in 21 patients (75%), diarrhoea and anorexia in 19 (67.9%) respectively, abdominal and pain in 18 (64.3%), weight loss in 16 (57.1%) and hepatomegaly in 8 (28.6%).

A total of 19 (67.9%) presented cutaneous GVHD demonstrated by biopsy, 9 (32.1%) bronchiolitis obliterans and 14 (50%) had clinical criteria of hepatic GVHD. The diagnosis of GI GVHD was made by upper endoscopy in 11 (39.3%), lower endoscopy in 9 (32.1%) and both of them in 8 (28.6%). No side effects of the endoscopy were notified.

The types of GVHD were classic acute GVHD in 14 (50%), acute and persistent or recurrent GVHD in 3 (10.7%), classic chronic GVHD in 4 (14.3%), and overlap (both acute and chronic GVHD were present) in 7 (25%).

Most of the patients received several treatments, including methylprednisolone in 26 (92.8%), budesonide in 7 (25%), beclomethasone in 2 (7%), photopheresis in 19 (67.9%), etanercept in 17 (60.7%), calcineurin inhibitors in 13 (46.4%), ruxolitinib in 7 (25%), mycophenolate mofetil, antithymocyte globulin and mesenchymal stem cells infusion and immunoglobulin in 3 patients (10.7%) respectively, and sirolimus in 1 (3.6%). These treatments were totally effective in 15 patients (53.6%), partially effective in 8 (28.6%) and non-effective or refractory in 5 (17.9%).

		Transplanted patients who developed GVHD (n=28)	Transplanted patients who did not develop GVHD (n=149)	p
Type of HSCT	Haploindentical allogeneic	11 (39,3%)	59 (39,6%)	0,8625
	HLA-matched allogeneic related	5 (17,9%)	27 (18,1%)	0,8231
	HLA-mismatched related	0	2 (1,3%)	1
	HLA-matched allogeneic non-related	10 (35,7%)	13 (8,7%)	0,0003
	HLA-mismatched unrelated	2 (7,1%)	9 (6%)	0,8415
Underlying condition	Acute lymphoblastic leukemia (ALL)	11 (39,3%)	38 (25,5%)	0,2059
	Acute myeloid leukemia (AML)	12 (42,9%)	29 (19,5%)	0,0400*
	Hodgkin Lymphoma	1 (3,6%)	5 (3,4%)	1
	Myelodysplastic syndrome	1 (3,6%)	8 (5,4%)	1
	Immunodeficiency	1 (3,6%)	1 (0,7%)	0,3001
	Hurler syndrome	1 (3,6%)	3 (2%)	0,5011*
	Medullary aplasia	1 (3,6%)	3 (2%)	0,5011
	Other	0	62 (41,6%)	0,0001*

[Table 1]

Conclusion: The treatments for GI GVHD are not always effective. A higher percentage of patients who received an HLA-identical unrelated allogeneic HSCT and who had ALL in the group that developed GVHD when compared to those who did not develop GVHD was observed (differences statistically significant), suggesting a possible association with these factors. Most patients with GI GVHD also presented cutaneous GVHD.

References: Jaramillo-Esparza, C et al. (2018). Gastrointestinal tract and liver graft-versus-host disease in pediatric patients with hematopoietic progenitor cell transplantation at a tertiary care center in Mexico. Revista De Gastroenterología De México 83(4), 385-392. Levine et al. (2013). Low Paneth cell numbers at onset of gastrointestinal graft-versus-host disease identify patients at high risk for nonrelapse mortality. Blood, 122(8), 1505-1509. Ma, C., Maluf, H., & Liu, T. (2015). Acute graft-versus-host disease is more prevalent and severe in the lower than the upper gastrointestinal tract. Human Pathology, 46(10), 1480-1487. Myerson, D. et al (2017). Graft-versus-Host Disease of the Gut: A Histologic Activity Grading System and Validation. Biology Of Blood And Marrow Transplantation, 23(9), 1573-1579. Rodriguez-Otero, P et al. (2012). Fecal calprotectin and alpha-1 antitrypsin predict severity and response to corticosteroids in gastrointestinal graft-versus-host disease. Blood, 119(24), 5909-5917. Sultan, M. et al(2012). Endoscopic Diagnosis of Pediatric Acute Gastrointestinal Graft-Versus-Host Disease. Journal Of Pediatric Gastroenterology And Nutrition, 55(4), 417-420. Washington, K. et al (2009). Pathology of graft-versus-host disease in the gastrointestinal tract. Human Pathology, 40(7), 909-917.

Disclosure: Nothing to disclose

Oesophageal, Gastric and Duodenal Disorders III

09:00-14:00 / Poster Exhibition - Hall 7

P1919 THE DYNAMICS OF CHINESE GUT MICROBIAL COMMUNITIES: THE EXPEDITION IN TRINIDAD AND TOBAGO

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Introduction: The human gut microbiome consists of trillions of microbiota and the majority of these microbiota reside in the gut. Many previous researches have received considerable attention to the association between gut metagenome and chronic diseases, such as obesity, inflammatory bowel disease, and other diseases. The roles of gut microbiota in human health not only in influencing the normal processes, but also associating with the occurrence and development of disease. With the increasing number of Chinese travelers around the world, there is undoubtedly drastic change of their diet as well as living environment, which would profoundly affect the gut microbial communities of these Chinese travelers. In general, when a person to a new environment, his/her may be feel inadaptability and the body has discomfort with a few symptoms, such as dizzy, flummoxed and emesis, and the time of inadaptability vary from person to person. We human are known to be inadaptable for the changing environments and foods. However, the mechanisms behind the inadaptability phenomenon remain unclear. Researches have already revealed that for short-term travelers, our gut microbial communities have been profoundly affected by the changing environments, and they have also asserted powerful feedbacks for our adaptation. Yet for mid- or long-term stays, the effect of changing environments on gut microbial communities as well as their feedback remain elusive.

Aims & Methods: In this study, we have followed a Chinese medical team's expedition from China to Trinidad and Tobago, stay in half a year, and come back again. During the whole monitoring duration of more than 9 months, we have collected 184 feces samples from Chinese medical team, 28 feces samples from native of Trinidad and Tobago and 5 food and water samples from Trinidad and Tobago, as well as 57 feces samples from native of Beijing, China. To characterize the taxonomic profile of the gut microbiome, the V4 hypervariable region of the bacterial 16S rRNA gene were amplified using the universal bacterial/archaeal primers 515F (5'- GTGC-CAGCMGCCGCGGTAA-3') and 806R (5'- GGACTACHVGGGTWTCTAAT-3'). To characterize gut microbiome functional potential, 61 faecal samples were selected and performed shotgun metagenome sequencing, mainly including the faecal samples of MT3, MT6, and MT10 people.

Results: The number of OTUs and PD_whole_tree varied from 511 to 6,695 and from 42.21 to 330.42, respectively. Whilst, the Shannon index and Simpson index ranged from 1.51 to 7.06 and 0.58 to 0.98, respectively. These differences revealed that the most significant changes of the gut microbiota occur directly after the shift of diet and locations. The mantel test between composition data (taxonomical composition and functional composition) and diet information showed that the changes of the gut microbiota community was strongly associated with diet, especially dairy products, pickled food, salty snack and sodas.

Conclusion: Based on which taxonomical structure profiling and association studies have been conducted, we have found that (i) the most significant changes of the gut microbiota occur directly after the shift of diet and locations; (ii) the stable states of the gut microbiota were diet dependent, while those states were related more with hosts than with enterotype; (iii) there were obvious differences in gut microbiota between Chinese groups with short stay and those with long stay in Trinidad and Tobago; (iv) there were obvious differences in gut microbiota between Chinese (with short and long stay in Trinidad and Tobago) and those natives.

Disclosure: On behalf of all the authors ,there is no conflict of the interest

P1920 SCREENING FOR *H. PYLORI* AND CLARITHROMYCIN RESISTANCE BY PCR FROM GASTRIC BIOPSIES: COMPARATIVE STUDY OF 2 KITS, AMPLIDIAG H. PYLORI+CLARIR (MOBIDIAG) AND RIDAGEN HELICOBACTER PYLORI (R-BIOPHARM)

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Introduction: Because of the increasing rate of clarithromycin- resistant *Helicobacter pylori* strains in France, the HAS French guidelines recommend antimicrobial susceptibility testing before starting the first-line eradication treatment. We evaluated the feasibility of this new approach in our hospital by studying 2 qualitative PCR kits : Amplidiag H. pylori+clariR kit (MOBIDIAG) targeting the 23S rRNA gene and SNPs in 2142 and 2143 positions, mostly involved in clarithromycin resistance, and RIDAGENE Helicobacter pylori kit (r-biopharm) targeting 16S rRNA and 23S rRNA genes.

Aims & Methods: Patients with indication for endoscopy with gastric biopsies were included in this study. Two antral and 2 corpus biopsies were analysed by PCR, and 2 additional biopsies were used for histological analysis. The 4 biopsies dedicated for PCR, were pooled, extracted on an iPrep extractor, and DNA amplifications were performed on a Rotorgene thermocycler.

Results: Among the 50 screened patients, 37 were *H. pylori* negative with both PCR kits (35 were confirmed negative and 1 was found positive by histology, 1 had no histological analysis), 13 were *H. pylori* positive with both PCR kits without detection of clarithromycin resistance (12 were confirmed positive and 1 was found negative by histological analysis).

Conclusion: Preliminary results of this study prove the feasibility of *H. pylori* and clarithromycin resistance screening by PCR from gastric biopsies, and show a good correlation between the 2 kits and histology results. They are both easy to use and give rapid results (1h45 for MOBIDIAG kit and 70 min for RIDAGEN kit). Samples can be tested in triplicate with the MOBIDIAG kit. We are currently working to complete these results with additional samples, to evaluate the PCR performances for clarithromycin resistance detection.

Disclosure: Nothing to disclose

P1921 SELECTIVE MICROBIOTA TRANSPLANTATION INDUCES RADIATION ENTERITIS IMPROVEMENT: A PILOT STUDY

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Introduction: The intestinal microbiota is implicated in the pathogenesis of radiation-induced bowel toxicity. Microbiota transplantation might be a therapeutic option for radiation enteritis.

Aims & Methods: This study aimed to assess the efficacy and safety of selective microbiota transplantation (SMT) through mid-gut in patients with radiation enteritis through a prospective cohort study. Eighteen patients with a median age of 56 (IQR, 49.8-63.5) years, were included after informed consent and institutional ethics approval according to registered trial (NCT03516461). The prepared 200ml selective microbiota suspension (mixed species of cultured bacteria) was infused daily into the distal duodenum through the nasojejunal transendoscopic enteral tubing (TET) tube for 3 days. Clinical and endoscopic data were collected during the follow-up. Endoscopic evaluations were assessed using the Vienna Rectoscopy Score (VRS). Fecal metatranscriptomes and metagenomes analysis were performed to assess associated microbial changes. The urinary metabolic profiles of those patients were generated using nuclear magnetic resonance (NMR) spectroscopy.

Results: 66.7 (12/18), 66.7% (12/18), 61.1% (11/18) and 44.4% (8/18) patients responded to SMT [≥1 grade reduction in Radiation Therapy Oncology Group (RTOG) European Organization for Research and Treatment of Cancer (EORTC) Radiation Toxicity Scales] at week 1, 2, 3 and 4 weeks, respectively. The stool frequency per day reduced from 5.9 ± 0.7 (mean ± SE) to 3.4 ± 0.6 four weeks after SMT (p < 0.001). The improvements in

quality of life was demonstrated by a decreased European Organization for Research and Treatment of Cancer Quality of Life Module for Proctitis-21 items questionnaire (EORTC QLQ PRT21) score from 56.8 ± 2.0 to 47.8 ± 3.1 four weeks after SMT (p = 0.001). Patients with VRS ≤ 2 at baseline achieved significantly more response than those with VRS ≥ 3 [100 % (5/5) vs. 23.1% (3/13), p = 0.007]. SMT was associated with a significantly higher response rate in patients with EORTC QLQ PRT21 score ≤ 63 at baseline than those > 63 [61.5% (8/13) vs. 0.0 % (0/5), P = 0.029]. Microbiota analysis showed that SMT altered the composition greatly. SMT induced significant alterations in urinary metabolic profiles. No serious adverse event related to SMT occurred during treatment and follow-up.

Conclusion: SMT induces clinical and endoscopic improvement in radiation enteritis and is associated with distinct microbial and metabolic changes that relate to outcome. SMT is a promising novel therapeutic option for radiation enteritis.

Disclosure: Nothing to disclose

P1922 A POLIT STUDY OF AN UPPER GASTROINTESTINAL MONITORING SYSTEM FOR TRACKING UPPER GASTROINTESTINAL BLEEDING

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Introduction: Second-look endoscopy would be scheduled, if rebleeding is suspected after primary endoscopic hemostasis of upper gastrointestinal (UGI) bleeding. However, the routine second-look endoscopy is a high-cost intervention and could even increase unnecessary risk. Thus, we aimed to develop a novel continuous UGI monitoring system to improve the tracking of UGI bleeding.

Aims & Methods: The UGI monitoring system consisted of a tiny and thin tube camera, a wearable host device, and a mobile display device. The tube camera was connected to the host device and then inserted into stomach via nasal tunnel. The host device was set to acquire images every minute and sent the images to the mobile device, in which an image analysis application was installed for rebleeding detection.

Patients with Rockall scores ≥ 3 were eligible for this study. They were put on the UGI monitoring system by the trained medical staff. The monitoring period was ≤ 3 days because most of rebleeding occurred within 3 days. The comfort level was scaled from 0 to 5 by the patients.

Results: Eight patients who had UGI bleeding and received primary endoscopy hemostasis were included in this study (age 41±83, 6 males, Rockall score 3-9) and the trial is still ongoing. From the images, how the contents inside the stomach changed over time was observed. Coffee-ground, blood clots, red blood, and food contents were photographed. Up to date, the included patient had not rebleeding during the system monitoring. However, this system could confirm no active bleeding in stomach 1-4 days earlier than observation of melena. Moreover, the comfort level of using the UGI monitoring system was less than 2 in average.

Conclusion: This UGI monitoring system could confirm no active gastric bleeding earlier. It is potential to evaluate various scenarios in the UGI tract with an endurable comfort level.

Disclosure: Nothing to disclose

P1923 BLEEDING AFTER GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION AND NECESSITY OF ENDOSCOPIC EXAMINATION (2ND LOOK) ON THE FOLLOWING DAY

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Introduction: Endoscopic submucosal dissection (ESD) has become the standard treatment for early gastric cancer in Japan. Hemorrhage is often encountered after ESD, and endoscopic hemostasis is required in some cases. Some institutions do not perform upper gastrointestinal endoscopy after ESD (hereinafter referred to as 2nd look), and some authors have reported that 2nd look on the day after ESD is unnecessary. In our department, however, exposed blood vessels and blood clots without active bleeding in the post-dissection ulcer floor have been recognized in addition to active bleeding after resection. In addition to active bleeding, we consider that exposed and/or observable vessel findings and clots on the ulcer floor after resection are important risk factors for hemorrhage. Here, we report comparison and examination of the frequency of active bleeding and "ulcer after resection with a risk of bleeding" on the day after ESD in relation to their risk factors. We also discuss the necessity of 2nd look after ESD.

Aims & Methods: In this paper, 2nd look refers to upper gastrointestinal endoscopy examination on the day after ESD. We examined 447 cases with 2nd look retrospectively in patients treated with ESD in our department during the period from August 2008 to March 2018. Active bleeding was examined in 447 cases. After excluding 51 cases with active bleeding, the occurrence of ulcers after resection with a risk of bleeding was examined in 396 cases. Patient background and pathological findings were checked on electronic medical records, and images and endoscopic findings were checked using a device for recording images of endoscopic findings (Solemio ENDO; Olympus, Tokyo, Japan).

Results: Active bleeding was seen in 51 cases (11.4%). Site of lesion, resected specimen size, and history with/without antithrombotic drug administration were found to be factors that significantly determined the occurrence of active bleeding. In cases with upper body lesions, hazard ratio (HR) was 0.259 (P = 0.0256) with a low risk of bleeding. For specimens resected by ESD exceeding 30 mm in size, HR was 2.736 (P = 0.0019) indicating a higher risk of bleeding. This suggested that larger specimens are associated with higher risk of bleeding. Patients with a history of antithrombotic drug administration showed an increased risk of active bleeding (HR = 1.957, P = 0.0477). We found 88 cases (22.2%) of "post-dissection ulcer floor with a risk of bleeding." HR was 0.318 (P = 0.0074) for upper body lesions. Thus the frequency of "post-dissection ulcer floor with a risk of bleeding" was low. Conversely, HR was 1.868 (P = 0.0120) for lesions in the antrum with a higher risk of bleeding. HR for specimen length >30 mm was 1.982 (P = 0.0060), and the frequency of "post-resection ulcer with a risk of bleeding" was high.

Conclusion: The results of this study indicated that the frequencies of active bleeding after ESD and "ulcer with a risk of bleeding" were higher than expected. In addition, their risk factors were elucidated. We believe that 2nd look is necessary to safely discharge patients.

References: none

Disclosure: no any Conflict of Interest

P1924 EFFECTIVENESS OF THE TREATMENT WITH SOMATOSTATIN ANALOGUES AND / OR THALIDOMIDE FOR INTESTINAL ANGIODYSPLASIAS IN CLINICAL PRACTICE

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Introduction: Pharmacological therapy with thalidomide or somatostatin analogues is indicated in patients with intestinal angiodysplasias, who did not respond to standard endoscopic treatment with argon-plasma coagulation. Previous studies support the efficacy of these therapies, but this has not been proven in real clinical practice.

Aims & Methods: The aim of this study was to evaluate the effectiveness of thalidomide and/or octreotide-LAR in patients with intestinal angiodysplasias not responding to standard endoscopic therapy in the daily clinical practice.

Methods: A retrospective, single-center, cohort study was designed. Patients diagnosed with intestinal angiodysplasias between 2012 and 2018 at the University Hospital of Santiago de Compostela, Spain, who were treated with thalidomide and/or octreotide-LAR were included. Hemoglobin levels, transfusion needs (red blood cells units per month), intravenous iron, and bleeding episodes were analyzed. Results are shown in percentages, mean and standard deviation, and analyzed by Student-t or U-Mann Whitney test.

Results: 31 patients were included (19 males, median age 77.3 years). 25% of the patients suffered from liver cirrhosis, 32% had chronic renal injury, 13% ischemic heart disease, and 25% aortic stenosis. Three patients were initially treated with thalidomide 100mg/24h, and 28 with octreotide-LAR 20mg/month. Eight patients, who did not respond to octreotide-LAR switched to thalidomide. Compared with baseline before treatment, hemoglobin levels increased with octreotide-LAR (0.98, 95%CI 0-1.97, p=0.05). However, needs per month of packed red blood cells (0.29, 95%CI -0.60-1.19, p>0.05), intravenous iron (-0.01, 95%CI -0.49-0.47, p>0.05) and bleeding episodes (-0.03, 95%CI -0.16-0.10, p>0.05) did not decrease.

No significant benefit was either observed after thalidomide therapy (needs of packed red blood cells per month 1.47, 95%CI -1.77-4.72, p>0.05; hemoglobin levels 0.59, 95%CI -0.64-1.82, p>0.05 and bleeding episodes per month 0.05, 95%CI -0.29-0.18, p>0.05). There were two mild adverse reactions in patients with octreotide-Lar and four with Thalidomide.

Conclusion: Effectiveness of pharmacological treatment with octreotide analogues or thalidomide of intestinal angiodysplasias refractory to endoscopic therapy in clinical practice is questionable. These results have to be confirmed in larger multicenter studies.

Disclosure: Nothing to disclose

P1925 ATP-DEPENDENT POTASSIUM CHANNELS, SOLUBLE GUANYLYL CYCLASE AND ENDOGENOUS PROSTAGLANDINS IN CARBON MONOXIDE-MEDIATED PREVENTION AGAINST OXIDATIVE ISCHEMIA/REPERFUSION-INDUCED GASTRIC DAMAGE

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Introduction: Carbon monoxide (CO), produced endogenously or released from tricarbonyldichlororuthenium (II) dimer (CORM-2) was shown to protect gastric mucosa against injury caused by NSAIDs or stress. However, the role of this gaseous transmitter in prevention of oxidative ischemia/

reperfusion (I/R)-induced gastric damage has not been extensively elucidated. Therefore, we determined the effect of pretreatment with CORM-2 on gastric lesions formation induced by 30 min of I followed by 3 h of R.

Aims & Methods: Thirty minutes before I/R, male Wistar rats were pretreated i.g. withvehicle, CORM-2 (1-10 mg/kg) or ZnPP (10 mg/kg) as an inhibitor of endogenous CO-producing heme oxygenase (HO) administered alone or combined with ODQ (10 mg/kg i.p.), inhibitor of soluble guanylyl cyclase (sGC), indomethacin (5 mg/kg), non-selective inhibitor of cyclooxygenases (COXs), L-NNA (15 mg/kg), inhibitor of nitric oxide (NO) synthase or glibenclamide (10 mg/kg), ATP-dependent potassium channels (K-ATP) blocker. Gastric lesions area, mucus production and gastric blood flow (GBF) were assessed by planimetry, AB/PAS staining and laser flowmetry, respectively. Gastric mucosal mRNA and/or proteinexpression for HO-1, HO-2 and Nrf-2, but also COX-1, COX-2, iNOS, TNF-a, IL-1b, K-ATP subunits Sur2 and Kir6.1 and sGC subunits alpha-1 and beta-1 were determined by real-time PCR and/or Western blot or IHC. 8-hydroxydeoxyguanosine (OHG) level in gastric mucosa as a molecular marker of oxidative DNA damage and PGE2 concentration were determined by ELISA. CO content in gastric mucosa was determined by gas chromatography. Serum concentration of 11 pro- and anti-inflammatory cytokines and TGFb1-3 was determined by Luminex platform.

Results: Pretreatment with CORM-2 (5 mg/kg) but not ZnPP increased CO content in gastric mucosa, decreased I/R-induced gastric damage, increased GBF, decreased OHG, increased PGE2 content and mRNA expression of COX-2, iNOS, TNF-a, IL-1bmRNA as compared with vehicle-control. CORM-2 maintained physiological mucus production. Glibenclamide and L-NNA but not indomethacin or ODQ reversed gastroprotective effects of CORM-2. Exposure to I/R decreased gastric mucosal mRNA expression for Sur2 and Kir6.1 previously decreased by exposure to I/R. CORM-2 decreased blood concentration of 11 cytokines and TGFb3 elevated by I/R.

Conclusion: We conclude that CO released from CORM-2 prevented gastric mucosa against oxidative I/R-induced damage by the maintenance of gastric microcirculation only in part dependently on sGC activity. These gastroprotective and hyperemic effects of CO against I/R-injury involve biosynthesis of endogenous NO but not co-activity of COXs. However, CO maintained physiological level of protective PGE2 under I/R conditions. Since increased bioavailability of CO did not modulated mRNA expression for K-ATP subunits and pharmacological blockade of these channels reversed protective and hyperemic effect of CORM-2 we conclude that this molecule acts via K-ATP activity. CO attenuated I/R-induced inflammatory response and DNA oxidation in gastric mucosa and on systemic level confirming its strong anti-inflammatory and anti-oxidative properties. [Funding source: National Science Centre, Poland (UMO-2016/23/N/NZ4/01890)].

Disclosure: Nothing to disclose

P1926 BALLOON TAMPONADE IN THE MANAGEMENT OF UNCONTROLLED VARICEAL HAEMORRHAGE - A 12 YEARS RETROSPECTIVE STUDY

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Introduction: Variceal hemorrhage is a life-threatening emergency and a major cause of death. Currently, the use of Sengstaken-blakemore (SB) tube is recommended as a temporary measure in uncontrolled variceal bleeding when endoscopic therapy fails or is not possible. Even though it is recommended, there are no recent studies about the outcomes of its use.

Aims & Methods: The aim of this study was to evaluate the safety and efficacy of SB tube placement, as well as the rebleeding rate and associated mortality. We also sought to identify associated predictors of hemostasis and mortality.

It was done a retrospective analysis of all the patients treated with SB tube for uncontrolled variceal hemorrhage at a single tertiary care hospital between 01/01/2007 and 31/12/2018.

Results: Over a twelve-year period, 34 patients underwent SB tube placement, 26 males, average age of 56 (±13.5) years old, 88% (30/34) had portal hypertension due to cirrhosis with an average Child-Pugh score of 10.6 (±2.1) and average MELD-Na score of 20.9 (±7.6). 86% of these patients had alcohol-related cirrhosis and 50% had active alcohol consumption.

At the time of the insertion of the SB tube, all the patients were medicated with a vasoactive drug and 94% (32/34) had active hemorrhage. Successful initial hemostasis was achieved in 62% (21/34) of the cases, despite rebleeding in 43% (9/21). The SB tube use was associated with complications in 32% of the cases, 8% of them was severe. The overall mortality rate within 30 days was 70% and within 1 year was 84%.

Univariate analysis indicated as potential predictors of mortality at 1 year the octreotide use (vs terlipressina; p = 0,02), hepatocellular carcinoma (p=0,006), and active alcohol consumption (p=0,04). Multivariate analysis did not point out any predictor of hemostasis or mortality.

Conclusion: SB tube seems to be a beneficial option as a rescue therapy for uncontrolled variceal bleeding but it is associated with a high rate of complications and bleeding recurrence.

Disclosure: Nothing to disclose

P1927 GASTROINTESTINAL BLEEDING INDUCED BY MALLORY-WEISS SYNDROME ANALYSIS

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Introduction: Mallory-Weiss syndrome (MWS) is characterized by superficial non-perforated mucosal laceration, commonly at gastroesophageal junction, and is estimated to be the cause of 8% to 15% of upper gastrointestinal bleeding of non-varicose origin[1,2]. The mechanism behind the injury is the sudden and repeated increase in intra-abdominal pressure caused by nausea, vomiting, hiccups, tension, coughing, abdominal or thoracic trauma[2]. Laceration originates at the gastroesophageal junction and may extend proximally into the esophagus or distally into the stomach[1]. The main predisposing factor is alcoholism, present in 30% to 70% of cases[2,3]. The severity of bleeding appears to be greater in the presence of portal hypertension and esophageal varices. Other related causes include bulimia nervosa, hyperemesis gravidarum and gastroesophageal reflux disease[1]. In most cases, it has a self-limiting course and does not require emergency endoscopy or surgical intervention.

Aims & Methods: Characterize the epidemiological profile of the patient in a university hospital that presents gastrointestinal bleeding due to MWS, from September 2017 to January 2019. A retrospective study was carried out with data collection of medical records and the protocol implanted in 772 patients of the Digestive Hemorrhage Service. In September 2017, this hospital became a unique reference for acute cases of gastrointestinal bleeding in Curitiba-PR and metropolitan region. Descriptive and statistical analysis of the prevalences according to age, sex, need for transfusion, death, symptomatology of entry, smoking, alcoholism, medications, comorbidities, clinical-surgical management, endoscopic diagnosis, endoscopic treatment was made.

Results: Of the 772 patients evaluated, 15 (1.9%) presented endoscopic reports confirming MWS, composing the sample. The most prevalent gender was male (13 patients) and the most affected age group was between 61-70 years (26.7%). The median age was 52 years (SD16.5). One man died (6.7%), non-related to MWS. Transfusion of red blood cells was necessary in 4 patients (26.7%), all male. The most present entry symptom was hematemesis with 14 cases (93.3%) and the most common association was hematemesis and melena with 4 cases (26.7%). The mean hemoglobin level at admission was 11.7 g / dL (5.1 - 16.4). Of the 15 patients, 10 were alcoholics, all men, for 27 years on average. As for smoking, 5 people smoked and 2 were ex-smokers, accounting for 46.7% of the sample. Cirrhosis was observed in only one individual, having the alcoholism as the etiology. The continuous medication more associated with bleeding was the use of anti-inflammatory drugs with 2 cases (13.3%). The most prevalent diagnosed etiology os MWS was alcoholism, corresponding to 8 cases (53.3%), followed by unidentified causes in 3 patients (20%), acute

gastroenterocolitis and gastroesophageal reflux disease, each with 2 cases (13.3%). At the endoscopy exam, in addition to MWS, 3 patients presented with enanthematous gastritis, one with erosive gastritis, one with esophageal varices and another with healing gastric ulcer.

Conclusion: The results set the profile of patients with MWS as men, alcoholics, presenting with hematemesis associated or not with melena and median age of 52 years. It is important to recognize this entity in cases of upper gastrointestinal bleeding, especially of non-varicose origin in alcoholic patients.

References: 1. Rawla P, Devasahayam J. Mallory Weiss Syndrome. [Updated 2019 Mar 25]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2019 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK538190/ 2. Rich K. Overview of Mallory-Weiss syndrome. J Vasc Nurs [Internet]. 2018;36(2):91-3. Available from: https://doi.org/10.1016/j.jvn.2018.04.001 3. Cybułka B. Mallory-Weiss Syndrome based on own experience-diagnostics and modern principles of management. Pol Prz Chir Polish J Surg. 2016;88(2):77-86

Disclosure: Nothing to disclose

P1928 ACUTE UPPER GASTROINTESTINAL BLEEDING - ADHERENT CLOTS, ADHERENCE TO GUIDELINES

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Introduction: Acute upper gastrointestinal haemorrhage secondary to peptic ulcer disease carries a significant mortality risk. The management of peptic ulcers with adherent clots (Forrest IIB) remains uncertain. ESGE recommends consideration of endoscopic clot removal. We aim to describe the demographics and outcomes of patients with adherent clots at a district general hospital.

Aims & Methods: Data for patients admitted to our Trust and diagnosed with a peptic ulcer over the last 3 years was obtained from the coding department using ICD-10 codes (K25.0, K25.2, K26.0, K26.2, K27.0 and K27.2). 89 patients that had undergone inpatient endoscopy were identified.

Results: 89 patients; female 28 (31.5%), mean age 72.9 (23 - 96). 17 (19.1%) patients were taking anticoagulants/antiplatelets (8 warfarin, 4 DOACs, 5 clopidogrel / ticagrelor). Mean length of stay 12.7 days. 6 (6.7%) patients had rebleeds, 2 (2.2%) patients underwent surgery and 6 (6.7%) patients died.

29 (32.6%) patients had adherent clots found at endoscopy.

Of 29 patients with adherent clots; 3 (10.3%) had documented endoscopic removal; 14 (48.3%) had documented not removal and 12 (41.4%) had no documentation of adherent clot management. 13 of the 14 adherent clots (93%) that were not removed were located in D1. 8 (27.6%) patients with an adherent clot received monotherapy.

	Adherent Clot (n=29)	No adherent clot (n=60)	*p value
Indication (Haematemesis & Melaena), n (%)	15 (51.7)	10 (16.7)	0.0006
Size (cm), mean (range)	1.5 (0.5 - 5)	1.1 (0.5 - 3)	0.009
Transfused, n (%)	26 (89.7)	42 (70.0)	0.04

[Table 1. Adherent Clot versus No Adherent Clot - Demographics and ulcer outcomes]

Conclusion: Patients with adherent clots presented with more severe symptoms, had larger ulcers and required more transfusions. Only 10% of adherent clots had documentation of endoscopic removal and almost half of adherent clots were not removed. Clearer documentation is required for future practice. Ambiguous guidelines could be contributing to variability in practice and suboptimal management.

Disclosure: Nothing to disclose

P1929 OUTCOMES ON THE USE OF HEMOSPRAY IN GASTROINTESTINAL BLEED POST ENDOSCOPIC THERAPY: OUTCOMES FROM THE MULTICENTRE INTERNATIONAL HEMOSPRAY REGISTRY

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Introduction: With increasing advances and complexity of endoscopic therapy, there is an increased risk of post procedure bleeding. Hemospray (Cook Medical, North Carolina, USA) is a novel haemostatic powder for GI bleeding. The aim of this study is to look at outcomes in patients with upper Gastrointestinal bleeds (UGIBs) following endoscopic therapy treated with hemospray in 14 centres worldwide.

Aims & Methods: Data was prospectively collected on the use of hemospray from specialist centres (Jan'16-September'18). Hemospray was used during emergency endoscopy for UGIBs post endoscopic therapy at the discretion of the endoscopist as a monotherapy, dual-therapy with standard haemostatic techniques or rescue therapy once standard methods have failed. Haemostasis was defined as the cessation of bleeding within 5 minutes of the application of hemospray. Rebleeding was defined as a sustained drop in Hb (>2g/l), haematemesis or melaena with haemodynamic instability after the index endoscopy.

Results: 59 patients had UGIBs post endoscopic therapy (41 male,18 female, 34/59 (58%) post Endoscopic mucosal resection (EMR), 5/59 (9%) post ESD, 5/59 (9%) post biliary sphincterotomy). The median Blatchford score at baseline was 4 (IQR,0-8). The average Rockall score was 6 (IQR, 5-7).

Haemostasis following the application of hemospray was achieved in 60/60 (100%) of patients. 14/59 (24%) patients had monotherapy with hemospray, 32/59 (54%) had combination therapy and 13/59 (22%) had rescue therapy. 2/46 (4%) had a rebleed post hemospray, one was following oesophageal EMR and the other post duodenal EMR. There were no patients' deaths within 30 days.

Conclusion: Hemospray is effective in achieving immediate hoemostasis following endoscopic therapy, with a low rebleed rate and no 30-day mortality.

Disclosure: Nothing to disclose

P1930 VERY EARLY ENDOSCOPY IN UPPER GASTROINTESTINAL BLEEDING

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Introduction: Acute upper gastrointestinal bleeding is a common condition in the emergency unit and has significant associated morbidity and mortality. Worldwide the most common causes of UGIB are nonvariceal, from peptic ulcers, Mallory Weiss syndrome, angiodysplesia or malignancy of the upper GI tract. ESGE guideline recommends performing early endoscopy (< 24 hours) after hemodynamic resuscitation. Very early endoscopy (< 12 hours) is recommended in patients with high risk clinical features like persistent hypotension and tachycardia after volume resuscitation.

Aims & Methods: The aim of the study was to evaluate the causes of UGIB, assess the time for early endoscopy and the hemostatic techniques used. We performed a retrospective study between 1st September 2018 to 31th December 2018 and included 182 patients who were admitted in our department with upper gastrointestinal bleeding.. We divided them into variceal bleeding (69 patients) and nonvariceal bleeding (113 patients).

Results: The mean age in the variceal bleeding lot was 55 years old, the youngest being 28 years old and the oldest 79 years old. 8 patients had bleeding from gastric varices GOV I and in one case was used injection of Glubran and in the other 7 patients band ligation. 61 patients had haemorrhage from esophageal varices and band ligation was performed.

The average time passed from presentation until the performance of the therapeutic endoscopy in patients with variceal bleeding was 3 hours and 55 minutes and the hospitalization period was around 3 days. From 69 patients with variceal bleeding 7 died, but they were having important comorbidities related mainly to advanced cirrhosis (hepatic cirrhosis Child B or C and hepatocarcinoma) .

In the non variceal lot, the average age was 59 years old, the youngest being 18 years old and the oldest patient being 90 years old. The most common causes were gastric ulcer (30 cases) or duodenal ulcer (35 cases), followed by 16 patients with Mallory Weiss lesions, 7 with Dieulafoy lesions and 6 with bleeding from gastric angiodysplasia. Rare causes of UGIB were haemorrhage from vater ampullary cancer, gastric polyps and hemosuccus pancreaticus. The therapeutic tools used in UGIB from ulcers were injection of epinephrine 1:10.000 in saline, followed by a second hemostatic procedure, like electrocoagulation using GoldProbe and application of endoscopic hemoclips

In patients with bleeding from Dieulafoy lesions and gastric angiodysplasia we used diluted epinephrine injection followed by electrocoagulation with GoldProbe and in Mallory Weiss lesions we frequently used dilute adrenaline injection and hemoclips.

The time passed from presentation until we performed the therapeutic endoscopy in the nonvariceal group was on average 5 hours, and the duration of hospitalization was on average 4 days. We had 8 deaths, 5 with duodenal ulcer and 3 with Dieulafoy lesion, related to cardiovascular comorbidities and anticoagulation drugs.

Conclusion: Very early endoscopic approachment seems to lowers the mortality rate and the duration of hospitalization, especially in patients with active bleeding or important comorbidities. From our experience, a good patient orientated rapid hemeodynamic echilibration and early endoscopy seems to be the best management for the UGIB.

Disclosure: I have nothing to disclose.

P1931 RISK FACTORS FOR EARLY MORTALITY IN VARICEAL BLEEDING

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Introduction: Acute haemorrhage from ruptured esophageal varices is most probably the most serious consequence of uncontrolled portal hypertension in cirrhotic patients, with a significant mortality. Overall survival is improving, due to new therapeutic approaches and improved medical care. However, early mortality after an episode of acute variceal bleeding remains high.

Aims & Methods: The aim of this study was to evaluate the risk factors affecting 5-day mortality rate after acute variceal bleeding in unselected cirrhotic patients.

537 cirrhotic patients admitted in our department with variceal bleeding were evaluated, 351 men and 186 women, with a mean age of 58.8 years, during a 7 years period. We divided the group of patients into three groups: group A, who died due to severe variceal bleeding (n=32), group B, the survivors (n=452), and group C, patients who died from other complications (n=53).

We tried to identify prognostic factors for massive, uncontrollable variceal hemorrhage by comparing patients' characteristics among the three groups.

Results: Total in hospital mortality rate was 15.8% (n=85), with a death rate of 5.9% (n=32) due to severe bleeding, while 9.8% of patients died from other complications.

There were no significant differences regarding the proportion of grade 3 EV and grade 2 EV in group A vs. group B vs. group C, nor regarding the mean age. The proportion of class Child Pugh class C in group A was significantly higher than in group B, but similar to group C. The MELD score was significantly higher in group A than in group B, but similar to group C. Severe thrombocytopenia (< 50.000/mmc) and haemorrhagic shock at admission were significantly more frequent in group A than in group B, but similar to group C.

Characteristics	Group A (32p) vs. Group B (452p)	Group A (32p) vs. Group C (53p)
EV grade 3	11/32 vs. 195/452 p= NS	11/32 vs. 22/53 p= NS
EV grade 2	20/32 vs. 257/452 p= NS	20/32 vs. 31/53 p= NS
Age	58 y/o vs. 59 y/o p= NS	58 y/o vs. 59 y/o p= NS
Child Pugh Class C	22/32 vs. 151/452 p=0.0006	22/32 vs. 31/53 p= NS
Meld score	24.5 vs. 17.4 p= 0.0005	24.5 vs. 24.8 p= NS
Severe thrombocytopenia	10/32 vs. 76/452 p< 0.0001	10/32 vs. 11/52 p= NS
Haemorrhagic shock	24/32 vs. 12/452 p< 0.0001	24/32 vs. 13/53 p= NS

[Table]

Conclusion: Liver failure, severe thrombocytopenia and haemorrhagic shock at admission were the risk factors we identified for in hospital 5-day mortality rate due to variceal bleeding.

Disclosure: Nothing to disclose

P1932 EVALUATION OF OUR IN-PATIENT ENDOSCOPY WORKLOAD AND MEETING NATIONAL STANDARDS FOR THE MANAGEMENT OF UPPER GASTROINTESTINAL BLEEDING IN A UNIVERSITY HOSPITAL

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Introduction: The 2015 United Kingdom (UK) National Confidential Enquiry into Patient Outcome and Death (NCEPOD) report, 'Time to get control' and National Institute for Health and Care Excellence (NICE) clinical guideline (CG141), England highlighted the need for endoscopy within 24 hours for patients presenting with suspected acute upper gastrointestinal bleeding (AUGIB). However, endoscopy demand has increased in recent years. We set out to evaluate our in-patient endoscopy procedure mix, workload, assess the timeliness of endoscopy and intervention rates for patients with AUGIB following a revised service arrangement. The updated service offers gastroenterology in-reach ward rounds on the acute medical units and once daily dedicated emergency inpatient endoscopy list at the University Hospitals of Leicester, UK NHS Trust which serves a catchment population of 1.1 million.

Aims & Methods: Patients referred for inpatient endoscopy from 1st of January to 31st of December 2017 were retrospectively identified via our online Integrated Clinical Environment (ICE) referral system, inpatient endoscopy procedure books and consultant's call out time sheets. ICE referrals and endoscopy database records were reviewed and cross referenced. Basic demographics, indications, number and type of endoscopic procedures including intervention rates for AUGIB were analysed. Time to endoscopy was defined as time of ICE referral to time of completion of endoscopy report. Simple regression analysis and Chi-Square test were used for statistical analysis.

Results: The total number of in-patient endoscopic procedure performed was 2033 with a mean number of 169 (1400 OGDs, 585 flexible-sigmoidoscopies, and 48 colonoscopies). 745 OGDs were performed for suspected AUGIB with a mean number of 61 procedures per month. Median and mean time to endoscopy was 5.2 hours (Interquartile Range [IQR] 3-21.9h) and 13.1 hours respectively. 84% of OGDs for AUGIB were performed within 24 hours. Overall intervention rate was 27.2%. The intervention rate was lower for procedures done outside of 24 hours compared to procedures done within 24 hours (17.6% versus 29.2% p = 0.010). 81.9% of ICE referrals were logged during in hours (9:00 to 17:00) and 18.1% were logged out of hours (17:00 to 08:00). We did not find an association between the timing of referral with timing of endoscopy (p = 0.912).

Conclusion: Despite proactive emergency working arrangements, a large proportion of endoscopies for patients with AUGIB were performed outside the time frames set by NICE guidelines and the NCEPOD report. Overall intervention rate was high but lower in procedures performed outside of 24 hours suggesting a degree of triage in utilizing the in-patient endoscopy list. To meet the 24 hour standard, an all-day rolling emergency endoscopy list maybe needed, a luxury few UK NHS Trusts can afford at times of severe constraints on endoscopy services.

Disclosure: Nothing to disclose

P1933 WITHDRAWN

P1934 ENDOSCOPIC MANAGEMENT OF UPPER GASTROINTESTINAL BLEEDING AS PART OF A MULTIDISCIPLINARY TEAM IN AN EMERGENCY TERTIARY CARE HOSPITAL: A SINGLE-CENTER COHORT STUDY

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Introduction: Upper gastrointestinal bleeding (UGIB) represents the main endoscopic emergency worldwide and despite the development of new therapeutic methods its treatment can still be very challenging.

Aims & Methods: The aim of this paper is to assess the patients with UGIB, both variceal and non-variceal who underwent early endoscopic treatment (< 12 hours) in a tertiary care emergency hospital. This is a retrospective analysis that enrolled patients with UGIB from January 2015 to December 2018, hospitalized in the Bucharest Clinical Emergency Hospital in Romania. Both the variceal and non-variceal bleeding were evaluated in terms of the type of lesion and the follow-up of the endoscopic treatment: rebleeding, admission in Intensive Care Unit (ICU), surgical treatment and death.

Results: The study included a total of 1677 patients, which were separated into two groups, non-variceal bleeding (1066 patients) and variceal bleeding (611 patients). In the non-variceal bleeding group, 32.74% had gastric ulcer, 30.86% had duodenal ulcer, 10.22% had Mallory-Weiss lesions, 7.61% of patients were bleeding from vascular lesions (angiodysplasias and Dieulafoy lesions), 6.56% from tumours (oesophagial, gastric and

duodenal tumours), 3.29% from esophageal ulcers, 3.19% had endoscopic retrograde cholangio-pancreatography (ERCP) post-sphincterotomy bleeding, 3.18% had acute hemorrhagic gastroduodenitis, while smaller percentages had acute necrotizing oesophagus (1.03%), post-gastric polypectomy bleeding (0.94%) and arterial fistulas or aneurysms (0.38%). Only 85.55% required endoscopic treatment and all patients received proton pump inhibitors drugs. Rebleeding was assessed in 48 patients (5.26%), mostly from gastric ulcers (24 patients), duodenal ulcers (14 patients) and ERCP post-sphincterotomy (3 patients). ICU admission was needed in 7.42% of total cases. A mortality rate of 12.29% (131 patients deceased) was recorded, mostly because of major comorbidities. Emergency surgery was needed in 22.92% of the patients with rebleeding, of which 27.27% of patients had good outcome and 72.73% of patients had deceased.

In the variceal bleeding group, from the total of 611 patients receiving endoscopic treatment in our unit, 529 had esophageal varices (EV), 49 had gastroesophageal varices type 1 (GOV1), 20 had gastroesophageal varices type 2 (GOV2) and 13 had isolated gastric varices (IGV). All the patients received adequate endoscopic treatment as well as medical treatment (vasoactive drugs such as terlipressin). The rebleeding rate was of 2.12% and was evaluated considering each type of varices: 8 patients with EV, 3 patients with IGV, 1 patient with GOV1 and 1 patient with GOV2. Sengstaken-Blakemore tube was necessary in 9 patients (1.47%) and admission in the ICU was required in 5% of the patients. We assessed the outcome of these patients: 94.44% had a positive outcome and were discharged and 5.56% deceased.

Conclusion: Our experience as an emergency tertiary care center with UGIB emphasizes the importance of early endoscopic approach as a safe and effective procedure with a high success rate, reducing the need for surgery. However, the mortality rate in both variceal and non-variceal bleeding remains high, therefore a multidisciplinary management (endoscopists, surgeons and anesthesiologists) is still considered the best approach for these patients.

Disclosure: Nothing to disclose

P1935 GASTROINTESTINAL BLEEDING IN PATIENTS ON ORAL ANTICOAGULATION THERAPY: CLINICAL AND DEMOGRAPHIC CHARACTERISTICS

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Introduction: There is frequent and growing use of medications that prevent abnormal blood clotting, including anticoagulants and antiplatelets[1]. However, their therapeutic benefits must be balanced against the risks[2]. The reported incidence of hemorrhagic complications in patients treated with anticoagulated drugs ranges from 12 to 40%[3]. The commonest site of significant bleeding is the gastrointestinal tract.

Aims & Methods: The aim of this study was to assess the clinical and demographic characteristics of anticoagulated patients hospitalized with gastrointestinal bleeding in a university hospital. A retrospective study was carried out with data collection of medical records and the protocol implanted in 772 patients of the Digestive Hemorrhage Service. From September 2017 to January 2019, 39 patients with gastrointestinal bleeding (GIB) were hospitalized while on oral anticoagulants. The patients were categorized according to age, sex, need for transfusion, death, symptomatology of entry, alcoholism, medications, comorbidities, endoscopic diagnosis, endoscopic treatment. The clinical outcome of these patients was compared with those of 591 patients hospitalized in the same time with GIB who were not taking anticoagulation or antiplatelets.

Results: 39 patients used oral anticoagulants (5%). The most prevalent gender was the female (51%). The mean age was 74 years (19-91). Eleven patients died (28.3%), mostly men (9). Transfusion of red blood cells was necessary in 27 patients (69.2%) and the higher international normalized ratio (INR) didn't increase the number of blood bags or the mortality. The most common entry symptoms were hematemesis with 24 cases (61.5%) and melena (53.8%). The mean hemoglobin level at admission was 8.8 g / dL (4.1-17.2). Warfarin was the mostly used anticoagulant (50%). Of the

39 patients, 10 were alcoholics (25.6%), all men. Cirrhosis was observed in only one individual, having the alcoholism as its etiology. The most frequent comorbidity was systemic arterial hypertension (64%). At endoscopic examination, 21 presented mucosal lesions (53.8%), 9 with peptic ulcers (23%), 2 with duodenal ulcers, 1 with esophageal ulcer, 2 with gastric varices and one sclerotherapy was needed. We found no significant difference between the death rate between anticoagulated (28.3%) and non-anticoagulated patients (20.3%; p=0.22).

Conclusion: Acute gastrointestinal bleeding is a severe complication in patients receiving long-term oral anticoagulant therapy, with high mortality. These patients usually bleed from mucosal disease, a non-varicose cause. However, in this study, there was no statistically significant difference between the death rate between anticoagulated and non-anticoagulated.

References: 1. Pedro Raquel, Sobral Maria Ana. Novos anticoagulantes orais e risco de hemorragia gastrointestinal: uma realidade? Rev Port Med Geral Fam [Internet]. 2015 Ago; 31(4): 286-288. Available from: http://www.scielo.mec.pt/scielo.php?script=sci_arttext&pid=S2182-51732015000400009&lng=pt. 2. Chang HY, Zhou M, Tang W, Alexander GC, Singh S. Risk of gastrointestinal bleeding associated with oral anticoagulants: population based retrospective cohort study. BMJ [Internet]. 2015 Apr 24;350:h1585. Available from: http://dx.doi.org/10.1136/bmj.h1585 3. Levine MN, Raskob G, Landefeld S, Kearon C. Hemorrhagic complications of anticoagulant treatment. Chest. 2001;119(1 Suppl.):108S-21S. Available from: https://doi.org/10.1378/chest.119.1_suppl.108S

Disclosure: Nothing to disclose

P1936 PLATELETS TRANSFUSION NEED IN CIRRHOTIC PATIENTS WITH GASTROINTESTINAL BLEEDING

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Introduction: Upper gastrointestinal bleeding (UGIB), defined as bleeding from lesions in the digestive tract proximal to the Treitz ligament is a medical emergency with high mortality rates[1]. Of the cases of UGIB, 10% to 30% have varicose origin, and these varicose veins are present in 50% of cirrhotic patients[2]. Volemic reposition is used as the initial management of UGIB and should be more carefully chosen in patients with varicose UGIB, as they have a persistent state of hypervolemic circulation, with splanchnic vasodilation and low effective arterial volume, tending to arterial hypotension. Formal platelet transfusion indications are bone marrow failure or secondary hemorrhagic manifestations treatment[3].

There is no consensus, however, some authors indicate that values above 50,000 platelets/mm^{3} are safe for performing invasive procedures[3], and at least 20,000 platelets/mm^{3} for performing non-invasive procedures. Transfusion, therefore, is only indicated below 50,000 platelets/mm^{3} in invasive procedures and below 20,000 platelets/mm^{3} in non-invasive procedures. There is no indication of prophylactic transfusion in cases other than these.

Aims & Methods: To characterize the need for platelet transfusion in the cirrhotic patient with gastrointestinal bleeding treated in a university hospital from September 2017 to January 2019. This is a retrospective study with data gathering from the 772 patients of the Digestive Hemorrhage Department of the Hospital Universitário Evangélico Mackenzie, Curitiba, Brazil. In September 2017, this hospital became a unique reference for acute cases of gastrointestinal bleeding in Curitiba. Descriptive and statistical analysis was made of the prevalences according to age, sex, need for transfusion, death, symptomatology of entry, smoking, alcoholism, comorbidities, clinical-surgical management, endoscopic diagnosis, endoscopic treatment.

Results: Of the 772 patients, 12 presented with cirrhosis and were subject to platelet transfusion (1.5%), composing the sample 10 men (83.3%) and 2 women (16.7%). At admission, the average platelet count of these patients was 98,000/mm^{3} (15,000-285,000). Only one patient had platelets below 20,000/mm^{3} (8.3%) and other 3 patients had platelets equal to or below 50,000/mm^{3} (33.3%). Therefore, there were 8 platelets transfusions without indication (66.6%). The median age was 51.5 years (SD = 8.8). 4

patients died (33.3%). The mean hemoglobin level at admission was 7.4 g/dL (3.7-9.7). Red blood cell transfusion was required in 11 patients (91.6%). The most present entry symptom was hematemesis with 11 cases (91.6%) and the most common association was hematemesis and melena with 7 cases (58.3%). Of the 12 patients, 9 were alcoholics (75%), all of them cirrhotic. At endoscopic examination, the most prevalent cause of UGIB was esophageal varices, corresponding to 10 cases (83.3%), of which 3 needed elastic ligature, followed by portal hypertensive gastropathy with 4 patients (33.3%).

Conclusion: The profile of the cirrhotic patient with gastrointestinal bleeding and platelet transfusion need is of men with a mean age of 51.5 years, alcoholics, presenting with hematemesis. The Department, facing so many platelet transfusions without indication, decided to better educate residents and attending physicians, as well as to restrict transfusion to extreme thrombocytopenia (less than 15,000 platelets/mm³) and to wait for the improvement of platelet metrics with drugs, to perform procedures, invasive or not.

References: 1. Lourenço, K., & Oliveira, R. (2003). ABORDAGEM DO PACIENTE COM HEMORRAGIA DIGESTIVA ALTA NÃO VARICOSA. Medicina (Ribeirao Preto. Online), 36(2/4), 261-265. 2. LUZ, Haroldo Luiz Jordelino da et al. FATORES PROGNÓSTICOS E MORTALIDADE EM PACIENTES CIRRÓTICOS QUE FORAM INTERNADOS COM HEMORRAGIA DIGESTIVA ALTA VARICOSA EM UM HOSPITAL PÚBLICO. Arquivos Catarinenses de Medicina, [S.l.], v. 46, n. 1, p. 97-106, jul. 2017. ISSN 18064280. Disponível em: 3. Ministério da Saúde. Guia para Uso de Hemocomponentes 2010, 1ª Edição.

Disclosure: Nothing to disclose

P1937 EFFECTIVENESS OF MANAGEMENT STRATEGIES FOR UNINVESTIGATED DYSPEPSIA: SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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Introduction: Dyspepsia is common in the community, causing a substantial impact on quality of life for sufferers as well as financial implications for society. The initial management of dyspepsia in primary care is a classical medical decision-making problem, with a number of competing strategies for the physician to consider. However, there is equipoise between some of these, and current guidelines do not agree on which approach should be used first-line.

Aims & Methods: Our aim was to conduct a network meta-analysis to compare the effectiveness of first-line strategies for the management of patients with uninvestigated dyspepsia.

MEDLINE, EMBASE, EMBASE Classic, the Cochrane central register of controlled trials, and clinicaltrials.gov were searched through March 2019 to identify randomised controlled trials (RCTs) assessing effectiveness of five management strategies (prompt endoscopy, "test and treat", "test and scope", empirical acid suppression, or symptom-based management) for uninvestigated dyspepsia. Trials reporting a dichotomous assessment of symptom status at final point of follow-up (≥12 months) were included.

Data were pooled using a random effects model. Effectiveness was reported as a pooled relative risk of remaining symptomatic at final follow-up, with 95% confidence intervals (CIs) to summarise effectiveness of each comparison tested, and ranked according to P-score. We also analysed likelihood of patients in each treatment arm requiring endoscopy, dissatisfaction with management, and rates of upper gastrointestinal cancer.

Results: We identified 15 eligible RCTs, containing 6162 patients. Of the five strategies, "test and treat" was ranked first, using both an intention-to-treat and per protocol analysis (P-score 0.79 for both) (Figure), but none of the strategies were significantly less effective than "test and treat", or more effective than each other, on direct or indirect comparison. Prompt endoscopy ranked second, but performed similarly (P-score 0.71 and 0.69 on intention-to-treat and per protocol analysis).

Patients assigned to "test and treat" were significantly less likely to require subsequent endoscopy (P-score 0.98), compared with all other strategies on indirect comparison. Dissatisfaction rates were significantly lower among patients randomised to prompt endoscopy, compared with "test and treat" and empirical acid suppression on indirect comparison. Only 20 upper gastrointestinal cancers (0.4%) were detected in 11 RCTs reporting this endpoint, containing 5028 patients. Detection rates were broadly similar between treatment arms.

Conclusion: In a network meta-analysis of RCTs, "test and treat" and prompt endoscopy performed similarly in terms of effect on symptoms at last point of follow-up, but "test and treat" was ranked first, and led to significantly fewer endoscopies than all other approaches. This suggests, of the five management strategies we studied, "test and treat" is the likely to be the most cost-effective.

Disclosure: Nothing to disclose

P1938 FUNCTIONAL DYSPEPSIA, PEPTIC ULCER AND *HELICOBACTER PYLORI* INFECTION IN A RURAL BANGLADESHI COMMUNITY: AN ENDOSCOPY-ASSISTED HOUSEHOLD SURVEY

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Introduction: The epidemiology including the prevalence and risk factors of dyspepsia varies in different population. Moreover, functional dyspepsia (FD), though is commoner than organic in hospital studies, community data, particularly from rural areas, are lacking in Asia due to difficulty in performing endoscopy in the community. Hence, we performed a rural community study in Bangladesh with the following aims:
(1) to study the prevalence of uninvestigated dyspepsia (UD), FD and structured dyspepsia (SD) in the community,
(2) to evaluate the frequency of *H. pylori* in FD and peptic ulcer (PU),
(3) to study its virulence-associated genes (CagA, vacA and specifically the vacA allelic variants) among patients with FD as compared to PU, and
(4) to determine the risk factors for dyspepsia.

Aims & Methods: This prospective cross-sectional house-to-house survey was undertaken by trained field interviewers among adult population (>18-y) in three villages (Charcharia, Churain of Dhaka district and Kharrah of Munshiganj district of Bangladesh) using enhanced Asian Rome III questionnaire and General Health Questionnaire-28 translated and validated in Bengali language. Dyspepsia, functional heartburn (FH) and IBS were defined by Rome III criteria.

Dyspeptic subjects were offered an upper gastrointestinal endoscopy including tests for *H. pylori* (rapid urease test, histology and multiplex polymerase chain reaction, PCR; infection was diagnosed if PCR or two other tests were positive) and its genotyping by PCR for CagA, vacA and specifically the vacA allelic variants. SD was diagnosed in presence of duodenitis or erosions, PU and erosive esophagitis.

Results: 3351/3559 subjects responded [(94.15%), mean age 40.41±16.05 y, female, 1924 (57.4%)]. 547 (16.3%) had UD [female 346 (18%) vs male 201 (14%); p=0.002)]. 201 (6%), 88 (2.6 %,) and 258 (7.7%) had postprandial distress syndrome (PDS), epigastric pain syndrome (EPS) and PDS-EPS overlap, respectively.

