



Original article

Risk factors for major complications after surgical treatment of primary ileocecal Crohn's disease. A multicentric Latin American experience[☆]



Nicolás Avellaneda,^{a,b,*} Claudio Saddy Rodrigues Coy,^c Henrique Sarubbi Fillmann,^d Rogerio Saad-Hossne,^e Juan Pablo Muñoz,^f Rafael García-Duperly,^g Felipe Belloio,^h Nicolás Rotholtz,ⁱ Gustavo Rossi,^j Juan Ricardo Marquez V,^k Mariano Cillo,^l Antonio Lacerda-Filho,^m Augusto Carrie,^a Beatriz Yuki Maruyama,ⁿ Lucio Sarubbi Fillmann,^d Marcela Maria Silvino Craveiro,^e Ezequiel Ferro,^f Eduardo Londoño-Schimmer,^g Andrés Iglesias,^h Camila Bras Harriott,ⁱ Juan Pablo Campana,^j Daniel Londoño Estrada,^m Rogini Balachandran,^b Paulo Gustavo Kotzeⁿ

^a General Surgery Department, Hospital Universitario CEMIC, Argentina

^b Colorectal Surgery Department, Aarhus University Hospital, Denmark

^c Colorectal Surgery Unit, Campinas State University (UNICAMP), Campinas, Brazil

^d Surgery Department, Pontificia Universidad Católica de Rio Grande do Sul, Brazil

^e Colorectal Surgery Department, Paulista State University UNESP, Brazil

^f Colorectal Surgery Department, Nueva Proctología, Argentina

^g Colorectal Surgery Department, Fundación Santa Fé de Bogotá, Colombia

^h Coloproctology Unit, Digestive Surgery Department, Pontificia Universidad Católica de Chile, Chile

ⁱ Colorectal Surgery Service, General Surgery Department, Hospital Aleman de Buenos Aires, Argentina

^j Section of Colorectal Surgery, Department of General Surgery, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina

^k Coloproctology Institute, Clínica Las Américas, Colombia

^l Colorectal Surgery Department, Hospital Británico de Buenos Aires, Argentina

^m Department of Colorectal Surgery, Felício Rocho Hospital, Belo Horizonte, Brazil

ⁿ Colorectal Surgery Unit, Pontificia Universidade Católica do Paraná (PUCPR), Curitiba, Brazil

ARTICLE INFO

Article history:

Received 6 January 2023

Accepted 5 April 2023

Available online 25 May 2023

A B S T R A C T

Introduction: Complications after ileocecal resection for Crohn's disease (CD) are frequent. The aim of this study was to analyze risk factors for postoperative complications after these procedures.

[☆] Please cite this article as: Surgical IBD Latam Consortium. Risk factors for major complications after surgical treatment of primary ileocecal Crohn's disease. A multicentric Latin American experience. Cir Esp. 2023. <https://doi.org/10.1016/j.cireng.2023.05.002>.

* Corresponding author.

E-mail address: n.avellaneda86@gmail.com (N. Avellaneda).

<http://dx.doi.org/10.1016/j.cireng.2023.05.002>

2173-5077/© 2023 AEC. Published by Elsevier España, S.L.U. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

Keywords:

Crohn

Ileocecal

Resection

IBD

Risk

Complication

Materials and methods: We conducted a retrospective analysis of patients treated surgically for Crohn's disease limited to the ileocecal region during an 8-year period at 10 medical centers specialized in inflammatory bowel disease (IBD) in Latin America. Patients were allocated into 2 groups: those who presented major postoperative complications (Clavien-Dindo > II), the "postoperative complication" (POC) group; and those who did not, the "no postoperative complication" (NPOC) group. Preoperative characteristics and intraoperative variables were analyzed to identify possible factors for POC.

Results: In total, 337 patients were included, with 51 (15.13%) in the POC cohort. Smoking was more prevalent among the POC patients (31.37 vs. 17.83; $P = .026$), who presented more preoperative anemia (33.33 vs. 17.48%; $P = .009$), required more urgent care (37.25 vs. 22.38; $P = .023$), and had lower albumin levels. Complicated disease was associated with higher postoperative morbidity. POC patients had a longer operative time (188.77 vs. 143.86 min; $P = .005$), more intraoperative complications (17.65 vs. 4.55%; $P < .001$), and lower rates of primary anastomosis. In the multivariate analysis, both smoking and intraoperative complications were independently associated with the occurrence of major postoperative complications.

