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Original Article

UNEXPECTED FINDINGS DURING LAPAROTOMY SURGERY AND URGENT SURGICAL INDICATIONS ARE ASSOCIATED WITH POSTOPERATIVE COMPLICATIONS IN PATIENTS WITH CROHN'S DISEASE

ACHADOS INESPERADOS DURANTE LAPAROTOMIAS E INDICAÇÃO CIRÚRGICA DE URGÊNCIA ESTÃO ASSOCIADOS COM COMPLICAÇÕES PÓS-OPERATÓRIAS EM PACIENTES COM DOENÇA DE CROHN

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ABSTRACT – BACKGROUND: Patients undergoing Crohn's disease (CD) surgery may develop a higher rate of postoperative complications (POC) than other patients. **AIMS:** The aim of this study was to investigate factors determining POC in patients with CD undergoing urgent laparotomy. **METHODS:** This is a retrospective cohort study conducted on adult patients undergoing urgent laparotomy for CD. Clinical and surgical variables, medication history, American Society of Anesthesiologists classification, and POC were investigated. Data collection and management were carried out using the REDCap software (REDCap electronic data capture tools) hosted at the hospital institution. For statistical analysis, the χ^2 (or Fisher's exact) test, Student's t-test, Mann-Whitney test, and simple and multiple multilevel logistic regression analyses were used. **RESULTS:** There was an association regarding the history of adalimumab use (p=0.04, OR 2.8, 95%CI 1.03–7.65), previous use of prednisone (p<0.01, OR 2.03, 95%CI 2.00–2.05), urgent surgery indications (p<0.01, OR=4.32, 95% CI=1.58–11.82), mechanical anastomosis (p=0.02, OR=0.22, 95%CI 0.06–0.80), unexpected intraoperative findings (p=0.02, OR 10.46, 95%CI 1.50–72.99), length of hospital stay greater than 10 days (p<0.01, OR 16.86, 95%CI 2.99–94.96), unplanned intensive care unit (ICU) admission (p=0.01, OR 15.06, 95%CI 1.96–115.70), and planned ICU admission (p<0.01, OR 18.46, 95%CI 3.60–94.51). On multivariate analysis, there was an association between the indication of urgent surgery (or emergency) (p=0.01, OR 4.38, 95%CI 1.43–13.37) and unexpected intraoperative findings (p=0.03, OR 8.11, 95%CI 1.21–54.50). **CONCLUSIONS:** Unexpected changes and urgent surgical indications are considered risk factors for POC in patients with CD.

HEADINGS: Crohn's Disease. Laparotomy. Postoperative Complications. Risk Factors.

Central Message

Patients undergoing Crohn's disease surgery may develop a higher rate of postoperative complications (POC) than other patients, mainly intra-abdominal sepsis, possibly due to the use of corticosteroids, immunobiologicals, and multiple previous resections. The most common POC are anastomotic leakage, bleeding from the intestinal suture line, adynamic ileus, complications with stoma, surgical-site infections, and genitourinary complications.

Perspectives

The findings of our study allow us to conclude that prior treatment with prednisone and adalimumab, Harvey-Bradshaw Index>3.5, urgent (or emergency) surgical indications, failure to perform mechanical anastomosis, identification of unexpected intraoperative findings, length of hospital stay longer than 10 days, and the need for postoperative care in the intensive care unit were considered risk factors for postoperative complications (POC). The presence of unexpected intraoperative findings and indications of urgent or emergency surgeries were considered determining factors of POC in Crohn's disease patients undergoing laparotomy.

RESUMO – RACIONAL*:* Pacientes submetidos à cirurgia de doença de Crohn podem desenvolver mais complicações pós-operatórias do que outros pacientes. **OBJETIVOS*:*** Investigar fatores determinantes de complicações pós-operatórias em portadores de doença de Crohn submetidos à laparotomias de urgência. **MÉTODOS*:*** Estudo de coorte retrospectivo desenvolvido com pacientes adultos submetidos a laparotomias de urgência por doença de Crohn. Foram investigadas variáveis clínicas e cirúrgicas, histórico medicamentoso, classificação da *American Society of Anesthesiology* e complicações pós-operatórias. A coleta e o gerenciamento dos dados foram realizados através do software REDCap (ferramentas eletrônicas de captura de dados REDCap*)* hospedadas na instituição hospitalar. Para a análise estatística foram utilizados os testes χ^2 (ou Exato de Fisher), Teste *t* de Student, Mann-Whitney *e* análise de regressão logística multinível simples e múltipla. **RESULTADOS*:*** Houve associação quanto ao histórico de uso de adalimumabe (p=0.04, OR 2.8, IC95% 1.03–7.65), uso prévio de prednisona (p<0.01, OR 2.03, IC95% 2.00–2.05), cirurgia de urgência (emergência) (p<0.01, OR 4.32, IC95% 1.58–11.82), anastomose mecânica (p=0.02, OR 0.22, IC95% 0.06–0.80), achados inesperados no intraoperatório (p=0.02, OR 10.46, IC95% 1.50–72.99), tempo de internação hospitalar maior que 10 dias (p<0.01, OR 16.86, IC95% 2.99–94.96), admissão em uti não-planejada (p=0.01, OR 15.06, IC95% 1.96–115.70) e admissão em uti planejada (p<0.01, OR 18.46, IC95% 3.60–94.51)**.** Pela análise multivariada verificou-se associação para indicação de cirurgia de urgência (e emergência) (p=0.01, OR 4.38, IC95% 1.43–13.37) e achados inesperados (p=0.03, OR 8.11, IC95% 1.21–54.50). **CONCLUSÕES*:*** Alterações inesperadas e indicação cirúrgica de urgência são fatores de risco para complicações pós-operatórias em pacientes com doença de Crohn.

