

# Abdominal Surgery in Crohn's Disease: Risk Factors for Complications

Cintia Mayumi Sakurai Kimura<sup>a</sup> Arceu Scanavini Neto<sup>a</sup>  
Natalia Sousa Freitas Queiroz<sup>b</sup> Natally Horvat<sup>c</sup>  
Mariane Gouvea Monteiro Camargo<sup>a</sup> Marcelo Rodrigues Borba<sup>a</sup>  
Carlos Walter Sobrado<sup>a</sup> Ivan Ceconello<sup>a</sup> Sergio Carlos Nahas<sup>a</sup>

<sup>a</sup>Department of Colon and Rectal Surgery, Hospital das Clínicas, University of São Paulo Medical School, São Paulo, Brazil; <sup>b</sup>Department of Gastroenterology, Hospital das Clínicas, University of São Paulo Medical School, São Paulo, Brazil; <sup>c</sup>Department of Radiology, Hospital das Clínicas, University of São Paulo Medical School, São Paulo, Brazil

## Keywords

Crohn's disease · Inflammatory bowel disease · Postoperative complications · Biologics · Surgery for Crohn's disease

## Abstract

**Introduction:** Abdominal surgery in patients with Crohn's disease (CD) is challenging, especially in the biologic era. The aim of this study was to evaluate factors associated with increased risk for postoperative complications in CD. **Methods:** A retrospective study was conducted with consecutive patients who underwent abdominal surgery for CD from January 2012 to January 2018. **Results:** Of 103 patients, 32% had postoperative complications. Gender, age, disease location and phenotype, hemoglobin and albumin levels, previous abdominal surgery, and preoperative optimization did not differ between the groups with or without complications. Thirty-five percent of the patients were under anti-TNF therapy, and this medication was not associated with increased risk for postoperative complications. Time since the onset of the disease was significantly higher in patients with complications (12.9 vs. 9.4,  $p = 0.04$ ). In multivariate analysis, creation of ostomy and urgent surgery were the only vari-

ables independently associated with increased risk for complications (OR 3.2, 95% CI 1.12–9.46 and OR 2.94, 95% CI 0.98–9.09, respectively). **Conclusion:** Urgent surgery for CD should preferably be performed in specialized centers, and creation of stoma is not necessarily associated with lower rate of postoperative complications but rather less severe complications.

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## Introduction

Abdominal surgery in patients with Crohn's disease (CD) is challenging even for surgeons with high expertise in a multidisciplinary setting. Currently, the complexity of surgery is increasing in the biologic era [1]. Patients with CD are frequently malnourished, in a proinflammatory state, and with multiple previous surgeries, and some of them are also immunocompromised due to biologics in combination or not with corticosteroids and immunomodulators [2]. Consequently, the surgical complication rate among these patients is usually higher than that among patients undergoing colorectal abdominal surgery for other reasons [3, 4].

Since the advent of biologic therapy, there has been a growing concern whether patients under biologics are at a greater risk of postoperative complications [5, 6]. This risk needs to be assessed, as 15–33% of the patients under the use of biologics will eventually need surgery [7–9]. However, it is important to emphasize that many other factors may also play a relevant role in potentiating this risk and must be taken into consideration in order to elaborate strategies to optimize the outcomes. The aim of this study was to evaluate whether the use of biologic therapy increases the risk of postoperative complications after abdominal surgeries in patients with CD and what other factors are associated with postoperative complications in this population.

## Materials and Methods

### *Study Population*

Our institutional review board approved this retrospective study and waived the requirement for informed consent (reference No. 97253018.3.0000.0068). The inclusion criterion was patients who underwent abdominal surgery due to CD at our institution from January 2012 to January 2018. The exclusion criteria were inaccessible clinical or surgical data and absence of follow-up at least 30 days after the surgery. This research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki.

### *Clinical and Laboratorial Data*

Clinical and laboratorial data were obtained from a detailed and standardized review of the medical records of the patients. This review was performed by a colorectal surgeon with 5 years of experience, who was blinded to the surgical outcomes of the patients. The following preoperative data were assessed: age, gender, Montreal classification of the CD, time since the onset of the disease, medications in use, comorbidities, hemoglobin level, serum C-reactive protein level, serum albumin, and preoperative nutritional optimization.

