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Hendel, Kristoffer; Kjærgaard, Sebastian; El-Hussuna, Alaa

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A systematic review of pre, peri and postoperative factors and their implications for the lengths of resected bowel segments in patients with Crohn’s disease

Kristoffer Hendel a,*, Sebastian Kjærgaard a, Alaa El-Hussuna b

a University of Copenhagen, Blegdamsvej 3B, 2200 Copenhagen N, Denmark
b Aalborg University Hospital, Klinik Kirurgi og Kæftbehandling, Hobrovej 18-22, 9100 Aalborg, Denmark

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A B S T R A C T

Aim: Several pre, peri and postoperative factors may have implications for the lengths of resected small bowel segments in Crohn’s disease patients. It might also affect patient outcome. We reviewed the current literature on factors and their implications for the lengths of resected small bowel segments and possible correlations with postoperative outcome.

Method: Searches were independently engineered by the authors and a research-librarian in MEDLINE and OVID databases using PubMed and EMBASE engines in compliance with PRISMA recommendations. All original articles, reviews and guidelines published in the period of 1985–2016 with last search date 13th of February 2016 on bowel resection in Crohn’s disease patients were assessed for inclusion.

Results: We identified 52 studies for synthesis. Preoperative: Perforation as indication for surgery and increased visceral obesity may be factors resulting in longer lengths of resected small bowel segments. Administration of total parenteral nutrition might reduce resection lengths. Perioperative: No difference in resection lengths in elective versus acute surgery, laparoscopic versus open approaches or in case of intra-operative blood transfusions. Stapled anastomoses might conserve more bowel than sutured ones. Postoperative: The lengths of the resected small bowel segments most likely have no impact on recurrence rates.

Conclusion: No pre, peri or postoperative factors were found to have definitive implications for the lengths of resected small bowel segments. Correlation between the lengths of resection and recurrence is weak.

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1. Introduction

Crohn’s disease (CD) is becoming more prevalent [1] with continually higher incidence rates argued to be 3.1 to 14.6 cases per 100,000 person-years [2,3]. While both medical and surgical treatments for CD is improving, the disease still presents itself with increased morbidity and an increasing burden of disease [4]. Surgical intervention has been shown to still be required in up to two-thirds of CD patients [5]. Furthermore, early surgery can be a factor in better patient outcome [4]. While it appears that strictureplasty procedures for CD have become an accepted treatment option, small bowel (SB) resection is still widely used and considered the only option in penetrative disease phenotypes and long affected segments [6–8]. Pre, peri and postoperative factors may have implications for the lengths of resected small bowel segments in Crohn’s disease patients. There are a limited number of studies on the subject with conflicting reports [9].

Repeated bowel resections can lead to intestinal failure [10], yet it appears there is a lack of quality registries and statistical data on factors that might lead to resection of longer SB segments. Although two thirds or more of CD patients undergo repeated bowel resection during a life-time [9,11], measurements and documentation of the resected bowel segments remain scarce; this makes planning for additional resections more difficult.

A recent shift in favour of laparoscopic surgical approaches and even a single port approach has naturally demanded research comparing the laparoscopic versus open approaches in CD-related surgery [12–14]. A recent review on this includes only a single article reporting on a possible correlation between the two approaches and lengths of the resected segments [15].

While it has been argued that lengths of resection margins do
not affect surgical recurrence [16–18], a newer study suggests that the use of correct resection margins is crucial to avoid recurrence [19]. This further strengthens the need for data on the lengths of resected SB segments in CD patients, especially when margins can be as low as 2 cm [20].

Objectives: To review the current literature for pre, peri and postoperative factors and their implications for the lengths of resected SB segments and possible correlations with postoperative outcome.

2. Materials and methods

Search strategy: (KH) executed a broad-spectrum search strategy (see below) in the MEDLINE and EMBASE records with no limits using the Ovid EMBASE and PubMed search engines. An external research-assistant librarian repeated the search to ensure validity, integrity and robustness of the search strategy. All articles were screened for title and abstract by two authors (KH and SK), and select articles were included for review based on full-text assessment by two authors (KH and SK). All authors participated in the final selection of included studies (KH, SK and AE). Fig. 1 shows our PRISMA flowchart.

