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In-hospital clinical outcomes after upper gastrointestinal surgery: Data from an international observational study

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Abstract

Aims: Previous research suggests that patients undergoing upper gastrointestinal surgery are at high risk of poor postoperative outcomes. The aim of our study was to describe patient outcomes after elective upper gastrointestinal surgery at a global level.

Methods: Prospective analysis of data collected during an international seven-day cohort study of 474 hospitals in 27 countries. Patients undergoing elective upper gastrointestinal surgery were recruited. Outcome measures were in-hospital complications and mortality at 30-days. Results are presented as n(%) and odds ratios with 95% confidence intervals.

Results: 2139 patients were included, of whom 498 (23.2%) developed one or more postoperative complications, with 30 deaths (1.4%). Patients with complications had longer median hospital stay 11 (6-18) days vs. 5 (2-10) days. Infectious complications were most frequent, affecting 368 (17.2%) patients. 328 (15.3%) patients were admitted to critical care postoperatively, of whom 161 (49.1%) developed a complication with 14 deaths (4.3%). In a multivariable logistic regression model we identified age (OR 1.02 [1.01-1.03]), American Society of Anesthesiologists physical status III (OR 2.12 [1.44-3.16]) and IV (OR 3.23 [1.72-6.09]), surgery for cancer (OR 1.63 [1.27-2.11]), open procedure (OR 1.40 [1.10-1.78]), intermediate surgery (OR 1.75 [1.12-2.81]) and major surgery (OR 2.65 [1.72-4.23]) as independent risk factors for postoperative complications. Patients undergoing major surgery for upper gastrointestinal cancer experienced twice the rate of complications compared to those undergoing other procedures (224/578 patients [38.8%] versus 274/1561 patients [17.6%]).

Conclusions: Complications and death are common after upper gastrointestinal surgery. Patients undergoing major surgery for cancer are at greatest risk.

Introduction

1
2 Currently, 310 million patients undergo surgery worldwide each year, with more procedures taking
3 place in high-income countries.[1,2] Estimates of mortality following in-patient surgery vary from 1
4 to 4%,[3-10] but it is now recognised that selected high-risk patient groups are more likely to
5 develop life threatening complications. Postoperative complications increase treatment
6 costs,[11,12] and reduce both life expectancy and quality of life at a societal level.[3,14] Whilst
7 technical errors are unusual during surgery and anaesthesia, poor patient outcomes persist for a
8 variety of reasons. Improvements in the quality of perioperative care for high-risk patients may
9 therefore lead to better patient outcomes.

10
11 Patients undergoing surgery to treat cancer of the upper gastrointestinal tract are an important
12 high-risk group. This includes cancers of the oesophagus, and stomach, which have a poor long-term
13 prognosis. Worldwide, oesophageal cancer is the sixth leading cause of death from cancer.[15]
14 Surgical resection remains the only potentially curative treatment, and is integrated in a multimodal
15 therapy, particularly for advanced disease. Recent data from the United Kingdom suggest one third
16 of patients undergoing oesophageal and gastric surgery for cancer, experience postoperative
17 complications, with hospital mortality rates in the region of 3%.[16] Other reports describe
18 complication rates between 40 and 80%, depending on age, gender, type of surgery, and the
19 presence of chronic disease.[17,18]

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21 The need remains to better understand patient outcomes following upper gastrointestinal surgery,
22 to ensure the planning of effective perioperative care, including appropriate patient selection,
23 surgical approach and postoperative provision of critical care.[14] The International Surgical
24 Outcomes Study (ISOS) was recently conducted to evaluate the incidence and risk factors for
25 complications and death after in-patient elective surgery at a global level, and to describe current
26 standards of postoperative care.[19] ISOS included a prospective sub-group analysis to describe in
27 detail, the clinical outcomes and standards of perioperative care following upper gastrointestinal
28 surgery at a global level, and to describe factors associated with complications during the hospital
29 stay and death in this population.

Patients and Methods

Project organisation

ISOS was approved by the Yorkshire & Humber Research Ethics Committee (Reference:13/YH/0371). We then conducted a sub-group analysis of data collected during this international seven-day cohort study of outcomes following elective adult in-patient surgery. Regulatory requirements differed between countries with some requiring research ethics approval and some requiring only data governance approval. Each participating country selected a single data collection week between April and August 2014. Patient data included only that recorded as part of routine care. Local investigators were supported by national co-ordinators, the international study management group, and via a website which provided all study documentation and guidance on study procedures (www.isos.org.uk/documents). The main ISOS project was registered prospectively with an international trial registry (ISRCTN51817007). The manuscript has been prepared according to the STROBE statement.[20]

The inclusion criteria were all adult patients (age ≥ 18 years) undergoing elective surgery with a planned overnight stay in hospital. Patients undergoing emergency surgery, day-case surgery or radiological procedures were excluded. We aimed to recruit as many hospitals and countries as possible and asked investigators in those hospitals to enrol all eligible patients. No formal sample size calculation was performed. Only hospitals returning valid data describing ≥ 20 patients and countries with ≥ 10 participating hospitals were included in the primary analysis of the ISOS dataset.[19] In this sub-group analysis, we included all patients who underwent upper gastrointestinal surgery by the thoracic or abdominal route, using either an open or laparoscopic technique, identified via the e-CRF.[19] We also investigated whether there were any differences in outcomes between high-income countries, and low or middle-income countries.