### *Surgical Data*

The surgical data were assessed by the same colorectal surgeon 1 month after the evaluation of the clinical information. All surgical procedures were performed by colorectal surgery fellows, oriented by colorectal surgeons with vast experience in inflammatory bowel disease. The following information was obtained: type of surgery (open or laparoscopic, elective or urgent, intestinal resection with or without stoma creation, and strictureplasty), presence of postoperative complications within 30 days after the surgery, and type of complication.

### *Statistical Analysis*

Qualitative variables were described as frequencies, and their association was assessed by  $\chi^2$  test or Fisher's exact test as appropriate. Quantitative variables were described as mean  $\pm$  standard deviation and were assessed with Student's *t*-test or the Mann-Whitney test, when appropriate.

The odds ratio for each variable and the respective risk for postoperative complication were calculated by bivariate logistic regression, with their respective 95% confidence interval. The results in this analysis that showed significance level inferior to 0.2 ( $p < 0.2$ ) were then assessed by a full-model multiple logistic regression.

The analysis was performed using the IBM-SPSS software for Windows, version 22.0, and Microsoft Excel 2010. A *p* value of 0.05 or inferior was considered statistically significant.

## Results

The study population consisted of 103 patients with abdominal surgeries for CD. The mean age of the patients was  $40.6 \pm 15$  years, and 57/103 (55%) were male. The mean time since the onset of CD was  $10.5 \pm 9.1$  years. Most of the patients had ileocolic disease [38/103 (36.8%)], and the most common disease behavior was penetrating [40/103 (38.8%)]. Also, 32/103 (31%) of the procedures were performed in urgent settings. Patients' clinical characteristics are detailed in Table 1.

With regard to medications in use, 36/103 (34.9%) of the patients were under biologics, receiving either infliximab (22.3%) or adalimumab (12.6%) in combination or not with other medications; 7/103 (6.7%) were receiving biologics in combination with corticosteroids, and 5/103 (4.8%) were receiving biologics associated with corticosteroid and azathioprine. The patients were receiving biologics for an average of  $100 \pm 81.2$  weeks.

Regarding the abdominal surgeries, 90/103 (87.5%) were open and 71/103 (68.9%) elective. Of the 103 patients, 72 (70%) underwent intestinal resection without stoma creation, 26/103 (25.2%) with stoma creation, and 5/103 (4.8%) strictureplasty.

Postoperative complications within 30 days after surgery occurred in 33/103 (32%) of patients. There were 27/33 (81.8%) surgical complications and 6/33 (18.2%) clinical complications. Clinical complications were 4/6 (66.6%) postoperative ileus, 1/6 (16.7%) deep venous thrombosis, and 1/6 (16.7%) pneumonia. Among the surgical complications, 14/27 (51.8%) were related to the abdominal wound, and 13/27 (48.2%) were related to infection and/or dehiscence.

The group of patients who presented postoperative complications was similar to the group without complications regarding gender, age, localization and phenotype of the disease, hemoglobin and albumin levels, previous abdominal surgery, and the need for preoperative nutritional optimization (Table 1). Also, on bivariate analysis, the use of biologics was not significantly associated with postoperative complications (Table 1). Time since onset