On multivariate analysis increasing age, female gender, being married, lower education of less than class V, lower family income, use of non-steroidal anti-inflammatory drugs, history of acute gastroenteritis in last year and presence of psychological distress were found as risk factors for UD. Of 346 (63.25%) agreeing for endoscopy; 232 (67.05%) and 114 (32.95%) had FD and SD [PU 99 (28.61%); EE, 13 (3.76%) and both peptic ulcer and EE, 4 (1.16%)] respectively. Of 232 FD subjects, 35 (15%), 73 (31%) and 124 (54%) had EPS only, PDS only and EPS-PDS overlap, respectively. *H pylori* was positive among 266/342 (78%) dyspeptics [FD, 173 /230 (75.2%) vs SD, 92/114 (82.1%) (p=0.169)]. *H. pylori* infected patients with PU had higher frequency of Cag A and vac A genotype s1m1 positivity than those with FD (p< 0.05). Of the 547 UD subjects, 203 (37%) had FH, 110 (20%) had IBS and 52 (9.5 %) had both FH and IBS.

Conclusion: 16%, 11% and 5% rural adult population of Bangladesh had UD, FD and PU, respectively. About half of the patients with dyspepsia had PDS-EPS overlap and 20% had overlap with IBS. About third of the subjects with UD had SD, mostly PU. Patients with PU had more virulent *H. pylori* compared to those with FD.
Disclosure: Nothing to disclose

P1939 EVALUATION OF MINDFULNESS BASED COGNITIVE THERAPY IN PATIENTS WITH FUNCTIONAL DYSPEPSIA IN A TERTIARY REFERRAL CENTRE IN SINGAPORE

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Introduction: Functional dyspepsia (FD) is a disorder of the brain-gut axis characterised by symptoms of abdominal discomfort. Mindfulness-based therapies use meditation and relaxation to achieve a state of consciousness, mindfulness, during which one consciously attends to his or her moment-to-moment experience. Its efficacy for FD treatment is uncertain.
Aims & Methods: To determine the effectiveness of group mindfulness based intervention in improving the symptoms and quality of life in patients with functional dyspepsia. We performed an assessor-blinded randomised treatment-as-usual waitlist controlled trial. Patients who fulfilled Rome-3 FD were prospectively recruited from a tertiary care gastroenterology unit in Singapore and randomised to undergo Mindfulness Based Cognitive Therapy (MBCT) or Treatment-as-Usual (TAU). Subjects in the MBCT arm underwent weekly 2-hour-long standardised MBCT sessions for 8 weeks and 1 half-day retreat conducted by 2 accredited psychologists. Outcomes were assessed using Short Form Nepean Dyspepsia Index (NDI-SF) and the EuroQOL VAS scale which were administered pre and post treatment by assessors blinded to the treatment assignment. The Primary outcome was change in NDI-SF and EuroQoL at end of treatment compared to baseline. Ethics Board review was obtained.
Results: Fifty three patients were referred and 27 (59.9%) patients were recruited over 3 months. Amongst those who did not agree to recruitment, 10 were not fluent in English, 10 cited time constraints and unsuitability of the MBCT schedules, and 6 had no cited reasons. 21 of 27 patients (78%) completed the intervention. Of those who withdrew, 5 found difficulty in attending the intervention schedule due to time commitments, 1 had difficulty in following with the intervention instructions, 1 lost interest, and 2 were unable to complete "homework" due to time constraints.
There was significant difference in change of NDI-SF at end of treatment compared to baseline between MBCT and TAU (mean change: -11.33 (7.53) Vs -2.0 (9.16), p< 0.01) (see table) indicating that participants in the MBCT arm experienced a greater symptom improvement as compared to those in the TAU arm. There was no significant difference in change of EuroQOL VAS scale between baseline and post-treatment assessment between groups.

		Mean Baseline (SD)	Mean End of MBCT (SD)	Mean change baseline to end (SD)	Mean difference between MBCT and TAU (SD)	p
NDI-SF	MBCT	28.14 (9.54)	16.81 (4.75)	-11.33 (7.53)	6.19 (8.38)	<0.01
	TAU	25.00 (8.72)	23.00 (9.58)	-2.0 (9.16)		
EuroQoL-VAS	MBCT	57.79 (21.43)	61.45 (15.34)	3.66 (18.64)	1.8 (18.45)	0.53
	TAU	62.69 (16.91)	63.25 (19.50)	0.56 (18.25)		

[Table of Results]

Conclusion: FD patients who underwent MBCT experienced a greater improvement in their symptoms compared to those in the TAU arm. Language proficiency and time constraints were the major barriers to attendance of MBCT. Modifications to the intervention to address these limitations and careful patient selection should be considered in future studies.
Disclosure: Nothing to disclose

P1940 DYSPEPSIA E-LEARNING: NOVEL TOOL FOR DYSPEPSIA MANAGEMENT

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Introduction: Digital educational tools hold several advantages over non-digital information. Patient engagement in self-management is an important application of digital tools. Dyspepsia is a condition primarily managed by lifestyle intervention, making patient engagement and educational motivation essential. Adoption of an educational tool depends on its development process and information transfer methods. We provide a detailed description of a successful dyspepsia e-learning development process.
Aims & Methods: We assessed users' needs by focus groups and interviews, followed by scientific validation of information against a systematic literature review. Subsequently, we developed the content based on most important themes, provided by the focus group participants and current literature. All content was organized into chapters and we supplemented information with text, videos, and 3D visualizations. The e-learning was pilot-tested and adjusted accordingly.
Results: We performed a focus group both with dyspeptic patients (n = 5) and general practitioners (n = 5). Main themes revealed were 1) Reassurance; 2) Pathophysiology of dyspepsia; 3) Prevalence, symptoms and prognosis of dyspepsia; 4) Lifestyle interventions; 5) Availability and value of therapy and diagnostics; 6) Psychosocial factors in dyspepsia, and 7) Peers' experiences. We wrote short text blocks providing information per item and added videos of a gastroenterologist, dietician and patient, explaining gastric function, dietary interventions and patient experiences. We created 3D visualizations of dyspepsia prevalence, upper gastrointestinal endoscopy procedure, gastric anatomy, function and mucosal damage, and pharmacological mechanisms of acid-reducing drugs.
Conclusion: The dyspepsia e-learning is a novel multi-media educational tool to assist patients and physicians in management of dyspepsia. This tool may be deployed to stimulate patient engagement and improve health outcomes. The presented protocol can be used to guide development of future e-learnings for dyspepsia, or similar conditions.
https://elearning-gastroscopiestaging.medify.eu/mdl/index_elearning-cwz_nl.html
Disclosure: Nothing to disclose

P1941 EDUCATING DYSPEPTIC PATIENTS REDUCES NEED FOR UPPER GASTRO-INTESTINAL ENDOSCOPY WITH > 40%: A MULTI-CENTER RANDOMIZED CONTROLLED TRIAL

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Introduction: Upper gastro-intestinal (GI) endoscopy is frequently performed in dyspeptic patients. Diagnostic yield is low and clinical implications are limited. Therefore, dyspeptic patients are exposed to an avoidable invasive procedure. Symptom comprehension and lifestyle modifications potentially reduce patients' need for upper GI endoscopy.
Aims & Methods: Our aim was to study whether education of dyspeptic patients by e-learning reduces upper GI endoscopies in patients referred for direct-access upper GI endoscopy. We performed a multi-center, randomized, controlled trial in dyspeptic patients aged 18-70 years, referred for direct-access upper GI endoscopy. We excluded patients with alarming features or family history of upper GI malignancy. We recruited patients from four district hospitals in the Netherlands and randomly assigned (1:1 ratio) patients to receive either e-learning education (intervention) or endoscopy (control). Primary outcome was the difference in proportion of cancelled upper GI endoscopies at 12 weeks. Secondary outcomes included

symptom type and severity (PAGI-SYM), dyspepsia-related quality of life (SF-NDI) and health anxiety (SHAI). NCT03205319.

Results: We randomized a total of 119 patients (median age 48 yrs [IQR:37-56], male 40%, Western European ethnicity 90%, use of acid-suppressive drugs 74%, previous upper GI endoscopy 24%). There were no baseline differences between study groups (intervention n=62; control n=57) with respect to symptom type/severity, quality of life and health anxiety. At 12 weeks, 61% of patients in the intervention group had cancelled endoscopy, vs. 14% of controls (RR 0.44 [95% CI 0.31-0.62], p < 0.001). No GI malignancy was detected.

Conclusion: E-learning education of dyspeptic patients effectively and safely reduces 47% of upper GI endoscopies. Education by e-learning may be broadly implemented in clinical practice to improve efficient use of upper GI endoscopies.

Disclosure: Nothing to disclose

P1942 PHARMACOLOGICAL PROFILE OF NALDEMEDINE, A PERIPHERAL ACTING µ-OPIOID RECEPTOR ANTAGONIST-COMPARISON WITH NALOXONE AND NALOXEGOL

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Introduction: Opioid-induced constipation (OIC), a common side effect of opioids, is due to the activation by opioids of the µ-opioid receptors in the enteric nervous system[1]. Peripherally acting µ-opioid receptor antagonists (PAMORAs) can reverse OIC by blocking the peripheral action of opioids in the gastrointestinal tract without affecting centrally mediated analgesia[2]. Naldemedine[3] is a PAMORA indicated for OIC in adult patients with chronic non-cancer pain in the US, in patients with chronic non-cancer pain and cancer in Japan and in adult patients who have previously been treated with a laxative in EU.

Aims & Methods: This study evaluated the in vitro and in vivo pharmacological profiles of naldemedine compared with those of naloxone and naloxegol.

In vitro binding affinity, antagonistic activity, Schild plot analysis of antagonism, and binding kinetics were evaluated for naldemedine, naloxegol, and naloxone. In vivo effects of each opioid antagonist on rat small intestinal transit (SIT) as well as withdrawal symptoms in morphine-dependent rats were also evaluated.

		Naldemedine	Naloxone	Naloxegol
Binding affinities/ Antagonist activities	µ (nM)	0.34/ 0.50	1.52/ 4.05	5.04/ 38.35
	δ (nM)	0.43/ 0.27	56.90/ 41.74	99.16/ 145.93
	κ (nM)	0.94/ 0.44	2.63/ 18.43	40.78/ 38.51
Shild analysis of antagonism	Schild slope	1.42	0.88	0.93
Binding kinetics to human µ-opioid receptor	Kon(nM⁻¹min⁻¹)	0.041	0.350	0.056
	Koff(min⁻¹)	0.023	0.290	0.390
	T1/2(min)	30.78	2.44	1.78

[Summary of in vitro pharmacological profile of naldemedine compared with naloxone and naloxegol in human opioid receptors]

Results: *In vitro*, the antagonist activity of naldemedine at human µ, δ or k opioid receptors were 0.50, 0.27 or 0.44 nM, respectively. These values are more potent compared with those of other compounds. The Schild plot analysis indicated that naldemedine antagonized the effect of opioid agonist in a non-competitive manner while other compounds antagonized in a competitive manner. In receptor binding kinetics analysis, naldemedine showed slower K_{on} and K_{off} profile than other compounds. In vivo, naldemedine dose-dependently ameliorated the morphine-induced SIT inhibition. This effect was not dependent on the dose of morphine between 1 and 3 mg/kg. On the contrary, the dose-response curve of naloxegol was significantly shifted between the doses of morphine. This difference in inhibition pattern of naldemedine and naloxegol could be attributed to type of antagonism. In morphine-dependent rats, naldemedine caused peripheral and central withdrawal symptoms at doses higher than 0.3 and 3 mg/kg, respectively, while the ED_{50} for preventive effect of constipation was 0.03 mg/kg. Naldemedine showed slower onset and lower severity of diarrhea, which is a peripheral withdrawal symptom, than other compounds at each ED_{50} in the SIT model. These differences could be attributed to binding kinetics.

Conclusion: Naldemedine acted differently with the mu-opioid receptor when compared with naloxegol and naloxone as demonstrated by slower kinetics and acting as a non-competitive antagonist. These results may explain the clinical profile observed in the clinical trials with naldemedine.

References: 1 Bell T, Annunziata K, and Leslie JB (2009) Opioid-induced constipation negatively impacts pain management, productivity, and health-related quality of life: findings from the National Health and Wellness Survey. J Opioid Manag 5:137-44. 2 Streicher JM, Bilsky EJ (2017) Peripherally Acting µ-Opioid Receptor Antagonists for the Treatment of Opioid-Related Side Effects: Mechanism of Action and Clinical Implications. J Pharm Pract. 31:658-669 3 Kanemasa T, Koike K, Arai T, Ono H, Horita N, Chiba H, Nakamura A, Morioka Y, Kihara T, Hasegawa M (2019) Pharmacologic effects of naldemedine, a peripherally acting µ-opioid receptor antagonist, in in vitro and in vivo models of opioid-induced constipation. Neurogastroenterol Motil. 31:e13563

Disclosure: TK: Participated in research design KK: Conducted experiments and performed data analysis KT: Conducted experiments and performed data analysis TA: Conducted experiments and performed data analysis AN: Participated in research design YM: Participated in research design MH: Participated in research design

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P1943 EFFECT OF NALDEMEDINE ON FREQUENCY OF SPONTANEOUS BOWEL MOVEMENTS AND ASSOCIATED SYMPTOMS

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Introduction: Opioid-induced constipation (OIC) is a well-known side effect of opioid therapy. NAL is a peripherally-acting µ-opioid receptor antagonist approved for the treatment of OIC in patients with chronic non-cancer pain.

Aims & Methods: To assess the effect of naldemedine (NAL) 0.2 mg once daily vs placebo (PBO) on the frequency of bowel movements (BMs), specifically the frequency of spontaneous BMs (SBMs), complete spontaneous BMs (CSBMs), SBMs without straining, and SBMs with a Bristol Stool Scale (BSS) score of 3 or 4 based on pooled results from the COMPOSE-1 and COMPOSE-2 studies during 12 weeks of treatment.

Two randomized, double-blind PBO controlled 12-week studies (NCT01965158 and NCT01993940), assessed the effect over time of NAL 0.2 mg once daily vs PBO in the frequency of SBMs, CSBMs, defined as SBMs with a perception of complete evacuation, SBMs without straining, and SBMs with a BSS score of 3 or 4 in adult (age 18-80 years) subjects with chronic non-cancer pain and OIC. Subjects were required to not be on laxatives at screening or to agree to discontinue laxatives upon signing informed consent. The mean changes in the frequency per week from baseline to each week was compared between NAL and PBO, with a mixed-effects model repeated measures with opioid dose strata and study as a covariate and treatment group, time, time-by-treatment group interaction as fixed effects. Safety was assessed based on the incidence of adverse events (AEs).

Results: In the two studies pooled, 1095 subjects were randomized 1:1 to NAL (N=549) or PBO (N=546) for 12 weeks. In all four endpoints, NAL was associated with a significantly (P≤0.0001) greater improvement from baseline at each week relative to PBO, starting at Week 1 and up to Week 12. The overall incidence of AEs was generally similar between groups. Treatment with NAL was associated with a greater incidence of gastrointestinal AEs (abdominal pain, diarrhea, nausea) compared with PBO.

Conclusion: Treatment with NAL over 12 weeks compared with placebo improved the frequency of bowel movements as well as the signs and symptoms of OIC frequently reported with bowel movements including perception of incomplete evacuation, need for straining, and hard stools. NAL was generally well tolerated.

P1944 SAFETY AND EFFICACY OF NALDEMEDINE FOR THE TREATMENT OF OPIOID-INDUCED CONSTIPATION IN PATIENTS WITH CHRONIC NON-CANCER PAIN RECEIVING OPIOID THERAPY: A SUBGROUP ANALYSIS OF PATIENTS ≥65 YEARS OF AGE

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Introduction: Chronic non-cancer pain (CNCP) is commonly managed with opioid analgesics, yet opioid-induced constipation (OIC), one of the most common side effects, is under-recognized and undertreated in elderly patients. Naldemedine (NAL), an oral peripherally acting μ-opioid receptor antagonist, is indicated for treatment of OIC in adult patients with CNCP in the US and in patients with CNCP and cancer in Japan.
Aims & Methods: To evaluate the safety and efficacy of NAL for up to 12 weeks in a subgroup of elderly patients from an integrated analysis across 3 global phase 3 trials.
Results up to 12 weeks from 3 double-blind, randomized, placebo (PBO)-controlled trials were integrated. Patients aged 18-80 years (y) with CNCP treated with opioids for ≥3 months and OIC received oral NAL 0.2 mg or PBO once daily. Patients aged ≥65 y were included in this subgroup analysis. Safety assessments from the 3 studies up to 12 weeks (safety population) included overall incidence of treatment-emergent adverse events (TEAEs), TEAEs in Gastrointestinal (GI) Disorders System Organ Class (SOC), and TEAEs of opioid withdrawal (OW) or possible OW. Efficacy was based on the primary endpoint from the two 12-week studies (intent-to-treat population), ie, proportion of responders. A responder was defined as having ≥3 spontaneous bowel movements (SBMs)/week and ≥1 SBM/week increase from baseline (BL) for ≥9 of 12 weeks and ≥3 of the last 4 weeks.
Results: At BL, 14.8% (344/2328) of patients in the safety population were ≥65 y. The incidence of TEAEs in the NAL vs PBO groups was 45.9% vs 51.6% (≥65 y) and 47.1% vs 45.6% (overall), and the incidence of GI disorder SOC TEAEs in the NAL vs PBO groups was 20.2% vs 16.1% (≥65 y) and 21.8% vs 13.8% (overall), respectively. The incidence of TEAEs of OW in the NAL vs PBO groups was 1.1% vs 0% (≥65 y) and 1.0% vs 0.6% (overall), and the incidence of TEAEs of possible OW was 1.1% vs 0.6% (≥65 y) and 1.6% vs 0.5% (overall), respectively. The proportion of responders was higher in the NAL vs PBO groups for patients ≥65 y (51.8% vs 37.6%; difference [95% confidence interval]: 12.6 [-2.3, 27.5]) and overall (50.1% vs 34.1%; 16.0 [10.2, 21.8]), respectively.
Conclusion: This integrated analysis across 3 phase 3 clinical trials up to 12 weeks confirmed that OIC treatment with NAL 0.2 mg was generally well tolerated and effective in patients aged ≥65 y with CNCP. The incidence of OW and possible OW was low and similar between NAL and PBO. Safety and efficacy results were consistent with the overall population.
Disclosure: James Wild received a one-time stipend from Shionogi for performing a review of the clinical study report. Lynn Webster was a consultant and received travel reimbursement from Shionogi Inc. Tadaaki Yamada is an employee of Shionogi Inc. who may or may not own stock options. Martin Hale was a consultant to Shionogi Inc. and received a stipend for review of the clinical study report.

P1945 SAFETY OF NALDEMEDINE FOR THE TREATMENT OF OPIOID-INDUCED CONSTIPATION IN SUBJECTS WITH CHRONIC NON-CANCER PAIN RECEIVING OPIOID THERAPY: RESULTS OF THREE GLOBAL PHASE 3 CLINICAL TRIALS

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Introduction: Opioid-induced constipation (OIC) is a common side effect of opioids in the treatment of chronic non-cancer pain (CNCP). Effective treatment of OIC can be impacted by how particular treatments are tolerated. Nalemedine (NAL), an oral, peripherally acting μ-opioid receptor antagonist, is approved for the treatment of OIC in adult patients with CNCP in the US.
Aims & Methods: To evaluate the safety and tolerability of NAL from integrated analysis across three global phase 3 trials up to 12 weeks.
Results from three phase 3, double-blind, randomized, placebo (PBO)-controlled trials were integrated to evaluate the safety and tolerability of NAL up to 12 weeks. Subjects 18 to 80 years old, with CNCP and OIC, taking opioids for ≥3 months, received either NAL 0.2 mg (N=1163) or PBO (N=1165) taken orally once daily with or without food. Tolerability and adverse events, including potential opioid withdrawal (OW) were analyzed.
Results: The majority of subjects completed the trial (NAL, 88.7%, PBO, 88.4%) and the proportion that discontinued was similar across treatment groups. The duration of treatment was similar across treatment groups with a mean exposure of 76.6 and 77.2 days in the NAL and PBO groups respectively, approaching the maximal possible exposure of 84 days for the 12-weeks of study. Adverse Drug Reactions were reported more frequently in the NAL group compared with PBO across the studies and in the pooled population (NAL, 20.1%, PBO, 13.6%, 95% CI of difference: 3.4, 9.5). The assessment of summary measures of Treatment Emergent Adverse Events (TEAEs) demonstrated that the overall incidence was similar between groups in all studies and associated primarily with the gastrointestinal system. TEAEs reported for ≥1% of subjects in at least one treatment group and at a higher incidence in the NAL group compared to PBO are shown in Table 1. TEAEs with ≥ 1% difference between the NAL and PBO groups were limited to abdominal pain, diarrhea, and nausea. In general, TEAEs were mild to moderate in severity and short in duration. The majority of reports of diarrhea occurred early in the study, reports of abdominal pain occurred early and only once, and nausea generally occurred early but with reports throughout the study. The incidence of OW was low in the NAL and PBO groups (NAL, 1.0%, PBO, 0.6%).
Conclusion: An integrated analysis across three Phase 3 trials demonstrated that treatment of OIC with NAL in subjects with CNCP was well tolerated with the majority of TEAEs occurring early, of short duration, mild to moderate in nature and generally limited to the gastrointestinal system. Furthermore, the incidence of OW was low and similar between NAL and PBO.

Treatment Emergent Adverse Events	Naldemedine 0.2 mg (%)	Placebo (%)
Diarrhea	7.7	2.4
Abdominal Pain	6.4	1.9
Nausea	5.3	3.3
Abdominal Pain - Upper	2.7	1.5
Back Pain	2.7	2.2
Headache	2.2	2.1
Vomiting	2.3	1.4
Nasopharyngitis	1.8	1.6
Abdominal Distension	1.7	1.6
Hyperhydrosis	1.5	0.7
Arthralgia	1.5	1.2
Viral Gastroenteritis	1.4	0.6
Influenza	1.1	0.9
Drug Withdrawal Syndrome	1.0	0.6
Bronchitis	1.0	0.9

[Treatment Emergent Adverse Events reported for ≥1% of subjects]

P1946 CLINICAL, IMAGING AND PHYSIOLOGICAL CHARACTERISTICS OF CHRONIC INTESTINAL PSEUDO-OBSTRUCTION IN SYSTEMIC SCLEROSIS, AMYLOIDOSIS AND PARANEOPLASTIC SYNDROMES: A TERTIARY CARE CENTER EXPERIENCE

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Introduction: Chronic intestinal pseudo-obstruction (CIPO) is a rare disabling disorder characterized by a severe impairment of intestinal motility, mimicking mechanical obstruction in the absence of an obstructing luminal lesion.

Aims & Methods: To describe the clinical correlates, imaging findings, and physiological studies (scintigraphic transit and manometry) in pseudo-obstruction associated with systemic sclerosis (SSc), amyloidosis and paraneoplastic syndromes evaluated at a single large tertiary referral center. A retrospective cohort of patients with intestinal pseudo-obstruction associated with SSc, amyloidosis or paraneoplastic syndromes treated at our institution between Jan 1, 2008-Aug 1, 2018 was assembled. Subjects with an alternative luminal or systemic etiology for bowel dilatation were excluded. Demographics, clinical characteristics, autoimmune serologies, imaging, physiological testing and biopsy results were abstracted from electronic medical records using a standardized data abstraction form.

Results: We identified 100 cases of pseudo-obstruction {mean age 58 y, 54% female, 86% Caucasian}; 55 associated with SSc, 27 with amyloidosis and 18 with paraneoplastic syndromes. The clinical features, radiological and physiological study findings were as listed in the table below. Female preponderance was seen in SSc, in comparison to male dominance in the other two groups. The most common symptom was abdominal bloating in all 3 groups. Vomiting and weight loss were more common in SSc compared to the other two groups. Diarrhea was less common in paraneoplastic syndromes compared to the other two groups. Only small bowel dilation was seen in 70%, 32% & 44% of patients in SSc, amyloidosis and paraneoplastic, respectively. Only large bowel dilation was seen in 44% & 44% of patients in amyloidosis and paraneoplastic, respectively. Remaining had both small and large bowel dilations. 5/8 were myopathic in SSc group and 3/5 were neuropathic in paraneoplastic group on gastroduodenal manometry.

Conclusion: Small bowel is more commonly involved than large bowel both on imaging and transit studies in SSc patients, whereas both small and large bowel showed equal involvement in the other 2 groups. Myopathic involvement was more common in SSc, whereas neuropathic involvement was more common in paraneoplastic syndromes.

Disclosure: Nothing to disclose

P1947 MANOMETRY DATA OF THE LOWER ESOPHAGEAL SPHINCTER LINEARLY CORRELATE WITH CLINICAL SEVERITY IN TYPE I AND II ACHALASIA

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Introduction: Achalasia is a very heterogeneous disease, with no obvious correlation between symptom duration, symptom severity, radiology and manometric data. The aim of our study was to investigate possible correlations between symptom severity (Eckardt score) and manometric data.

Aims & Methods: We analysed a cohort of 61 consecutive patients with achalasia, diagnosed according to the Chicago classification v 3.0; 41 patients had achalasia type II, 17 had type I and only 3 patients had achalasia type III. Due to the low number of type III achalasia patients we included in the analysis only patients with type I and II. The patients were divided according to the Eckardt score in two groups, with a score ≤ 6 and with a score > 6 (representing clinically severe achalasia). The manometric data of the two groups were compared using Mann-Whitney U-testand student t-test and multivariate analysis. A $p < 0.05$ was considered significant.

Results: All the manometric variables of the esophagogastric junction [LES resting (LESP) and residual (LESRP) pressure and integrated relaxation pressure (IRP)] showed differences between the two groups, in the sense of higher values corresponding to the Eckardt score > 6 (p = 0.029 for LESP, p = 0.0009 for LESRP, p = 0.003 for IRP). The univariate analysis showed linear correlations between IRP (r^2 = 0,17; p = 0,004), LESRP (r^2 = 0,26; p = 0,0004), LESP (r^2 = 0,08; p = 0,048) and the Eckardt score. The multivariate analysis of the correlations between the Eckardt score and the manometric variables at the level of the LES was done by multiple regression and found that LES resting pressure is not an independent predictor for the severity of the Eckardt score (regression coefficient -0.03, p = 0.08), while IRP (regression coefficient 0.04; p = 0.0004) and LESRP (regression coefficient 0.09; p = 0.002) are independent predictors of the Eckardt score. The distal contractility integral showed no significant differences between the two groups (p = 0.97).

Conclusion: Our resuts have shown that in type I and II achalasia there is a linear correlation between the degree of incompleteness of LES relaxation and the clinical severity measured by the Eckardt score. These results validate the Eckardt score as a sensitive tool in determining the severity of achalasia before treatment and underline that the main determinant of symptoms in achalasia is the absence of relaxation of the LES, with a superior pathophysiological importance compared to that of aperistalsis.

Disclosure: Nothing to disclose

		Systemic Sclerosis (n=55)	Amyloidosis (n=27)	Paraneoplastic Syndromes (n=18)
Sex	Male, Female	29.1%(n=16), 70.9%(n=39)	74%(n=20), 26%(n=7)	55.6%(n=10), 44.4%(n=8)
Age at pseudo-obstruction		52.8(12.1)	60(13.5)	52.6(20.2)
Clinical features	Bloating, Distension, Pain, Nausea, Vomiting, Constipation, Diarrhea, >5%weight loss	82.7%(n=52), 69.2%(n=52), 71.2%(n=52), 82.7%(n=52), 73.1%(n=52), 51.9%(n=52), 67.3%(n=52), 77.6%(n=49)	80.8%(n=26), 73.0%(n=26), 53.8%(n=26), 61.5%(n=26), 46.2%(n=26), 30.8%(n=26), 80.8%(n=26), 30.8%(n=26)	72.2%(n=18), 72.2%(n=18), 72.2%(n=18), 61.1%(n=18), 50%(n=18), 44.4%(n=18), 27.8%(n=18), 11.1%(n=18)
Diameter of dilated small bowel in cm (SD) (n=no. of dilated bowels/total no. of observations)	Duodenum, Jejunum, Ileum	4.4(1.6)(n=46/47), 4.5(1.6) (n=44/47), 4.5(1.7)(n=42/47)	3.6(1.2)(n=13/25), 4.0(1.2) (n=13/25), 4.0(1.1)(n=12/25)	3.7(0.8)(n=9/18), 4.4(1.3) (n=9/18), 4.2(0.9)(n=7/18)
Diameter of dilated large bowel in cm (SD) (n=no. of dilated bowels/total no. of observations)	Caecum, Ascending colon, Transverse colon, Descending colon, Sigmoid colon	7.3(2.1)(n=8/47) 6.5(3.1)(n=8/47) 7.0(3.1)(n=7/47) 4.3(0.9)(n=4/47) 5.2(1)(n=4/35)	8.1(4)(n=13/25) 6.6(3)(n=13/25) 8.7(4.8)(n=12/25) 13.3(5.5) (n=4/25) 5.1(n=1/25)	7.8(2.5)(n=9/18) 6.5(1.1) (n=9/18) 7.6(2.8)(n=9/18) 6.5(2.8)(n=5/18) 4.9(n=1/18)
Gastric emptying, %	1 hr, 2 hrs, 4 hrs	24%(23%), 45%(32%), 71%(29%)	25%(29%), 46%(34%), 70%(28%)	27%(12%), 53%(17%), 84%(17%)
Small bowel transit, colonic filling	6 hrs	28%(34%)	16%(12%)	35%(21%)
Colonic transit, geometric center, GC	4 hrs, 24 hrs, 48 hrs	0.4(0.8), 1.7(1.3), 1.8(1.6)	0.10(0.1), 0.57(0.7), 0.95 (0.5)	0.2(0.2), 2.1(0.4), 2.7 (0.6)
Manometry findings		Total 8: 7 were abnormal (5 myopathic type, 1 neuropathic, 1 both)	Only 1 finding is available which is abnormal (neuropathic type)	Total 5: 4 were abnormal (3 neuropathic, 1 mechanical)

[P1946 Table 1]

P1948 DELAYED ESOPHAGO-GASTRIC JUNCTION RELAXATION IN PATIENTS WITH JACKHAMMER ESOPHAGUS SUGGESTS THAT THE HYPERCONTRACTILE PERISTALSIS MAY BE A COMPENSATORY MECHANISM

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Introduction: Jackhammer esophagus (JE) is a major disorder of esophageal motility, characterized by hypercontractile peristalsis, diagnosed by high resolution manometry (HRM) showing ≥ 20% swallows with increased contractile vigor (distal contractile integral (DCI) > 8000 mmHg/s/cm). We hypothesize that the hypercontractile peristalsis in JE could be a compensatory mechanism for impaired EGJ relaxation, which even when integrated relaxation pressure (IRP) is normal (< 15 mmHg) may be expressed by a delayed onset of relaxation.

Aims & Methods: Our aim was to assess and compare time to onset of EGJ relaxation in JE patients with normal IRP, "control" patients (presenting for evaluation of esophageal symptoms) with normal HRM, and asymptomatic healthy volunteers.

We evaluated time to onset of EGJ relaxation in 44 patients (24 with JE, 20 with normal HRM) who presented to our motility lab for evaluation of esophageal symptoms, and in 21 asymptomatic healthy volunteers who underwent HRM. Demographic characteristics and validated esophageal questionnaires (GERDQ, BEDQ, Eckardt) were collected for all subjects. HRM was performed with a solid-state catheter with 36 pressure sensors; ten 5-ml liquid swallows administered, Chicago Classification version 3.0 used to diagnose JE and normal esophageal motility. Time to onset of EGJ relaxation after swallow initiation was measured in seconds, from the time of upper esophageal sphincter opening to EGJ opening. EGJ opening was determined at an isobaric contour of 23 mmHg, based on analysis in the healthy volunteers showing persistent EGJ effacement at this value in 100% of the volunteers. Median times to onset of relaxation for the study groups were compared by Wilcoxon rank sum test.

Results: Demographics and questionnaire scores are shown in Table 1; patients were older and had higher scores compared to healthy volunteers. HRM metrics were different among the study groups with the exception of DL (Table 1). Median times to onset of relaxation after swallow initiation are shown in figure 1. There was no significant difference in median time to onset of relaxation for healthy volunteers compared to patient controls with normal HRM (0.20 s versus 0.90 s, p = 0.149). Median time to onset of relaxation was significantly longer in JE patients compared to healthy volunteers and patient controls (3.30s vs 0.20 s vs 0.90 s, p=0.001).

	Healthy Volunteers	Control patients with normal HRM	Jackhammer Esophagus	p
Age	35 (28 - 41)	55 (40 - 67)	64.5 (59.5 - 71)	0.001
BMI	24.34 (23.01 - 28.08)	25.40 (21.75 - 29.17)	27.26 (24.36 - 29.57)	0.543
BEDQ	0 (0 - 0)	0 (0 - 4)	8 (0.5 - 17)	0.001
GERDQ	0 (0 - 0)	7.50 (1.50 - 15.50)	10 (4 - 18.5)	0.001
Eckardt	0 (0 - 0)	2.5 (1 - 3.5)	2 (2 - 3.5)	0.001
IRP	8 (3.30 - 13.30)	4.95 (4.95 - 6.95)	9.10 (5.85 - 13.70)	0.044
DCI	1081 (568 - 1676)	1635 (1409 - 2128)	8635 (7143 - 11370)	0.001
DL	6.50 (5.60 - 7.30)	6.35 (5.75 - 7)	6.35 (5.80 - 7.65)	0.779
EGJ	22.4 (14.5 - 27.9)	23 (21.75 - 29.15)	36.95 (29.05 - 52.10)	0.001
Seconds	0.20 (0 - 3.30)	0.90 (0.30 - 2.50)	3.30 (2.80 - 5.30)	0.001

[Table 1]

Conclusion: Patients with Jackhammer esophagus and normal EGJ relaxation by IRP have significantly delayed onset of EGJ relaxation compared to healthy subjects and control patients with normal HRM. These findings suggest that hypercontractile peristalsis in these JE patients could be a compensatory mechanism to overcome outflow obstruction manifested as delayed EGJ relaxation. Therefore, if our findings are confirmed, therapies to address impaired EGJ relaxation could be considered for these patients.
Disclosure: Nothing to disclose

P1949 THE VALUES OF ESOPHAGOGASTRIC JUNCTION CONTRACTILE INDEX IN THE DIAGNOSIS OF EGJ OUTLET OBSTRUCTION

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Introduction: The diagnosis of EGJ outlet obstruction (EGJOO) is mainly based the high 4 second integrated relaxation pressure (IRP4s) with peristaltic contraction during wet swallows. In some situations, the IRP4s was hard to get because patients couldn't well accomplish the wet swallows. EGJ contractile index (EGJCI) is a newly defined metric to reflect the function of EGJ in resting state.

Aims & Methods: The aims of this study were to analyze the values of EGJCI in the diagnosis of EGJOO.

One hundred and seven EGJOO patients and 103 non-EGJOO subjects were enrolled in this study. All subjects completed the CRF questionnaire, blood tests, gastroendoscopy and HRM. The values of EGJCI were compared between the two groups. The correlations between EGJCI, LES rest pressure and IRP4s were analyzed respectively and furtherly the AUC value of EGJCI in diagnosing EGJOO was analyzed by ROC curve.

Results: There was significant difference of the EGJCI values between the EGJOO group and the non-EGJOO subjects (34.85±2.95 vs. 14.42±1.38, P< 0.001). Among these 210 subjects, significant positive correlation between ECJCI and IRP4s was found (r=0.574, P< 0.001) while no significant correlation was found between IRP4s and LES rest pressure (r=0.107, p=0.085). Further analysis showed the AUC of EGJCI was 0.778. And the cutoff value of EGJCI was 14.02 to differentiate the EGJOO and non EGJOO with sensitivity of 0.804 and specificity of 0.66.

Conclusion: EGJCI is an effective metric to represent the EGJ function of both resting state and the swallowing state. When the cutoff was 14.02, EGJCI can help to differentiate the EGJOO patients from non-EGJOO subjects with a high sensitivity.
Disclosure: Nothing to disclose

P1950 MINIMALLY INVASIVE ASSESSMENT OF GASTROPARESIS DURING WHOLE-GUT EXAMINATION WITH A 3D-TRANSIT SYSTEM IN NORMATIVE DATA

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Introduction: Gold standard for diagnosis of gastroparesis is gastric emptying scintigraphy. Unfortunately, the association between symptoms and results of scintigraphy is poor. The Motilis 3D-Transit system allows minimally invasive and completely ambulatory description of transit patterns throughout the whole gastrointestinal tract.

Aims & Methods: The aim was to establish normative data for gastric emptying time and contractility patterns assessed with the 3D-Transit system and determine if gastric emptying time and contractility patterns were affected by age, BMI, gender or the content of the test meal.

3D transit recordings from 130 healthy were reanalysed using newly developed software.

Results: The median gastric emptying time was 2.7hours (range 0.1-21). In 90% the capsule passed the pylorus within the fasting period of 6 hours after ingestion. The median contraction frequency in the stomach was 3.1 contractions pr. Minute (range 2.6-3.9). The frequency was highest in women and increased with age (p< 0.05). The median amplitudes was 35°(range 4-85) based on rotation of the capsule and 11mm (range 6-31) based on capsule position. The amplitude based on rotation higher in women and decreased with increasing BMI (p< 0.05). The amplitude was higher in women, increased with the total amount of calories in the test meal and decreased with increasing BMI and age (p< 0.05). We did not find any systematical day-to-day variation (p>0.05). Inter-rater variability was minimal.

Conclusion: The 3D-Transit is a safe, minimally invasive, radiation free and ambulatory system for assessment of GE. Vi have established normative data on gastric emptying and motility. In future studies with 3D-transit, gender, age, BMI should be matched and the test meal should also be standardized.

Disclosure: Schlageter V is co-owner of Motilis Medica SA and has been technical partner in terms of improving and creating new system software but had no influence on the study itself. Other authors have no competing interests.

P1951 FREE DRINKING AND SOLID SWALLOWS PERFORMED DURING HIGH-RESOLUTION MANOMETRY HELP BETTER DEFINE THE CLINICAL RELEVANCE OF ESOPHAGOGASTRIC JUNCTION OUTFLOW OBSTRUCTION

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Introduction: Esophagogastric junction outflow obstruction (EGJOO) is a high-resolution manometry (HRM) derived diagnosis with unclear clinical implications; some require invasive therapy similar to achalasia, while others are of little significance. We hypothesized that adjunctive testing during HRM (free drinking and solids) would help determine EGJOO that is relevant and warrants therapy.

Aims & Methods: Between July 2015 and December 2018, all those with EGJOO on HRM at a tertiary center in London were assessed. HRM was performed with ten 5mL water swallows followed routinely by a rapid drink challenge (RDC; 200mL water drunk freely) and then solid swallows (either five 1cm³ buttered bread or 200g rice). EGJOO was defined as raised integrated relaxation pressure (IRP) during 5mL swallows (median IRP >15mmHg), RDC (IRP>8mmHg) and/or solid swallows (IRP>25mmHg in at least 2 swallows) with preserved peristalsis.[1] EGJOO was divided into Functional or Secondary (anatomic/mucosal disorder). Eckardt symptom score, stasis on barium swallow, presence of peristaltic dysfunction and therapeutic outcome were assessed.

Results: From a total of 1705 HRM studies performed, 78 subjects (4.6%) were identified as having EGJOO (median age 55y; 29 males). Dysphagia was the primary symptom in 54 (69%). Hiatus hernia >2cm was present in 30 (38%). Fifty-four (70%) had functional EGJOO, of whom 19 were opioid users. 17 had Secondary etiologies; post-fundoplication (N=7), crural diaphragm impingement within a hernia (N=3), stricture (N=3) and eosinophilic esophagitis (N=4). Secondary EGJOO had a significantly lower mean IRP during single water swallows compared to functional EGJOO (12.1 vs 18.2mmHg, P< 0.01).

In 26 patients (31%), raised IRP was evident only with RDC or solids and not with 5mL water; this occurred in a larger proportion of Secondary compared to Functional EGJOO subjects (65% vs. 25% respectively; P=0.003). 7 received endoscopic therapy with significant improvement in

median Eckardt score (6 pre and 2 post-therapy; P=0.02). On the other hand, 13 (17%) with raised IRP during 5mL water swallows had normal IRP with RDC/solids, 11 of whom had no concomitant peristaltic abnormalities or holdup of barium at the EGJ and did not require any form of therapy. Fifty-two subjects (69%) had normal esophageal body motility, while 24 (31%) exhibited hypertensive, fragmented or ineffective patterns with any swallow modality. Of the 55 who had subsequent barium studies, patients with peristaltic abnormalities exhibited holdup of contrast significantly more often than those with normal peristalsis (42% vs. 16% respectively; P=0.02).

19 (35%) of Functional EGJOO patients had endoscopic therapy (7 botulinum toxin, 13 pneumatic dilatation and 1 per-oral endoscopic myotomy) leading to a reduction in mean Eckardt score from 5.9 to 1.0 at a minimum of 3 months post-therapy (P<0.0001). Of the Secondary EGJOO subjects, 5 (29%) received endoscopic therapy: 2 balloon or Savary-Gilliard dilatation (mucosal stricture) and 3 pneumatic dilatation (tight fundoplication). This led to a reduction in mean Eckardt score from 6.2 to 3.0 at a minimum of 3 months post-therapy (P=0.03).

Conclusion: The addition of adjunctive testing to the HRM protocol (RDC/solids) increases the likelihood of identifying clinically relevant EGJOO, by increasing both sensitivity and specificity of its diagnosis. These findings, along with abnormalities in esophageal motor pattern during RDC and solid swallows as a further discriminating factor may assist in better determining who might benefit from therapy.

References: 1. Hollenstein M, Thwaites P, Bütikofer S, Heinrich H, Sauter M, Ulmer I, Pohl D, Ang D, Eberli D, Schwizer W, Fried M, Distler O, Fox M, Misselwitz B. Pharyngeal swallowing and oesophageal motility during a solid meal test: a prospective study in healthy volunteers and patients with major motility disorders. Lancet Gastroenterology & Hepatology 2017; 2(9):644-653

Disclosure: Nothing to disclose

P1952 GASTRIC PERORAL ENDOSCOPIC PYLOROMYOTOMY FOR REFRACTORY GASTROPARESIS: A SYSTEMATIC REVIEW WITH POOLED ANALYSIS

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Introduction: Gastroparesis (GP) is a chronic debilitating condition. Current pylorus-targeted procedures are either invasive or have questionable efficacy. Gastric per-oral pyloromyotomy (G-POEM) has been proposed as a minimally invasive intervention for refractory GP.

Aims & Methods: We performed a systematic review and pooled analysis to evaluate the efficacy and safety of G-POEM for GP.

Electronic databases (Medline, Scopus, EMBASE) were searched up to January 2019. Only studies including patients who underwent G-POEM for GP were eligible. The primary outcome of interest was the technical success rate. Secondary outcomes included the mean procedural time, the rate of clinical success and the rate of adverse events, namely intra- and post-procedural bleeding, perforations and strictures. The pre- and post- procedural Gastroparesis Cardinal Symptom Index (GCSI) scores and results of Gastric Emptying Scintigraphy (GES), if provided, were also assessed.

Procedural, clinical and safety outcomes were assessed by pooling data by means of a random- or fixed-effect models according to the degree of heterogeneity to obtain a proportion with a 95% confidence interval (CI).

Results: Ten studies were eligible for inclusion (292 patients), only 2 of which were prospective. Seven studies were performed in the United States, 2 in France and 1 in China. All studies but 2 were single-center experiences. Endoscopic pyloromyotomy was technically successful in all patients. Significant symptomatic improvement was achieved after 83.9% of the procedures (mean follow up period 7.8±5.5 months). Six studies reported the pre- and post- procedural Gastroparesis Cardinal Symptom

Index score: the mean pre-procedural GCSI score was 3.3±0.6 and dropped to 1.61±0.61 after G-POEM (p<0.001). When comparing the mean values of pre- and post-procedural scintigraphic evaluation, there was a significant decrease in the residual percentage at both 2 and 4 hours: 74.9±5.2 % vs 52.5±10.8 % (p<0.001) and 44.1±13.0 % vs 20.6±9.5 % (p<0.001), respectively. The overall adverse event rate was 6.8%. Immediate and post-procedural bleeding occurred in 1.9% (I^2=27.8%) and 2.6% (I^2=0%) of procedures, respectively. Gastric ulcers were reported in 5 cases, with a pooled rate of 2.3% (I^2=0%). Moreover, perforations were reported in 3 cases and a peritoneal abscess occurred in 1 case. Late events such as pyloric strictures were reported after 1% (I^2=0%) of cases.

Conclusion: In the short-term, G-POEM appears to be a promising technique in terms of safety and efficacy outcomes. While comparison to other pylorus-directed interventions in large controlled trials is awaited, G-POEM should be considered as a therapeutic option when dealing with refractory gastroparesis.

Disclosure: Nothing to disclose

P1953 OESOPHAGEAL BIOPSY RESULTS IN PATIENTS UNDERGOING PER ORAL ENDOSCOPIC MYOTOMY (POEM) FOR ACHALASIA: A RETROSPECTIVE SINGLE CENTRE EXPERIENCE

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Introduction: There is literature suggesting an association between oesophageal motility disorders and eosinophilic oesophagitis (EoE) with a few cases reporting patients with co-existing oesophageal achalasia and EoE.[1-3]

Aims & Methods: The aim of this study was to undertake a histological evaluation for the presence of eosinophils in oesophageal biopsies (mucosal and muscle) in patients with achalasia who underwent POEM to determine if any association of eosinophilic oesophagitis and achalasia existed in our cohort.

All patients undergoing POEM for achalasia from 2013 onwards were included, with data extracted from the hospital electronic patient record. Patients had routine pre-treatment assessment with high resolution manometry, barium swallow and Eckardt score. Results of oesophageal biopsies (mucosal and oesophageal) that were taken were recorded.

Histology samples were processed by our local histopathology department. Samples were routinely fixed in formalin and embedded in paraffin wax before sectioning onto glass slides for review.

Results: 105 patients underwent POEM at our institution from November 2013 onwards (45F; mean age 51± 14 yrs). Mean duration of disease was 4.9± 4.5 yrs and the most common sub-type of achalasia according to Chicago Classification was Type II (71 patients). The mean Eckardt score pre-POEM was 8±2 points.

44 (42%) patients underwent oesophageal biopsies (39 mucosal, 5 muscle) in our cohort. 21 patients underwent oesophageal biopsies prior to undergoing POEM, 5 had oesophageal biopsies taken during POEM and 18 underwent oesophageal biopsies post POEM (during their Day 1 post POEM oesophagogastroduodenoscopy).

31 patients had both lower and mid oesophageal biopsies, 6 only had lower oesophageal biopsies and 2 only mid oesophageal biopsies. The 5 that had muscle biopsies taken had their sample taken from mid oesophagus. No patient had oesophageal biopsies that contained eosinophils. 20 samples were reported as normal, 19 biopsies chronic inflammation, 2 biopsies with diathermy effect and therefore not interpretable, 1 fibrosis and 2 with other diagnoses (leukoplakia and candidiasis).

Conclusion: In our cohort no oesophageal biopsies reported eosinophils. Most biopsies either had evidence of chronic inflammation or no abnormality. Our study could not identify a link between eosinophilic oesophagitis and achalasia. The main finding of chronic inflammation is in keeping with stasis related inflammation that occurs in achalasia. Our finding could challenge the need to do routine oesophageal biopsies in work up endoscopy for achalasia patients who already have a confirmed diagnosis with high resolution manometry. This could have significant cost and time saving benefits. Further research is required to determine the utility of oesophageal muscle biopsies, a novel resource uncovered by submucosal endoscopy.

References: 1.Cools-Lartigue, J., Chang, S. Y., Mckendy, K., Mayrand, S., Marcus, V., Fried, G. M., & Ferri, L. E. (2013). Pattern of esophageal eosinophilic infiltration in patients with achalasia and response to Heller myotomy and Dor fundoplication. Diseases of the Esophagus, 26(8), 766-775. 2. Savarino, E., Gemignani, L., Zentilin, P., De Bortoli, N., Malesci, A., Mastracci, L., ... & Savarino, V. (2011). Achalasia with dense eosinophilic infiltrate responds to steroid therapy. Clinical gastroenterology and hepatology, 9(12), 1104-1106. 3. Mandaliya, R., DiMarino, A. J., & Cohen, S. (2013). Association of achalasia and eosinophilic esophagitis. Indian Journal of Gastroenterology, 32(1), 54-57.

Disclosure: Nothing to disclose

P1954 SYMPTOM PROFILE OF NON-CARDIAC CHEST PAIN DEPENDS ON PATHOPHYSIOLOGY OF ESOPHAGEAL DISEASES

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Introduction: Non-cardiac chest pain (NCCP) is one of major symptoms in patients with esophageal motility disorders (EMDs) or gastroesophageal reflux disease (GERD), but, the symptom profile of NCCP in different diseases is not fully understood.

Aims & Methods: A total of 91 consecutive patients (57 females, mean age: 54 years) with NCCP who underwent esophageal manometry using high resolution manometry (HRM) between March 2009 and February 2018 at Gunma University Hospital were enrolled. Most of the patients (92%) had dysphagia as well as NCCP. NCCP was assessed by a questionnaire concerning location, time and duration of NCCP. Esophagogastroduodenoscopy (EGD) was performed in all patients. When reflux esophagitis was seen on EGD or when a proton pump inhibitor (PPI) was effective, patients were diagnosed as GERD. When eosinophil infiltration (≥15/HPF) in the esophageal mucosa was seen, patients were diagnosed as eosinophilic esophagitis (EoE) regardless of presence of EMDs or GERD. Esophageal motility was assessed retrospectively according to the Chicago classification v3.0. Major EMDs were divided into five groups based on HRM findings: Achalasia type I or II, achalasia type III, esophago-gastric junction outflow obstruction (EGJOO), spastic esophageal motility disorders (SMDs) and absent contractility (AC). When major EMDs were found, it was considered that NCCP was caused by EMDs. When a PPI was not effective and there was no abnormal finding on both EGD and HRM, a 24-hour esophageal pH-impedance monitoring was performed. When abnormal esophageal acid exposure or positive symptom association were found, patients were diagnosed as GERD. When neither of those was present, patients were diagnosed as functional chest pain (FCP).

Results: There were 33 achalasia (type I or II), 8 achalasia (type III), 8 EGJOO, 7 SMDs, 3 AC, 7 EoE, 22 GERD and 3 FCP. Fifty seven (63%), 45 (49%), 32 (35%) and 27 (30%) patients had pain in the lower part, middle part, back or upper part of the chest, respectively. The location of pain was not significantly different among patient groups. The time of pain was significantly different among groups (p<0.05).

	Within 1 minute	1-5 minutes	5-10 minutes	10-30 minutes	More than 30 minutes
Type I or II achalasia	27%	18%	21%	9%	24%
Type III achalasia	0%	50%	25%	13%	13%
Esophago-gastric junction outflow obstruction	13%	50%	13%	13%	13%
Spastic esophageal motility disorders	29%	29%	29%	14%	14%
Absent contractility	0%	33%	0%	33%	33%
Eosinophilic esophagitis	14%	14%	14%	29%	29%
Gastroesophageal reflux disease	27%	9%	9%	0%	55%
Functional chest pain	33%	0%	33%	0%	33%

[Duration of chest pain among groups]

Most patients had pain between meals or during or after meals. Some patients with achalasia or EoE had pain in the wake-up period; patients with EGJOO or SMDs did not have pain in the wake-up period. Patients with type I or II achalasia tended to have pain during nighttime as well as during post prandial periods. The duration of pain was also significantly different among groups (p<0.05, Table). It was shorter in patients with type III achalasia, EGJOO or SMDs, while, it was longer in patients with GERD.
Conclusion: The symptom profile of NCCP was different among patient groups. The NCCP profile may represent pathophysiology of diseases.
Disclosure: Nothing to disclose

P1955 INCREASED OESOPHAGEAL SYMPTOMS AND MANOMETRIC ABNORMAL PATTERNS IN OPIOIDS USERS: EXPERIENCE OF A LARGE TERTIARY REFERRAL CENTRE

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Introduction: Opioid induced oesophageal dysfunction is increasingly recognized. The inability to discontinue opioids pauses a challenge in the management of these patients. Opioids mainly affect organization of peristalsis and relaxation of the lower oesophageal sphincter. The relationship between type of opioids intake, symptoms and manometric pattern is still unclear.
Aims & Methods: To record the prevalence of major and minor oesophageal disorders in patients using opioids and compare this to non-users.
We identified 155 patients on opioids registered on our HRM database between October 2013 and March 2019. Type of opioids, symptoms and manometric features were reviewed and compared between opioids users and non-users (n= 6465). Patients with an incomplete test, studied following fundoplication or with a known major motility disorder were excluded.
Results: The prevalence of opioid use in our patient population was 2.3%. Opioids used included Tramadol (n=50), Codeine (n=45), Morphine Sulphate (n=12), Co-dydramol (n=9), Fentanyl (n=7), Oxycodone (n= 6) and Combination therapy (n=26). The commonest reason for opioid use was a musculoskeletal disorder (55%). The main complaint was dysphagia in 21%, chest pain in 10%, heartburn and regurgitation in 35%, cough in 8% and other (abdominal pain, vomiting, belching, globus) in 26%. Another 42.5% reported dysphagia as secondary symptom. Compared to non-users of opioids, dysphagia was the main complaint in 13.5% and chest pain in 4.8%, whilst another 21% reported dysphagia as secondary symptom. There was a significant difference in the prevalence of all major and minor manometric abnormalities between opioid users and non-users (p< 0.0001). The incidence of GOJ obstruction was 11.6% vs 1.6% respectively, Jackhammer oesophagus and Distal Oesophageal Spasm 4.5% vs 1.2%, Achalasia type 3 1.9% vs 0.18%, Absent peristalsis 1.3% vs 0.09%, Nutcracker oesophagus 3.9% vs 0.17%, IEM 29.6% vs 10%. Amongst opioid users whose main complaint was dysphagia or chest pain, Achalasia type 3 was present in 6% and GOJ obstruction in 19%. Although numbers are relatively small, more portent opiates (Fentanyl, Oxycodone) and combinations of opiates appeared associated with a greater risk of major motility disorders.
Conclusion: The prevalence of symptoms and oesophageal dysmotility was higher in opioids users. This highlights the awareness physicians and physiologists should have about an increasing problem in our patient group.
Disclosure: Nothing to disclose

P1956 PATHOPHYSIOLOGY OF SWALLOWING DYSFUNCTION AND DOPAMINERGIC EFFECTS IN PARKINSON'S DISEASE

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Introduction: The pathophysiology of OD and the effect of dopaminergic medication on swallowing dysfunction are not fully understood in Parkinson's disease.
Aims & Methods: Our aim was to describe the pathophysiology of impaired safety of swallow in Parkinson's disease (PD) and to assess whether the OFF/ ON state related to dopaminergic medication affects swallow function.
We studied 50 patients with PD and 12 healthy volunteers (HV). Videofluoroscopic (VFS) signs and kinematics of swallow response were assessed. In 40 patients with PD, all tests were performed in OFF (12 hours without any medication) and ON (1 hour after usual dopaminergic medication) state.
Results: Mean age of PD patients was 70.46±10.03yr (24 women), mean time of disease 5.094±3.86yr, the Hoehn-Yahr stage 2.32±0.81 and mean dose of dopamine 567.10±302.35mg. Mean age of HV was 40.20±2.50 yr (six women). PD Patients had high prevalence of impaired safety of swallow (36% of penetrations in PD, higher PAS mean 2.16± (1.35), delayed laryngeal vestibule closure time (LVC, 293.33±90.07ms) when compared to HV (164.00±39.78ms), both unaffected by dopaminergic treatment (305.00±105.90ms). A cutoff level of delayed LVC≥380.00ms predicts unsafe swallow with sensitivity=0.67; specificity=0.79 and AUC of 0.80. There was no significant difference in swallow between OFF and ON states for VFS signs of efficacy and safety, or kinematics of swallow response. In both situations patients presented similar high prevalence of oral residue (OFF: 92.50%; ON: 90.00%), piecemeal swallow (OFF: 75.00%; ON: 80.00%) and pharyngeal residue (OFF: 85.00%; ON: 85.00%).
Conclusion: Swallowing function appears to be severely impaired in the initial stages of PD and do not improve by dopaminergic treatment. Patients with PD require new strategies for active treatment of the severe swallowing dysfunction they suffer from the initial stages of the disease.
Disclosure: Nothing to disclose

P1957 COMPARISON OF SAFETY OF TREATMENT OPTIONS FOR END-STAGE ACHALASIA OR SIGMOID ESOPHAGUS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: End-stage achalasia is characterized by massive esophageal dilatation with loss of the esophageal straight axis giving rise to a sigmoid appearance. Several effective treatment options are available for early achalasia. However, these interventions might be technically difficult and associated with higher complication rates in the management of end-stage achalasia.
Aims & Methods: We aimed to compare the relative safety of various treatment modalities used in patients with end-stage achalasia and sigmoid esophagus through a systematic review and meta-analysis.The meta-analysis was performed using the Preferred Reporting Items for Systematic Reviews for Meta-analyses (PRISMA) guidelines. We searched PubMed, Embase, Cochrane library, Medline, Google Scholar, and Science Citation Index to identify relevant studies between January 2012 and January 2018. Keywords used were "sigmoid esophagus", "end stage achalasia", "achalasia", "Laparoscopic Heller myotomy (LHM)", "esophagectomy", "esophageal resection", "peroral endoscopic myotomy (POEM)" and "advanced achalasia". Statistical analysis was performed using Review Manager Version 5.3 (RevMan) software.

Results: Using the predefined search strategy, 33 studies were included in the meta-analysis. A total of 1987 patients were included of which 1497 underwent esophagectomy, 386 had LHM and 104 had POEM. Based on the meta-analysis, POEM was found to be most effective treatment option in terms of major complications [OR = 0.51, 95% confidence interval (CI) = 0.28 to 0.89], length of hospital stay [standardized mean difference (SMD) = -1.1, 95% CI = - 1.18 to - 0.07] and operative time [SMD = - 1.82, 95% CI - 2.76 to - 0.11] (table 1). P score ranking result showed that POEM was ranked top in major complications, hospital stay and operative time (P score = 0.907, 0.996, 0.991, respectively)(table 2).