Conclusion: This study shows that risk factors for complications after primary ileocecal resections for Crohn's disease in Latin America are similar to those reported elsewhere. Future efforts in the region should be aimed at improving these outcomes by controlling some of the identified factors.

© 2023 AEC. Published by Elsevier España, S.L.U. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

Factores de riesgo para complicaciones mayores posteriores al tratamiento quirúrgico de enfermedad de Crohn con afectación ileocecal. Trabajo retrospectivo, multicéntrico en Latinoamérica

R E S U M E N

Palabras clave:

Crohn

Ileocecal

Resección

EII

Riesgo

Complicación

Introducción: Las complicaciones posteriores a resección ileocecal por enfermedad de Crohn (EC) son frecuentes. El objetivo de este estudio fue analizar los factores de riesgo para presentar complicaciones postoperatorias después de estos procedimientos.

Materiales y métodos: Se realizó un análisis retrospectivo de pacientes operados por enfermedad de Crohn limitada a la región ileocecal durante un período de 8 años en diez centros especializados en enfermedad inflamatoria intestinal (EII) de América Latina. Los pacientes fueron divididos en dos grupos, los que presentaron complicaciones postoperatorias mayores (Clavien-Dindo > II) (denominado grupo de complicaciones postoperatorias - POC) y los que no (grupo sin complicaciones postoperatorias - NPOC). Se analizaron las características preoperatorias y las variables intraoperatorias para identificar posibles factores relacionados a POC.

Resultados: Se incluyeron 337 pacientes, 51 (15,13%) en el grupo con POC. El grupo POC presentó mayor índice de tabaquismo (31,37 vs. 17,83, $p = 0,026$), quienes presentaron más anemia preoperatoria (33,33 vs. 17,48%, $p = 0,009$), urgencias (37,25 vs. 22,38, $p = 0,023$) y menores niveles de albúmina. Los procedimientos por enfermedad complicada se asociaron con una mayor morbilidad postoperatoria. Los pacientes con POC tuvieron un tiempo operatorio más largo (188,77 vs. 143,86 minutos, $p = 0,005$), más complicaciones intraoperatorias (17,65 vs. 4,55%, $p < 0,001$) y menores tasas de anastomosis primaria. En el análisis multivariado, tanto tabaquismo como complicaciones intraoperatorias se asociaron de forma independiente con la aparición de complicaciones mayores postoperatorias.

Conclusión: Este estudio demuestra que los factores de riesgo de complicaciones posteriores a resecciones ileocecales primarias por EC en América Latina son similares a los reportados en otros lugares. Los esfuerzos futuros en la región deben estar dirigidos a mejorar estos resultados mediante el control de algunos de los factores identificados.

© 2023 AEC. Publicado por Elsevier España, S.L.U. Este es un artículo Open Access bajo la licencia CC BY (<http://creativecommons.org/licenses/by/4.0/>).

Introduction

Crohn's disease (CD) is a chronic condition associated with transmural inflammation, which commonly affects the ileocecal region.¹ In these patients, repeated flare-ups of the disease are associated with complications (fibrotic stenosis or fistulae). Surgery is still needed in a significant percentage of patients, even despite significant advances in medical therapy.²

As in other parts of the world, the prevalence of Crohn's disease is rising in Latin America, with some of the highest numbers reported in Brazil and Argentina (approximately 24 and 15 patients/100 000 persons).³

Ileocecal resections for complicated disease are associated with higher rates of postoperative complications compared to luminal disease.^{4,5} Therefore, several studies have aimed to identify risk factors associated with higher postoperative morbidity.⁶

Data regarding the surgical management of inflammatory bowel disease (IBD) in Latin America is scarce. Information about indications and outcomes of ileocecal resections for CD, use of minimally invasive approaches, types of anastomosis, etc., are lacking.⁷

The aim of this study was to identify possible risk factors associated with postoperative complications in a large cohort of patients who had undergone primary ileocecal resections due to CD in different countries in Latin America.