**Table 1.** Clinical data and odds ratio for postoperative complication, with their respective bivariate *p* value

Variable	Total ( <i>n</i> = 103)	Complication ( <i>n</i> = 33)	No complication ( <i>n</i> = 70)	OR (95% CI)	Bivariate <i>p</i> value
Age, years	40.6±15.0	43.5±16.4	39.2±14.3	1.02 (0.99–1.05)	0.24
Male, <i>n</i> (%)	57 (55.3)	20 (60.6)	37 (52.8)	1.37 (0.62–3.23)	0.46
Previous abdominal surgery, <i>n</i> (%)	60 (58.2)	20 (60.6)	40 (57.1)	1.25 (0.50–3.10)	0.65
Time since the onset of CD, years	10.5±9.1	12.9±9.7	9.4±8.6	1.04 (0.99–1.10)	0.04
Disease localization, <i>n</i> (%)					
Ileocolonic	38 (36.8)	9 (27.3)	29 (41.4)	1.0	0.09
Ileocolic and perianal	26 (25.2)	8 (24.2)	18 (25.7)	1.19 (0.38–3.73)	
Ileum	18 (17.5)	8 (24.2)	10 (14.3)	3.22 (0.98–10.58)	
Colon	7 (6.8)	2 (6.1)	5 (7.1)	1.61 (0.25–10.30)	
Ileum and perianal	6 (5.8)	3 (9.1)	3 (4.3)	3.22 (0.55–18.85)	
Jejunum and ileum	5 (4.8)	1 (3.0)	4 (5.7)	0.81 (0.08–8.16)	
Colon and jejunum	2 (1.9)	2 (6.1)	0 (0.0)	6.44 (0.52–79.64)	
Colon and perianal	1 (0.9)	0 (0.0)	1 (1.4)	–	
Phenotype, <i>n</i> (%)					
Penetrating	40 (38.8)	14 (42.4)	26 (37.1)	1.20 (0.42–3.45)	0.33
Strictureing	28 (27.2)	8 (24.2)	20 (28.6)	1.0	
Penetrating and stricturing	29 (28.1)	9 (27.3)	20 (28.6)	1.32 (0.43–4.04)	
Nonstricturing and nonpenetrating	6 (5.8)	2 (6.1)	4 (5.7)	1.25 (0.19–8.23)	
Hemoglobin, g/dL	11.5±2.0	11.2±2.0	11.7±2.0	0.84 (0.67–1.05)	0.22
Serum albumin, g/dL	3.3±0.8	3.2±0.9	3.4±0.7	0.99 (0.61–1.61)	0.36
C-reactive protein, mg/dL	38.4±58.4	50.4±73.8	32.7±49.3	1.00 (0.99–1.01)	0.27
Preoperative nutritional optimization, <i>n</i> (%)	32 (31.1)	12 (36.4)	20 (28.6)	1.43 (0.59–3.44)	0.45
Biologic, <i>n</i> (%)	36 (34.9)	12 (36.4)	24 (34.3)	1.03 (0.44–2.43)	0.94
Corticosteroid, <i>n</i> (%)	28 (27.2)	6 (18.2)	22 (31.4)	0.49 (0.18–1.34)	0.16
Immunomodulator, <i>n</i> (%)	60 (58.2)	15 (45.4)	45 (64.3)	0.46 (0.20–1.07)	0.07
Laparoscopic surgery, <i>n</i> (%)	13 (12.6)	1 (0.03)	12 (17.2)	0.15 (0.02–1.22)	0.06
Creation of ostomy, <i>n</i> (%)	26 (25.2)	13 (39.4)	13 (18.5)	1.5 (0.21–10.51)	0.06
Urgent surgery, <i>n</i> (%)	32 (31.1)	13 (39.4)	19 (27.1)	1.88 (0.78–4.52)	0.21

CD, Crohn's disease.

of the disease was significantly higher in patients with complications (12.9 vs. 9.4, *p* = 0.04). However, on multivariate analysis, this variable was not relevant as an independent risk factor for complications, as demonstrated in Table 2. On this analysis, the only factors that were independently associated with increased risk for postoperative complications were creation of ostomy (OR 3.26, 95% CI 1.1–9.5) and urgent surgery (OR 2.94, 95% CI 0.98–9.09).

Furthermore, we compared patients who underwent surgery in an elective versus urgent setting (Table 3). Both groups were similar regarding age, gender, use of biologics, and corticosteroids. However, patients undergoing urgent surgery were less likely to have a previous abdominal surgery than patients undergoing elective surgery (34.4 vs. 69%, *p* = 0.01), and laparoscopic approach was slightly more common in this group (18.7 vs. 9.8%), although this was not statistically significant (*p* = 0.20).

**Table 2.** Multivariate analysis of risk factors for postoperative complications

Variable	Odds ratio	95% CI	<i>p</i> value
Corticosteroid	0.56	0.17–1.79	0.32
Immunomodulator	0.71	0.27–1.85	0.48
Urgent surgery	2.94	0.98–9.09	0.05
Creation of ostomy	3.26	1.12–9.46	0.03
Laparoscopic surgery	0.12	0.01–1.15	0.06
Time since the onset of CD, years	1.04	0.99–1.09	0.15

CD, Crohn's disease.

Time since onset of CD was longer in the group undergoing elective surgery (11.4 vs. 8.4 years, *p* = 0.04).