(KH) performed data extraction and (AE) re-checked it. Differences were resolved by discussion.

OVID EMBASE and OVID MEDLINE search by authors:

1. crohn* OR inflammatory bowel disease OR IBD-all fields.
2. resection OR resected OR small bowel length OR short bowel OR segment-keyword.
3. 1 AND 2

PubMed MEDLINE search by authors: (((crohn* OR inflammatory bowel disease OR IBD) AND length of resection).all fields.

In total 719 results of which 63 were duplicates resulting in a yield of 656 unique results for the internal searches.


2.1. Inclusion criteria

All original articles, reviews and guidelines published in the period of 1985–2016 with last search date 13th February 2016 about bowel resection in CD patients were included. Inclusion criteria for full-text evaluation:

1. Studies/articles reporting the effect of pre, peri, and postoperative factors on the lengths of resected SB segments.
2. Studies/articles reporting the effect of resected segment length on short- and long-term postoperative outcome.

We retrieved these articles for full-length text reading and their reference lists screened for other relevant articles.

2.2. Exclusion criteria

We excluded articles that did not meet the above stated criteria as well as case reports, editorials, letters to editor, conference abstracts and articles where full text was not available.

2.3. Assessment of risk of bias

The quality of bias control in the included observational studies was assessed using the Newcastle-Ottawa scale (NOS). All the included studies present a high risk of bias.

3. Results

We included 52 articles in this review, please see Fig. 1 for a PRISMA flow-diagram. The following subsections and paragraphs present our findings in segments divided by types of comparisons made. Any article may appear in two or more segments if applicable. It was not possible to conduct meta-analysis of the included studies because of heterogeneity in outcome measurements, methodology and reporting of outcome measurements. An overview of the following results is available as Table 1.

3.1. Preoperative factors

3.1.1. Studies comparing the lengths of resected SB segments and different preoperative factors [11,21–28]

One study found that structuring versus fistulising indications for surgery does not affect the lengths of the resections [21]. Another study found the difference based on perforating versus stenotic indications to be of significance, the former patient group having more lengths resected p < 0.001 [22]. Both studies lack adjustment for other factors that might influence resection lengths. Another factor that shows an effect on the lengths of resected SB segments is visceral obesity (BMI and CT-scan evaluation); longer SB segments were resected in patients with visceral obesity VFA ≥ 130 cm squared, p = 0.04 tested in univariate analysis. The results were not adjusted for other factors [23]. This appears, however, not to be related to preoperative lipid profile after adjusting for confounding factors in multivariate analysis [24]. Furthermore, the post-surgical lipid profile also seems to be unaffected [28].

Preoperative medical treatment and the lengths of resected SB segments: One study showed no link between the use of a preoperative immunosuppressant and the lengths of the resected segments p = 0.33 in univariate analysis [22]. However, with the added cost of longer lengths of stay, total parenteral nutrition (TPN) administration appears to reduce the lengths of resected SB segments in patients undergoing ileo-coelic resection p < 0.001, and near-significantly in patients undergoing segmental SB resection p < 0.09 when tested in multivariate analyses [25].

While initial SB lengths and postoperative residual SB lengths appear not to influence the likelihood of recurrence [26,27], one study found a correlation between preoperative extent of diseased segments and extent at recurrence r = 0.7, p < 0.001 [11]. This result has however not been adjusted for other factors.

3.2. Perioperative factors

3.2.1. Studies comparing the lengths of resected SB segments in patients undergoing elective vs acute surgery [10,22,29]

A single-centre retrospective study found no difference in the lengths of resected SB segments based on whether the surgery was elective or acute p = 0.14 [29]. Another retrospective study analysed patients with intestinal failure and found in agreement with this,
that residual lengths of SB were the same regardless of elective vs acute indication for surgery $p < 0.001$ [10]. These findings were cemented in a multi-centre retrospective study that showed no difference $p = 0.07$ [22]. All three studies failed to provide multivariate analyses.

