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ORIGINAL ARTICLE

Post-operative morbidity in Crohn's disease: what is the impact of patient-, disease- and surgery-related factors?

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Abstract

Purpose Over 50% of patients suffering from Crohn's disease (CD) require surgery in their lifetime. Predictors/risk factors of post-operative morbidity and mortality in CD are poorly investigated. We aimed to assess the risk factors of post-operative morbidity/mortality in CD.

Methods We performed a retrospective cohort study in which all CD patients operated and followed up at our tertiary Inflammatory Bowel Disease Centre from 2014 to 2019 were enrolled. For each patient, we evaluated patient-dependent, disease-dependent and surgery-dependent variables. All patients underwent small bowel and/or colic resections.

Results Of the 165 operated patients, forty-two (25.5%) developed post-operative complications (major complication rate = 9.8%) including wound infection (12.1%), respiratory complications (4.8%), prolonged ileum (4.2%), anastomotic leak (3.6%), urinary infections (3%), abdominal abscess (2.4%), anastomotic bleeding (3.6%), abdominal bleeding (1.2%) and obstruction (0.6%). Two subjects (1.2%) required re-operation within 30 days, and one died. A surgery duration < 141 min was predictive of a better post-operative outcome (sensitivity 80.9%, specificity 43.1%, PPV 32.7%, NPV 86.9%). The multivariable analysis showed stricturing/fistulizing behaviour (OR 3.7, 95% CI 1.6–6.4, $p = 0.02$), need for total parenteral nutrition (OR 4.1, 95% CI 2.4–9.2, $p = 0.01$), pre-operative bowel cleansing (OR 0.6, 95% CI 0.41–0.83, $p = 0.01$) and surgery duration < 141 min (OR 0.2, 95% CI 0.08–0.7, $p = 0.03$) as the only risk factors associated with post-operative morbidities.

Conclusions About 25% of CD patients develop post-operative complications. Several patient-related, disease-related and surgery-related factors should be considered risk factors for post-operative morbidity. The recognition of these factors, as well as a multidisciplinary approach to the pre-operative management of CD, could reduce post-operative complications.

Keywords Crohn's disease · Surgery · Morbidity · Post-operative complications

Introduction

Optimal management of inflammatory bowel disease (IBD) requires strict collaboration between gastroenterologists, surgeons and other specialists such as radiologists, nutritionists and dermatologists [1].

Despite the huge advances in the medical therapy of Crohn's disease (CD) and change in its course, especially due to the introduction of biologics, over 50% of patients still require surgery in their lifetime [1, 2]. Moreover, although the rate of colectomies for the treatment of ulcerative colitis seems to have decreased the biologics era, the number of intestinal resections in Crohn's disease has not significantly improved [3].

At the same time, the burden of post-operative morbidity is still consistent in some case series, and this might counterbalance the benefits of an "early surgery" strategy. Morbidity in IBD surgery is often associated with both patient- and disease-related factors, whose pre-operative identification is crucial to improving patient care and choosing the best risk/benefit profile option.

Scientific evidence has so far been heterogenous, with many factors likely associated with post-operative morbidity

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in Crohn's Disease. For example, several studies have tried to address the association between pre-operative biologics and the increase in post-operative infectious complications [4–7], with controversial results obtained sometimes. On the other hand, hypoalbuminemia, anaemia [8, 9], stoma formation and pre-operative steroids [10] are more clearly associated with surgical morbidity.

In this paper, we report our retrospective series in an IBD referral centre over a 6-year period. We aimed to evaluate all the possible factors associated with surgical morbidity, including patient-dependent, disease-dependent and surgery-dependent factors. Both major and minor complications are carefully reported and analysed. The identification and possible correction of some of these factors might be helpful in careful patient selection, optimization of treatment strategies and timing, with further improvement in overall results.