Treatments	Major Complications	Hospital Stay	Operative time
Esophagectomy	0.438	0.428	0.456
LHM	0.176	0.478	0.526
POEM	0.907	0.996	0.991

[P score rankings]

Conclusion: Our results show that POEM is safer and is associated with shorter length of hospital stay compared to esophagectomy and LHM in treating sigmoid esophagus or end-stage achalasia. We believe this is the first meta-analysis to compare the safety of treatment options in end-stage achalasia with sigmoid esophagus. Further studies are needed to assess the efficacy of these interventions in this patient population.
Disclosure: Nothing to disclose

P1958 OUTCOME OF PER ORAL ENDOSCOPIC MYOTOMY FOR TREATMENT OF ACHALASIA - NORWEGIAN SINGLE CENTER EXPERIENCE WITH MEDIAN FOLLOWING-UP OF 24 MONTHS

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Introduction: Long term effects of Per Oral Endoscopic Myotomy (POEM) are still unknown. The aim of this study was to investigate and report the feasibility, safety, efficacy and complications of POEM from the introductory phase in a tertiary referral center in Norway.
Aims & Methods: Collected prospective data from the first 68 patients with achalasia who underwent POEM at Haukeland University Hospital from February 2014 until December 2017 were analyzed. The patients were followed up for 12 months with respect to acute and delayed complications, and efficiency of the treatment. The diagnosis was based on findings on high resolution manometry (HRM) and timed barium swallow X-ray (TBS). We repeated HRM, TBS, in addition to impedance and 24-hours pH measurement 12 months after POEM. Reflux was regarded as pathological if the acid exposure (pH< 4) time was more than 6%. Eckardt score was used for symptom evaluation before, and at 6, 12 and up to 56 months after POEM.
Results: 41 males and 27 females with symptomatic achalasia and Eckardt score ≥6 were included. The mean age was 44,6y. Based on HRM, 15 patients had achalasia type I, 34 type II and 19 with type III. 36 patients (53%) were naïve to other treatment, while 11 (16%) had been previously treated with botulinum toxin injection, 14 (22%) with pneumatic balloon dilatation, and 10 (15%) with Heller's myotomy. The average resting pressure over lower esophageal sphincter (LES) was median 25 mmHg (0-72) prior to POEM, and 6,5 mmHg (0-23.1) after. Dysphagia improved in all patients on follow up. The Eckardt score was significantly reduced from median 7 (4-12) before POEM to 1 (0-9) at 12 months after POEM (p < 0.0001). The median myotomy length was 11 cm (4-20). 43 patients (63%) patients had posterior myotomy, while 25 (27%) anterior. The procedure time was mean 130 min, and admission time was mean 3 days. We did not experience any serious complications but observed capnoperitoneum and capnothorax in 10 patients (15%). 3 patients (4%) required peritoneal decompression during POEM (Grade 2 complication). At 12 months, 86.8% had Eckard score ≤3, and 75,5% Eckardt score ≤2. 24 -hours pH monitoring was recorded on 55 patients (80%). 12 months post-POEM pathological reflux was measured in 45%, but only 37% reported reflux symptoms, 22% needed proton pump inhibitors (PPI) daily while 9% needed PPI occasionally.

Conclusion: Results with 12-56 months following-up from our cohort of consecutive patients show that POEM is safe and relieves symptoms of achalasia significantly, but the risk of reflux is higher than what is previously reported in the literature. Further studies are needed to confirm the findings in a long-term follow-up.
Disclosure: Nothing to disclose

P1959 CAN OESOPHAGEAL HYPOMOTILITY EXPLAIN UNDERLYING CAUSE OF SMALL INTESTINAL BACTERIAL OVERGROWTH?

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Introduction: It is known that Small Intestinal Bacterial Overgrowth (SIBO) is linked with gut hypomotility as well as long term use of acid suppressants. However, due to difficulties for investigating small intestinal motility, identifying the underlying cause for SIBO in patients remains mainly unknown and speculative.
Aims & Methods: The aim of this study is to investigate the relation of oesophageal motility findings with SIBO, as an indicator of gut hypomotility.
Methodology
Patients referred to Guy's Hospital London for upper GI investigation who completed oesophageal high resolution manometry, lactulose test to rule out SIBO and also 24hr impedance-pH reflux monitoring from June 2017 to Dec. 2018. Diagnoses were made based on: Chicago classification for oesophageal motility disorders v3 [1], the North American consensus guideline for Hydrogen and Methane breath testing 2017 [2], and the Lyon consensus on reflux monitoring 2017 [3].
Statistical analysis was made using Graphpad Prism tool to obtain ROC analysis, two tailed Fisher's exact test and demographic analysis. P value < 0.05 was considered significant.
Results: 71 patients completed both HRM and SIBO testing (F:M= 46:25, median age 49, 25-70 years old). 25/71 patients were diagnosed with SIBO out of whom 17 (68%) had also ineffective oesophageal motility, 6 (24%) normal oesophageal motility and 2 (8%) oesophagogastric outflow obstruction.
57 patients completed both 24hr impedance-pH reflux monitoring and SIBO test. 20/57 diagnosed with SIBO of whom, pathological gastroesophageal reflux was confirmed in 5 (20%). ROC curve analysis revealed that detection of distal contractile integral (DCI) < 450mmHg.cm.s has a sensitivity was 63.64% and specificity of 52% in predicting SIBO (95% CI: 47%-77%).
There was statistically significant different number of patients with SIBO diagnosed with IOM as opposed to having normal motility (P < 0.004). However majority of the SIBO patients were not suffering from GORD (GORD vs having no GORD: P < 0.008). Lower oesophageal sphincter basal pressure and DCI were not significantly different between patients with and without SIBO.
Gender had a slight impact on presence of SIBO (female with SIBO 39%, male with SIBO 24%). Highest prevalence of SIBO was detected in patients in their 50s (50%) but there was a dramatic reduction beyond the age 60 (18%).
Conclusion: SIBO is significantly associated with poor oesophageal body motility. This can be due to underlying poor small intestinal motility in a group of patients with IOM. A further study with larger sample size and concomitant investigation of small intestinal as well as oesophageal motility testing is required to further confirm these findings before use of oesophageal motility as a surrogate to determine small intestinal motility.
References: [1] Neurogastroenterol Motil. 2015 Feb;27(2):160-74. doi: 10.1111/nmo.12477. Epub 2014 Dec 3. The Chicago Classification of esophageal motility disorders, v3.0 [2] Am J Gastroenterol. 2017 May;112(5):775-784. doi: 10.1038/ajg.2017.46. Epub 2017 Mar 21. Hydrogen and Methane-Based Breath Testing in Gastrointestinal Disorders: The North American Consensus. [3] Gut. 2018 Jul;67(7):1351-1362. doi: 10.1136/gutjnl-2017-314722. Epub 2018 Feb 3. Modern diagnosis of GERD: the Lyon Consensus.
Disclosure: Nothing to disclose

P1960 FUNCTIONAL DYSPEPSIA AND DUODENAL EOSINOPHILIA ARE ASSOCIATED WITH INCIDENT ANXIETY: PROSPECTIVE 10 YEAR FOLLOW-UP OF THE KALIXANDA STUDY

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Introduction: Functional dyspepsia (FD) is a common condition in the population. It is associated with duodenal eosinophilia[1] and it has been shown that anxiety at baseline is associated with new-onset functional dyspepsia in long term.[2] Innate immunity response is linked with gut-brain/brain-gut regulation and psychological distress.[3]

Aims & Methods: Our aim was to investigate whether FD (Rome III) is associated with new-onset anxiety and/or depression and if this can be predicted by duodenal inflammation in a population based 10-year follow-up study.

Participants of the study (n=3000) were randomly selected from the national Swedish population register and surveyed in 1998 by a validated abdominal symptom questionnaire (ASQ) and hospital anxiety and depression scale (HADS). 1000 individuals were randomly selected to complete an esophagogastroduodenoscopy in 1999-2001. All eligible from the latter cohort (n=887, response rate 79%) were invited to a follow-up in 2010 with the ASQ and HADS. In a case-control study of 213 subjects (FD vs. healthy controls), histology from the oesophagus, stomach and the duodenum was evaluated at baseline (the pre-specified cut off being the mean, 23 eosinophils in duodenal bulb (D1) and 24 eosinophils in second part of the duodenum (D2)). The cut off for gastric eosinophilia was also the mean, 11 eosinophils in all three locations: cardia, corpus and antrum. The possible association of FD and duodenal eosinophilia to incident anxiety was analysed. Data were analyzed by Fisher's exact test and logistic regression.

Results: FD was reported by 89 subjects (42%), duodenal eosinophilia in D1 was found in 78 subjects (37%) and in 84 subjects in D2 (39%) at baseline. Incident anxiety was found in 12 subjects (6%) and depression only in 2 subjects (1%). None of the study subjects had oesophageal eosinophilia. Duodenal eosinophilia was not associated with gastric eosinophilia (OR=0.18, 95 CI 0.02-1.70, P=0.135).

Incident anxiety was associated with baseline functional dyspepsia (10/83 vs. 2/116, p=0.004), especially postprandial distress syndrome (10/65 vs. 2/134, p< 0.001) but not with epigastric pain syndrome (1/27 vs. 11/172, p=1.0). Incident anxiety was also associated with duodenal eosinophilia in D1 at baseline (9/75 vs. 3/124, p=0.011, OR=5.2, 95% CI 1.31-20.4, adjusting for age, gender and FD).

Conclusion: : Incident anxiety is significantly associated with baseline FD and duodenal eosinophilia is associated with a 5-fold increased risk of anxiety in a 10-year follow-up supporting the concept that mucosal immune system can regulate the bidirectional gut-brain communication.

References: 1. Talley, N.J., Walker, M.M., Aro, P., et al. Non-ulcer dyspepsia and duodenal eosinophilia: an adult endoscopic population-based case-control study. Clin Gastroenterol Hepatol 5, 1175-1183 (2007). 2. Aro, P., Talley, N.J., Johansson, S.E., Agreus, L. & Ronkainen, J. Anxiety Is Linked to New-Onset Dyspepsia in the Swedish Population: A 10-Year Follow-up Study. Gastroenterology 148, 928-937 (2015). 3. Powell, N., Walker, M.M. & Talley, N.J. The mucosal immune system: master regulator of bidirectional gut-brain communications. Nat Rev Gastroenterol Hepatol 14, 143-159 (2017).

Disclosure: Nothing to disclose

P1961 BURDEN OF GASTROINTESTINAL SYMPTOMS AND DISEASE IN TURKEY: CAPPADOCIA COHORT STUDY

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Introduction: There are no population-based studies determine the prevalence of gastrointestinal symptoms and associated diseases, in Turkey. It is necessary to know the prevalence of the diseases in the community for health professionals and their providers, in order to establish forward-looking targets and to use the resources correctly. Therefore, this study was designed to determine the frequency of the most common gastrointestinal system (GIS) symptoms, and diseases in a community-based sample.

Aims & Methods: The study is a cross-sectional cohort study. The ''Cappadocia cohort'' consisting of Avanos and Gülşehir districts of Nevşehir is shown to represent exactly the Turkey, in terms of population distribution. Therefore, it was found appropriate for the sample. The study was conducted between October 2017 and July 2018. Volunteers over 18 years of age were included in the study. The ''Gastrointestinal Symptom Questionnaire'' consisting of 16 questions for the upper GIS and 18 questions for the lower GIS was applied by the contracted research company by phone or face to face. It was accepted that the symptom was present if the symptom severity was ≥2 on a 6 scale, and gastrointestinal disease was accepted if the symptoms were present in at least 3 areas. The questionnaire was questioned for the last month. Body mass indexes were calculated.

Results: A GI symptom questionnaire was performed in 3369 (81.7%) of total 5042 people, who met the study criteria and accepted to participate, and 2797 people (67.8%) were evaluated for height and weight. The 39% of the participants were male , 61% were female and the median age was 52 years. The median BMI was 29.6 kg/m2 and 35% of the participants were overweight and 45% were obese. The rate of smokers was 24%, and the rate of alcohol drinkers was 5.2%. The use of aspirin and NSAIDs was 52%, PPI use was 25.5%, and the rate of H2RA use was 6.2%. The 70.5% of the population had at least one GIS symptom. The most common symptoms of upper GIS were bloating, burning and pain, and the most common symptoms of lower GIS were abnormal defecation, gurgling and swelling. The presence of upper GIS disease associated with symptom severity was 32.7%, the presence of lower GI disease was 12.9%, and the presence of both were 9.9%. The frequency was significantly higher in women (p < 0.001). The presence of symptoms and the presence of upper GIS disease were directly proportional to BMI. There was a significant decrease in upper gastrointestinal symptoms and upper GIS disease frequency with age.

Conclusion: This community-based cross-sectional cohort study, evaluating the gastrointestinal symptoms and the burden of disease, which was held in Turkey for the first time, has revealed that gastrointestinal symptoms were 70% among the community. The study showed that 1/3 of the population had upper GIS disease, 1/10 had lower GIS disease, and this frequency increased significantly in women. There was a linear relationship between weight gain and symptoms and presence of upper GI disease. It has been found that the prevalence of gastroenterological diseases is high and they are serious in terms of public health in Turkey.

Disclosure: Nothing to disclose

P1962 ROLE OF ENVIRONMENTAL FACTORS ON THE OUTCOME OF GASTROESOPHAGEAL REFLUX DISEASE: A 6 MONTHS PROSPECTIVE STUDY

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Introduction: Gastroesophageal reflux disease (GERD) is claimed to be a multifactorial disease involving both environmental and dietary factors [1] [2], but the scientific literature on this topic is lacking.
Aims & Methods: Aim of the study is to assess the impact of such factors in the outcome of GERD in a population of patients in a secondary care setting.
We enrolled 208 GERD patients in a private gastroenterological ward in North-East Italy; we selected GERD patients with problems at work (harassment, mobbing, interpersonal conflict, bullying, low motivation and job satisfaction, discrimination, etc.)or who did night work or smokers (10 to 20 cigarettes per day) or heavy coffee drinkers (3 or more daily). Patients were singled out in 4 groups according to the factors involved in their clinical history: group A in which problems at work played an important role, group B that experienced discomfort due to night shifts; group C with the smokers and group D composed of heavy coffee drinkers. The observation time was divided into 2 periods marked by 3 symptom evaluations carried out with the Visual Analogue Scale (VAS) (ranged from 0 to 10 with increasing gravity of pain) and with a Symptomatic Score (SS) that considered only heartburn and regurgitation (the score ranged from 0 to 6 with the single symptom score ranging from 0 to 3 with increasing gravity); the first period lasted 6 months, in which all patients performed therapy with antacids or PPI only when needed; symptoms were assessed at baseline and at the end of 6 months; in the second period, which lasted 6 months, patients were made to change their habits, changing profession, being diverted to daily shifts, quit smoking and stop drinking coffee. The clinical outcome of GERD has been evaluated through VAS and Symptomatic Score modifications.
Results: We selected 208 pts (M: 108, mean age 48 years, range 19-73 years) divided into 4 groups according with the study design: group A: 43 pts (M: 19, mean age 46 years, range 19-52) that have changed their occupation during the follow-up; group B: 37 pts (M: 28, mean age 41 years, range 24-54) that changed shift; group C: 61 pts (M: 27, mean age 52 years, range 25-73) that quit smoking and group D: 67 pts (M: 34, mean age 54 years, range 23-71) that stopped drinking coffee. Table 1 summarizes the results (expressed as mean value (m.v.)) before and after the critical environmental event.
Conclusion: The study seems to confirm the importance of environmental factors on GERD outcome, focusing on the crucial role of break through life events like shift and carrier changes; dietary and voluptuous factors such as drinking coffee and smoking seem to be less important in improving these patients' quality of life.

	To (Baseline)	T1 (Environmental event)	T2 (After 6 months)
Group A VAS m.v.	5	6	2
Group A SS m.v.	5	5	1
Group B VAS m.v.	5	6	1
Group B SS m.v.	4	5	1
Group C VAS m.v.	5	6	5
Group C SS m.v.	4	5	6
Group D VAS m.v.	6	5	5
Group D SS m.v.	5	4	5

[Table 1.]

References: [1] Bradley, Laurence A., et al. "The relationship between stress and symptoms of gastroesophageal reflux: the influence of psychological factors." American Journal of Gastroenterology88.1 (1993). [2] Sonnenberg, Amnon. "Effects of environment and lifestyle on gastroesophageal reflux disease." Digestive Diseases 29.2 (2011): 229-234.
Disclosure: Nothing to disclose

P1963 BOTULINUM TOXIN PROVIDES SYMPTOMATIC RELIEF FOR PATIENTS WITH TYPE 3 SPHINCTER OF ODDI DYSFUNCTION

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Introduction: Type 3 Sphincter of Oddi dysfunction, or biliary visceral hypersensitivity, causes considerable morbidity. However in the wake of the EPISOD study, which refuted the role of sphincterotomy, there is lack of clarity regarding whether any endoscopic intervention is beneficial. We therefore performed a retrospective single centre study of papillary injection of botulinum toxin for management of Type 3 Sphincter of Oddi dysfunction.
Aims & Methods: Electronic endoscopy records were searched from 2015-2018 for cases of botulinum toxin injection for Type 3 Sphincter of Oddi dysfunction. All had received injections of 100 units of botulinum toxin into the papilla, during duodenoscopy. Electronic patient records were retrospectively reviewed for symptomatic response, duration of response, further procedures and adverse events.
Results: 19 patients were identified. All underwent at least one procedure, with 11 undergoing repeat procedures . Following first procedure, (63.2% N=12/19) reported complete resolution of symptoms)and (15.7%, N=3/19) reported a partial response. Median duration of response was 4 months (IQR 4-4.5). Following repeat procedures, (36.4%, N= 4/11) reported total response, and (18.2%, N=2/11) reported partial response. There were no serious adverse events identified.
Conclusion: 78.9% patients reported symptomatic improvement following first injection with botulinum toxin. 54.6% reported improvement after a follow up procedure. Papillary botulinum toxin injection may be a useful and relatively safe treatment option for Type 3 Sphincter of Oddi dysfunction, however placebo controlled trials are required to further evaluate benefit, especially regarding repeat procedures.
Disclosure: Nothing to disclose

P1964 HOW LONG SHALL WE MAKE MYOTOMY FOR GASTRIC SIDE TO PREVENT REFLUX ESOPHAGITIS AFTER POEM?

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Introduction: According to guideline of Peroral endoscopic myotomy (POEM), the endopoint of the myotomy is recommended from 1 to 2cm into the gastric side. GERD after POEM is one of adverse event, because fundoplication is not performed in POEM as compared with Heller-Dor operation. Previous papers have reported that GERD occurs 13 to 60% after POEM.
Aims & Methods: The aim of this study is to evaluate the effect of short length myotomy for gastric side.
Forty-two cases of Achalasia or non-achalasia esophageal motility disorders treated by POEM from December 2012 to December 2017 were enrolled in this study.
The length of myotomy was decided by esophagography and/or high resolution manometry (HRM). 1cm myotomy was performed for gastric side.
When balloon dilatation (BD) and/or re POEM were performed, it was defined as recurrence.
Gender (Male / Female) was 24 and 18, respectively. Median age was 55 (19-92) years old. Previous treatment is as follows; BD: 10, medication: 10, medication plus BD: 2, BD plus operation: 1. Type of disease is as follow; Achalasia: 31 (Type I: 9, Type II: 12, unknown type: 10 because of without HRM), DES: 5, Jackhammer esophagus: 1, others: 5. Median duration of symptoms was 48 (1-480) months. Median follow up periods was 19 (1-72) months.
Results:
1. Median procedure time was 58 (28-131) mins.
2. Median length of myotomy was 7 (4-19) cm.
3. Complication: a. Four cases (9.5%) had the mucosal laceration. Three cases were treated by endo clip and/or PGA sheet, and one case was treated by laparoscopic drainage. b. There was no severe bleeding.
4. Median eckardt score (ES) of pre-POEM and post-POEM were 5 (1-11) and 0 (0-4), respectively. Clinical success rate (ES≦2 or reduced more than 4 points) was 95% (40/42).

5. EGD was performed 1 year after POEM. Nine cases (24%) had GERD-A, and 5 cases (14%) had GERD-B.

6. Only two cases (5%) had heart burn. Both cases had GERD-B.

7. Three cases (7%) had recurrence. BD was performed, and 2 cases were improved. However, BD for 1 case was not effective, and re-POEM was performed.

8. Peristalsis was partially recovered in 19% of the patients after POEM. Median length of myotomy for these cases was 6(4-10) cm.

Conclusion: Clinical success rate of short gastric myotomy was fare, and GERD was lower as compared with previous reports. Therefore, short gastric myotomy is acceptable.

References: None

Disclosure: Nothing to disclose

P1965 INSUFFICIENT ROME CRITERIA TO DIAGNOSE PURE FUNCTIONAL ABDOMINAL PAIN AND EPIGASTRIC PAIN SYNDROME: THE NEED OF RULING OUT CHRONIC ABDOMINAL WALL PAIN

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Introduction: There is firm evidence that chronic abdominal wall pain (CAWP) is one of the major cause of chronic abdominal pain. CAWP has been easily ignored and the physician may misdiagnose CAWP as functional abdominal pain syndrome (FAPS) or even as epigastric pain syndrome (EPS). We investigated whether there is a difference between clinical response for local anesthetic injection or a somatic nerve block (a major therapeutic option for CAWP) in CAWP alone and in CAWP-FAPS overlap.

Aims & Methods: From January 2012 to April 2017, patients complaining of abdominal pain were undergone relevant studies. CAWP with negative screening exams were enrolled. Greenbaum's criteria were adopted to diagnose CAWP while FAPS was diagnosed according to the Rome III criteria. For eligible patients, Rome IV criteria of EPS were surveyed also if they were Rome III-based EPS. CAWP alone group and CAWP-FAPS overlap group were treated by tap block. Baseline and post-treatment pain sore were recorded by 10-Likert scale. The 0.1% lidocaine mixture was used for the local anesthetic injection. After the local treatment, the responsiveness was assessed and 1 or 2 sessions of additional injection were performed if it is warranted. Clinical responsiveness was defined by over 50% degree reduction in symptom score.

Results: A total of 595 Patients complained with chronic abdominal pain were underwent EGD, colonoscopy, blood exam and imaging study (US or CT scan). Among them, 49 participants without obvious abnormal result to explain the pain were enrolled (11 of overlap, 38 of CAWP only). Mean age was 49.5+/-11.2 and female were predominant by 1.45 fold. The most frequently affected area was epigastrium followed by right iliac in both groups. Kaplan-Meiser analysis of unresponsiveness after the local treatment revealed no significant difference between the two groups (p= 0.781). The responsiveness at 3 months after the treatment also was not significantly different. When we diagnosed with Rome III criteria, EPS-CAWP overlap was less common (p= 0.035, McNemar test).

Conclusion: Clinical responsiveness to the local anesthetic injection was not different between CAWP-FAPS overlap and CAWP alone. Rome III criteria of EPS is more suitable to discriminate EPS from CAWP than Rome IV criteria.

Disclosure: Nothing to disclose

P1966 ANALYSIS OF POST-POEM REFLUX PREDICTORS AND PPI CONSUMPTION

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Introduction: Post-POEM reflux (reflux) appears in 16-68% of the patients and it is the main burden after POEM. There is scarce evidence of factors predicting reflux.

Aims & Methods: 22 patients with complete pre and post-POEM procedure work up - upper endoscopy, high-resolution manometry (MMS®, 22 channels water perfused), barium swallow, 24 h pH testing - were selected from our POEM prospective cohort (june 2016-april 2019, n=52). OGJ-CI as by Nicodeme. Symptoms: Eckardt and GERDQ score. Reflux diagnosis: Lyon consensus criteria. Parametric data expressed as mean, ±SD, t-test for mean comparison. Non-parametric data expressed as median (IQR), Mann-Whitney test for median comparison. Pearson test was used for correlation analysis. Significant variables p < 0.05, possibly associated variables p < 0.2.

Results: POEM was successful in all patients except one, who needed a second POEM procedure due to a mistaken manometric diagnosis. Reflux was found in 11/22 (50%) patients. Age was significantly associated with reflux, with older patients within this group. Post-POEM body mass index (BMI) was also higher in patients with reflux. Gender, time from symptoms onset, previous BMI, BMI increment, previous treatments, anaesthetic risk and antiplatelet agents intake were not different between groups. Basal (pre-POEM) reflux symptoms were lower in patients with reflux, however, no differences were noticed after POEM with a GERDQ median of 1 in patients with reflux and 3 in non-reflux patients. Only one patient with reflux scored more than 3 in GERD-Q. No differences were shown in tunnel length nor oesophageal/gastric myotomy. Reflux incidence was unaffected by learning curve since it was equal in the first eleven procedures compared to the second half. Basal mean lower oesophageal sphincter pressure (LOSP) was lower in the reflux group, as well as the basal OGJ-CI and the basal 4sIRP. Manometric diagnosis, post-POEM LOSP, decrease of LOSP, post-POEM 4sIRP, decrease of 4sIRP, post-POEM OGJ-CI and decrease of OGJ-CI were similar between groups. Post-POEM 5 min barium column, but not basal nor decrease of barium column, was lower in reflux patients. See table 1. The most significant correlations were found for age (p 0.065) and post-POEM BMI (p 0.078) with distal oesophageal acid exposure time. Endoscopic studies revealed grade A oesophagitis in 2 patients and grade C in 1 patient. All patients controlled reflux symptoms with a single PPI dose. 4 patients consumed PPI because of antiplatelet agent treatment. Overall, there were fewer patients on PPI after POEM procedure - 14/22 vs 18/22. 7 non-reflux and 1 reflux patients ceased PPI consumption.

Conclusion: PostPOEM procedure reflux is common. Older age and a low basal GERD-Q score are associated with reflux appearance. There are no significantly associated variables in the work-up test, observing lower basal LOSP, 4s-IRP pressures and shorter post-POEM barium column in the reflux group. Reflux burden is debatable, since globally there were less reflux related symptoms after the procedure and the PPI consumption decreased. All patients controlled their symptoms with a single dose of PPI.

Variable (unit)	Non-reflux	Reflux	p
Age (years)	46 (11)	65 (22)	0.01
Post BMI (kg/m2)	24.1 ± 5	28.8 ± 4	0.135
Basal GERD-Q	6.9 ± 2.5	4.3 ± 2	0.035
Basal LOSP (mmHg)	37.8 ± 14.7	28.3 ± 12.2	0.125
Basal 4s-IRP (mmHg)	22.5 ± 14	15.8 ± 6.2	0.171
Basal OGJ-CI (mmHg/cm)	51.3 ± 32	29 ± 23	0.096
Post POEM barium column (cm)	2.6 (6.5)	0 (0)	0.161

[Table 1. Significant and possibly associated with reflux variables.]

References: 1. Estremera-Arevalo F, Albeniz E, Rullan M et al. Efficacy of peroral endoscopic myotomy compared with other invasive treatment options for the different esophageal motor disorders. Rev Esp Enferm Dig. 2017 Aug;109(8):578-586. doi: 10.17235/reed.2017.4773/2016. 2. Nicodème F, Pipa-Muniz M, Khanna K et al. Quantifying esophagogastric junction contractility with a novel HRM topographic metric, the EGJ-Contractile Integral: normative values and preliminary evaluation in PPI non-responders. Neurogastroenterol Motil. 2014 Mar;26(3):353-60. doi: 10.1111/nmo.12267. Epub 2013 Dec 3. 3. Wang D, Xu H, Tang T et al. Assessment of the esophagogastric junction (EGJ) using the EGJ contractile integral (EGJ-CI) following per-oral endoscopic myotomy (POEM) in achalasia. Rev Esp Enferm Dig. 2018 Nov;110(11):706-711. doi: 10.17235/reed.2018.5560/2018.

Disclosure: Nothing to disclose

P1967 MACROPHAGE PLASTICITY AND POLARIZATION IN DIFFERENT CLINICAL VARIANTS OF GASTROESOPHAGEAL REFLUX DISEASE

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Introduction: In gastroesophageal reflux disease (GERD) the refluxate provokes active esophageal mucosa inflammation with moderate immune cells infiltration, which includes macrophages (M), obtaining M1 or M2 phenotype. Considering the modern concept of immune response development, changes of M phenotype strongly correlate with Th1/Th2 systemic immune response. So, M of different phenotypes can greatly influence esophageal mucosa inflammation and affect GERD clinical variants.

Aims & Methods: Analysis of M polarization and phenotypic plasticity in patients with different clinical variants of GERD.

Patients with non-erosive reflux disease (NERD; n=26; 41.2±3.6 y.o.), erosive reflux disease (ERD; n=25; 41.9±3.1 y.o.), and Barrett's esophagus (BE; n=19; 43.7±4.2 y.o.) were included in the study. M phenotype and polarization was assessed by in vitro model included adding refluxates of patients (n=70) with different pH (4.6-8.1) to peritoneal M of C57/BL6 mice (n=70) culturing in standard conditions for 36 hours. M polarization analysis included secretory function assessment (Th1/Th2 cytokines in culture medium, Antigenix, USA), receptor characteristics - typical M1/M2 CD markers (CD80 / CD206, respectively) performed by flow cytometry (FC500, Beckman Coulter). Phenotypic plasticity was measured as changes of CD expression (CD80/CD206) and cytokine production (IL-12p70/IL-10) during 36 hours of M reprogramming in the presence of 0%, 10%, 40% standard FBS. Changes in 0% FBS vs 10% FBS reflected plasticity towards M1 phenotype, in 40% FBS vs 10% FBS - to M2 phenotype. Mean pH values of refluxates were assessed for all patients' groups.

Results: Analysis of M polarization in different variants of GERD by cytokine production and CD markers expression revealed the prevalence of Th1 and Th1/Th2 bivalent cytokines and M1 markers expression in all groups with variable changes of indices probably due to various mean pH values of the refluxates (6.53±0.41 in ERD, 5.52±0.24 in BE, 5.44±0.32 in NERD). Analysis of macrophage plasticity showed the ability of macrophages to change their phenotype both towards M1 and M2 in all groups, but max changes were observed in production of IL-10 in 40% FBS in all groups (increased as compared to 10% FBS standard conditions in 3.77 in NERD group, 3.8 - in BE and 3.4 - in ERD). The level of CD markers expression also changed in various FBS concentrations, but the changes were significant only for CD206 in 40% FBS in all groups. The data were comparable between the groups: CD206 expression increased in 1.6 in NERD, in 1.5 in BE, in 1.6 ERD.

Conclusion: Analysis of macrophage polarization in different variants of GERD showed that secretion and receptor profile of the cells is typical for M1 phenotype with some variations of different cytokines production and CD markers expression that may be due to the type and pH value of the refluxate influencing macrophages. Macrophages in all GERD variants can change their phenotype according to the micro-environment. Phenotypic plasticity of the cells was confirmed by changing the cytokine production and CD markers expression. The highest phenotypic plasticity was shown

towards M2 phenotype for macrophages in all groups. These data can indicate the possibility to influence macrophage-mediated immune response in different clinical variants of GERD.

Disclosure: Nothing to disclose

P1968 NOCTURNAL SYMPTOMS OF GASTROESOPHAGEAL REFLUX ARE RELATED TO PROXIMAL EXTENT OF LIQUID REFLUXATE DURING NIGHTTIME

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Introduction: Patients with gastroesophageal reflux disease (GERD) often have nocturnal symptoms. However, pathophysiology of nocturnal symptoms is not fully understood.

Aims & Methods: A total 25 subjects were enrolled (11 females, median age 58 year-old). Subjects were divided into five controls, six reflux esophagitis (RE) patients without nocturnal reflux symptoms and 14 RE patients with nocturnal reflux symptoms. We evaluated esophageal motility, and gastroesophageal reflux (GER) and esophago-pharyngeal reflux (EPR) events with a high-resolution impedance manometry system using a Unisensor catheter. The system has 36 pressure sensors and 16 impedance measurement sites. Pharyngeal and esophageal pH sensors were located 1.5 cm above the proximal border of the upper esophageal sphincter (UES) and 5 cm above the proximal border of the lower esophageal sphincter (LES) to detect EPR and GER events. Sleep stages were assessed using polysomnogram. These measurements were concurrently recorded for about 6-hours post-prandially in the supine position during sleep. Subjects, who took proton pump inhibitors (PPIs), were made to stop taking PPIs at least one week prior to the study. Subjects had a standard meal (1000 kcal) before recording. The presence of RE was evaluated by esophagogastro-duodenoscopy and the severity of nocturnal symptoms was assessed by nocturnal gastro-esophageal reflux disease symptom severity and impact questionnaire (N-GSSIQ) in all subjects. The number of transient LES relaxation (TLESR), GER, EPR events and the length of proximal extent of liquid refluxate from the proximal border of the LES in each liquid or mixed GER event were evaluated. Data is shown as median (25%, 75%).

Results: Most GER events were associated with TLESR events and they occurred during awakening or just after arousals. There was no acid EPR event. The incidences of TLESR, TLESR with liquid or mixed GER, TLESR with acid GER and TLESR with UES relaxation were not different among three groups (Table). The length of the proximal extent of liquid refluxate in RE patients with nocturnal symptoms was significantly longer than other groups (p< 0.05).

	Controls	RE patients without nocturnal reflux symptoms	RE patients with nocturnal reflux symptoms
Number of subjects	5	6	14
Number of TLESR events	11 (6, 20)	19 (14, 25)	12 (9, 18)
Number of TLESR events with liquid or mixed GER events	8 (4, 14)	14 (6, 18)	11 (8, 18)
Number of TLESR events with acid GER	0 (0, 6)	2 (0, 6)	5 (0, 8)
Number of TLESR events with UES relaxation	1 (1, 4)	3 (0, 6)	0 (0, 1)
Length of proximal extent of liquid refluxate	5 (4, 11)	5 (3, 13)	8 (5, 14)*

[Number of events among groups]

Conclusion: Nocturnal reflux symptoms are related to the proximal extent of liquid refluxate during nighttime. Acid EPR event is not common during nighttime.

Disclosure: Nothing to disclose

P1969 THE ROLE OF ESOPHAGEAL EPITHELIAL INTEGRITY ON PROTON PUMP INHIBITOR RESPONSE IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE

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Introduction: 20-30% of patients with gastroesophageal reflux disease (GERD) do not adequately respond to proton pump inhibitors (PPI). It is not known whether esophageal epithelial integrity is one of the determinant of the response.

Aims & Methods: We evaluated the relationship between PPI response rate and esophageal epithelial integrity in GERD patients.

24 healthy controls (HC) 16 functional heartburn, 11 reflux hypersensitivity, 35 true non-erosive reflux (NERD), 48 erosive GERD A-B (ERD AB) and 12 erosive GERD C-D (ERD CD) in total 146 subjects were included. GERD and QoL questionnaires, high-resolution esophageal manometry, off-PPI intra-esophageal 24-h impedance-pH monitoring, upper gastrointestinal endoscopy with distal esophageal biopsies performed in all patients. Esophageal epithelial resistance (TEER) and tissue permeability via fluorescein diffusion within 2 hours were measured by mini-Ussing chamber system. Patients were analysed according to phenotypes and PPI responses; >80% very good, 50-79% good, < 50% no response.

Results: TEER of all GERD patients were significantly lower than the healthy controls. TEER of all GERD groups were decreased compared to HC however only ERD groups were significant. The tissue permeability of all phenotypes and functional heartburn was significantly higher than controls. According to PPI response, TEER was significantly lower and tissue permeability was significantly higher than the controls. Tissue permeability in >80% responder group was significantly lower compared to "good" and "no response" groups. While TEER results of "17-34" age group were higher but insignificant than older patients (>55 yo) (p=0.072), tissue permeability was significantly lower. In addition, the tissue permeability of patients ≤50 yo healthy controls was significantly lower than older healthy controls.

	TEER (ohm)	Permeability (pmols)
Healthy controls	166,8 ± 46,2	36,9 ± 13,5
PPI response ≥80%	147,0 ± 39,1**	45,9 ± 23,8*
PPI response 50-79%	136,0 ± 37,6**	57,6 ± 33,1* ^^
No response <50%	138,9 ± 51,8**	60,1 ± 38,9** ^
ERD (all)	129,3 ± 33,3*	51,7 ± 30,7 **
ERD A/B	133,7 ± 34,1* ¥¥	46,9 ± 28,1***
ERD C/D	112,1 ± 37,1* ¥	60,1 ± 38,9**
NERD	151,4 ± 48,0	57,5 ± 32,9**
Reflux hypersensitivity	153,6 ± 46,5	65,4 ± 34,1**
Functional heartburn	159,5 ± 55,1	54,5 ± 34,1***
All patients	141,8 ± 39,4**	55,0 ± 32,8*
GERD patients 17-34 yo	150,1 ± 39,4	50,4 ± 25∞
GERD patients >55 yo	133,0 ± 51,6	67,5 ± 43,2

* p≤ 0.001 vs HC, ** p<0.01 vs HC, *** p<0.05 vs HC ¥ p≤ 0.01 vs NERD, ¥¥ p<0.05 vs NERD ^ p≤ 0.01 vs Very good PPI response, ^^ p≤ 0.05 vs Very good PPI response ∞ p< 0.05 vs >55 aged

[Transepithelial resistance and permeability results of the groups]

Conclusion: Tissue resistance was lower and tissue permeability higher in all GERD patients compared to healthy controls implicates that tissue integrity decreases in GERD. Although the PPI response criteria in the literature have been determined in "50% and above" range; this rate is not adequate at the clinical level. We found that a higher and clinically more significant level which is >80% range was significantly related with a better epithelial integrity. This finding implicates that lower ion (H+) permeability might be related with higher PPI response. The tissue permeability of older healthy controls was higher than younger subjects implicates the importance of aging by itself.

Disclosure: Nothing to disclose

P1970 THE THICKNESS OF THE CRURAL DIAPHRAGM IS THINNER IN HELICOBACTER PYLORI INFECTED GERD PATIENTS

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Introduction: The crural diaphragm is an essential component of the esophagogastric junction (EGJ). Inspiratory EGJ pressure is lower in GERD and patients fail to increase EGJ pressure during graded increase in inspiratory resistance. Also, some reflux esophagitis patients may have a weaker and thinner crural diaphragm. Inflammation is an important factor of muscle dysfunction. One of the most common causes of human inflammation is the infection by *Helicobacter pylori*, which has a complex relationship with GERD.

Aims & Methods: The aim of this study is to measure the thickness of the crural diaphragm in GERD patients and analyze its relation to symptoms, gastric inflammation, and the infection with *H. Pylori*. Thirty patients (18 females, age 46.7 yr, weight 71.5 kg, in average) with GERD (distal esophageal acid exposure > 4.2%) were studied after approval by the local ethical committee (HUWC-Ceará Federal University, Fortaleza, Brazil). The right crus of the diaphragm (RC) is easily identified with an endoscopic ultrasound (EUS) probe positioned in the EGJ region during expiration (12 MHz, radial probe, Fujinon, Japan). The RC images were stored for posterior blinded measurement of its ortogonal section, in mm. GERD patients were categorized according to the RC thickness (cutoff=4mm, lower limit of our laboratory 95%CI). During the endoscopic procedure, biopsies of the antrum and gastric corpus (five different sites) were taken for blinded, four-points (0-3), hystologic analysis for each of the following items: inflammation, inflammatory activity (neutrofil infiltration), metaplasia, atrophy, and *H. pylori* infection. The total score of each hystologic item were summed up for statistical analysis. The maximal inspiratory oral pressure (maxIP, in cmH_2O) was measured with a digital manometer during maximal isometric inhalation in sitting position with nostrils closed, as marker of inspiratory muscles strength. The volunteers also completed two GERD questionnaires: RSI for atypical and RDQ for typical symptoms. Data were analyzed with Student t or Mann-Whitney Tests. Results are presented in mean ± SEM or median (minimum-maximum).

Results: Age and weight did not differ between patients with normal (n=23) or abnormal (n=7) RC thickness. Symptoms total scores did not differ significantly between the two groups: RDQ (9 (2-30) vs 20 (2-25), p=0,10) and RSI (13 (1-42) vs 21 (6-38), p=0.17). However, the epigastric burning sensation (RDQ item) and the respiratory difficulty (RSI item) were higher in the group with a thinner RC (0 (0-5) vs 3 (0-5), p=0.03; 0 (0-5) vs 5 (0-5), p=0.023; respectively). Inflammation, inflammatory activity, and *H. pylori* infecction scores were significantly higher in the patients with a thinner RC (5 (1-8) vs 5 (5-6), p=0.042; 0 (0-9) vs 5 (0-10), p= 0.003; 0 (0-13 vs 8 (0-15), p=0.008; respectively). Atrophy and metaplasia did not differ between the groups. The positivity of the rapid urease test was also higher in the patients with abnormal RC thickness (p=0.008). Acid exposure in the distal esophagus did not differ between the two groups of GERD patients. The maxIP were less negative in the patients with abnormal RC thickness ($-75.5±7.5\ cmH_2O$ vs $-56.1±3.9\ cmH_2O$).

Conclusion: In GERD patients, the thickness of the RC and the strength of inspiratory muscles were associated with gastric inflammation due to the infection with *H. Pylori*. The esophageal acid exposure and the typical symptoms of the two groups of GERD patients did not differ. These results brings about new evidence that may help interpret the complex relationship between *H. Pylori* infection and GERD.

References: Souza et al, Am. J. Physiol., DOI: 10.1152/ajpgi.00054.2013
Souza et al, NG&M, DOI: 10.1111/nmo.12899

Disclosure: Nothing to disclose

P1971 THE INFLUENCE OF CRURAL DIAPHRAGM ON ESOPHAGOGASTRIC JUNCTION FUNCTION AND GASTROESOPHAGEAL REFLUX DISEASE FEATURES. A PROSPECTIVE STUDY WITH HIGH RESOLUTION MANOMETRY AND IMPEDANCE-PH MONITORING

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Introduction: A normal function and morphology of the esophagogastric junction (EGJ) is essential in preventing gastroesophageal reflux disease (GERD). Crural diaphragm (CD) is responsible for a part of the antireflux barrier. High-resolution manometry (HRM) provides information on axial separation between lower esophageal sphincter (LES) and CD and can evaluate the EGJ antireflux barrier using the EGJ contractile integral (EGJ-CI). However, comprehensive data about the correlation between presence of LES-CD separation, EGJ-CI and GERD features determined at impedance-pH monitoring (MII-pH) are scarce.

Aims & Methods: To verify if a increasing distance of LES-CD separation and a decreasing EGJ-CI could better correlate with a positive MII-pH testing, with symptoms and the presence of esophagitis.

Consecutive patients with predominant typical GERD symptoms (heartburn and/or regurgitation) and a recent upper endoscopy were enrolled. Esophagitis was defined according to Los Angeles classification. The presence of further symptoms and PPIs response were recorded. All patients underwent HRM to assess the EGJ morphology, the EGJ-CI and 10 single water swallows to evaluate peristalsis and EGJ function, according to the Chicago Classification (CC) 3.0. EGJ Type I was further divided into Type I-CO, a complete overlap of LES and CD, and Type I-MS, a minimal separation, with LES located from the upper border of CD (in correspondence of pressure inversion point, 0.0 cm) to 1 cm above. Also, intra-hernia pressure and contractile integral of CD (CD-CI, when distinguishable from LES) were recorded.

The patients then underwent impedance-pH testing off-therapy. We recorded the esophageal acid exposure time (AET), number of total reflux episodes, mean nocturnal baseline impedance (MNBI), post-reflux swallow-induced peristaltic wave index (PSPW + if< 53%) and symptom association analysis using symptom association probability (SAP+ if ≥95%) and symptom index (SI+ if ≥50%).

McNemar test and Anova test were performed among groups determined according to LES-CD separation.

	EGJ Type I-CO (n=72)	EGJ Type I-MS (n=54)	EGJ Type II (n=42)	EGJ Type III (n=35)	P Value
Patients with GERD (%)	33.3	70.3	76.1	94.2	0.001* (n.s. type I-MS vs Type II)
Total number of reflux (mean ± S.D.)	29±15	48± 29	49±21	79±28	0.001* (n.s. type I-MS vs Type II)
AET % (mean ± S.D.)	2.7±0.8	4.8±2.2	11±12	17±13	0.001*
PSPW% (mean ± S.D.)	68± 25	45± 32	50± 37	28± 13	0.001* (n.s. type I-MS vs Type II)
MNBI (mean ± S.D.)	3211±895	1811±676	1796±943	1279±1285	0.001* (n.s. type I-MS vs Type II)
Patients with positive symptom association (%)	26	55	70.2	86.6	0.001*
EGJ-CI	21±8	15±11	15±14	5±10	0.001* (n.s. type I-MS vs Type II)

[Table 1]

Results: We enrolled 203 [96M/107F; mean age 46] consecutive patients and identified 72 (35.4%) patients with EGJ Type I-CO, 54 (26.6%) Type I-MS, 42 (20.7%) Type II and 35 (17.2%) Type III. Patients with Type III EGJ had lower EGJ-CI, decreased mean DCI, a higher median number of reflux episodes, a greater mean AET, a lower MNBI and PSPW and had more frequently a positive symptoms association compared to patients with Type II and Type I-CO/MS (Table 1). Type I-MS had a higher number of reflux episodes (48 vs. 29, p< 0.03), a greater mean AET (4.8 vs. 2.7, p< 0.05) and a greater positive symptom association (55% vs. 26%, p< 0.02) compared to Type I-CO. At Anova, PPI response was significantly linked to EGJ Type III, whereas dysphagia was linked to higher intra-hernia pressure and CD-CI values.

Conclusion: With increasing separation between LES and CD, patients had a gradually and significantly increase of reflux episodes and esophageal acid exposure. Even a minimal separation can be responsible for GERD development and supports the role of CD in preventing reflux.

Disclosure: Nothing to disclose

P1972 A NOVEL SUSCEPTIBILITY LOCUS NEAR *GRIK2* ASSOCIATED WITH EROSIVE ESOPHAGITIS IN A KOREAN COHORT

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Introduction: Erosive esophagitis is defined as esophageal mucosal breaks proven by endoscopy because of gastroesophageal reflux exposure. Through Genome-Wide Association Studies (GWAS), we aimed to identify genetic factors associated with erosive esophagitis, especially gender differences.

Aims & Methods: The GWAS was conducted with 4,242 healthy participants who underwent upper endoscopies for health check-ups; 3,620 subjects comprised the discovery set and 622 subjects comprised the replication set. Erosive esophagitis was diagnosed by endoscopy and assessed for severity. After the quality control and imputation, we used the multivariable linear regression and SNPs with $p < 5.0 \times 10^{-8}$ were considered significant genome-wide.

Results: We detected six genome wide significant SNPs associated with erosive esophagitis in male subjects; rs518309 ($p = 2.12 \times 10^{-8}$), rs654455 ($p = 2.12 \times 10^{-8}$), rs562589 ($p = 2.504 \times 10^{-8}$), rs594589 ($p = 2.786 \times 10^{-8}$), rs513126 ($p = 2.93 \times 10^{-8}$), and rs4445064 ($p = 5.864 \times 10^{-8}$). All the SNPs were replicated in the replicated set ($p < 0.05$). We could predict the severity of erosive esophagitis based on genetic risk score established by these SNPs. These SNPs were located in topologically associated domain of glutamate ionotropic receptor kainite type subunit 2 (*GRIK2*) gene on chromosome 6q16.3.

Conclusion: This is the first GWAS to identify SNPs associated erosive esophagitis diagnosed by endoscopy. We found six genome wide significant SNPs associated with erosive esophagitis and these variation could help predict its severity.

Disclosure: Nothing to disclose

P1973 GASTRIN ELEVATION DURING LONG TERM PROTON PUMP INHIBITOR THERAPY AND FUNDIC GLAND POLYPS

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Introduction: Proton pump inhibitor (PPI) therapy is usually associated with serum gastrin elevation. Prolonged use of PPI may promote a development of fundic gland polyps (FGPs). Concerns have been raised about the course of chronic gastrin elevation and relations to FGPs grow. Published studies regarding long term PPI use exceed 5 years interval rarely.

Aims & Methods: The aim of this study was to analyze the time evolution of gastrin elevation during long term PPI therapy of gastroesophageal reflux disease and consequences in FGPs development.

This prospective observational study included patients with gastroesophageal reflux disease (GERD) on long term PPI therapy. Patients followed 8 years and longer were selected for analysis. The level of serum gastrin during follow up was compared to dose of PPI, sex, H. pylori and presence of FGPs on endoscopy.

Results: The data from 109 patients (51 males) were available. Mean follow up was 10.9 years. Median serum gastrin level gently fluctuates about upper limit of gastrin (115 ng/l) during the period, without any significant progression in time. Mean gastrin was non-significantly higher in females than males (160 vs 109 (p 0,5)). In 55 patients FGPs were found on gastroscopy.

The mean serum gastrin in patients with and without FGPs was not different (131 vs 140 ng/l (p=0,82)). Lower than standard, standard and higher PPI doses were related to different gastrin elevation (mean 65 vs 125 vs 192 ng/l). Neither neuroendocrine tumor nor gastric cancer was recorded in the study cohort.

Conclusion: Gastrin elevation is mild without any significant progression in time during more than 10 years of PPI therapy of GERD. Although chronic PPI use is associated with development of fundic gland polyps, this was not related to serum gastrin level. The correlation between serum gastrin and PPI dose was observed.

Disclosure: Nothing to disclose

P1974 ETHNIC COMPARISON OF PHARMACOKINETICS AND PHARMACODYNAMICS OF DWP14012, A NEW POTASSIUM-COMPETITIVE ACID BLOCKER, AMONG KOREAN, CAUCASIAN AND JAPANESE

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Introduction: A potassium-competitive acid blocker (P-CAB), DWP14012, is under development for the treatment of acid-related esophageal-gastric disease. This study aimed to compare the pharmacokinetics (PK), pharmacodynamics (PD) and safety of DWP14012 among different ethnic groups.

Aims & Methods: A randomized, double-blind, placebo-controlled, single- and multiple-dose study was conducted in Korean, Caucasian and Japanese healthy subjects. Ten subjects in each dose group randomly received DWP14012 or placebo in a ratio of 8:2. Each subject was orally received DWP14012 (40 mg, 60 mg or 80 mg in Korean; 40 mg or 80 mg in Caucasian; 20 mg, 40 mg or 80 mg in Japanese) or placebo once-daily for 7 consecutive days. Serial blood samples were collected for PK evaluation. For PD evaluation, a 24-hour intra-gastric pH monitoring was performed at baseline (a day prior to first dose), after a single dose and steady-state after multiple doses. Safety profiles were assessed throughout the study. A general linear model was developed to compare PK and PD parameters. Geometric mean ratios (GMRs) and its 90% confidence intervals (CIs) of PK parameters for Caucasian and Japanese over Korean were calculated and the mean differences and its 90% CIs of PD parameters between each ethnic group was also calculated.

Results: After multiple treatment of 40 mg of DWP14012, the plasma concentration of DWP14012 and the gastric acid suppression was similar among the ethnic groups. The GMR (90% CI) of area under the curve within a dosing interval at steady-state (AUC_{tau}) for Caucasian and Japanese to Korean were 1.08 (0.76-1.53) and 1.07 (0.76-1.52), respectively. The mean percentages of time pH above 4.0 for DWP14012 in Korean, Caucasian and Japanese were 64.3%, 62.8% and 70.3%, respectively, and the mean difference of PD parameter for Caucasian and Japanese compared to Korean were not statistically significant (both $P > 0.05$).

After multiple treatment of 80 mg of DWP14012, the GMR (90% CI) of AUC_{tau} for Caucasian and Japanese were 0.70 (0.49-0.99) and 0.73 (0.52-1.04), respectively. . However, the gastric acid suppression was similar between each ethnic group (both $P > 0.05$); The mean percentages of time pH above 4.0 for DWP14012 in Korean, Caucasian and Japanese were 94.8%, 90. 6% and 90.6%, respectively.

The increased gastric acid suppression according to dose of DWP14012 and clear exposure-response relationship were observed in all ethnic groups. There were no serious adverse events and no clinically significant changes in tolerability parameters in all dose groups in every ethnicity.

Conclusion: After 7-day multiple administration of DWP14012 40 and 80 mg, the gastric acid suppression and the exposure-response relationship were similar among Korean, Caucasian and Japanese. These results suggested that the gastric acid suppression of DWP14012 may not be sensitive to ethnic factors.

Disclosure: Nothing to disclose

P1975 ON-DEMAND VERSUS HALF-DOSE CONTINUOUS THERAPY WITH VONOPRAZAN AS MAINTENANCE THERAPY FOR GASTROESOPHAGEAL REFLUX DISEASE

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Introduction: Although symptomatic gastroesophageal reflux disease (GERD) is a chronic clinical condition treated with initial and maintenance therapies, there has been no established consensus for a long-term maintenance therapy. Several studies have reported the efficacy of vonoprazan (VPZ), a novel potassium-competitive acid blocker, as an initial therapy for GERD; however, an optimal maintenance therapy with VPZ remains to be evaluated.

Aims & Methods: The aim of this study was to evaluate the efficacy of an on-demand therapy with VPZ as a maintenance therapy for mild symptomatic GERD. A retrospective observational study of case data from patients with upper gastrointestinal endoscopy-proven symptomatic GERD (defined as modified Los Angeles [LA] classification grades A or B, and more than 8 points on the Frequency Scale for the symptoms of GERD [FSSG]) was conducted. We included patients who achieved symptomatic remission, which was defined as an FSSG score ≤8 points, after receiving an initial therapy with 20 mg VPZ for 8 weeks. These patients were then treated with on-demand therapy by taking 20 mg VPZ only when reflux symptoms occurred (on-demand group), or with continuous therapy with 10 mg VPZ (continuous group) as maintenance therapy. Clinical symptoms were retrospectively compared between the two groups using the FSSG questionnaire at the start of the maintenance therapy, and after 4, 8, 12, 24, 48, and 52 weeks. An endoscopic evaluation using the modified LA classification system was also performed at 12 weeks in both the groups. Furthermore, health related quality of life (HRQOL) was assessed using reflex esophagitis specific HRQOL questionnaires at 52 weeks.

Results: Forty-eight patients (22 men, 26 women; mean age, 72.5 years [range, 32-88 years]; on-demand group, 31 patients; continuous group, 17 patients) completed the study. FSSG scores, modified LA classification grades at diagnosis of GERD, and FSSG scores at the start of the maintenance therapy were similar in both the groups (12.0 ± 3.5 vs. 12.8 ± 3.5, P = 0.20, grade A; 61.3% vs. 47.1%, P = 0.34; 3.3 ± 2.3 vs. 2.8 ± 2.2, P = 0.20; respectively). There was no significant difference in the persistence rate of maintenance therapy at week 52 between the groups (85.9% vs. 88.2%, P = 0.68). Two patients (6.5%) dropped out because of worsening of symptoms, and 3 patients (9.7%) changed regimen to continuous therapy on their own volition at remission state in the on-demand group. Moreover, two patients (11.8%) dropped out because of worsening of symptoms in the continuous group. The average number of VPZ tablets taken per week during the 28-52 weeks tended to be lower than that during the 0-28 weeks in the on-demand group (1.6 tablets ± 0.15 vs. 1.3 tablets ± 0.2, P = 0.13). Although FSSG scores after 4, 8, 24, 48, and 52 weeks were significantly higher in the on-demand group than in the continuous group, there was no significant difference in the endoscopic severity, evaluated by the modified LA classification system, after 12 weeks between the two groups (grade M; 75.0% in the on-demand group vs. 93.8% in the continuous group, P = 0.12), and no patients experienced symptomatic recurrence at 52 weeks in the on-demand group. Furthermore, there was no significant difference in HRQOL assessed by reflex esophagitis HRQOL questionnaires at 52 weeks between the two groups.

Conclusion: On-demand therapy with 20 mg VPZ was an effective alternative maintenance therapy for mild GERD that was comparable to half-dose continuous therapy with a sufficient persistence rate, symptom control rate, and HRQOL.

Disclosure: Nothing to disclose

P1976 A NOVEL ENDOSCOPIC FUNDOPLICATION FOR GASTROESOPHAGEAL REFLUX DISEASE: ANTI-REFLUX MUCOSAL ABLATION (ARMA)

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Introduction: As a treatment for gastroesophageal reflux disease (GERD), proton pump inhibitors (PPIs) are the mainstay of medical therapy. However, up to 40% of patients are reported to have persistent GERD symptoms despite PPI therapy. Several endoscopic procedures have been attempted but no procedure has been widely accepted as the standard endoscopic treatment for GERD. We developed Anti-reflux mucosal ablation (ARMA) as a minimally invasive treatment.

Aims & Methods: The aim of this study is to clarify the efficacy and safety of ARMA. The indication of ARMA is PPI refractory GERD patient without prominent sliding hernia. The purpose of ARMA is to narrow the space of hiatus hernia by performing ablation to the mucosa at the gastric cardia.

Step 1: marking of scheduled ablation area on the mucosa. Mucosal ablation is scheduled along the gastric cardia in butterfly shape to avoid stenosis. Markings on the mucosa were placed using Triangle Tip Knife J connected to the electrocautery generator (VIO300D ERBE) in soft coagulation mode, 50 W, effect1.

Step 2: Saline with indigo carmine dye was injected into submucosa along the markings using 25-Gauge needle. Correct submucosal saline injection was confirmed by lifting of the mucosal surface.

Step 3: Near circumferential (butterfly shape) mucosal ablation was made using Triangle Tip Knife J in spray coagulation mode, 50W, effect2.

The efficacy of ARMA was evaluated using the objective findings (flap valve grade: I/II/III/IV as point 0/1/2/3, 24-hour multi-channel intraluminal impedance-pH monitoring) and subjective findings (Frequent Scale for the Symptoms of GERD:FSSG, and GERD-HRQL).

Results: A total of 12 patients with median age of 54.5 (29-75), Female 5: Male 7, with PPI-refractory GERD were enrolled in this study between May 2018 and March 2019. The procedure time was 40.3 (20-69) minutes without any immediate complications. GERD-HRQL score improved significantly from median of 30.5 to 12 (p=0.0005), and the FSSG was significantly improved from median of 25 to 10.5 (p=0.0078) both at 2-month follow-up. The Hill's flap valve grade score significantly improved from 1.91 to 0.5 (p< 0.001). The DeMeester composite score improved from 33.5 to 2.8 (p=0.0547) and percent time clearance pH improved from 9 to 0.5 (p=0.0781) after ARMA. ARMA was successful in all cases and mild stenosis was observed in one patient which was managed by balloon dilatation, and no bleeding nor perforation were observed.