3.2.2. Studies investigating the lengths of resected SB segments, surgical approach, anastomosis type and blood transfusion [12–14,30–39]

Several retrospective studies have assessed the influence of open versus laparoscopic approach on the lengths of resected bowel segments and found no difference [12,14,30]. However, a Hungarian study [40] suggests that laparoscopic access resulted in shorter lengths of resected SB segments $p = 0.03$. None of these studies made correlation analyses. Two prospective studies failed to provide thorough statistical data [12,31], but came to the same conclusions as a randomised study finding no difference in multivariate analyses [32]. A systematic review also found no difference [39]. The type of laparoscopic approach whether it being a single-port or multi-port approach, had no effect on the lengths of the resected segments [33].

The only available research about anastomosis type is a retrospective study showing that shorter lengths of SB segments were resected using a stapled anastomosis vs a sutured one $p = 0.04$ [38]. Perioperative blood transfusion appears to have no effect on SB resection lengths in a retrospective study using multivariate analyses [34]. This is in agreement with a later meta-analysis [35].

3.3. Postoperative outcome

3.3.1. Studies investigating the length of resected SB segments and correlation with recurrence [9,11,17,18,26,27,34,35,39,41–64,65]

Although symptomatic recurrence correlated to preoperative affected segment length $p = 0.001$ in one retrospective study [11], the finding could not be reproduced in two prospective studies [26,27]. None of the studies above are adjusted for possible confounders in multivariate analyses.

Surgical recurrence: Two retrospective studies on surgical recurrence [41,42] found that more extensive resections correlate with lower rates of recurrence. While the former does not provide any statistical data, the latter reported statistically significant results at $p < 0.05$ based on 45 patients that had resection of $>25$ cm

Records identified through database searching
$(n = 336 + 383 + 2010 = 2729)$

Additional records identified through other sources
$(n = 30)$

Records after duplicates removed
$(n = 2319)$

Records screened
$(n = 2319)$

Records excluded
$(n = 2142)$

Full-text articles assessed for eligibility
$(n = 177)$

Full-text articles excluded, with reasons as stated in text
$(n = 125)$

Studies included in qualitative synthesis
$(n = 52)$

Studies included in quantitative synthesis (meta-analysis)
$(n = 0)$

Fig. 1. (a) first picture; (b) second picture.

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Year</th>
<th>Type</th>
<th>No. of patients</th>
<th>Follow-up in months</th>
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<th>Results of univariate analyses</th>
<th>Results of multi-variate analyses</th>
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<td>Prospective</td>
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<td>Difference</td>
<td>p = 0.07</td>
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<td>Agwuobhi et al.</td>
<td>2001</td>
<td>Retrospective</td>
<td>41</td>
<td>6–324</td>
<td>No difference</td>
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<td>2015</td>
<td>Retrospective</td>
<td>74</td>
<td>N/A</td>
<td>Stricture vs fistula</td>
<td>p = 0.91</td>
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<td>1995</td>
<td>Prospective</td>
<td>23</td>
<td>32–242</td>
<td>Extent of disease correlation with symptomatic recurrence</td>
<td>p = 0.001</td>
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<td>Prospective</td>
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<td>24–216</td>
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<td>Prospective</td>
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<td>N/A</td>
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<td>Prospective</td>
<td>28</td>
<td>N/A</td>
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<td>Horvath et al.</td>
<td>2014</td>
<td>Prospective</td>
<td>133</td>
<td>N/A</td>
<td>Open vs laparoscopy</td>
<td>ns</td>
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<td>RCT</td>
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<td>N/A</td>
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<td>Gardenbroek et al.</td>
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<td>Prospective</td>
<td>63</td>
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<td>Sica et al.</td>
<td>2001</td>
<td>Prospective</td>
<td>56</td>
<td>1–126</td>
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<td>Welsch et al.</td>
<td>2007</td>
<td>Prospective</td>
<td>100</td>
<td>60 (mean)</td>
<td>Correlation between &gt; 20 cm resection lengths and recurrence</td>
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<td>2012</td>
<td>Prospective</td>
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<td>12</td>
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<td>Silvis et al.</td>
<td>1994</td>
<td>Retrospective</td>
<td>148</td>
<td>56 (median)</td>
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<td>N/A</td>
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<td>Eshuis et al.</td>
<td>2009</td>
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<td>71</td>
<td>50–124</td>
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<td>Prospective</td>
<td>164</td>
<td>36</td>
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<td>1995</td>
<td>Retrospective</td>
<td>172</td>
<td>1–21</td>
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<td>Miro et al.</td>
<td>2008</td>
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<td>Buisson et al.</td>
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<td>Review</td>
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<td>Hollaar et al.</td>
<td>2011</td>
<td>Meta-analysis</td>
<td>(7) 622</td>
<td>72.8 (mean)</td>
<td>Correlation between resection lengths and recurrence</td>
<td>True</td>
<td>N/A</td>
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</tbody>
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(continued on next page)
correlating with lower rate of recurrence. Different literature reviews attained conflicting results [9,39,55,56], but most of these studies found no correlation between the lengths of the resected SB segments and recurrence.