DESCRITORES: Doença de Crohn. Laparotomia. Complicações Pós-Operatórias. Fatores de Risco.

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INTRODUCTION

Crohn's disease (CD) is an inflammatory intestinal disease that can affect any part of the digestive system, but, most commonly, the terminal ileum, colon, or perianal region, and may possibly develop in more than one of these organs concomitantly[38]. It is a disease with an increasing prevalence and different clinical manifestations. Patients may be asymptomatic to seriously ill, with a recurrent and inflammatory process that causes impairment of functions, malnutrition, and other irreversible consequences[34]. The most common symptoms, however, are chronic diarrhea and abdominal pain[45]. Pharmacological treatment is the first option in most cases; a wide range of medications is available, but mainly corticosteroids, immunomodulators, and immunobiologicals[13] have been used.

In the past, surgery was the initial treatment for CD. It was observed, though, that the recurrent inflammatory process led to repeated surgeries, with multiple intestinal resections potentially progressing to a short intestine[3,4]. Today, despite the evolution of treatments and the use of immunobiologicals, abdominal surgery is still frequently recommended for these patients, with 26.2% undergoing surgery within 10 years[44]. Thus, patients are currently operated on when they present with signs of subocclusion or obstruction due to a stenosing condition, with symptomatic fistulas or in the case of patients refractory to immunobiologicals, and with intracavitary abscesses that cannot be percutaneously drained[33]. In patients with a predominantly inflammatory pattern, laparoscopic ileal resection is an alternative to the use of anti-tumor necrosis factor (TNF) drugs[36,41].

Depending on the patient's condition and the manifestation of the disease, several types of abdominal procedures can be used in patients with CD. Single or combined intestinal resection surgeries (enterectomy, ileocolectomy, or colectomy), comprising manipulation or resection of adjacent organs due to the involvement secondary to fistulas and strictures, can be performed[2,42]. The most common postoperative complications (POC) are anastomotic leakage, bleeding from the intestinal suture line, adynamic ileus, complications with stoma, surgical-site infections, and genitourinary complications[21].

Patients undergoing CD surgery may develop a higher rate of POC than other patients, mainly intra-abdominal sepsis, possibly due to the use of corticosteroids, immunobiologicals, and multiple previous resections[4]. Another study has shown that POC were considered independent risk factors for endoscopic recurrence after primary CD surgery[9].

The objective of this study was to investigate the possible factors determining POC in patients with CD undergoing laparotomy.

METHODS

This was a retrospective cohort study carried out in a large referral hospital that serves a representative population of the country. The investigation was approved by the institution's ethics and research committee (number 51623021.4.0000.5481). Data were collected from the medical records. As an inclusion criterion, patients with CD who underwent laparotomy alone or in combination with other procedures were considered eligible. Such procedures included colon and/or small intestine resections with or without creation of a stoma; strictureplasty; intestinal transit reconstructions; corrections of paracolostomy hernias; drainage of abscesses via laparotomy; and surgical reapproaches via laparotomy. Such surgical procedures were performed at the institution hospital between the years 2000 and 2022 and were followed up for at least 30 days. Patients with little diagnostic differentiation, among other causes of colitis, were excluded from the study.

Initially, from a total of 220 CD patients undergoing outpatient follow-up, 117 patients with a history of surgery were identified. After reviewing the inclusion and exclusion criteria, the medical records of 72 adult CD patients who underwent 125 laparotomy surgeries in the last 20 years were considered eligible for participation in the study (Figure 1).