Materials and methods

Ethical considerations

This study was approved by institutional review boards from all included centers and was conducted in accordance with good clinical practice standards.

Study design and setting

This is a retrospective multicenter study that included consecutive surgical patients treated primarily for CD limited to the ileocecal region, from 10 specialized IBD teaching hospitals in 4 Latin American countries (Argentina, Brazil, Chile and Colombia) over an 8-year period (2012–2020).

An initial analysis of this cohort was performed comparing outcomes of patients operated on for either luminal involvement alone or for disease complications.⁸

Participants

Inclusion criteria: Patients who had undergone primary ileocecal resections due to CD, either conventional or laparoscopic, with luminal, stenotic, or penetrating phenotypes.

Exclusion criteria: Previous abdominal procedures associated with CD, missing data on the electronic health records, and age younger than 18 years.

Patient stratification

Patients were allocated into 2 groups according to the presence of major postoperative complications (Clavien–Dindo > II)⁹

within 30 days of the procedure (POC: postoperative complications, NPOC: no postoperative complications).

Data collection and management

Information regarding patients' comorbidities and operative procedures were collected in an electronic database, which was validated by 3 experts in colorectal surgery and biostatistics to identify key issues and to maximize completeness and accuracy of data. Local investigators compiled their specific databases, which were combined by the primary author (NA). The lead investigators (NA and PGK) checked the accuracy of all cases to ensure data quality. When missing data were identified, the local lead investigator was contacted and asked to complete the records.

Variables analyzed

Preoperative variables included patient demographics (comorbidities stratified by Charlson's Comorbidity Index), smoking status, preoperative anemia and albumin levels, ASA score and history of previous abdominal procedures.

Variables associated with Crohn's disease included time from CD diagnosis to surgery (disease duration), Montreal classification, exposure to biological agents before surgery and within 12 weeks of the operative procedure, history of perianal disease, previous exposure to corticosteroids at the time of surgery (defined as receiving more than 20 mg/day of Prednisolone for more than 6 weeks),¹⁰ and requirement of preoperative nutrition optimization before the procedure (defined as patients who needed to be hospitalized in order to receive enteral or parenteral nutrition before surgery). Percentage of early surgery (for luminal involvement, as defined by Maruyama et al.)¹¹ or surgery for disease complications (stenoses or fistulae) were also evaluated.

Intraoperative factors included operative time, character of surgery (urgent or elective), operative approach and conversion rate, presence of intraoperative complications and their respective stratification following the CLASSIC Classification,¹² requirements of associated procedures and rates of primary anastomosis. Decisions regarding the specific type of anastomosis and management of the colonic stump in patients who did not receive an anastomosis were also considered between the 2 groups.

Postoperative factors included length of hospitalization, readmission, reoperation rates, and mortality within 30 days of the procedure.

Outcomes

The main outcome of the study was to compare preoperative and intraoperative characteristics between the POC and NPOC groups, aiming to identify possible risk factors associated with 30-day postoperative major complications.

Statistical analysis

Statistical analysis was performed using Stata Software (v11.1, Statacorp, College Station, Texas, USA). The categorical variables were described as percentages whereas numerical variables

were described as mean or median (accordingly) with their range. The normality of each numerical variable was evaluated visually and with the Kolmogorov-Smirnov test.

We used the chi-square or Fisher's exact tests, as appropriate, for the comparison of categorical variables, and the Student's T or Fisher's exact test for continuous variables. OR with respective 95% CI were also calculated.

A multivariable analysis using a logistic regression model was performed including all the variables compared with a P value $<.05$ and those variables considered clinically significant by the investigators. A P value $<.05$ was considered statistically significant. Our primary outcome variable was the presence of major postoperative complications.

Results

In total, 337 patients met the inclusion criteria, 51 of which (15.13%) presented major complications and comprised the POC group. Fig. 1 describes the patient selection process, and

Appendix 1 describes the number of patients included per study center.

