



## Original Article

# Postoperative complication rates between Crohn's disease and Colorectal cancer patients after ileocolic resections: a comparative study<sup>☆</sup>



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### ABSTRACT

**Introduction:** Ileocolic resection (ICR) is the most common surgical procedure performed for Crohn's disease (CD). Similarly, right-sided Colorectal cancer (CRC) is treated by the same operation. The primary aim of this study was to analyze and compare the frequency and profile of early postoperative complications of ICR between patients with CD and CRC.

**Methods:** Retrospective and observational study with patients submitted to ICR from two Brazilian tertiary referral units in colorectal surgery. We included patients with diagnosis of CD or CRC, treated with ICR, at any stage of follow-up. Variables analyzed: age at surgery, gender, diagnosis, surgical approach (open or laparoscopy), type of anastomosis (hand-sewn/stapled; end-to-end/side-to-side), presence and type of early postoperative complications (30 days) and mortality, among others.

**Results:** 109 patients were included, 73 with CD (67%) and 36 with CRC (33%). CD patients were younger ( $42.44 \pm 12.73$  years vs.  $66.14 \pm 11.02$  years in the CRC groups,  $p < 0.0001$ ) and had more previous resections ( $20 \pm 27.4$  in CD and 0 in CRC,  $p = 0.001$ ). There were no significant differences between the groups in terms of overall early postoperative complications [17/73 (23.3%) in the CD and 5/36 (13.9%) in the CRC groups ( $p = 0.250$ )]. There was no significant difference between the groups in relation to anastomotic leakage ( $p = 0.185$ ), surgical site infections ( $p = 0.883$ ), other complications (0.829) and deaths ( $p = 0.069$ ).

<sup>☆</sup> Studied carried out at Pontifícia Universidade Católica do Paraná (PUCPR), Hospital Universitário Cajuru, Serviço de Coloproctologia (SeCoHUC), Curitiba, PR, Brazil.

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Conclusions: There was no significant difference in early postoperative complications in patients with CD or CRC submitted to ICR.

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## Complicações pós-operatórias após ressecções ileocólicas na doença de Crohn e no câncer colorretal: um estudo comparativo

### R E S U M O

Palavras-chave:  
Doença de Crohn  
Câncer colorretal  
Complicações  
Pós-operatório

**Introdução:** A ileocectomia direita (ICD) é a operação mais realizada no manejo cirúrgico da doença de Crohn (DC). Da mesma forma, é o procedimento de escolha no tratamento do câncer colorretal (CCR) quando localizado à direita. O objetivo deste estudo foi analisar e comparar as complicações cirúrgicas em pacientes submetidos a ICD por DC e CCR em uma coorte de pacientes.

**Método:** Estudo longitudinal, retrospectivo e observacional, de uma coorte de pacientes submetidos a ICD provenientes de 2 centros de referência em coloproctologia. Os critérios de inclusão foram pacientes com DC ou CCR, submetidos a ICD, em qualquer estágio de acompanhamento. As variáveis analisadas foram: idade à cirurgia, gênero, diagnóstico, abordagem (aberta ou laparoscópica), tipo de anastomose, presença e tipo de complicações pós-operatórias precoces (até 30 dias) e óbito.

**Resultados:** Foram incluídos 109 pacientes, 73 com DC (67%) e 36 com CCR (33%). Os grupos foram homogêneos em todas as variáveis, à exceção da idade ( $42,44 \pm 12,73$  na DC e  $66,14 \pm 11,02$  no CCR,  $p < 0,0001$ ). Não houve diferença entre os grupos em relação às complicações precoces, com 17/67 (23,3%) na DC e 5/36 (13,9%) no CCR,  $p = 0,250$ . Da mesma forma, não houve diferença entre os grupos em relação a deiscência de anastomose ( $p = 0,185$ ), infecções do sítio cirúrgico ( $p = 0,883$ ), outras complicações (0,829) e óbitos ( $p = 0,069$ ).

**Conclusões:** Não houve diferença nas complicações pós-operatórias em pacientes submetidos a ICD entre portadores de DC e CCR.