Study procedures and variables studied

The following information was collected: demographic data, hospital records, gender, age, educational data, smoking and drinking habits, comorbidities, age at disease diagnosis and onset of symptoms, family history of inflammatory bowel disease (IBD) and autoimmune diseases, history of medications already used establishing the CD treatment, previous abdominal surgeries, medications for CD in use at the time of surgery, location and pattern of the disease, presence of extra-intestinal manifestations, and weight, height, and body mass index (BMI) classified according to the cutoff points defined by the WHO (<18.5 kg/m^2: underweight; 18.5–24.9 kg/m^2: normal; 25.0–29.9 kg/m^2: overweight; 30.0–34.9 kg/m^2: Grade 1 obesity; 35.0–39.9 kg/m^2: Grade 2 obesity; and =40 kg/m^2: Grade 3 obesity)[48]. Laboratory hemoglobin tests were also collected (<12.0 g/L for women and <13.0 g/L for men)[49]; hematocrit (<36% for women and <39% for men)[24]; and albumin (>3.5: well nourished and <3.5: malnourished)[7].

The disease-affected areas (colon, small intestine, and/or perianal region) were classified according to the pattern of CD manifestation, as follows: penetrating, stenosing, penetrating and stenosing, or nonpenetrating and nonstenosing. The extra-intestinal manifestations included arthralgia or arthritis, uveitis, erythema nodosum, pyoderma gangrenosum, aphthous ulcer, anal fissure, or perianal fistula. The Crohn's Disease Activity Index (CDAI)[5] and the Harvey-Bradshaw Index (HBI)[6] were calculated. The American Society of Anesthesiologists (ASA) classification was reviewed as follows: ASA I: normal health; ASA II: mild systemic disease; ASA III: severe nondisabling systemic disease; ASA IV: severe, disabling, life-threatening systemic disease; ASA V: dying patient, with minimal survival expectancy; and ASA VI: cadaver organ donor[15].

Surgical variables

Previous abdominal surgeries were divided into surgeries performed due to CD and surgeries required due to other etiologies. In both cases, the type of surgery was specified.

Regarding the surgical procedures, information was collected regarding preoperative laboratory tests for hemoglobin, hematocrit, and albumin; prescription of preoperative enteral or parenteral nutrition; preoperative blood transfusion; type of surgery; presence of anastomosis and/or stoma; surgical nature; surgical time; intraoperative complications; unexpected intraoperative findings; length of hospital stay; admission and time in the intensive care unit (ICU); and identification of POC.

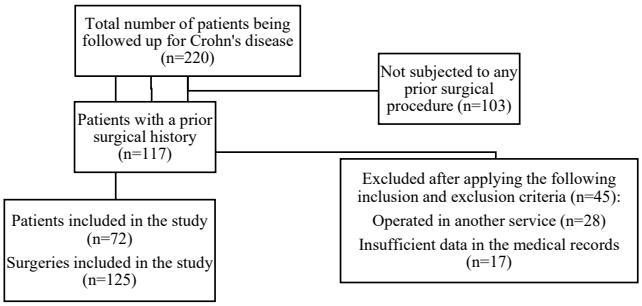

Figure 1 - Inclusion and exclusion criteria for patients with Crohn's disease.

The type of surgery was initially described in five categories, depending on the anatomical structure involved. The first category involved operating exclusively on the small intestine and the second, solely on the colon. The third covered ileocolectomy surgery. For the fourth category, laparotomy with procedures on more than one organ was selected. The fifth category included laparotomy to release fibrous adhesions, cavity washings, nontherapeutic laparotomies, or parastomal hernias with access to the abdominal cavity. The nature of the surgery was divided into elective and urgent, according to the records of the relevant hospitalizations.

To define unexpected intraoperative findings, based on the descriptive recording of the surgical procedure, information about the abdominal cavity inventory that was found as being not consistent with the clinical condition or previous imaging examinations was considered. POC were defined and classified according to the method proposed by Clavien-Dindo[14], which stratifies them according to the therapy required for their treatment. POC were considered to be those manifested in the first 30 days following laparotomy.

Statistical analysis

In this study, data collection and management were carried out using the REDCap software (REDCap electronic data capture tools) hosted at the hospital where this investigation was conducted[22,23]. The REDCap (Research Electronic Data Capture) is a secure, web-based data capture tool designed to support information capture for research studies, offering an intuitive interaction area, audit trails for export methodology and element scanning, automated procedures for continuous data downloads for common statistical packages, and mechanisms for interaction with external sources[22,23].

Data were described considering the mean, standard deviation, and median for quantitative variables and frequency tables for qualitative variables. The characteristics of the patients and procedures were related to complications using the χ^2 (or Fisher's exact) test for categorical variables and Student's *t*-test (or Mann-Whitney test) for numerical variables.