Conclusion: This case series suggests that endoscopic anti-reflux mucosal ablation (ARMA) may represent an effective anti-reflux procedure safely, with the added advantage of simplicity, low cost, less invasive, and leaving no artificial prostheses in situ. Larger studies with long-term follow up are warranted to confirm this result.

Disclosure: Nothing to disclose

P1977 FIXED COMBINATION OF HYALURONIC ACID, CHONDROITIN-SULPHATE AND ALUMINUM HYDROXIDE RESTORES ESOPHAGEAL MUCOSAL INTEGRITY IN PATIENTS WITH PROVEN GASTROESOPHAGEAL REFLUX DISEASE - A RANDOMIZED, CONTROLLED, PATHOPHYSIOLOGICAL AND CLINICAL STUDY

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Introduction: Esophageal intraluminal baseline impedance (BI) is determined by the conductivity of esophageal wall and is considered a surrogate marker of mucosal integrity, which impairment is associated to the development of gastro-esophageal reflux disease (GERD). Indeed, patients with GERD exhibit decreased distal BI as compared to healthy controls and this finding has been correlated with abnormal distal esophageal acid exposure time (AET). Current research is being focused on novel compounds able to protect the esophageal mucosa and restore its integrity. Recently, a new medical device based on a combination of hyaluronic acid, chondroitin-sulphate and aluminum hydroxide, in a single melt in mouth tablet (GERDOFF®, Sofar) has been marketed

Aims & Methods: We aimed to investigate whether GERDOFF® was able to modify the esophageal mucosal integrity in patients with GERD. This was a prospective, single center, randomized, controlled study (EC approval 4203/AO/17). Within 1-5 days from the upper endoscopy carried out off-therapy, 32 patients with typical reflux symptoms and evidence of erosive esophagitis greater than Los Angeles (LA) grade B, completed the Reflux Disease Questionnaire (RDQ) to assess severity and frequency of GERD symptoms, the GERD health-related quality of life (GERD-HRQL) and underwent high-resolution impedance manometry (HRIM) followed by a 10 minutes impedance-pH recording. Thereafter, they were randomized in a 1:1 ratio to receive GERDOFF®, 6 tablets per day, to be administered after each daily meal, at mid-morning and mid-afternoon and at bedtime (Group A), or an oral antacid or alginate on as needed basis for 14±2 days (Group B). Thereafter, patients repeated the questionnaires, filled in a VAS scale to measure the palatability of GERDOFF® and underwent a 24-hour impedance-pH monitoring. Tracings were blindly and manually reviewed and BI was measured at distal (at 3cm), mid (at 9cm) and proximal (at 15cm) esophagus off-therapy (10 minutes recording) and after 14±2 days of treatment. Secondary study parameters were: symptoms relief after 14±2 days of treatment, palatability, safety and tolerability of GERDOFF®.

Results: Two patients did not complete the study and were excluded. So far, data from 30 patients [18M/12F; mean age 54 (27-72) years; mean BMI 26 (18-34)] were further analyzed. Seventeen patients had Grade B, 4 grade C, 2 grade D esophagitis and 7 had short-segment Barrett Esophagus. Demographic, clinical and conventional impedance-pH features did not differ between Group A and Group B (p=ns). Also BI at distal, mid and proximal esophagus was similar (p=ns) between the two groups (1553Ω vs. 1284Ω, 1639Ω vs. 1769Ω, 2140Ω vs. 2303Ω, respectively). In contrast, after treatment BI at distal, mid and proximal esophagus was different (p<0.05) between the two groups (2093Ω vs. 1247Ω, 2337Ω vs. 1751Ω, 2785Ω vs. 2212Ω, respectively). Twelve out of 15 (80%) patients treated with GERDOFF® showed a significant increase of BI after treatment, whereas only 2/15 (14%) had a similar effect (p<0.0007). The palatability, safety and palatability of GERDOFF® were good.

Conclusion: Our data showed that in patients with proven GERD, GERDOFF® treatment for two weeks is able to restore the esophageal mucosal integrity in the majority of the patients, at both distal and proximal esophagus. These data provide a clear rationale for GERDOFF® use in the management of GERD.

Disclosure: Edoardo Savarino served as consultant for SOFAR

P1978 FIXED COMBINATION OF HYALURONIC ACID, CHONDROITIN-SULPHATE AND ALUMINUM HYDROXIDE IMPROVES REFLUX SYMPTOMS AND QUALITY OF LIFE IN PATIENTS WITH PROVEN GASTROESOPHAGEAL REFLUX DISEASE – A RANDOMIZED, CONTROLLED, PATHOPHYSIOLOGICAL AND CLINICAL STUDY

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Introduction: Proton pump inhibitors represents the current mainstay of gastroesophageal reflux disease (GERD) treatment. However, there is increasing evidence of their failure (i.e. 20-40% of the cases) and adverse events. Thus, current research is being focused on novel compounds able to protect the esophageal mucosa and reduce the damaging effect of the refluxate. Recently, a new medical device based on a combination of hyaluronic acid, chondroitin-sulphate and aluminum hydroxide, in a single melt in mouth tablet (GERDOFF®, Sofar) has been marketed.

Aims & Methods: We aimed to investigate whether GERDOFF® was able to modify the esophageal mucosal integrity in patients with GERD. This was a prospective, single center, randomized, controlled study (EC approval 4203/AO/17). Secondary study parameters were: symptoms relief after 14±2 days of treatment, palatability, safety and tolerability of GERDOFF®. Within 1-5 days from the upper endoscopy carried out off-therapy, 32 patients with typical reflux symptoms and evidence of erosive esophagitis greater than Los Angeles (LA) grade B, completed the Reflux Disease Questionnaire (RDQ) to assess severity and frequency of GERD symptoms, the GERD health-related quality of life (GERD-HRQL) and underwent high-resolution impedance manometry (HRIM) followed by a 10 minutes impedance-pH recording. Thereafter, they were randomized in a 1:1 ratio to receive GERDOFF®, 6 tablets per day, to be administered after each daily meal, at mid-morning and mid-afternoon and at bedtime (Group A), or an oral antacid or alginate on as needed basis for 14±2 days (Group B). Thereafter, patients repeated the questionnaires, filled in a VAS scale to measure the palatability of GERDOFF® and underwent a 24-hour impedance-pH monitoring. Tracings were blindly and manually reviewed and BI was measured at distal (at 3cm), mid (at 9cm) and proximal (at 15cm) esophagus off-therapy (10 minutes recording) and after 14±2 days of treatment.

Results: Two patients did not complete the study and were excluded. So far, data from 30 patients [18M/12F; mean age 54 (27-72) years; mean BMI 26 (18-34)] were further analyzed. Demographic, clinical and conventional impedance-pH features did not differ between Group A and Group B. In particular, mean RDQ [28.6 (15-45) vs. 27.6 (4-42), p=0.7800] and mean GERD-HQRL [20.2 (3-35) vs. 22.2 (4-35), p=0.864] were similar at baseline. In contrast, after treatment mean RDQ [28.6 (15-45) vs.16.9 (1-36), p=0.0054] and mean GERD-HQRL [20.2 (3-35) vs.12.3 (2-24), p< 0.0030] decreased compared to baseline only in the GERDOFF® group, whereas no variation was observed in the control group [27.6 (4-42) vs. 31.5 (5-70) and 22.2 (4-35) vs. 22.9 (0-33), p=0.1767 and p=0.6451, respectively]. The palatability [6.6 (2-10)], safety and tolerabilty of GERDOFF® were good

Conclusion: Our data showed that in patients with proven GERD, GERDOFF® treatment for two weeks is able to improve GERD-related symptoms and quality of life. Larger studies are necessary to confirm these preliminary clinical data

Disclosure: Edoardo Savarino serve as consultant for SOFAR

P1979 WITHDRAWN

P1980 MEASUREMENT OF SERUM GASTRIN LEVELS AND HISTOLOGIC EVALUATION OF THE DEGREE OF PARIETAL CELL DEGENERATION AND ECL CELL HYPERPLASIA ARE THE MOST IMPORTANT INDICATORS TO EVALUATE THE RISK OF DEVELOPING NET WHEN CONSIDERING THE USE OF MORE POTENT GASTRIC ACID SECRETION INHIBITORS

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Introduction: The situation surrounding upper gastrointestinal tract diseases is about to change completely due to the decrease in *H. pylori* infection rate and the spread of eradication in Japan. In the future, it is expected that the use of gastric acid secretion inhibitors will continue to increase due to the further increase of gastroesophageal reflux disease (GERD). On the other hand, the negative effect and verification of safety associated with more potent acid suppression and long-term acid suppression have not been sufficiently obtained. Potassium Competitive Acid Blocker (P-CAB) is the most potent acid secretion suppressant among similar acid secretion inhibitors (PPIs and H2 blockers), the use of P-CAB has been increasing rapidly in Japan and some countries. But, the negative effect of P-CAB (for example progression to neuroendocrine tumors (NET) have been remain unknown, so it is necessary to pay attention to the unknown side effects of P-CAB

Aims & Methods: We aimed to find out an index for avoiding the risk of developing neuroendocrine tumor (NET) under the long time use of gastric acid secretion inhibitors. We think hypergastrinemia as one of the side effects of acid secretion inhibitors is the most important factor of NET induction. In addition, the appearance of ECL cells hyperplasia and degeneration of parietal cells are important precursors of NET, and the presence of ECL micronest may be considered as a preneoplastic status of NET onset. We examined the serum gastrin levels (normal range≦200 pg / ml) and gastric biopsy specimens in 55 cases using gastric acid secretion inhibitors for GERD from April 2017 to March 2019. We compared the serum gastrin levels and the presence of parietal cell degeneration and ECL cell hyperplasia on each drug. We examined whether it could be an important index for avoiding the risk of developing NET.

Results: All 55 cases were divided into 20 cases in the P-CAB group and 35 cases in the PPI group, we compared the serum gastrin levels in fasting conditions. In the P-CAB group the serum gastrin levels were significantly higher (160~35,000 median 2,600) than in the PPI group (40~2,000 median 280) (*p* < 0.01). Furthermore, in 26 cases (10 cases in the P-CAB group and 16 cases in the PPI group) where stomach biopsy specimens were present, 90% (9/10) of the P-CAB group and 50% (8/16) of PPI group showed the presence of parietal cell degeneration and ECL cell hyperplasia. In addition, the results of comparing the degree of parietal cell degeneration and ECL cell hyperplasia showed severe changes in P-CAB group 67% (6/9) rather than PPI group 25% (2/8). Two cases of short-term use of P-CAB (6 months) were included, it was suggested that histological changes due to short-term use of P-CAB occurred in the gastric gland. In summary, significant hypergastrinemia associated with strong inhibition of gastric acid secretion was revealed, and histologically, parietal cell degeneration and ECL cell hyperplasia had been occurred at high rates. Furthermore, it became clear that more pronounced changes appeared due to the stronger suppression of acid secretion. We believe that long-term potent inhibition of acid secretion may increase the risk of developing NET.

Conclusion: More potent gastric acid secretion suppression resulted in marked hypergastrinemia, hyperplasia of ECL cells and degeneration of parietal cells. Therefore, when continuing strong suppression of gastric acid secretion, it is recommended that serum gastrin levels and histologic evaluation be performed to reduce the risk of developing NET.

Disclosure: Nothing to disclose

P1981 ALTERED GUT MICROBIOTA IN CANDIDATES FOR ANTIREFLUX SURGERY

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Introduction: Antireflux surgery is an option for patients with symptoms of gastroesophageal reflux disease (GORD) who have an unsatisfactory response to proton pump inhibitor (PPI) therapy or seek an alternative to lifelong medication. However, long-term PPI therapy is associated with an altered gut microbiota.[1,2] Candidates for antireflux surgery are not routinely screened for dysbiosis of the gut microbiota. We performed a hydrogen and methane breath test (HMBT) in patients under consideration for antireflux surgery with a history of PPI use.
Aims & Methods: 138 patients on long-term PPIs (>6 months) and referred for antireflux surgery performed a lactulose HMBT. A positive result for small intestinal bacterial overgrowth (SIBO) and/or excessive methane production was indicative of dysbiosis (determined by a rise in hydrogen ≥10 ppm above baseline within 60 minutes after ingestion of substrate and determined by methane levels ≥10 ppm at any interval, respectively). Patients who underwent a complete 24-hour ambulatory pH study and HMBT were analysed for association with GORD (determined by a distal acid exposure time of >4%) and reflux symptom association (determined by a symptom index of ≥50% and symptom association probability of ≥95%) statistically using Pearson Chi-Square test.
Results: In total 59.4% of subjects (82/138) had gut dysbiosis (25.3% were positive for SIBO, 19.6% were positive for excessive methane production and 14.5% had concomitant SIBO and excessive methane). 63 patients provided a complete 24-hour pH study and HMBT. The presence of dysbiosis was not associated with an abnormal AET ($p=$>0.05) but was associated with a positive reflux-symptom association (p=0.001). Belching and regurgitation were the most frequently reported symptoms associated with reflux episodes.
Conclusion: A large proportion of patients considering antireflux surgery as a management strategy present with altered gut microbiota as determined by HMBT. Those patients with dysbiosis are more likely to have a positive association between reflux episodes and symptoms. Breath testing may be a useful adjunctive test in the pre/post-operative assessment of antireflux surgery. Although, further prospective study is required to determine the impact of altered gut microbiota on clinical outcomes following antireflux surgery.
References: 1. Jackson MA, Goodrich JK, Maxan M-E, Freedberg DE, Abrams JA, Poole AC, et al. Proton pump inhibitors alter the composition of the gut microbiota. Gut. 2016;65(5):749. 2. Imhann F, Bonder MJ, Vich Vila A, Fu J, Mujagic Z, Vork L, et al. Proton pump inhibitors affect the gut microbiome. Gut. 2016;65(5):740.
Disclosure: Nothing to disclose

P1982 RISK FACTORS FOR EROSIVE TOOTH WEAR IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE (GORD) SYMPTOMS: A PROSPECTIVE CROSS-SECTIONAL CASE CONTROL STUDY

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Introduction: The most common oral manifestations of patients with GORD symptoms is erosive toot wear (ETW). It is not clear why a group of patients with GORD symptoms develop ETW whereas others don't. The aim of this study is to assess the risk factors associated with developing ETW in patients with GORD symptoms, and to identify the predictive factors for ETW.
Aims & Methods: Consecutive patients referred for assessment of GORD to the Oesophageal Laboratory at Guy's Hospital were recruited (REC Ref 18/NE/0099). After consenting, validated self-reported Reflux Symptom Questionnaire 7-day recall (RESQ-7) was used to assess the frequency and intensity of GORD symptoms. Patients underwent 24hr impedance-pH reflux monitoring; acid exposure times, Symptoms index (SI) and symptoms association probability (SAP) were reported.

A clinical assessment of ETW was done using Basic Erosive Tooth Wear Examination (BEWE) protocol; a validated index in which the mouth is divided into 6 areas each scored from 0 to 3 (0= no ETW, 1= initial loss of surface texture, 2= loss of hard tissue < 50% of surface area and 3= loss of hard tissue ≥ 50% of surface area). Those with a cumulative score of ≥12 and at least 1 oral area scoring 3 were included in the ETW group (ETW) and the rest were included in the NETW group (No ETW).
Data were analysed using STATA software, mean (SD), t-test analysis and ROC curve analysis were applied. P< 0.05 was considered significant.
Results: 121 patients were recruited: ETW (n=64), NETW (n=57). Patients reported a range of 9 symptoms more commonly: heartburn, chest pain, regurgitation, cough, hoarseness, acid taste, throat burning, belching and epigastric pain. (mean±SD) of intensity and frequency of individual symptoms of heartburn, hoarseness and coughing were significantly higher in ETW group:
Heartburn intensity (ETW: 12.7±0.9 vs NETW: 9.7±0.9; P= 0.03), frequency (ETW: 14.3 ±1.0 vs NETW: 10.3 ±1.0; P= 0.007). Hoarseness intensity (ETW: 2.25±0.2 vs NETW: 1.32 ±0.2; P= 0.004), frequency (ETW: 2.8 ±0.2 vs NETW: 1.5±0.2; P= 0.0004). Coughing intensity (ETW: 3.0 ±0.2 vs NETW: 1.6± 0.2; P= 0.004, frequency (ETW: 3.5 ±0.2 vs NETW: 1.98 ±0.2; P= 0.0001).
ROC curve analysis, considering all symptoms on RESQ-7, showed that patients with total frequency of >25 (54.01% were correctly classified with a specificity of 30.88% and sensitivity of 76.8%) and/or total intensity of >36 (61.36% were correctly classified with a specificity of 81.5% and sensitivity of 41.8%) are more likely to develop ETW amongst GORD patients.
119/121 patients completed impedance-pH testing, total acid exposure time was significantly higher in ETW (1.48± 0.06) patients vs NETW (1.28±0.06); P=0.02. However, there was no significant difference between the two groups when upright and/or supine acid exposure time was considered individually.
Conclusion: This study demonstrates that there are three predictive values of developing ETW in GORD patients:
1) Heartburn, hoarseness and coughing as opposed to other reflux symptoms. Hoarseness and cough may indicate progression of reflux to proximal oesophagus and oral cavity.
2) Abnormal total acid exposure time, regardless of the body position or diurnal changes, on reflux monitoring.
3) Total frequency >25 and/or intensity >36 of all symptoms on RESQ-7; although not yielding in high accuracy.
Disclosure: Nothing to disclose

P1983 THE NATURAL HISTORY OF LOW-GRADE DYSPLASIA IN PATIENTS WITH BARRETT'S OESOPHAGUS: A TERTIARY CENTRE EXPERIENCE

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Introduction: Barrett's Oesophagus (BE) is associated with increased risk of oesophageal cancer (EAC). The optimal management of low-grade dysplasia (LGD) arising in BE remains controversial. We performed a retrospective study from a tertiary referral centre for BE neoplasia, to estimate time to progression in patients with confirmed LGD compared to down-staged LGD.
Aims & Methods: We carried out retrospective analysis of tertiary BE LGD referrals in a single tertiary centre (July '06-October '18). Patients underwent high definition white light endoscopy with chromoendoscopy with targeted and Seattle protocol biopsies following referral. All biopsies were reviewed by at least two expert pathologists. We carried out analysis in ablation naïve patients with at least one follow-up endoscopy post index procedure. The primary end point was time to progression to high grade dysplasia (HGD)/EAC.
Results: 141 LGD patients were included.13 were diagnosed during surveillance at our centre. 128 were tertiary referrals. 43/128(34%) were upstaged at index endoscopy after referral to HGD/intramucosal adenocarcinoma

(IMC). 12 were upstaged to IMC, all had endoscopic mucosal resections at index.

44/128(34%) were down-staged, 28/128(34%) to non-dysplastic Barrett's oesophagus (NDBO), 15/128(12%) to indefinite for dysplasia (IND), one had no BE on index endoscopy. In the NDBO/IND group, 34 had no ablations and at least one follow-up endoscopy during surveillance at our centre, 5/34(15%) progressed to HGD/IMC over a median time of 36 months (IQR,13-42).

41/128(32%) of all referrals had confirmed LGD at index endoscopy. There was 54/141(38%) confirmed "true" LGD including patients diagnosed under our surveillance programme. In this cohort 34 had no ablations and at least one follow-up endoscopy during follow-up surveillance. 10/34(32%) progressed to HGD/IMC over a median time of 10 months (IQR,4-16). The remainder of this cohort had a median follow up of 27 months (IQR,14-45), and average number of 2 follow-up endoscopies with biopsies.

	'True' LGD (n=34)	IND (n=13) (Downstaged cohort)	NDBO (n=21) (Downstaged cohort)
Mean age, years	66	71	69
Male sex	30/34 (88%)	12/13 (92%)	16/21 (76%)
Medan progression time to HGD/IMC (months)	10 (IQR, 4-16)	19 (IQR, 11-28)	42 (IQR, 28-72)
Median months of follow-up	17 (IQR, 6-39)	31 (IQR, 15-46)	17 (IQR, 6-31)

[Analysis of ablation treatment naive patients]

Conclusion: Our data shows the variability in the diagnosis of LGD from referring centres, with 32% of referrals with confirmed LGD. The cumulative incidence of progression to HGD/IMC and time to progression varied across subgroups. Confirmed LGD had a shorter progression time compared to the down-staged group (NDBO/IND). It is important to differentiate these subgroups so that decisions on surveillance/endotherapy can be more personalised and resources utilised more wisely.
Disclosure: Nothing to disclose

P1984 THE UTILITY OF A METHYLATION PANEL IN THE ASSESSMENT OF CLINICAL RESPONSE TO THE RADIOFREQUENCY ABLATION FOR BARRETT'S OESOPHAGUS

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Introduction: Barrett's oesophagus (BE) is the main risk factor for oesophageal adenocarcinoma (OAC). The presence of dysplasia significantly increases the risk of BE malignant progression, hence, endoscopic treatment such as radiofrequency ablation (RFA) is recommended in those cases. After RFA, random 4-quadrant biopsies at the gastro-oesophageal junction (GOJ) are taken to detect residual disease. It is debatable whether intestinal metaplasia (IM) at the GOJ is a reliable marker of residual disease since it is subjective and patchy in nature. We have previously shown that methylation panel is accurate in identifying IM within the oesophageal tissue[1].
Aims & Methods: In this single-centre, retrospective study we aimed to investigate whether a methylation panel in GOJ biopsies could be used to stratify patients after RFA. We analysed paraffin-embedded 4-quadrant BE and GOJ biopsies from adult patients with BE who underwent RFA, achieved remission, and had at least 2 follow-up endoscopies with biopsies taken at the GOJ. Biopsy sets from each treatment time-point (pre-RFA, 1st and 2nd follow-up) were included. The extent of IM was classified using a dedicated 4-tier histological score (IM-Score) and immunochemistry score using trefoil factor-3 staining (TFF3-score). The IM-Score was based on number of glands with goblet cells (1, 2-5 or >5 glands) and number of biopsies with IM (0=no IM, 1=focal, 2=moderate

and 3=extensive) and a total score of 0-1 was regarded as 'focal IM' and 2-3 as 'diffuse IM'. TFF-3 was scored as positive in the presence of intense cytoplasmic staining. Promoter methylation at 3 genes (ZNF345, TFP12, ZNF569) was assessed by Methylight and a mean value was generated (Meth-Score). Methylation levels were compared using one-way ANOVA and Wilcoxon test, where appropriate. The accuracy of methylation panel in predicting diffuse IM after RFA treatment was assessed by calculating the area under the receiver operating characteristic curve (AUC). The correlation between Meth-score and IM-Score / TFF3 was assessed using Spearman's method.
Results: We included 45 patients, who achieved endoscopic remission after RFA. The pre-RFA grades included: non-dysplastic BE (NDBE; 24.4%), low-grade dysplasia (LGD; 31.1%), and high-grade dysplasia/intramucosal carcinoma (HGD/IMC; 44.4%). Overall, the methylation levels correlated with the degree of dysplasia, with a Meth-Score of 40.5%, 63.0% and 80.6% in NDBE, LGD, HGD/IMC, respectively (P<0.001). One-hundred-and-five GOJ biopsy sets (post-RFA) were analysed, of which 87 (82.9%) had focal IM, and 18 (17.1%) had wide-spread IM, with corresponding mean methylation levels of 2.4% and 35.5%, respectively (P=.018). The accuracy of methylation panel in predicting wide-spread IM at the GOJ was high (AUC 91.6%, 95%CI 87.0%-96.2%). Within the GOJ biopsy sets we found a significant correlation between methylation levels and amount of IM, measured both with IM-Score (rho=66.0%, P<0.001) and TFF3 positivity (rho=75.6%, P<0.001).
Conclusion: The methylation panel can differentiate grades of dysplasia in Barrett's and significantly correlates with the extent of IM at the GOJ. We propose the Meth-Score as an objective measure of residual and recurrent disease following RFA.
References: 1) Chettouh H, Mowforth O, Galeano-Dalmau N, et al. Methylation panel is a diagnostic biomarker for Barrett's oesophagus in endoscopic biopsies and non-endoscopic cytology specimens. Gut. 2018;67:1942-1949.
Disclosure: Nothing to disclose

P1985 RISK FACTORS FOR PROGRESSION OF CONFIRMED LOW GRADE DYSPLASIA IN A BARRETT'S TERTIARY REFERRAL CENTRE

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Introduction: Barrett's Oesophagus (BE) is associated with an increased risk of oesophageal cancer (EAC). The optimal management of patient's with low-grade dysplasia (LGD) arising in BE remains controversial. In the past 3 years there is a shift toward offering endoscopic eradication therapy to avoid cancer progression. We performed a retrospective study from a tertiary referral centre for BE neoplasia, our aim was to look at risk factors for progression of 'true' low grade dysplasia (LGD confirmed at endoscopy by two expert Barrett's histopathologists).
Aims & Methods: We carried out a retrospective analysis of all confirmed LGD BE in a single tertiary centre (July 2006-October 2018) and assessed risk factors which may affect rates of progression. Extent was defined as unifocal (One endoscopic level of LGD) or multifocal (>1 endoscopic level of LGD in BE segment). All patients underwent high definition white light endoscopy with chromoendoscopy with targeted and Seattle protocol biopsies following referral. All biopsies were reviewed by at least two expert pathologists. The primary end point was time to progression to high grade dysplasia (HGD)/EAC.
Results: A total of 54 patients had confirmed low grade dysplasia following index endoscopy, 34 patients (30m, 4f) were ablation treatment naïve and had at least one follow-up endoscopy. The average age of this cohort was 66 . Patients had an average of 2 (IQR,1-3) follow-up endoscopies with biopsies following index endoscopy at our centre. Their median follow-up time was 22 months (IQR,8-39).
16/34 (47%) patients had multifocal low-grade dysplasia. 8(50%) of these patients progressed to HGD/EAC over a median time of 14 months (IQR,6-19). 2/18 (11%) patients with unifocal low grade dysplasia progressed to HGD/EAC over a median time of 2 months (IQR, 2-3). There was significant difference in numbers that progressed between both groups (P < 0.05).

6/34 (18%) patients had nodularity in Barrett's at baseline. 4/6 (67%) of these patients progressed to HGD/EAC over a median time of 8 months (IQR, 3-14). Most of these patients (75%) had an endoscopic mucosal resection for staging. 6/28 (21%) patients with no nodularity progressed to HGD/EAC over a median time of 11 months (IQR,5-21). There was a significant difference in the numbers that progressed between the two cohorts (P < 0.005).

5/34 (15%) patients had a short segment of Barrett's (< 3cm). 1/5 (20%) of these patients progressed to EAC after one month. 9/29 (31%) patients with a long segment of BE (≥ 3cm) progressed to HGD/EAC over a median follow up time of 13 months (IQR, 4-17).

	Unifocal LGD	Multifocal LGD	Short BE segment	Long BE segment	Nodularity	No nodularity	Male	Female
Number progressed to HGD/EAC (%)	2/18 (11%)	8/16 (50%)	1/5 (20%)	9/29 (31%)	4/6 (67%)	6/28 (21%)	9/30 (30%)	1/4 (25%)
P- value	P < 0.05		P = 0.6		P < 0.05		P = 0.8	

[Analysis of radio frequency ablation naive patients]

Conclusion: LGD in BE can be difficult to accurately diagnose pathologically and therefore management can often be variable. Robust prognostic markers are needed to differentiate those patients that need surveillance or endotherapy. Multifocal LGD and nodularity were associated with a significant risk of progression to HGD/EAC. The presence of a longer segment of BE was associated with a higher progression risk.
There is an argument that the treatment of LGD with endotherapy should be indivualised given the possible risks associated. Identifying key risk factors of progression will tailor treatment in a specific, higher risk cohort.
Disclosure: Nothing to disclose

P1986 COLUMNAR EPITHELIUM MORPHOLOGY AFTER ESOPHAGECTOMY: CLINICAL INSIGHT INTO THE DEVELOPMENT OF BARRETT'S ESOPHAGUS

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Introduction: The mechanism of development of Barrett's esophagus (BE) has been investigated in animal experiments; however, clinical studies are rare. Acid reflux is considered to play a major role in the development of BE, but there is little evidence to prove this. Given that changes in columnar epithelium due to acid reflux are used as a surrogate marker of BE, we investigated the link between the development of BE and acid reflux.
Aims & Methods: This retrospective study involved 158 patients who underwent esophagectomy in a single institution between 2004 and 2018. Patients without detailed data such as operative method, patients without an intact stomach, and patients without endoscopic follow-up were excluded. Patients were divided into two groups. The first group comprised 106 patients who had undergone esophagectomy and gastric pull-up reconstruction (St), while the second group comprised 52 patients who had undergone esophagectomy and ileocolic interposition (Ic). The incidence of BE, the interval between surgery and the development of BE, and the severity of BE and reflux esophagitis were analyzed. BE was defined as an endoscopic columnar epithelium extending to the oral side from the site of anastomosis. Scheduled endoscopic examination was performed as follow-up once or twice a year.
Results: Clinical characteristics were as follows: mean age 64.7 years in St, 61.3 years in Ic (p=0.017); male patients 95 (90%) and 43 (83%), respectively (p=0.31); mean follow-up period 67.6 and 51.3 months, respectively (p=0.013); and mean number of endoscopic examinations 8.8 and 7.7, respectively (p=0.17). Occurrence of BE was seen in 47 cases (44.3%) and 1 case (1.9%), respectively (p< 0.01). Reflux was observed in 68 cases and 1 case, respectively (p< 0.01). The median interval to development of BE was 524 (168-3002) days. The mean length of BE was 11.7 mm. Univariate and multiple logistic analysis revealed that the method of reconstructive surgery (odds ratio 22.6) and reflux (odds ratio 4.91) were independent risk factors. There was no incidence of Barrett's adenocarcinoma during follow-up.

Conclusion: The development of BE is closely linked to reflux, including gastric acid reflux, and is rarely observed in ileocolic interposition.
Disclosure: Nothing to disclose

P1987 DIAGNOSTIC YIELD OF SEATTLE PROTOCOL AND TARGETED BIOPSY – COMPARATIVE STUDY IN BARRETT'S ESOPHAGUS SURVEILLANCE

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Introduction: Endoscopic surveillance in Barrett's Esophagus (BE) is recommended according to the Seattle protocol (SP) with random 4-quadrant biopsy specimens obtained every 1-2 cm to detect dysplasia, complemented with targeted biopsies (TB) of suspicious lesions.
Narrow-Band Imaging (NBI) has the potential to increase diagnostic acuity, although it is not routinely recommended. The main limitations of SP are sampling error and costs associated with histology.
Aims & Methods: The main aim was compare diagnostic yield (DY), defined by dysplasia in the histology, of SP with TB alone.
Cross-sectional study, which consecutively included patients undergoing BE surveillance between 2015 and 2018. Exams were executed with high resolution scopes under white light (WL) or NBI according to endoscopist's preference and experience. Surveillance of BE was made according to SP in all patients. TB were performed if suspected focal lesions were identified.
Results: A total of 127 surveillance exams referring to 94 patients were included. Mean age was 60±15 years and most patients were male (74.5%). WL evaluation was complemented with NBI in 40.2% (n=51). Random biopsies were performed in 112 (88.2%) and targeted biopsies in 15 (11.8%). DY of SP was very low (2.7%, n=3) and dysplasia was confirmed in a subsequent examination in only 1 case (0.9%). TB demonstrated a significantly higher DY (40%; n=6) (p < 0.001). Considering only patients in whom WL evaluation was complemented with NBI, SP maintained a significantly lower DY (SP-2.6%, TB-41.70%, p=0.002). There was a significant association between TB surveillance and dysplasia identification in histology, both in WL (p < 0.001) and NBI assessment (p = 0.002).
Conclusion: Targeted biopsies had a significantly higher diagnostic yield, either under WL or with NBI, compared to Seattle Protocol.
Disclosure: Nothing to disclose

P1988 BARRETT'S OESOPHAGUS SURVEILLANCE AT A LARGE UNIVERSITY HOSPITAL IN THE UNITED KINGDOM

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Introduction: Barrett's oesophagus represents the most important risk factor for the development of oesophageal cancer. According to NICE, surveillance should be considered for Barrett's diagnosed endoscopically and on biopsy[1]. British Society of Gastroenterology (BSG) guidelines recommend Barrett's surveillance to be performed at specific prescribed intervals dependent upon the length and histology[2]. Additionally, the BSG has proposed the use of a Minimum Endoscopic Dataset (MED) for reporting endoscopic findings[2].
Aims & Methods: The main aims of this service improvement project were to:
1. Evaluate whether Barrett's surveillance is being conducted within recommended levels of tolerance at our hospital.
2. Assess the standard of our endoscopy reporting in comparison to the BSG MED.
A total of 137 Barrett's cases diagnosed endoscopically at Queen Elizabeth Hospital Birmingham (QEHB) between 2015 and 2018 were identified. The QEHB serves as the primary teaching hospital for the University of Birmingham and is one of the largest single-site NHS hospitals in the UK.
Patients found to have Barrett's with dysplasia were excluded from surveillance. In addition, patients who were subsequently diagnosed with

oesophageal cancer (as identified from the Somerset Cancer Registry) were excluded. Adherence of the endoscopy report findings to the criteria outlined in the BSG MED was assessed including documentation of the Prague endoscopic classification and concordance with Seattle protocols for biopsy.

Results: Of the 137 Barrett's cases, 50 (36%) were excluded from the surveillance programme. As shown in Table 1, these included 23 patients with dysplasia and a single patient with subsequent oesophageal cancer diagnosed on biopsy. 57 of the remaining 87 patients (66%) were identified to be overdue for surveillance. Of these 57 cases, 11 (19%) had the Prague classification documented, while 2 (4%) had biopsies taken.

Total no. of Barrett's cases:	137	Proportion of cases
No. excluded:	50/137	36%
-Dysplasia	23/50	46%
-Subsequent diagnosis of oesophageal cancer	1/50	2%
-Previous diagnosis of oesophageal cancer (i.e. under cancer surveillance)	2/50	4%
-Endoscopy report unavailable	11/50	22%
-Other (e.g. failed endoscopy or inconclusive Barrett's)	13/50	26%
No. eligible for surveillance:	87/137	64%
No. with surveillance overdue:	57/87	66%
-Prague classification	11/57	19%
-Biopsies	2/57	4%

[Table 1: Breakdown of Barrett's cases diagnosed at QEHB in 2015-18]

It is clear that a significant proportion of Barrett's patients at our hospital are overdue their surveillance endoscopy outside of tolerance. Furthermore, most of them have neither been properly reported nor sampled according to BSG standards at their last endoscopy. The latest National Oesophago-cancer Gastric Audit reported a decreased number of Barrett's patients diagnosed with dysplasia in 2012-17 in the West Midlands (in contrast to the rest of the UK)[3]. Our results suggest that poor Barrett's surveillance at our hospital in recent years could have at least partially contributed to this decline.

Conclusion: An unacceptable number of Barrett's patients at our hospital are overdue their surveillance as per BSG guidelines. Efforts to implement a co-ordinated surveillance programme and improve our standard of endoscopy reporting are now underway. Barrett's patients identified to have surveillance overdue have been entered into a prospective database for prioritised follow-up in order to bring our Barrett's surveillance service back to tolerance.

References: 1. Gastro-oesophageal reflux disease and dyspepsia in adults: investigation and management. NICE Clinical Guideline 2014 [CG184] 2. British Society of Gastroenterology guidelines on the diagnosis and management of Barrett's oesophagus. Fitzgerald RC, di Pietro M, Ragunath K, et al. Gut 2014;63:7-42 3. National Oesophago-cancer Gastric Audit - Annual Report 2017

Disclosure: Nothing to disclose

P1989 NARROW BAND IMAGING IN SCREENING OF BARRETT'S ESOPHAGUS IN GASTROESOPHAGEAL REFLUX DISEASE PATIENTS

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Introduction: Seattle protocol described as targeted and random four-quadrant biopsies every 2 cm has long been considered as the gold standard of screening and surveillance of Barrett's esophagus (BE) to minimize sampling error (1), however its difficulty limits its applicability in practice specially as a screening tool for BE among specific populations. With the rising need to do selective screening in gastroesophageal reflux disease (GERD) patients with certain risk factors other protocols as Narrow band imaging (NBI) guided biopsy need to be investigated.

Aims & Methods: To validate the utility of NBI guided biopsy as a screening protocol for BE among certain GERD patients compared to Seattle protocol. Endoscopy and biopsy taking was done in 2 different sessions 2 weeks apart to allow mucosa to heal for 100 patients in Alexandria, Egypt. In the first session Seattle protocol was applied and in the second session NBI guided biopsy was done. Patients had at least one of the following: Chronic Gastroesophageal reflux disease (more than 5 years), frequent Gastroesophageal reflux disease (more than once weekly), two or more of the following risk factors for Barrett's esophagus: Old age >50 years, central obesity (waist circumference >102 cm in males and >88 cm in females), current or past history of smoking and family history of BE or esophageal adenocarcinoma (EAC) and family history of BE or EAC (2). All patients with known Barrett's esophagus were excluded. Suspicious lesions were defined as follows: in Seattle protocol mucosal irregularities (e.g. nodules/ulcers) (3), in NBI suspicious lesions were defined as per Barrett International NBI Group (BING) classification as any lesion with irregular/absent mucosal pattern and/or any lesion with irregular vascular pattern (focally or diffusely distributed vessels not following normal architecture of the mucosa) (4).

Results: Considering the overall worst diagnosis by histopathology as the true diagnosis, Of the 100 consecutive GERD patients, 17 patients had Barrett's esophagus either by one of the two techniques or by both, 35.3% by both methods, 41.2% by narrow band imaging alone and 23.5% by Seattle protocol alone (p< 0.001, κ= 0.461). Sensitivity, specificity, negative predictive value and positive predictive value for Seattle protocol were 58.8%, 100%, 92.2%, 100% vs 76.5%, 100%, 95.4%, 100% respectively for narrow band imaging. A mean of 7.73 samples/patient were taken in Seattle protocol vs 3.42 samples in narrow band imaging (p< 0.001). A mean of 8.63 minutes was consumed in Seattle protocol vs 2.65 minutes in narrow band imaging (p< 0.001). No statistically significant difference in the detection rate of dysplasia between the two techniques was found.

Conclusion: Though this study has some limitations due to the relatively small number of patients beside the lack of magnifying NBI which leaded to some difficulty in detection of abnormal vascular pattern, this study indicates that NBI guided biopsy might be a valid alternative to Seattle protocol and further multicentric larger studies are needed.

References: 1. Gould JC, Wendling MR, Oeschlager BK, Mittal SK, Komanduri S, Perry KA, et al. Advances in the Diagnosis and Treatment of Barrett's Esophagus and Early Esophageal Cancer; Summary of the Kelly and Carlos Pellegrini SSAT/SAGES Luncheon Symposium. J Gastrointest Surg. 2017;21(8):1342-9. 2. Shaheen NJ, Falk GW, Iyer PG, Gerson LB. ACG Clinical Guideline: Diagnosis and Management of Barrett's Esophagus. Am J Gastroenterol. 2016;111(1):30-50; quiz 1. 3. Wolfsen HC, Crook JE, Krishna M, Achem SR, Devault KR, Bouras EP, et al. Prospective, controlled tandem endoscopy study of narrow band imaging for dysplasia detection in Barrett's Esophagus. Gastroenterology. 2008;135(1):24-31. 4. Sharma P, Bergman JJ, Goda K, Kato M, Messmann H, Alsop BR, et al. Development and Validation of a Classification System to Identify High-Grade Dysplasia and Esophageal Adenocarcinoma in Barrett's Esophagus Using Narrow-Band Imaging. Gastroenterology. 2016;150(3):591-8

Disclosure: Nothing to disclose

P1990 AN AUTOMATED, QUANTITATIVE MULTIPLEX IMMUNOFLUORESCENCE ASSAY ACCURATELY RISK STRATIFIES BARRETT'S ESOPHAGUS PATIENTS WITH A COMMUNITY-BASED DIAGNOSIS OF LOW-GRADE DYSPLASIA AT A RATE COMPARABLE TO EXPERT PATHOLOGISTS

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Introduction: Low-grade dysplasia (LGD) in Barrett's esophagus (BE), is the strongest predictor of malignant progression, yet an accurate histological diagnosis of LGD is challenging. The majority of community-based LGD diagnoses are down-staged to non-dysplastic (ND)BE when reviewed by an expert pathologist, whereas patients in whom the diagnosis of LGD is confirmed have a 10% annual risk of progression to high-grade dysplasia (HGD) or cancer (Ca), justifying the consideration of prophylactic endoscopic ablation. Although guidelines recommend expert pathologist review of all LGD cases, expert review is poorly defined, prone to observer

variation, and not widely available. Recent studies suggest that an automated, quantitative multiplex immunofluorescence assay may identify NDBE patients with an increased risk of malignant progression. We investigated if this assay also allows objective risk stratification for cases with a community-based diagnosis of LGD at a rate comparable to expert pathologists.

Aims & Methods: A blinded nested case-control cohort was derived from the screening cohort of the SURF-study, a randomized controlled trial of SUrveillance vs. RadioFrequency ablation for BE patients with LGD. 60 patients with a community-based diagnosis of LGD of whom 30 progressed to HGD/EAC (progressors) and 30 patients who did not progress (non-progressors) were matched for age, sex and maximal BE length. All random biopsy levels of the baseline endoscopy and subsequent endoscopies were independently reviewed by 3 expert pathologists with an international reputation. All levels of the baseline endoscopy were additionally tested by a multiplex biomarker assay (TissueCypher Barrett's Esophagus Assay, Cernostics). The assay integrates quantitative biomarker and morphology scores extracted from whole slide images of multiplex immunofluorescence-labeled standard formalin-fixed paraffin-embedded biopsies to classify patients as low-risk (LR), intermediate-risk (IR) and high-risk for progression to HGD/EAC within 5 years. A histological revision diagnosis of NDBE was considered as low- (LR), while indefinite for dysplasia (IND) and LGD were considered as high-risk (HR) for progression.

Results: 60 BE patients (52 male), mean age 63±9 years, were studied. Clinical characteristics were similar between progressors and non-progressors. Median time between baseline endoscopy and progression was 2.5 years (1.3-5.4). Accuracy, sensitivity and specificity of the biomarker assay vs. the 3 expert pathologists were 73% vs 72-77%, 66% vs 77-80% and 80% vs 63-77%, respectively. 20/26 (78%) patients classified as IR/HR by the biomarker panel and 69-77% classified as HR (IND/LGD) by the 3 expert pathologists progressed to HGD/EAC.

Conclusion: A quantitative multiplex immunofluorescence assay risk stratified BE patients with a community-based diagnosis of LGD with an accuracy comparable to three renowned expert pathologists. The assay allows for automated, objective risk stratification which may be a practical and effective solution to the lack of standardization of expert pathology review of LGD as advocated by all guidelines.

Disclosure: R.J. Critchley-Thorne and E.A. Bossart have ownership interest (stock or stock options) in, and are salaried employees at Cernostics, Inc. Y. Zhang is a paid consultant to Cernostics, Inc.

P1991 SAFETY AND EFFICACY OF MULTI-BAND MUCOSECTOMY FOR VISIBLE LESIONS IN BARRETT'S ESOPHAGUS: A SYSTEMATIC REVIEW WITH POOLED ANALYSIS

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Introduction: The incidence of esophageal adenocarcinoma (EAC) has been increasing over the past decades. Current consensus states that all visible lesions in the context of Barrett's Esophagus (BE) should be endoscopically resected due to the high likelihood of containing significant pathology. Conversely, extensive resection aiming for metaplasia eradication should not be preferred over ablation strategies given the higher risk of subsequent stricturing. Current methods of mucosal resection include the cap-assisted technique and more recently multi-band mucosectomy (MBM). Since its first description, several prospective and retrospective series have been published, but data on efficacy and safety of MBM has yet to be systematically reviewed.

Aims & Methods: We performed a systematic review with pooled-analysis to evaluate the efficacy and safety of MBM in patients with BE. Electronic databases (Medline, Scopus, EMBASE) were searched up to March 2019. Studies including patients with BE who underwent MBM were eligible. The primary outcome was the rate of adverse events such as intra- and

post- procedural bleeding, perforation and stricture. Of note, we developed subgroup meta-analytic models selecting a priori variables which could affect the outcomes, such as the indication for performing MBM (focal lesion resection vs metaplasia eradication). Secondary outcomes were focused on MBM performed for resecting visible lesions. The rates of complete resections and R0 resections were assessed. The endoscopic resection was considered macroscopically complete if the visible lesion was entirely removed. The absence of neoplastic invasion at deep and lateral margins of the resected specimens was considered as an R0 resection for lesions resected in an en-bloc fashion. In cases of piecemeal resections, R0 at the deep margin of all resected specimens derived from a single lesion was required. Primary and secondary outcomes were assessed by pooling data by means of a random- or fixed-effect model according to the degree of heterogeneity to obtain a proportion with a 95% confidence interval (CI).

Results: Thirteen studies were eligible for inclusion, providing data on 1334 procedures performed in 986 patients; 839 out of 1334 procedures were performed in order to resect focal lesions on BE. Ten studies were performed in Europe and 3 in North America. All studies but 3 had a retrospective design. According to data reported by 6 studies, there was a mean number of 4.2±1.6 specimens per procedure. Considering the histological findings, 52.2% of the lesions were adenocarcinomas and 31.3% were HGD. The overall adverse event rate was 5.3%(I²:83.4%). Immediate and post-procedural bleeding occurred in 0.2% (I²:0%) and 0.7% (I²:0%) of procedures, respectively. Moreover, perforations and strictures were reported in 0.3% (I²:0%) and 3.9% (I²: 80.4%) of procedures, respectively.

The sensitivity analysis focused on focal lesion resection (8 studies, 584 procedures) reported an overall adverse event rate of 5.5% (I²=0%), with rates of bleeding, perforation and stricture of 1.6%, 1.0% and 3.3%, respectively. Focal lesions were resected at a complete rate of 97.6%(I2: 49.9%) with an R0 resection rate of 94.1% (I2 81.7%).

Conclusion: Our results confirm MBM as a safe and effective technique to treat visible lesions in patients with Barrett's esophagus. Further studies with longer follow-up periods are still necessary to provide definitive reassurance in terms of long term efficacy.

Disclosure: Nothing to disclose

P1992 THE RISK OF PREVALENT AND INCIDENT NEOPLASIA IN PATIENTS WITH A DIAGNOSIS OF BARRETT'S ESOPHAGUS INDEFINITE FOR DYSPLASIA

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Introduction: Barrett's esophagus (BE) is a well-established precursor condition to esophageal adenocarcinoma and the presence of dysplasia is the main risk factor for malignant progression. The BE with indefinite for dysplasia (BE-IND) diagnosis is used when the significance of epithelial abnormalities is uncertain due to inflammation or technical artifact. The natural behaviour of BE-IND is poorly understood.

Aims & Methods: In this retrospective, single-center study we aimed to characterize the risk of prevalent and incident neoplasia in patients with BE-IND. We reviewed the BE research database to identify patients diagnosed with BE-IND. We excluded patients under 18 years old, with a follow-up of less than 1 year, with a previous diagnosis of definitive dysplasia, and previous endoscopic therapy. Times and rates of progression to neoplasia were calculated and categorized as prevalent neoplasia when the progression occurred within 1 year of follow-up (FU), and incident neoplasia, for progression after >1 year FU. A multivariable regression model adjusted for age, sex, length of BE segment, the extent of IND (focal vs multifocal) and baseline IND diagnosis was used to identify risk factors for both prevalent and incident neoplasia.

Results: In total, 345 patients with ≥1 diagnosis of BE-IND were identified between 1999 and 2018, of which 147 (42.6%) were excluded, and the remaining 198 (57.4%) were analyzed. Hundred-fifty-one patients (76.3%) showed regression to a non-dysplastic epithelium at the first follow-up biopsies and 19 patients (9.6%) had prevalent dysplasia of any grade including 17 low-grade dysplasia (LGD) and two cases of advanced neoplasia (1.0%): 1 high-grade dysplasia (HGD) and 1 intramucosal cancer (IMC). Twenty-eight patients (14.1%) had incident dysplasia progressing to LGD (21), HGD (5), and IMC (2) after a median FU of 32.8 months (range 12.3 - 124.5), yielding an incidence rate of dysplasia (any grade) and advanced neoplasia (HGD/IMC) of 3.9 and 1.3 cases per 100 patient-years, respectively. The length of BE segment was associated with the increased risk of prevalent dysplasia (odds ratio 1.14; 95%CI 1.00-1.30, P=.046), however not incident dysplasia, for which none of the analyzed risk factors were found predictive.

Conclusion: Patients with BE-IND, especially with a long segment of BE, should be closely monitored as nearly 10% harbor prevalent dysplasia. A significant proportion of patients with BE-IND will progress to more advanced stages and molecular biomarkers are required for stratification, as clinical criteria to predict patients at high-risk for progression are lacking.

Disclosure: Nothing to disclose

P1993 ENDOSCOPIC SUBMUCOSAL DISSECTION FOR RESECTION OF T1B N0 ESOPHAGEAL CANCER: RETROSPECTIVE MULTICENTER STUDY

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Introduction: While esophagectomy is the standard treatment for submucosal (T1b) esophageal adenocarcinoma (EAC) and squamous cell cancer (SCC), many elderly patients -the age group that esophageal cancer tends to affect- are not candidates for surgery.

Endoscopic submucosal dissection (ESD) is a minimally invasive procedure that allows for en-bloc resection of early esophageal cancer and allows for precise histopathologic staging of the tumor. ESD could be curative in submucosal cancer without lymph node metastasis, and it allows for precise histopathologic staging.

Aims & Methods: We aimed to evaluate the long-term outcomes of ESD in patients with EUS-staged T1b esophageal cancer.

A retrospective multicenter study was performed at three academic hospitals in the U.S. Patients who underwent ESD with a pre-procedural or post-procedural histopathologic diagnosis of T1b N0 M0 EAC or SCC were included in the study. Data was collected on demographics, tumor and procedure characteristics, procedure pathology, and follow-up. Local recurrence was confirmed by endoscopic findings and pathological analysis. Metastasis was confirmed by cross-sectional imaging.

The main outcome was a composite of rate of metastasis and local recurrence. Follow-up time was defined as months from initial procedure to recurrence or last follow-up visit if recurrence-free. A time-to-event analysis was performed to evaluate recurrence. A Cox proportional hazard ratio regression analysis was performed to identify predictors of recurrence.

Results: Thirty-seven patients underwent ESD (mean age 70 years +/-9; 25 males; median tumor size 25 mm). Based on available comorbidity data, 42% patients were not fit for surgery, as determined by an age-adjusted Charlson Comorbidity Index > 6. En bloc and R0 rates were 73% and 52%, respectively. Twenty tumors (54%) were found to be HGD or T1a on post-ESD specimen analysis, while one was staged as T2. Immediately after ESD, 4 patients were referred for surgery, 2 underwent chemoradiation therapy, and 4 radiation alone. Patients were followed for a median of 9 months, and the calculated 12- and 48-month recurrence rate was 13% and 30%, respectively. Not achieving en bloc resection was identified as a predictor for recurrence.

Conclusion: This multicenter trial showed that ESD for T1b esophageal cancer can be acceptable for patients who deemed not surgical candidates. However, close follow up is necessary. ESD can also serve as a staging procedure, as our data confirms inaccurate EUS-staging of T1b cancer, with 54% of tumors being down-staged to T1a, as has been previously reported.

Disclosure: Nothing to disclose

P1994 REASONS FOR LONG TIME TO REFERRAL FROM PRIMARY CARE FOR OESOPHAGEAL AND GASTRIC CANCER PATIENTS IN THE NETHERLANDS

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Introduction: In gatekeeper healthcare systems, an efficient diagnostic process in primary care is pivotal for reducing cancer related disease burden.

Aims & Methods: This study aims to explore reasons for long time to referral for upper gastrointestinal (GI) cancer patients in Dutch primary care.

A retrospective cohort study, using anonymized free text primary care records of 6 routine primary care databases in the Netherlands. Patients diagnosed with oesophageal- or gastric cancer (2010-2015), who symptomatically presented in primary care, were included. Based on manual free text exploration, time from presentation to referral in primary care was determined. Duration was calculated per characteristic (median, IQR). We performed uni- and multivariable log-binomial regression analyses to find associations of patient- and presentation characteristics with relatively "long duration" (≥75th percentile value). Routes to referral of patients with relatively "longest durations" (≥90th percentile value) were explored using thematic free text analyses.

Results: 174 symptomatic oesophageal cancer patients and 138 symptomatic gastric cancer patients were included. Longer median durations and/or univariable association with ≥P75 were found for;
(1) patients without alarm symptoms (both types),
(2) female sex, higher socio-economic status score (SES) and psychiatric comorbidity (oesophageal cancer),
(3) youngest age category (gastric cancer). In multivariable analysis, presentation without alarm symptoms showed a statistically significant association with "long duration" (≥P75) for both cancer types. For oesophageal cancer, high SES was associated with long duration. Thematic exploration of routes to diagnosis for patients with "longest durations" (≥P90) showed one dominating theme: "an initial low clinical suspicion of cancer", and only few preventable factors for long duration.

Conclusion: The main reason for long time to referral of oesophageal and gastric cancer patients is an initial low cancer suspicion. Absence of alarm symptoms is the main contributor to this lower suspicion and therefore, the longer times to referral.

Only few preventable factors for delayed referral could be identified. These findings reflect a well-functioning gatekeeper system, with most to be gained from improving upper GI cancer recognition among those with non-alarm symptoms.

Disclosure: Nothing to disclose

P1995 A PROSPECTIVE STUDY OF SM2 CARCINOMA DIAGNOSIS USING THE EXTENT OF TYPE B2 VESSELS IN THE JAPAN ESOPHAGEAL SOCIETY CLASSIFICATION

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Introduction: Although the Japan Esophageal Society (JES) classification for superficial squamous cell carcinoma has been simplified and is now widely used, the low diagnostic accuracy of invasion depth on the basis of type B2 vessels is a topic of concern. Based on the fact that in pSM2 carcinoma type B2 vessels appear at a similarly high rate to type B3 vessels, and the larger the area they cover, the higher the possibility of invasion,

we have previously reported that the extent of type B2 vessels in cases of pSM2 carcinoma is significantly larger than that in cases of pMM/pSM1 carcinoma, and that the appropriate cut-off value is 7 mm.

Aims & Methods: In the present study, we carried out a prospective study of the accuracy of the diagnosis of invasion depth based on the extent of these type B2 vessels. We examined 99 lesions in 78 patients who underwent endoscopic submucosal dissection in our department between April 2016 and September 2018. The patients were 71 men and 7 women of median age 70 years (range 50-89 years). The main macroscopic tumor type was IIa in 12 cases, IIb in 35, IIc in 47, Is in 4, and III in 1; the main tumor location was the cervical esophagus (Ce) in 4 cases, the upper thoracic esophagus (Ut) in 9, the middle thoracic esophagus (Mt) in 57, the lower thoracic esophagus (Lt) in 27, and the abdominal esophagus (Ae) in 2; the circumferential ratio was < 1/2 the circumference of the esophagus in 61 cases, < 2/3 of the circumference in 13, ≥2/3 of the circumference in 21, and circumferential in 4; and the mean tumor diameter was 20 mm (range 3-100 mm). The region of interest containing the highest concentration of atypical vessels was marked with two points, the invasion depth at this point was diagnosed, and the diagnostic accuracy was investigated. For type B2 vessels in particular, both ends of the largest region were marked, and the distance between these marks was then measured by using biopsy forceps. The largest diameter was also measured under stereoscopic microscopy. In this study, type B2 vessels were defined as irregularly branched vessels corresponding to type 4 vessels in the Arima classification.

Results: The vessels in the region of interest were type B1 in 75 lesions, type B2 in 21, and type B3 in 3. Of the 75 lesions with type B1 vessels, the tumor had invaded to EP or LPM in 69 cases, MM in 4, and SM2 in 2, and the diagnostic accuracy was 92% (69/75). All 3 lesions with type B3 vessels had invaded the submucosa to a depth of ≥200 mm (SM2), and the diagnostic accuracy was 100% (3/3). Both these results were similar to those of previous studies. However, of the 21 lesions with type B2 vessels, 14 had invaded either the MM or the submucosa to a depth of < 200 mm (SM1) and 7 were SM2, and following the conventional procedure the diagnostic accuracy was only 66.7% (14/21). However, when the extent of the vessels was taken into account, 15 lesions had type B2 vessels with an extent of < 7 mm. The invasion depth for these 15 lesions was MM/SM1 in 14 and SM2 in 1, and the diagnostic accuracy was 93% (14/15). The invasion depth of all 6 lesions with type B2 vessels with an extent of ³7 mm was SM2, and the diagnostic accuracy was 100% (6/6). Taking the extent of type B2 vessels into account significantly improved diagnostic accuracy from 68% to 95% (*p* < 0.01).

Conclusion: Although our prospective study involved only a small number of cases, it suggested that the extent of type B2 vessels may be useful for the diagnosis of invasion depth. The designation of irregularly branched vessels as type B2 may also be an important assessment criterion.

Disclosure: Nothing to disclose

P1996 RELATIONSHIP BETWEEN ABDOMINAL FAT DISTRIBUTION AND PROGRESSION OF BARRETT'S ESOPHAGUS TO ADENOCARCINOMA

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Introduction: Obesity was known to be the risk factor of the incidence of Barrett's esophagus (BE) and Barrett's esophageal adenocarcinoma (BEA). Especially excessive visceral fat have recently reported to promote some cancers, including BEA, development and progression because of metabolic disruption. It elaborates cytokines, adipokines and growth factors, resulting in systemic inflammation which could be carcinogenesis. To our best knowledge, there is no report to mention to the differences of relationship between abdominal fat distribution and progression of BEA based on the length of BE.

Aims & Methods: This study aimed to clarify the impact of abdominal fat distribution on progression of BE to adenocarcinoma in long-segment BE (LSBE) and short-segment BE (SSBE).