Methods

Study design and population

We performed a retrospective cohort study using a prospectively maintained database, with all consecutive patients affected by CD from January 2014 to December 2019 enrolled. Each patient was operated and then followed up for at least 1 year at our Tertiary Centre for Inflammatory Bowel Disease, School of Medicine Federico II, Naples (IT). The indication for surgery was made in accordance with current guidelines [11–13]. In particular, CD patients underwent surgery for treatment-refractory disease or for disease complications, such as strictures, fistulas or abscesses. Patients who underwent surgery for perianal disease alone were excluded from the analysis.

For each included patient, we evaluated patient-dependent (comorbidities, smoking, drugs, nutritional status), disease-dependent (disease duration, location, behaviour, extension) and surgery-dependent variables (duration, emergency/election, laparoscopy/laparotomy, bowel/colic resection, length of intestinal resection).

We assessed both surgical and medical complications, which were retrospectively graded using the Clavien–Dindo staging system [14, 15]. Major complications were defined as those of grade III and higher (i.e. grades III, IV and V—those requiring at least endoscopic, radiographic or surgical intervention, those requiring ICU admission and those leading to death). Overall complications, number of patients with any complication and percentage of each single complication were detected. Particularly, we examined the following complications: anastomotic leak, urinary infections, pneumonia, respiratory complications, abdominal abscess, wound infection, other infections, prolonged ileum, obstruction, abdominal bleeding, anastomotic bleeding, need for re-operation within 30 days and death.

Statistical analysis

Data were analysed using the Statistical Package for Social Sciences (SPSS software v.15.0, Chicago, IL, USA) for Windows and the StatsDirect statistical software (vers. 3.0). The descriptive statistics used included determination of the mean values and standard deviations (SD)—or of the medians and interquartile ranges (IQR)—for the continuous variables and of the percentages and proportions for the categorical variables. Statistical analysis was performed using the X^2 or Mann–Whitney U test as appropriate. Receiver operating characteristic (ROC) curves were constructed to identify the best cut-off values for the surgery duration, body mass index (BMI), length of resection and age at surgery that could predict post-operative morbidity. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and area under the curve (AUC), with each 95% confidence interval (CI), were calculated. Binary logistic regression was used to examine the relationship between complication as a dependent variable and the possible risk factors as independent variables. Further supplementary multivariable analyses were performed to establish the risk factors of each specific complication (i.e. wound infection, urinary infection).

Results

We enrolled 165 CD patients that underwent surgery during the study period.

Patient-dependent variables

There were more male patients (54.5%). The mean age of all patients was 39.05 ± 15.9 years. A high percentage of patients were active smokers (38.8%) and had a positive familial history of IBD (12.2%). As for comorbidities, 6.7% of the patients suffered from diabetes. The mean pre-operative BMI was 21.7 ± 3.08 kg/m^2, and a remarkably high percentage of patients (77.6%) had a BMI value < 24 kg/m^2. The patient-dependent variables are summarized in Table 1.

Disease-dependent variables

The mean disease duration was 103.4 ± 95.6 months. Sixty-one patients (37%) had ileal Crohn's disease, 22 patients (13.3%) had a colic location, 78 patients (47.3%) had ileocolic disease, and only 3 subjects (1.8%) had upper gastrointestinal location. As far as the disease location is concerned, 38 patients were affected by perianal fistulizing Crohn's disease (23%).

Table 1 Baseline features of the study population (Crohn's disease $n = 165$)