Subsequently, intra-patient procedures were considered dependent, and therefore, to relate the characteristics of the patients, simple (to verify the effect of just one characteristic) and multiple (to verify the joint effect of the characteristics) multilevel logistic regression analyses were used. For the multiple multilevel logistic regression analysis, only variables that presented a p-value less than 0.05 in the simple analysis or that presented clinical validity defined by the researchers were selected. The odds ratio (OR) and the respective 95% confidence intervals (CIs) were estimated. A significance level of 0.05 was considered, and the data were analyzed using SPSS v25, R v4.1.2, and the lme4 package. Variables such as albumin, hemoglobin, hematocrit, BMI, surgical time, and hospital stay were classified into two categories, considering the cutoff points indicated by the receiver operating characteristic (ROC) curve (in relation to the occurrence or not of the complication). The ROC curve area, sensitivity, specificity, positive predictive value, negative predictive value, and accuracy (with their respective 95% CIs) were calculated for these points.

RESULTS

Population

A total of 40 patients (55.5%) underwent only one laparotomy. The other 32 patients had been operated more than once; 18 of them (25%) had undergone the surgery twice, 10 (13.8%) were operated three times, two (2.7%) had the surgery four times, one (1.3%) was operated five times, and another patient (1.3%) underwent the surgery six times. During the eligible patients' data collection, we observed that some information was missing in the medical records due to the absence of entries at the time of care. Therefore, when characterizing the distribution of some variables, the rates were calculated considering only the available data.

Male gender prevailed in 61.1% (n=44) of patients, 4.8% (n=3) reported a family history of IBD, and none of them had a family history of autoimmune diseases. Other characteristics of the study population are summarized in Table 1. The 125 surgeries in the study were performed in patients who had diseases affecting the small intestine in 74.4% (n=93), the colon

Table 1 - Characteristics of the studied population (n=72 patients, n=125 surgeries).

Variables	n	%
Gender		
Female	28	38.9
Male	44	61.1
Education		
Completed primary education	2	2.7
Completed high school	13	18.0
Completed higher education	43	59.7
No registry	14	19.4
Comorbidities		
No	52	72.2
Yes	13	18.0
No registry	7	9.7
Family history of IBD		
No	59	81.9
Yes	3	4.1
No registry	10	13.9
Family history of autoimmune diseases		
No	62	86.1
Yes	0	0
No registry	10	13.9
ASA surgical risk classification		
I	0	0
II	64	88.9
III	8	11.1
IV	0	0
V	0	0
Previous surgery for CD in another service		
No	48	66.6
Yes	24	33.3
Previous abdominal surgery for another reason		
No	63	87.5
Yes	9	12.5
Location of the disease		
Small intestine	93	74.4
Colon	60	48.0
Perianal	20	16.0
Disease pattern		
Stenosing	48	38.4
Fistulizing	33	26.4
Inflammatory	30	24.0
Stenosing and fistulizing	14	11.2
Extra-intestinal manifestations		
No	116	92.8
Yes	9	7.2
Drug treatment		
No	16	12.7
Yes	109	87.3

IBD: Inflammatory bowel disease; ASA: American Society of Anesthesiologists; CD: Crohn's disease

in 48% (n=60), and the perianal region in 16% (n=20); there were a few cases in which the patient had more than one organ affected (Table 1). The perianal region cases (n=20) included perianal involvement in 8.8% (n=11), perianal fistulas in 5.6% (n=7), and perianal abscesses and anal fissures in 1.6% (n=2) of the patients. The average age at the onset of symptoms and at diagnosis was 28.3±9.4 and 28.7±9.9 years, respectively. The mean CDAI was 199.5±132.6 and the HBI was 4.6±4.2.

Regarding drug treatment, 59.7% (n=43) of the patients had previously used immunobiologicals. The medications included infliximab (20.8%, n=15), adalimumab (18%, n=13), vedolizumab (13.9%, n=10), ustekinumab (4.2%, n=3), and certolizumab (2.8%, n= 2). There was a history of corticosteroid therapy in 41 individuals, mostly prednisone (54.2%, n=39) and budesonide (2.8%, n=2). Previous use of immunosuppressants was detected in 34.7% (n=27) of the patients: azathioprine in 33.3% (n=24), methotrexate in 2.8% (n=2), and mercaptopurine in 4% (n=1) of the patients.