Data collection

Data describing consecutive patients were collected until hospital discharge on paper case record forms. Data were censored at 30 days following surgery for patients who remained in hospital. Data were anonymised before entry onto a secure internet-based electronic case record form designed specifically for ISOS, which incorporated automated checks for plausibility, consistency and completeness.

Outcome measures

1 The primary outcome measure was in-hospital postoperative complications assessed using
2 predefined criteria and graded according to the Clavien-Dindo classification.[21,22] The secondary
3 outcome measure was in-hospital mortality. Process measures were admission directly to critical
4 care after surgery, admission to critical care for treatment of a postoperative complication, and
5 duration of hospital stay. A single prospective definition of critical care was used for all countries (a
6 facility routinely capable of admitting patients who require invasive ventilation overnight).
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10 11 12 *Statistical analysis*

13 Statistical analysis was performed using SPSS (version 20.0) and R: A language and environment for
14 statistical computing (R Foundation for Statistical Computing, Vienna, Austria). Categorical variables
15 are presented as number (%) and continuous variables as mean (SD) where normally distributed and
16 median (IQR) where not normally distributed. Univariable analysis was used to select risk factors for
17 postoperative complications. Multivariable logistic regression analysis was used to develop a generic
18 model in which all previously determined risk factors were entered. The threshold for inclusion of
19 variables in the multivariable analysis was $p < 0.05$. All predictors were entered into the model using
20 forced simultaneous entry. With the expected sample size, a limited number of factors could be
21 included in the model without over fitting, and these were selected based on clinical suitability and
22 assessment of correlated variables. Bootstrapping was used to assess the reliability of the models.
23 Goodness-of-fit tests were performed using the Hosmer-Lemeshow test. A process of forward and
24 backward selection, based on minimisation of Akaike's Information Criterion (AIC), was used to
25 derive the final model.[23] Results are presented as odds ratios with 95% confidence intervals. For
26 variables included in our final model, univariable logistic regression was then performed to generate
27 unadjusted odd ratios for comparison with the multivariable model. In the main ISOS database, data
28 describing baseline risk factors were missing for a very small proportion of patients [451/44 814
29 (1%)]. Due to the low proportion of missing data, we performed a complete case analysis where
30 patients with missing data were excluded from the analysis.[19]
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Results

Data describing 44 814 patients were collected in 474 hospitals in the following countries and regions: Australia, Austria, Belgium, Brazil, Canada, China, Denmark, France, Germany, Greece, Hong Kong, Indonesia, Italy, Malaysia, Netherlands, New Zealand, Nigeria, Portugal, Romania, Russia, South Africa, Spain, Sweden, Switzerland, Uganda, United Kingdom, and the United States of America. Fewer than ten hospitals participated in India, Iraq and Mexico and in accordance with the prospective statistical analysis plan, patients recruited in these countries were excluded from the primary analysis. 2139 patients who underwent upper gastro-intestinal surgery in 369 centres were identified in the ISOS database (4 [2-7] patients per centre; Figure 1). Baseline patient data are presented in Table 1.

Process measures

The median stay in a post-anaesthetic care unit was 2 (1-3) hours. 328 (15.3%) patients were admitted to a critical care unit as routine immediately after surgery, with a median critical care stay of 1 (1-4) days. Of these patients, 161 (49.1%) developed a complication with 14 (4.3%) deaths. 121 patients were admitted to a critical care unit to treat complications, of whom 17 (14%) died. The median duration of critical care stay for patients admitted to treat a complication was 5 (1-10) days.

The median overall hospital stay was 5 (2-10) days, increasing to 11 (6-18) days amongst those patients who developed complications.

Clinical outcomes

In total, 498 (23.2%) patients developed complications in hospital, and 30 died before hospital discharge (1.4%). 297 (13.9%) patients developed a single postoperative complication whilst 201 (9.4%) patients developed two or more complications. Data describing postoperative complications are presented in Table 2. There were 368 infectious complications affecting 254 patients, the most frequent being pneumonia and superficial surgical site infections of varying severity (Table 2). There were 125 complications affecting 97 patients related to technical aspects of surgery, such as postoperative bleeding and anastomotic leak (Table 2). The "All other" category of complications were not specified and included deep vein thrombosis, ileus, pancreatitis etc. Nine patients experiencing complications in this category died, however, all had additionally experienced infectious, cardiovascular, or other complications related to the technical aspects of the procedure. In the initial univariable regression analysis, age (OR 1.03 [1.02-1.04]), American Society of Anesthesiologists (ASA) physical status score III (OR 3.33 [2.32-4.78]) or IV (OR 5.51 [3.07-9.88]), surgery for cancer (OR 2.60 [2.11-3.21]), non-laparoscopic surgery (OR 1.79 [1.45-2.21]),

intermediate surgery (OR 1.81 [1.19-2.75]), major surgery (OR 4.34 [2.91-6.48]) and cirrhosis (OR 2.28 [1.05-4.95]) were identified as risk factors for postoperative complications. However during the multivariable logistic regression analysis when adjusted for cofounders, only age, ASA status, surgery for cancer, non-laparoscopic surgery, intermediate and major surgery were identified as independent risk factors for postoperative complications (Table 3). This indicated major upper gastrointestinal surgery to treat cancer as a sub-population at particular risk of poor outcomes (Supplementary Table 1), with twice the rate of complications (224/578 major cancer patients [38.8%] versus 274/1561 [17.6%] patients undergoing minor, intermediate, or major non-cancer procedures (Figure 2). In the major cancer surgery group, 122 (21.1%) patients developed one complication, whilst 102 (17.6%) patients developed two or more complications during their postoperative stay in hospital. Of 2139 patients who underwent upper gastrointestinal surgery, 30 died (1.4%). Non-survivors were older, had higher ASA scores and underwent major surgery (Supplementary Table 2).