Patient-dependent variables	
Male gender, *n* (%)	90 (54.5%)
Mean age, years ± SD	39.05 ± 15.9
Active smokers, *n* (%)	64 (38.8%)
Familial history, *n* (%)	20 (12.1%)
Any comorbidity, *n* (%)	17 (10.3%)
Diabetes, *n* (%)	11 (6.7%)
Pre-operative BMI, mean ± SD	21.7 ± 3.08
Pre-operative BMI < 24, *n* (%)	128 (77.6%)
Disease-dependent variables	
Disease duration, months ± SD	103.4 ± 95.6
Perianal disease, *n* (%)	38 (23%)
Age at diagnosis A1 – A2 – A3	52 – 81 – 32
Disease behaviour B1 – B2 – B3	22 – 72 – 71
Disease Location (CD) L1 – L2 – L3 – L4	62 – 22 – 78 – 3
Pre-operative anaemia, *n* (%)	64 (38.8%)
Pre-operative hypoalbuminemia, *n* (%)	36 (21.8%)
Pre-operative TPN (at least 15 days), *n* (%)	17 (10.3%)
Pre-operative TPN (at least 30 days), *n* (%)	14 (8.5%)
Surgery-dependent variables	
Previous surgery, *n* (%)	55 (33.3%)
Pre-operative bowel cleansing, *n* (%)	131 (79.4%)
Emergency surgery, *n* (%)	23 (13.9%)
Laparoscopy, *n* (%)	47 (28.5%)
- *Laparoscopy 2015–2017*	(28.5%)
- *Laparoscopy 2018–2019*	(71.5%)
Ileal resection, *n* (%)	37 (22.4%)
Ileocolic resection, *n* (%)	111 (67.3)
Colectomy, *n* (%)	13 (7.9)
Proctectomy, *n* (%)	2 (1.2)
Rectosigmoid resection, *n* (%)	2 (1.2)
Length of ileal resection, cm (mean ± SD)	24.39 ± 17.87
Surgical duration, min (mean ± SD)	147.12 ± 60.89

n number, *SD* standard deviation, *CD* Crohn's disease, *L1* ileal location, *L2* colic location, *L3* ileocolic location, *L4* upper gastrointestinal location, *TNP* total parenteral nutrition

A total of 64 patients presented with pre-operative anaemia (38.8%) and 36 with pre-operative hypoalbuminemia (21.8%). Seventeen patients (10.3%) needed pre-operative total parenteral nutrition (TPN). The disease-dependent variables are summarized in Table 1.

Surgery-dependent variables

As ours is a tertiary centre, the majority of patients (86.1%) underwent an elective surgery. A laparoscopic approach was used in 28.5% of cases throughout the entire study duration; from 2018, the laparoscopy rate adoption increased to 71.5%. About 33.3% of CD patients had already undergone surgery for their conditions. Pre-operative bowel cleansing was administered in 131 patients (79.4%). The surgery-dependent variables are summarized in Table 1.

Pre-operative medical treatment

Twenty-seven patients (16.4%) were on steroid therapy at the time of surgery; 22 patients (13.3%) underwent steroid therapy for at least 6 weeks before surgery. Azathioprine (AZA) was administered in a lower percentage of patients (6.1%). As for biologics, 2 patients (1.2%) received infliximab (IFX), 7 patients (4.2%) received adalimumab (ADA), and 2 patients (1.2%) received vedolizumab (VDZ). The low rate of patients under biologic treatment at the time of surgery was the result of our protocol, which consisted in interrupting biologic treatment at least 6–8 weeks before surgery.

Both pre-operative antibiotics and antithrombotic prophylaxis were widely used in all patients: a cycle of metronidazole 500 mg i.v. t.i.d. for 5–7 days and enoxaparine (from 4000 IU/daily to 8000 IU/daily according to the patient's weight) was administered. Seventeen patients (10.3%) received antibiotic therapy for abscess treatment before surgery, with previous abscess drainage in 4 cases. The pre-operative medical treatments are summarized in Table 2.

Post-operative complications

The overall morbidity, re-operation and readmission rates were identified. The overall morbidities and their grading are summarized in Table 3. Forty-two patients (25.5%) developed post-operative complications; thus, the overall complications were 70. The overall morbidity is reflective of the number of patients who had at least 1 complication; thus, patients who had at least 1 complication were counted only once. The rate of incidence of major complications was 9.8%. One patient died. The following complications were described: wound infection (12.1%), respiratory complications (4.8%), prolonged ileum (4.2%), anastomotic leak (3.6%), urinary infections (3%), pneumonia (3.6%), abdominal abscess (2.4%), anastomotic bleeding (1.2%), other infections (3%), abdominal bleeding (2.4%) and obstruction (0.6%). Two subjects (1.2%) required re-operation within 30 days (Table 4). Only 4 patients needed intraoperative transfusions, while 11 patients (6.7%) needed post-operative ones. Three patients needed endoscopic review because of bleeding. Only 3 patients (1.8%) required hospitalization in the intensive care unit, whereas 130 patients (78.8%) were discharged in 6 days.