Endoscopic recurrence: A prospective study of 29 patients [47] investigated endoscopic recurrence and found a correlation with extensive resection at > 100 cm ($p = 0.03$), increasing the risk of recurrence. Even less aggressive resections (20 cm) may carry risk of recurrence at 0.42 (CI 0.21-0.84) as shown in another study [45].

These findings are supported by retrospective studies [17,34,35,43,44,46,48–53] that found no correlation in addition to a meta-analysis [54] reviewing three articles including one of the above cited articles [48].

On resection margins: Indirectly connected to the matter on the lengths of resected SB segments is data on resection margins. Five studies [17,18,53,57,65] found no difference in recurrence based on different lengths of resection margins, cemented by reviews of the literature [39,55]. Conversely, four studies [43,58–60] found that conservative or non-radical margins are linked to higher rates of recurrence at $p < 0.01$ and $p = 0.003$.

On gallstones: Patients undergoing gallbladder surgery are more likely to have gallstones requiring surgery $p < 0.001$ in multivariate analysis [61]. This might be due more to the total loss of length than the incremental loss of length; it is however yet another reason in favour of a conservative approach.

<table>
<thead>
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<th>Author(s)</th>
<th>Year</th>
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<td>Strong et al. [55]</td>
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<td>Review</td>
<td>(6)</td>
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<td>Review</td>
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<td>Carlstedt et al. [62]</td>
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<td>12–312</td>
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<td>Retrospective</td>
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</tr>
<tr>
<td>Martin et al. [43]</td>
<td>1994</td>
<td>Retrospective</td>
<td>286</td>
<td>55 (mean)</td>
<td>Recurrence in correlation to conservative &gt; radical margins of resection</td>
<td>$p = 0.003$</td>
<td>None</td>
</tr>
<tr>
<td>Fazio et al. [65]</td>
<td>1996</td>
<td>Prospective</td>
<td>131</td>
<td>55 (median)</td>
<td>Recurrence in correlation to resection margins 2 cm vs 12 cm</td>
<td>ns</td>
<td>N/A</td>
</tr>
<tr>
<td>Recurrence and additional surgeries: Ellis et al. [41]</td>
<td>1984</td>
<td>Retrospective</td>
<td>18</td>
<td>7–384</td>
<td>Correlation between loss of length and additional hospitalisations</td>
<td>ns</td>
<td>N/A</td>
</tr>
<tr>
<td>Mappes et al. [63]</td>
<td>1994</td>
<td>Retrospective</td>
<td>65</td>
<td>N/A</td>
<td>Correlation between additional surgeries and loss of length</td>
<td>$r = 0.8$</td>
<td>None</td>
</tr>
<tr>
<td>Elriz et al. [22]</td>
<td>2011</td>
<td>Retrospective</td>
<td>38</td>
<td>N/A</td>
<td>Correlation between first and last resection in loss of length</td>
<td>$p &lt; 0.001$</td>
<td>None</td>
</tr>
<tr>
<td>Pelletier et al. [64]</td>
<td>2011</td>
<td>Retrospective</td>
<td>24</td>
<td>N/A</td>
<td>Correlation between additional surgeries and loss of length</td>
<td>$p = 0.005$</td>
<td>None</td>
</tr>
</tbody>
</table>
On ileostomy: In a patient population in need of long-term ileostomy for either CD or UC, no association was demonstrated between the lengths of resected SB segments and ileostomy complications [62].