Comparison of high-income and low or middle-income countries:

Using the World Bank classification, eight were classed as low or middle-income countries (Brazil, China, Indonesia, Malaysia, Nigeria, Romania, South Africa, and Uganda), and 19 were classed as high-income countries (Australia, Austria, Belgium, Canada, Denmark, France, Germany, Greece, Hong Kong, Italy, Netherlands, New Zealand, Portugal, Russia, Spain, Sweden, Switzerland, United Kingdom, and the United States of America).[24] Patient outcomes for major cancer surgery in high-income countries were similar to the overall international sub-group with 326/1270 patients (25.7%) developing complications with six deaths (2.3%). In this post-hoc analysis, complication rates were lower in the low or middle-income countries 172/869 (19.8%) $p < 0.001$. When explored this we found that although age was similar in both the high and low or middle-income countries 57 (44-68) vs 58 (46-66) years, ASA distribution significantly differed with more ASA 2, 3 and 4 patients being operated in the high income countries (Supplementary Figure 1). Patients in high-income countries underwent fewer minor procedures (Supplementary Figure 2). There were no significant differences between high or low and middle-income countries in terms of risk of complications in the univariable analysis.

Discussion

We report data from an international prospective cohort study describing detailed postoperative outcomes for a population of more than 2,000 patients undergoing elective upper gastrointestinal surgery in 27 countries worldwide. The principal findings were that one in four patients experienced a complication before hospital discharge, compared to one in six of the overall surgical population in the parent study.[19] Surgery involving the upper gastrointestinal tract was associated with higher risk of complications compared to the reference category of orthopaedic surgery in the complete ISOS dataset.[19] According to our results, complications in the upper gastrointestinal surgery group were associated with a two-fold increase in hospital stay, and one in fifteen patients who developed a complication died before hospital discharge. Patients undergoing major cancer surgery are at particular risk, with twice the postoperative complication rate of other patients undergoing upper gastrointestinal surgery. In the univariable analysis, risk of complication was similar when high-income countries were compared to low and middle-income countries. Our results suggest that the greater crude complication rates in high-income countries largely relate to differences in casemix. This finding suggests that measures to reduce complication rates remain important in all countries, regardless of income status.

The complication rates observed in this analysis are lower than those reported in recently studies from Sweden, Japan, Australia and the UK.[16,25-27] The Australian, Japanese and UK studies all reported complications during hospital stay, similar to our methods. Unlike our contemporary snapshot of practice, these studies collected information on patients over several years.[25-27] The ongoing change and improvement in clinical practice over the last decade might partly account for the lower observed complication rates in our series.[28] Infectious complications such as surgical site infections and pneumonia remain commonplace, and are associated with prolonged hospital stays. In previous studies, pneumonia rates as high as 22.5% were reported following oesophagectomy, whereas in our series the rate was only 4.0%, even in the major cancer surgery sub-group.[16,25-27] Similarly, technical complications of surgery were less frequent in this dataset, although this may relate to differences in casemix and improvements in surgical technique and perioperative care compared to the standards observed in previous studies in this international patient sample. [16,25-27]

Mortality rates were lower than expected given the observed complication rates. It is possible that this relates to improvements in the care of patients who develop complications, although this may also be affected by the duration of critical care stay for patients who develop life threatening

1 complications after major elective surgery, which may now routinely exceed 30 days before
2 treatment is withdrawn for reasons of futility. In this context, 30-day mortality may not truly reflect
3 the seriousness of eventual patient outcomes. The risk factors for postoperative complications
4 identified in the ISOS study are well recognised. Age has been shown to be independently associated
5 with higher post-operative morbidity and mortality after major upper gastrointestinal
6 procedures,[29-31] although age alone should not be viewed as a reason to deny patients a
7 definitive surgical treatment. A recent Australian study did not demonstrate any correlation
8 between age and long-term survival, even though postoperative complications were more frequent
9 amongst elderly patients.[31] The findings from our larger international study are consistent with
10 this previous work, confirming the high incidence of complications early after upper gastrointestinal
11 surgery amongst elderly patients. ASA score has been highlighted as a strong predictor of
12 postoperative complications.[32] It is interesting to note that a relatively large proportion of patients
13 undergoing upper gastrointestinal surgery were classed as ASA III or IV, in both cancer and non-
14 cancer cancer groups, with a corresponding increase in the frequency of complications. Similar
15 findings have recently been reported in the UK, with one third of patients undergoing
16 oesophagectomy falling into ASA III and IV categories.[33] Recent recommendations for the
17 treatment of upper gastrointestinal cancer recommend careful patient selection based on
18 physiological reserve and pre-existing co-morbid disease.[34,35] One in six patients in this cohort
19 were admitted to a critical care unit immediately after surgery, half of whom experienced
20 postoperative complications. Although significant progress has been made in the development of
21 perioperative pathways to improve patient outcomes, it remains uncertain what the most
22 appropriate level of postoperative care should be for this high-risk patient group. This is highlighted
23 in the findings of a recent analysis of a large US dataset, which did not identify any benefit of routine
24 critical care admission immediately after major upper gastrointestinal cancer surgery.[36] The
25 secondary analysis of the ISOS dataset also failed to signal any mortality benefit of routine critical
26 care admission following high-risk elective surgery.[37]