Factors associated with surgical morbidities

The ROC curve analysis identified a surgery duration < 141 min as the best cut-off value for the prediction of a

Table 2 Pre-operative medical treatment

	Crohn's disease (165)
Steroids at diagnosis, *n* (%)	67 (40.6%)
Previous AZA, *n* (%)	68 (41.2%)
Previous IFX, *n* (%)	39 (23.6%)
Previous ADA, *n* (%)	48 (29.1%)
Previous VDZ, *n* (%)	9 (5.5%)
Previous UST, *n* (%)	2 (1.2%)
Pre-operative steroids (at least 2 weeks), *n* (%)	27 (16.4%)
Pre-operative steroids (at least 6 weeks), *n* (%)	22 (13.3%)
Pre-operative AZA, *n* (%)	10 (6.1%)
Pre-operative IFX, *n* (%)	2 (1.2%)
Pre-operative ADA, *n* (%)	7 (4.2%)
Pre-operative VDZ, *n* (%)	2 (1.2%)
Pre-operative combo, *n* (%)	1 (0.6%)
Pre-operative antibiotics, *n* (%)	126 (76.4%)
Antithrombotic prophylaxis, *n* (%)	159 (96.4%)

Table 4 Thirty-day surgical complications

Complications	Patients (*n*, %)
Number of patients with any complication, *n* (%)	42 (25.5%)
Overall complications, *n*	70
Anastomotic leak	6 (3.6%)
Urinary infections	5 (3%)
Polmonitis	6 (3.6%)
Respiratory complications	8 (4.8%)
Abdominal abscess	4 (2.4%)
Wound infection	20 (12.1%)
Other infection	5 (3%)
Prolonged ileum	7 (4.2%)
Obstruction	1 (0.6%)
Abdominal bleeding	2 (1.2%)
Anastomotic bleeding	6 (3.6%)
Need for reoperation within 30 days, *n* (%)	2 (1.2)
Death, *n* (%)	1 (0.6)

better post-operative outcome (sensitivity 80.95%, 95% CI 65.9–91.4%, specificity 43.1%, 95% CI 34.2–52.3%, PPV 32.7%, 95% CI 28.2–37.5%, NPV 86.9%, 95% CI 77.5–92.7%, AUC 0.62, 95% CI 0.53–0.73) (Fig. 1). Moreover, a BMI cut-off value < 24 was associated with a worse outcome (sensitivity 50%, 95% CI 33.8–66.2%, specificity 65.2%, 95% CI 55.9–73.8%, PPV 32.8%, 95% CI 21.3–46%, NPV 79.4%, 95% CI 69.9–86.9%, AUC 0.55, 95% CI 0.44–0.65). The binary logistic regression showed stricturing/fistulizing behaviour (OR 3.7, 95% CI 1.6–6.4, $p = 0.02$), need for total parenteral nutrition (OR 4.1, 95% CI 2.4–9.2, $p = 0.01$), pre-operative bowel cleansing (OR 0.6, 95% CI 0.41–0.83, $p = 0.01$) and surgery duration < 141 min (OR 0.2, 95% CI 0.08–0.7, $p = 0.03$) as the only factors associated with post-operative morbidities (Table 5). A pre-operative BMI < 24 was also associated with anastomotic leak (OR 4.3, 95% CI 1.8–8.6, $p = 0.02$) (Supplementary Table 1), pre-operative hypoalbuminemia was associated with urinary infections (OR 2.5, 95% CI 1.8–7.9, $p = 0.04$) (Supplementary Table 2), pre-operative infliximab was associated with pneumonia (OR 3.8, 95% CI 2.2–6.3, $p = 0.01$) (Supplementary Table 3), and diabetes (OR 5.7, 95% CI 2.3–9.8, $p < 0.01$) and pre-operative steroids (OR 6.1, 95% CI 1.8–11.4, $p < 0.01$) were associated with wound infection (Supplementary Table 4).

