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ORIGINAL ARTICLE

Preoperative factors associated with prolonged postoperative in-hospital length of stay in patients with Crohn's disease undergoing intestinal resection or strictureplasty

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Abstract

Purpose To investigate factors that influence postoperative in-hospital length of stay (LOS) in patients with Crohn's disease (CD) undergoing bowel surgery. Furthermore, the study aimed to evaluate LOS as a surrogate for postoperative outcome.

Methods This is a multicentre retrospective cohort study. Inclusion criteria were adult patients with CD who underwent bowel surgery with either anastomosis or stricturoplasty. All timings of surgeries were included regardless of the method of access to the abdominal cavities. Patients with stoma were excluded. Demographic data, preoperative medications, previous operations for CD, preoperative sepsis, and operation were recorded. Primary outcome was LOS while secondary outcome variable was postoperative complications.

Results A total of 449 patients who underwent abdominal surgery for CD were included. Of the 449 patients, 265 were female (59%). Median age was 37 years (IQR = 20), median LOS was 7 days (IQR = 6). Patients with longer LOS had higher rates of re-laparotomy/re-laparoscopy (45/228 (19.7%) versus 9/219 (4.1%) $p = 0.01$). In multivariate analysis, age (OR = 1.024 [CI 95% 1.007–1.041], $p = 0.005$), preoperative intra-abdominal abscess (OR = 0.39 [CI 95% 0.185–0.821], $p = 0.013$), and previous laparotomy/laparoscopy (OR = 0.57 [CI 95% 0.334–0.918], $p = 0.021$) were associated with prolonged LOS. LOS correlated with postoperative complications after adjustment for age, gender, previous laparotomy/laparoscopy, and preoperative intra-abdominal abscesses (OR = 1.28 [CI 95% 1.199–1.366], $p < 0.0001$).

Conclusion Age, preoperative intra-abdominal abscess, and previous laparotomy/laparoscopy significantly prolonged LOS. LOS correlated with postoperative complications and can therefore be used in epidemiological or register-based studies as a surrogate for postoperative outcome.

Keywords Crohn's disease · Length of postoperative stay in hospital · Postoperative complications · Inflammatory bowel disease · Surgery

Introduction

The probability of surgical intervention in patients with Crohn's disease (CD) 1 and 5 years after diagnosis is 16.3% and 33.3%, respectively, with a 10-year cumulative probability of surgery ranging between 38–50% in the literature. Two thirds of those patients may require a second surgical procedure [1–4]. A more recent epidemiological study suggests a decrease in resection rate during the last decades, revealing a resection rate 1 to 10 years after diagnosis of 13% and 22%, respectively [5]. In patients with CD, surgery is indicated in several clinical scenarios, including stricturing CD with obstructive symptoms, fistulizing/perforating CD, perianal CD with infectious complications, issues related to the drainage of

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an abscess, lack of response to medical therapy, steroid dependence, or, rarely, malignant transformation [6].

Following surgery for CD, patients are often hospitalized for several days with a median postoperative length of hospital stay (LOS) ranging from 7–12 days [7, 8]. Risk factors associated with prolonged LOS are hypoalbuminemia, cortisone usage, and comorbidities [9–11]. Other factors have also been shown to prolong the LOS, such as age, preoperative narcotics, laparotomy, and handsewn end-to-end bowel anastomosis [12–15]. The postoperative complications following surgery for CD include anastomotic leakage, wound rupture and infection, intra-abdominal septic complications (IASC), postoperative ileus (POI), and cardiovascular events. The risk of postoperative complications in CD ranges between 20–25% in the literature [16, 17]. IASC, mainly postoperative abscess and fistulas, further prolong the LOS [18, 19]. Patients with CD are also more likely to have a longer LOS compared with those operated for colon cancer (CC), possibly due to an enhanced postoperative inflammatory response [20].

Although postoperative complications prolong LOS, there is a lack of evidence of correlation between prolonged LOS and postoperative complications in patients with CD undergoing bowel surgery. Postoperative complications are usually used as a quality indicator and consequently are used as primary outcome variables in surgical literature. However, postoperative complications might not be accurately registered, leading to weakness in registry data and the studies built on them. Complete registration of data is another factor that affects the use of postoperative complications as an indicator of outcome in big data registries.

The aim of this study was to investigate pre- and perioperative risk factors that might influence the postoperative LOS in patients with CD undergoing bowel surgery. Furthermore, the study aims to evaluate LOS as a surrogate of postoperative outcome by examining its correlation with postoperative complications.