In 109 of the 125 procedures (87.2%), drug treatment for CD was prescribed. Prednisone was used in 35.2% (n=44) of the surgeries. Immunobiologicals were administered in 34.4% (n=43) of the surgeries, with adalimumab in 12.8% (n=16), infliximab in 12% (n=15), vedolizumab in 6.4% (n=6), ustekinumab in 3.2% (n=4), and certolizumab in 1.6% (n=2) of the surgeries. Aminosalicylates were used in 31% (n=37) of the surgeries, with oral mesalazine in 20.8% (n=26), sulfasalazine in 8% (n=10), and rectal mesalazine in 0.8% (n=1) of the surgeries. In 22.4% (n=28) of laparotomies, treatment with ciprofloxacin was prescribed and in 21.6%, (n=27) treatment with azathioprine was prescribed.

Variables related to surgeries

Regarding preoperative laboratory tests, the level of albumin was 3.6±0.7 g/dL, hemoglobin was 11.9±2 g/dL, and hematocrit was 36±6%. BMI was 20.4±7.6 kg/m^2. Among the 125 laparotomies, 39.2% (n=49) involved only the small intestine, 24% (n=30) involved the terminal ileum and colon, 15.2% (n=19) involved exclusively the colon, 12% (n=15) involved more than one viscera, and 9.6% (n=12) involved other organs. Regarding the nature of the surgeries, 78.5% (n=95) were elective, 20.7% (n=25) were urgent, and only 0.8% (n=1) was considered emergency. An abdominal drain was placed in 8.3% (n=10) of laparotomy surgeries.

Primary anastomosis occurred in 72.6% (n=90) of the surgeries, with 60.5% (n=75) of them with a mechanical suture and 12% (n=15) with a manual suture. Terminal stoma creation was adopted in 14.5% (n=18) of the procedures, with 15 ileostomies, two terminal colostomies, and one Mikulicz ileostomy and colostomy. Protective ileostomies were performed in 7.2% (n=9) of laparotomy surgeries. Unexpected intraoperative findings were observed in 7.2% (n=9) of surgeries, with 2.4% (n=3) of minor stenosis, 1.6% (n=2) of enterocolic fistulas, 1.6% (n=2) of colon perforations, and 2.4% (n=2) of intracavitary collections. Surgical complications were recorded in 2.4% (n=2) of the procedures, characterized as enterotomies secondary to small-loop adhesions.

The mean age at the time of laparotomy was 38.9±1.7 years. The average time between the onset of symptoms and surgery and the time between the diagnosis and surgery were 12.7±10 and 11.8±9.7 years, respectively. In 14.3% (n=24) of hospitalizations, there was admission to the ICU for postoperative care, with an average stay of 4±3 days. The duration of hospital stay was 13.6±21.4 days, with a median of 8 days. One of the patients had a hospital stay of 131 days due to complications from the disease.

Postoperative complications

There were 20% of POC in the study population (n=125 surgeries). Other characteristics related to POC are shown in Table 2.

Table 2 - Incidence of postoperative complications and distribution according to the Clavien-Dindo classification[14].

Variables	n	%
POC		
No	100	80.0
Yes	25	20.0
Clavien-Dindo classification		
I	9	7.2
II	9	7.2
IIIa	0	0
IIIb	6	4.8
IVa	0	0
IVb	1	0.8
V	0	0
Degree I		
Adynamic ileum	6	4.8
Superficial abdominal wall collection	1	0.8
Enterorrhagia with spontaneous resolution	1	0.8
Central venous access infection	1	0.8
Degree II		
Postoperative blood transfusion	5	4
Abdominal wall infection with antibiotic therapy	1	0.8
Parental nutrition due to adynamic ileus	1	0.8
Pulmonary thromboembolism	1	0.8
Enterocutaneous fistula with antibiotic therapy	1	0.8
Degree IIIb		
Anastomotic leakage	3	2.4
Laparotomy for anastomosis revision	2	1.6
Intracavitary infection	1	0.8
Degree IVb		
Marrow aplasia	1	0.8

POC: postoperative complications.

Association between variables and the presence of postoperative complications

In the analysis of the association between the studied variables and the presence of POC, a significant difference was found only for higher education (p=0.050) and a history of drug treatment with the drug adalimumab (p=0.035). In the analysis of the association between all nutritional variables and laboratory tests, in patients who did or did not present POC, there was no significant difference. When reviewing the association between variables related to the disease and the presence or absence of POC, a significant difference was found in CDAI (p=0.023) and HBI (p=0.019). There was no significant association between current drug treatment and the presence of POC.

When analyzing the association between variables related to surgery and the presence or absence of POC, a significant difference was found regarding the nature of the surgical indication (p=0.002); presence of unexpected intraoperative findings (p=0.016); preoperative blood transfusions (p=0.030); length of hospital stay (p<0.001); and ICU admission requirement (p<0.001).