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The strengths of this study have been discussed in detail in our previous publication.[19] We used a very simple data set consisting primarily of categorical variables to aid data collection and minimising empty data fields. Patient-level variables were selected on the basis that they were objective, and routinely available to local investigators. We carefully defined surgical procedure categories to identify patients undergoing major upper gastrointestinal surgery by either the abdominal or thoracic route. We also asked investigators to confirm whether the indication for surgery was cancer. The study also has a number of weaknesses. The ISOS project was prospectively

1 designed to allow us to clearly identify patients undergoing upper gastrointestinal surgery, but its'
2 main objective was to evaluate all elective in-patient surgery. Baseline data were not specific to the
3 upper gastrointestinal surgical procedure category, and our multivariable model may not fully
4 account for high mortality rates in hospitals specialising in more complex surgery due to the low
5 number of patients recruited in each centre. It is possible, that given the pragmatic nature of ISOS
6 study looking at only complications during the hospital stay, we missed some of the later events,
7 possibly resulting in an under-estimate of the incidence of postoperative complications. Also, due to
8 the pragmatic nature of the study, external verification of the imputed data was not possible,
9 potentially resulting in misreporting of complications. However, the similar studies from different
10 countries also limited their data collection period to in-hospital stay or 30 days postoperatively and
11 suffered from lack of external data verification.[16,25-28]

21 *Conclusions*

22 The findings of this international cohort study indicate that a large number of patients develop
23 complications after elective in-patient upper gastrointestinal surgery. Patients undergoing major
24 cancer surgery were at particular risk with complication rates approaching one in two patients. To
25 improve patient outcomes, the concept of perioperative medicine is being adopted more widely to
26 ensure safe and effective patient care throughout the perioperative care pathway.[39] International
27 datasets help to set out the baseline for further quality improvement initiatives and can be used for
28 perioperative decision-making and informed consent during upper gastrointestinal surgery.
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Conflict of interest statement

RP has given lectures and/or performed consultancy work for Nestle Health Sciences, Medtronic, Edwards Lifesciences, GlaxoSmithkline and BBraun, and has received research funding from Nestle Health Sciences, BBraun, and Edwards Lifesciences, and is a member of the Associate editorial board of the British Journal of Anaesthesia. All other authors declare they have no conflicts of interest.

11

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13 research grant, and by a National Institute for Health Research (UK) Professorship held by RP. The
14 study was sponsored by Queen Mary University of London. The study funders and sponsor had no
15 involvement in the study design, in the collection, analysis and interpretation of the data, in the
16 writing of the manuscript; and in the decision to submit the manuscript for publication. The
17 International Surgical Outcomes Study group investigators (collaborators listed in the Supplementary
18 Appendix) were entirely responsible for study design, conduct and data analysis. The authors had full
19 data access and were solely responsible for data interpretation, drafting and critical revision of the
20 manuscript, and the decision to submit for publication.
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Contributors

31 RP conceived the analysis and designed this with TS and JP. Patient recruitment and data collection
32 were performed by the members of the International Surgical Outcomes Study group (see
33 Appendix). TS and JP performed the data analysis. The manuscript was drafted by TS and RP, and
34 then revised following critical review by all co-authors.
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Data sharing

43 The authors are happy to consider data sharing requests from bona fide researchers. Participant
44 consent was not obtained but the presented data are anonymised and risk of identification is low.
45 Enquiries should be addressed to the chief investigator at: admin@isos.org.uk.
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References

1. Weiser TG, Regenbogen SE, Thompson KD, et al. An estimation of the global volume of surgery: a modelling strategy based on available data. *Lancet* 2008;372:139-44.
2. Weiser TG, Haynes AB, Molina G, et al. Estimate of the global volume of surgery in 2012: An assessment supporting improved health outcomes. *Lancet* 2015;385:S11.
3. Pearse RM, Moreno RP, Bauer P, et al. Mortality after surgery in Europe: a 7 day cohort study. *Lancet* 2012;380:1059-65.
4. Findlay G, Goodwin A, Protopappa K, et al. Knowing the Risk; A review of the peri-operative care of surgical patients. National Confidential Enquiry into Patient Outcome and Death 2011.
5. Jhanji S, Thomas B, Ely A, et al. Mortality and utilisation of critical care resources amongst high-risk surgical patients in a large NHS trust. *Anaesthesia* 2008;63:695-700.
6. Pearse RM, Harrison DA, James P, et al. Identification and characterisation of the high-risk surgical population in the United Kingdom. *Crit Care* 2006;10:R81.
7. Glance LG, Lustik SJ, Hannan EL, et al. The Surgical Mortality Probability Model: derivation and validation of a simple risk prediction rule for noncardiac surgery. *Ann Surg* 2012;255:696-702.
8. Jencks SF, Williams MV, Coleman EA. Rehospitalizations among patients in the Medicare fee-for-service program. *N Engl J Med* 2009;360:1418-28.
9. Noordzij PG, Poldermans D, Schouten O, et al. Postoperative mortality in The Netherlands: a population-based analysis of surgery-specific risk in adults. *Anesthesiology* 2010;112:1105-15.
10. Yu PC, Calderaro D, Gualandro DM, et al. Non-cardiac surgery in developing countries: epidemiological aspects and economical opportunities--the case of Brazil. *PLoS One* 2010; 5(5):e10607.
11. Scally CP, Thumma JR, Birkmeyer JD, et al. Impact of Surgical Quality Improvement on Payments in Medicare Patients. *Ann Surg* 2014;262:249-52.
12. Sadique Z, Harrison DA, Grieve R et al. Cost-effectiveness of a cardiac output-guided haemodynamic therapy algorithm in high-risk patients undergoing major gastrointestinal surgery. *Perioper Med* 2015;4:13.
13. Head J, Ferrie JE, Alexanderson K, et al. Diagnosis-specific sickness absence as a predictor of mortality: the Whitehall II prospective cohort study. *BMJ* 2008;337:a1469.
14. Pearse RM, Holt PJ, Grocott MP. Managing perioperative risk in patients undergoing elective non-cardiac surgery. *BMJ* 2011;343:d5759.
15. Siegel R, Ma J, Zou Z, et al. Cancer statistics, 2014. *CA Cancer J Clin* 2014;64:9-29.
16. Chadwick G, Taylor A, Groene O, et al. The National Oesophago-Gastric Cancer Audit. An Audit of the care received by people with Oesophago-Gastric Cancer in England and Wales. . 2014.
17. Smith RC, Creighton N, Lord RV, et al. Survival, mortality and morbidity outcomes after oesophagogastric cancer surgery in New South Wales, 2001-2008. *Med J Aust* 2014;200:408-13.
18. Markar SR, Schmidt H, Kunz S, et al. Evolution of standardized clinical pathways: refining multidisciplinary care and process to improve outcomes of the surgical treatment of esophageal cancer. *J Gastrointest Surg* 2014;18:1238-46.
19. ISOS group investigators. Global patient outcomes after elective surgery: Prospective cohort study in 27 low-, middle- and high-income countries. *Br J Anaesth* 2016;117:601-609.
20. von Elm E, Altman DG, Egger M et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *PLOS Med* 2007;4:e296.