Material and methods

Study design

This is a multicentre retrospective cohort study of patients with CD who underwent abdominal operations in four tertiary Danish centers. The primary outcome was defined as LOS measured in days after surgical intervention. The day of operation is considered as day 0. Secondary outcome was defined as all the postoperative complications.

Patients

Inclusion and exclusion criteria: adult patients with CD who underwent bowel surgery as part of the treatment for CD were included. Urgent, expedited, and elective surgeries were included regardless of the method of access to the abdomen (open, laparoscopic, or converted). Only patients who had an anastomosis or stricturoplasty were included. Patients with stoma (defunctioning or permanent) were excluded because stoma construction prolongs LOS [21, 22] and might be a strong confounding factor [23].

Teaching the patients how to manage their stoma is required by Danish guidelines and it usually prolongs the in-hospital length of stay in Danish hospitals.

Demographic data, preoperative medications, previous operations for CD, preoperative sepsis, and operation were recorded. Part of this cohort was previously investigated by El-Hussuna et al. [24], which examined the data collected in 2000 to 2007. The cohort which is presented in this study comprises more data and investigates different outcome variables.

Patients were divided into two groups for comparison of LOS. As patients were not normally distributed, the median was used for this comparison. LOS was dichotomized to facilitate comparison.

Group 1: Patients who had LOS shorter than median LOS

Group 2: Patients who had LOS equal or longer than median LOS

All the participating hospitals followed a standard postoperative enhanced recovery pathway as recommended by the health regulator in Denmark (Sundhedsstyrelsen). Appendix 1 shows the details of this (Danish). All the patients received a single dose of intravenous antibiotics at the start of anaesthesia and received thrombosis prophylaxis during their stay at the hospital.

Statistical analysis

The SPSS program version 22 was used for analysis of data. Continuous variables were reported using median and interquartile range. For the univariate analysis, Pearson chi-square and Fischer's exact tests were used. Continuous data were compared with the Mann–Whitney *U* test. Multivariate logistic regression was used to investigate postoperative outcome and LOS, and adjustment for confounding was done by stepwise backwards elimination, starting with a model including all pre- and perioperative characteristics deemed clinically and/or statistically significantly different between the two treatment groups. Variables were then removed one by one until all variables had $p < 0.05$.

Logistic regression analysis was used to identify independent predictors of outcome. A two-sided *p* value less than 0.05 was considered as statistically significant. The correlation between LOS and postoperative complication was investigated using logistic regression.

Table 1 Patients' characteristics in 447 patients with CD. The tables show a comparison between the two groups depending on their LOS dichotomized using median value to facilitate comparison. LOS was unknown for 2/449 patients included in the cohort