Regarding laboratory studies, patients in the elective group had higher hemoglobin levels (12.0 vs. 10.6 g/dL,

**Table 3.** Comparison of patients' characteristics according to urgent or elective surgery

Variable	Total ( <i>n</i> = 103)	Urgent ( <i>n</i> = 32)	Elective ( <i>n</i> = 71)	<i>p</i> value
Age, years	40.6±15.0	41.2±15.7	40.3±14.9	0.78
Male, <i>n</i> (%)	57 (55.3)	15 (46.8)	44 (61.9)	0.22
Previous abdominal surgery, <i>n</i> (%)	60 (58.2)	11 (34.3)	49 (69.0)	0.01
Time since the onset of CD, years	14.2±9.2	8.4±9.5	11.4±8.8	0.04
Laparoscopic, <i>n</i> (%)	13 (12.6)	6 (18.7)	7 (9.8)	0.20
Biologic, <i>n</i> (%)	36 (34.9)	8 (25.0)	28 (39.4)	0.16
Corticosteroid, <i>n</i> (%)	28 (27.2)	10 (31.2)	18 (25.3)	0.45
Azathioprine, <i>n</i> (%)	60 (58.2)	13 (40.6)	47 (66.2)	0.03
Hemoglobin, g/dL	11.5±2.0	10.6±2.1	12±1.9	0.02
Serum albumin, g/dL	3.3±0.8	3.05±1.2	3.6±0.72	0.08
C-reactive protein, mg/dL	38.4±58.4	52.8±77.8	31.2±45.1	0.04
Creation of ostomy	26 (25.2)	10 (31.2)	20 (28.2)	0.93

CD, Crohn's disease.

$p = 0.02$ ) and lower C-reactive protein (31.2 vs. 52.8 mg/dL,  $p = 0.04$ ). Serum albumin was higher in the elective group (3.6 vs. 3.05 g/dL), but this difference did not reach statistical significance ( $p = 0.08$ ). Both groups had the same rate of ostomy creation.

### Discussion/Conclusion

It is well described that postoperative complications are more common in patients with CD, than in patients undergoing colorectal abdominal surgery for other reasons [3, 4]. Until 2 decades ago, when biologic therapy was not yet available, malnutrition, corticosteroid use, penetrating disease, and intra-abdominal infection were the main factors associated with postoperative complications among these patients [5, 10]. It was already difficult to standardize CD patients back then due to the multiple disease phenotypes, and surgical management of CD was, consequently, also difficult to standardize.

As biologics were introduced in the market, defining the timing for surgical management for these patients became even more complex, and the safety of biologics in the perioperative period became an issue of growing concern. Recently published results from the PUCCINI trial, a large prospective multicenter cohort study to determine risk factors for postoperative infection in inflammatory bowel disease, concluded that exposure to anti-TNF prior to the surgery does not independently increase the risk for postoperative infectious complications [11]. Many other studies also support this finding [12–15]. In accordance,

in our study, patients who received biologic therapy were not at increased risk for complications.

It is very complex to compare patients under anti-TNF therapy since the same dose of anti-TNF might reach different serum concentrations in different patients and its effects can last even after the medication is already cleared out [16–18]. Nevertheless, current literature indicates that the use of anti-TNF therapy should be interpreted more as an indicator of disease severity, rather than an indication, by itself, for delaying surgery, avoiding anastomosis, or creating diverting stoma [19].

In the present study, stoma creation was associated with increased risk for complications. This finding should be interpreted with caution. While it is believed that creation of stoma can reduce postoperative abdominal sepsis, it is also true that diverting stomas are more frequently performed in patients who the surgeon believes have increased risk for complications [5, 17, 20]. Also, the creation of stoma is related to other postoperative complications, such as dehydration, infection of abdominal wound, mucocutaneous separation, and parastomal abscess, which are usually less severe than anastomotic dehiscence [21, 22]. Therefore, the association between creation of stoma and higher complication rate was probably due to the fact that those patients were in poorer conditions at the time of the surgery, and they would probably have suffered more serious complications if the stoma was not created.

Another factor that has been largely associated with increased complication rates is surgery in an urgent setting [23], which occurred in 31% of the cases in our study.

Complications were indeed more frequent in this group, underscoring the importance of these surgeries being performed in specialized centers in order to minimize morbimortality [24, 25].

Regarding the other variables analyzed in the present study, we did not find any other significant risk factor associated with postoperative complications. A review of the literature on risk factors for complications following abdominal surgery for CD over the last 10 years found conflicting results on this matter, likely due to differences in study design and heterogeneous cohorts.