Univariate logistic regression analysis

In the study of the risk factors assessed by univariate logistic regression for POC associated with patients' demographic characteristics, personal history, and nutritional and laboratory parameters (n=125 surgeries), it was found that only low hematocrit values were associated with POC (p=0.01, OR 1.24, 95%CI 1.23–1.26) (Table 3).

Regarding the history of drug treatment, no statistical association was observed while assessing the type of drug. An association was found regarding the history of adalimumab use (p=0.04, OR 2.8, 95%CI 1.03-7.65) and previous use of prednisone (p<0.01, OR 2.03, 95%CI 2.00-2.05). No medication in use at the time of surgery was decisive for complications (Table 4).

Table 3 - Study of risk factors for postoperative complications using univariate regression analysis (patients' demographic characteristics, personal history, and nutritional and laboratory parameters) (n=125 surgeries).

Variables	p-value	OR	95%CI
Male	0.96	0.99	0.35-2.71
University education	0.09	4.07	0.77-21.35
Comorbidities	0.24	1.98	0.63-6.18
Smoking	0.17	0.97	0.93-1.01
ASA III	0.27	2.13	0.55-8.23
Previous surgery for CD in another service	0.47	0.67	0.23-1.98
Previous abdominal surgery	0.86	1.14	0.26-5.00
Albumin<3.2 (ROC)	0.27	1.91	0.60-6.09
Mild hypoalbuminemia (3-3.5)	0.91	0.92	0.22-3.88
Moderate hypoalbuminemia (2.4-2.9)	0.99	1.01	0.24-4.32
Severe hypoalbuminemia (<2.4)	0.13	6.73	0.56-81.39
Anemia (literature)	0.73	0.83	0.28-2.42
Hemoglobin<10.95 (ROC)	0.13	2.17	0.80-5.85
Low hematocrit (literature)	0.01	1.24	1.23-1.26
Hematocrit<32.5 (ROC)	0.13	0.46	0.17-1.27
Preoperative parenteral nutrition	0.09	2.85	0.85-9.52
Preoperative enteral nutrition	0.17	5.09	0.50-51.64
Underweight (BMI<18.5)	0.71	1.26	0.58-2.78
Overweight (BMI=25-29.9)	0.87	0.87	0.15-4.95
Obesity (BMI=30)	0.11	5.12	0.67-39.08
BMI=23.5 (ROC)	0.38	0.59	0.19-1.89
Two surgeries	0.82	1.11	0.38-3.23
Three surgeries	0.62	0.65	0.11-3.47
Four surgeries	0.86	1.24	0.11-14.18
Five surgeries	0.38	3.82	0.19-77.58
Six surgeries	0.38	3.82	0.19-77.58
Age=60 years	0.57	0.52	0.06-4.86
Age at symptom onset	0.36	1.03	0.96-1.11
Age at diagnosis	0.6	1.02	0.95-1. 08
Interval between symptom onset and surgery (=18.86)	0.08	3.16	0.87-11.43
Interval between diagnosis and surgery (=14.88)	0.24	1.99	0.63-6.31

OR: odds ratio; CI: confidence interval; ASA: American Society of Anesthesiologists; CD: Crohn's disease; BMI: body mass index; ROC: receiver operating characteristic curve.

Table 4 - Study of risk factors for postoperative complications using univariate regression analysis, related to previous and current drug treatment (n=125 surgeries).

Variables	Previous treatment			Current treatment		
	p-value	OR	95% CI	p-value	OR	95% CI
No treatment	0.51	0.57	0.10-3.14	0.24	2.01	0.62-6.53
Prednisone	<0.01	2.03	2.00-2.05	0.95	1.03	0.41-2.66
Aminosalicylates						
Mesalazine PO	0.88	1.08	0.40-3.03	0.89	0.92	0.30-2.81
Sulfasalazine	0.96	0.97	0.30-3.10	0.66	0.79	0.28-2.24
Ciprofloxacin	0.62	0.73	0.20-2.69	0.85	1.11	0.38-3.14
Immunosuppressants	0.65	1.27	0.45-3.49	0.72	0.86	0.28-2.59
Azathioprine	0.24	0.52	0.18-1.61	0.8	0.87	0.29-2.63
Methotrexate	0.99	1.02	0.08-12.49	-	-	-
Immunobiologicals	0.4	0.64	0.22-1.85	0.64	0.79	0.29-2.14
Adalimumab	0.04	2.8	1.03-7.65	0.4	0.51	0.11-2.45
Certolizumab	0.56	2.28	0.14-37.93	0.33	4.05	0.24-68.20
Infliximab	0.09	2.37	0.85-6.73	0.51	1.52	0.43-5.31
Vedolizumab	0.91	1.09	0.24-4.87	0.42	2.05	0.35-12.14
Ustekinumab	-	-	-	0.81	1.32	0.13-13.48

OR: odds ratio; CI: confidence interval; POC: postoperative complications.