Patients' characteristics	LOS < median 219/449 (48.8%)	LOS ≥ median 228/449 (50.8%)	Uni-variate *p* value	Multi-variate OR (CI 95%)
Age	Median 34.00 IQR 20	Median 39.00 IQR 22	0.000	1.024 (1.007–1.041) $p = 0.005$
Female	130/219 (59.4%)	133/228 (58.3%)	0.825	
Cortinson treatment	84/219 (38.4%) (missing 2)	81/228 (35.5%)	0.487	
Prednisolon	78/219 (35.6%)	75/228 (32.9%)		
Solu-Medrol	3/219 (1.4%)	5/228 (2.2%)		
Other cortisons	3/219 (1.4%)	1/228 (0.4%)		
Immuno treatment	84/219 (38.4%)	93/228 (40.8)	0.599	
Imurel	80/219 (36.5%)	77/228 (33.8%)		
Methotrexate	4/219 (1.8%)	11/228 (4.8%)		
Puri-nethol	-	4 (1.8%)		
Others	-	1 (0.4%)		
Biological treatment	25/219 (11.4%)	19/228 (8.3%)	0.544	
Infliximab	22/219 (10.0%)	17/228 (7.5%)		
Adalimumab	3/219 (1.4%)	2/228 (0.9%)		
Preoperative sepsis	32/219 (14.6%)	54/228 (23.7%)	0.015	
Preoperative fistula	23/219 (10.5%)	43/228 (18.9%)	0.013	
Preoperative abscess	14/219 (6.4%)	35/228 (15.4%)	0.002	0.39 (0.185–0.821) $p = 0.013$
Previous laparotomy/laparoscopy	101/219 (46.1%)	133/228 (58.3%)	0.01	0.57 (0.334–0.918) $p = 0.021$
Operation urgency			0.196	
Acute/urgent	68/219 (31.1%)	84/228 (36.8%)		
Elective	151/219 (68.9%)	144/228 (63.2%)		
Disease localization (Montreal)	(Missing 2)			
Ileum (L1)	110/219 (50.2%)	105/228 (46.1%)	0.602	
Colon (L2)	16/219 (7.3%)	28/228 (12.3%)		
Ileo-colic (L3)	55/219 (25.1%)	65/228 (28.5)		
Upper GI (L4)	11/219 (5.0%)	9/228 (3.9%)		
L1 + L4	4/219 (1.8%)	7/228 (3.1%)		
L2 + L4	-	2/228 (0.9%)		
L3 + L4	-	1/228 (0.4%)		
Disease in remission*	-	11/228 (4.8%)		
Type of resection with location		(Missing 1)	0.67	0.986 (0.665–1.462) $p = 0.945$
SM + IC	136/219 (62.1%)	108/228 (47.4%)		
Colectomy and/or rectal	18/219 (8.2%)	36/228 (15.8%)		
SM + IC + colectomy	60/219 (27.4%)	82/228 (36.0%)		
Stoma closure	5/219 (2.3%)	1/228 (0.4%)		
Anastomosis site	(Missing 27)	(Missing 36)	0.045	1.161(1.016–1.326) $p = 0.028$
Small bowel	23/219 (10.5%)	31/228 (13.6%)		
Ileo-colic	153/219 (69.9%)	129/228 (56.6%)		
Ileo-rectal	4/219 (1.8%)	10/228 (4.4%)		
Colo-colic	7/219 (3.2%)	7/228 (3.1%)		
Colo-rectal	-	1/228 (0.4%)		
Small bowel & ileo-colic	2/219 (0.9%)	6/228 (2.6%)		
Small bowel & ileo-rectal	-	1/228 (0.4%)		
Small bowel & colo-rectal	-	1/228 (0.4%)		
Ileo-rectal & colo-colic	3/219 (1.4%)	4/228 (1.8%)		
Ileo-colic & strictureplasty of small bowel	-	1/228 (0.4%)		
	-	1 /228 (0.4%)		

Table 1 (continued)

Patients' characteristics	LOS < median 219/449 (48.8%)	LOS ≥ median 228/449 (50.8%)	Uni-variate *p* value	Multi-variate OR (CI 95%)
Ileo-colic, colo-colic, and strictureplasty of small bowel				
Postoperative complications				
Any postoperative complication	33/219 (15.1%)	117/228 (51.3%)	$p < 0.001$	5.266 (3.191–8.69) $p < 0.001$
Death within 3 months	-	4/228 (1.8%)	0.049	
Anastomosis leak	2/219 (0.9%)	29/228 (12.7%)	0.000	
Postoperative abscess	6/219 (2.7%)	30/228 (13.2%)	0.000	
Postoperative enteric fistula	4/219 (1.8%)	6/228 (2.6%)	0.565	
Paralytic ileus	3/219 (1.4%)	30/228 (13.2%)	0.000	
Wound rupture	5/219 (2.3%)	25/228 (11.0%)	0.000	
Wound infection	19/219 (8.7%)	38/228 (16.7%)	0.011	
Other postoperative information	5/219 (2.3%)	41/228 (18%)	0.000	
Postoperative thrombosis	-	2/228 (0.9%)	0.165	
Pulmonary embolism	1/219 (0.5%)	-	0.307	
Cardiovascular complications	1/219 (0.5%)	3/228 (1.3%)	0.335	
Septic complications	22/219 (10.0%)	72/228 (31.6%)	0.000	

SM small bowel resection, *IC* ileo-colic/ileo-cecal resection, *IQR* inter-quartile range

Results

A total of 449 patients who underwent abdominal surgery for CD were included in this study (Table 1). These operations included resections with anastomosis, stoma closure with anastomosis, and stricturoplasty. Of the 449 patients, 265 were female (59%). Median age at the time of operation was 37 years (IQR 20). The median LOS was 7 days (IQR 6). There were no significant differences between the two groups regarding preoperative medical treatment (steroids, immunomodulators, and/or biological therapy).

Postoperative complications significantly prolonged LOS ($p < 0.001$). Group 1 consisted of 219/449 (48.8%) patients. Of those 219 patients, 33 (15.1%) had postoperative complications compared with 117/228 (51.3%) in group 2. Patients in group 2 had higher rates of postoperative surgical reintervention in the form of laparotomy/laparoscopy: 45/228 (19.7%) in group 2 versus 9/219 (4.1%) of patients in group 1 ($p = 0.01$). No difference was shown in readmission rates between the two groups ($p = 0.62$).