Preoperative variables

Information of included patients prior to surgery are described in detail in Table 1. No differences between POC and NPOC groups were identified regarding sex, Charlson comorbidity score, other comorbidities, ASA score, previous abdominal procedures, and time from CD diagnosis to surgery.

We created an additional analysis that stratified time from diagnosis to surgery into 3 categories (less than 2 years, 2-5 years, and more than 5 years), which also showed no differences between groups.

On the other hand, POC patients presented higher rates of smoking (31.37% vs. 17.83%, $P = .026$, OR: 2.11), preoperative anemia (33.33% vs. 17.48%, $P = .009$, OR: 2.36), and urgent surgery (37.25% vs. 22.38%, $P = .023$, OR: 2.06). Operations for complicated disease (when compared to luminal phenotype) were also more frequent in the POC group. Albumin levels were lower in the POC

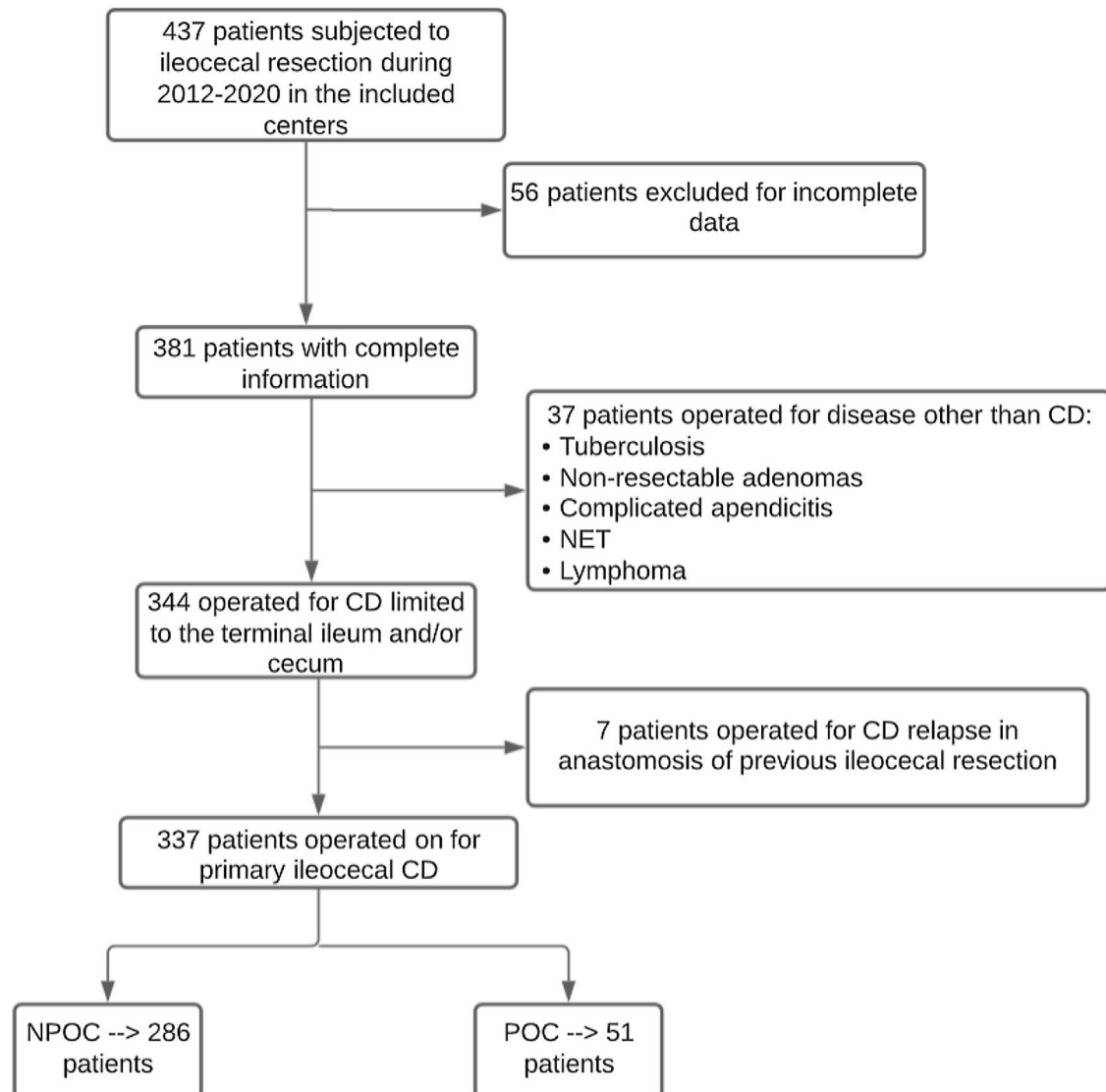


Fig. 1 – Patient selection process.

Table 1 – Preoperative variables.

Variables	All patients N = 337 (100%)	NPOC N = 286 (84.87%)	POC N = 51 (15.13%)	P value	OR (95% CI)
Sex (female)	177 (52.52)	154 (53.85)	23 (45.10)	0.249	0.70 (0.39–1.28)
Age (median, range)	39.78 (18–89)	39.16 (18–89)	43.22 (18–77)	0.095	
Smoking	67 (19.88)	51 (17.83)	16 (31.37)	0.026	2.11 (1.08–4.12)
BMI (median, 95% CI)	22.87 (13.96–37)	23.09 (14.84–37)	21.70 (13.96–30.10)	0.189	
Hypertension	25 (7.42)	18 (6.29)	7 (13.73)	0.806	2.37 (0.93–6.04)
Dyslipidemia	11 (3.26)	8 (2.80)	3 (5.88)	0.253	2.17 (0.55–8.52)
Charlson comorbidity score (median, range)	0.60 (0–8)	0.59 (0–8)	0.63 (0–6)	0.843	
Anemia	67 (19.88)	50 (17.48)	17 (33.33)	0.009	2.36 (1.21–4.59)
Other comorbidities	30 (8.90)	23 (8.04)	7 (13.73)	0.189	1.81 (0.73–4.51)