History of previous abdominal surgery was identified as a risk factor by some authors. The rationale is that it predisposes to more intra-abdominal adhesions, increased operative time, postoperative ileus, and increased risk for incidental bowel lesions during the surgical procedure [10, 26, 27]. However, our study, along with others in the literature, has not found significant difference in complication rates among patients with previous abdominal surgery [28, 29].

Also, in the present study, we found a tendency toward worst outcomes among patients with longer time since onset of CD, which was not confirmed by the multivariate analysis. A study by Shental et al. [29] concluded that patients with disease duration of more than 10 years were at increased risk for intra-abdominal septic complications. We believe that the cumulative effect of many years of inflammation may predispose to worst outcomes. Although this information is unlikely to have an impact on clinical management, it might be useful for preoperative assessment of the patients, when consenting them before the surgery, and when aligning the expectations for postoperative recovery [30].

Penetrating disease was the most frequent phenotype in our population, and it has been associated with increased risk for postoperative complications in many studies [31, 32]. In our experience, however, there was no association between this phenotype and worst outcomes, but it might be related to our relatively small sample size and possibly due to the fact that surgeons tend to be more conservative in dealing with patients with penetrating CD.

Regarding drug therapy, there is strong evidence to support that immunomodulators are not associated with increased rate of postoperative complications [2, 12, 33], and our results are in accordance with these studies. In contrast, the use of corticosteroids is known to increase the risk of complications [15]. More recently, a study by Yoon et al. [20] showed that whereas no immunosuppressive medication alone was independently associated with

increased risk for postoperative septic complications, patients using multiple immunosuppressives were at significantly increased risk. In our cohort, none of the medications was associated with increased morbidity, not even corticosteroids. One hypothesis is that as continuous use of corticotherapy is usually reserved for the most refractory patients and they usually undergo preoperative optimization and progressive reduction of the dosage prior to the surgery, this might have diminished their risk. In addition, it is likely that the surgical approach for these patients was more conservative.

Regarding laboratorial data, even though patients with complications had lower levels of hemoglobin and albumin and higher levels of serum C-reactive protein, the differences were not statistically significant, again probably due to the sample size. Several studies, with larger cohorts, have found that these variables might influence the postoperative outcome and should be taken into consideration when evaluating the need for preoperative optimization [10, 24, 34].

Finally, one important aspect to be highlighted is that the more severe the disease is, and the poorer the conditions of the patient are preoperatively, the more intense the preoperative care will be [35–37]. Our clinic is a national referral center for the treatment of inflammatory bowel disease, and the patients are often malnourished and with very advanced disease by the time they are referred to our service. For this reason, they are usually hospitalized for days, or even weeks, before the procedure in order to receive nutritional optimization, physiotherapy, and psychological support, which notably have the potential to improve postoperative outcomes [10, 38]. This is probably the reason why there were so few factors associated with significant increased risk for complications in this study. Moreover, the experience of the multidisciplinary team in dealing with these patients might have played a significant role [39–41].

This study has some limitations, especially due to its retrospective nature and relatively small cohort. The patients were very heterogeneous, and each of them received a specific preoperative treatment. Consequently, it is difficult to precisely identify the factors that contributed the most to postoperative complications. On the other hand, it reflects the routine of professionals who treat patients with CD. Also, the small number of patients who had undergone laparoscopic surgery is an important limitation of this study. As the majority of our patients had previous abdominal surgery and a significant number of them were operated in an urgent setting, the number of laparoscopic procedures was small. Several studies

report same or lower morbidity for laparoscopic surgery than open surgery for CD [20, 42–46]. In our experience, patients undergoing laparoscopic surgery indeed had a lower rate of complications, but due to the small number of events, it would be precipitated to draw any conclusion on this matter. Last, the results presented were from a very specific population of patients with advanced and refractory CD treated in the largest hospital of Latin America. Therefore, our results may not reflect the reality of current practice in other international centers.

In conclusion, our study showed that creation of stoma is not always necessarily associated with lower rate of postoperative complications but probably with less severe complications. Also, urgent surgery should always be faced as a procedure with increased morbidity. The decision on the surgical management of patients with CD should be taken after an integrated evaluation of the patient, considering the overall nutritional status, immunologic therapy, personal history, and presentation of the disease, highlighting the importance of an experienced multidisciplinary team.

### Statement of Ethics

The institutional review board of our hospital approved this retrospective study and waived the requirement for informed consent (reference No. 97253018.3.0000.0068). This research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki.