Serious complications that require reoperation may prolong LOS and introduce a bias in the results. Therefore, all the patients with Clavien-Dindo classification IIIb-IV complications were excluded, and statistical analysis was redone to compare group 2 to group 1 as a subgroup analysis. The subgroup analysis showed a high risk of prolonged LOS in older patients (median 38 years (IQR 20) versus median 34 years (IQR 20), $p = 0.002$), patients with preoperative intra-abdominal abscess (21/141 (14.9%) versus 2/172 (1.2%) $p = 0.023$), patients who had previous laparotomy/laparoscopy (81/141 (57.4%) versus 79/172 (45.9%) $p = 0.043$), and those who had POI (14/141 (9.9%) versus 1/172 (0.6%) $p < 0.01$).

Nine patients in group 1 underwent reoperation for the following causes: two of them due to anastomotic leakage, 5/9 due to intra-abdominal abscess leading to entero-enteric fistula with intra-abdominal abscess, and 2/9 because of POI (Table 1). There were no deaths in group 1 compared with 4 deaths in group 2.

In multivariate analysis, age (OR = 1.024 [CI 95% 1.007–1.041], $p = 0.005$), preoperative intra-abdominal abscess (OR = 0.39 [CI 95% 0.185–0.821], $p = 0.013$), and previous laparotomy/laparoscopy for treatment for CD (OR = 0.57 [CI 95% 0.334–0.918], $p = 0.021$) were factors that prolonged LOS (Table 1). These factors continued to be significant after adjustment for different possible confounders, such as laparotomy versus laparoscopy, urgency of operation, disease localization, type of resection, anastomosis site, preoperative medical treatment, and gender. The multivariate analysis conducted again after excluding all the patients who had complications thus obtaining a homogenous group of 297 patients with no postoperative complications. The results shown in Table 2 continued to point at age, preoperative abscess and previous laparotomy/laparoscopy for treatment for CD.

LOS correlated with postoperative complications in multivariate regression analysis after adjustment for age, gender, previous laparotomy/laparoscopy, and preoperative intra-abdominal abscess (OR 1.28 [CI 95% 1.199–1.366] $p < 0.0001$).

Table 2 Patients' characteristics in 297 patients with CD. The tables show a comparison between the two groups depending on their LOS. LOS dichotomized using median value to facilitate comparison. Patients with postoperative complications were excluded from this analysis to obtain a homogenous group of patients with CD who had uneventful postoperative recovery

Patients' characteristics	LOS < median	LOS ≥ median	Uni-variate *p* value	Multi-variate OR (CI 95%)
Age	35.05 ± 12.69 (missing 1)	39.95 ± 14.786	0.007	1.024 (1.005–1.044) $p = 0.012$
Female	106/186 (57.0%)	60/111 (54.1%)	0.622	
Cortinson treatment	68/186 (36.6%) (missing 2)	42/111 (37.8%)	0.879	
Prednisolon	64/186 (34.4%)	38/111 (34.2%)		
Solu-Medrol	1/186 (0.5%)	4/111 (3.6%)		
Other cortisons	3/186 (1.6%)	-		
Immuno treatment	74/186 (39.8%)	44/111 (39.6%)	0.980	
Imurel	70/186 (37.6%)	38/111 (34.2%)		
Methotrexate	4/186 (2.2%)	6/111 (5.4%)		
Puri-nethol	-	-		
Others	-	-		
Biological treatment	19/186 (10.2%)	11/111 (9.9%)	0.538	
Infliximab	17/186 (9.1%)	11/111 (9.9%)		
Adalimumab	2/186 (1.1%)	-		
Preoperative abscess	12/186 (6.5%)	18/111 (16.2%)	0.007	0.39 (0.176–0.865) $p = 0.014$
Preoperative fistula	19/186 (10.2%)	20/111 (18.0%)	0.054	
Previous laparotomy/laparoscopy	86/186 (46.2%)	67/111 (60.4%)	0.018	0.557 (0.333–0.931) $p = 0.038$
Operation urgency			0.357	
Acute/urgent	59/186 (31.7%)	41/111 (36.9%)		
Elective	127/186 (68.3%)	70/111 (63.1%)		
Disease localization (Montreal)	(Missing 1)		0.732	
Ileum (L1)	94/186 (50.5%)	57/111 (51.4%)		
Colon (L2)	13/186 (7.0%)	10/111 (9.0%)		
Ileo-colic (L3)	46/186 (24.7%)	30/111 (27.0%)		
Upper GI (L4)	11/186 (5.9%)	5/111 (4.5%)		
L1 + L4	3/186 (1.6%)	3/111 (2.7%)		
L2 + L4	-	-		
L3 + L4	-	1/111 (0.9%)		
No disease	18/186 (9.7%)	5/111 (4.5%)		
Type of resection with location			0.265	
SM + IC	121/186 (65.1%)	60/111 (54.1%)		
Colectomy and/or rectal	13/186 (7.0%)	14/111 (12.6%)		
Both	48/186 (25.8%)	37/111 (33.3%)		
Stoma closure	4/186 (2.2%)	-		