Previous abdominal surgery	81 (24.04)	70 (24.48)	11 (21.57)	0.654	0.85 (0.41–1.74)
Time from diagnosis to surgery (months, median, range)	63.36 (0–504)	62.14 (0–300)	70.18 (0–504)	0.475	
Character of surgery (Urgent)	83 (24.63)	64 (22.38)	19 (37.25)	0.023	2.06 (1.09–3.90)
Luminal vs. complicated disease (Complicated)	277(82.20)	230 (80.42)	47 (92.16)	0.044	2.86 (0.98–8.34)
Montreal classification					
A1	21 (6.23)	20 (6.99)	1 (1.96)	0.171	0.27 (0.03–2.04)
A2	235 (69.73)	197 (68.88)	38 (74.51)	0.420	1.32 (0.67–2.60)
A3	81 (24.04)	69 (24.13)	12 (23.53)	0.927	0.97 (0.48–1.95)
B1	60 (17.80)	56 (19.58)	4 (7.84)	0.044	0.35 (0.12–1.02)
B2	155 (45.99)	131 (45.80)	24 (47.06)	0.868	1.05 (0.58–1.91)
B3	101 (29.97)	84 (29.37)	17 (33.33)	0.569	1.20 (0.64–2.27)
B2–3	21 (6.23)	15 (5.24)	6 (11.76)	0.076	2.41 (0.88–6.58)
Perianal CD	93 (27.60)	81 (28.32)	12 (23.53)	0.481	0.78 (0.39–1.56)
Previous steroids	128 (37.98)	105 (36.71)	23 (45.10)	0.256	1.42 (0.77–2.59)
Previous exposure to biological agents	180 (53.41)	153 (53.50)	27 (52.94)	0.942	0.98 (0.54–1.78)
Number of previous biologics					
1	114 (63.33)	95 (33.22)	19 (37.25)	0.574	1.19 (0.64–2.22)
2	58 (32.22)	52 (18.18)	6 (11.76)	0.263	0.60 (0.24–1.49)
3	8 (4.44)	6 (2.10)	2 (3.92)	0.431	1.90 (0.37–9.75)
Exposure to biologics within 12 weeks before surgery	115 (63.89)	98 (64.05)	17 (62.96)	0.913	0.95 (0.41–2.23)
Requirement of preoperative nutritional optimization	50 (14.84)	40 (13.99)	10 (19.61)	0.298	1.50 (0.69–3.24)
Albumin level (median, range)	3.48 (1.2–5.2)	3.54 (1.9–5.2)	3.23 (1.2–4.5)	0.04	
ASA score					
I	62 (18.40)	55 (19.23)	7 (13.73)	0.350	0.67 (0.28–1.57)
II	239 (70.92)	202 (70.63)	37 (72.55)	0.781	1.10 (0.56–2.14)
III	34 (10.09)	27 (9.44)	7 (13.73)	0.349	1.53 (0.62–3.72)
IV	2 (0.59)	2 (0.70)	0	0.549	0.000