### References

- 1 Øresland T, Faerden AE. Surgery in the age of biological treatment. *Scand J Gastroenterol*. 2015;50(1):121–7.
- 2 Ahmed Ali U, Martin ST, Rao AD, Kiran RP. Impact of preoperative immunosuppressive agents on postoperative outcomes in Crohn's disease. *Dis Colon Rectum*. 2014;57(5):663–74.
- 3 Kirchhoff P, Clavien PA, Hahnloser D. Complications in colorectal surgery: risk factors and preventive strategies. *Patient Saf Surg*. 2010;4(1):5.
- 4 Bellolio F, Cohen Z, Macrae HM, O'Connor BI, Huang H, Victor JC, et al. Outcomes following surgery for perforating Crohn's disease. *Br J Surg*. 2013;100(10):1344–8.
- 5 Yamamoto T, Allan RN, Keighley MR. Risk factors for intra-abdominal sepsis after surgery in Crohn's disease. *Dis Colon Rectum*. 2000;43(8):1141–5.
- 6 Alves A, Panis Y, Bouhnik Y, Pocard M, Vicaud E, Valleur P. Risk factors for intra-abdominal septic complications after a first ileocecal resection for Crohn's disease: a multivariate analysis in 161 consecutive patients. *Dis Colon Rectum*. 2007;50(3):331–6.
- 7 Schnitzler F, Fidler H, Ferrante M, Noman M, Arijs I, Van Assche G, et al. Long-term outcome of treatment with infliximab in 614 patients with Crohn's disease: results from a single-centre cohort. *Gut*. 2009;58(4):492–500.
- 8 Peyrin-Biroulet L, Salleron J, Filippi J, Reenaers C, Antunes O, Filipe V, et al. Anti-TNF monotherapy for Crohn's disease: a 13-year multicentre experience. *J Crohns Colitis*. 2016;10(5):516–24.
- 9 Wong DJ, Roth EM, Feuerstein JD, Poylin VY. Surgery in the age of biologics. *Gastroenterol Rep*. 2019;7(2):77–90.
- 10 Huang W, Tang Y, Nong L, Sun Y. Risk factors for postoperative intra-abdominal septic complications after surgery in Crohn's disease: a meta-analysis of observational studies. *J Crohns Colitis*. 2015;9(3):293–301.
- 11 Cohen B, Fleshner P, Kane S, Herfarth H, Palekar N, Farraye F, et al. 415a: anti-tumor necrosis factor therapy is not associated with postoperative infection: results from prospective cohort of ulcerative colitis and Crohn's disease patients undergoing surgery to identify risk factors for postoperative infection I (Puccini). *Gastroenterology*. 2019;156–80.
- 12 Colombel JF, Loftus EV, Tremaine WJ, Pemberton JH, Wolff BG, Young-Fadok T, et al. Early postoperative complications are not increased in patients with Crohn's disease treated perioperatively with infliximab or immunosuppressive therapy. *Am J Gastroenterol*. 2004;99(5):878–83.

### Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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### Author Contributions

Cintia M.S. Kimura contributed to the concept of the study, performed collection of the data and statistical analysis, interpreted the data, wrote the manuscript, and is accountable for all aspects of the work. Arceu Scanavini Neto contributed to the design of the study, revised the manuscript, approved the version to be published, and is accountable for all aspects of the work. Natalia S.F. Queiroz contributed to the design of the study, revised the manuscript, approved the version to be published, and is accountable for all aspects of the work. Natally Horvat contributed to the interpretation of the results, revised the manuscript, approved the version to be published, and is accountable for all aspects of the work. Mariane M.G.M. Camargo contributed to the interpretation of the results, revised the manuscript, approved the version to be published, and is accountable for all aspects of the work. Marcelo R. Borba contributed to the conception of the study, revised the manuscript, approved the version to be published, and is accountable for all aspects of the work. Carlos W. Sobrado contributed to the conception of the study, revised the manuscript, approved the version to be published, and is accountable for all aspects of the work. Ivan Ceconello contributed to the conception of the study, revised the manuscript, approved the version to be published, and is accountable for all aspects of the work. Sergio C. Nahas contributed to the conception and design of the study, revised the manuscript, approved the version to be published, and is accountable for all aspects of the work.