Study 1: We retrospectively reviewed the 124 patients with pathologically defined superficial BEA who underwent endoscopic resection, including 4 endoscopic mucosal resection (EMR) and 85 endoscopic submucosal dissection (ESD), or surgical operation (35 esophagectomy) in our institution between January 2004 and December 2018. 124 BEA cases included 34 LSBE (length ≥3 cm) cases and 90 SSBE (length ≥1 and < 3 cm) cases. Using computed tomography volumetry, we measured areas of visceral (VFA) and subcutaneous (SFA) fat at the level of the umbilicus, and calculated the VFA/SFA ratio in each patient, defining high-VFA/SFA ratio (≧1.0) and low-VFA/SFA ratio (< 1.0). We also measured body mass index (BMI) and waist circumference (WC). VFA/SFA ratio, BMI and WC in the patients were compared and analyzed between BEA with LSBE group and BEA with SSBE group.

Study2: We divided 62 patients who had LSBE into two groups based on prognosis of BEA; BEA with LSBE (34 patients) and non-BEA with LSBE group (18 patients). Abovementioned parameters were compared and analyzed between these two groups.

Results: Study1: High VS ratio were seen in 22 (64.7%) patients among BEA with LSBE group and 34 (37.8%) patients among BEA with SSBE group, which is statistically significant (p = 0.0072). However, difference of BMI or WC were not significant between BEA with LSBE group and BEA with SSBE group as follow; median BMI (range) 24.2 (13.1-31.8) kg/m² vs. 23.2 (16.2-36.9) kg/m², WC (range) 85.8 (59.8-122.6) cm vs. 86.0 (62.4-151.4) cm. Study2: In non-BEA with LSBE group, BMI (range) and WC (range) were 23.7kg/m² (18.8-26.8) kg/m² and 86.1 (77.0-104.9) cm. These were not significant either, compared to BEA with LSBE group. High VS ratio were seen in 6 (33.3%) patients among non-BEA with LSBE group. This result was statistically significant compared to BEA with LSBE group (0.038).

Conclusion: High VFA/SFA ratio was significantly associated with progression of long-segment Barrett's esophagus to esophageal adenocarcinoma.

References: [1]Beddy P, Howard J, McMahon C, Knox M, de Blacam C, Ravi N, et al. Association of visceral adiposity with oesophageal and junctional adenocarcinomas. Br J Surg2010; 97:1028-1034. [2] Long E, Beales L.P. I . The role of obesity in oesophageal cancer development Therap Adv Gastroenterol. 2014 Nov; 7(6): 247-268.

Disclosure: Nothing to disclose

P1997 OUTCOME OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR SUPERFICIAL PHARYNGEAL SQUAMOUS CELL CARCINOMA - ESPECIALLY FOR THE SCC LOCATED ANTERIOR SIDE OF EPIGLOTTIS

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Introduction: ESD for pharyngeal SCC (PSCC) is difficult, because of narrow space and poor maneuverability. Especially, ESD for PSCC located in the anterior side of epiglottis is extremely difficult. Because, the intubated tube elevates the epiglottis, and working space of anterior side of epiglottis will become narrow.

Aims & Methods: The aim of this study is to clarify the usefulness of ESD for pharyngeal SCC, especially located in the anterior side of epiglottis.

119 pharyngeal SCC in 91 patients treated by ESD from Apr. 2006 to Mar. 2019 in Saku Central Hospital Advanced Care Center were enrolled to this retrospective study.

Male/Female was 90/1. Mean age was 68.5 (40-92). Mean size of tumor and specimen were 20.0 (1 - 51) and 29.1 (8 - 90) mm, respectively.

Location: pyriform sinus, middle pharynx epiglottis, and were 55, 58 and 6.

All ESD was performed by a hook knife under intubated general anesthesia.

ESD for the SCC located in anterior side of epiglottis: An intubated tube elevated epiglottis, and the approach to anterior side of epiglottis becomes impossible. Therefore, a temporary tracheotomy was performed before ESD. Clip with line was used to get enough traction. Autocut mode was used for dissection to prevent burning effect to the cartilage of epiglottis.

Surveillance: 1 - 2 endoscopy, CT scan and neck US were performed as surveillance after ESD.

Results:

1. En bloc resection rate was 100%. R0 resection (En bloc + lateral margin negative) rate was 96.6% (115/119)

2. Complication: Delayed bleeding rate was 1.1% (1/91). Re-intubation was needed for the hemostasis. Dysphasia was shown in 3.3% (3/91). Two patients had mild dysphagia and improved in two weeks. The remaining one patient had severe dysphagia. The patient had a big SCC, 50mm in size, and the SCC extend from light piriform sinus to ary-epiglotic fold.

3. Invasion depth: Epithelial (EP) and subepithelial (SEP) SCC were 57% (68/119) and 43% (51/119), respectively.

4. The rate of lymph-duct involvement of EP and SEP were 0% and 5.7% (5/119), respectively.

5.The rate of venous involvement of EP and SEP were 0% and 2.9% (1/35), respectively. The only patient who had venous involvement was 92 years old, and followed up without an additional therapy.

6. Local recurrent rate was 0 %.

7. LNM rate of EP and SEP was 0% and 4.7% (2/43 cases), respectively. A cervical LNM was diagnosed 6 months after ESD. Lymph node dissection and CRT was performed for the patient. The patient died of other disease without recurrence of pharyngeal SCC. The other patient also had a cervical LNM and treated by LND + CRT. The patient is alive without recurrence for 10 years.

8. Prognosis and distant metastasis

One patient died of lung metastasis. The patient had SEP SCC with lymph duct involvement.

9. ESD for SCC in anterior side of epiglottis

A temporary tracheotomy was performed before ESD. Clip with line was used to get enough traction for all cases. All of six cases were completed successfully without any complications.

Conclusion: ESD is a safe and useful treatment for superficial pharyngeal SCC, even if SCC located in anterior side of epiglottis. We have to observe carefully to detect such superficial pharyngeal SCC when we insert endoscope.

Disclosure: Nothing to disclose

P1998 CLINICOPATHOLOGICAL STUDIES OF ESOPHAGEAL SQUAMOUS CELL CARCINOMA DEVELOPING FROM ACHALASIA: ANALYSIS OF ITS CARCINOGENESIS AND MORPHOLOGICAL CHARACTERISTICS

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Introduction: Achalasia of the esophagus is a benign disease caused by dyskinesia of an esophageal motor disorder characterized by insufficient relaxation of the lower esophageal sphincter and the absence of progressive peristalsis. Achalasia is presumed to be a premalignant lesion and esophageal carcinoma is the most serious late complication clinically. Chronic inflammation by retained food may induce carcinogenesis of the esophageal squamous epithelium. Carcinoma may develop progressively from hyperplastic and dysplastic changes of esophageal achalasia. However, the detailed mechanism of carcinogenesis in achalasia patients has not been clarified yet.

Aims & Methods: We analyzed 21 cases of achalasia-associated carcinoma of the esophagus clinically, and examined pathological and morphological characteristics of carcinogenesis in achalasia, surgically or endoscopically resected, using endoscopic, histological and immunohistochemical procedures. The invasive parts of each carcinoma, in situ carcinoma, dysplasia as well as hyperplasia were examined for histological mapping, and with immunohistochemical expression for p53 protein.

Results: The patients ranged in age from 43 to 76 years, with a mean age of 60 years. The mean interval between the diagnosis of achalasia and carcinoma was 21.7 years. Nine of the 21 cases were superficial cancers, and the other 12 cases were advanced cancers invading the adventitia. Radiographically, 10 of the 21 cases were sigmoid type, the other 11 cases were straight (flask) type. Six cases were grade III, the other 15 cases were grade II, and none was grade I. Surgical treatment for achalasia was 12 cases, balloon dilatable bouginage was 6 cases, and 3 cases were no treatment. Endoscopically, 8 cases of carcinomas were protruding type, and the

others were superficial depressed type and ulcerative type. Twelve cases were composed of squamous cell carcinoma and the other one was basaloid-squamous carcinoma. Histological mapping of the resected specimens demonstrated marked hyperplastic changes of stratified squamous epithelium and multiple foci of dysplastic changes. The squamous cell carcinomas showed well to moderately differentiated type with low-grade atypia, closely associated with dysplastic foci. Immunohistochemical overexpression of p53 was detected in the invasive parts of the carcinoma, in situ carcinoma, and dysplasia, and was not detected in the hyperplastic epithelium.

Conclusion: Chronic inflammatory irritation by retained food in achalasia may induce chronic hyperplastic esophagitis and eventually malignant transformation of esophageal epithelial cells, associated with dysplasia-carcinoma sequence. Achalasia seems to be a risk factor for developing squamous cell carcinoma of the esophagus, even if after surgically treated. Careful long-term follow-up to detect and treat early stage cancer for patients with achalasia by endoscopic screening is recommended.

Disclosure: Nothing to disclose

P1999 LONG-TERM RESULTS OF ENDOSCOPIC TREATMENT VS. ESOPHAGECTOMY WITH LYMPHADENECTOMY IN PATIENTS WITH HIGH-RISK EARLY ESOPHAGEAL CANCER INCLUDING DETAILED ANALYSIS OF LYMPH NODE MICROMETASTASES

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Introduction: Esophagectomy is a standard treatment for patients with 'high-risk' early esophageal cancer (EEC) despite a growing evidence that endoscopic treatment could be a safe alternative even for these patients.

Aims & Methods: The aims were 1. to prospectively assess results of endoscopic vs. surgical treatment in consecutive patients with 'high-risk' EEC and 2. to determine lymph node (LN) metastases and micrometastases (including risk factors) in those who underwent surgery. Firstly, patients with EEC underwent endoscopic resection (ER) or submucosal dissection (ESD). Those patients with 'high-risk' EEC without contraindications were referred to surgery, the remaining patients continued in endoscopic treatment, if necessary. 'High-risk' cancer was defined as any cancer with sm invasion or mucosal cancer with at least one of the following: poor differentiation (G3/G4), invasion to blood (A+) or lymphatic vessels (L+) and high tumor cell dissociation (TCD3). The patients have been followed up for a median of 32,5 months (range 1-171). LNs were processed as a sentinel LN, thus it was completely cut into 2-3 mm thick slices and embedded into paraffin blocks. Serial levels were stained for hematoxylin-eosin to evaluate metastases and for immunohistochemistry to evaluate micrometastases and isolated tumor cells.

Results: A total of 67 patients was included, 18 (26,9%) had T1a cancer with 'high-risk' features and 49 (73,1%) had T1b cancer with sm invasion; 48 had adenocarcinoma (EAC), 18 had squamous carcinoma (SCC) and 1 had mixed adenoneuroendocrine carcinoma (MANEC); 27 patients (40,3%) were referred to surgery and 40 (59,7%) continued in endoscopic treatment.

Endoscopy: Complete local remission (CLR) was achieved in 35/40 patients (87,5%). Four patients without CLR continued endoscopic therapy with a palliative intent and one patient died due to other comorbidity. Tumor generalization occurred in 2 patients (1 EAC and 1 SCC, both with sm3 invasion, G3, TCD3, A+ and L+) and local relapse occurred in 1 patient (EAC, sm1, G3, TCD3). All of the remaining patients with CLR (n=32; 21 EAC, 10 SCC, 1 MANEC) have not experienced either local relapse or generalization. Tumor-free survival was 28,5 months (range 1-131).

Surgery: Among 27 patients who were referred for esophagectomy, one patient had generalization revealed during the operation. The remaining 26 patients underwent esophagectomy; local residua of malignancy were present in 5/26 patients (19,2%, expected residua as these patients did not achieved CLR). A total of 532 LNs were evaluated, LN metastases were

detected in 1 (16 LNs) (EAC: G3-4, sm3, TCD3, A+, L+) and micrometastases in another 2 patients (EAC: sm3, G3, TCD 2, A+, L+; SCC: sm2, G2, TCD1, A+). Surgery related mortality was 3,9% (1/26, the cause of death was anastomotic dehiscence).

Conclusion: Endoscopic treatment provided long-term remission (or cure) in considerable number of patients with high risk EAC and it may represent a valid alternative to surgery. The risk of LNs metastases/micrometastases was low. The risk of metastatic progression increased with rising amount of risk features (Prob > |t| 0.0366). None of the patients with sm1 invasion or well-differentiated tumor (G1) have experienced generalization, thus advanced sm invasion (sm2, sm3) and poor differentiation may be crucial factors.

Disclosure: Nothing to disclose

P2000 YIELD OF REGIONAL MALIGNANT LYMPH NODE METASTASIS BY EUS AND FNA FOR THE DETECTION OF RESIDUAL DISEASE AFTER NEOADJUVANT CHEMORADIOTHERAPY FOR ESOPHAGEAL CANCER

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Introduction: Endoscopic ultrasound (EUS) and EUS-guided fine-needle aspiration (FNA) are potential tools for detection of residual disease after neoadjuvant chemoradiotherapy (nCRT) in patients with esophageal cancer. This is the first prospective study that investigated the yield of EUS and FNA for detection of malignant lymph nodes (LNs) 10-12 weeks after nCRT.

Aims & Methods: EUS was performed 10-12 weeks after nCRT. ^{18}F-FDG PET-CT was used to guide targeting of suspicious LNs. If suspicious LN were identified with radial EUS, a linear EUS was performed with concurrent FNA-sampling. Endoscopic nodal staging was compared to histopathological examination of the resection specimen (ypN). Primary outcome was the proportion of correctly identified patients with malignant LNs (ypN+).

Results: 101 consecutive patients were included. Seventy-nine patients had ypN- residual disease, of whom 62 were classified correctly by EUS (specificity 78%). Twenty-two patients had ypN+ residual disease of whom 11 were identified by EUS (sensitivity 50%). Six of these patients had ≥1 LN not fulfilling the EUS-criteria for malignant LNs (round, hypo-echogenic, >5mm). Malignant LNs in falsely negative patients were predominantly located at the distal LN stations. Specificity and sensitivity of FNA were 100% (10/10) and 75% (3/4), respectively.

	ypN-	ypN+	Total
yuN-	62	11	73
yuN+	17	11	28
Total	79	22	101

[Positive and negative findings by EUS (yuN) and histopathological examination of the resection specimen (ypN).]

Conclusion: EUS detected 50% of ypN+ patients 10-12 weeks after nCRT. Remarkably, in 55% (6/11) of these patients ≥1 suspect LNs did not meet EUS-criteria for malignant LNs. To optimize sensitivity and minimize the risk of missing residual disease after nCRT, FNA of local LNs should be performed even in cases of low suspicion.

Disclosure: Nothing to disclose

P2001 EFFICACY AND SAFETY OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR ESOPHAGEAL LESIONS UNDER GENERAL ANESTHESIA

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Introduction: Endoscopic submucosal dissection (ESD) is a well-established treatment for early-stage malignant lesions of the stomach, esophagus, and colorectum with no risk of lymphatic metastasis. ESD requires precise and complicated maneuvers. But the esophageal wall is thinner than the stomach and moves with respiration and heartbeat, swallowing, peristalsis in a narrow space. It couses difficult maneuverability of devices.

Therefore, intraoperative management of the patient's general condition is very important during esophageal ESD. In Japan, ESD is usually performed under conscious sedation in the endoscopy room.

However, it is difficult to control patient movement completely because of insufficient effect of sedation, and it has a risk of aspiration pneumonia. Any patient movement during the procedure can result in complications such as perforation and hemorrhage. Therefore, we perform ESD under general anesthesia with mechanical ventilation.

Aims & Methods: The aim of this presentation is to evaluate the effect and safety of Esophageal ESD under general anesthesia.

In the past 10 years from January 2008 to December 2017, 371 lesions (277 patients) had undergone ESD under general anesthesia for diseases of the esophagus. We retrospectively investigated the efficacy and safety of esophageal ESD under general anesthesia.

Results: The male: female ratio was 244:33 (88.1%:11.9%) and the patients' average age was 68.1 ± 8.5 years (42-89 years). The diameter of the resected specimen was 43.0 ± 18.3 mm (8-115 mm) and average circumference rate of resected specimen was three-fifth (one-fifth to whole circumference). The *en bloc* resection rate was 89.0%. The average operating time was 113.8 ± 62.3 min (25-340 min), and the average anesthesia time was 146.4 ± 67.6 min (50-370 min). The location of the lesion was cervical in 20 lesions, upper esophagus in 53 lesions, middle esophagus in 169 lesions, lower esophagus in 97 lesions, esophagogastric junction in 32 lesions. The pathological findings was squamous cell carcinoma in 280 lesions and adenocarcinoma in 20 lesions, neoplasia in 56 lesions, others in 11 lesions. The invasion depth of carcinoma was M in 266 lesions, SM in 34 lesions. Average postoperative hospital stay was 7.7 days (2-64). Average years of experience as a doctor was 13 years (6-21). About one-third of the patients were performed ESD by a non-expert doctor (6-8 years of experience as a doctor). With regard to complications, intraoperative perforation occurred in 3 (1.1%) patients, delayed perforation occurred in 1 (0.4%), delayed bleeding occurred in 4 (1.4%). These complications were occurred in patient performed ESD by expert doctor (over 11 years of experience as a doctor), because of difficulty factor to perform ESD (location, size, severe comorbidities, etc).

Conclusion: For ordered management of accidental events during esophageal ESD, general anesthesia might be a crucial option for a better clinical outcome even when administered by non-experienced operators.

Disclosure: Nothing to disclose

P2002 A NOVEL MAGNIFIED ENDOSCOPIC FINDING FOR THE DIFFERENTIAL DIAGNOSIS BETWEEN INFLAMMATION AND SUPERFICIAL ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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Introduction: Magnified endoscopic findings were subclassified into type B1, B2 and B3 in Japanese esophageal society (JES) classification to diagnose invasion depth of esophageal superficial squamous cell carcinoma (ESCC). Type B2 is defined as irregular vessels without a loop-like formation, and it diagnoses as T1aMM/T1bSM1 SCC.

Sometimes T1aESCC has erosion / inflammation, and NBI magnified endoscopy revealed non loop irregular vessels. If it is judged as JES type B2,

the lesion was overdiagnosed as T1aMM/T1bSM1. Therefore, we have to investigate the differential diagnosis between SCC and erosion, when non loop irregular vessels were observed.

Aims & Methods: The aim of this study is to investigate the characteristics of type B2 vessels.

Four hundred ninety-nine ESCC in 298 patients were treated by ESD from January 2011 to May 2018. Precise comparison between magnified endoscopic findings and histology is necessary to measure the target vessels correctly. We selected consecutive 53 ESCC in 51 patients which had type B2, and precious comparison was possible.

The distance between top of IPCL and surface, the density and minor axis of type B2 using CD34 staining were investigated.

Based on endoscopic findings, we subclassified B2 into B2 pure and B2 inflammation (B2 i.) B2 pure was defined as non-loop irregular vessels. B2 i was defined as thin vessels with high density.

B2 pure was 44 lesions, and B2 i was 9 lesions. Macroscopic type; 0-IIa, 0-IIb, 0-IIc and 0-III were 10, 2, 31, 1 and 0, 0, 9, 0 respectively. Location; Ce, Ut, Mt, Lt and Ae were 6, 4, 26, 6, 2 and 0, 0, 7, 2, 0, respectively. Mean tumor size was 37mm and 39mm, respectively. There was no significant difference in background between B2 pure and B2 i.

Results:

1. Histological findings of B2 area: All of the pathological diagnosis in 44 lesions which showed B2 pure were SCC. Pathological diagnosis of 9 lesions which showed B2 i were SCC in 2, and erosion or inflammation in 7 lesions.

2. How deep can we observe by NBI magnified endoscopy? The distance between top of IPCL and surface was measured in 66 points of non-neoplastic squamous epithelium randomly. The mean distance was 88 (31-174) μm. Therefore, we concluded that we can observe at least 100 μm under the surface.

3. Maicrovessles which exist 100 μm under the surface in B2 i (n=6) and B2 pure (n=16) were investigated.

a. Density was calculated using CD34 staining. The mean density was 3.35/mm in B2 pure and 8.22 /mm in B2 i, respectively (p=0.001).

b. Minor axis of vessels was measured using CD34 staining. The mean minor axis of vessels was 12.3 μm and 6.65 μm, respectively. (p=0.0028). B2 i has thin vessels with high density, and B2 pure has thick vessels with low density.

Conclusion: B2i is an important parameter to show erosion in superficial ESCC. B2 should be subclassified into B2 pure and B2 i to prevent overdiagnosis.

Disclosure: Nothing to disclose

P2003 TUMOR SIZE INCREASES THE RISK FOR LYMPH NODE METASTASES IN T1B ESOPHAGEAL ADENOCARCINOMA

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Introduction: The decision to give adjuvant therapy after endoscopic resection of T1b esophageal adenocarcinoma (EAC) who are not surgical candidates is largely based on a lesion's risk of lymph node metastasis (LNM). However, risk factors for LNM in esophageal T1b EAC are still not clearly defined.

Aims & Methods: The aim of this study is to evaluate risk factors for LNM in T1b EAC patients who underwent esophagectomy or endoscopic resection with ≥ 5 years of follow-up post-procedurally. This was a single center, retrospective analysis carried out at a large tertiary referral center. Our pathology database assisted in identifying patients who underwent esophagectomy or ER with ≥ 5 years follow-up, with histologically proven T1b EAC between 2010 and 2017.

Patients were excluded from the study if they (a) received chemoradiation prior to esophagectomy (b) received chemoradiation before or after ER (c) had any other primary cancer treated within the preceding 5 years. LNM was considered positive if there was histologically or radiologically confirmed metastasis (a) in esophagectomy specimens or (b) within 5 years of follow up post ER. All pathologic specimens were reviewed by an expert gastrointestinal pathologist for T1b accuracy and depth of submucosal invasion.

Results: A total of 40 patients [median age 69y (IQR 61.5-76); 87% males] formed the study cohort of which 36 patients (90%) underwent esophagectomy and 4 patients who were not surgical candidates (10%) underwent endoscopic resection. Of the total, seven (17.5%) patients developed LNM per study criteria (Table 1). Tumor size was significantly (p-value 0.019) associated with the risk of LNM. Applying a non-parametric ROC curve, 3 cm is the optimal threshold at which the size of the tumor is positively associated with metastasis. No other risk factors including lymphovascular invasion, differentiation on pathology, macroscopic appearance, infiltration growth pattern, or tumor distance from the gastroesophageal junction were significant risk factors for LNM.

Conclusion: In T1b esophageal adenocarcinoma, tumor size greater than 3 cm appears to be the variable with the most potential as a risk factor for metastasis at five years following surgical or endoscopic resection. Adjuvant therapy should be considered in patients with tumor size greater than 3 cm.

Disclosure: Nothing to disclose

P2004 MICA HAS A PROTECTIVE EFFECTIVE TO NON-STEROIDAL ANTI-INFLAMMATORY DRUGS ENTEROPATHY VIA REGULATING LONG NON-CODING RNA-NCRUPAR AND PAR2

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Introduction: NSAIDs (non-steroid anti-inflammatory drugs) have a wide range of clinical applications. Studies have shown that the incidence of small intestine injury in patients with long-term NSAIDs is about 70%. Currently, the prevention and treatment methods are limited, thus it is of great significance to elucidate its pathogenesis for the safe clinical application of NSAIDs.

Aims & Methods: Caco-2 cells were cultured and divided into the following six groups:

Group A: blank control group;
Group B: diclofenac sodium treatment group;
Group C: Control RNAa group;
Group D: ncRuPAR over expression group;
Group E: diclofenac sodium+mica containing serum group; and
Group F: diclofenac sodium treatment+PAR-2 (proteinase-activated receptor-2) blocker FSLLRY-NH2 group.

Transwell detected the intestinal epithelial cell permeability, western-blot detected the expression of PAR-2, Occludin and Claudin-1, and qRT-PCR detected the expression of ncRuPAR and PAR-2 mRNA.

Results: After diclofenac sodium treatment, intestinal epithelial cell permeability increased (143.02±1.70 vs 100±4.43, P< 0.05), the expression of Occludin (0.29±0.02 vs 0.45±0.01, P< 0.05) and Claudin-1 (0.20±0.01 vs 0.31±0.01, P< 0.05) decreased. The expression of ncRuPAR mRNA (7.01±1.17 vs 1.17±0.81, P< 0.05) and PAR-2 mRNA (5.52±0.92 vs 1.03±0.29, P< 0.05) also increased. Mica medicated serum and PAR-2 blocker FSLLRY-NH2 inhibited the increase of intestinal epithelial cell permeability induced by diclofenac sodium (108.18±1.96 ; 111.29±4.23, P< 0.05), as well as its effect on the expression of ncRuPAR mRNA (3.40±1.89; 4.18±0.35, P< 0.05), PAR-2 mRNA (2.73±0.39; 3.60±0.69, P< 0.05), Occludin (0.38±0.02;0.35±0.01, P< 0.05) and Claudin-1 (0.25±0.01;0.24±0.02, P< 0.05). After ncRuPAR over expression, intestinal epithelial cell permeability increased (147.93±1.96, P< 0.05), the expression of PAR-2 mRNA (24.71±4.17, P< 0.05) and ncRuPAR mRNA (4686.48±1191.9, P< 0.05) increased, while the expression of occludin (0.35±0.02, P< 0.05) and claudin-1 (0.18±0.01, P< 0.05) decresed.

Conclusion: Small intestinal epithelial cell permeability increased and mucosal mechanical barrier function is impaired in NSAIDs enteropathy. NcRuPAR affect the mechanical barrier function of intestinal mucosa by regulating the expression of PAR-2, and mica may play a preventive role by affecting the expression of ncRuPAR.

Disclosure: Nothing to disclose

P2005 IMPLEMENTATION OF PROTON PUMP INHIBITOR DEPRESCRIPTION PROTOCOL AT HOSPITAL DISCHARGE: THE DE-PIBP PROJECT

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Introduction: Proton pump inhibitors (PPIs) are among the most pre-scribed drugs. Despite a safe profile, their prolonged use has been associated with some complications such as enteric infections and fractures. It is hence recommended to adjust their prescription according to the existing guidelines of scientific societies.

Aims & Methods: Objectives: To evaluate the applicability of a deprescription algorithm in hospitalized patients with chronic consumption of PPIs, and to determine the number of patients who maintain deprescription after 4, 12 and 24 weeks, as well as the factors associated with the lack of compliance with the deprescription algorithm.

Methodology: prospective study with consecutive inclusion of patients who were under PPI treatment for at least 8 weeks and had been admitted to the Gastroenterology Department (GED) of the University Hospital Miguel Servet (Zaragoza, Spain). PPI prescription was classified as adequate or inadequate according to the criteria of the Spanish Association of Gastro-enterology. Those with inadequate prescription who agreed to participate in the study completed the Spanish version of the Gastrointestinal Short Form Questionnaire (GSF-Q). Exclusion criteria were: GSF ≥13, occasional use of PPI (≤2 times / week), severe comorbidity (ASA IV or higher), advanced cognitive impairment, pregnancy, and hospital stay less than 24 hours. Patients without exclusion criteria were included in the deprescription protocol based on the recommendations of the Canadian Primary Care Society, with follow-up at 4, 12 and 24 weeks to assess the reappearance of symptoms, necessity to reintroduce PPIs and why. The protocol was approved by the Ethics Committee.

Results: Between September 2018 and April 2019, 1173 patients were admitted more than 24 hours to the GED, of whom 513 (43.73%) consumed PPIs chronically. 142 met some other exclusion criteria. 371 patients were included, 54% males, with mean age 74.4 (SD 12.5) years. The prescription was considered adequate in 284 patients (76.55%), being over 60 year old individuals taking antiaggregant drugs the most frequent group (76.05%). The prescription was inadequate in 87 patients (23.45%), the majority because of polypharmacy (52%). 12 patients refused to participate in the deprescription protocol. 35 patients stopped PPI treatment immediately while 26 gradually reduced the treatment, 7 switch to on-demand treatment and 7 decreased dosed indefinitely. Sex was not a risk factor for inadequate prescription (p = 0.251), while age> 75 years was indeed associated with inadequate prescription(p = 0.025). Follow-up information, which was available at 4 weeks for 64 patients, showed that 53 individuals (82.81%) complied with the deprescription protocol while 11 subjects had reintroduced PPIs again at the previous dose (7 without justified cause). At 12 weeks, 32 out of 45 patients (71.1%) with follow-up information complied with the deprescription protocol. No patient presented serious adverse effects attributable to deprescription.

Conclusion: Inadequate indication of PPI is very common in patients admitted to a Gastroenterology ward. The application of algorithm of deprescription is a safe and effective strategy to reduce the inadequate consumption of PPIs in the medium term.

Disclosure: Nothing to disclose

P2006 PROTON PUMP INHIBITORS: IMPLEMENTATION OF A DE-PRESCRIBING STRATEGY

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Introduction: Proton pump inhibitors (PPI) are the most consumed drugs in Spain. Prescribing a PPI without indication contributes to polypharmacy and drug interactions.

Aims & Methods: Our objective was to develop a strategy in order to optimize the use of PPI in a northern region of Spain (616,758 inhabitants). Methods: A so-called "PPI optimization strategy" was implemented including the following activities:

1) A multidisciplinary group (gastroenterologists, general practitioners (GPs) and primary care pharmacists (PCP)) was established to design the strategy;

2) Evidence on PPIs and gastroprotection was assessed;

3) Criteria for selection of candidates for intervention was agreed (patients with PPI prescribed for more than 12 months without authorized indication);

4) Pharmacists presented the program and gave a training session to GPs and nurses.

5) Patient-oriented support materials were provided to doctors (explanatory leaflets for candidates and general public too);

6) Candidates for intervention were retrieved through an in-house developed software called Observa (Observatory of medication safety), that interacts with all clinical records in our province;

7) A message was sent through this tool to GPs whose patients met the inclusion criteria asking to withdraw the drug in November'17 for patients >65 years. In June'18 a message was sent for patients < 65 years meeting the inclusion criteria and a second message to those patients > 65 years for whom there had not been an answer after the first invitation;

8) A mass media campaign supporting the strategy was launched that included press release for local newspapers.

9) PPIs withdrawal was monitored and evaluated.

Results: A total of 15,794 patients were candidates for the intervention; 9,325 >65 years and 6,469 patients < 65 years. A 53% (n: 8,293) of deprescription invitations were answered; 40% were accepted, 11% rejected and 2% non-valid.

Among patients >65 years, who were invited twice to withdraw PPIs, 62% of deprescription invitations were answered (n: 5,735) and 47% of all the proposals were accepted, 76% of those answered. (n: 4,631). In patients younger than 65 years, who got a single invitation, there were a 40% of answers (n:2,558) and a 30% of proposals were accepted (n:1,912), 74% of those that had been answered.

The strategy was started in the end of 2017. During 2018 the amount of defined daily dose (DDD) for PPIs in our region descended a 13% compared to 2017.

Conclusion: There is a high use of PPI in general population, quite often without meeting any medical criteria for it. The use of web tools such as Observa can contribute to the optimization of pharmacotherapy and avoids PPI overuse. A 75% of the evaluated proposals of de-prescribing were accepted, which has had an impact on the consume of PPIs in our region.

Disclosure: Nothing to disclose

P2007 CLINICOPATHOLOGICAL AND IMMUNOHISTOCHEMICAL STUDY OF THE MECHANISM OF SPORADIC FUNDIC GLAND POLYP PROLIFERATION AND ENLARGEMENT IN LONG-TERM PPI-USERS

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Introduction: An association between sporadic fundic gland polyps (SFGP) and long-term PPI use has previously been suggested, and SFGP with dysplasia-carcinoma in rare cases has recently been reported.
Aims & Methods: To investigate the relationship between SFGP and PPI, we enrolled 86 SFGP patients (32 PPI-users of more than 6 months and 54 non-users) and compared clinical and endoscopic characteristics and histological findings including parietal cell protrusion (PCP), number and size of microcysts, parietal cell nuclear density, and MIB1 and β-catenin immunohistochemistry of biopsy specimens.
Results: All patients were *H. pylori*-negative, with no or slight gastric atrophy. The proportion of patients with cobble stone-like appearance in background mucosa and with more than 20 polyps were significantly higher among PPI-users (66% of users vs. 6% of non-users and 63% of users vs. 19% of non-users, respectively).The maximum diameter of the polyps was significantly larger in PPI-users than non-users (5.3 mm vs. 3.6 mm, respectively). Histologically, the number of microcysts and ratio of patients with PCP was significantly greater in PPI-users than non-users (8.4 vs. 4.9 and 53% vs. 13%, respectively). There was no difference in the maximum diameter of microcysts, parietal cell nuclear density, or MIB1-index between the two groups. At no point was nuclear accumulation of β-catenin observed.
Conclusion: Our results suggest that an increased number of microcysts drives the enlargement and proliferation of SFGP in long-term PPI-users. The proliferative activity of the neck zone and β-catenin immunohistochemistry did not differ between users and non-users. There was no parietal cell hyperplasia; however, parietal cell hypertrophy was found in PPI-associated SFGP.
Disclosure: Nothing to disclose

P2008 QUANTIFYING EARLY GASTRIC CANCER IN AUSTRALIA: WHAT IS THE POTENTIAL NEED FOR GASTRIC ESD IN THE WEST?

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Introduction: Endoscopic submucosal dissection (ESD) can be curative in early gastric cancer (EGC), particularly in lesions with favourable histology. (1) ESD provides an *en bloc* specimen, enabling accurate staging, and has significantly lower morbidity and mortality compared to gastrectomy.(2) It is the recommended treatment for EGC in multiple international guidelines and is widely performed in Asia where gastric cancer has high prevalence.(3-5) ESD is not commonly performed in Western countries.(6)
One proposed reason is that a lower proportion of gastric cancer present at early stage than in high prevalence regions. To assess the potential need for ESD, the incidence of EGC must be established.
Aims & Methods: This study aims to evaluate the proportion of gastric cancer that met histological criteria for EGC, and proportion of EGC that were suitable for and treated by endoscopic resection in a Western population.
This is a retrospective analysis of all gastric cancers reported to Victorian Cancer Registry, a mandatory reporting process of new cancer diagnoses in the state of Victoria (26% of the population).(6) All EGCs (T1a and T1b lesions) diagnosed between January 2011 to December 2016 were identified from histological reports. Demographic, tumour characteristics and treatment data were collected. Japanese and European ESD guidelines (3,5) were applied to assess the number of potential ESD candidates.
Results: 1779 gastric cancers were reported. 237 (13.3%) were EGCs, with mean annual incidence of 47 cases. 33 endoscopic and 149 surgical resection specimens were available. On application of ESD resection criteria, 132 (72.5%) met extended and 84 (46.2%) met standard criteria. Of these, 26 (19.7%) were treated endoscopically and 106 (80.3%) by surgery. Tumour location, depth and involvement of pathologic margins was significantly

different between treatment strategies (Table 1). Endoscopic resections were performed using snare-based technique and ESD in 93.4% and 6.6%, respectively.

		Surgical, n = 149	Endoscopic, n = 33	P value
Age at diagnosis (median, range)		68.7 (25.5 - 92.9)	70.9 (50.9 - 87.8)	0.168
Male (n, %)		105 (70.5)	23 (69.7)	0.690
Location of tumour (n, %)	Antrum/Incisura	60 (40.3)	3 (9.09)	<0.005
	Lesser curvature	6 (4.0)	4 (12.1)	<0.005
	Greater curvature	27 (18.1)	2 (6.06)	NS
	Fundus	5 (3.4)	1 (3.03)	NS
	GOJ/cardia	42 (28.2)	16 (48.5)	<0.005
Depth of tumour (n, %)	Tis	3 (2.0)	4 (12.1)	NS
	T1a	55 (36.9)	20 (60.6)	NS
	T1b	91 (61.1)	9 (27.3)	<0.005
Differentiation (n, %)	Well/Moderate	64 (43.0)	15 (45.4)	0.205
	Poor	37 (24.8)	3 (9.09)	0.145
	Not reported	48 (32.2)	15 (45.5)	0.305
Diameter (mm, median, range		21.2 (0.2 - 65)	17.6 (6 - 90)	0.179
Lymphovascular invasion (n, %)		24/146 (16.4)*	4/31 (12.9)*	0.346
Perineural invasion (n, %)		4/134 (3.0)*	0/24 (0)*	0.015
Pathologic margins clear (n, %)		143 (96)	23/30 (76.7)*	<0.005

*not reported in all cases. NS; not significant

[Table 1. Comparison of early gastric cancers treated with surgical versus endoscopic resection]

Conclusion: In this State Cancer Registry study, 237 EGCs were diagnosed over a 5-year period, representing 13.3% of gastric cancers. Within limitations of retrospective analysis, most EGCs fulfilled criteria for ESD. Advanced resection techniques should be considered part of the management algorithm for EGC, ideally after discussion at a multidisciplinary meeting involving an Interventional Endoscopist. To increase the utilisation of ESD, patients should be referred to centres with expertise in lesion assessment and advanced endoscopic resection, and systems implemented to improve training, accreditation and access to ESD.
References: 1. Yada T, Yokoi C, Uemura N. The current state of diagnosis and treatment for early gastric cancer. Diagn Ther Endosc. 2013;2013:241320. 2. Choi MK, Kim GH, Park DY, Song GA, Kim DU, Ryu DY, et al. Long-term outcomes of endoscopic submucosal dissection for early gastric cancer: a single-center experience. Surg Endosc. 2013;27(11):4250-8. 3. Hu J, Zhao Y, Ren M, Li Y, Lu X, Lu G, et al. The Comparison between Endoscopic Submucosal Dissection and Surgery in Gastric Cancer: A Systematic Review and Meta-Analysis. Gastroenterol Res Pract. 2018;2018:4378945. 4. Pimentel-Nunes P, Dinis-Ribeiro M, Ponchon T, Repici A, Vieth M, De Ceglie A, et al. Endoscopic submucosal dissection: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy. 2015;47(9):829-54. 5. Japanese Gastric Cancer A. Japanese gastric cancer treatment guidelines 2014 (ver. 4). Gastric Cancer. 2017;20(1):1-19. 6. Ono H, Yao K, Fujishiro M, Oda I, Nimura S, Yahagi N, et al. Guidelines for endoscopic submucosal dissection and endoscopic mucosal resection for early gastric cancer. Dig Endosc. 2016;28(1):3-15. 7. Statistics ABo. Australian Demographic Statistics, Sep 2018. Canberra, Australia2019.
Disclosure: Nothing to disclose

P2009 ENDOSCOPIC SURVEILLANCE AFTER TOTAL GASTRECTOMY FOR GASTRIC CANCER: IS IT NECESSARY?

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Introduction: Endoscopic surveillance after total gastrectomy for gastric cancer is routinely performed for detecting tumor recurrence or adverse effects of surgery.[1] But, there were only a few reports for clinical benefits of endoscopic surveillance.[2-5]
Aims & Methods: We investigated the necessity for endoscopic surveillance after total gastrectomy for gastric cancer. We reviewed the medical records of 385 patients who underwent total gastrectomy for gastric cancer between January 2011 and December 2011 in single tertiary hospital. Finally, we enrolled 143 early gastric cancer (EGC) patients and 175 advanced gastric cancer (AGC) patients who received surveillance programs after total gastrectomy including endoscopy and abdominopelvic computed tomography with contrast (APCT).
Results: Median follow-up period of APCT was 58.4 months and endoscopy was 55.5 months. We performed an R0 resection in 313 of 318 patients. Tumor recurrence was confirmed in 59 patients (19%), all of which were confirmed by APCT. Of 59 patients, four patients were EGC and 55 patients were AGC patients. The sites of recurrences were as follows: peritoneum in twenty-five, distant metastasis in twenty-one, loco-regional recurrence in six, and mixed recurrence in seven. Endoscopically confirmed recurrences were in five patients. Only one patient was confirmed recurrence by endoscopy earlier than APCT. This patient was performed R1 resection with the involvement of proximal margin. The postoperative benign stricture was confirmed by endoscopy in 2 patients (1%) without symptom and endoscopically passage disturbance. Other postoperative adverse effects including surgical stump or anastomosis site leakage, jejunal intussusception, and mechanical ileus were confirmed by APCT in 7 patients (2%).
Conclusion: Endoscopic surveillance after total gastrectomy with R0 resection for gastric cancer is a limited role for detecting tumor recurrence or adverse effects of surgery. Abdominopelvic computed tomography with contrast is maybe sufficient for surveillance modality after total gastrectomy with R0 resection for gastric cancer.

References: 1. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines), Gastric Cancer, Version 1.2019, NCCN.org. 2. Kodera Y, Ito S, Yamamura Y, et al. Follow-up surveillance for recurrence after curative gastric cancer surgery lacks survival benefit. Annals of surgical oncology. 2003;10(8):898-902. 3. Bennett JJ, Gonen M, D'Angelica M, Jaques DP, Brennan MF, Coit DG. Is detection of asymptomatic recurrence after curative resection associated with improved survival in patients with gastric cancer? Journal of the American College of Surgeons. 2005;201(4):503-510. 4. Park SJ, Park YS, Jung IS, et al. Is endoscopic surveillance necessary for patients who undergo total gastrectomy for gastric cancer? PLOS ONE. 2018;13(6):e0196170. 5. Lee SY, Lee JH, Hwang NC, et al. The role of follow-up endoscopy after total gastrectomy for gastric cancer. European journal of surgical oncology : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology. 2005;31(3):265-269.
Disclosure: Nothing to disclose

P2010 RISK FACTORS OF GASTRIC CANCER AFTER ERADICATION OF Helicobacter pylori EVALUATED FROM THE BACKGROUND GASTRIC MUCOSA: A PROPENSITY SCORE-MATCHED CASE-CONTROL STUDY

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Introduction: It is well known that eradication of *Helicobacter pylori (H. pylori)* reduces the risk of gastric cancer (GC) development. In contrast, *H. pylori* eradication does not prevent gastric cancer development in all individuals. There would be some risk factors in the background gastric mucosa after eradication of *H. pylori*. However, it is still unclear that histological features of the background gastric mucosa would be a predictable marker for the development of GC after eradication of *H. pylori*. Thus, we investigated risk factors of early GC development after eradication of *H. pylori* based on the histological characteristics of gastric mucosa.
Aims & Methods: 61 patients who underwent endoscopic submucosal dissection of GC after successful *H. pylori* eradication (defined as group A), and 122 patients without developing gastric neoplasm over 3 years after successful *H. pylori* eradication for control group, (defined as group B) were analyzed. Moreover, we used propensity score-matching analysis to adjust significant differences in the baseline clinical characteristics of patients. Before and after propensity score-matching, we compared the score in the histological evaluation of these enrolled patients between group A and group B. Three biopsy specimens were obtained from the greater curvature of the antrum, the lesser curvature of the corpus, and the greater curvature of the corpus.
Gastric mucosa samples were evaluated according to the updated Sydney system.
Results: Comparison of clinical characteristics between two groups revealed that males, elderly patients were significantly higher, and years after successful eradication were longer, although not significantly, in group A.
Updated Sydney system scores of group A were significantly higher than group B at all site except for intestinal metaplasia (IM) in the greater curvature of the corpus. However, there may be some bias, because of the difference depending on gender, age, and years after successful eradication. Therefore, we matched to reduce the influence of confounding these factors. After propensity score-matching, 54 patients with gastric cancer and 54 patients without gastric cancer were included in each group. Inflammation (mononuclear cells infiltration) in background gastric mucosa of Group A were significantly higher than the scores for the matched group B with the greater curvature of the antrum (0.78 ± 0.57 vs 0.28 ± 0.45, $p < 0.01$), the lesser curvature of the corpus (0.89 ± 0.42 vs 0.64 ± 0.59, $p < 0.01$) and greater curvature of the corpus (0.59 ± 0.60 vs 0.35 ± 0.48, $p=0.03$). Other significant differences were observed in atrophy of the greater curvature of the antrum (1.13 ± 0.87 vs 0.64 ± 0.77, $p < 0.01$), the lesser curvature of the corpus (1.61 ± 1.01 vs 0.92 ± 1.01, $p < 0.01$), and in IM of the greater curvature of the antrum (0.78 ± 0.82 vs 0.46 ± 0.77, $p=0.02$), the lesser curvature of the corpus (1.57 ± 1.19 vs 0.85 ± 0.98, $p < 0.01$).
Conclusion: Continuous high level of inflammation in the background gastric mucosa would be a risk factor of gastric cancer onset after *H. pylori* eradication.
Disclosure: Nothing to disclose

P2011 THE EFFECTS OF WARFARIN AND DIRECT ORAL ANTICOAGULANT IN ENDOSCOPIC SUBMUCOSAL DISSECTION CASES FOR GASTRIC NEOPLASM

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Introduction: The number of the cases who take warfarin or direct oral anticoagulant (DOAC) is increasing because they have cardiovascular diseases. Japanese guidelines for gastroenterological endoscopy have recommended continuation of warfarin and temporary withdrawal of DOAC on the day of endoscopic submucosal dissection (ESD). However, anticoagulants were temporarily withdrawn until the guidelines were revised in 2017. In Japan, DOAC has been used since 2011, however, the effect on endoscopic treatment is not clear. In this study, we evaluated the effect of warfarin and DOAC.
Aims & Methods: 417 patients with gastric neoplasms underwent ESD at the Nippon Medical School from January 2012 to February 2018. We excluded 32 patients who underwent injection of triamcinolone into ulcer after ESD, 27 patients who took NSAIDs, and 9 patients who had been on dialysis. Among them, 96 cases were taking antithrombotic drugs. 21 patients taking anticoagulant drugs were divided into two groups; warfarin group (13 patients; male 10) and DOAC group (8 patients; male 8). The

types of DOAC were dabigatran, apixaban, edoxaban or rovaroxaban. We compared retrospectively the post-bleeding rate, blood data, and complications between two groups.

Results: The post-bleeding rate were no differences between warfarin group (15.3%; 2/13) and DOAC group (12.5%; 1/8). No perforation occurred in both groups. The warfarin group had a slight longer ESD procedure time than the DOAC group. There were no differences in the rate of increase on the next day after ESD with platelet counts, PT (%) and APTT, but D-dimer was significantly increased in the warfarin group (61.0% vs 15.4%; p = 0.04). There were no complications such as thromboembolism in both groups.

Conclusion: Although there was no thromboembolism, withdrawing warfarin made anticoagulant action unstable and may be risk of thromboembolism.

Disclosure: Nothing to disclose

P2012 ENDOSCOPIC ULTRASOUND IN THE DIAGNOSIS AND FOLLOW-UP OF GASTRIC SUBEPITHELIAL LESIONS: RESULTS FROM A REGIONAL CENTRE

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Introduction: Gastric subepithelial lesions (SEL) found on conventional endoscopy or CT have a broad differential including malignant disease. Endoscopic ultrasound (EUS) +/- fine needle aspiration (FNA) has become an important modality in assessing SELs and guiding management. The optimum assessment and follow-up strategy for smaller lesions remains unclear. Our aim was to assess outcomes of patients undergoing EUS for gastric SELs in our regional centre. Secondary aims included assessing the use of EUS FNA, surveillance strategy and outcomes by lesion size (<10, 10-20 and >20mm).

Aims & Methods: We undertook a retrospective analysis of our prospectively collated regional EUS database, to identify patients who underwent EUS for SELs. Electronic patient records were analysed to obtain relevant data including imaging, cytopathology and follow-up. Patients with SELs out-with the stomach and patients undergoing EUS for investigation of known (or strongly suspected) malignancy were excluded.

Results: Between 1/1/14 and 31/12/17, 70 patients were referred for EUS due to the identification of an SEL on endoscopy (97%) or CT scan (3%). Mean age was 60 years with 44% (n=31) male. 56% (n=38) patients also underwent endoscopic biopsy together with EUS. All patients were followed up for a minimum of 12 months. Mean lesion size on EUS was 24.8mm. 15.7% (n=11), 42.9% (n=30) and 40% (n=28) of lesions were < 10mm, 10-20mm and >20mm respectively. One patient had mucosal thickening only, and one patient had incidental lung adenocarcinoma diagnosed at EUS. Table 1 shows the EUS diagnosis according to size of lesion.

31.4% (n=22) patients underwent FNA of lesion, (0%,4.2% and 27.1% patients for lesion size < 10mm 10-20mm and >20mm respectively). 4.2% (n=3) patients had biopsies within biopsies and 5.7% (n=4) patients were not sampled due to patient factors.

68% (n=15) of EUS-FNAs were diagnostic. 62.5% (n=10) FNAs were diagnostic of GIST, with 12.5% (n=2) leiomyoma, and one each adenocarcinoma, lymphoma, and lipoma.

All patients with lesions < 20mm (n=42) were alive and well with at least one-year follow-up, or had died of unrelated causes. 19 underwent repeat EUS or surveillance CT/endoscopy, 19 had no planned follow up due to lesions being deemed low risk or patient choice, one had a resection and two died of other causes. Of the 27 patients with lesions >20mm, 11 underwent resection/received Imatinib and 11 underwent EUS/CT/endoscopy surveillance due to patient co-morbidities or lesion being deemed low risk on EUS, with static size of lesion. Three lesions >20mm were cysts requiring no follow-up, two received other chemotherapy/surgery and one died of unrelated causes.

Conclusion: EUS is a useful tool in the assessment, diagnosis and follow-up of small SELs. Management of lesions < 2cm remains controversial, however in our series, patients with SEL within this size range had no clinical sequelae and no EUS findings of concern during follow-up of at least one-year.

EUS imaging diagnosis (n)	Size of lesion <10mm	Size of lesion 10-20mm	Size of lesion >20mm	Total
Probable GIST	1	6	14	21
Benign lesion	5	15	1	21
Indeterminate	0	0	4	4
Pancreatic rest	1	5	0	6
Lipoma	1	3	1	5
Suspicion of malignancy	0	0	5	5
Cyst	0	0	3	3
Normal	1	0	0	1
Polyp	1	2	0	3

[Table 1. EUS results according to size]

Disclosure: Nothing to disclose

P2013 CLINICAL IMPACT OF ENDOSCOPIC SUBMUCOSAL DISSECTION USING CLUTCH CUTTER WITH OVER-THE-SCOPE-CLIP CLOSURE FOR SUPERFICIAL NON-AMPULLARY DUODENAL EPITHELIAL TUMOR

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Introduction: Endoscopic submucosal dissection (ESD) for superficial non-ampullary duodenal epithelial tumor (SNADET)is often caused high rate of delayed complications.We reported that ESD using a scissor-type knife was efficient for gastrointestinal tumors andESD with prophylactic laparoscopic closure is one of the minimally invasive treatments for SNADET. In contrast, there have been some reports with regard to the usefulness of the over-the-scope clip (OTSC) for prevention of delayed complications after endoscopic treatment.

Aims & Methods: The consecutive patients with SNADET who underwent ESD at the hospital of Kyoto Prefectural University of Medicine were retrospectively enrolled between January 2009 and April 2019.The inclusion criteria were SNADETs larger than 10mm without submucosal invasion with a low risk for lymph node metastasis clinically. We had mainly performed ESD using a needle-type knife (Flush Knife) between January 2009 and September 2017, or using a scissor-type (Clutch Cutter) between October 2017 and April 2019. The mucosal defect was prophylactically closed using conventional clips, laparoscopic hand-saw suturing, or OTSC.

The primary endpoint was to evaluate the rate of en block resection, intra-operative complications (perforation and bleeding) between Flush Knife cases and Clutch Cutter cases. The secondary end point was to evaluate the rate of delayed complications among three closing methods. All patients provided written informed consent.

This study was approved by the ethical committee of Kyoto Prefectural University of Medicine.

Results: A total of 77 lesions in 75 patients (male/female 54/23 and median age 67 years) were resected by ESD. There were 37 and 40 cases resected using the Flush Knife and the Clutch Cutter, respectively. Moreover, there were 14, 13, and 50 cases using conventional clip, laparoscopic hand-sewn suturing, and OTSC for prophylactic closure of the mucosal defect after ESD, respectively. Histopathological diagnosis (adenoma/ T1a cancer/ T1b cancer) in Flush Knife and Clutch Cutter cases revealed 2/33/2 and 1/34/5, respectively. In Flush Knife and Clutch Cutter cases, the rate of R0 resection was 83.8% and 97.5%, respectively, with no significant difference. Median resection time in Clutch Cutter cases was significantly shorter than that in Flush Knife cases (40 min and 54 min, respectively, P< 0.01). The rates of complete closurewere 78.6%, 92.3%, and 98.0% for the conventional clip, the laparoscopic closure, and OTSC, respectively, with no significant difference (P=0.13).

However, the closing time for OTSC was significantly shorter than that of the conventional clip and the laparoscopic closure (P< 0.01). Adverse events such as delayed perforation and delayed perforation was 15.4%,

7.7%, and 2.3%, and 0%, 0%, and 2.3% for the conventional clip, the laparoscopic closure, and OTSC, respectively, with no significant difference (P=0.56 and P=1).

Conclusion: ESD using Clutch Cutter with OTSC closure is safe and feasible for the less invasive treatment of SNADET.

Disclosure: Yuji Naito received collaboration research funding from Fujifilm Medical Co., Ltd. (J132001115, J132001139). Naohisa Yoshida received a research grant from Fujifilm Medical Co., Ltd. (J162001222). Yoshito Itoh were affiliated with a department that was partially funded by Fujifilm Medical Co., Ltd. (J082003006).

P2014 PRECEDING ENDOSCOPIC SUBMUCOSAL DISSECTION DOES NOT AFFECT FOR THE PROGNOSIS OF PATIENTS WITH GASTRIC CARCINOMA WITH SUBMUCOSAL DEEP INVASION AFTER ADDITIONAL SURGERY: A PROPENSITY SCORE-MATCHED ANALYSIS

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Introduction: In Japan, the guidelines for gastric cancer treatment specify several criteria for curative resection of endoscopic submucosal dissection (ESD), and additional surgery after endoscopic ESD is recommended for all patients who did not meet the curative criteria for gastric cancer. The submucosal deep invasion (SM-d; depth of submucosal invasion≧500μm) is one of the risk factors for the predicted lymph node metastasis, and is used in the new curative criteria "eCura system" in the Japanese Gastric Cancer Treatment guidelines 2018 (ver.5). However, the data about the long-term outcomes of the preceding ESD for the patients with pathological SM-d (pSM-d) gastric cancer is insufficient. In this study, we analyzed the influence of preceding ESD on the prognosis of patients with pSM-d gastric cancer after additional surgery using propensity score-matching.

Aims & Methods: We retrospectively assessed 316 consecutive patients with 319 pSM-d gastric cancers who underwent ESD prior to additional surgery or surgery alone between February 2002 and February 2017 at the Hiroshima University Hospital. Of the patients after ESD, patients who did not meet curative criteria of the guidelines were advised to undergo additional surgery. Of the 316 patients, 63 patients were treated by ESD alone because of various reasons (refusal to surgery, comorbidity and/or advanced age), and they were excluded. Finally, 248 patients with pSM-d gastric cancer who underwent ESD prior to additional surgery (Group A: n=101) or surgical resection alone (Group B: n= 147) were included in this study. Propensity score-matching was used to control for potential confounders. After matching the propensity scores, we analyzed pathological characteristics between the 2 groups and the prognoses of patients with≧60 month follow-up period was analyzed.

Results: The baseline characteristics before propensity score matching were following: There were significantly more male in Group A than Group B, and the patients in Group A were significantly older than the patients in Group B. A higher proportion of patients in group B had tumors located in the middle third of the stomach. Likewise, depressed type tumors and undifferentiated type tumors in Group B were significantly more than tumors in Group A, the mean tumor diameter in Group B were significantly larger than that in Group B and the mean depth of submucosal invasion in Group B was significantly deeper than in Group A. The en bloc resection rates in Group A were 91% (93/102) and the rates of vertical margin positive were 23% (23/102). Perforation occurred in 5% (5/102) and all cases could be improved by conservative treatment. Local recurrence had not occurred but metastasis to lymph nodes or other organs occurred in 2% (2/102) in Group A and 3% (4/147) in Group B. Propensity scores were calculated using a logistic regression model, and the variables included in the model were age, sex, tumor size, and gross type in Group A. After propensity score-matching, 80 patients in group A and 80 patients in group B were picked up. There were no significant differences in 5-year overall survival rates (87.5% vs. 91.2%) and 5-year disease-specific survival rates (96.3% vs. 96.4%) after treatment of pSM-d gastric cancer between 2 groups.

Conclusion: Preceding ESD for patients with pSM-d gastric cancer did not affect their clinical outcomes adversely after additional surgery.

Disclosure: Nothing to disclose

P2015 GERMLINE MUTATIONS IN TWO FAMILIAL EARLY-ONSET GASTRIC CANCER FAMILIES

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Introduction: Gastric cancer (GC) is highly heterogeneous and most cases are sporadic. While only 10% cases showed family aggregation overall, the frequency of hereditary GC can rise up to 25% in early-onset GC patients. At present, the only known cause of hereditary diffuse gastric cancer is *CDH1* germline mutation in the Caucasian population. Recent studies using next-generation sequencing have identified several recurrent somatic genes mutated in sporadic GC. However, germline mutations of familial gastric cancer (FGC) have not been thoroughly investigated in Chinese patients.

Aims & Methods: We searched our previously published cohorts of 152 young GC patients1 and identified two FGC families. In each family, two patients were re-admitted to our hospital. Patients' demographics, clinical results, detailed family history, and endoscopic-pathological findings were gathered and analyzed. Patients' peripheral blood was collected to extract DNA for whole-genome sequencing. The sequencing data were aligned with the reference genome sequence, filtered out synonymous alterations, and compared with previously published results in the literature and the TCGA data of the Unites Stated National Institute of Health.

Results: In four patients (two male patients and two female probands, average age: 50.2 years), three had poorly differentiated adenocarcinoma with mixed mucinous and signet ring carcinoma components; the other was moderately differentiated adenocarcinoma in the cardia. Tumor stages ranged from pI to pIIA. All 4 patients were well at the last follow up. Whole-genome sequencing demonstrated 8 shared non-synonymous SNPs and Indels among all four patients, 4 unique variations shared in the first family and 7 in the second family. Go analysis showed that the genes for cytoskeleton, actin binding, myosin complex, keratin filament, cytoskeletal protein binding and intercellular non-membrane-bounded organelle terms were significantly associated with FGC. Two germline genes, 1) Leukocyte immunoglobulin-like receptor subfamily A member 4 (*LILRA4*) with a missense mutation (NM_012276.4:c.953-2A>G), 2) Myomesin-2 (*MYOM2*) with a missense mutation (NM_003970.3:c.3695A>G), were validated by PCR Sanger Sequencing. No CDH1 mutation or p53 alterations were found in any 4 Chinese patients.