On repeated surgeries: It is still controversial whether the lengths of resected SB segments in repeated surgeries correlates with that of resected SB segments in primary surgery. There are few studies supporting such correlation [41,63] and few that do not [27,64].

4. Discussion

We present a systematic review of the literature on pre, peri and postoperative factors and their implications for the lengths of resected SB segments and outcome in CD patients. Due to high risk of bias and a highly heterogeneous pool of data for comparable parameters, meta-analysis was not an option for the present review.

As shown in our results, most factors do not appear to have any implications for the lengths of resected SB segments. However, due in part to the already stated problems with the included studies, great caution must be taken accepting this conclusion. Generally, the studies researching the same parameters differed greatly in methodology, objectives and outcome reporting. Often, investigated factors only accounted for a minor part of a greater study and many articles lacked proper multivariate analyses. Most of the included studies did not differentiate between different phenotypes of CD. These are all limitations to this review while strengths include a very broad-spectrum search strategy and very generous inclusion criteria.

Considering the above, the present review most importantly exposes a lack of homogenous well-researched data on resection surgery in CD patients. Furthermore, different practices of resection lengths, lengths of clear margin and supportive care appear to be based on speculation.

To properly research methods to increase quality of life, outcome and evaluate pharmacological treatment for CD patients in need of surgery, we believe it is of great importance to report the lengths of resected SB segments in CD surgery in addition to factors like phenotype, loss of blood and length of remaining SB. This is often neglected due to the traditional view that surgery and SB resection is only a consequence of non-response to medical treatment. In this traditional view, the surgeon’s role is to resect SB and return the patient to a medical gastroenterologist for further management. This concept has been challenged in the last few years. Multi-disciplinary team management is becoming the gold standard in leading IBD centres with a IBD-surgeon as part of the operative management of duodenal Crohn’s disease. Dis Colon Rectum 2013 Feb;56(2):519–25.


Considering the above, the present review most importantly exposes a lack of homogenous well-researched data on resection surgery in CD patients. One third of CD patients may need medical treatment to another for long periods of time may lead to poor quality of life as well as longer lengths of SB resections. This can only be confirmed or ruled out if SB length is reported.

Claims that biologics decrease the lengths of resected SB segments have not been properly investigated due to lack of recording of such data.

Postoperative recurrence and its correlation with lengths of resected SB segments have been investigated in small series studies with high risk of bias. More well-designed studies cannot be conducted properly without an emphasis on reporting resected SB lengths.

The traditional fear of repeated surgeries leading to short bowel syndrome has led to extended periods of medical treatment attempts before the patient is assessed for both initial and repeated surgical resections. In an era of bowel sparing surgery, this route of treatment options is not based on well-researched evidence; regardless of various kinds of approaches, the best course of action cannot be properly assessed without studies comparing the lengths of resected SB segments using different modalities.

Nowadays, different national and international cancer register databases exist. These databases report many factors like ASA score, performance level, perioperative blood loss and site of ligation of blood vessels etc. With a challenging disease like CD, the need for such databases is essential to provide better treatment options. Lengths of resected SB segments is one of the parameters that should be reported in such databases and be investigated in future studies.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.ijso.2017.04.002.

References