Discussion

Despite that the rate of surgical treatment of CD seems to have been decreasing over the last decades, mostly due to medical therapy optimization, at least 40% of patients with CD still require surgery within 10 years from the diagnosis

Table 3 Clavien–Dindo classification of surgical complications

Classification	Definition	% of patients
Grade 1	Any deviation from the normal post-operative course without the need for pharmacologic treatment or surgical, endoscopic and radiologic interventions. Allowed therapeutic regimens are drugs as antiemetics, antipyretics, analgetics and diuretics, and electrolytes and physiotherapy. This grade also includes wound infections opened at the bedside	6.3%
Grade 2	Requiring pharmacologic treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included	9.4%
Grade 3	Requiring surgical, endoscopic or radiologic intervention	8%
3a	Intervention not under general anaesthesia	
3b	Intervention under general anaesthesia	
Grade 4	Life-threatening complication (including CNS complications) requiring IC/ICU management	1.2%
Grade 5	Death as a result of complications	0.6%
Overall		25.5%

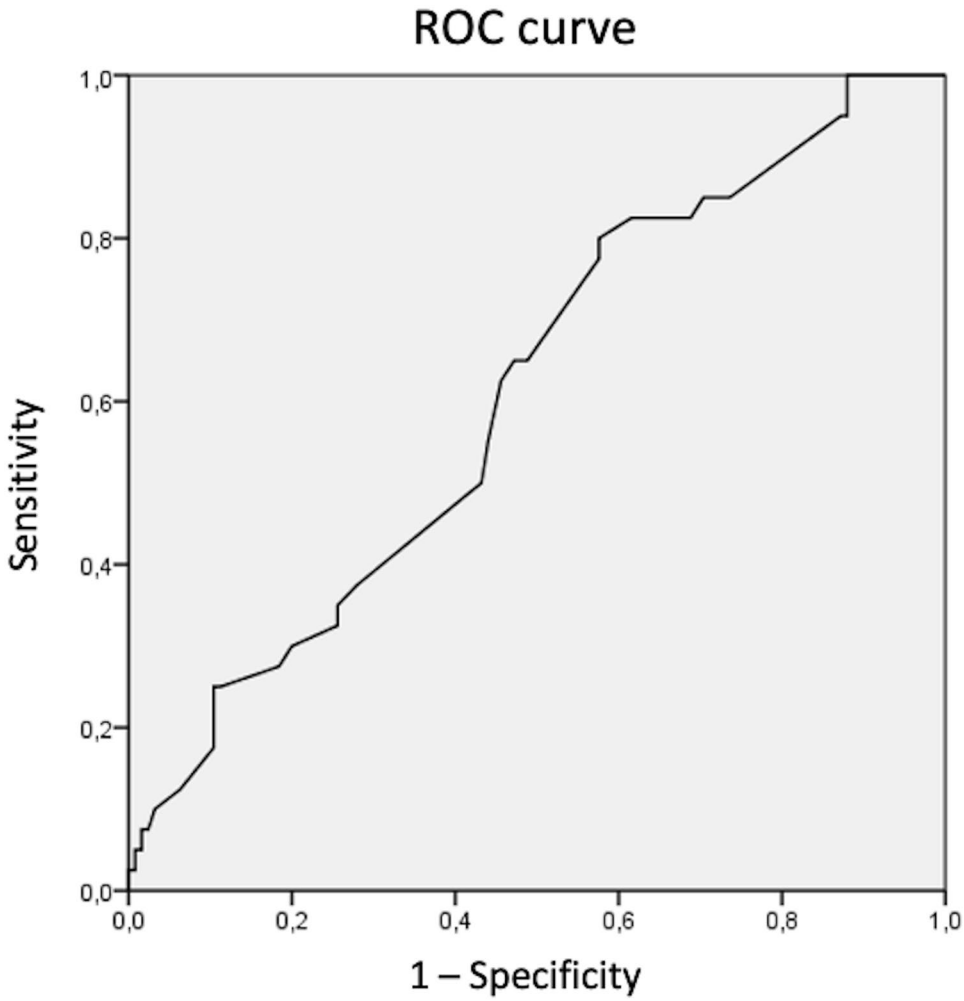

Fig. 1 A surgery duration < 141 min was predictive for a better post-operative outcome (sensitivity 80.95% (95% CI 65.9–91.4%), specificity 43.1% (95% CI 34.2–52.3%), PPV 32.7% (95% CI 28.2–37.5%), NPV 86.9% (95% CI 77.5–92.7%), with an AUC of 0.62 (95% CI 0.53–0.73))

[1]. Evidence from old and long-term follow-up studies have also demonstrated that surgery could be the only therapeutic option in some cases, and up to 50% of patients might not require further surgery after primary ileocolic resection, observations that were true even in the pre-biologic era [16–19]. On the other hand, despite the enormous improvements in medical therapy, IBD specialists should be very cautious when administering prolonged biological therapy, especially to patients with an acceptable surgical risk, because of complications mainly related to immunosuppression; these risks