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## Introduction

Crohn's disease (CD) is a systemic autoimmune chronic inflammation that affects the gastrointestinal tract, with crescent incidence and prevalence in developing countries.<sup>1</sup> This disease can affect any portion of the gastrointestinal tract. However, it is more frequent (50%) in the terminal ileum and caecum.<sup>1-3</sup>

Strategies aiming disease control in CD management are evolving, mostly based on novel therapeutic drugs, as biological agents (monoclonal antibodies). Despite significant advances in medical management of CD, surgery is still necessary in a significant proportion of patients.<sup>4</sup> Up to 50% of patients are submitted to an intestinal resection after 10 years of diagnosis.<sup>5</sup>

The most common performed surgical procedure for CD is the ileocolic resection (ICR), that can be either performed with minimally invasive techniques (multiport laparoscopy, single-port or robotics) or by conventional approach.<sup>2,3</sup> This operation can often be challenging. The significant inflammatory process caused by failure to medical therapy may result in complications as abscesses, fistulas and adhesions, what

can technically lead to difficulties in the surgical approach. These difficulties usually tend to increase surgical postoperative complication rates.<sup>2,6</sup>

Colorectal cancer (CRC), when located in the cecum, ascending or proximal transverse colon (right segments of the large bowel), is usually treated by the same surgical method (ICR). Similarly, this operation in the management of CRC can be performed by open approach, or by minimally invasive techniques.<sup>7</sup> Some oncological principles may be different between cancer and CD, but the operations *per se* are considered similar in the management of both diseases.<sup>6,7</sup>

Patients submitted to ICR may present numerous postoperative complications. Minor ones, such as fever, surgical site and urinary tract infections can usually be managed without significant problems. However, major complications such as anastomotic leakage, sepsis and pneumonia can lead to prolonged hospitalization or even to death.<sup>8,9</sup> These complications can be a result of many variables: patient's age, smoking habits, previous use of certain types of medication, other comorbidities, surgical characteristics (elective or emergency), disease phenotype (fistulas, stenosis, abscesses), type of the anastomosis, among others.<sup>6-11</sup> Multiport laparoscopic surgery resulted in a decrease in the postoperative

complication rates, as it ensured a better patient satisfaction and shorter hospital stay in the postoperative period, as compared to the conventional approach.<sup>7-11</sup>

Due to the greater complexity of the cases, as big inflammatory masses, internal, external fistulas and phlegmons can be a consequence of uncontrolled inflammation, it is speculated that patients with CD may present higher rates of postoperative complications in comparison to other diagnoses, due to intraoperative technical difficulties.<sup>6,7</sup> This can also be related to associated medical therapy, leading to immunosuppression at the time of surgery.<sup>8,9</sup> However, this was not confirmed in the literature. A study from the United States with more than 700 patients demonstrated that despite associated immunomodulators and biologics, postoperative complication rates were not higher in ICR for CD in comparison to other diagnoses.<sup>6</sup>

The primary aim of this study was to analyze and compare the frequency and profile of early postoperative surgical complications of ICR between patients with CD and CRC.

## Methods

### Study design

This was a longitudinal, retrospective and observational study with patients submitted to ICR from two Brazilian tertiary referral units in colorectal surgery, in a 5-year period (between January of 2011 and April 2016).

### Inclusion and exclusion criteria

The eligibility criteria were patients with diagnosis of CD or CRC, confirmed by imaging and endoscopic tests, treated with ICR, by conventional or laparoscopic approach (with primary anastomosis) at any stage of follow up. Patients with other diagnoses except from CD and CRC, or submitted to other surgical procedures, those who were younger than 18 years of age, with diverting stomas, who lost follow-up or had lack of data in the charts were automatically excluded.

### Variables of interest

Concurrently with data collection, comparative Excel charts were created embracing patient's name and other demographic characteristics, such as age at surgery, gender, diagnosis, surgical approach (open or laparoscopy), type of anastomosis (hand-sewn/stapled; end-to-end/side-to-side), presence and type of early postoperative complications (30 days) and mortality, among others.

### Group definition

After initial identification in the units' operating lists, patients had their records accessed, and were allocated into two groups (CD and CRC). Early postoperative complications were then analyzed (according to the frequency and type of complication) and compared between the two groups.

## Statistical analysis

Pearson chi-square test and Mann-Whitney's *U* test were used to verify group homogeneity. The student's *t* test was used to compare the complication rates between the groups.  $p < 0.05$  values were considered significant.

## Ethical considerations

The study protocol was approved by the ethics committee of the Catholic University of Paraná (PUCPR), in June/2016, under protocol number CAAE 56444216.7.0000.0020, at the ministry of health *plataforma brasil* website.

## Results

Initially, 118 patients were identified from the surgical lists, and considered eligible for the study. Four patients were subsequently excluded for lack of data in the charts and five were also excluded due to diverting stomas, as a result of the procedure. Therefore, the study's population was composed by 109 patients (Fig. 1): 73 with CD (67%) and 36 with CRC (33%).