Conclusion: These findings showed that 2 germline genes, *LILRA4* and *MYOM2*, may act as tumor suppressor genes and might be used as a diagnostic marker for FGC. Further validation of these two genes mutations in FGC is obligatory and on-going.

References: 1 Fan Zhou#, Jiong Shi, Cheng Fang, Xiaoping Zou*, Qin Huang*. Gastric Carcinomas in Young (Younger than 40 Years) Chinese Patients: Clinicopathology, Family History, and Postresection Survival, Medicine (Baltimore), 2016, 95(9): e2873.

Disclosure: Nothing to disclose

P2016 THE PREVALENCE AND SIGNIFICANCE OF JEJUNAL POLYPOSIS AFTER DUODENECTOMY IN FAMILIAL ADENOMATOUS POLYPOSIS

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Introduction: Duodenal adenocarcinoma is the second leading cause of cancer in familial adenomatous polyposis (FAP). Spigelman stage (SS) of duodenal polyposis predicts cancer risk. Advanced SS requires consideration of duodenal resection. Post-duodenectomy data indicate polyps occur in the post-anastomotic jejunum, distal to the flow of bile, but limited data exists regarding their significance. Our study aims to evaluate the prevalence, natural history, and severity of polyposis of the jejunum after duodenectomy in patients with FAP.

Aims & Methods: We identified consecutive FAP patients following duodenal resection, including Whipple procedure, pancreas-sparing duodenectomy (PSD), or segmental duodenectomy, at Cleveland Clinic between 08/1978 and 01/2018 from the David G. Jagelman Inherited Colon Cancer Registries. Patients without endoscopic follow up data were excluded. Medical records were used to determine demographics, time to diagnosis of jejunal polyps, length of post-operative endoscopic follow up, and maximal SS of jejunal polyposis (neo-Spigelman stage). The Spigelman and neo-Spigelman stage (0-IV) was calculated according to cumulative points (1,2,3) for each category within the following characteristic: largest polyp size (1-4 mm, 5-10 mm, > 10 mm), polyp number (1-4, 5-20, > 20), histology (tubular adenoma, tubulovillous adenoma, villous adenoma), degree of dysplasia (1 for low grade, 3 for high grade). Stage I is 1-4 points, II is 5-6 points, III is 7-8 points and IV is 9-12 points.

Results: 64 patients were identified; mean age 61.7 ±12.3 years, 53% male, 83% white. 28% underwent Whipple, 61% PSD, and 11% segmental duodenectomy. Advanced polyposis (81%, SS III-IV) was the most common indication for surgery. Post-operatively 38/64 (59%) developed jejunal polyposis (Table 1), with median time to diagnosis of 55 months and follow up time of 127 months. On most recent endoscopy, neo-Spigelman stage was I in 29%, II in 50%, III in 18.4%, and IV in 2.6%. No cases of high-grade dysplasia or carcinoma were noted during surveillance. 48% of jejunal polyps were treated with endoscopic resection or ablation. One patient with neo-Spigelman stage III jejunal polyposis had Whipple procedure 21 years after initial PSD for progressive polyposis of the jejunum, with surgical specimen demonstrating high grade dysplasia.

		Number of patients (%)
Time to diagnosis, median months [Q1, Q3]		55 [22, 84]
Duration of post-operative endoscopic follow up, median months [Q1, Q3]		127 [78, 175]
Neo-Spigelman stage	Stage I	11 (29)
	Stage II	19 (50)
	Stage III	7 (18.4)
	Stage IV	1 (2.6)
Carcinoma/ HGD on surveillance biopsy		0
Management of jejunal polyposis	Surveillance	18 (47.4)
	Endoscopic resection/ ablation	19 (50)
	Surgical resection	1 (2.6)
Q1 first quartile; Q3 third quartile; HGD high grade dysplasia		

[Table 1. Jejunal polyposis detected on post-operative surveillance (N=38)]

Conclusion: In spite of surgical management of duodenal polyposis, jejunal polyposis occurs in the majority of patients after surgical duodenectomy and is advanced in 1 in 5 patients. Further studies are required to evaluate the significance and risk of polyposis of the jejunum in FAP patients. In the meantime, continued endoscopic surveillance is indicated.
Disclosure: Nothing to disclose

P2017 THE PREVALENCE AND SIGNIFICANCE OF DUODENAL BULB POLYPOSIS AFTER DUODENECTOMY IN PATIENTS WITH FAMILIAL ADENOMATOUS POLYPOSIS

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Introduction: Consideration of prophylactic duodenal surgery is recommended in patients with Familial Adenomatous Polyposis (FAP) and Spigelman stage IV duodenal polyposis to prevent cancer. Pylorus-sparing approaches of pancreatoduodenectomy (PD) and pancreas-sparing duodenectomy (PSD) are often performed over a complete Whipple procedure. Pylorus-sparing techniques, with the benefit of reduced rates of gastric

dumping syndrome, create a duodeno-jejunal anastomosis at the apex of the duodenal bulb, which remains at risk of recurrent adenoma. Our study aims to evaluate the prevalence and severity of polyposis of the duodenal bulb after pylorus-sparing duodenectomy.
Aims & Methods: We identified consecutive FAP patients following duodenal resection (PD, PSD, or segmental duodenectomy) at Cleveland Clinic, between 05/1992 and 01/2018 from the David G. Jagelman Inherited Colon Cancer Registries. Those who had a pylorus-sparing procedure with a remnant duodenal bulb on post-operative anatomy were included in the study. Those without endoscopic follow up data after surgery were excluded. Medical records data was used to determine time to occurrence, maximal size, histology, and dysplasia of duodenal bulb polyps in patients after duodenal resection.
Results: 55 FAP patients had a pylorus-sparing duodenal resection and were included in the study (20% PD, 69% PSD, 11% segmental duodenectomy). Mean age was 61.5 ±12.6 years, 56% were male, and 82% were white. 6/55 (11%) patients with duodenal bulb polyposis were identified (Table 1). All patients were post-PSD. Median time to polyp occurrence in the duodenal bulb was 43 months [IQR 19-62]. All 6 patients developed large polyps > 20 mm. 1 of 6 had tubulovillous adenoma, the remainder tubular adenoma on biopsy. Endoscopic resection with submucosal injection was attempted on 5 of 6 cases, and complete resection was achieved in one case. The remaining 4 lesions demonstrated no lift on submucosal injection. In one case, initial endoscopic resection was successful, but recurrent adenoma at the site of resection after 12 months was not amenable to resection due to fibrosis. There were no cases of carcinoma or surgical resection for duodenal bulb polyps.

Patient	Time to polyp detection (months)	No. of post operative EGDs	Maximal size (mm)	Maximal histology	Success of endoscopic therapy
1	19	16	60	TA	No
2	43	4	20	TA	Yes
3	56	2	40	TA	No
4	62	12	50	TA	No
5	14	7	25	TVA	No
6	105	9	35	TA	Not attempted

[Table 1: Bulb polyp characteristics (N=6)]

Conclusion: A minority of patients develop polyps in the duodenal bulb after pylorus-sparing duodenectomy. They are difficult to manage endoscopically due to failure of endoscopic resection with frequent non-lifting with submucosal injection. This could be secondary to the proximity to the surgical anastomosis, prevalence of Brunner's glands in the proximal duodenum, and previous attempted removal. Optimal approaches to prevent duodenal bulb polyps after pylorus-sparing duodenectomy are needed.
Disclosure: Nothing to disclose

P2018 VONOPRAZAN VERSUS PROTON PUMP INHIBITORS FOR THE MANAGEMENT OF GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION-INDUCED ARTIFICIAL ULCER: A SYSTEMATIC REVIEW WITH META-ANALYSIS

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Introduction: Vonoprazan, a novel potassium-competitive acid blocking agent, has been used in the management of endoscopic submucosal dissection (ESD)-induced artificial ulcers. This study aimed to perform a systematic review and meta-analysis for the comparison of the effects of vonoprazan and proton pump inhibitors (PPI) in treating ESD-induced artificial ulcers and preventing delayed bleeding in randomized controlled trial and cohort studies.
Aims & Methods: We searched OVID-MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), Google Scholar, and clinical trial registries in April 2018 to identify all studies that assess and compare the effects of vonoprazan and PPI in treating ESD-induced artificial ulcers and

preventing delayed bleeding. Primary outcome of ulcer healing rate and secondary outcomes of shrinkage rate, ulcer size, and delayed bleeding were studied.

Results: A total of 1265 patients from 12 studies was included in the final analysis. Healing rate at 4 weeks post-ESD was significantly higher in the vonoprazan group than in the PPI group (RR 1.20 (1.03-1.40)). However, healing rate at 8 weeks post-ESD was significantly higher in the PPI group than in the vonoprazan group (RR 0.68 (0.48-0.97)).

There was no evidence of significant difference between groups in shrinkage rate at 4 weeks post-ESD, shrinkage rate at 8 weeks post-ESD, delayed bleeding, ulcer size at 0 weeks post-ESD, and ulcer size at 8 weeks post-ESD.

Conclusion: There was no substantial difference in ulcer healing and post-ESD bleeding between vonoprazan and PPIs. However, vonoprazan more rapidly and effectively treated artificial ulcers after ESD than did PPIs.

References: J Neurogastroenterol Motil. 2019 Jan 31;25(1):6-14. doi: 10.5056/jnm18139. Mori H, Suzuki H. Role of Acid Suppression in Acid-related Diseases: Proton Pump Inhibitor and Potassium-competitive Acid Blocker. J Neurogastroenterol Motil. 2019 Jan 31;25(1):6-14.

Disclosure: Nothing to disclose

P2019 WITHDRAWN

P2020 THE VALUE OF ENDOSCOPIC BIOPSIES IN ROUTINE UPPER GASTROINTESTINAL ENDOSCOPY

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Introduction: The United Kingdom BSG and AUGIS quality standards in upper gastrointestinal endoscopy recommend taking biopsies for histological examination to diagnose inflammatory, pre- or malignant lesions which may or may not be visible to the naked eye [Beg, Gut 2018]. This may increase the duration and cost of the procedure and potentially reduce the focus on mucosal inspection. This study aimed to investigate the diagnostic value (changes in diagnosis and contribution to management) added by histology and its cost.

Aims & Methods: Patients under going consecutive diagnostic gastroscopies performed by four fellows were recruited. Incomplete, surveillance or therapeutic procedures, procedures for dysphagia and those arranged in order to obtain histology (eg. positive coeliac serology) were excluded. Biopsies were performed according to BSG quality standards [Beg, Gut 2018]. The utility of biopsies (changes in diagnosis and contribution to management) were examined from endoscopic and histological findings.

Results: Of 509 patients examined, 314 were included. Gastroscopies was performed for dyspepsia (66%), anaemia (26%), weight loss (16%), diarrhoea (2%) and vomiting (1%). Biopsies occurred in 86% of patients with an mean of 1.5 samples per patient biopsied. Biopsy sampling provided additional pathological information not evident at endoscopy in 28% of cases. However, if benign pathologies are excluded (mostly chemical or Helicobacter gastritis or duodenitis), this falls to 6.7% (n=18: dysplasia n=3, adenocarcinoma n=1, gastric intestinal metaplasia (GIM) n=7, villous atrophy (VA) n=2, Barretts n=5). In total, management change occurred in 19% consequent on histological findings, but this falls to 12% (n=34: adenocarcinoma n=2, dysplasia n=3, GIM, n=10, Barretts n=15, VA n=3, peptic stricture n=1) where Helicobacter pylori (which can be detected by other non-invasive methods) eradication is excluded.

Fifty seven focal lesions were biopsied where dysplasia or cancer was diagnosed in 7% (1/14 oesophageal, 2/35 gastric and 1/8 duodenal). Barretts (58% vs 0% p=0.02), GIM (81% vs 18% p=0.05) and VA (20% vs 1% p=0.02) were found more commonly in abnormal compared to normal mucosa. The overall cost of tissue sampling approximates to £17,100 (£82 per person). Routine biopsies of patients with only normal mucosa costed over £3,500.

Conclusion: Although 86% undergoing gastroscopy have biopsies taken, contributing to aetiopathological understanding in 28%, only a small minority (6.7%) have pre-malignant or malignant pathologies and result in a change in management in only 12%. Non-targeted biopsies are of limited value and costly when sampled from normal mucosa.

References: Beg S, Ragunath K, Wyman A, et al. Quality standards in upper gastrointestinal endoscopy: a position statement of the British Society of Gastroenterology (BSG) and Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland (AUGIS). Gut 2017; 66(11): 1886-99.

Disclosure: Nothing to disclose

P2021 ROUTINE EXAMINATION OF STOMACH AND DUODENUM IN PATIENTS ATTENDING FOR BARRETT'S SURVEILLANCE- IS IT REALLY INDICATED?

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Introduction: Patients undergoing OGD for Barrett's surveillance have examination upto D2 before detailed examination of Barrett's mucosa and Seattle protocol biopsies. This may lead to less time dedicated to examine Barrett's segment potentially leading to reduction in the yield of dysplasia. Most patients undergo such procedures with throat spray or sedation, hence potentially reducing the compliance of patients towards the end of procedure when examination of Barrett's segment is performed in routine practice.

Aims & Methods: Our aim is to find out what percentage of surveillance OGDs incidentally pick up significant pathologies in stomach and duodenum (cancer, pyloric stenosis, polyp with dysplasia, benign ulcer and varix) compared with their index procedures; whether we could potentially avoid examination of stomach and duodenum during surveillance procedures and focus this time on longer inspection of Barrett's segment

We retrospectively analysed all OGD reports retrieved from hospital's Endoscopy reporting tool for patients who underwent OGD within last 10 years (January 2009- December 2018) for Barrett's surveillance. Data was extracted electronically using the endoscopy audit tool on the reporting system. We analysed all these OGDs for presence of significant pathologies in stomach and duodenum that were found incidentally. Procedures with Barrett's oesophagus as index diagnosis or OGD earlier than the proposed surveillance interval for other indications were excluded. Reports of all procedures with a diagnosis of Barrett's oesophagus over a period of one year(2018) were individually validated manually to confirm accuracy of the electronic data set and to get a gross estimate of surveillance procedures over 10 years.

Results: Yearly procedure count was 155 patients undergoing Barrett's surveillance OGD which approximates to about 1550 procedures over 10 years. The median age was 68 years. Average surveillance interval was 3.45± 1.12 years. There were no cases of gastric or duodenal cancer, however 1 patient had incidental follicular lymphoma (0.06%), single case of gastric adenoma with focal HGD (0.06%) and 2 patients with duodenal adenoma (0.1%) were found over 10 years. Incidental benign ulcers (gastric and duodenal) were found in 4% (n =61) and gastric varices in 5 patients (0.3%, all with known chronic liver disease).

Conclusion: Our study demonstrates that incidental findings of significant pathology during surveillance OGD for Barrett's oesophagus is very rare. Hence in patients undergoing Barrett's surveillance, a focussed examination of oesophagus and gastro-oesophageal junction rather than examination of stomach and duodenum may be more appropriate with an aim to increase pick up rates of dysplasia. Previous studies have demonstrated that longer inspection time is associated with increase in detection rate of high grade dysplasia and cancer (1).

A shortcoming in our study is the retrospective nature of data. We also noted a longer surveillance interval than what we expected. This could be explained by surveillance procedures performed outside our local authority, but this would not have influenced our results other than the overall numbers. We do not have any data regarding separate time intervals for the completion of OGD and examination of Barrett's segment. We would recommend detailed prospective data collection for these aspects. Multi-centre data may further validate the above results.

References: 1. Longer inspection time is associated with increased detection of high-grade dysplasia and esophageal adenocarcinoma in Barrett's esophagus. Gupta, Neil et al. GIE , Volume 76 , Issue 3 , 531 - 538

Disclosure: Nothing to disclose

P2022 WHAT AFFECTS THE SATISFACTION AND EXPERIENCE OF OUR PATIENT DURING UPPER-ENDOSCOPY: AN EXPLORATORY RESEARCH

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Introduction: Recent guidelines on quality in endoscopy recommend a regular assessment of patient experience. Nevertheless, there is a paucity of data in this research area. Most studies did not question the experience from the patient perspective. The aim of this study was to develop a satisfaction questionnaire in order to identify the main elements affecting patient experience and satisfaction during an upper-endoscopy.
Aims & Methods: Based on literature review and information collected from exploratory interviews with patients, before and after the examination, a satisfaction questionnaire was created. This questionnaire includes an interactive part with 11 variables about patient experience classified by importance by the patients. This questionnaire was administered by the same interviewer to outpatients undergoing upper-endoscopy after discharge from Saint-Pierre Hospital, Brussels, Belgium from the 14th of march to the 4th of april 2019. An informed consent validated by local ethics committee was presented before each interview. The statistical analyses were performed with IBM SPSS.
Results: Out of the 54 consecutive interviewed patients, 52 fully responded (35 women). 46.1% of the sample was aged between 26 and 45 years old. The mean of the global satisfaction was 8.82 out of 10 with a standard deviation of 0.989. Perceived « Kindness of the care team », « Professionalism of the care team » and « Explanation of the results right after the examination » were considered as the 3 most important factors influencing the global satisfaction of the patient, by respectively 84.6%, 57.7% and 50% of the sample. On the other hand, « Fasting the day of the exam », « Waiting time before the exam » and « Pain » were considered as the 3 least important factors influencing the global satisfaction of the patient, by respectively 57.7 %, 57.7% and 36.5%. There is a statistically significant difference in rank between both the 11 variables (p< 0.001), and the 3 most important factors (p=0.001). There is a significant difference between « Kindness of the care team » and « Professionalism of the care team » (p=0.006).
Conclusion: Patient satisfaction is a key quality indicator of upper-endoscopy. It is necessary to draw attention on how patients feel before and after an endoscopy procedure and not only focus on the exam itself. Our interesting results show that kindness and communication stand out as the most important factors of patient satisfaction during upper-endoscopy. Larger studies should confirm these results in order to design a validated questionnaire.
References: Bisschops, R., Areia, M., Coron, E., Dobru, D., Kaskas, B., Kuvaev, R., Pech, O., Ragunath, K., Weusten, B., Familiari, P., Domagk, D., Valori, R., Kaminski, M., Spada, C., Bretthauer, M., Bennett, C., Senore, C., Dinis-Ribeiro, M. and Rutter, M. (2016). Performance measures for upper gastrointestinal endoscopy: a European Society of Gastrointestinal Endoscopy (ESGE) Quality Improvement Initiative. Endoscopy, 48(09), pp.843-864. Brown, S., Bevan, R., Rubin, G., Nixon, C., Dunn, S., Panter, S., & Rees, C. (2015). Patient-derived measures of GI endoscopy: a meta-narrative review of the literature. Gastrointestinal Endoscopy, 81(5), 1130-1140.e9.
Disclosure: Nothing to disclose

H. Pylori III
09:00-14:00 / Poster Exhibition - Hall 7

P2023 DIFFERENTIAL *HELICOBACTER PYLORI* PLASTICITY IN THE GASTRIC NICHE OF SUBJECTS AT INCREASED GASTRIC CANCER RISK

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Introduction: Histopathological changes in gastric mucosa during *Helicobacter pylori* (HP) infection can be associated with HP fitness adaptation through genetic events leading to reduced virulence as precancerous lesions develop.
Aims & Methods: In this study we dissected the heterogeneity of the HP genotypes in patients (pts) at higher gastric cancer (GC) risk to understand if they exploit an increased genetic stability and consequent virulence. 14 Autoimmune Gastritis (AG), 25 First Degree Relatives of GC pts (FDR), 39 GC and 13 Dyspeptic pts without familiarity (D) were investigated. Gastric biopsies were grown in HP selective medium; HP was identified by standard methods. As representation of HP strain heterogeneity, 10-12 colonies-forming-unit (CFU)/pt were isolated and analyzed by PCR. A total of 915 CFU were examined. Three CagPAI loci (*cagA, cagE, virB11*) were studied as proxy marker of CagPAI plasticity. *VacA s, i* and *m* regions, *homB/A* alleles were also evaluated as markers of additional virulence. A stable CagPAI was defined by simultaneous presence of *virB11, cagE, cagA* genes in ≥9 isolated CFU/pt. Increased virulence was determined with ≥9CFU with *vacA s1i1mx* aplotype (vs. *sxi2m2* or *vacA* deletion) or ≥9CFU with *homB* gene. Histological grading of gastritis was made by Sidney system. OR and 95% confidence intervals (C.I.) were calculated.
Results: FDR status was associated with significant higher atrophy (OR=6.3, 95%C.I.:1.2-31.9) and neutrophil infiltration (activity) (OR=7.2, 95%C.I.:1.2-44.7) than D, while metaplasia and mononuclear cell infiltration were comparable. Moreover, FDR showed a reduced risk to host mixed infections (OR=2.7, 95%C.I.:0.03-0.81). Additionally, FDR exhibited a higher frequency of subtypes carrying the CagPAI-vacA s1i1mx-homB positive profile (OR=2.7, 95%C.I.:1.7-4.4). Conversely, AG patients presented a lower frequency of subtypes carrying a stable CagPAI and vacA s1i1mx.
Conclusion: These results underline H. pylori different plasticity in the gastric niche of populations at risk of GC, suggesting a different host-bacterium interaction capacity that might affect the outcome of the infection.
Disclosure: Nothing to disclose

P2024 HELICOBACTER PYLORI CAGA PROMOTES GASTRIC CANCER TUMORIGENESIS VIA THE P-ERK/AUF1/GKN1 PATHWAY

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Introduction: Helicobacter pylori (HP) was the carcinogen of gastric cancer ,especially the cagA-positive HP. Gastrokine1(GKN1), an important tumor suppressor, is downregulated in HP infected gastric mucosa. However, the underlying mechanism that HP cagA promotes carcinogenesis by influencing the anti-tumor gene GKN1 was not clearly elucidated.
Aims & Methods: We investigated whether GKN1 was downregulated during HP infection in vivo and in vitro by real-time PCR , western blot and immunohistochemistry. The AUF1 gene was knocked down in GES-1 and BGC-823 cells , we measured GKN1 expression by real-time PCR and western blot to find their inner relationship.
In addition , we conducted RNA-Protein Pull-Down and RNA-immunoprecipitation to judge whether AUF1 can bind GKN1. By measuring turnover and luciferase activity ,we explored the GKN1mRNA stability while AUF1 was knockdown. During HP infection ,we measured AUF1, GKN1 and p-ERK expression. We also observed the cell proliferation, migration, cell cycle

when AUF1 was knockdown. Furthermore, we conducted the cagA knockout HP and measured the expression of AUF1, GKN1 and p-ERK.

Results: we suggested that GKN1 was downregulated during HP infection. In addition, GKN1 expression was negatively correlated with AUF1. RNA-Protein Pull-Down and RNA-immunoprecipitation experiment proved AUF1 can bind with GKN1mRNA. Further investigation revealed that AUF1 can influence the GKN1mRNA stability to regulate its expression. Moreover, We observed AUF1 was induced during HP infection and biological function studies demonstrated that AUF1 can promote cell proliferation ,migration and accelerated G1/S phase transition. What's more, HP cagA can activate the p-ERK/AUF1/GKN1 pathway and the expression of AUF1 and GKN1 can be rescued by p-ERK inhibitor.

Conclusion: These data showed that HP cagA may promote gastric cancer tumorigenesis via the p-ERK/AUF1/GKN1 pathway. The AUF1/GKN1 axis might serve as a prognostic biomarker as well as a novel potential target in the treatment of gastric cancer.

Disclosure: Nothing to disclose

P2025 OPTIMUM SECOND-LINE REGIMENS FOR *HELICOBACTER PYLORI* ERADICATION: INTERIM RESULTS OF AN ON-GOING COCHRANE SYSTEMATIC REVIEW

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Introduction: *H. pylori* infection represents a significant healthcare burden, and first-line eradication treatment often fails, mainly due to antibiotic resistance.

Aims & Methods: To evaluate the effects of second-line treatments on *H. pylori* (Hp) eradication through systematic review of randomised controlled trials (RCTs).

We searched electronic databases and other sources up to January 2019. Selection criteria: RCTs comparing the efficacy of at least two different second-line Hp treatments. The previous failed first-line regimen should have contained at least two antibiotics. We excluded studies assessing a second-line therapy based on bacterial antibiotic susceptibility or resistance or the use of any type of adjuvant in any of the treatments. We determined the effects on Hp eradication rates based on intention-to-treat analysis. We attempted to combine results by meta-analysing risk differences (RD). We stratified results by first-line therapy used. Meta-analysis was conducted with at least two studies based on the Mantel-Haenszel method. We planned to explore sources of heterogeneity by subgroup analysis. We assessed risk of bias of the included studies with the Cochrane risk-of-bias tool for RCTs.

Results: Up to now, the review has included 41 RCTs. In total, we have evaluated 39 comparisons of second-line different antibiotic combinations, which are stratified by five different first-line therapy failures. *Effects on Hp eradication rates:* The table below summarises the meta-analyses performed for the 9 second-line therapy comparisons after failure of a first-line standard triple therapy. Two comparisons improved eradication rates. Triple therapy with amoxicillin and metronidazole was more effective than triple with amoxicillin and levofloxacin (2 studies, I^2=0%; High risk of bias). Also, standard bismuth quadruple therapy during 14 days was more effective as compared to 7 days (3 studies, I^2=53%; High risk of bias).

Experimental arm	Control arm	RD [95%CI]	Nº of studies1
PPI + A + M	PPI + A	0.01 [-0.23, 0.22]	3
PPI + A + M	PPI + A + L	0.21 [0.09, 0.33]*	2
PPI + A + Ma	PPI + A + Mb	0.03 [-0.08, 0.14]	3
E + A + Mox	E + M + Tc + TDB	0.03 [-0.16, 0.09]	3
O + Bs + A + M	O + A + Tc + Bs	0.12 [-0.01, 0.24]	2
PPI + M + Tc + Bs (14 days)	PPI + M + Tc + Bs (7 days)	0.16 [0.07, 0.26]*	3
PPI + L + Azit	PPI + M + Tc + Bs	-0.08 [-0.40, 0.24]	2
PPI + L + T	PPI + M + Tc + Bs	0.04 [-0.36, 0.45]	2
PPI + A + L	PPI + M + Tc + Bs	0.04 [-0.27, 0.36]	3

1- Number of studies included in each comparison; RD-risk difference; CI-confidence interval; PPI-proton pomp inhibitor; A-amoxicillin; Azit- azithromycin; Bs-bismuth salts; C-clarithromycin; E-esomeprazole; L-levofloxacin; Mox-moxifloxacin; M-metronidazole; Ma-metronidazole 750mg; Mb-metronidazole 500mg; O-omeprazole; T-tinidazole; Tc-tetracycline; TDB-tripotassium dicitrate bismuthate; * significance level p≤0.05

[Meta-analyses for the 9 second-line therapy comparisons after failure of a first-line standard triple therapy]

Conclusion: There is an amalgam of anti-*H. pylori* second-line treatments used in the clinical setting. After a first-line standard triple therapy (PPI, clarithromycin and amoxicillin) failure, triple therapy with a PPI, amoxicillin and metronidazole showed higher eradication rates than the combination of a PPI, amoxicillin and levofloxacin. Standard quadruple therapy during 14 days, as compared to 7 days, showed better results. However, these are preliminary results and need to be read cautiously due to the limited number of studies included for each comparison and their high risk of bias.

Disclosure: Nothing to disclose

P2026 REAL LIFE DATA EVALUATING HELICOBACTER PYLORI ERADICATION RATES AFTER APPLICATION OF MAASTRICHT V GUIDELINES

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Introduction: Helicobacter pylori (Hp) eradication is challenging, especially in high clarithromycin (Cla)-resistant areas where the classical triple therapy has to be abandoned.

Aims & Methods: Evaluation of real-life data for Hp eradication in patients who applied Maastricht V treatment guidelines in a high Cla-resistant area. Consecutive patients evaluated prospectively for Hp eradication after receiving 1st, 2nd or 3rd line treatments according to Maastricht V guidelines during a period of 31 months (08/2016-03/2019). Cla-resistance was 30% in our population by means of culture and/or PCR. Hp eradication was evaluated with ^{13}C urea breath test (UBT) at least 4 weeks after treatment. Medications offered for 1st line treatment were: Esomeprazole (Eso) 40mg, Amoxicillin (Amo) 1gr, Metronidazole (Metro) 500mg and Cla 500mg all bid in different quadruple combinations or a commercial combination of Bismuth subcitrate potassium, Metro, Tetracycline hydrochloride (BMT) 3 pills qid administered with Eso 40mg bid. For 2nd line they received either Eso and Amo bid plus Levofloxacin 500mg (Levo) qd (Eso/Amo/Levo) or Eso/BMT for 10 days and for 3rd line: only Eso/BMT for 10 days. Results 371 out of 387 patients received treatment according to Maastricht V guidelines, mean age 55.8±14.8 years, 46% males. Overall Hp eradication after the 3 lines of treatment was achieved in 306 patients with an intention to treat (ITT) and per protocol (PP) analysis success rates of 82.5% (95% C.I. 78.6-86.4) and 89.7% (86.5-93.0) respectively. For 1st line treatment 252 received Eso/Amo/Cla/Metro bid for 10 days (CONCO10), 27 received Eso/Amo bid for 7days and then Eso/Cla/Metro bid for another 7 days (SEQ14), 44 received Eso/Amo bid for 7days and then Eso/Amo/Cla/Metro bid for another 7 days (HYBRID14) and 6 received Eso/BMT for 10 days. For 2nd line treatment 34 patients received Eso/Amo/Levo for 10 days and 2 Eso/BMT for 10 days while for 3rd line treatment all 6 received Eso/BMT for 10 days.

Results: Overall 1st line eradication rates for 329 patients were 82.7 (95% C.I. 78.6 - 86.8) in ITT and 90.1 (95% C.I. 86.7-93.4) in PP analysis. Details are depicted in the table.

	CONCO10 (252)	SEQ14 (27)	HYBRID14 (44)	ESO/BMT(6)
ITT%(95%C.I.)	84.5(80.1-89.0)	88.9 (77.0 -100)	65.9(51.9-79.9)	100
PP%(95% C.I.)	90.0 (86.5-94.0)	88.9 (77.0 -100)	87.9(76.7 - 99)	100

[1st Line Treatment]

For second line 26 eradicated with Eso/Amo/Levo [ITT = 76.5% (95% C.I. 62.2-90.7) and PP = 83.9% (95% C.I. 70.9-96.8)] and all 2 (100%) with Eso/BMT while in the 3rd line 6 out of 6 eradicated Hp (100%) with Eso/BMT. Univariate analysis revealed that younger age (OR=3.4) and alcohol consumption (OR=2.12) were associated with non-compliance regarding reevaluation with UBT. 19.6 % of patients reported side effects (16 % dysgeusia, 12% nausea, 8% soft or frequent bowel movements, 1% rush). No patient discontinued treatment due to side effects.

Conclusion:
1) Real life Hp eradication rates are satisfactory in high clarithromycin resistant areas when Maastricht V guidelines are applied
2) The most frequently used 1st line treatment regimen is ten day concomitant with a high eradication rate
3) Bismuth subcitrate combination had a success rate of 100% in all 3 lines of treatment when administered, although limited by low availability in many countries.

Disclosure: Nothing to disclose

P2027 CONCOMITANT THERAPY, SEQUENTIAL THERAPY OR HIGH DOSE ESOMEPRAZOLE AND AMOXICILLIN DUAL THERAPY FOR FIRST LINE HELICOBACTER PYLORI ERADICATION A PROSPECTIVE RANDOMIZED STUDY

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Introduction: The resistance of Helicobacter pylori to antibiotics has increased the need for new first line treatment. The aim of this study was to assess and compare the efficacy and safety of concomitant treatment with sequential therapy and dual therapy with high dose esomeprazole and amoxicillin.

Aims & Methods: This prospective randomized study was performed during July 2016 to September 2018. Consecutive naïve helicobacter pylori infected patients were included. Patients included were randomized and divided into 3 groups using a high dose PPI based on esomeprazole 40mg twice daily:
BT group: dual therapy= PPI + amoxicillin 1g 3/d for 14 days
*SQ group: sequential therapy= PPI + amoxicillin 1g twice daily for 5 days followed by PPI + clarithromycin 500mg and metronidazole 500mg twice daily for 5 days.
*CT group: concomitant therapy= PPI + amoxicillin 1g + clarithromycin 500mg + metronidazole 500mg twice daily for 10 days.
At the end of the treatment, compliance to therapy and reported side effect were evaluated. At least 6 weeks after the end of the treatment a C13 urea breath test (UBT) was performed to assess H. pylori eradication rate.

Results: A total of 393 patients agreed to participate in the study. The Mean age of patients was 43.9 +/- 15 years (16-90 years). Sex ratio was= 1. Groups BT, SQ and CT included respectively 130, 132 and 131 patients. They were comparable in terms of age, sex, clinical and endoscopic presentation. The eradication rate in intention to treat (ITT) was 63.1%, 86. 4% and 90.8% respectively in the BT, SQ and CT groups (P = 0.0001).
The corresponding rate of eradication by protocol was 67. 7%, 88.5% and 95.3% (P = 0.00016). No significant results were seen in the eradication rate between CT and SQ both in PP analysis and in ITT analysis (P= 0.09). The prevalence of the side effects following the concomitant treatment was

38. 2% significantly higher (P = 0.001) than BT group (13. 80%) and SQ group (22%). Therapeutic compliance was 94%, 98.5% and 95. 4% respectively in patients receiving the BT, SQ and CT protocol (P= 0.16).

Conclusion: This study demonstrated that concomitant therapy led to a non-statistically significant over sequential therapy, with higher side effects.

Disclosure: Nothing to disclose

P2028 HIGH TREATMENT SUCCESS OF STANDARD HELICOBACTER PYLORI-ERADICATION REGIMENS DESPITE PROVEN ANTIMICROBIAL RESISTANCE: FOLLOW UP RESULTS OF A PROSPECTIVE MULTICENTER CLINICAL STUDY

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Introduction: Antimicrobial resistance may reduce response to Helicobacter pylori (HP) eradication therapy. Recently, a prospective multicenter clinical study revealed high rates of clarithromycin (21%) and/or chinolone (13%) resistant Helicobacter pylori (HP) species in a large treatment-naïve Austrian patient population.

Aims & Methods: The aim of this subsequent study was to assess the clinical impact of this antimicrobial resistance on the actual HP-eradication treatment success of study subjects. Follow-up data of patients participating in the afore mentioned prospective clinical trial were analyzed regarding HP-eradication treatment regimen, treatment success rates and subsequent HP-eradication therapies. Of note, results of antimicrobial resistance testing (as assessed by real-time PCR in the previous study) were not yet available when subjects underwent individual HP-eradication therapy.

Results: Four study centers provided their follow-up data on a total of 116 HP-positive patients. 108/116 pts. (93%) received HP-eradication treatment: sequential therapy, 58/108 (54%); clarithromycin triple therapy, 26/108 (24%); levofloxacin sequential therapy, 20/108 (19%). Treatment response was tested in 54/108 pts. (50%) by histology, stool antigen or urea breath test. Among these 54 patients, 20 subjects (37%) had been identified to have clarithromycin (15/54, 28%) and/or quinolone (6/54, 11%) resistant HP species. Nevertheless, eradication was successful in 50/54 pts. (93%) including 10 patients with proven antimicrobial resistance against antibiotic compounds used for eradication. Those 4/54 pts. (7%) who failed initial HP-eradication (most likely due to proven clarithromycin resistance) underwent another treatment course of the same eradication regimen and cleared HP upon final investigation.

Conclusion: This follow-up study revealed high success rates of standard HP-eradication therapy despite proven antimicrobial resistance against antibiotic compounds used for eradication. Although reporting a small number of subjects, these results warrant further investigation regarding selection of compounds and treatment duration for HP-eradication therapy in the future.

References: Bilgilier C, Stadlmann A, Makristathis A, Thannesberger J, Kastner MT, Knoflach P, et al. Prospective multicentre clinical study on inter- and intrapatient genetic variability for antimicrobial resistance of Helicobacter pylori. Clin Microbiol Infect. 2018 Mar;24(3):267-272.

Disclosure: Nothing to disclose

P2029 FOURTEEN DAY SEQUENTIAL THERAPY CONTAINING RABEPRAZOLE VERSUS 10 AND 14 DAY CONCOMITANT THERAPY IN THE FIRST LINE TREATMENT OF HELICOBACTER PYLORI INFECTION: AN OPEN LABEL, SINGLE CENTER, RANDOMIZED CLINICAL TRIAL

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Introduction: Helicobacter Pylori infection remains currently a common infection worldwide.

The decline in the efficacy of traditional triple therapies has generated since 2010 new combinations of antibiotics. The last guidelines of Maastricht V recommend concomitant quadritherapy or bismuth quadritherapy to reach an eradication rate of at least 90%. These values remain higher than those obtained with standard sequential therapy, but with a higher cost and more adverse effects.

Aims & Methods: We aimed to compare a modified sequential therapy to 10 and 14 day quadritherapies currently recommended in terms of efficacy, incidence of adverse effects and cost.

We conducted an open-label prospective study at gastroenterology II department in Military teaching hospital of Rabat from January 2016 to March 2019 and randomized patients with confirmed Helicobacter pylori infection to 3 groups (1:1:1): The first group received quadruple therapy of twice-daily (bid) Omeprazole 20mg, Amoxicillin 1g, Clarythromycin 500mg and Metronidazol 500mg for 10days (QT-10), the second group received a 14 day quadruple therapy following the same regimen (QT-14), and the third received an optimized sequential therapy consisting on a bid Rabeprazole 20 mg plus amoxicillin 1g for 7 days, followed by bid Rabeprazole 20 mg, clarithromycin 500 mg and metronidazole 500mg for the next 7days (OST-14). Adverse events (AEs) were recorded throughout the study, and the H.pylori eradication rate was determined 6 weeks after treatment using the 13C urea breath test.

Results: There was no significant difference in relation to demographic, clinical, endoscopic and histologic findings between the three groups.

In intention to treat analysis (ITT), eradication rate was 87%, 92,3% and 95,8% respectively in QT-10, QT-14 and OST-14 groups, with no significant difference between the groups. In the per protocol analysis, and compared to QT-10, QT-14 and OST-14 showed a significant higher eradication rate with 91,2%, 95% and 96,8% respectively (p=0,03). The overall incidence of AEs was also significantly lower in the OST-14 group, compared to QT-10 and QT-14 groups (21,2%, 37,2% and 41,6% respectively, *p=0,02*).

Conclusion: Optimizing standard sequential therapy in terms of duration and using a second-generation Proton Pomp Inhibitor is a safe and effective alternative that allows an eradication rate comparable to those currently recommended by the Maastricht V guidelines, while causing fewer adverse effects and allowing a gain in term of cost. Further studies are needed to substantiate these findings.

Disclosure: Nothing to disclose

P2030 PREVALENCE OF HELICOBACTER PYLORI INFECTION IN PATIENTS WITH FUNCTIONAL DYSPEPSIA AND EFFECTS OF ERADICATION ON SYMPTOMS – URBAN INDIAN SCENARIO

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Introduction: Functional dyspepsia (FD) is classically defined as continuous or frequently recurring epigastric pain or discomfort centred in upper abdomen for which no organic cause can be determined. The last Consensus of an International panel of clinical investigators on gastroduodenal functional disorders (Rome III) recommended Helicobacter Pylori (HP) eradication in all infected patients with non ulcer dyspepsia diagnosed at upper endoscopy, also suggesting non-invasive testing followed by HP eradication (test and treat) in those patients with no alarm features, although many infected patients with FD may not gain symptomatic benefit.

Aims & Methods: Effect of eradication of HP on symptoms of functional dyspepsia is uncertain, and the data in Asian scenario are scanty. The study aimed to see HP positivity rate in patients of functional dyspepsia and primarily the effect of its eradication on symptoms.All patients who were diagnosed with functional dyspepsia of more than 3 months duration were enrolled into this study. Patients of functional dyspepsia were tested for HP infection by the urease breath test by Heliprobe analyser, Sweden. These patients had no alarm symptoms, red flags to warrant an endoscopy. Symptoms were documented on our standard Performa and symptoms on a seven-point Likert scale, ranging from extremely improved compared with the baseline period to extremely aggravated compared with the baseline period.HP positive patients were treated with standard triple therapy for 15 days with amoxicillin, ornidazole and clarithromycin.

Results: HP positivity rate in functional dyspepsia was 274/994 (27.5%). Repeat UBT was performed between 12-14 weeks (off PPI for 2 weeks) 19 patients were lost to follow up in the treatment arm and 86 patients in the HP negative arm at 6 months.At 12 weeks, the eradication rate for HP in triple therapy was 201/255 (78.8%).The patients who were H pylori negative were treated with standard dose PPI and prokinetic (domperidone). On intention-to-treat analysis, the symptom resolution at 24 weeks in the HP positive group and negative group was (187/255) [73.3%] and 136/634 [21.4%] respectively (X=209.380; p value< 0.001). Symptom resolution/ improvement was defined as a 3 point reduction in the Likert scale.

Conclusion: 187/255 (73.3%) patients who had helicobacter pylori eradication had resolution of symptoms vs. the population of HP negative patients 136/634 (21.4%) at 6 months (p value< 0.001). Complete resolution of symptoms occured in 38/187 (20.3%) of the HP treated patients.Of the various upper GI symptom clusters epigastric pain resolved the most and bloating the least on Likert scale.There is a high HP positivity rate in patients of a presumed diagnosis of functional dyspepsia. The eradication of H pylori seems to resolve the symptoms (albeit partially) of functional dyspepsia.The number needed to treat/harm is 2.

Disclosure: Nothing to disclose

P2031 EFFICACY IN SECOND-LINE REGIMENS IN SPAIN: RESULTS FROM THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG)

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Introduction: The use of an optimal second-line regimen to eradicate *Helicobacter pylori (H. pylori)* infection refractory to the previous treatment prescribed is crucial in order to save antibiotics for future infections, specially considering the relevance of antibiotic resistance growth worldwide.

Aims & Methods: The aim was to evaluate the efficacy of the second-line treatments more frequently prescribed in a Spanish cohort arising from routine clinical practice. We conducted an observational, prospective, multicenter study, carried out in 48 Spanish hospitals as part of the 'Pan-European Registry on *H. pylori* management'. The project was provided by AEG-REDCap. Patients were included from February 2013 to January 2018 by Spanish gastroenterologists. A multivariate analysis was performed considering the most efficacious therapies. The sex of the patient, type of PPI (first vs. second-generation), type of PPI dose (simple vs. double), treatment duration (10 vs. 14 days), compliance and penicillin allergy, were considered for evaluation.

Results: 1,868 patients received a second-line eradication therapy in our cohort: 67% of them were women, 6% had penicillin allergy and their median age was 50±14 years. 90% of the patients had previously received a therapy containing clarithromycin. The therapies most frequently prescribed were (all of them including a proton pump inhibitor, PPI): triple therapy comprising levofloxacin and amoxicillin (T-LA, 43%), quadruple therapy adding bismuth to the triple therapy mentioned (Q-BLA, 22%), three-in-one single capsule bismuth containing metronidazole, bismuth and tetracycline (Q-SINGLE, 15%), triple therapy combining moxifloxacin and amoxicillin (T-MXA, 5%), and the non-bismuth quadruple concomitant therapy (Q-NBCT, 5%). 10% of the remaining patients received other minority therapies. Efficacy of these therapies was analyzed on a modified ITT (mITT) and PP basis. Results are shown in Table 1, depending on treatment duration. Good compliance was associated with higher efficacy in Q-BLA and T-LA therapies (p< 0.05). The longer treatment duration (14 days) was also associated with higher efficacy in T-LA therapy (p< 0.001).

	Duration (days)	mITT efficacy		PP efficacy	
		N included	mITT (95% C.I)	N included	PP (95% C.I)
T-LA	10	593	70% (66-74%)	564	73% (69-76%)
	14	193	86% (80-90%)	180	92% (87-95%)
Q-BLA	14	408	86% (82-89%)	375	91% (87-93%)
Q-SINGLE	10	263	82% (77-87%)	232	92% (88-95%)
T-MXA	14	69	86% (75-93%)	66	89% (79-96%)
Q-NBCT	10	39	77% (61-89%)	37	78% (62-90%)
	14	46	80% (66-91%)	45	82% (68-92%)

[Table 1: Efficacy obtained in mITT and PP basis with the five more common treatments used as second-line regimens.]

Conclusion: The best efficacy results (closer to 90%) as second-line therapies were obtained using quadruple therapy combining levofloxacin and bismuth, and triple therapies with amoxicillin and a quinolone (levofloxacin/moxifloxacin), all of them prescribed for 14 days.

Disclosure: Dr. Gisbert has served as a speaker, a consultant and advisory member for or has received research funding from Casen Recordati, Mayoly, Allergan, Advia, Diasorin. Dr McNicholl has received retributions from Allergan and MSD for training activities, and he is an advisor for Mayoly. The rest of co-authors have no conflict of interests to declare.

P2032 PAN-EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG): FIRST-LINE TREATMENT USE AND EFFICACY TRENDS IN 2013-2018

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Introduction: The impact of consensus, prescription choices and efficacy trends on clinical practice over time has not been studied in depth.

Aims & Methods: International multicenter prospective non-interventional registry starting in 2013 aimed to evaluate the decisions and outcomes of *H. pylori* management by European gastroenterologists. All infected adult patients were systematically registered at AEG-REDCap e-CRF. *Variables included*: Patient's demographics, previous eradication attempts, prescribed treatment, adverse events, and outcomes. Intention-to-treat analyses were performed. Data monitoring was performed to ensure the quality of the data.

Results: So far 25,256 patients from 27 European countries have been included, 19,754 (77%) were naïve empirical prescriptions. Although, overall, the most common prescribed treatments in the 2013-18 period were triple therapies, a shift in antibiotic regimens was identified. Triple therapies decreased from over 50% of prescription in 2013/14 to less than 25% in 2017/18 while Pylera® has increased from 0-1% (2014/2015) to 25% (2018). Full description of most common treatments is shown in Table 1. Regarding the efficacy of each treatment no trend has been identified (data now shown), however there has been a 5% overall improve in first-line efficacy (Table 1).

Conclusion: European gastroenterological practice is constantly adapting to the newest published evidence and recommendations, and although this shift is delayed and slow, it improves clinical practice outcomes.

Treatment	2013	2014	2015	2016	2017	2018
Triple C+M	116	271	317	262	41	8
Triple C+A	1,541	2,192	1,478	1,127	1,002	196
Triple A+M	164	181	75	31	19	1
Triple A+L	76	104	117	75	11	1
Sequential C+A+T	231	263	236	61	302	69
Sequential C+A+M	354	156	54	21	6	1
Quadruple M+Tc+B	70	83	12	2	6	1
Quadruple C+A+T	6	31	91	34	8	7
Quadruple C+A+M	753	910	943	786	663	65
Quadruple C+A+B	42	83	195	766	408	148
Pylera	1	1	21	502	788	183
Other	136	189	239	200	174	47
mITT	85.8%	86.3%	86.2%	88.3%	89.7%	90.4%

[Treatment prescription and overall eradication trends 2013-2018 (Hp-EuReg)]

P2033 FIRST-LINE *H. PYLORI* ERADICATION THERAPY IN EUROPE: RESULTS FROM 21,487 CASES OF THE EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG)

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Introduction: The best approach for *Helicobacter pylori* management remains unclear. Audit processes are essential to ensure that clinical practice is aligned with best standards of care.

Aims & Methods: International multicenter prospective non-interventional registry starting in 2013 aimed to evaluate the decisions and outcomes of *H. pylori* management by European gastroenterologists. All infected adult patients were systematically registered at AEG-REDCap e-CRF. *Variables included*: Patient's demographics, previous eradication attempts, prescribed treatment, adverse events, and outcomes. Intention-to-treat and per-protocol analyses were performed. Data monitoring was performed to ensure the quality of the data.

Results: So far, 21,487 first-line prescriptions from 27 European countries have been evaluated. Average age was 49 years, 60% women, and 18% had peptic ulcer. Pre-treatment resistance rates were: 24% to clarithromycin, 34% metronidazole, and 14% both. Drug prescription and efficacy is shown in the table. Triple therapy with amoxicillin and clarithromycin was the most commonly prescribed(45%), achieving, overall, < 80% eradication rate. Over 90% eradication was obtained only with 10-day bismuth quadruple therapies or 14-day concomitant treatment. Longer treatment duration, higher acid inhibition and compliance were associated with higher eradication rates in the multivariate analysis.

Conclusion: Triple therapies account for the majority of prescriptions, however, only quadruple therapies lasting at least ten days are able to achieve over 90% eradication rates.

Treatment	N	% Use	ITT	mITT	PP
PPI + C+A	8,374	39%	68.4%	84.2%	84.7%
PPI + C+A+M	4,156	19%	86.1%	90.0%	90.5%
PPI + C+A+B	1,525	7.1%	78.6%	92.8%	93.1%
PPI + M+Tc+B s.c.	1,520	7.1%	82.9%	94.7%	95.3%
PPI + C+A+T seq	1,166	5.5%	76.9%	91.3%	91.9%
PPI + C+M	1,043	4.9%	70.0%	81.1%	81.5%
PPI + C+A+M seq	608	2.8%	74.8%	81.0%	83.2%
PPI + A+M	560	2.6%	65.8%	85.4%	85.5%
PPI + A+L	404	1.9%	76.6%	81.4%	81.8%
PPI + M+Tc+B	188	1.3%	77.6%	93.1%	93.7%
PPI + C+A+T	172	0.9%	83.6%	94.9%	96.1%

ITT - intention to treat, PP - per-protocol, 95%CI - 95% confidence interval, PPI - proton pump inhibitor, Seq - sequential, C - clarithromycin, M - metronidazole, T - tinidazole, A - amoxicillin, L - levofloxacin, B - bismuth , Tc - tetracycline, s.c. - single capsule

[Overall first-line eradication rate per by treatment]

Disclosure: Prof. Gisbert has served as a speaker, consultant and advisor to, or has received research funding from, Almirall, Nycomed, AstraZeneca, Casen Recordati, Mayoly, and Allergan. Dr McNicholl has received retributions from Allergan and MSD for training activities, and he is an advisor for Mayoly.

P2034 WITHDRAWN

P2035 APPLICATION OF SCREENING AND SCORING SYSTEM FOR THE ANALYSIS OF A NEW TYPE OF GASTRIC CANCER

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Introduction: Approximately 500,000 deaths from gastric cancer reports in china annually. In addition, almost 680,000 new cases - half of which globally - attributed to the low rate of early screening and detection. High-risk groups over the age of 40 get screening for gastric cancer every year. Risk factors include having previously gastric illnesses suffering, immediate family member with gastric cancer, or antibodies for the Helicobacter pylori (Hp) bacteria. In China, almost 90 percent of the patients when detected for gastric cancer are already in the progressive stage.

Aims & Methods: To explore the screening and scoring system of a new type of gastric cancer and its application in gastric cancer screening for comprehensive analysis.

The 451 screened patients at gastric cancer risk from April 2018 to October 2018 were selected. According to the survey, serum pepsinogen (PGI, PGII, PGI/PGII) and gastrin 17 (G17) were determined by enzyme-linked immunosorbent assay. *Helicobacter pylori* positive rate was tested by a 13C urea breath test. According to the "China Early Gastric Cancer Screening Process Expert (of Shanghai) Consensus, 2017" scoring standard, the patients were

divided into three groups, i.e. low-risk groups (n=306), intermediate risk group (n=130) and high-risk group (n=15). All patients underwent gastroscopy, biopsy and pathological diagnosis for suspicious lesions under endoscopy.

Results: In the low-risk group, we detected 11 cases of low-grade intraepithelial neoplasia (detection rate was 3.6%). In case of the intermediate-risk group, one was differentiated with adenocarcinoma (progressive phase), four were high-grade tumors (detection rate 3.1%) and 23 were found low-grade tumors (detection rate 17.7%). While in the high-risk group, there were two high-grade tumors (detection rate 13.3%) and nine low-grade tumors (detection rate 60%). Among them, the infection rate of *Helicobacter pylori* for the low-risk group, intermediate-risk group and high-risk group found was 33%, 51%, and 60%, respectively that showed an upward trend.

Groups	Total Cases	Hp		Hp Infection Rate	Main Pathology				
		Positive	Negative		Advanced Cancer	High Level Intra-epithelial Neoplasia	Low Level Intra-epithelial Neoplasia	Atrophic Gastritis
low-risk group	306	204	102	0.333333	/	/	11	227
Intermediate-risk group	130	64	66	0.507692	1	4	23	80
High-risk group	15	6	9	0.6	/	2	9	4

[*Statistical* Results:]

Conclusion: According to our study, the high-risk groups of new gastric cancer screening and scoring system can effectively improve the detection rate of early gastric cancer. Furthermore, it will be helpful to secure a large number of therapeutic assets/resources in gastric cancer screening.
Disclosure: Nothing to disclose

P2036 EVALUATION OF A "PHONE CALL STRATEGY" FOR THE PATIENTS WITH GASTRIC PRECANCEROUS LESIONS LOST FOR FOLLOW-UP: A PROSPECTIVE STUDY IN A SINGLE CENTER IN FRANCE

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Introduction: Early detection and adequate surveillance of gastric precancerous lesions (GPL) may prevent the development of gastric cancer (GC) and reduce GC-related mortality. However, some patients with GPL are lost for follow up. The aims of this prospective study were:
1) to evaluate the feasibility and efficacy of a "phone-call" strategy to rescue the patients lost for follow-up, and
2) to assess the evolution of GPL in these patients.
Aims & Methods: Among all the patients diagnosed with GPL (atrophic gastritis, AG, intestinal metaplasia, IM, low grade dysplasia, LGD) in our center between January 2000 and December 2015, we identified those who according to the European MAPS guidelines [1]should undergo a surveillance endoscopy, who were under the age of 80, and who had no severe comorbidities. They were all contacted by phone (three calls) by a medical doctor, and invited to undergo a surveillance endoscopy. In those who accepted, the upper endoscopy was performed during which 5 random gastric biopsies (2 from the antrum, 1 from the angulus, and 2 from the corpus) were obtained for histological analysis performed by an expert pathologist with the evaluation of the presence of GPL and their severity. The results were compared to those of the initial endoscopy.
Results: Among the 535 patients with a GPL,134 fulfilled the inclusion criteria and were contacted by telephone. Among them, 62 could not be joined, 16 were followed in another center, 8 agreed to participate but never came, 8 refused endoscopy, and 3 had endoscopy but without biopsies. Thus finally, 36 patients (27%) were included in the analysis. There were 22 males (61%), the mean age was 57 years at index endoscopy and 63 years at inclusion, and the mean duration of follow up was 65 months. At index endoscopy, 3 patients had AG, 27 IM, and 6 LGD. Nine patients (25%) were *H. pylori* positive and in all of them the bacterium was successfully eradicated. During the follow up, 7 patients (19%) showed a progression of GPL [(1 from AG to IM, 4 from antrum- or corpus-limited IM to pangastric IM, 1 from IM to LGD, and 1 from extensive IM to GC which could be treated curatively (pT2pN0)]. Eleven patients (31%) showed regression of GPL (1 from AG to normal mucosa, 6 from IM to normal mucosa, 1 from pangastric- to corpus limited-IM, 3 from LGD to IM), and 18 patients (50%) showed stability of the lesions.
Conclusion: This study shows that:
1) despite several phone calls, a follow-up endoscopy could only be performed in a quarter of patients who had indication for control endoscopy according to the current guidelines, and
2) most of the patients showed stability of the GPL, but one patient progressed to GC and thanks to this strategy, he could be diagnosed on time and successfully treated.
References: Dinis-Ribeiro M, Areia M, de Vries A, Marcos-Pinto R, Monteiro-Soares M, O'Connor A, et al. Management of precancerous conditions and lesions in the stomach (MAPS): guideline from the European Society of Gastrointestinal Endoscopy (ESGE), European Helicobacter Study Group (EHSG), European Society of Pathology (ESP), and the Sociedade Portuguesa de Endoscopia Digestiva (SPED). Endoscopy 2012;44:74-94. doi:10.1055/s-0031-1291491
Disclosure: Nothing to disclose

P2037 LONG-TERM OUTCOME OF WATCH AND WAIT STRATEGY FOR GASTRIC ANTIBIOTIC-RESISTANT MUCOSA-ASSOCIATED LYMPHOID TISSUE LYMPHOMA

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Introduction: Although *Helicobacter pylori* (HP) eradication therapy (antibiotic therapy) has been established as the first line therapy for gastric mucosa-associated lymphoid tissue (MALT) lymphoma regardless of their HP infection status, therapeutic strategy for superficial gastric MALT lymphoma in patients not responding to antibiotic therapy (non-responders) has been an important issue to be solved. Watch & wait strategy has been assumed to be a choice after antibiotic therapy, however, the malignant potential of the disease remains uncertain.
Aims & Methods: We analyzed the long-term outcome of watch & wait strategy for non-responders. During the period between January 1995 and January 2017, 119 patients received antibiotic therapy as the first-line therapy for superficial gastric MALT lymphoma. Among them, we selected 45 patients who met the inclusion criteria;
a) the first-line therapy of antibiotic therapy could not lead complete response of the disease,
b) watch & wait strategy was subsequently applied for at least a year in case no disease progression,
c) the disease confined to either mucosal layer or submucosal layer under endoscopic ultrasonography.
Clinical data were collected by reviewing electrical medical records, and long-term outcome of superficial gastric MALT lymphoma occurring in HP-negative patients (HP-negative disease) was analyzed by comparing the outcome occurring in HP-positive patients (HP-positive disease).
Overall survival rate (OSR) and progression free survival rate (PFSR) were calculated by the Kaplan-Meier method and the values were compared using the log-rank test. We also compared clinicopathological features between HP-negative and HP-positive diseases.
Results: The study subjects comprised 25 HP-negative disease and 20 HP-positive disease, and the mean follow-up period was 56 months [range; 9-224 months]. OSR of the study subjects at 5 and 10 years after HP eradication were 100% and 92%, and PFSR at 5 years was 53%. PFSR was significantly higher in HP-negative disease than in HP-positive disease (PFSR at 5 years; 73% vs 27%, p=0.0026). Age ≤ 60 years (16/25 vs 5/20), the disease confined to the mucosal layer (20/25 vs 8/20), and superficially spreading

type in morphology (22/25, 11/20) were significantly more frequent in HP-negative disease than in HP-positive disease. Eleven patients (55%) in HP-positive disease and 4 patients (16%) in HP-negative disease experienced disease progression. Interestingly, the progression pattern was obviously different between HP-positive disease and HP-negative disease (enlargement of gastric leision/extra-gastric leision, 10/1 vs 0/4, p=0.0027)

Conclusion: Careful follow-up by EGD seems appropriate to monitor disease progression of superficial gastric MALT lymphoma in non-responders. In HP-negative patients with MALT lymphoma, watch & wait strategy can be reasonable after antibiotic therapy, however, careful follow-up using systemic imaging modalities should be necessary.