While reviewing the OR of POC associated with variables related to CD (location and pattern of the disease, CDAI, and HBI), a statistical association greater than 3.5 (p=0.03, OR 3.58, 95%CI 1.13-11.34) was observed only for HBI. The stenosing pattern and IADC greater than or equal to 450 (indicating severe active disease) did not show a statistical association (data not shown in table).

Table 5 shows the study of risk factors for variables related to surgery. There was a statistical association regarding urgent surgical indications (p<0.01, OR 4.32, 95%CI 1.58-11.82), mechanical anastomosis (p=0.02, OR 0.22, 95%CI 0.06-0.80), unexpected findings in intraoperative events (p=0.02, OR 10.46, 95%CI 1.50-72.99), length of hospital stay greater than 10 days (p<0.01, OR 16.86, 95%CI 2.99-94.96), unplanned admission

to ICU (p=0.01, OR 15.06, 95%CI 1.96-115.70), and planned ICU admission (p<0.01, OR 18.46, 95%CI 3.60-94.51) (Table 5).

Multivariate logistic regression analysis

Table 6 shows the study of risk factors for POC with the use of a multivariate analysis. There was a statistical association between urgent surgical indications (p=0.01, OR 4.38, 95%CI 1.43-13.37) and unexpected findings (p=0.03, OR 8.11, 95%CI 1.21-54.50).

The multivariate analysis initially included the variables that were valid (significant association) in the univariate regression analysis. As extended hospital stay and ICU admission are, according to the Clavien-Dindo[14] definition, already considered as POC, we decided to exclude them from this multivariate regression analysis.

DISCUSSION

A total of 125 abdominal surgeries due to CD were evaluated; similar Brazilian studies that investigated risk factors for surgical complications after abdominal surgeries due to CD included 44 and 103 surgeries[25,39]. Regarding the recurrence of laparotomy surgeries, a study reported that 58.2% of the patients underwent surgery only once, 26.5% twice, and 15.3% more than twice[12]; similar results were found in our investigation. Another study showed that 26.6% of the patients required at least one reoperation[27], and another study showed that 6.3% (n=7) of patients were reoperated within 36 months[35].

Characteristics of patients with Crohn's disease

Data from our study showed an association between higher education and a history of drug treatment with adalimumab and the incidence of POC, whereas no association was observed between educational level and complications in another investigation[25].

In surgeries due to CD conditions, a greater risk of complications in the elderly was not identified in our work; similar findings were observed in another investigation[39]. Other studies have shown that frailty is a stronger predictor of postoperative morbidity than advanced age in patients undergoing intestinal resection for CD[47]; similar findings were observed comparing the postoperative outcome of CD patients of different age groups[30].

In our study, albumin level was found to be 3.6±0.7 g/dL, and surgeries involving patients with hypoalbuminemia accounted for 38.5% of cases; no statistical association was observed with POC. However, other investigations reported in the literature indicate low serum albumin levels and malnutrition as risk factors for POC[29,40,51].

Drug treatment

In this investigation, drug treatment was divided into two groups: medications that the patient had already used (history) and current medications. An association was verified by a simple regression in relation to the history of previous use of prednisone or adalimumab. No drug therapy used during laparotomies resulted in a significant association. Some studies have shown that the use of corticosteroids can interfere with the postoperative outcome: the use of corticosteroids prior to the surgical procedure was associated with a greater chance of anastomotic leakage[28]; an increased risk of intra-abdominal sepsis with the use of corticosteroids associated with immunomodulators[52] and a risk of reoperation within 30 days in patients receiving corticosteroid therapy were observed[19].

Other studies have reported contradictory results regarding the risk of postoperative morbidity in CD patients using anti-TNF; they indicated that the therapy with immunobiologicals increases the chance of total infectious complications and surgical wound infections[46]. Another study reported that these medications are risk factors for general POC in patients with IBD; however, they observed that immunobiologicals, when administered 4 weeks in advance of the surgical procedure, do not interfere with the postsurgical outcome[37]. And another investigation suggested that the use of infliximab 8 weeks in advance of surgery is considered a risk factor for infectious complications in CD patients[43], with no greater risk of postsurgical complications being observed in patients with IBD using anti-TNF, as shown in another literature[8].

Factors related to surgery

In our study, 21.5% of the 125 laparotomies were performed urgently or emergently. After multivariate logistic regression, it was observed that urgent surgery was considered a risk factor for POC while comparing urgent or emergency surgeries with

Table 5 - Study of risk factors for postoperative complications using univariate regression analysis, for variables related to surgery (n=125 surgeries).