Table 1 demonstrates the baseline characteristics of the patients in detail. As observed, the groups were not 100% homogeneous. There was a difference in the median age at surgery ( $42.44 \pm 12.73$  in the CD and  $66.14 \pm 11.02$  in the CRC groups,  $p < 0.0001$ ) and in the number of previous resections ( $20 \pm 27.4$  in CD and 0 in CRC,  $p = 0.001$ ). The surgical characteristics of the patients were also comparable between the groups. Laparoscopic procedures were performed in 20-25% of the patients, and the stapled side-to-side was the most frequent anastomosis performed. All patients with diagnosis of CD were using or an immunomodulator (azathioprine), a biological agent, or both in combination.

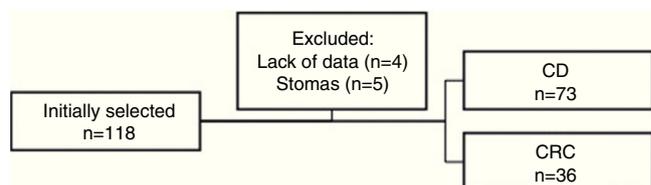
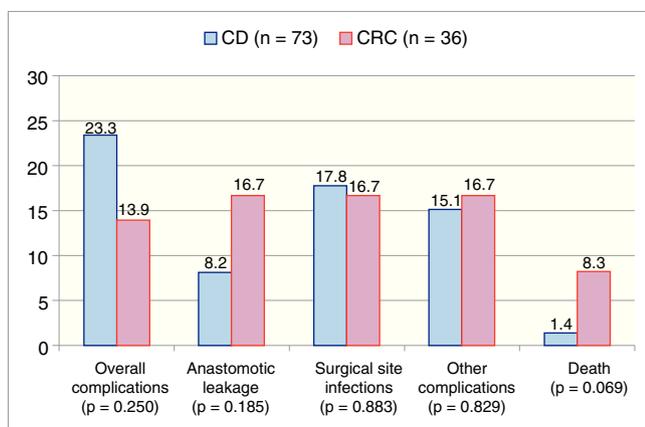


Fig. 1 – Study flowchart and group definition.

Table 1 – Baseline characteristics of the 109 patients.

Variable	CD (n = 73)	CRC (n = 36)	p Value
Age (mean ± SD)	42.44 (±12.73)	66.14 (±11.02)	<0.001 <sup>a</sup>
Female gender (n%)	40 (54.8)	20 (55.6)	0.940
Previous resections (n%)	20 (27.4)	0(0.0)	0.001 <sup>a</sup>
Laparoscopic surgery (n%)	15 (20.5)	9 (25.0)	0.598
Hand-sewn end-to-end anastomosis	3 (4.1)	2 (5.6)	0.210
Hand-sewn side-to-side anastomosis	6 (8.2)	7 (19.4)	
Stapled side-to-side anastomosis	64 (87.7)	27 (75.0)	

<sup>a</sup> Pearson's chi-square test.



**Fig. 2 – Postoperative complications between the groups. No significant statistical difference was found (Student's t test).**

Regarding the primary outcome of our study, there was no significant differences between the groups in terms of early postoperative complications. Overall complications were found in 17/73 (23.3%) in the CD and in 5/36 (13.9%) in the CRC groups ( $p=0.250$ ). Likewise, according to the specific type of complication analyzed, there was no significant difference between the groups in relation to anastomotic leakage ( $p=0.185$ ), surgical site infections ( $p=0.883$ ), other complications (0.829) and deaths ( $p=0.069$ ). These data are illustrated in detail in Fig. 2.

## Discussion

ICRs are widespread operations, performed due to a myriad of different diagnosis in the daily practice of general and colorectal surgeons.<sup>6</sup> The surgical procedure *per se* is not significantly different between different diseases. Peculiarities in CRC patients should also be of notice, mainly regarding the discussion of extended mesocolic resection in order to respect oncological surgical principles. ICR can be performed by conventional (open) approach or by minimally invasive techniques (multiport laparoscopy, single-port or robotics), independently of the diagnosis. Several studies demonstrated the feasibility of minimally invasive procedures even in complicated cases of CD.<sup>3,10,11</sup>

In our study, the majority of the patients submitted to ICR had a diagnosis of CD (67%) as compared to CRC (only 33% of the population). This was not observed in other series in the literature, as CRC tend to be a more common reason for ICR in general surgical practice. In a snapshot audit from the European Society of Coloproctology (ESCP) with 3208 patients, only 11.7% ( $n=371$ ) were operated due to CD, whereas 78.4% ( $n=2515$ ) had right-sided CRC.<sup>12</sup> In a retrospective series ( $n=131$ ) from a general surgeon's perspective, the same pattern was observed: the majority of patients had malignancy (92/131 – 70.3%), while CD was the indication for surgery in the minority (39/131 – 29.7%).<sup>13</sup> Our sample had a majority of patients of CD possibly due to a referral bias, as both units are tertiary referral centers for inflammatory bowel diseases (IBD) medical and surgical management. Another possible reason is that more general and digestive surgeons in our country

do operations for CRC, but not as much for complicated CD, what could explain this important difference of our study in comparison to other series.