- 1 21. Jammer I, Wickboldt N, Sander M, et al. Standards for definitions and use of outcome
2 measures for clinical effectiveness research in perioperative medicine: European
3 Perioperative Clinical Outcome (EPCO) definitions: A statement from the ESA-ESICM joint
4 taskforce on perioperative outcome measures. *Eur J Anaesthesiol* 2015;32:88-105.
- 5 22. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal
6 with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004;240:205-
7 13.
- 8 23. Akaike H. Akaike's Information Criterion. *In: International Encyclopedia of Statistical*
9 *Science*. Berlin: Springer; 2011:p25-5.
- 10 24. World Bank classification of national income (2016). <http://www.worldbank.org/en/country>
11 (accessed 3rd November 2016).
- 12 25. Booka E, Takeuchi H, Nishi T, et al. The Impact of Postoperative Complications on Survivals
13 After Esophagectomy for Esophageal Cancer. *Medicine (Baltimore)* 2015;94:e1369.
- 14 26. Hii MW, Smithers BM, Gotley DC, et al. Impact of postoperative morbidity on long-term
15 survival after oesophagectomy. *Br J Surg* 2013;100:95-104.
- 16 27. Rutegard M, Lagergren P, Rouvelas I, et al. Surgical complications and long-term survival
18 after esophagectomy for cancer in a nationwide Swedish cohort study. *Eur J Surg Oncol*
19 2012;38:555-61.
- 20 28. Markar SR, Karthikesalingam A, Low DE. Enhanced recovery pathways lead to an
21 improvement in postoperative outcomes following esophagectomy: systematic review and
22 pooled analysis. *Dis Esophagus* 2015;28:468-75.
- 23 29. Abunasra H, Lewis S, Beggs L, et al. Predictors of operative death after oesophagectomy for
24 carcinoma. *Br J Surg* 2005;92:1029-33.
- 25 30. McLoughlin JM, Lewis JM, Meredith KL. The impact of age on morbidity and mortality
26 following esophagectomy for esophageal cancer. *Cancer Control* 2013;20:144-50.
- 27 31. O'Grady G, Hameed AM, Pang TC, et al. Patient Selection for Oesophagectomy: Impact of
28 Age and Comorbidities on Outcome. *World J Surg* 2015;39:1994-9.
- 29 32. Sauvanet A, Mariette C, Thomas P, et al. Mortality and morbidity after resection for
30 adenocarcinoma of the gastroesophageal junction: predictive factors. *J Am Coll Surg*
31 2005;201:253-62.
- 32 33. Fischer C, Lingsma H, Hardwick R, et al. Risk adjustment models for short-term outcomes
33 after surgical resection for oesophagogastric cancer. *Br J Surg* 2016;103:105-16.
- 34 34. Alldinger I, Sisic L, Hochreiter M, et al. Outcome, complications, and mortality of an
35 intrathoracic anastomosis in esophageal cancer in patients without a preoperative selection
36 with a risk score. *Langenbecks Arch Surg* 2015;400:9-18.
- 37 35. Atkins BZ, Shah AS, Hutcheson KA, et al. Reducing hospital morbidity and mortality following
38 esophagectomy. *Ann Thorac Surg* 2004;78:1170-6.
- 39 36. Wunsch H, Gershengorn HB, Cooke CR, et al. Use of Intensive Care Services for Medicare
40 Beneficiaries Undergoing Major Surgical Procedures. *Anesthesiology* 2016;124:899-907.
- 41 37. Kahan BC, Koulenti D, Arvaniti K et al. Relationship between critical care provision and
42 mortality following elective surgery: Prospective analysis of data from 27 countries.
43 *Intensive Care Med* 2016 in press
- 44 38. Greco M, Capretti G, Beretta L, et al. Enhanced recovery program in colorectal surgery: a
45 meta-analysis of randomized controlled trials. *World J Surg* 2014;38:1531-41.
- 46 39. King AB, Alvis BD, McEvoy MD. Enhanced recovery after surgery, perioperative medicine,
47 and the perioperative surgical home: current state and future implications for education and
48 training. *Current Opinion in Anaesthesiology*. 2016;29:727-32.