might become even higher when patients require subsequent surgery under these drugs. A meta-analysis by Kopylov et al. [4], for example, includes 8 studies and 1641 patients operated for Crohn's disease (423 treated with infliximab vs 1219 not treated with infliximab) and shows a significant increase in infective complications in patients pre-treated with biologics and an insignificant increase in overall complications. Similar results have been achieved in a more recent study by Brouquet et al. [5]. This study, funded by GETAID, enrolled 92 patients with CD from 19 hospitals over a 3-year period and demonstrated how taking anti-TNF (anti-tumour necrosis factor) drugs less than 3 months to surgery was associated with the overall post-operative morbidity and intra-abdominal septic complications. Controversially, Bafford et al. reported that neither anti-TNF biologics nor a combination immunosuppressive therapy increased post-surgical morbidity. In the study, 177 procedures out of 197 (64.8%) were performed on patients who received perioperative immunomodulation. Patients exposed to steroids within 6 weeks of surgery ($p = 0.21$), those exposed to thiopurines ($p = 0.10$) or anti-TNF agents ($p = 1.0$) within 90 days of surgery or any combination had neither a higher rate of overall morbidity nor septic complications when compared with those who did not receive these medications pre-operatively [6].

In our series, we found that pre-operative infliximab was a risk factor for pneumonia (OR: 3.8). Despite some inconsistencies in the literature about the association between pre-operative biologics and post-operative complications [20–22], most of the studies and meta-analyses show an increase in the overall and infectious complications after the administration of pre-operative biologics, including pelvic sepsis and anastomotic leak. A prudent approach that aims to discontinue biologic use at least 4 weeks before surgery, or

Table 5 Predictors of post-operative morbidities in the whole cohort of 165 CD patients