In the present study, the groups were homogeneous for important surgical variables, mainly the surgical approach and the type of anastomosis. CRC patients were significantly older than CD patients, what clearly could be expected, as the prevalence of CD is increased in the younger, whilst the incidence of malignancy tends to be higher in the elderly. Moreover, patients with CD had more previous resections than those with CRC, what was also expected, as the natural history of recurrence of CD usually tends toward repeated operations over time, mainly if not adequate postoperative medical therapy was used.

In regards to the primary objective of our study, no differences were observed in overall early postoperative complications between CD (23.3%) and CRC (13.9%) –  $p=0.250$ . This was in accordance to a large series of patients with comparison between the outcomes of CD vs. non-CD patients. Mascarenhas et al. found that major complication rates were not different between the CD (5.4%) and non-CD patients (4%) –  $p=0.58$ . The same pattern was observed for minor complications (5.4% vs. 9.9%, respectively,  $p=0.16$ ). Our higher rates of complications, in comparison to this series, can be probably explained by two factors: first, referral bias due to more complicated cases of CD and advanced tumors in the CRC group, as both units are referral centers from the public system in a developing country (tendency to more advanced and severe cases); secondly, the teaching hospital profile of the units, where residents tend to perform procedures under supervision.

In our sample of patients, anastomotic leakage was found in 8.2% of the CD and in 16.7% of the CRC resections performed. In the biggest series of the literature to date (ESCP snapshot study), the overall leakage rate was 8.1% (7.2% for CRC and 9% for CD, with 15.8% for other indications).<sup>12</sup> The expected tendency of higher anastomotic problems in CD in comparison to CRC, mostly due to the complexity of the procedures (inflammatory masses, phlegmons, fistulas) malnutrition, anemia or preoperative steroids, was not found in our study. Maybe with a wider sample of patients, this difference could be encountered (possible type II error in our study, as no sample calculation could be made due to the observational design).

There is controversy if the type of anastomosis can affect the rates of anastomotic leakage. A prospective study by McLeod et al. demonstrated no differences in complications between the two different techniques.<sup>14</sup> A meta-analysis published in 2014 demonstrated that stapled side-to-side anastomosis tend to be safer than hand-sewn end-to-end anastomosis in several aspects, mainly in dehiscence, with an Odds Ratio (OR) of 0.45, with 95% confidence interval (CI) 0.20–1.00.<sup>2</sup> The ESCP snapshot study came to opposite results, with higher risk for dehiscence in patients with stapled anastomosis (OR 1.43, 95% CI 1.04–1.95,  $p=0.03$ ) in multivariate analysis.<sup>12</sup> In our study, we could not check the relation between anastomotic leakage and the type of anastomosis due to the small numbers, mainly of the hand-sewn technique, or intrinsic heterogeneity among them (hand-sewn end-to-end and side-to side were performed).

Another important point is that all CD patients in our study had previous immunosuppression with a thiopurine, a biological agent or both, and this did not affect the postoperative complication rates. This is in accordance to the study from Mascarenhas et al.,<sup>6</sup> and with other two retrospective studies we published aiming the impact of immunomodulators and biological agents in postoperative outcomes in CD.<sup>15,16</sup>

Our study has important limitations that might be considered in the analysis of the results. All biases from retrospective chart reviews from two different units, that could impair data collection, should be taken into account. The reduced sample of patients could not lead to proper subgroup analysis, regarding type of anastomosis and laparoscopic procedures, for example. We also could not have precise data from preoperative medication in the CD group, what could also contribute to the study's results. However, our study's strength is based on the precise methodology, as few studies aimed this specific comparison between the two different diseases.

In summary, our retrospective comparative study did not demonstrate any differences in postoperative complications between CD and CRC patients submitted to ICR. No differences in anastomotic leakage were found, as well as in mortality rates. The experience of these two teaching hospitals in colorectal surgery can stimulate prospective data in our country in to order outline possible differences in the surgical management of CD and CRC, what could lead to optimization of individualized therapy for each patient.

### Conflicts of interest

EFM is a speaker for Abbvie, Janssen and Takeda. RSH and LS are speakers for Abbvie and Janssen. PGK is a speaker and consultant for Abbvie, Ferring, Janssen, Pfizer and Takeda.

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