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Table 1. Baseline patient characteristics. Data presented as n (%) or mean (SD). ASA, American Society of Anesthesiologists physical status score; COPD, chronic obstructive pulmonary disease. We compared patients with or without complications, using Mann-Whitney U and Chi-square tests as appropriate. * signifies p<0.05 compared to patients with complications.

	All patients (n=2139)	Patients with complications (n=498)	Patients without complications (n=1641)
Age	56 (16)	61 (15)	55 (16)*
Male	1034 (48.3%)	271 (54.5%)	761 (46.3%)*
Female	1108 (51.7%)	227 (45.6%)	881 (53.7%)*
Smoker	397 (18.8%)	101 (20.3%)	295 (18.3%)
Black ethnicity	190 (9.0%)	32 (6.5%)	158 (9.8%)*
ASA score			
I	337 (15.8%)	43 (8.7%)	294 (17.9%)*
II	1104 (51.7%)	219 (44.1%)	884 (54.0%)*
III	631 (29.5%)	206 (41.4%)	424 (25.9%)*
IV	65 (3.0%)	29 (5.8%)	36 (2.2%)*
Severity of surgery			
Minor	297 (13.9%)	30 (6.0%)	267 (16.3%)*
Intermediate	857 (40.0%)	145 (29.1%)	712 (43.4%)*
Major	985 (46.0%)	322 (64.7%)	661 (40.3%)*
Chronic disease			
Ischaemic heart disease	189 (8.9%)	59 (11.8%)	130 (8.0%)*
Heart failure	83 (3.9%)	28 (5.6%)	55 (3.4%)*
Diabetes mellitus	309 (14.5%)	79 (15.9%)	229 (14.0%)
Cirrhosis	27 (1.3%)	11 (2.2%)	16 (1.0%)*
Surgery for Cancer	750 (35.1%)	269 (54.0%)	479 (31.7%)*
Metastatic cancer	140 (6.6%)	54 (10.8%)	86 (5.3%)*
Stroke	73 (3.4%)	22 (4.4%)	51 (3.1%)
COPD/Asthma	240 (11.3%)	62 (12.4%)	178 (10.9%)
Other chronic disease	926 (43.4%)	259 (52.0%)	630 (38.6%)*
Blood test results			
Haemoglobin (g/dL)	12.7 (2.1)	12.3 (2.2)	12.9 (2.1)*
Creatinine (µmol/L)	79 (53)	84 (54)	77 (52)*
Sodium (mmol/L)	139 (6)	139 (8)	140 (5)
Leucocytes (x10⁹/mm³)	7.7 (4.6)	8.4 (7.6)	7.4 (2.9)
Laparoscopic technique	936 (43.7%)	165 (33.1%)	770 (47.0%)*

Table 2. Complication rates for patients undergoing elective upper gastrointestinal surgery using the Clavien-Dindo classification (I to V). Percentages expressed as a proportion of all patients included in the analysis (n=2139). ARDS, acute respiratory distress syndrome.

	Severity class I	Severity class II	Severity class III	Severity class IV	Severity class V	Cumulative complication rate
Infection						
Pneumonia N (%)	31 (1.4%)	46 (2.1%)	0 (0%)	21 (1.0%)	10 (0.5%)	108 (5.0%)
Superficial surgical site N (%)	42 (2.0%)	28 (1.3%)	5 (0.2%)	3 (0.1%)	1 (0.1%)	79 (3.7%)
Body cavity N (%)	24 (1.2%)	19 (0.9%)	0 (0%)	19 (0.9%)	2 (0.1%)	64 (3.0%)
Deep surgical site N (%)	12 (0.6%)	25 (1.2%)	0 (0%)	12 (0.6%)	4 (0.2%)	53 (2.5%)
Bloodstream N (%)	11 (0.5%)	14 (0.7%)	1 (0.1%)	9 (0.4%)	6 (0.3%)	41 (1.9%)
Urinary tract N (%)	12 (0.6%)	14 (0.7%)	0 (0%)	1 (0.1%)	4 (0.2%)	31 (1.4%)
Cardiovascular						
Arrhythmia N (%)	35 (1.6%)	36 (1.7%)	3 (0.1%)	8 (0.4%)	6 (0.3%)	88 (4.1%)
Pulmonary oedema N (%)	14 (0.7%)	4 (0.2%)	0 (0%)	3 (0.1%)	1 (0.1%)	22 (1.0%)
Cardiac arrest N (%)	-	-	-	5 (0.2%)	9 (0.5%)	14 (0.7%)
Myocardial infarction N (%)	1 (0.1%)	2 (0.1%)	0 (0%)	3 (0.1%)	2 (0.1%)	8 (0.4%)
Pulmonary embolism N (%)	1 (0.1%)	3 (0.1%)	0 (0%)	2 (0.1%)	0 (0%)	6 (0.3%)
Stroke N (%)	1 (0.1%)	0 (0%)	0 (0%)	2 (0.1%)	3 (0.2%)	6 (0.3%)
Other complications						
Post-operative bleeding N (%)	-	56 (2.6%)	0 (0%)	11 (0.5%)	14 (0.7%)	81 (3.8%)
Acute kidney injury N (%)	24 (1.1%)	22 (1.0%)	0 (0%)	10	12 (0.6%)	68 (3.2%)
Anastomotic leakage N (%)	12 (0.6%)	12 (0.6%)	5 (0.2%)	20 (0.9%)	6 (0.3%)	55 (2.6%)
Gastro-intestinal bleeding N (%)	23 (1.1%)	11 (0.5%)	0 (0%)	1 (0.1%)	4 (0.2%)	39 (1.8%)
ARDS N (%)	8 (0.4%)	8 (0.4%)	0 (0%)	3 (0.1%)	5 (0.2%)	24 (1.1%)
All others N (%)	84 (3.9%)	80 (3.7%)	7 (0.3%)	11 (0.5%)	9 (0.4%)	191 (8.9%)
Total N (%)	434 (20.3%)	380 (17.8%)	21 (1.0%)	139 (6.5%)	30 (1.4%)	