Baseline factors	Univariate analysis			Binary logistic regression		
	Odds ratio	95% CI	*p*	Odds ratio	95% CI	*p*
Male gender	0.7	0.53–1.08	0.8			
A1 vs A2/A3	0.9	0.69–1.35	0.9			
B2/B3 vs B1	2.4	1.3–6.9	**0.01**	3.7	1.6–6.4	**0.02**
L1 vs L2/L3	0.9	0.71–1.44	0.8			
Perianal disease (yes vs not)	1.2	0.85–1.76	0.3			
Previous surgery (yes vs not)	1.1	0.78–1.85	0.9			
Smoking habits (yes vs not/ex)	1.5	0.88–2.1	0.5			
Comorbidities (yes vs not)	1.3	0.74–1.96	0.5			
Diabetes (yes vs not)	1.2	0.65–1.87	0.7			
BMI < 24 (yes vs not)	1.1	0.65–1.89	0.6			
Pre-operative anaemia (yes vs not)	1.4	0.78–2.21	0.5			
Pre-operative hypoalbuminaemia (yes vs not)	1.3	0.69–1.79	0.7			
TPN > 30 days (yes vs not)	3.5	2.4–8.5	**<0.01**	4.1	2.4–9.2	**0.01**
TPN > 15 days (yes vs not)	2.3	1.7–5.55	**0.04**	1.3	0.87–3.68	0.09
Pre-operative steroids (at least 2 weeks) (yes vs not)	1.1	0.68–1.86	0.5			
Pre-operative steroids (at least 6 weeks) (yes vs not)	1.3	0.72–2.21	0.2			
Pre-operative AZA (yes vs not)	3.2	1.2–6.8	**0.01**	1.2	0.89–2.21	0.2
Pre-operative IFX (yes vs not)	1.4	0.67–1.98	0.4			
Pre-operative ADA (yes vs not)	1.3	0.71–2.2	0.3			
Pre-operative VDZ (yes vs not)	1.1	0.56–1.87	0.4			
Pre-operative combo (yes vs not)	1.3	0.67–1.89	0.5			
Pre-operative bowel cleansing (yes vs not)	0.5	0.21–0.87	**0.01**	0.6	0.41–0.83	**0.01**
Emergent surgery (yes vs not)	1.3	0.67–2.13	0.6			
Laparoscopy (yes vs not)	0.8	0.45–2.13	0.2			
Surgery duration < 141 min (yes vs not)	0.5	0.2–0.7	**<0.01**	0.2	0.08–0.7	**0.03**

Statistically significant results have been highlighted in bold

CD Crohn's disease, *CI* confidence interval, *A1* age < 16, *A2* age 17–40, *A3* age > 40, *B1* inflammatory behaviour, *B2* stricturing behaviour, *B3* fistulizing behaviour, *L1* ileal location, *L2* colonic location, *L3* ileocolonic location, *BMI* body mass index, *TNP* total parenteral nutrition, *AZA* azathioprine, *IFX* infliximab, *ADA* adalimumab, *VDZ* vedolizumab, *combo* combination therapy (azathioprine plus biologics)

otherwise opt for multi-stage procedures, is also suggested by recent guidelines [11–13].

Steroids are also a recognised risk factor for post-operative morbidity, with an increased risk of infectious complications, independently from the concomitant use of other immunosuppressants [23, 24]. A meta-analysis of seven observational studies that included a total of 1532 patients has also demonstrated that patients operated on a high dose of corticosteroids (> 40 mg of prednisolone) are at an increased risk of the overall complications [25]. In our study population, pre-operative steroid use was only associated with an increased rate of wound infections; this was certainly due to our strict policy to opt for multi-stage procedures and diverting stomas when operating on patients under steroids, after attempting to wean them off the drugs as much as possible.

Optimization of pre-operative nutritional status is another key factor for improving surgical outcomes. Our data showed that a pre-operative BMI less than 24 was associated with anastomotic leak (OR: 4.5) and a low albumin level was associated with urinary tract infection. Of course, it is well known that a BMI of 24 stands for normal nutritional status. From a statistical point of view, this was the cut-off value that indicated a significant association between the BMI and post-operative leak. Several patients, in fact, had a much lower BMI. Nevertheless, this data needs to be interpreted as showing a trend towards an increased surgical complication rate with lower BMI levels. Malnutrition is a well-known risk factor for both surgical morbidity and mortality, including a higher infection rate and longer hospital stay. It is generally defined as a 10–15% weight loss in the previous 6 months, besides a low BMI and a low serum albumin level [26, 27]. With regard to patient optimization, Ghoneima et al. investigated the role of pre-operative Hb, albumin and CRP values in determining septic complications after surgery for CD. In the study, patients with none or one pre-operative abnormal blood results (low Hb, low

Alb and high CRP) were categorized as "low risk", while patients with two or three abnormal results were defined as "high risk". The results demonstrated a statistically significant higher rate of intra-abdominal septic complications (10.6% vs 30.77%, respectively, $p < 0.0001$), surgical site infections (10.6% vs 30.77%, respectively, $p < 0.0001$) and overall complications (25.76% vs 53.85%, respectively, $p < 0.0001$) in patients with two or more pre-operative blood result abnormalities [28].