Disclosure: Nothing to disclose

P2038 PROSPECTIVE STUDY SHOWING THE CORRELATION BETWEEN THE SEVERITY OF HP GASTRITIS AND PRE-NEOPLASTIC LESIONS IN A MOROCCAN POPULATION

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Introduction: Helicobacter pylori (Hp) is a pathogenic bacterium that contributes to an inflammatory reaction of the gastric mucosa. The extent and severity of gastric mucosal inflammation, as well as the occurrence of preneoplastic lesions (atrophy and intestinal metaplasia), depend on a number of factors that are related to the bacterium, host, and environmental factors.

Aims & Methods: The aim of this work is to study the gastric lesions associated with Hp infection, and to determine the relationship between bacterial density and the appearance of gastric histological lesions.
We performed a single-centric prospective study from March 2014 and March 2019. We included 406 patients who benefited from high endoscopy and who had Hp infection documented on a histological study of gastric biopsies.

Results: The average age of patients was 43.9 years (range, 15 to 87 years). The sex ratio (H / F) was 1.23. Chronic smoking was found in 17.9% of cases. The frequency of antritis and moderate to severe chronic funditis was 78.5% and 40.5% respectively. Moderate to severe activity was noted in 48.5% at the antrum in 21% at the fundus. The incidence of gastric atrophy and intestinal metaplasia was 12.7% and 7.2%, respectively. The density of HP was higher in the antrum than in the fundus (67.2% vs. 26.8% respectively). In univariate analysis, only antral and fundic gastritis activity was significantly associated with bacterial density (OR: 4.3, 95% CI (2.7 - 6.8) p < 0.001, OR: 5.9. 95% CI (3.5 - 9.9) p < 0.001 respectively).

Conclusion: In our study the density of Helicobacter pylori significantly influences the activity of gastritis. We found no correlation between bacterial density and gastric pre-neoplastic lesions. Other studies with large case series including other factors, including the genetic profile of Helicobacter pylori, are needed.

Disclosure: Nothing to disclose

P2039 IS IT WORTH TO SCREEN THE PATIENTS FOR PRENEOPLASTIC GASTRIC LESIONS AND HELICOBACTER PYLORI?

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Introduction: In spite of declining incidence in the last years, gastric cancer (GC) is still the fifth most common cancer in the world, however, GC is the third worldwide cause of mortality from malignant diseases.
The prevention of GC includes the primary prevention: eradication of Helicobacter pylori(HP) and secondary prevention: the detection, surveillance and/or treatment of the preneoplastic lesions.
As it is known, the first step in carcinogenesis initiation process is the colonization of the gastric mucosa with HP. Identifying and surveillance in patients with these gastric preneoplastic lesions leads to early diagnosis of gastric cancer with more treatment options and an improvement in survival rate.

Aims & Methods: The purpose of this study was to determinate the incidence of gastric preneoplastic lesions from several points of view: gender, age, histopathology type, and the presence of the HP and to evaluate the best time for screening.
Upper digestive endoscopy has been performed in **12541** patients with dyspeptic syndrome in First Gastroenterology Clinic from Târgu Mureș, from 2014-2018. Patients with hemorrhage were excluded from the study. In all the patients gastric biopsies and histopatological exam were made, OLGA classification was used.

Results: In 2131 patients (52,9% males and 47,1% females) were found gastric changes. Histopathologically, 32,7% of the patients had atrophic gastritis, 43,1% intestinal metaplasia (23,7% complete metaplasia and 19,4% incomplete metaplasia) and 0,7% dysplasia. Active gastritis/pangastrits with HP was identified in 59,3% of the patients. In 4,8% of cases there were revealed polyps (hyperplastic, adenomatous) and were removed. The incidences of preneoplastic lesions reported to the total numbers of patients were: 5.55% atrophic gastritis, 7.30% intestinal metaplasia and 0,11% dysplasia.
The premalignant lesions were present mostly in the patients between 60 and 70 years. There was no statistically significant difference between males and females (P>0.05) regarding the incidence of preneoplastic lesions.

Conclusion: HP was identified in more than half of the patients, so HP has still a high incidence in Romania. After the age of 60 is worth to screen the patients by endoscopy or to perform non-invasive tests like pepsinogen. Women are as much exposed as man to premalignant gastric lesions after 60 years

References: 1. Malfertheiner P, Megraud F, O'Morain CA, et al. Management of Helicobacter pylori infection-the Maastricht V/Florence Consensus Report. Gut. 2017;66:6-30. 2. Dinis-Ribeiro M, Areia M, de Vries AC, et al. Management of precancerous conditions and lesions in the stomach (MAPS): Endoscopy. 2012;44:74-94. 3. Shiotani A, Cen P, Graham DY. Eradication of gastric cancer is now both possible and practical. Semin Cancer Biol. 2013;23:492-501

Disclosure: Nothing to disclose

Small Intestinal III
09:00-14:00 / Poster Exhibition - Hall 7

P2040 A SPECIALTY PHARMACY COHORT STUDY EVALUATING THE EFFECTIVENESS OF TEDUGLUTIDE IN SUBGROUPS OF SHORT BOWEL SYNDROME PATIENTS RECEIVING PARENTERAL SUPPORT DEFINED BY BOWEL ANATOMY

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Introduction: This specialty pharmacy cohort study assessed the effectiveness of teduglutide in reducing parenteral support (PS) in patients with short bowel syndrome-associated intestinal failure (SBS-IF) across anatomy subgroups.

Aims & Methods: Adult patients with SBS-IF who received PS and teduglutide (2013Q1-2017Q2) from Option Care, a specialty pharmacy in the United States, were classified into anatomy subgroups as defined in Jeppesen et al. 2018: 1) stoma group (defined as 0% colon remaining, stoma, and no colon-in-continuity), 2) ≥50% colon remaining group (defined as ≥ 50% colon remaining, no stoma, and colon-in-continuity), 3) >0-< 50% colon remaining group. Response (≥20% reduction in weekly PS volume) and weaned off (weekly PS volume of 0) rates during follow-up and time to first response/weaned off were summarised.

Results: The 23 patients in the study included 10 in the stoma group (mean±SD age, 57.2±9.0 years) and 13 in the ≥50% colon remaining group (54.2±16.2 years). No patients had colon remaining between 0% and 50%. Crohn's disease was the most common reason for bowel resection in patients with stoma (70.0%) and patients with ≥50% colon remaining (36.4%). Before teduglutide initiation, mean duration of SBS was 11.4±10.6 and 12.2±12.6 years, duration of PS was 4.4±2.5 and 9.5±10.7 years, and PS volume was 12.4±6.3 and 11.5±5.5 L/week in patients with stoma and ≥50% colon remaining, respectively. After teduglutide initiation, among 10 patients with stoma (mean follow-up duration 24.2±18.1 months), 7

(70.0%) achieved response and 5 (50.0%) weaned off PS; mean time to first response and weaning off was 9.8±11.5 and 17.7±14.7 months, respectively. Among 13 patients with ≥50% colon remaining (mean follow-up duration, 32.0±14.8 months), 10 (76.9%) achieved response and 6 (46.2%) weaned off PS; mean time to first response and weaning off was 2.7±2.6 and 10.2±14.2 months, respectively.

Conclusion: Teduglutide reduced weekly PS volume and patients with SBS-IF achieved weaning off across anatomy subgroups. The response rate to teduglutide is consistent with findings from prior clinical trials but time to response and PS-wean off differ, which may reflect differences in SBS-IF management between clinical trials and real world use, and care with or without the expertise of a Center of Excellence multidisciplinary team. Further research is warranted to confirm current findings.

References: Jeppesen PB, Gabe SM, Seidner DL, Lee HM, Olivier C. Factors associated with response to teduglutide in patients with short-bowel syndrome and intestinal failure. Gastroenterology. 2018;154(4):874-885.

Disclosure: K Chen is an employee of Shire Human Genetic Therapies, Inc., a member of the Takeda group of companies. H Yang, J Zhao, and A Briggs are employee of Analysis Group, Inc., which received payment for contracted research from Shire Human Genetic Therapies, Inc., a member of the Takeda group of companies. This research was funded by Shire Human Genetic Therapies, Inc., a member of the Takeda group of companies.

P2041 PREDICTIVE POTENTIAL OF BIOMARKERS OF INTESTINAL BARRIER FUNCTION FOR THERAPEUTIC MANAGEMENT WITH TEDUGLUTIDE IN PATIENTS WITH SHORT BOWEL SYNDROME

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Introduction: Teduglutide, an analog of glucagon-like peptide 2, improves intestinal rehabilitation in chronic intestinal failure frequently caused by short bowel syndrome (SBS). However, the mechanisms in the intestinal barrier related to regulation of intestinal permeability (IP) during adaptive response or therapy are not well understood. We analyzed whether measurement of IP or gene expression analysis from mucosal biopsies of selected candidate genes likely associated with IP are useful biomarkers to describe the regulation mechanisms in the intestinal barrier in patients with SBS with or without teduglutide therapy.

Aims & Methods: IP was assessed using a sugar drink test containing lactulose and mannitol and urinary recovery rate was used to determine lactulose/mannitol ratio. Gene expression analyses of mucosal biopsies was performed using qRT-PCR Quantitec Primer Assays for tight junction genes and epithelial markers.

Results: SBS patients (n=29) showed increased Lac/Man ratio compared to healthy controls (HC, n=34),(p=0.0001). Mannitol recovery was decreased in SBS (Mean HC 13.8% vs. SBS 5.4%, p= 0.0001), whereas lactulose recovery was similar to HC (mean HC 0.21% vs. SBS 0.36% p= 0.2). qRT-PCR analyses showed significant differences in gene expression between SBS patients (n=30) and HC (n=7) for YBX3 p=0.048, CRB3 p=0.009, CDK4 p=0.048, CASK p=0.03, and SI p=0.02.

For 12 patients, gene expression data were analyzed before and after up to 12 month of teduglutide treatment. Significant differences in gene expression were received for CASK p=0.01 and SI p=0.028. Further, analysis of citrullin levels in this cohort showed increased citrullin levels in patients with teduglutide therapy (p=0.012).

Conclusion: The analysis of IP gave first insights into changes of intestinal sugar absorption but has not yet been established in SBS patients. Further paired and controlled studies are required to evaluate the specifc influence of both altered bowel anatomy and/or changes in barrier function. Furthermore, altered specific gene expression was shown for both, tight junction formation and genes involved in nutrient transport and should be further analyzed.

Disclosure: Nothing to disclose

P2042 GOTHENBURG INTESTINAL TRANSPLANT ENDOSCOPY SCORE: A PROSPECTIVE, SINGLE CENTER EVALUATION

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Introduction: The results of intestinal transplantation have drastically improved during the last decade. However, the major factor that influences the survival is the presence of acute rejection. In the absence of timely treatment rejection may rapidly evolve towards mucosal loss, which is associated with a poor outcome.

Microscopic examination of the endoscopic biopsies forms the basis of acute cellular rejection monitoring today. Nevertheless, the findings during endoscopy in acute cellular rejection (ACR) are well-known, but a grading system for its severity is lacking. Gothenburg Intestinal Transplant Endoscopy Score (GITES) is a novel, five-stage endoscopic score constructed by us aiming to describe and categorize the endoscopic findings after intestinal transplantation[1]. In theory, this system could result in a more objective evaluation of the visual findings and subsequently a faster diagnosis of rejection

Aims & Methods: We prospectively graded the endoscopic findings with GITES in 13 adult patients (3 isolated intestinal grafts,10 multivisceral grafts) at one single center using white light high definition endoscopy systems. The scoring was performed by the endoscopist at the time of endoscopy and later we correlated the results with histology. Our aim with this study was to establish the usefulness of GITES in diagnosing acute cellular rejection.

Results: Eighty-five ileoscopies were performed between January 2015 to feb 2019. In 52 (61%) cases the endoscopic findings were normal. Twenty-three (69%) out of the 33 abnormal endoscopies revealed mild alterations represented by mild/moderate edema, erythema or blunted villi (GITES 1 and 2). Acute rejection was found in biopsies from 11 (14%) endoscopy sessions (4 mild & 7 moderate/severe) and in three specimens the biopsies revealed CMV enteritis. GITES above 1 (erythema, edematous villi) had 91% sensitivity and 94% specificity for ACR whereas positive (PPV) and negative predictive values (NPVs) were 78% and 98%, respectively. During moderate and severe ACR, GITES revealed an 87% sensitivity and 94% specificity whereas positive (PPV) and negative predictive values (NPVs) were 78% and 98% respectively

Conclusion: This study suggest that evaluation of the endoscopic findings with GITES results in a satisfactory identification and stratification of rejection. A prospective, multicentre evaluation is needed.

References: Varkey J, Stotzer PO, Simren M, Herlenius G, Oltean M. The endoscopic surveillance of the transplanted small intestine: a single center experience and a proposal for a grading score. Scand J Gastroenterol. 2018;53(2):134-139.

Disclosure: Nothing to disclose

P2043 PREVENTIVE EFFECT OF *LACTOBACILLUS SALIVARIUS* WB21 ON SMALL BOWEL INJURIES IN SUBJECTS WHO TAKE BOTH NSAID AND PPI: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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Introduction: We previously demonstrated an exacerbating effect of proton pump inhibitors (PPI) on small bowel injuries by nonsteroidal anti-

inflammatory drugs (NSAID) in the randomized, double-blind, placebo-controlled trial [1]. However, when considering the prevention of upper GI damage by NSAIDs, simultaneous medication of NSAID and PPI is reasonable. Thus, preventive measures for small bowel injuries by NSAID and PPI need to be determined.

Aims & Methods: We aimed to ascertain the influence of *Lactobacillus salivarius* WB21 on small bowel injuries using capsule endoscopy (CE) in subjects who take both NSAID and PPI.

Sixty healthy subjects were randomly assigned into two groups; one given celecoxib (200 mg, twice daily), rabeprazole (20 mg, once daily) and placebo for 2 weeks (placebo group, n=30), and the other given celecoxib, rabeprazole and *Lactobacillus salivarius* WB21 (7.0×10^{8}CFU, twice daily) for 2 weeks (WB21 group, n=30). The subjects completed questionnaires about GI symptoms, and laboratory tests and CE before and after 2 weeks' medication. We then compared the incidence and the numbers of small bowel mucosal lesions determined by second CE between WB21 and placebo groups. We also compared positive rates of GI symptoms and anemia between the two groups. In the present study, patients in whom small bowel mucosal lesions were identified by initial CE were omitted in the data analysis.

Results: Fifty-seven patients (27 subjects in the WB21 group and 30 subjects in the placebo group) underwent the full analysis. The incidence rate of small bowel ulcers was significantly lower in the WB21 group than the placebo group (14.8% vs. 40.0% respectively; $P=$ 0.043). In addition, the mean number of ulcers was significantly smaller in the WB21 group than the placebo group (0.7 vs. 1.1 respectively; P=0.049). However, the incidence rates and the mean number of small bowel erosion did not differ between the two groups. GI symptom score by Gastrointestinal Symptom Rating Scale did not differ between the two groups, and no subject developed anemia after the medication.

Conclusion: *Lactobacillus salivarius* WB21 seems to exert preventive effect on small bowel mucosal injuries in subjects taking NSAID and PPI simultaneously.

UMIN clinical trial registry number: UMIN000026358

References: 1. Washio E, et al. Clin Gastroenterol Hepatol 2016; 14: 809-815.

Disclosure: Nothing to disclose

P2044 RESULTS OF A MULTICENTRIC RETROLECTIVE STUDY OF TEDUGLUTIDE TREATMENT IN BENIGN SHORT BOWEL SYNDROME IN GERMANY

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Introduction: Teduglutide (TED) is a medical treatment for functional rehabilitation of short bowel syndrome (SBS) in patients with chronic intestinal failure (cIF). Its application and effectivity is routinely monitored by a structured home care service program within a multicentric approach in Germany.

Aims & Methods: From these prospectively documented data, a retrolective data base was generated in order to study treatment characteristics and outcome parameters in a clinical routine setting of TED-treated cIF-patients. An interim analysis for TED treatment characteristics up to one year is presented. Statistical analyses were performed with SPSS by using Friedman-Test with subsequent Bonferroni-adjusted post-hoc analyses and Spearman's Rank-Order Correlation.

Results: So far, 44 patients (f:26 / m:18, median age 53 years) were included in this interim analysis. Causes of SBS included vascular (n=13) and inflammatory diseases (n=16), ileus (n=6), injury (n=5) and others (n=4). Median time on parenteral support (PS) before TED was 31 (range 3 - 301) months. At TED start, 64% of patients (28/44) received individually compounded parenteral nutrition (PN), 18% (8/44) received standard-

ized PN; the remaining patients received either no parenteral support although medically indicated (n=3), solely intravenous fluid support (n=3) or support details were unknown (n=2). PS was administered by patients themselves (n=17), by relatives (n=3), by nurses (n=13) or others/unknown (n=3/5). TED treatment resulted in a significant reduction in PN calories and volume requirements as well as reduced infusion days per week and shortened infusion times (see Table 1).

	i.v.-Volume per week [L]	i.v.-Energy per week [kcal]	PN-Infusion time per serving [h]	PN days per week
Baseline	12.8 (±7.5)	7,119 (±4,475)	10.6 (±3.8)	5.0 (±2.4)
Week 12 ± 1	11.3 (±7.1)	6,315 (±4,454)	10.3 (±4.0)	4.4 (±2.3)*
Week 24 ± 3	10.4 (±6.8) **	5,425 (±4,517) **	9.5 (±4.9)	3.8 (±2.6)***
Week 49 ± 6	9.6 (±7.3) **	5,254 (±4,719) **	7.9 (±5.5) **	3.6 (±2.8)***

*[Parenteral support characteristics on teduglutide treatment. n=34; p<0.05, ** p<0.01, *** p<0.001 vs. baseline; PN = parenteral nutrition; Mean (SD)]*

The reduction of infusion time was positively correlated with the reduction of PN volume (p< 0.001; r=0.63) and calories (p=0.001; r=0.58) after one year of TED treatment. After one year, 29 of 39 patients (74%) were considered responders to TED treatment (with a minimum of 20% i.v.-volume reduction).

Conclusion: In this multicentric real-world analysis of PS-dependent SBS/cIF-patients, TED shows effectivity in improving intestinal absorptive function as indicated by significantly reduced weekly i.v.-volume and calorie requirements. In addition, the findings demonstrate a reduction of effective infusion days and times, which both importantly affect patients' well-being. These data indicate the effectivity of TED treatment in a national routine treatment setting in concordance with clinical trial data and guideline recommendations.

Disclosure: S. Pevny, J. Wehkamp, I. Blumenstein, M.W. von Websky, I. Schiefke S. Maasberg and U.-F. Pape: Consultant for Shire; U.-F. Pape: Grant / Research Support from Shire

P2045 BONE MARROW MESENCHYMAL STEM CELL CONDITIONED MEDIUM WITH INFLAMMATORY ACTIVATION FOR REPAIR OF RADIATION-INDUCED IEC-6 CELL INJURY

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Introduction: Conditioned medium from mesenchymal stem cells (MSC-CM) may represent a promising alternative to MSCs transplantation. Our previous study has demonstrated that MSC-CM with inflammatory activation improves the structural and functional restoration of the small intestine after radiation-induced intestinal injury, improve the survival status of rats with acute radiation injury, but its potential cellular mechanism has not been further explored.

Aims & Methods: To observe the effect of MSC-CM with inflammatory activation on the proliferation and apoptosis of intestinal epithelial cells (IEC-6) after radiation injury and to investigate the cellular mechanism of pre-activated MSC-CM in repairing the small intestinal mucosa. : IEC-6 cells were divided into four groups: control group, radiation injury group, normal MSC-CM (MSC-CMIEC-6(NOR)) group and inflammatory pre-activated MSC-CM (MSC-CMIEC-6(IR)) group. IEC-6 cells in the latter three groups were exposed to 10 Gy X-ray irradiation and cultured in DMEM-F12 medium, MSC-CMIEC-6(IR) and MSC-CMIEC-6(NOR) respectively. Cells in the control group were only cultured in DMEM-12 medium. Cultured cells were collected at 3 days after radiation to observe the proliferation of IEC-6 cells by using proliferating cell nuclear antigen immunofluorescence staining, and to observe the apoptosis by using TUNEL apoptosis staining and western blot assay.

Results: Compared with the radiation injury group, in the MSC-CMIEC-6(IR) group, the number of cells positive for proliferating cell nuclear antigen increased significantly (P<0.05), the number of TUNEL positive cells decreased significantly (P<0.05), and the expression of Caspases-3 decreased significantly (P<0.05), However, there was no significant difference between the MSC-CMIEC-6(NOR) group and radiation injury group (P>0.05).

Conclusion: Taken together, MSC-CMIEC-6(IR), but not non-activated MSC-CM, significantly promotes the proliferation and reduces apoptosis of intestinal epithelial cells after radiation injury and therefore repair the injured intestinal tissue.
Disclosure: Nothing to disclose

P2046 GINSENOSIDE RG1 ENHANCES THE PARACRINE EFFECTS OF BM-MSCS ON RADIATION INDUCED INTESTINAL INJURY

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Introduction: Radiation induced intestinal injury(RIII) is commonly seen in patients with intra-abdominal and/or pelvic malignancy.However, there are still no effective stategies in treating this life-threatening disease.stem cell therapy using pleiotropic mesenchymal stromal cell(MSCs) seems to be one of the most promising therapies for treating the adverse effects related to the radiotherapy,However, the amounts of active molecules secreted by MSCs under normal condition are too low to reach the effective therapeutic concentrations, and thus couldn't exert its beneficial effect on tissue reparation.Ginsenoside Rg1 is available to promote proliferation and differentiation of stem cells and plays an important role in tissue repair. Therefore, it's becoming an ideal stimulatory factor for stem cells to enhance the therapeutic effect of MSCs[18, 19]. There were few studies reporting that RG1 could increase the concentrations of VEGF, G-CSF around the damaging tissue, raising the idea of its potential on regulating paracrine[18, 20, 21].Therefore, we used RG1 to stimulate MSC and explored whether the paracrine effect was improved and if there's any therapeutic benefits on RIII.
Aims & Methods: We used RG1 to stimulate MSC and explored whether the paracrine effect was improved and if there's any therapeutic benefits on RIII. For all the vivo experiments, 2 ml DMEM-F12 or concentrated conditioned medium with different concentrations of RG1, RG1 with or without neutralizing antibodies were injected intraperitoneally,
Results: Systemic infusion of Rg1-MSC-CM, but not MSC-CM, significantly improved intestinal damage and survival of RIII rats,we found that the level of VEGF and IL-6 were significantly higher in RG1-MSC-CM than MSC-CM. Further antibody neutralizing investigations confirmed that VEGF and IL-6 were two most key factors in RG1-MSC-CM-mediated tissue repair. we explored the mechanism and enhancing effects of RG1 on MSC paracrine. It has been found that PI3K/Akt signaling pathway is essential in epithelial survival and neoangiogenesis[24]. What's more, the activation of PIK3-AKT pathway can enhance the expression of VEGF and IL-6[25]. Some investigators found that RG1 could activate thePI3K-AKT pathway by binding to glucocorticoid receptor[20, 27]. As expected, through examing the related molecules involved in this pathway, we found that the concentration of phosphorylated-AKT, IKK increased significantly with the utilization of RG1. In addition, nuclear translocation was enhanced by activating NF-kB. On the contrary, after using the corresponding inhibitor of NF-kB(BAY11-7082), the increased expression of IL-6 and VEGF and even the therapeutic effect of RG1-MSC-CM were canceled out. This suggested that the PI3K-AKT/NF-kB pathway was critical in the RG1-mediated paracrine enhancement of MSC. Further investigation on CHIP studies showed that there were several binding sites for NF-kB on the gene promoter of VEGF and IL-6, which further confirmed the hypothesis that RG1 could activate NF-kB via the PI3K-AKT pathway, increase the expression of VEGF and IL-6 secreted by MSC and thus paly a role in RIII.
Conclusion: The present study showed that RG1 could enhance the paracrine effect of MSC for VEGF and IL-6, which helped to promote tissue repair in RIII. This indicated that RG1 could be served as a promoter in stem cell therapy for treating RIIII.
Disclosure: Nothing to disclose

P2047 IN ADULT COELIAC DISEASE HISTOLOGICAL RECOVERY AND PERSISTENT VILLOUS ATROPHY SEEM SIMILAR AFTER 1 AND 2-3 YEARS OF ADEQUATE GLUTEN-FREE DIET

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Introduction: In adult coeliac disease (CD) the gold standard to assess duodenal mucosal recovery after gluten-free diet (GFD) should be histological control through duodenal biopsies taken by esophagogastroduodenoscopy. Timing and effective need of this follow-up is nowadays debated. Only a limited percentage of CD patients achieve complete histological recovery after 1 year of adequate GFD[1]. Refractory CD is defined as persistent villous atrophy associated to malabsorptive signs or symptoms despite adequate GFD for more than 12 months, but data on the timing and occurrence after GFD are scarce and conflicting [2,3]
Aims & Methods: The study's first aim was to verify if longer histological control is able to obtain higher percentage of complete histological recovery. Second aim was to determine number of patients with refractory coeliac disease at 1 and 2-3 years of follow-up.
Longitudinal cohort study of 168 CD adult patients (F=72%; median age=38, range18-71 years) followed from 2009 to 2018, who randomly underwent endoscopic/histological control after adequate GFD (Biagi-questionnaire score 3-4) at 1 year (Group 1 n=113 patients; mean follow-up 13±1.6 months) or 2-3 years (Group 2 n= 55 patients; mean follow-up 27.2±4.8 months). Anthropometric, clinical, serological data and duodenal histology (at baseline and follow-up) were compared between Group 1 and Group 2. Total histological recovery was defined as absence of villous atrophy and < 30/100 intraepithelial lymphocytes, partial histological recovery as improvement of at least one grade of the Marsh classification while no histological recovery as the total absence of improvement compared to the baseline histology at CD diagnosis. Refractory coeliac disease was defined as persistence of villous atrophy associated to gastrointestinal symptoms and biochemical alterations, when excluded other causes of villous atrophy.
Results: Total and partial histological recovery were similar in Group 1 and Group 2 (Total recovery: 61.9% vs 54.5%, respectively; p=0.40; partial recovery 36.3% vs 38.2%, respectively; p=0.86). No histological recovery was slightly more frequent in Group 2 although statistical significance was not reached (1.8% in Group 1 vs 7.3% in Group 2; p=0.09). Features at baseline and at follow-up (gender, median age, GI symptoms, CD specific antibodies and Marsh 3C) were similar between groups. Villous atrophy persisted in 27 (23.9%) Group 1 patients and in 14 (25.5%) Group 2 patients (p=0.84). In 1 (0.9%) Group 1 patient and 1 (1.8%) Group 2 patient (p=0.59) with persisting villous atrophy, presence of severe gastrointestinal symptoms, antibodies positivity and/or biochemical alterations were associated, thus displaying a clinical picture of refractory CD. Between patients with no histological recovery, 2 (100%) patients in Group 1 and 3 patients (75%) in Group 2 reported improvement or resolution of their diagnosis symptoms.
Conclusion: Total, partial and no histological recovery similarly occurs after 1 and 2-3 years of adequate GFD. Villous atrophy persists in about one forth of patients in both Groups. Features of refractory celiac disease are infrequent (1.2% of the total population) and occur in similar proportions after 1 or 2-3 years of adequate GFD. Thus, in adult CD patients histological recovery and occurrence of refractory CD after adequate GFD seem not to be time-dependent, and the first histological follow-up after 2-3 years of adequate GFD seems to be safe.
References: 1) Galli G, Esposito G, Lahner E, et al. Histological recovery and gluten-free diet adherence: a prospective 1-year follow-up study of adult patients with coeliac disease. Aliment Pharmacol Ther. 2014 Sep;40(6):639-47 2) Rubio-Tapia A, Hill ID, Kelly CP et al. ACG clinical guidelines: diagnosis and management of celiac disease. Am J Gastroenterol. 2013 May;108(5):656-76 3) Alberto Rubio-Tapia and Joseph Murray. Classification and management of refractory celiac disease. Gut 2010 Apr;59(4):547-557
Disclosure: Nothing to disclose

P2048 UNDERSTANDING CELIAC DISEASE OUTCOMES AND MONITORING PATTERNS AFTER DIAGNOSIS: A MULTINATIONAL REAL-WORLD STUDY

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Introduction: The objective of the study is to describe celiac disease (CeD) outcomes and monitoring patterns in patients with CeD in the United Kingdom (UK), USA, and Norway.

Aims & Methods: A retrospective medical chart review study was performed at three gastroenterology centres. Data from medical charts of patients with biopsy-confirmed CeD, who were diagnosed between 2008 and 2012 and who had at least one follow-up before December 31, 2017, were collected. Patients were classified into four groups at diagnosis and follow up: 1: no symptoms & normal duodenal histology; 2: no symptoms & abnormal duodenal histology; 3: symptoms & normal duodenal histology; and 4: symptoms & abnormal duodenal histology. Any biopsy results other than normal or increased intraepithelial lymphocytes were considered abnormal. Symptoms included in this classification were diarrhoea, abdominal pain/distention, poor appetite, weight loss, tiredness/lethargy, brain fog, malabsorption and bloating.

Results: To date, 200 eligible patients were included (100 in Norway, 100 in the USA). Data collection is currently ongoing at the UK site. Patients were 72.5% female with a median age at diagnosis of 35 years (IQR: 23-48), and a median follow-up of 26.5 months (IQR: 12-51.5). Overall, 52% presented with diarrhoea, 49% had abdominal pain, 38.5% had nutritional deficiencies, 32% experienced bloating and 11.5% presented with anaemia. At diagnosis, 17.5% and 82.5% were in class 2 and 4 respectively. All patients were advised to commence a gluten free diet (GFD) after diagnosis, and 4 patients discontinued the GFD during follow-up. Adherence to the GFD was not assessed. Ninety-three (46.5%) patients reported symptoms following acute gluten exposure while attempting to follow a GFD.

After esophagogastroduodenoscopy (55%), bone densitometry was the next most frequent (33.5%) procedure performed during follow-up, where 45% of US patients received this procedure compared to 22% of Norwegian patients. One hundred and eight (54%) patients underwent at least one follow-up duodenal biopsy, which comprised 26% of US and 82% of Norwegian patients respectively. Of these 108 patients, 4% of US patients and 25% of Norwegian patients had ≥ 2 follow-up biopsies after diagnosis. However, the US site had a greater number of follow-up visits and longer follow-up duration compared to the Norway centre. During follow-up, 68% had persistent CeD-related gastrointestinal symptoms, 40.5% had nutritional deficiencies, and 26.5% had tiredness/lethargy indicated in their charts. Of the patients with a follow-up biopsy, the median follow-up time from diagnosis to last biopsy result within the study period was 25.5 months (IQR: 12-45), and 38 patients (36%) had persistent villous atrophy at this time regardless of symptoms (Table 1). Patients with persistent atrophy were significantly older at diagnosis (43 vs. 35 years old, p<0.01).

Baseline disease class	N[†]	During follow-up, n (%)			
		Class 1	Class 2	Class 3	Class 4
Class 2 (n=35)	18	9 (50%)	2 (11.1%)	4 (22.2%)	3 (16.7%)
Class 4 (n=165)	88	34 (38.6%)	14 (15.9%)	21 (23.9%)	19 (21.6%)

Class 1: No symptoms & normal duodenal histology; Class 2: No symptoms & abnormal duodenal histology; Class 3: Symptoms & normal duodenal histology; Class 4: Symptoms & abnormal duodenal histology. *Considered only the last symptoms and biopsy results available during the follow-up period. 17 subjects in class 2 and 75 subjects in class 4 at baseline did not have any available biopsy results during the follow-up period. [†]2 subjects with follow-up biopsy results as ‚other‘ were excluded from this analysis.

[Changes in celiac disease class from baseline through follow-up (N=108)]*

Conclusion: Follow-up biopsy is not universally conducted even at large referral centres. Initial findings suggest a large proportion of patients continue to have abnormal duodenal histology and/or ongoing symptoms after diagnosis despite GFD. Further, the majority of patients continue to experience gastrointestinal symptoms after diagnosis.

P2049 BURDEN OF ILLNESS AND TREATMENT EXPERIENCES IN CELIAC DISEASE - RESULTS FROM A MULTI-COUNTRY PATIENT SURVEY STUDY

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Introduction: Strict adherence to a gluten-free diet (GFD) is the sole treatment option for patients with celiac disease (CeD). Many patients still experience symptoms and develop complications of the disease, as well as bear additional burden due to maintaining the GFD (1-6).

Aims & Methods: The objective of the study is to assess the burden of CeD and treatment experiences through a multi-country patient survey. A cross-sectional survey was developed, in collaboration with patient advocates, clinicians, outcomes researchers and patients with CeD. Survey questions included socio-demographic and clinical characteristics, symptoms, and patient-reported outcome (PRO) measures, e.g., the Celiac Symptom Index (CSI), Celiac Dietary Adherence Test (CDAT), and Work Productivity and Activity Impairment Questionnaire (WPAI). CeD severity was self-reported as mild, moderate, severe, or very severe. Adult participants were eligible if they had self-reported biopsy-confirmed CeD (or serology with family history of CeD) and on a GFD for ≥6 months. Participants are being recruited through patient advocacy groups and patient panels in the US, UK, Spain, and Germany.

Results: To date, 101 UK and 100 US patients have completed the survey. The UK sample's mean age was 35.5 years, with 73% female and 84% White-British. The US sample's mean age was 37.2 years, with 60% female and 78% White/Caucasian-American. Most patients were diagnosed by biopsy (80% of UK, 80% of US). Seventy three percent of US patients and 85.2% of UK patients self-reported their CeD severity as "moderate", "severe" or "very severe".

		UK (N=101)	US (N=100)
Method of Diagnosis:	Biopsy via endoscopy	40%	19.8%
	Blood tests for serology/antibodies related to CD	20%	19.8%
	Biopsy and blood tests	40%	60.4%
Self reported CeD severity:	Mild	14.9%	27%
	Moderate	30.7%	30%
	Severe	30.7%	31%
	Very Severe	23.8%	12%
CSI means score (SD)		41.9 (11.4)	41.7 (11.8)
CDAT mean score (SD)		16.0 (4.1)	15.6 (4.7)
WPAI mean score (SD):	Impairment at Work	35% (25.1%)	39.9% (27.8%)
	Work Productivity Loss	41.3% (29.4%)	47.4% (30.9%)
	Overall Activity Impairment	36.6% (25.4%)	44% (26.4%)

[US and UK Demographics and PRO scores]

The majority of patients (72.2% of UK, 75% of US) reported having CeD-related symptoms more than once a month, with 63% of UK patients and 57% of US patients reporting at least one episode of symptomatic suspected gluten exposure within the last month. 19.8% of UK patients and 23% of US patients experienced CeD-related symptoms at daily basis, and more patients (37.6% of UK, 30% of US) reported having a couple of symp-

toms at weekly basis. The most frequently reported symptoms experienced in the past month for both US and UK patients included abdominal pain, tiredness, flatulence, diarrhoea, and bloating, with the most bothersome being tiredness, abdominal pain and concentration issues.

Table 1 illustrates that only 18 (17.8%) UK and 31 US patients (31%) were considered to have excellent/very good adherence (CDAT< 13). Mean WPAI scores indicated relatively high work productivity and activity impairment reported in both US and UK patients' prior week. The US general population estimates for average percent lost productivity at work was 14%, (absenteeism=4%, presenteeism=10%) [7].

Conclusion: In this preliminary analysis of an on-going patient survey, the large majority of adult patients with CeD in the US and UK have significant burden of disease including frequent symptoms, challenges with GFD adherence, and diminished work productivity.

References: 1. Rubio-Tapia A, Hill ID, Kelly CP, Calderwood AH, Murray JA. ACG clinical guidelines: diagnosis and management of celiac disease. Am J Gastroenterol 2013;108:656-76. 2. Guandalini S, Tundia N, Thakkar R, Macaulay D, Essenmacher K, Fuldeore M. Direct costs in patients with celiac disease in the USA: a retrospective claims analysis. Dig Dis Sci 2016;61:2823-30. 3. Ukkola A, Kurppa K, Collin P, et al. Use of health care services and pharmaceutical agents in coeliac disease: a prospective nationwide study. BMC Gastroenterol 2012;12:136. 4. Mattila E, Kurppa K, Ukkola A, et al. Burden of illness and use of health care services before and after celiac disease diagnosis in children. J Pediatr Gastroenterol Nutr 2013;57:53-6. 5. Missbach B, Schwingshackl L, Billmann A, et al. Gluten-free food database: the nutritional quality and cost of packaged gluten-free foods. PeerJ 2015;3:e1337. 6. Burden M, Mooney PD, Blanshard RJ, White WL, Cambray-Deakin DR, Sanders DS. Cost and availability of gluten-free food in the UK: in store and online. Postgrad Med J 2015;91:622-6. 7. Tundia N, Hass S, Fuldeore M, Wang L.L, Cavanaugh T, Boone J, Heaton P, Validation and U.S. population norms of health-related productivity questionnaire, Value in Health, Volume 18, Issue 3, May 2015, Page-A24

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P2050 INCREASED SEROREACTIVITY TO MICROBIAL MARKERS IN FIRST-DEGREE RELATIVES OF CELIAC DISEASE PATIENTS

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Introduction: Relatives of celiac disease (CD) patients are at higher risk of developing the disease due to genetic predisposition and possible environmental factors. We have previously reported increased seropositivity to *Saccharomyces cerevisiae* (anti-*Saccharomyces cerevisiae* antibodies, ASCA), *Pseudomonas fluorescence* (anti-I2 antibodies) and *Bacteroides Caccae* (anti-OmpW antibodies) in CD.

Aims & Methods: We hypothesized that also relatives of CD patients could show hyperreactivity to these three microbial markers. Frequency of seropositivity and concentrations of ASCA IgA and IgG, IgA-class anti-I2 and anti-OmpW antibodies were compared between 463 first-degree relatives of CD patients, 58 untreated and 55 treated CD patients and 80 non-CD controls. In addition, CD-associated HLA haplotypes and tissue transglutaminase (tTGab) and endomysium (EmA) antibodies were determined.

Results: Altogether 49 relatives of CD patients were positive for tTGab and/or EmA and were analyzed as a separate group. Among the 414 CD autoantibody negative relatives, one or more of the three microbial markers was positive in 73%, in 97% of untreated and in 87% of treated CD patients and 44% of non-CD controls. The relatives also had higher median ASCA IgA (8.90 vs 4.50 U/ml, p< 0.001), ASCA IgG (8.37 vs 5.75 U/ml, p< 0.001) and

anti-I2 antibody (absorbance 0.71 vs 0.32, p<0.001) concentrations than the controls. The percentage of seropositivity (86%) and concentrations of microbial markers were somewhat higher in the autoantibody positive group (median ASCA IgA 11.1 U/ml, ASCA IgG 12.8 U/ml, median absorbance for anti-I2 antibodies 0.93 and for anti-OmpW antibodies 1.00). In this subgroup, also anti-OmpW antibody concentrations were higher than in the control group. There was a weak positive correlation between tTGab and ASCA IgA (r=0.31, p<0.001). Seropositivity of relatives was not significantly associated with HLA genotypes (DQ2.5, DQ8, DQ2.2, DQ2+DQ8 or DQ2 and DQ8 negative).

Conclusion: Relatives of CD patients demonstrated higher frequency of seropositivity and increased concentrations of ASCA, anti-I2 and anti-OmpW antibodies compared with non-CD controls. These findings were not associated with HLA DQ2 or DQ8, suggesting the role of environmental factors and other genetic variants.

Disclosure: Nothing to disclose

P2051 FACTORS ASSOCIATED WITH NON ADHERENECE TO GLUTEN FREE DIET IN ADULT CELIAC PATIENTS IN ISRAEL

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Introduction: The cornerstone of the recommended treatment for celiac disease (CD) is a lifelong strict gluten-free diet (GFD). We aimed to identify prospectively the demographic, clinical, social and psychological profile associated with non adherence to a GFD in adult CD patients in Israel

Aims & Methods: An anonymous online questionnaire has been sent via the Israeli Celiac association and through social networks. Only CD patients≥18 years old were included. Socio-demographic, laboratory and clinical data as well as anxiety and depression score were reported. Adherence to GFD was assessed by Biagi questionnaire.

Results: 301 patients completed the questionnaire, mean age of 37.5 ± 14.9 years, 79.2% female. The most common presenting symptoms were: anemia (59.7%), abdominal pain (50.8%) and diarrhea (42.8%). According to the Biagi score, 82% of patients were found to be high adherent to GFD (Biagi 3-4) and 18% were low adherent (Biagi-0-2). Univariate analysis revealed that: age of patient, age at diagnosis, duration of disease, education, income level, origin, smoking, gastroenterological follow up and membership in a supporting group, were all significantly associated with adherence to GFD.However in multivariate analysis, only age at diagnosis and smoking were significantly associated with adherence to GFD (HR 1.083, 0.287, respectively).

Conclusion: Understanding risk factors for non adherence in celiac disease in an important issue. Intervention strategies in young adult celiac patients as well as in smokers might improve adherence and reduce future complications with better quality of life.

Disclosure: Has been accepted to present as well in the international celiac disease symposiun ICDS 2019 in Paris.

P2052 HEMORHEOLOGICAL ALTERATIONS IN CELIAC DISEASE AND INFLAMMATORY BOWEL DISEASE

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Introduction: Hemorheological changes predispose to the development of arterial thrombotic events; however, limited information is available on the status of these changes in celiac disease (CeD) and inflammatory bowel disease (IBD).

Aims & Methods: In this study, we aimed to describe the hemorheological profile of CeD and IBD patients to investigate whether any alterations contribute to elevated cardiovascular risk. This is a case-control study involving newly diagnosed and followed CeD and IBD patients with non-CeD, non-IBD subjects. In addition to routine laboratory parameters, hemorheological parameters i.e. erythrocyte deformability and aggregation (with LORCA), viscosity of whole blood and plasma (with Brookfield viscometer) were measured from venous blood. We calculated mean±standard deviation (for continuous variables) and frequencies (for categorical variables) and used two-sample t-test and linear correlation in the statistical analysis. Registration number: ISRCTN49677481.

Results: Study participants included 52 CeD, 41 IBD (73% with Crohn's disease) and 54 control patients. There was no difference in age and gender distribution between CeD and control patients, nor in hematocrit (41.2±3.5% vs. 41.4±3.6%, respectively; p=0.717), viscosity of plazma (1.24±0.16 mPa·s vs. 1.27±0.14 mPa·s, respectively; p=0.253), viscosity of whole blood (4.07±0.43 mPa·s vs. 4.13±0.46 mPa·s, respectively; p=0.534) and erythrocyte aggregation. In contrast, erythrocyte deformability was impaired at three different levels of shear. Patients with IBD were younger than controls (36±14 years vs. 44±17 years, respectively; p=0.013) with male dominance (46.3% vs. 62.9%, respectively; p=0.029), there was no difference in hematocrit (40.3±3.9% vs. 41.4±3.6%, respectively; p=0.159), viscosity of plasma (1.31±0.17 mPa·s vs. 1.27±0.14 mPa·s, respectively; p=0.234), viscosity of whole blood (4.14±0.49 mPa·s vs. 4.13±0.46 mPa·s, respectively; p=0.896) and erythrocyte aggregation between groups. In contrast, aggregation index and γ were higher (p=0.008), while $t_{1/2}$ was lower in IBD patients (p=0.024). In Crohn's disease, viscosity of plasma positively correlated with disease activity (rho=+0.579, p=0.001).

Conclusion: An impaired erythrocyte deformability in CeD, an increased aggregability in IBD, and an activity-dependent increase in viscosity of the plasma in Crohn's disease may predispose to thrombus formation.

Disclosure: Nothing to disclose

P2053 EFFECT OF *BIFIDOBACTERIUM INFANTIS* NSL SUPER STRAIN IN HIGHLY SYMPTOMATIC CELIAC DISEASE PATIENTS ON LONG-TERM GLUTEN-FREE DIET. A PILOT STUDY

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Introduction: A strict gluten-free diet (GFD) is currently the only recommended treatment for celiac disease (CeD). Despite apparent compliance with the diet, 30-50% of treated patients have gastrointestinal (GI) symptoms. A recent DBPC trial showed that oral administration of *Bifidobacterium infantis*NLS super strain (*B. infantis* NSL-SS) alleviated symptoms in newly diagnosed CeD patients consuming gluten, and that this effect could be attributed to the modulation of innate immunity.

Aims & Methods:
Aim: We explore the effect of a three-week course of *B. infantis* NSL-SS on persistent symptoms in patients with CeD following a long-term GFD.
Methods: We conducted a prospective, randomized, cross-over, double-blind, placebo-controlled trial. Adult patients were enrolled if they were on a GFD for at least two years and were symptomatic at screening according to the GI symptom rate score (GSRS) (>3 points in the mean global score or >2 for any individual syndromes). Patients voluntarily consuming gluten, with complications, other treatments that might have affected results, or limitations for following protocol or collecting stool or urine samples were excluded. After a one-week run-in period, patients were randomized to receive *B. infantis* NSL-SS (Natren LIFE START 2 Natren Inc. CA.) (2 capsules 3 t.i.d.; 2 x 10 CFU/capsule) or placebo for 3 weeks. After a 2-week wash-out period, patients switched treatment for the next 3 weeks. Outcome was assessed based on changes (Δ) in the celiac symptoms index (CSI) for each treatment. Stool and urine samples were also collected at the end of each period for detection of gluten immunogenic peptide (GIP) excretion.

Results: Eighteen patients were enrolled; 2 were excluded due to intentional transgressions and 4 due to inconsistence in symptoms questionnaire reports. In the per protocol analysis (n=12), there were no significant changes in the CSI total score and subscales comparing probiotics vs. placebo. However, there was a significant improvement of specific CeD symptoms in *B. infantis* treatment compared to placebo (median Δ [range]: 5.0 points [0 to 9] vs. 2.5 [-7 to 4], respectively; *p*<0.03; Mann-Whitney) when this analysis was restricted to patients with total CSI scores above the median. There was a significant placebo effect in general health subscale (*p*<0.04). Globally, we observed a non-significant carryover effect when probiotics was the first treatment. GIP excretion in stools and urine was similar in both treatments. No side effects were detected in either intervention.

Conclusion: This exploratory study suggests that *B. infantis* NSL-SS may improve specific CeD symptoms in a subgroup of GFD treated patients with higher symptomatic

Disclosure: Nothing to disclose

P2054 REAL LIFE PATTERNS OF GLUTEN-FREE DIET ADHERENCE IN CELIAC PATIENTS USING GIP EXCRETION

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Introduction: Patients with celiac disease (CeD) treated with a gluten-free diet (GFD) are often exposed to gluten contamination. However, the frequency of such transgressions in a real life scenario is unclear.

Aims & Methods: Aim: To explore the pattern of fecal and urinary excretion of gluten immunogenic peptide (GIP) during a 4-week period in CeD patients on long-term GFD.

Methods: This prospective study enrolled consecutive series of adult CeD patients on a GFD for more than two years. At baseline, patients completed a celiac symptom index (CSI) questionnaire to determine presence of symptoms. Patients collected stool and urine samples for 4 weeks. The collection protocol was designed to ensure coverage of gluten excretion during week-days and week-ends.

Thus, the last stool on Fridays, and two urine samples during Sunday morning and evening, were collected. Urine samples were pooled in one single week-end assay. An ELISA test for stool (iVYLISA GIP-S , Biomedal S.L. Spain) and point-of-care tests (GlutenDetect; Biomedal S.L., Spain) for urine were used for GIP detection.

Results: We enrolled 23 patients who were on a GFD for a median time of 7 yrs. The median number of transgressions for the overall population was 3/4w. (IQR: 1-5). GIP excretion in week-end (urine samples) was positive in 21/23 patients (91.3%), while GIP in stools collected during weekdays was detected in 11/23 patients (47.8%) (*Fisher's Exact test*: $p<0.004$). While 41/92 (44.6%) GIP determinations in urine were positive, GIP was detected in 24/92 (26.0%) of stools (*Chi square* test: $p<0.02$). Frequency of GIP excretion for each of the 4 weeks, progressively increased as the study progressed (1 vs. 4 week GIP excretion in either stool and/or urine: $p<0.05$).

No differences were observed comparing symptomatic (CSI scores >35 points) vs. asymptomatic patients. A significant correlation was observed between frequency of transgressions and baseline serology (*rho*: vs. IgA tTG $p<0.04$; vs. IgA DGP $p<0.0009$).

Conclusion: The study shows evidence of a high frequency of dietary indiscretions in CeD patients on long term treatment with GFD, independently of the presence of symptoms. Ingestion of gluten was notably more frequent during week-end than during week-days. We show evidence of a relaxation of dietary control along the 4-week study.

Disclosure: Nothing to disclose

P2055 INTRODUCING A DIRECT ACCESS GASTROSCOPY PATHWAY FOR PRIMARY CARE PHYSICIANS SIGNIFICANTLY REDUCES DELAYS IN DIAGNOSIS OF COELIAC DISEASE

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Introduction: UK guidelines recommend that patients with suspected coeliac disease should have endoscopy and biopsy within 6 weeks of referral. This helps to avoid adult patients abstaining from gluten products prior to establishing a histological diagnosis. Our unit traditionally receives written referrals from primary care for a specialist review prior to gastroscopy and biopsy. This resulted in diagnostic delays leading to non-compliance with the national 6-week target. Therefore, we have introduced a new direct access gastroscopy service for primary care physicians to bypass the first specialist consultation with the aim of streamlining the process, thus improving patient experience and meeting the national target.

Aims & Methods: We retrospectively reviewed cases of newly elevated TTGs from primary and secondary care between 2014 and 2018 (n=108). Of these, 52 patients were referred for specialist review for probable coeliac disease. 43 of these were referred from primary care physicians (the other 9 were excluded as they were internal hospital referrals) however 1 of the direct access referrals refused endoscopy. We then compared the performance of the new direct access gastroscopy service to the traditional referral route, using an unpaired t-test to compare time to endoscopy.

Results: Patients referred via the traditional pathway (n=21) took a mean time of 94.4 days (95% C.I. 46.58 to 142.22) to undergo a gastroscopy and biopsy. Conversely, patients referred on the direct access gastroscopy pathway (n=21) took a mean time of 39.7 days (95% C.I. 16.63 to 62.77), which was significantly quicker than the traditional pathway (p=0.04). 17 patients (81%) seen on the direct access pathway and 16 patients (76.1%) on the indirect access pathway demonstrated a positive histology.

Conclusion: The direct access gastroscopy pathway enabled the unit to meet national standards and improve the patient experience by instigating earlier introduction of gluten free diet.

Disclosure: Nothing to disclose

P2056 STUDY OF GUT MICROBIOTA AND SERUM BIOMARKERS IN CELIAC DISEASE

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Introduction: Celiac disease (CD) is autoimmune, genetic pathology of digestive system, that characterized by primary or secondary dysbiosis.

Aims & Methods:

Aim: To investigate of fecal microbiota composition and to identify candidate biomarkers of CD by serum metabolomics analysis.

Methods: Fresh fecal samples were collected from 43 CD patients on a gluten-free diet and 42 healthy controls (HC). The quantitative real-time polymerase chain reaction (qRT-PCR) was used for fecal microbiota assessment. Serum metabolomic assays were conducted using the GC-MS.

Results: CD patients had lower butyrate-producing *Faecalibacterium prausnitzii* and *Bifidobacterium* spp. counts than HC. Taxonomic dysbiosis in CD was characterized by a higher *Bacteroides fragilis/Faecalibacterium prausnitzii* ratio compared to HC. Serum of CD patients showed significant increases in stearic acid, 2-hydroxyisovaleric acid (2-HIVA), succinate, fumarate and benzoate compared to HC. The ratio of arachidonic acid (AA) to eicosadienoic acid (EDA) (C20:4n-6/C20:2n-6) was increased in CD. Oral butyrate plus inulin (as supplement for 28 days) significantly enhanced fecal butyrate-producing bacteria (evaluated as BCoAT gene content), reduced elevated baseline *B. fragilis/F. prausnitzii* ratio and lowered serum levels of pro-inflammatory succinate and 2-HIVA in CD patients.

Conclusion: An increased *B. fragilis/F. prausnitzii* ratio can serve as available biomarker for intestinal proinflammatory dysbiosis in CD. Low counts of butyrate-producing *F. prausnitzii* suggest the desirability of co-treatment with oral butyrate or butyrate-enhancing agents (probiotics, prebiotics, metabiotics) in CD. Treatment that increases colonic bifidobacteria (e.g., some *Bifidobacterium* probiotics or inulin-type prebiotics) can be considered in CD. Significant changes in serum levels of microbial and endogenous metabolites, reflecting some metabolic pathways disturbances (glycolysis, TCA cycle, fatty acid metabolism, ketone body metabolism, phenylalanine, tyrosine and tryptophan metabolism, microbial metabolism) are observed in CD. Some metabolites (e.g., a microbial metabolite 2-HIVA), as well as a new metabolomic index (AA/EDA ratio), reflecting the balance between pro-inflammatory and anti-inflammatory components of the omega-6 fatty acid pool, may be considered as candidate biomarkers of chronic intestinal inflammation and metabolic dysbiosis in CD.

Disclosure: No Conflict of Interest

P2057 CLINICOPATHOLOGICAL FEATURES OF THE MUCIN PHENOTYPES IN SPORADIC NON-AMPULLARY DUODENAL SUBMUCOSAL INVASIVE CARCINOMA

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Introduction: We previously revealed the clinicopathological difference of non-ampullary duodenal neoplasia between the oral and anal side of the papilla of Vater. However, the reason of the difference by tumor location is not clarified. There are some reports about the differences of mucin phenotype of non-ampullary duodenal epithelial neoplasia depending on tumor location. However, previous studies have targeted only superficial tumors, like adenoma and mucosal carcinoma.

Aims & Methods: We tried to reveal the clinicopathological features and the significance of mucin phenotype in carcinoma with submucosal invasion. We retrospectively collected all the case of non-ampullary duodenal carcinoma (NADC) which invaded into submucosal layer at 4 institutions in Japan between January 2003 and December 2018. Moreover, we investigated consecutive mucosal NADCs in Okayama University Hospital as a control group during the same period. The mucin expression of MUC5AC, MUC6, MUC2, CDX2, and CD10 and the proliferative activity of Ki-67 were evaluated in both submucosal and mucosal carcinomas by immunohistochemistry. Tumors were classified into gastric, gastric and intestinal mixed, and intestinal phenotype according to combination of mucin expression. We measured the distribution of tumor cells stained for Ki-67 to assess the proliferative activities of tumor cells.

Results: There were 11 submucosal carcinomas at 4 institution, and 12 mucosal carcinomas in Okayama University Hospital. Among the patients with submucosal carcinoma, 8, 1, and 2 received radical resection with lymphadenectomy, partial resection without lymphadenectomy, and endoscopic resection, respectively. There were no significant differences in sex, age, tumor size, macroscopic type, or histological type between the submucosal and mucosal groups.

However, all the submucosal carcinomas were located on the oral side of the papilla of Vater (oral-Vater), and the proportion of NADCs on oral-Vater was significantly higher in submucosal carcinoma than mucosal carcinoma (100% vs. 58.3%, P = 0.0016). These lesions were classified gastric type (n=8) and mixed type (n=3), and no lesions were intestinal type. The proportion of gastric and mixed type was significantly higher in submucosal carcinoma than in mucosal carcinoma (100% vs. 41.7%, P = 0.0024). The distribution of Ki-67 expression showed that the diffusely stained pattern was more frequently seen in submucosal carcinoma than mucosal carcinoma (66.7% vs. 9.1%, P = 0.0047).

	Submucosal (n=11)	Mucoal (n=12)	P-value
Tumor location (oral-Vater/anal-Vater) (%)	11/0 (100/0)	7/5 (58.3/41.7)	0.016
Mucin phenotype (gastric+mixed/intestinal) (%)	11/0 (100/0)	5/7 (41.7/58.3)	0.0024
Ki-67 (superficial type/diffuse type) (%)	1/10 (9.1/90.9)	8/4 (66.7/33.3)	0.0047

[Table. Comparison of clinicopathological features between submucosal and mucosal carcinomas]

Conclusion: Our date clarified the differences in the clinicopathological features such as tumor location, mucin phenotype, and proliferation behavior of tumor between submucosal and mucosal carcinoma. That might suggest there is different origin and pathway in the carcinogenesis of submucosal invasive carcinoma from mucosal carcinoma.

References: Matsueda et al. J Gastroenetrol Hepatol. 2019 Epub ahead of print.

Disclosure: Nothing to disclose

P2058 ENDOSCOPIC RESECTION OF AMPULLARY AND DUODENAL ADENOMAS: ARE WE DOING IT RIGHT?

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Introduction: Duodenal and ampullary adenomas have the potential for malignant transformation to carcinomas by an adenoma-to-carcinoma sequence as seen elsewhere in the gastrointestinal tract. Endoscopic resection of these lesions is increasingly being used in place of invasive surgery. However, endoscopic resection in the duodenum can be challenging due to its anatomy and may be associated with a higher risk of complications. This study aims to evaluate the safety and efficacy of endoscopic resection of such lesions.

Aims & Methods: All patients with ampullary and large non-ampullary (>10mm) duodenal polyps who underwent endoscopic resection in a tertiary referral centre were included in the study. A retrospective analysis on data including demographics, size, histology, location, method of resection and complications was performed.