- 13 Marchal L, D'Haens G, Van Assche G, Vermeire S, Noman M, Ferrante M, et al. The risk of post-operative complications associated with infliximab therapy for Crohn's disease: a controlled cohort study. *Aliment Pharmacol Ther.* 2004;19(7):749–54.
- 14 Fumery M, Seksik P, Auzolle C, Munoz-Bongrand N, Gornet JM, Boschetti G, et al. Post-operative complications after ileocecal resection in Crohn's disease: a prospective study from the REMIND group. *Am J Gastroenterol.* 2017;112(2):337–45.
- 15 Lightner AL, McKenna NP, Alsughayer A, Harmsen WS, Taparra K, Parker ME, et al. Biologics and 30-day postoperative complications after abdominal operations for Crohn's disease: are there differences in the safety profiles? *Dis Colon Rectum.* 2019;62(11):1352–62.
- 16 Waterman M, Xu W, Dinani A, Steinhart AH, Croitoru K, Nguyen GC, et al. Preoperative biological therapy and short-term outcomes of abdominal surgery in patients with inflammatory bowel disease. *Gut.* 2013;62(3):387–94.
- 17 Chang MI, Cohen BL, Greenstein AJ. A review of the impact of biologics on surgical complications in Crohn's disease. *Inflamm Bowel Dis.* 2015;21(6):1472–7.
- 18 Appau KA, Fazio VW, Shen B, Church JM, Lashner B, Remzi F, et al. Use of infliximab within 3 months of ileocolic resection is associated with adverse postoperative outcomes in Crohn's patients. *J Gastrointest Surg.* 2008;12(10):1738–44.
- 19 Barnes EL, Lightner AL, Regueiro M. Perioperative and postoperative management of patients with Crohn's disease and ulcerative colitis. *Clin Gastroenterol Hepatol.* 2020;18(6):1356–66.
- 20 Yoon YS, Stocchi L, Holubar S, Aiello A, Shawki S, Gorgun E, et al. When should we add a diverting loop ileostomy to laparoscopic ileocolic resection for primary Crohn's disease? *Surg Endosc.* 2020.
- 21 Formijne Jonkers HA, Draaisma WA, Roskott AM, van Overbeeke AJ, Broeders IA, Consten EC. Early complications after stoma formation: a prospective cohort study in 100 patients with 1-year follow-up. *Int J Colorectal Dis.* 2012;27(8):1095–9.
- 22 Cottam J, Richards K, Hasted A, Blackman A. Results of a nationwide prospective audit of stoma complications within 3 weeks of surgery. *Colorectal Dis.* 2007;9(9):834–8.
- 23 Gutiérrez A, Rivero M, Martín-Arranz MD, García Sánchez V, Castro M, Barrio J, et al. Perioperative management and early complications after intestinal resection with ileocolonic anastomosis in Crohn's disease: analysis from the PRACTICROHN study. *Gastroenterol Rep.* 2019;7(3):168–75.
- 24 Chowdhury MM, Dagash H, Pierro A. A systematic review of the impact of volume of surgery and specialization on patient outcome. *Br J Surg.* 2007;94(2):145–61.
- 25 Gutiérrez A, Rivero M, Martín-Arranz MD, García Sánchez V, Castro M, Barrio J, et al. Perioperative management and early complications after intestinal resection with ileocolonic anastomosis in Crohn's disease: analysis from the PRACTICROHN study. *Gastroenterol Rep.* 2019;7(3):168–75.
- 26 Luong TV, Grandt SD, Negoii I, Palubinskas S, El-Hussuna A. Preoperative factors associated with prolonged postoperative in-hospital length of stay in patients with Crohn's disease undergoing intestinal resection or stricture-plasty. *Int J Colorectal Dis.* 2019;34(11):1925–31.
- 27 Abdalla S, Brouquet A, Maggiori L, Zerbib P, Denost Q, Germain A, et al. Postoperative morbidity after iterative ileocolonic resection for Crohn's disease: should we be worried? A prospective multicentric cohort study of the GETAID chirurgie. *J Crohns Colitis.* 2019;13(12):1510–7.
- 28 Kanazawa A, Yamana T, Okamoto K, Sahara R. Risk factors for postoperative intra-abdominal septic complications after bowel resection in patients with Crohn's disease. *Dis Colon Rectum.* 2012;55(9):957–62.