In our study, we found 70 overall complications, and the number of patients with any complication was 42 (25.5%). We also graded the complications according to the Clavien–Dindo classification [14]. Thus, considering only severe complications (grades III and IV), which are those that require endoscopic intervention, radiologic intervention, surgical intervention or ICU management, our major morbidity rate was 9.8%.

In our study, 86.1% of patients underwent elective surgery, which was performed laparoscopically in 28.5% of such cases. The laparoscopy rate increased greatly in the last 2 years (71.5%). In fact, until 2018, we used small right lower quadrant transverse incision for Crohn's surgery, with satisfactory results achieved in respect of complications, the post-operative course and cosmetics [29]. Nevertheless, since 2018, this technique has been abandoned in favour of a full laparoscopic approach, which is less invasive overall [30–32].

We also found that a shorter operative time, i.e. surgery duration less than 141 min, was a protective factor against post-operative morbidity (OR: 0.2). In their prospective nationwide cohort, Brouquet et al. [5] demonstrated that an operative time longer than 180 min was associated with almost three times higher post-operative morbidity (OR: 2.71). These results are perhaps not surprising, considering that longer operative times are usually associated with more complicated, recurrent or penetrating diseases, which are in turn associated with higher post-operative morbidity.

From this standpoint, results from the LIR!C trial [33] demonstrate the possibility of considering surgery at an early disease stage, and not only as a last resort, as an alternative to biologic therapy. Early surgery often translates into easier and faster operation, with theoretically lower morbidity. We recently demonstrated that a novel type of ileocolonic anastomosis, Kono-S anastomosis [34], could significantly reduce endoscopic recurrence at a 6-month follow-up, with excellent safety profiles [35–37]. Shimada et al. [38] recently demonstrated that Kono-S anastomosis was also associated with a significantly lower leak rate (5.1% vs 17.3% in the end-to-end group).

In our study population, only 6 patients (3.6%) experienced anastomotic leak, probably thanks to the multidisciplinary teamwork that ensured patients for surgery were in satisfactory nutritional condition and given appropriate medical therapy. In our centre, we tailor surgery according to the medical therapy, so we prefer to perform multi-stage procedures, even with diverting temporary stomas, for patients with known risk factors (steroids, biologics, malnutrition, etc.). Otherwise, when possible, we prefer to wait for a proper washout from biologics or steroids and nutritional status optimization [39, 40].

We registered only one death in our series. The patient had a recurrent fistulizing CD, for which we gave indication for surgery 1 year before, but the patient refused surgery and was followed up in peripheral hospitals, where he underwent prolonged biological therapy. He then returned to our attention with a late-stage complicated disease, a large retroperitoneal abscess, a fistula between the jejunum and a previous colorectal anastomosis and a chronic obstructive syndrome, with a transverse colon diameter of 8 cm; he was severely malnourished, with hypoalbuminemia, anaemia and septic status. He died of multi-organ failure 10 days after surgery despite being placed under intensive medical support in our ICU.

The main limitation of this study lies in its retrospective design. Moreover, as we included all patients operated on for abdominal CD, results came from different types of surgeries; besides having the potential to give rise to bias, this might have hidden tiny associations between risk factors and morbidities. On the other hand, we have reported results from a considerably wide cohort of patients operated on and followed up in an IBD referral centre. In addition to reporting our "case-series" results, we aimed to statistically detect patient-, disease- and surgery-related variables associated with complications. We believe this data might represent further tools to drive the multidisciplinary clinical decision-making, in order to provide optimal patient-tailored treatment.

Conclusion

Surgery for Crohn's disease is impaired by around 10% of major post-operative complications, especially infective complications. Several patient-related, disease-related and surgery-related issues should be considered relevant risk factors for post-operative morbidity. The recognition of these factors, as well as the adoption of a multidisciplinary and intensive approach to pre-operative management of the disease, could minimize these complications.

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