Results: A total of 122 patients underwent endoscopic resection of duodenal polyps. Out of these 37 underwent ampullectomy and 85 underwent resection for non-ampullary duodenal polyps >10mm.

Ampullary Adenomas

There were a total of 37 patients who underwent ampullectomy (median age 66 years [IQR 50-83]. 27 (73%) had a submucosal injection, whereas pancreato-duodenal stent was placed in 26 (73%) of the patients. 7 (20%) patients had adjunct tissue ablation (APC). 62% of the lesions were pure ampullary, whereas 38% polyps involved the duodenum.

The mean polyp size was 21.6mm [IQR5-80]. 75.7% (28/37) of the polyps were removed in a single session with an en-bloc resection rate of 43.2%.

.Non Ampullary Duodenal Adenomas

A total of 85 patients with polyps >10mm referred for endoscopic therapy (median age 64 years, [IQR] 27-87 years, 52% male). 58 (70%) underwent endoscopic mucosal resection (EMR) and 27 (30%) had knife assisted resection (KAR). The histology revealed 63 (77%) low grade dysplasia, 14 (14%) high grade dysplasia, 2(3%) carcinoids, 1(1%) Brunner gland hyperplasia and 5 (5%) hyperplastic polyps. The majority of the lesions were found in D2 (70,82%). 8/85 patients (10%) had a diagnosis of familial adenomatous polyposis syndrome.

The mean polyp size was 25.3 mm [IQR 10-80]. 93.5% (80/85) of the polyps were removed in a single session with an en-bloc resection rate of 40%.

Table 1 shows the complication and recurrence rates stratified by lesion size (< 30mm vs >30mm) for both ampullary as well as non ampullary lesions.

	Non ampullary duodenal adenomas		Ampullary adenomas	
Lesion size	< 30 mm	> 30 mm	< 30 mm	> 30mm
Number	53	32	28	9
Delayed Bleeding	2 (4%)	5 (16%)	1 (4%)	1 (11%)
Perforation	1 (2%)	1 (3%)	0 (0%)	0 (0%)
Pancreatitis	0 (0%)	0 (0%)	0 (0%)	1 (11%)
Recurrence	1 (2%)	5 (16%)	4 (14%)	3 (33%)

[Table 1]

The bleed rate was significantly higher in larger lesions. All complications in this series were managed endoscopically. The mean follow up period was 38 months for non ampullary duodenal adenomas and 16 months for ampullary adenomas. Recurrence rate was higher in the larger lesions in both sub groups and a majority of the recurrences (70%) were treated endoscopically.

Conclusion: Endoscopic resection of duodenal lesions is a safe and effective technique for complete removal of these polyps. Lesion assessment is crucial in patient selection for endoscopic removal as noted by the absence

of cancers in this cohort. The risk of complications, particularly bleeding is significantly higher in lesions greater than 3cm in size. Similarly, recurrence rates are also higher in this group. Nevertheless, we demonstrated that all complications and most recurrences were successfully managed endoscopically.
Disclosure: Nothing to disclose

P2059 A 20-YEAR SINGLE-CENTER EXPERIENCE OF TUMOR BLEEDING IN DUODENAL GASTROINTESTINAL STROMAL TUMOR

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Introduction: Upper gastrointestinal bleeding (UGIB) is one of the major manifestations of gastrointestinal stromal tumor (GIST)of gastrointestinal tract. Several studies have reported that GIST bleeding is associated with poor prognosis. However, only few reports have reported the prognosis of duodenal GIST and its hemostasis modalities for tumor bleeding.
Aims & Methods: To identify clinical outcome of duodenal GIST bleeding, we analyzed risk factors and prognosis of hemorrhagic duodenal GIST evaluating hemostasis methods. Total 179 patients histopathologically diagnosed with primary duodenal GIST between January 1998 and December 2017 were enrolled to this study and medical records were reviewed, retrospectively.
Results: Of 179 total patients, 49 (27.4%) patients showed UGIB. Endoscopic intervention and transarterial embolization were performed for initial hemostasis in 17 and 1 patients, respectively and other 31 were treated conservatively. In endoscopic treatment group, re-bleeding was found in 6 cases (35.3%) and all of the patients finally received surgery. Over a median of 48 months of follow-up, 7 patients in the bleeding group and 20 patients in the non-bleeding group died; the 5-year survival rate was 83.3% in the bleeding group and 85.7% in the non-bleeding group ($P = 0.431$). Multivariate analysis showed that significant risk factors for duodenal GIST bleeding was P53 positivity (hazard ratio [HR] = 2.601, $P = 0.019$) and risk factors for overall survival were old age (HR = 1.070, $P = 0.004$), large maximal diameter (HR = 1.197, $P = 0.002$), and mitotic count > 5/HPF (HR 5.029, $P = 0.002$). A tumor diameter of 5 cm was cut-off value in predicting overall survival with a sensitivity of 81.0 % and specificity of 65.3%.

	Total (n=179)	Bleeding group (n=49)	Non-bleeding group (n=130)	P value
Age (median, IQR)	55 (44-64)	55 (44-63)	55 (44-64)	0.792
Sex (male/female)	91/88	34/15	57/73	0.003
Size of tumor, cm	4.0 (3.0-6.0)	4.0 (3.0-6.0)	4.0 (3.0-6.0)	0.938
Mitotic count	2.0 (1.0-4.3)	3.0 (1.0-5.0)	2.0 (1.0-4.0)	0.112
Antithrombotic drugs	14 (7.8%)	4 (8.2%)	10 (7.7%)	1.000
Recurrence	27/163 (15.1%)	7/47 (14.9%)	20/116 (17.2%)	0.196
Recurrence free survival, months	40 (19-76)	49 (19-88)	39 (19-69)	0.226
Death	27 (15.1%)	7 (14.3%)	20 (15.4%)	1.000
Median survival, months	48 (21-77)	49 (23-99)	43 (20-75)	0.196

[Table. Clinicopathologic characteristics.]

Conclusion: Surgical removal of duodenal GIST should be considered when tumor bleeding is detected because re-bleeding rate is somewhat high after endoscopic hemostasis. And, in duodenal GIST patients with old age, large tumor diameter, and mitotic count > 5/HPF, managements should be performed carefully due to the poor prognosis.
Disclosure: Nothing to disclose

P2060 AN EVALUATION OF THE RISKS AND BENEFITS OF BIOPSY OF THE PAPILLA IN PATIENTS WITH FAMILIAL ADENOMATOUS POLYPOSIS (FAP)

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Introduction: Nearly all patients with FAP will develop duodenal adenomas. Ampullary and duodenal cancer are the leading cause of death in patients with FAP after colectomy. The risk of duodenal cancer can be predicted by the Spigelman stage of duodenal polyposis. International and national guidelines recommend upper endoscopic surveillance with forward and side viewing scopes to evaluate the duodenum and visualize the papilla for patients with FAP at a frequency according to the Spigelman stage. There is no consensus whether the papilla should be routinely biopsied or included in the Spigelman staging system of duodenal polyposis. Some endoscopists refrain from biopsy of the papilla due to a theoretical risk of pancreatitis. No data is available to support the risk of pancreatitis related to biopsy of the papilla.
Aims & Methods: We aim to identify the rate of pancreatitis after biopsy of the papilla in FAP patients and the effect of biopsy on Spigelman stage. This is a retrospective cohort study identifying consecutive FAP patients at the Cleveland Clinic, between 05/1992 and 01/2018 from the David G. Jagelman Inherited Colon Cancer Registries. All FAP patients who have undergone at least one endoscopy with biopsy of the duodenal papilla were included. Patients with previous history of ampullary carcinoma or in whom pathology results were not available were excluded. Medical records were used to determine demographics, endoscopic history, risk factors for pancreatitis, and Spigelman staging with and without biopsy. Post-procedural pancreatitis was defined as two out of three of:
i) typical symptoms of pancreatitis
ii) lipase three times the upper limit of normal or
iii) presence of radiography consistent with pancreatitis within 7 days of esophagogastroduodenoscopy (EGD).
Results: 77 FAP patients (51.9% male) were identified with a total of 120 individual upper endoscopies (range: 1-6 biopsies per patient) resulting in biopsy of the duodenal papilla. 1.6% (2/120) developed pancreatitis after ampullary biopsy. Normal papilla was biopsied in 49/120 EGDs. No patients with endoscopically normal appearing papilla developed pancreatitis. 71 abnormal duodenal papilla were biopsied with 2 episodes of pancreatitis post-biopsy. Both episodes of acute pancreatitis occurred in the same patient. Biopsy of the normal papilla changed Spigelman stage in 3 patients:
i) stage 1 to 2
ii) stage 2 to 3
iii) stage 3 to 4.
In the patient who was up-staged from Spigelman III to IV due to normal papilla biopsy underwent pancreas-sparing duodenectomy.
Conclusion: No FAP patients with biopsies of endoscopically normal papilla developed pancreatitis. Biopsy of normal duodenal papilla in FAP does have the potential to change management by increasing Spigelman stage. It should be further studied if multiple biopsies of the papilla affect this risk-benefit ratio.
Disclosure: Nothing to disclose

P2061 ROUX-EN-Y GASTRIC BYPASS AND PREVIOUS BARIATRIC SURGERY ARE RISK FACTORS FOR SYMPTOMATIC CHOLELITHIASIS AFTER BARIATRIC SURGERY

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Introduction: Bariatric surgery predisposes patients to development of cholelithiasis and therefore the need of a subsequent cholecystectomy; however, the incidence of cholecystectomy after bariatric surgery is debated.
Aims & Methods: Medical records of 601 patients hospitalized for bariatric surgery between January 1, 2010 and July 1, 2018 were reviewed. Our aim was to evaluate the incidence of cholecystectomy following different types of common bariatric procedures.

All patients who developed cholelithiasis and a subsequent cholecystectomy were included. Cholelithiasis was diagnosed by clinical criteria and characteristic ultrasound findings. We used the Israeli community medical data system "Ofek" in order to find patients' missing data. Twenty-one patients were excluded because of missing data.

Categorical variables were summarized with frequencies and percentages. Continuous variables were summarized using sample size, Mean, Standard deviation, Median, Minimum, Maximum and 95% C.I. Correlations between categorical variables and Incidence of cholelithiasis after surgery were tested for significance using the Chi-Square test. Correlations between Continuous variables and incidence of cholelithiasis after surgery were tested for significance using the independent T-Test.
Results: We evaluated retrospectively 580 patients with an average follow-up of 12 months (range 6-24 months). Mean age was 48±19 years (78% females). Twenty-nine patients (5%) underwent laparoscopic cholecystectomy (LC) before the bariatric surgery and 58 patients (10%) performed concomitant LC with the bariatric procedure due to symptomatic gallstone disease (including stones, sludge and polyps). There were 203 laparoscopic sleeve gastrectomy (SG) (35%), 175 laparoscopic gastric band (LAGB) (30%), 55 Roux-en-Y gastric bypass (RYGB) (9.5%) and 147 (25%) mini gastric bypass (MGB) procedures during the study period. At the follow-up period 36 patients (6.2%) developed symptomatic cholelithiasis while the most common clinical presentation was biliary colic.

Statistically, there was a significant difference between the type of the bariatric operation and the incidence of cholelithiasis after the operation. The incidence of symptomatic gallstones formation in patients who underwent RYGB was 14.5 %. This was significantly higher comparing to 4.4% following SG, 4.1% following LAGB and 7.5% following MGB (p=0.04). We did not find any predictive risk factors including smoking, BMI at surgery, change in BMI, comorbidities such as diabetes, hyperlipidemia, hypertension and COPD for gallstone formation or a subsequent cholecystectomy. Interestingly, previous bariatric surgery was a risk factor for gallstone formation and cholecystectomy [15.8% (13/82 patients) in those with previous bariatric surgery compared to 4.6% (23/492 patients) among those without previous bariatric operation (P< 0.001)].
Conclusion: Our data demonstrate that patients with previous bariatric surgery or patients planned for RYGB are at high risk to develop postoperative symptomatic gallbladder disease. Concomitant cholecystectomy during the bariatric procedure should be considered in those asymptomatic patients with cholelithiasis.
Disclosure: Nothing to disclose

P2062 POSSIBLE IMPACT OF VAGOTOMY ON POSTOPERATIVE WEIGHT LOSS AFTER SELECTED BARIATRIC SURGERY PROCEDURES. IMPORTANCE OF THE MODULATION OF THE SECRETION OF GASTROINTESTINAL HORMONES BASED ON ANIMAL EXPERIMENTAL MODELS

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Introduction: Obesity is one of the major health problems in the developed countries and bariatric surgery procedures are effective in the treatment of this disorder. Nevertheless, all present bariatric surgery procedures, with the exception of intra-gastric balloon insertion, have significant impact on the innervation of the vagus nerve. Many experimental studies have shown, that signals from the vagus nerve play an important role in the gastrointestinal hormones regulation and transmission of information between enteric nervous system and brain centers responsible for food intake regulation.
Aims & Methods: Therefore, we aimed to determine the effect of vagal innervation on the regulation of food intake and secretion of enterohormones in the pathophysiology of simple obesity as well as the change of these parameters after selected bariatric surgery procedures.

Male Wistar rats were fed with a high-caloric diet for 8 weeks to induce obesity (DIO). Next, sleeve gastrectomy (LSG), truncal varotomy with pyloroplasty (VAG) and intra-gastric balloon insertion were performed alone (BAL) or in combination with truncal vagotomy (VAG + BAL). Animals weight was monitored weekly. After 12 weeks, rats were sacrificed and gastrointestinal biopsies and serum samples from portal vein were collected. Glucagon-like peptide-1 (GLP-1), gastric inhibitory polypeptide (GIP), peptide YY (PYY), ghrelin, glucagon, insulin, leptin and pancreatic polypeptide (PP) concentration was measured using Luminex platform or ELISA.
Results: In rats with VAG, LSG, and BAL+VAG significant weight loss was observed during 4 and 12 weeks after surgery. However, in animals with BAL temporal reduction of weight observed after 4 weeks was reversed after 12 weeks. VAG alone decreased serum content of ghrelin, GIP, PYY and PP but did not affect glucagon, leptin or GLP-1 as compared with intact DIO. BAL increased GLP-1, GIP, decreased ghrelin but did not affect serum concentration of other enterohormones. LSG decreased content of ghrelin, PYY and PP. BAL combined with VAG decreased GLP-1, GIP, PYY, PP as compared with BAL alone.
Conclusion: We assume that the effect of VAG on weight loss was mediated by the modulation of particular enterohormones release. We conclude that VAG increased the effectivness of BAL implementation maintaining its weight loss effect 12 weeks after surgery via modulation of PYY and PP concentration possibly affecting food intake in these animals. [Funding source: National Science Centre, Poland (UMO-2016/23/N/NZ4/03252)].
Disclosure: Nothing to disclose

P2063 PREOPERATIVE UPPER ENDOSCOPY PLAYS AN IMPORTANT ROLE IN ASYMPTOMATIC PATIENTS UNDERGOING BARIATRIC SURGERY

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Introduction: Obesity is a global epidemic and is associated with greater morbidity and mortality. Surgically induced weight loss has become the best treatment for morbidly obese patients. Obesity has been shown to be an important risk factor for several gastrointestinal diseases. Many of these conditions can be clinically relevant and have a significant impact on

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patients undergoing bariatric surgery. The indication Esophagogastroduo-denoscopy (EGD) prior to bariatric surgery is controversial in particular in asymptomatic patients. ASMBS and ASGE recommends preoperative endoscopy in patients with symptoms and individualized H. Pylori screening however, most studies recommend its implementation in all patients. A lack of correlation between patient symptoms and endoscopic findings has been documented by many authors. However, considering the relatively weak clinical relevance of the majority of lesions discovered on routine EGDS and the cost and invasiveness of the procedure, several authors have instead advocated a non-endoscopic approach for asymptomatic patient. Furthermore, many surgeons consider reflux esophagitis or Barrett's oesophagus a contraindication to Laparoscopic Sleeve Gastrectomy (LSG)

Aim: The purpose of this study was to compare the prevalence of abnormal relevant findings and HP status in preoperative EGD before bariatric surgery in asymptomatic and symptomatic patients undergoing bariatric surgery.

Methods: Data was collected from a prospective database of a consecutive series of 212 obese patients undergoing bariatric surgery. The patients were divided into two groups according to gastrointestinal symptoms. *Group 1*: Upper gastrointestinal symptoms *Group 2*: asymptomatic. The endoscopic findings were classified by clinical relevance in: Not relevant findings (did not change the surgical approach) or Relevant findings (change surgical approach or postpone surgery). Moreover, Helicobacter Pylori (HP) assessment by histology was performed in all the patients. Gastric biopsies were performed in elective patients according to the endoscopic findings

Results: In the *Group 1* (symptomatic, 72 patients) 20% of the patients had a normal endoscopy and 37 % of the patients had relevant findings (mainly hiatus hernia, reflux esophagitis) that changed the surgical approach, 10 % of the patients had another major finding (gastric adenoma, Barrett's oesophagus, celiac disease). 62% were HP positive. 10% had intestinal metaplasia. In the *Group 2* (asymptomatic, 140 patients) 25 % of the patients had a normal endoscopy and 32 % of the patients had relevant findings (mainly hiatus hernia, reflux esophagitis). 12 % of the patients had another relevant finding (gastric adenoma, ulcers and Barrett's esophagus, celiac disease). 12% had intestinal metaplasia. 68% were HP positive.

Conclusion: Preoperative EGD in asymptomatic and symptomatic patients undergoing bariatric surgery revealed significant pathology in many patients that alter the medical and surgical management. Similar rates of relevant findings were found in asymptomatic and symptomatic patients. Our results support routine EGD in asymptomatic patients undergoing bariatric surgery

Disclosure: Nothing to disclose

P2064 GUT MICROBIOTA PROFILING IN A PROSPECTIVE POPULATION COHORT IN RELATION TO METABOLIC HEALTH

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Introduction: .Population-based studies have identified regional variations in individual compositions of the fecal microbiota, limiting the relevance of disease-associated signatures from currently available cross-sectional cohorts. KORA is a regionally confined and prospectively followed population study with a focus on cardiometabolic health. In an interval of 5-years, microbiota profiling was performed on consecutive stool samples using high-throughput sequencing

Aims & Methods: Bacterial profiling of two sampling time points (t_1=1,976 and t_2=701 samples) was performed by amplicon sequencing of the V3/V4 and V1/V2 regions of 16S rRNA genes. Data were adjusted to control over confounding variables such as metformin intake, physical activity, vitamin D, PPI, age and gender. To assess shifts in the microbiota linked to metabolic conditions, individuals were stratified based on body mass index (BMI), impaired glucose tolerance (HOMA, fasting glucose and OGTT) to discriminate between healthy, prediabetic and Type-2 diabetes (T2D) conditions.

Results: We obtained a total of 13,352 (V3-V4) and 14,379 (V1-V2) high-quality sequences per sample representing 370±76 OTUs and 255±55 OTUs, respectively, with a Shannon diversity of 4.71±0.37 and 3.99±0.37. Permutational multivariate analysis identified 46 subject-related variables that significantly explained nearly one third of the variations in gut microbiota profiles. Besides triglyceride concentration in blood and body weight, rural versus urban habitats strongly influenced compositional profiles (explaining 0.9% variations). Unsupervised clustering identified three distinct microbiota profiles characterized by significant differences in richness and in the relative abundance of dominant bacterial genera, including *Prevotella* (C1), *Bacteroides* (C2) and *Ruminococcus* (C3). Richness was highest in C1 (423±65 OTUs) associated with a significantly reduced prevalence of obese (p=0.004) and T2D individuals (p=0.015). Lowest diversity and richness was observed in C3 (333±72 OTUs). Richness and Shannon diversity was significantly reduced in obese individuals (BMI > 30).

Interestingly, microbiota profiles of T2D compared to metabolically healthy individuals revealed significantly reduced richness and Shannon diversity in populations with a BMI > 30. *Paired analysis of 701 prospective samples are in the process aiming to validate microbial risk profiles for the development of T2D.*

Conclusion: The microbial ecosystem in the human gut is characterized by a large variation influenced by environmental factors associated with geographic regions, lifestyle, and health conditions. BMI is an important variable to stratify the microbiota profiles of T2D. The prospective fecal microbiota analysis in KORA will allow the identification of microbial profiles that can be predictive of T2D development.

Disclosure: Nothing to disclose

P2065 INTRAGASTRIC BALLOON – HOW IMPORTANT IS MULTIDISCIPLINARY TEAM TO PREVENT WEIGHT REGAIN AFTER IGB USE?

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Introduction: Intragastric Ballon (IGB) has gained popularity recently, however, studies addressing long-term weight loss with IGB are scarce in the current literature. Although different studies cite the importance of the multidisciplinary team in the control and prevention of weight regimen, there are still no studies that quantify the benefits of this follow-up.

Thus, the objective of this study was to evaluate the long-term weight regimen, in a cohort of patients who underwent IGB, among those who did or did not follow the treatment with the multidisciplinary team.

Aims & Methods: Obese patients treated with intragastric balloon (IGB) for a six-month period who underwent balloon removal at least two years before the collection of data, were invited to participate in the study. Patients were stratified based on length of follow-up after IGB removal on the date of interview (2, 3, and 4 years), and relevant factors to weight control as well as behavioral habits were analyzed (A survey was conducted to evaluate the frequency and adherence of the behaviors stipulated by the psychologist and nutritionist, as well as the rhythm of physical activity, in all years of follow-up), and compared by using a logistic multivariate analysis.

Results: A total of 224 patients were included in the study. The mean weight regain was 4.66±4.91 kg, 8.66±6.96 kg, and 9.99±8.44 kg at follow-up on 2, 3 and 4 years, respectively. Multivariate logistic analysis determined risk factors for weight regain according to time span after IGB removal. After 2 years of balloon removal, the significant risk factor was lack of follow-up with a psychologist during treatment; increasing the chance of weight regain 1.13 times compared with those subjects that received psychological follow up (ODDS for 2 years: 1.13; p=0.02; IC95%: 0.55-1.89). An independent and significant risk factor for weight regain after 3 years of IGB removal was the lack of follow-up with a nutritionist after the use of IGB. Chance of weight regain was 3.36 times higher in this group than in individuals who did the nutritional follow-up (ODDS for 3 years: 3.36; p<0.01; IC95%: 1.42-7.94). After 4 years of IGB removal, sedentary behavior was an independent and significant risk factor, increasing the chance of weight regain 3.86 times compared with physically active behavior (ODDS for 4years: 3.86; p=0.03; IC95%: 1.13-12.67).

Conclusion: Weight regain occurs commonly after intragastric balloon removal in up to two-thirds of patients. Lack of psychological and nutritional follow up during and after treatment, as well as sedentary behavior are important risk factors for weight regain.

References: Moura D, Oliveira J, De Moura EG, et al. Effectiveness of intragastric balloon for obesity: A systematic review and meta-analysis based on randomized control trials. Surg Obes Relat Dis 2016;12:420-9. Genco A, Cipriano M, Bacci V, et al. Intragastric balloon followed by diet vs intragastric balloon followed by another balloon: a prospective study on 100 patients. Obes Surg 2010;20:1496-500. Genco A, Maselli R, Frangella F, et al. Intragastric balloon for obesity treatment: results of a multicentric evaluation for balloons left in place for more than 6 months. Surg Endosc 2015;29:2339-43. Crea N, Pata G, Della Casa D, et al. Improvement of metabolic syndrome following intragastric balloon: 1 year follow-up analysis. Obes Surg 2009;19:1084-8.

Disclosure: Nothing to disclose

P2066 INTRAGASTRIC BALLOON: USE OF PROPHYLACTIC NYSTATIN FOR THE PREVENTION OF FUNGAL COLONIZATION

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Introduction: The intragastric balloon (IGB) has been used for more than 20 years in Brazil as an endoscopic method for assisting weight loss, and some intercurrences were observed during more than 10,000 procedures performed. One of these intercurrences is the presence of fungi in the IGB, increasing the friability of the silicone and inducing the premature rupture of the IGB, as well as gas hyperinflation.

Aims & Methods: To evaluate the effectiveness of the use of antifungal (Nystatin), diluted in intragastric balloon filling saline solution, in order to prevent the appearance of fungi in silicon, 120 patients (76.7% women) who underwent adjustable intragastric balloon Spatz3 throughout the year 2017.

Patients were divided into two groups by randomized clinical trial: 60 patients had 50 nystatin mililiters (100,000 IU / ML) mixed with saline solution with Methylen Blue in the IGB filling and the other 60 patients had their IGB filled with saline solution and Methylene Blue. Only the nursing team knew which patients had received antifungals in the filling of the balloon (double-blind study).

The initial volume of IGB filling in all patients was 700ml.

Initial BMI started at 27 kg/m2 and IGB maximum period implant was 12 months.

When the IGB was removed, the Endoscopist described whether there was fungal colonization on the silicone surface and, when there was, divided the colonization on the silicone surface in 4 stages: less than 10% (insignificant), between 10% and 25% (light), between 20 and 50% (moderate) and more than 50% (accentuated). When there was insignificant colonization (up to 10%) it was described as normal in the database.

Results: 19 patients (15.84%) were excluded from the final analysis: 2 (1.66%) due to early removal, 15 (12.5%) did volume adjustment during the IGB and 2 (1,66%) balloon spontaneous deflation or leakage.

Among the 101 patients analyzed, 54 had antifungal in the IGB and 47 only saline and methylene blue.

In the group with antifungal the incidence of fungal colonization was 9.25% (n = 5).

In these 5 IGBs with fungal colonization, 4 (80%) presented light colonization (between 10% and 25% of the surface) and 1 (20%) with moderate colonization (between 25% and 50% of the surface).

In the group without the use of antifungal the incidence of fungal colonization was 19.15% (n = 9). In these 9 IGBs with fungal colonization, 4 (44.5%) presented light colonization (between 10% and 25% of the surface), 3 (33.3%) with moderate colonization (between 25% and 50% of the surface) and 2 (22.2%) with accentuated colonization (more than 50% of the surface).

There was no significant difference in outcomes between men and women and mean age was 30.49 years.

The mean weight loss was -20.64kg (+/- 16.8kg).

Conclusion: The use of mixed nystatin to the saline solution in the IGB filling reduced the fungal colonization in the silicone coating by half, demonstrating that this practice has a positive effect with low cost and significant difference in fungal prevention.

However, even associated with IGB friability, fungal colonization does not prove to be of such importance since balloon spontaneous deflation or leakage corresponded to only 1.66% of the total initial sample and the 14 patients who presented fungi in the IGB (13.86 %) did not present any clinical symptoms.

References: Crea N, Pata G, Della Casa D, et al. Improvement of metabolic syndrome following intragastric balloon: 1 year follow-up analysis. Obes Surg 2009;19:1084-8. 2.Mazure RA, Salgado G, Villarreal P, et al. Intragastric balloon and multidisciplinary team. Nutr Hosp 2009;24:282-7. 3.Sallet JA, Marchesini JB, Paiva DS, et al. Brazilian multicenter study of the intragastric balloon. Obes Surg 2004;14:991-8

Disclosure: Nothing to disclose

P2067 WITHDRAWN

P2068 VITAMIN D LEVELS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Recently it has been shown that Vitamin D has a role in immunomodulation processes. Namely it promotes differentiation of lymphocytes as well as different interleukins such as IL-10, and it may have an effect on production of interferon γ.

Aims & Methods: We aimed to assess Vitamin D levels in inflammatory bowel disease (IBD) patients as well as healthy individuals, and to examine is there a correlation of Vitamin D levels with disease activity. Complete medical records of all patients with histologically diagnosed IBD were evaluated. As a control group we analyzed medical records of age and sex matched healthy volunteers, who had done their annual health check up. A case-control study was preformed among 45 newly diagnosed IBD patients and the same number age, sex matched healthy controls. All patients underwent a total colonoscopy with ileoscopy. Complete blood count was obtained in addition to inflammatory markers (CRP, erythrocyte sedimentation rate-ESR) and serum levels of 25-hydroxyVitamin D. Mayo score, UCEIS and CDAI respectively were calculated for each patient.

Results: Vitamin D deficiency was noted in 60% of patients with IBD and 32% healthy individuals. Serum levels of Vitamin D were significantly lower (P< 0.05) in IBD patients than controls. There were no significant differences in values of Vitamin D in relation to age or gender (P>0.05), although the average values were lower in women. Additionally we have not found statistically significant differences in levels of Vitamin D in patients with UC compared to CD. Moreover serum levels of Vitamin D negatively correlated with CRP and ESR (P< 0.05). Additionally lower levels of Vitamin D negatively correlated with CDAI, UCEIS and Mayo score (P< 0.05).

Conclusion: Our results suggest that IBD patients may have micronutrient deficiency more common than assumed. Additionally patients with active disease have significantly lower levels of Vitamin D, so there is a need for adequate supplementation.

Disclosure: Nothing to disclose

P2069 THE CLINICAL SIGNIFICANCE OF HYPOPHOSPHATAEMIA AFTER INTRAVENOUS IRON INFUSIONS FOR IRON DEFICIENCY ANAEMIA

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Introduction: Intravenous (IV) iron is commonly used to treat iron deficiency in patients with severe symptomatic anaemia or intolerance to oral iron supplements [1]. Ferric carboxymaltose (FCM) is a high dose IV iron known to cause a drop in serum phosphate level that often leads to hypophosphatemia [2]. Hypophosphataemia following FCM administration has been reported to be up 75%, but its clinical significance remains unknown [3].

Aims & Methods: The purpose of this study was to investigate the proportion of patients developing hypophosphataemia following FCM administration and the potential clinical sequel in a tertiary university hospital. The medical records of inpatients that received an FCM infusion between Apr-2016 and Dec-2017 were retrospectively examined. Data on basic demographics, haematinics, phosphate and related biochemistry, were collected at baseline and five follow-up time points.

Results: A total of 321 patients received FCM during the audit period; 61.4% were females. Mean weight ± SD at baseline was 66.7 ± 20.3 kg, age 54.3 ± 23.8 years, haemoglobin 92.2 ± 0.8 g/L, ferritin 163.1 ± 288.5 µg/L, transferrin saturation 13. 2± 13.5%. 25% of patients had inflammatory bowel disease (IBD). Mean iron dose per administration was 902.8 ± 177.4 mg, and 19/321 (5.9%) of patients experienced a hypersensitivity reaction, of which 3/321 (0.9%) requiring IV steroids. Mean baseline phosphate was 1.1 ± 0.3 mmol/L and dropped to 0.97 ± 0.3 following FCM administration. 94/216 (43.5%) of patients with available records had a phosphate level of < 0.8 mmol/L, 63/216 (29.2%) < 0.65 mmol/L and 6/216 (2.8%) < 0.33 mmol/L at any time point up 90 days post-infusion. The temporal trend of phospate reduction is shown in Table 1.

Patients that had a phosphate of <0.65 mmol/L at any point hypophosphataemia (n=63)	% of patients with phosphate of <0.8 mmol/L	% of patients with phosphate of <0.65 mmol/L
0-7 days post FCM infusion (n with available data = 51)	42/51 (82.4%)	37/51 (72.6%)
8-14 days post FCM infusion (n with available data = 38)	25/38 (65.7%)	19/38 (50%)
15-29 days post FCM infusion (n with available data = 35)	23/35 (65.7%)	16/35 (54.3%)
30-60 days post FCM infusion (n with available data = 35)	27/35 (77.1%)	22/35 (62.8%)
>60 days post FCM infusion (n with available data = 11)	6/11 (54.5%)	5/11 (45.5%)

[Temporal trend of hypophospahatemia]

Of those developing hypophosphataemia, 11/94 (11.7%) received oral phosphate and 45/94 (47.9%) IV phosphate. Mean alkaline phosphatase increased from 113.3 IU/L at baseline to 130.0 IU/L at 0-7 days and 146.7 IU/L at 8-14 days post iron infusion (p< 0.05).

Conclusion: In the population examined, a high proportion of patients developed hypophosphataemia following FCM administration. In almost half of the cases that developed hypophosphataemia treatment with Oral/IV phosphate was necessary. A high proportion of those developing hypophosphataemia had a low phosphate up to 90 days post iron infusion. Our data suggest that FCM-induced hypophosphataemia is persistent and has important clinical consequences.

References: [1] Koduru P, Abraham BP. The role of ferric carboxymaltose in the treatment of iron deficiency anemia in patients with gastrointestinal disease. Therapeutic advances in Gastroenterology. 2016 Jan;9(1):76-85. [2] Hardy S, Vandemergel X. Intravenous iron administration and hypophosphatemia in clinical practice. International Journal of Rheumatology. 2015;2015. [3] Fang W, McMahon LP, Bloom S, Garg M. Symptomatic severe hypophosphatemia after intravenous ferric carboxymaltose. JGH Open. 2019.

Disclosure: Nothing to disclose

P2070 A EUROPEAN E-DELPHI SURVEY: EXPERT CONSENSUS ON MANAGEMENT OF IRON DEFICIENCY ANAEMIA IN PATIENTS WITH GASTROINTESTINAL BLEEDING

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Introduction: Gastrointestinal bleeding (GIB) is a common complication of many gastrointestinal conditions with a high mortality rate (5-11%), and one of the the most common causes of iron deficiency anaemia (IDA) (1, 2). While IDA is known to occur in different gastrointestinal disorders, recording and characterising GIB-related IDA (GIB-IDA) in heterogeneous GI conditions is challenging. Therefore, data are scarce and guidelines for diagnosis and management are lacking.

Aims & Methods: This study aimed to use Delphi methodology to obtain an expert consensus on the optimal management of GIB-IDA. An e-Delphi Survey was conducted among 26 European experts in gastroenterology and IDA. Potential participants were chosen based on publications, established clinical expertise and seniority in the workplace, and asked to complete a narrative questionnaire about their clinical practice and opinion on GIB-IDA management. Questionnaires were qualitatively analysed to identify unique propositions for optimal management of GIB-IDA, which were used to formulate a Delphi Questionnaire with 13 different categories including 126 core statements. Here, we present data from the 5 main categories (with 54 statements): 1) Iron treatment for iron deficiency and IDA; 2) Oral iron (reasons to use); 3) Oral iron (reasons not to use); 4) Intravenous (IV) iron (reasons to use); 5) IV iron (reasons not to use). Consensus was defined as at least 75% agreement on the proposition.

Results: Consensus was reached in support of 17 of the 54 statements proposed. The 5 statements with the strongest (>91%) consensus were: 1) In mild anaemia, oral iron may suffice; 2) Clinical findings which suggest the use of IV iron as part of the treatment of IDA include a history of malabsorption states associated with poor absorption of oral iron, such as coeliac disease; 3) First line IV iron treatment should be considered when adverse effects of oral iron occur; 4) The price of IV iron formulations is mostly the reason to use oral iron first line to treat anaemia due to GI bleeding, and 5) A consensus on methods for administration of available IV iron products is needed to reduce inappropriate blood transfusion.

Conclusion: Our study suggests that current use of iron therapy by experts in the field is driven by clinical and cost-orientated considerations, rather than by clinical assessment and therapeutic targets or treatment thresholds. Although experts recognise the importance and effectiveness of IV iron products, consensus is lacking regarding the use of IV iron as first-line therapy in patients with GIB-IDA, although studies show that it may be faster and more cost-effective than oral iron.[1,2] New guidance is therefore needed concerning the optimal therapy of GIB-IDA, including recommendations on the use of IV iron formulations.

References: 1. Pasha SF, Hara AK, Leighton JA. Diagnostic evaluation and management of obscure gastrointestinal bleeding: a changing paradigm. Gastroenterology & hepatology. 2009;5(12):839-50. 2. Rollhauser C, Fleischer DE. Nonvariceal upper gastrointestinal bleeding. Endoscopy. 2004;36(1):52-8.

Disclosure: A. Aksan has received congress expenses from Vifor Pharma. J. Stein has received fees for consultancy and lecturing from Pharmacosmos, and Vifor.

P2071 PROTEIN ENERGY MALNUTRITION ALTERS EPITHELIA-MICROBE INTERACTIONS IN THE INTESTINAL TRACT WITH LONG-LASTING CONSEQUENCES FOR INFLAMMATORY SUSCEPTIBILITY

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Introduction: Maintaining health requires a homeostatic equilibrium between the microbial community and the intestinal epithelium that serves as the regulatory interface with the host. Nutritional stressors such as malnutrition, starvation or caloric restriction disturb this equilibrium and thus provoke changes in the function of the intestinal microbiota and intestinal mucosa.
Aims & Methods: We aimed to elucidate the mechanisms underlying the complex tripartite interplay between microbiota, the intestinal epithelium and the environment (nutritional stressors). We therefore developed experimental protein energy malnutrition (PEM) models to investigate the effects of adult, postnatal and prenatal PEM on the microbiota and host physiology, in particular inflammatory susceptibility.
Results: We found that PEM induced drastic modifications of the host's gastrointestinal tract but also systemic immunity and metabolism. A single episode of PEM extensively changed the overall microbiota composition enriching for Gammaproteobacteria and Bacteroidaceae while depleting for Actinobacteria and Verrucomicrobia along with the functional metagenomic repertoire. The intestinal epithelial transcriptome was also largely reprogrammed in response to PEM. PEM-induced changes in the microbiota and epithelial transcriptome partially remained upon switching to control diet, indicating a "memory effect". Most important, the long lasting PEM-induced microbiome and transcriptome changes also altered the inflammatory susceptibility in an experimental colitis model *in vivo*. On-going experiments aim at determining whether PEM phenotypes are transmissible, for example from the mother to offspring or solely through the altered microbiome.
Conclusion: Our data identified alterations in the microbiome and epithelial transcriptome as potential molecular mechanisms underlying the long lasting physiologic consequences of PEM, thus paving the way to develop probiotic therapeutic interventions for malnutrition.
Disclosure: Nothing to disclose

P2072 DELIVERING PARENTERAL NUTRITION - REAL WORLD CHALLENGES

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Introduction: Parenteral nutrition (PN) is widely used to intravenously deliver nutrition to patients with non-functioning or inaccessible gut. The National Confidential Enquiry into Patient Outcome and Death (NCEPOD) report in 2010, "A Mixed Bag" found good practice regarding PN in only 19% of cases. It recommended an urgent need to deliver high quality nutrition to all patients in hospital.
Aims & Methods: This audit was designed to evaluate our Parenteral Nutrition Service against NCEPOD review. The primary aim was to establish whether the key recommendations of the NCEPOD report are being adhered to: documentation of indication and its appropriateness, consideration of enteral options, clinical and biochemical monitoring during PN, duration of PN and any complications. All adult inpatients who received PN at Darlington Memorial Hospital and University Hospital of North Durham between June- August 2018 were identified from 2 electronic databases viz. referrals to dietetics and electronic prescribing software.
Data collection was done from case notes, inpatient electronic prescription charts and pathology results. Baseline demographics, documented indication for PN, anticipated and actual duration of PN, reason for discontinuing PN and associated complications were recorded and analysed using Excel®.

Results: 49 in-patients were identified over the 3month period, an annualised PN workload of approx. 200 pts/yr. Mean age was 69.2y (46-93), mean weight prior to commencing PN 75.3kg (41.1-114.8kg). 22/49 pts were surgical, 1/49 medical and 16/49 on intensive care. 25/49 pts had a clearly documented indication (ITU 5/16, medicine 10/11, surgery 10/22) but only 1 patient had a documented anticipated duration for PN. Mean duration was 10 days (1-32) and mean length of inpatient stay was 21 days (4-53). Only 7/49 pts were reviewed by a Nutritional MDT team, although all pts were regularly reviewed by Dieticians.
Reasons for discontinuing PN: oral feeding resumed in 28 pts, death/end of life care commenced in 10 pts, NG/NJ/PEG feeding commenced in 6 pts, patient refusal in 2 pts and 3 pts transferred to a tertiary service.
Complications: Abnormal LFTs in 3 pts, abnormal electrolytes in 33 pts and 1 midline associated thrombophlebitis. 16/49 pts had daily testing of serum biochemistry. 30 day all-cause mortality from commencing PN was 18% (9/49).
Conclusion: Our study shows the need for a quality improvement program for PN including documentation of indications and goals of PN treatment. Patients commencing PN should be reviewed by a Nutrition MDT to improve initial assessment and monitoring. A decreased compliance with daily serum biochemistry correlates with an increased incidence of electrolyte abnormality.
Disclosure: Nothing to disclose

P2073 PRELIMINARY ANALYSIS OF THE QUALITY OF LIFE AND NUTRITIONAL STATUS IN PATIENTS REFERRED FOR PERCUTANEOUS ENDOSCOPIC GASTROSTOMY: BENEFICENCE OR NON-MALEFICENCE?

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Introduction: The Percutaneous Endoscopic Gastrostomy (PEG) is an option for long-term enteric feeding, specially in patients with neurologic conditions that affect swallowing or with oropharyngeal malignancies.
Aims & Methods: With this study, we intend to determine how the PEG affect health-related quality of life (HRQoL) and the nutritional status (NS) in patients who were submitted to the procedure. Prospective and unicentric study, designed to assessment HRQoL and NS in patients who received PEG between November 2018 and February 2019 as well as the impact of the procedure in these variables. The HRQoL was assessed with the portuguese version of EQ-5D questionnaire and the NS with *Mini Nutritional Assessment* (MNA), that were performed to the patient or his/her caregiver (in case of response incapacity of the patient), at the time of PEG perform and 2-3 months after that.
Results: A total of 21 patients were included, 52% of male gender, with a mean age of 71±18 years. The nasogastric tube was the main form of feeding (76%), with a median time of use of 5 months (IQR 2-12). In 31% of cases, the body mass index (BMI) was lower than normal (mean BMI of 20±4 kg/m²). According to MNA, 60% of patients were undernourished and 33% with risk of that; among these two groups, an early age was associated to undernourished (p=0.024). In 43% of cases, the health status was considered worse when compared with 12 months before the PEG perform. Nine patients were contacted after received the PEG, in a mean time of 3±1 months; 10% of cases were death, due to causes not related to the procedure. It was verified an improvement in NS with a paired increase of the mean value of MNA after PEG placement (p=0.027). In EQ-5D, it was verified an improvement in capacity of perform daily routine activities (p=0.046). Moreover, a subjective improvement in terms of physical, psychological and emotional welfare was reported (100%, 86% and 71%, respectively).
Conclusion: PEG placement was associated to an improvement in NS and also to one factor in terms of HRQoL. The subjective assessment, in terms of welfare, was overall positive.
Disclosure: Nothing to disclose

P2074 SIMPLE BEDSIDE PREDICTORS OF PERCUTANEOUS GASTROSTOMY TUBE INSERTION FOR SHORT-TERM MORTALITY

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Introduction: Percutaneous endoscopic gastrostomy (PEG) tube insertion has become the most common method for oral enteral nutrition and is mainly reserved for patients who are unable to maintain long-term adequate oral feeding for at least 2-3 weeks and for malnourished patients who are unable to satisfy the body energy requirements. The American Gastroenterological Association recommend PEG insertion in patients who are expected to survive for more than 1 month after the procedure.
Aims & Methods: We aimed to explore simple easily available clinical and laboratory predictors for shor-term survival (within 1- month) after PEG insertion. We performed a single center retrospective study of all patients 18 years old or older who underwent primary PEG insertion for various clinical indication at Galilee Medical Center from January 1st 2014 to December 30th 2018. Primary comparison was performed between patients who survived more than 1 month after PEG insertion (long-term survival)to patients who died within 1 month of the procedure (short-term mortality).
Results: A total of 272 patients who underwent primary PEG insertion. Sixty-four patients (23.5%) died within one month after PEG insertion (group A), compared to 208 patients (76.5%) survived more than 1 month (group B). The mean age in group A was 77.3 ± 14 years as compared to 70.4 ± 17 years in group B. Thirty-two patients (11.8%) were males in group A, compared to 103 patients (37.8%) in group B. The most common two indications for primary PEG insertion in groups A and B were dementia (43.7% vs. 34.6%) and stroke (40.6% vs. 35.6%), respectively.
In univariate regression analysis, only serum albumin and hemoglobin levels were positively correlated with long-term survival following PEG insertion (more than 1-month) (OR 2.973, 95% CI 1.641-5.387, P=0.0003, OR 1.294, 95% CI 1.101-1.520, P=0.0018), respectively. On the other hand, several predictors identified showed negative correlation with long-term survival. Older age (OR 0.971, 95% CI 0.952-0.991, P=0.005), ischemic heart disease (OR 0.494, 95% CI 0.273-0.893, P=0.0197), higher creatinine level (OR 0.438, 95% CI 0.249-0.772, P=0.0043), elevated CRP level (OR 0.992, 95% CI 0.988-0.996, P< 0.0001) and CRP to albumin ratio (OR 0.9, 95% CI 0.970 - 0.989, P< 0.0001). On multivariate logistic analysis, older age (OR 0.9, 95% CI 0.952-0.996, P=0.019), higher creatinine level (OR 0.63, 95% CI 0.379-1.046, P=0.074), and elevated albumin to CRP ratio (OR 0.9, 95% CI 0.974-0.994, P=0.002) correlated with short-term mortality after PEG insertion, while hemoglobin level remained positively correlated with long-term survival (OR 1.18 95% CI 0.995-1.401, P=0.05), with ROC of 0.7274.
Conclusion: We have showed that simple clinical and laboratory bedside parameters including old age, higher creatinine level and elevated CRP to albumin ratio could be useful aid in avoiding gratuitous PEG insertion in these patients population with high risk for short-term mortality.
Disclosure: Nothing to disclose

Paediatric: Upper GI III
09:00-14:00 / Poster Exhibition - Hall 7

P2075 VARIANTS OF THE CHRONIC HP-ASSOTIETED INFLAMMATORY PATHOLOGY OF THE STOMACH AND DUODENUM IN CHILDREN

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Introduction: The detailed location of the process in chronic inflammatory pathology of the stomach and duodenum it is important, because different variants of location have their own etiopathogenetic mechanisms and prognosis.

Aims & Methods: To give clinical, endoscopic and morphological characteristics of various variants of chronic inflammatory pathology of the stomach and duodenum in children.
Patients and methods. 112 children aged 6 - 17 with chronic inflammatory pathology of the stomach and duodenum were examined.
Results: Chronic inflammatory disorders of the stomach and duodenum in children presents 4 variants: isolated duodenitis, duodenogastric, antrum gastritis and pangastritis. In isolated duodenitis in children (17.9 %), morphologically, moderate or severe inflammation in the duodenum mucosa in the intact body and the antral region of the stomach is determined. Duodenogastric (19.6 %) characterizes by the appearance of a slight superficial inflammation in the antrum. In antrum-gastritis (10.7 %), it has a moderate or severe degree, and in some patients can be combined with an initial process in the body of the stomach.
Pangastritis (51.8 %) is characterized by the presence of moderate or severe common inflammation often hyperplasic with follicular or erosive bulbitis. Colonization of the gastric mucosa Hp has differences, depending on the topical version. In the body of the stomach, it is absent or insignificant in patients with the first three options, in pangastritis. Hp is determined in the body in all cases, and in a third of patients (34.4 %) a moderate or severe degree of colonization Of Hp of the body of the stomach is recorded. In antrum-gastritis and pangastritis 83.2 % of children found highly pathogenic strains of Hp. A common feature of all topic variants is the presence of chronic duodenitis. Insulated gastritis without involving in process of the mucosa of the duodenum in children is not detected. There are no significant differences in clinical manifestations of certain topical variants of chronic inflammatory pathology of the stomach and duodenum in children.
Conclusion: Chronic inflammatory disorders of the stomach and duodenum in children is heterogeneous and includes 4 variants: isolated duodenitis, duodenogastric, antrum gastritis and pangastritis. In the absence of differences in clinical manifestations, each variant is characterized by features of pathomorphology of the mucosa of the stomach and duodenum, as well as colonization of Hp.
Disclosure: Nothing to disclose

P2076 SAFETY AND EFFICACY OF THE RAPID REAL TIME 13C-UBT DIAGNOSTIC FOR H. PYLORI DETECTION IN CHILDREN

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Introduction: Helicobacter pylori (*H. pylori*) infection in children is often acquired in the first five years of life and differs from that in adults.
The ELISA stool antigen test is considered convenient for use in children due to lack of a more convenient method. The performance of the Urease breath test (UBT) was reported to be with a sensitivity of only 76.2%, due to antibiotic and PPI consumption.
Aims & Methods: Our aim was to investigate the safety and efficacy of the Exalenz Bioscience 13C-Urea Breath Test using the BreathID® Hp systems compared to the stool antigen test in the pediatric population.
Fifty three (53) children were enrolled to perform the 13C-Urea Breath Test via both the BreathID® Hp Point-of Care (POC) System and the BreathID® Hp Lab System means of breath collection. Results of both breath collection methods were compared with stool antigen testing
Results: BreathID® Hp POC System sensitivity was 93.3% [95% CI (68.05%; 99.83%)] and specificity was 100% [95% CI (86.77%; 100.00%)] compared to stool antigen. The overall agreement in detection of H.pylori using the BreathID® Hp POC System breath test compared to the stool antigen test was 97.56% [95% CI (87.14%; 99.94%)]. BreathID® Hp Lab System sensitivity was 93.3% [95% CI (68.05%; 99.83%)] and specificity was 100% [95% CI (87.23%; 100.00%)]compared to stool antigen. The overall agree-

ment in detection of H.pylori using the BreathID® Hp Lab System breath test compared to the stool antigen test was 97.62% [95% CI (87.43%; 99.94%)]. One minor possibly related adverse event was recorded
Conclusion: The 13C-Urea Breath Test is an accurate, safe, easy to perform, non-invasive method, which aids in confirming the presence or eradication of H. pylori infection. Both breath sample collection methods -the BreathID® Hp POC System and the BreathID® Hp Lab System- are safe and efficacious diagnostic tests in children, without serious adverse events (SAE). The substrate dose used in children is safe.
Disclosure: Nothing to disclose

P2077 THE INFLUENCE OF DIAGNOSTIC DELAYS ON GROWTH OF CHILDREN WITH COELIAC DISEASE IN CENTRAL EUROPE

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Introduction: Coeliac disease (CD) is one of the most common systemic immune-mediated disorders. Undiagnosed and untreated CD can seriously affect nutritional status and growth of affected children.
Aims & Methods: The aim of our study was to assess the influence of diagnostic delays on growth in newly diagnosed children with CD in the Central European (CE) region.
We conducted an anonymised multi-centre web-based survey that was filled out by paediatric gastroenterologists from five CE countries, providing us with data from medical records of CD patients aged < 19 years with CD diagnosis in 2016. Z-scores for weight and height of children with CD at the time of diagnosis were calculated, based on the WHO reference, and related to diagnostic delays measured as the time interval from the symptom onset to confirmation of the diagnosis. Statistical analysis was performed using IBM SPSS Statistics 22.0 for Windows.
Results: Data from 393 symptomatic children (65% female) diagnosed at a median age of 7 years (range 7m-18.5y) from Croatia, Hungary, Germany, Italy and Slovenia were included. The median delay from onset of symptoms to confirmation of the diagnosis was 6m (range 0m-10y). At the time of CD diagnosis, median z-score for weight was -0.44 (min -4.59; max 3.53) and for height -0.07 (min -4.60; max 7.29). No differences were found between girls and boys. Twenty-six of the included children (6.6%) had diagnostic delays longer than 3 years (Table 1). They had lower weight and shorter stature compared to those with the delays of less than one year (z-score for weight: -0.93 and -0.39 respectively, p< 0.05; z-score for height: -0.50 and -0.04 respectively; NS). There was a weak negative correlation between diagnostic delays and z-scores for weight (r=-0.105) and height (r=-0.115) (both p< 0.05).

DIAGNOSTIC DELAY	Number of patients (%)	Weight z-score (median)	Height z-score (median)
0-12 months	288 (73.3%)	-0.39	-0.04
13-24 months	58 (14.8%)	-0.45	-0.27
25-36 months	21 (5.3%)	-0.78	-0.29
>36 months	26 (6.6%)	-0.93*	-0.50
*significant difference vs. 0-12m delays (p<0.05)			

[The influence of diagnostic delays on weight and height of children with coeliac disease.]

Conclusion: Children with CD had slightly lower body mass at the time of diagnosis but similar height compared to healthy children. Longer diagnostic delays lead to progressively lower body mass and, to a lesser de-

gree, also to shorter stature. Efforts are needed to prevent long diagnostic delays and resulting complications, which may permanently affect child development as well as final height and health in adulthood.
*Study was co-financed by Interreg CE programme (CE 111, Focus IN CD)
Disclosure: Nothing to disclose

P2078 HOW LONG SHOULD WE FOLLOW CHILDREN WHO HAVE A FIRST-DEGREE RELATIVE WITH COELIAC DISEASE ?

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Introduction: Family members of patients with coeliac disease (CeD) have 10-40% risk of CeD during lifetime and most affected subjects develop the disease between the age of 2-6 years according to prospective cohort studies. In this study we investigated whether 9 and 12 years old children have new seroconversion and whether gluten consumption habits influence the prevalence.
Aims & Methods: First-degree family members (FDR) presenting for screening were prospectively enrolled and followed by measuring serum transglutaminase 2-specific (TGA) and endomysial (EMA) antibodies at age 3 and 6 years. Children currently aged 9 and 12 years were called for new blood drawings. The investigated cohorts included 134 children from the PREVENTCD study (www.preventcd.com) with randomised early gluten introduction at age 4 or 6 months, a wild cohort (n=302) born in the same years but starting gluten as wished by parents, and other FDR persons with multiple screenings. CeD diagnosis was confirmed by histology showing Marsh III lesions. Results were compared with prevalence data of cross-sectional FDR screening performed first time at the specified age timepoints. HLA-DQ testing was performed if a genetic sample was available.
Results: Altogether 1007 FDR children at risk had an evaluation by TGA testing at age 9 (n=506) or 12 (n=501), or both. No cases occurred in children who were negative for both HLA-DQ2 and DQ8 alleles and gluten introduction time did not influence prevalence. From the children who were still negative at age 3, 10.2% (19/185) developed CeD by age 6, and from those still negative at age 6, 12.0% (3/25) developed CeD by age 9, but no new cases occurred between 9 and 12 years of age. Higher proportions of positives were found at 9 years of age (66/362, 18.2%) or 12 years of age (51/326, 15.6%, p< 0.01), if screening has not been implemented before these timepoints or the index patient was diagnosed only at that time.
Conclusion: Periodic screening of children at risk should be continued until the age of 9 years.
Grant support: GINOP-2.3.2-15-2016-00015, NKFI 120392, EFOP-3.6.1-16-2016-00022, CE111 Interreg Focus in CD.
Disclosure: Nothing to disclose

P2079 EXPLORING THE PROFILE OF CELIAC DISASE BETWEEN ADULT AND PEDIATRIC CELIAC PATIENTS

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Introduction: Past studies reported differences in disease expression, epidemiology, coexisting diseases, complications, and association with obesity, between pediatric and adult patients with celiac disease (CD). The purpose of this study was to compare demographic, clinical and social data as well as adherence status between pediatric and adults celiac disease patients.
Aims & Methods: An anonymous online questionnaire has been sent via the Israeli Celiac association and through social networks. Socio-demographic and clinical data were reported. Adherence to GFD was assessed by Biagi questionnaire.

Results: 445 patients were included in the study, mean age 25.7±17.5 years, 71.9% female. Patients were divided into 6 different age groups- under 6 years old (134 patients) , 6-12 (79 patients), 12-18 (41 patients), 18-30 (81 patients), 30-45 (79 patients) and 45 + years old (23 patients). Abdominal pain, diarrhea, distended abdomen, anemia, TSH abnormalities and short stature had different prevalence among the different age groups. We found significant differences in – Gender (more females in the adult group- 78% vs 63%, P< 0.001) as well as in ethnicity (more Ashkenazy Jew in the adult group, 62% vs 45%, P< 0.001). The pediatric group had more frequent gastroenterology and dietitian follow up (p< 0.001 in both). Pediatric patients reported to be more frequent a part of a supporting group compared to adults (p=0.002). Finally, pediatric patients were found to be more compliant to GFD compared to adults (p< 0.001).

Conclusion: there are differences in the clinical profile of celiac disease between children and adults. Pediatric celiac patients are more adherent to GFD. Different management approach should be considered in the different age groups.

Disclosure: Has been accepted to present as well in the international celiac disease symposiun ICDS 2019 in Paris.

P2080 DOES SHORT SEGMENT COELIAC DISEASE CONFINED TO THE DUODENAL BULB HAVE A UNIQUE CLINICAL, SEROLOGICAL OR HISTOLOGICAL PROFILE?

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Introduction: Coeliac disease (CD) is a common autoimmune enteropathy with increased prevalence worldwide. The diagnosis is based on positive serological tests with proved histological findings in the duodenum. Due to possible patchy villous atrophy pattern, the histological features may be presented only at the duodenal bulb in about 11% of CD patients. So far, any possible association between isolated CD of the duodenal bulb and unique profile of such patients has not been fully explored.

We aimed in this study to investigate whether short segment coeliac disease (SSCD) confined only to the duodenal bulb in pediatric patients has a unique demographic, clinical, laboratory or histological profile at the time of diagnosis compared to more extensive CD.

Aims & Methods: We conducted a retrospective study which included all children, aged 1-18 years who underwent upper endoscopy with duodenal biopsies for a suspicious CD at the Pediatric Gastroenterology Unit in "Assaf Harofhe" Medical Center, Israel. Endoscopies were done between January 2013 and august 2108. The diagnosis of CD was made in accordance with the ESPGHAN criteria. Demographic, clinical data (celiac-associated symptoms), family history of CD and laboratory results (hemoglobin, ferritin, and coeliac serology) at diagnosis as well as histological data were recorded. Histological severity was assessed by MARSH classification.

Results: Out of 160 suspected CD patients, 22 and 19 children were excluded due to lack of serology or a diagnosis of potential CD respectively. Twenty two out of the remaining 113 children had disease confined only to the duodenal bulb-SSCD (19%). The only difference between SSCD to more extensive CD was that children diagnosed with SSCD had lower serum level of anti-TTG antibodies at presentation (p< 0.01).

No significant differences between the two groups were documented in the demographic, clinical and histological features.

Conclusion: SSCD is more common than previously reported in the literature. Despite lower serology titer the histological severity is similar. More prospective studies are needed to illuminate this issue.

Disclosure: Nothing to disclose

Index of Authors and Co-Authors
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