Table 3. Results of the multivariate logistic regression model for postoperative complications following upper gastrointestinal surgery.

ASA, American Society of Anesthesiologists physical status score. Data presented as adjusted odds ratios presented with 95% confidence intervals. 148 patients were omitted from the multivariable model due to missing data on one or more covariates. Age: no reference. Odds ratio for age is indexed to years of difference in age, so that in the multivariable model odds ratio for a ten-year increase in age is $1.021 = 1.18$. ASA was treated as a single ordered categorical variable with ASA I as the reference to all other categories (OR=1.0). Cirrhosis – reference: no cirrhosis. Intermediate surgery – reference: minor surgery. Major surgery – reference: minor surgery. Cancer surgery – reference: non-cancer surgery. Open Surgery – reference: laparoscopic surgery.

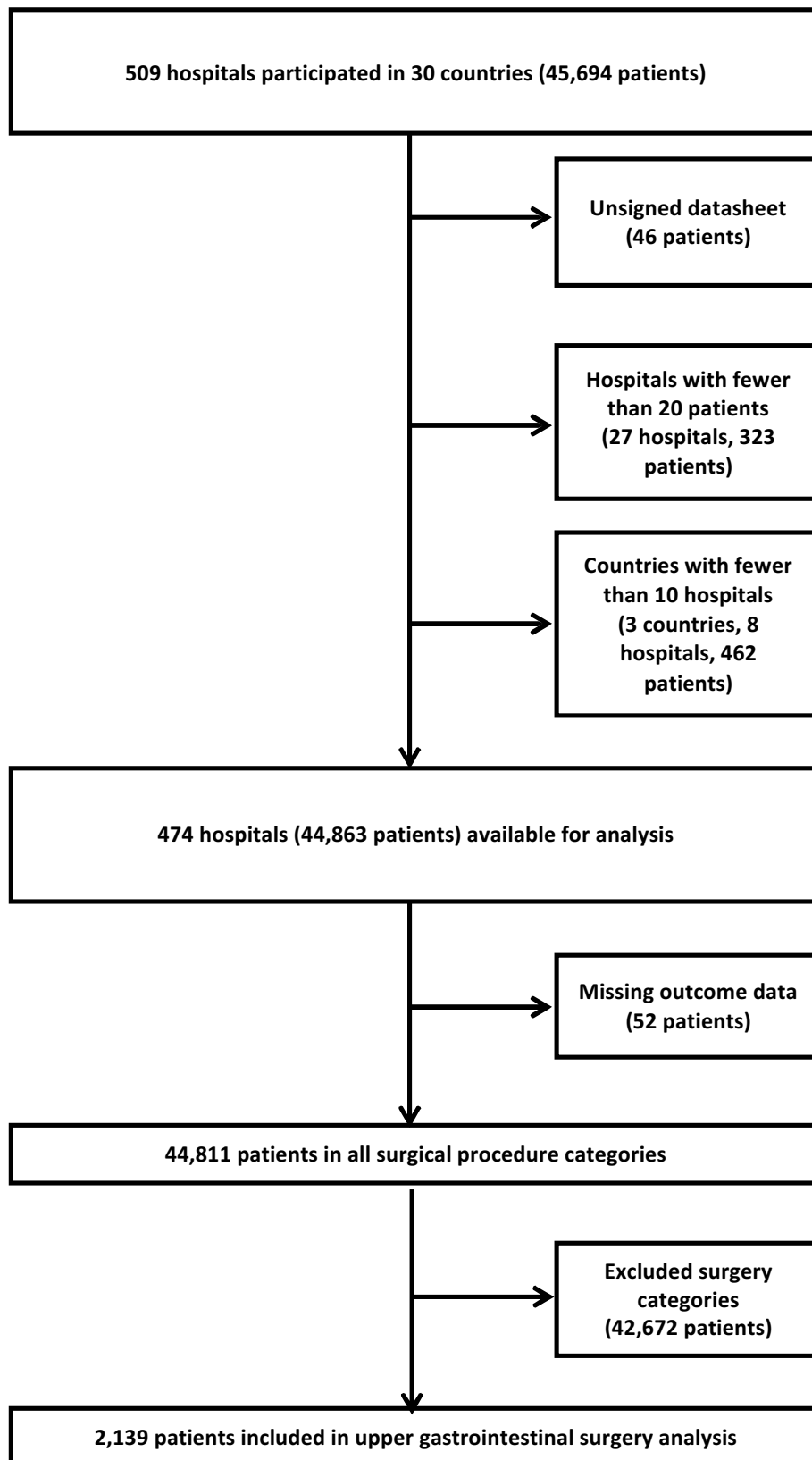
	Multivariable model OR (95%CI)	p-value
Age	1.02 (1.01-1.03)	<0.001
ASA II	1.13 (0.78-1.66)	0.540
ASA III	2.12 (1.44-3.16)	<0.001
ASA IV	3.23 (1.72-6.09)	<0.001
Cirrhosis	2.12 (0.91-4.78)	0.072
Intermediate surgery	1.75 (1.12-2.81)	0.016
Major surgery	2.65 (1.72-4.23)	<0.001
Cancer Surgery	1.63 (1.27-2.11)	<0.001
Open surgery	1.40 (1.10-1.78)	0.006