No disease: disease in remission

Discussion

This study showed that LOS correlates with postoperative complications in patients with CD who had undergone abdominal surgery as part of their treatment for CD. Higher age, preoperative intra-abdominal abscess, and previous laparotomy/laparoscopy for CD were associated with prolonged LOS in patients with CD with or without postoperative complications.

Patients with CD might have a longer LOS compared with those suffering from CC; although patients with CD are generally younger, have lower ASA grade, and have fewer comorbidities [25]. Our study showed three risk factors that prolong LOS and are discussed below.

There are two distinct populations of elderly patients with CD: (1) those diagnosed at a younger age who transition to older age with their disease; and (2) individuals diagnosed at an advanced age. It is increasingly recognized that the clinical presentation, the natural history of the disease, and the management differs in these two populations [26]. Management of multiple comorbidities, social issues, functional status, polypharmacy, and drug interactions in elderly patients may be challenging. However, our data shows a median age of only 37 years. Therefore, the prolonged LOS might be attributed to a longer disease duration rather than comorbidities. Unfortunately, data on comorbidity were not available for all the patients in this cohort to confirm our hypothesis.

The adjusted results showed that previous laparotomy/laparoscopy for CD is a risk factor that prolongs LOS. This might be related to a longer disease duration and a more complex surgical intervention in patients who have previously undergone surgery for CD. Disease burden can increase with years leading to a higher prevalence of psychiatric illness compared with the general population [27]. A systematic review found that people suffering from depression and anxiety also reported a more severe IBD-associated abdominal pain likely due to an increased sensitivity [28]. A recent study suggests that previous laparoscopy/laparotomy for CD does not affect LOS, but this study did not adjust for many possible risk factors that prolongs LOS [29].

The combination of intra-abdominal abscesses with active CD is a formidable challenge. Percutaneous drainage (PD) under ultrasonographic or computed tomographic guidance is a safe procedure with a very low complication rate, but it might be a factor that prolongs LOS. Management with PD may solve the infectious condition and almost 30% of patients with CD-related spontaneous intra-abdominal abscess may avoid subsequent surgery [30]. It is indicated for those that are technically accessible, well-defined, and of unilocular formation. There is a significant higher risk of abscess recurrence following PD alone compared with PD with elective surgery [30]. Surgery without prior PD is associated with a significantly higher rate of complications compared with initial PD followed by surgery [31]. The prolonged LOS in patients with an intra-abdominal abscess might be related to the complex management of these patients. Successful percutaneous drainage may be considered as a bridge to elective surgery, allowing nutritional and medical optimization of patients, with the aim of a more successful postoperative outcome for the patients.

Our study has several limitations. It is a retrospective study of a relatively small sample size. Other limitations are lack of data concerning comorbidity, disease severity, disease duration, preoperative optimization, and adherence to a postoperative enhanced recovery program. Additional large prospective studies are needed to explore LOS in CD patients undergoing surgery.

Incompleteness of registration, reporting bias, and mistakes in registration may weaken registry data. LOS is usually accurately documented in registries since it is related to social, economic, and administrative issues. By confirming the correlation between LOS and postoperative complications, this study can be used to trace postoperative outcome in registry data. In other words, it can be assumed that patients with longer LOS are more likely to have a higher complication rate even if the registry data about postoperative complications are missing.

Conclusion

Patients with CD with preoperative intra-abdominal abscess, previous laparotomy/laparoscopy, and higher age have a higher risk of prolonged LOS even after excluding postoperative complications. LOS correlated with postoperative complications in patients with CD undergoing bowel surgery and can therefore be used in epidemiological or register-based studies as a surrogate for postoperative outcome.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The project approved by Danish data agency (DataTilsynet HVH-2013-046 / 02515).

Statement of informed consent Not relevant to this retrospective study at the time of data collection.

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