- 29 Shental O, Tulchinsky H, Greenberg R, Klausner JM, Avital S. Positive histological inflammatory margins are associated with increased risk for intra-abdominal septic complications in patients undergoing ileocolic resection for Crohn's disease. *Dis Colon Rectum.* 2012;55(11):1125–30.
- 30 Ghoneima AS, Flashman K, Dawe V, Baldwin E, Celentano V. High risk of septic complications following surgery for Crohn's disease in patients with preoperative anaemia, hypoalbuminemia and high CRP. *Int J Colorectal Dis.* 2019;34(12):2185–8.
- 31 Schlüssel AT, Cherng NB, Alavi K. Current trends and challenges in the postoperative medical management of Crohn's disease: a systematic review. *Am J Surg.* 2017;214(5):931–7.
- 32 Yamamoto T, Spinelli A, Suzuki Y, Saad-Hossne R, Teixeira FV, de Albuquerque IC, et al. Risk factors for complications after ileocolonic resection for Crohn's disease with a major focus on the impact of preoperative immunosuppressive and biologic therapy: a retrospective international multicentre study. *United European Gastroenterol J.* 2016;4(6):784–93.
- 33 Aberra FN, Lewis JD, Hass D, Rombeau JL, Osborne B, Lichtenstein GR. Corticosteroids and immunomodulators: postoperative infectious complication risk in inflammatory bowel disease patients. *Gastroenterology.* 2003;125(2):320–7.
- 34 Carvello M, Di Candido F, Greco M, Foppa C, Maroli A, Fiorino G, et al. The trend of C-reactive protein allows a safe early discharge after surgery for Crohn's disease. *Updates Surg.* 2020.
- 35 Li Y, Zuo L, Zhu W, Gong J, Zhang W, Gu L, et al. Role of exclusive enteral nutrition in the preoperative optimization of patients with Crohn's disease following immunosuppressive therapy. *Medicine.* 2015;94(5):e478.
- 36 Spinelli A, Allocca M, Jovani M, Danese S. Review article: optimal preparation for surgery in Crohn's disease. *Aliment Pharmacol Ther.* 2014;40(9):1009–22.
- 37 Forbes A, Escher J, Hébuterne X, Kłęk S, Krznaric Z, Schneider S, et al. ESPEN guideline: clinical nutrition in inflammatory bowel disease. *Clin Nutr.* 2017;36(2):321–47.
- 38 Rombeau JL, Barot LR, Williamson CE, Mullen JL. Preoperative total parenteral nutrition and surgical outcome in patients with inflammatory bowel disease. *Am J Surg.* 1982;143(1):139–43.
- 39 El-Hussuna A, Iesalnieks I, Horesh N, Hadi S, Dreznik Y, Zmora O. The effect of pre-operative optimization on post-operative outcome in Crohn's disease resections. *Int J Colorectal Dis.* 2017;32(1):49–56.
- 40 Smedh K, Andersson M, Johansson H, Hagberg T. Preoperative management is more important than choice of sutured or stapled anastomosis in Crohn's disease. *Eur J Surg.* 2002;168(3):154–7.
- 41 Nguyen GC, Steinhart AH. The impact of surgeon volume on postoperative outcomes after surgery for Crohn's disease. *Inflamm Bowel Dis.* 2014;20(2):301–6.
- 42 Tiberi A, Pesi B, Giudici F, Zamboni D, Nelli T, Cupellini C, et al. Laparoscopic ileo-colic resection and right hemicolectomy for Crohn's disease and colon cancer: a preliminary comparative study on post-operative outcome. *Updates Surg.* 2020;72:821–6.
- 43 Bossuyt P, Debeuckelaere C, Ferrante M, Vanbeckevoort D, Billiet T, Wolthuis A, et al. The operative risk and natural history after the diagnosis of ileal penetrating Crohn's disease. *Eur J Gastroenterol Hepatol.* 2018;30(5):539–45.
- 44 Patel SV, Patel SV, Ramagopalan SV, Ott MC. Laparoscopic surgery for Crohn's disease: a meta-analysis of perioperative complications and long term outcomes compared with open surgery. *BMC Surg.* 2013;13:14.
- 45 Maartense S, Dunker MS, Slors JF, Cuesta MA, Pierik EG, Gouma DJ, et al. Laparoscopic-assisted versus open ileocolic resection for Crohn's disease: a randomized trial. *Ann Surg.* 2006;243(2):143–9; discussion 150–3.
- 46 Kristo I, Stift A, Argeny S, Mittlböck M, Riss S. Minimal-invasive approach for penetrating Crohn's disease is not associated with increased complications. *Surg Endosc.* 2016;30(12):5239–44.