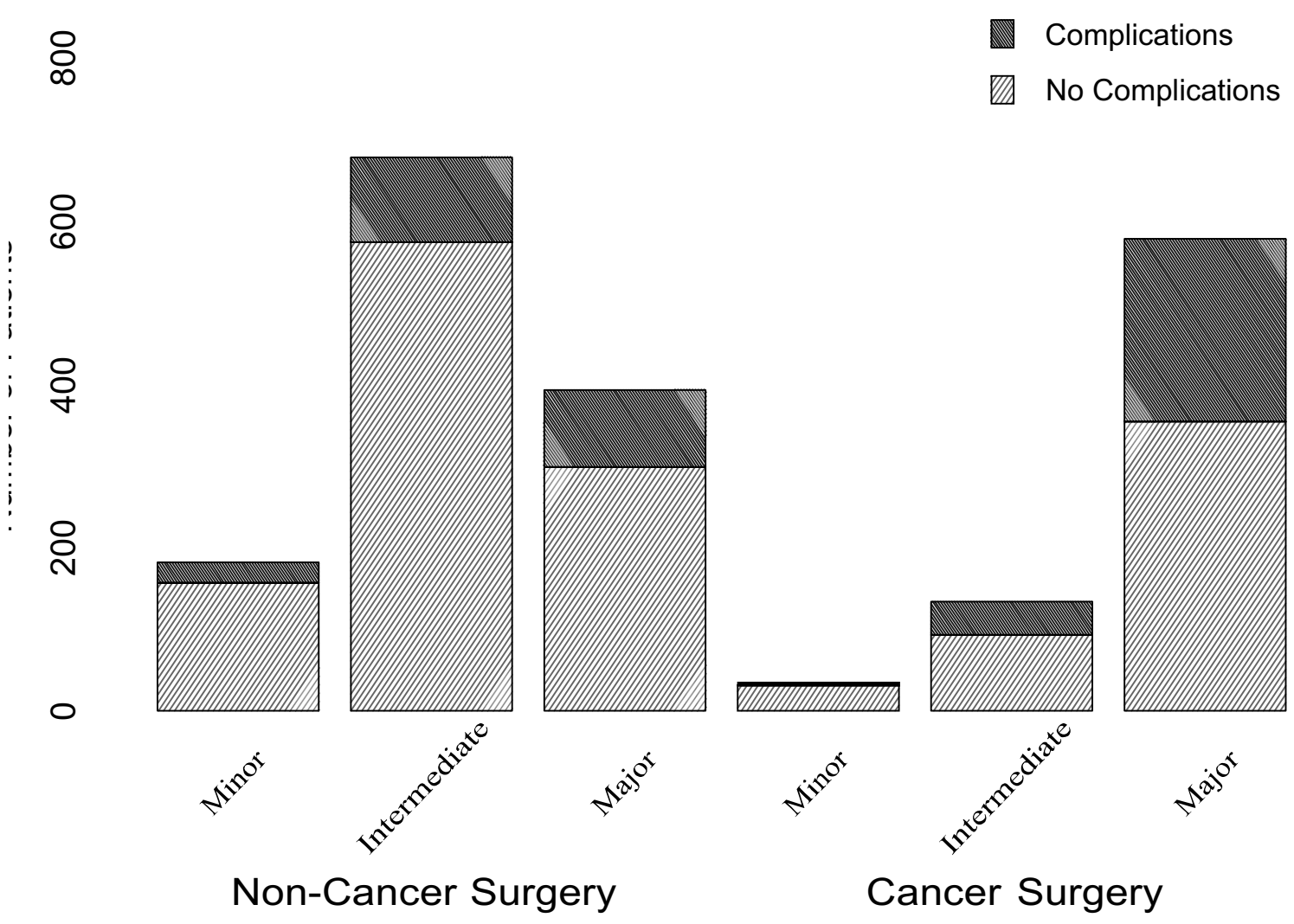
Figure legends

Figure 1. Patients, hospital and countries excluded from study.

Figure 2. Distribution of postoperative complications in major cancer surgery (n=578) and other upper gastrointestinal procedures (n=1561).

Figure 1. Patients, hospital and countries excluded from analysis.





Conflict of Interest statement

Conflict of interest statement

RP has given lectures and/or performed consultancy work for Nestle Health Sciences, Medtronic, Edwards Lifesciences, GlaxoSmithkline and BBraun, and has received research funding from Nestle Health Sciences, BBraun, and Edwards Lifesciences, and is a member of the Associate editorial board of the British Journal of Anaesthesia. All other authors declare they have no conflicts of interest.