Variables	p-value	OR	95%CI
Indication of urgency (or emergency)	<0.01	4.32	1.58-11.82
Time of surgery (ROC)	0.12	3.31	0.73-15.04
Anastomosis creation	0.51	1.73	0.34-8.88
Mechanical anastomosis	0.02	0.22	0.06-0.80
Terminal stoma creation	0.10	5.87	0.96-35.98
Protective ileostomy	0.29	2.40	0.48-12.14
Unexpected findings	0.02	10.46	1.50-72.99
Drain placement	0.83	0.82	0.14-4.94
Preoperative blood transfusion	0.07	4.93	0.86-28.44
Length of stay greater than 10 days (ROC)	<0.01	16.86	2.99-94.96
Unplanned ICU admission	0.01	15.06	1.96-115.70
Planned ICU admission	<0.01	18.46	3.60-94.51

OR: odds ratio; CI: confidence interval; ROC: Receiver operating characteristic curve; ICU: Intensive care unit.

Table 6 - Study of risk factors for postoperative complications using multivariate regression analysis.

Variables	p-value	OR	95%CI
Surgical indications of urgency (or emergency)	0.01	4.38	1.43-13.37
Unexpected findings	0.03	8.11	1.21-54.50

OR: odds ratio; CI: confidence interval.

elective surgeries. Similar findings were observed in other investigations, with 31.1% of surgeries being urgent[39] and an increased chance of postsurgical morbidity in CD patients when the surgeries are performed on an urgent basis[20,50].

In our study, 22 different types of surgery were performed, and it was observed that mechanical anastomosis showed a statistical association with the surgery. There are studies showing that mechanical anastomosis leads to a lower incidence of dehiscence in patients undergoing right colectomies[11], and other studies have not observed any difference in postoperative morbidity related to the anastomosis technique[10].

The identification of unexpected intraoperative findings was, at the end of the multivariate analysis, determined as a risk factor for POC. Among the 125 surgeries, there was a discrepancy between intraoperative findings and previous imaging examinations in 7.2% of cases (n=9 cases). This result differs from that obtained in a study that reported the presence of unexpected intra-abdominal findings in 279 of the 375 surgeries examined (74.4%), including 123 (30.4%) small fistulas with other structures and 33 (8.8%) abscesses[16]. The impact of these findings on postoperative outcomes was not described[16].

In the present study, although a length of hospital stay longer than 10 days was associated with POC in the simple regression, it was decided not to consider this variable in the multiple regression. Type 1 Clavien-Dindo[14] classification considers any deviation from the normal postoperative course as a complication. An extended hospital stay is generally not expected in the uncomplicated postoperative period of CD patients' surgeries. Therefore, it would become a confusing factor when interpreting the final result. The same rationale was applied considering the need for ICU admission.

Incidence of complications

POC occurred in 25 of the 125 laparotomy surgeries included in this study (20%). In comparison, national surveys with a similar methodological structure[25,39] reported complication rates of 32% and 40.9%, respectively. International retrospective studies reviewing the risk factors for postsurgical complications reported rates between 25.5% and 45.6%[1,17,18,20,31]. Some publications only considered septic POC[26,32,50], describing an incidence of 15.5%, 17%, and 8%, respectively. In our survey, four septic complications were observed (3.2%).

POC within 30 days after the surgical procedure occurred in 32% of patients in another retrospective study[39]. Out of these, 81.8% of the patients experienced surgical complications and 18.2% experienced clinical complications. Among the surgical complications, 51.8% were related to the abdominal wound, and 48.2% were associated with infection and/or dehiscence of suture lines. The creation of a stoma and urgent surgeries were considered risk factors for the complications[39].

As a strong point of our investigation, we highlight the fact that this work was developed in a hospital which is a referral center for the treatment of IBDs, especially in CD patients, and which attends a representative population of a large metropolitan region of the country. And, as limiting factors of the study, we can consider the surgeries of different procedures and the fact that the study is retrospective.

CONCLUSIONS

The findings of our study allow us to conclude, through the use of univariate analysis, that prior treatment with prednisone and adalimumab, HBI>3.5, urgent (or emergency) surgical indications, failure to perform mechanical anastomosis, identification of unexpected intraoperative findings, length of hospital stay longer than 10 days, and the need for postoperative care in the ICU were considered risk factors for POC. And according to the multivariate analysis, the presence of unexpected intraoperative findings and surgeries indicated on an urgent (or emergency) were considered determining factors of POC in CD patients undergoing laparotomy.

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