Univariate comparative analysis of preoperative characteristics between groups. Categorical variables described as percentages whereas numerical variables were described as mean or median (accordingly) with their range. Normality of each numerical variable was evaluated visually and with the Kolmogorov-Smirnov test. Chi square or Fisher exact tests, as appropriate, for the comparison of categorical variables, and the Student's T or Fisher's exact test for continuous variables. OR with respective 95% CI also calculated.

group (3.23 vs. 3.54, $P = .04$). The rate of exposure to steroids at the time of surgery was numerically higher in the POC group, but this difference was not statistically significant (45.10% vs. 36.71%, $P = .256$). Previous perianal CD, previous use of biological agents, exposure to these drugs within 3 months of surgery, and requirements of preoperative nutrition optimization were similar in POC and NPOC patients. Lastly, no difference was observed regarding exposure to different types of biologic agents and the presence of complications.

Intraoperative variables

Intraoperative information is described in detail in [Table 2](#).

Patients from the POC group had a significantly longer mean operative time (188.77 vs. 143.86, $P = .005$), numerically

higher rates of associated procedures (23.53% vs. 14.34%, $P = .097$) and intraoperative complications (17.65% vs. 4.55%, $P < .001$). In contrast, patients in the NPOC group presented a higher rate of primary anastomosis (93.71% vs. 82.35%, $P = .006$) and lower need for postoperative antibiotics (45.45% vs. 76.47%, $P < .001$, OR: 3.90).

The overall rate of minimally invasive surgery was 51.34%, with no difference between groups in terms of initial laparoscopic approach. Even though conversion rates were numerically higher in the POC group, the difference was not significant (16% vs. 9.46%, $P = .322$). Different types of anastomoses were included in the analysis. Side-to-side, anti-peristaltic stapled anastomosis was the most common anastomotic configuration. No differences were identified between the groups regarding the specific type of anastomo-

Table 2 – Intraoperative variables.

Variables	All patients N = 337 (100%)	NPOC N = 286 (84.87%)	POC N = 51 (15.13%)	P value	OR (95% CI)
Operative time (median, range)	151.43 (45–420)	143.86 (45–360)	188.77 (60–420)	0.005	
Approach					
Laparoscopic	173 (51.34)	148 (51.75)	25 (49.02)	0.719	0.90 (0.49–1.63)
Conventional	164 (48.66)	138 (48.25)	26 (50.98)	0.719	1.11 (0.61–2.03)
Conversion rate	18/173 (10.40)	14/148 (9.46)	4/25 (16)	0.322	1.82 (0.54–6.11)
Requirement of associated procedures	53 (15.73)	41 (14.34)	12 (23.53)	0.097	1.84 (0.89–3.82)
Intraoperative complications	22 (6.53)	13 (4.55)	9 (17.65)	0.000	4.50 (1.78–11.38)
CLASSIC Minor	19/22 (86.36)	13/22 (100)	6/9 (66.67)	0.025	
CLASSIC Major	3/22 (13.64)	0	3/9 (33.33)	0.025	
Primary anastomosis	310 (91.99)	268 (93.71)	42 (82.35)	0.006	0.31 (0.13 – 0.75)
Type of anastomosis					
Hand-sewn	47/310 (15.16)	38/268 (14.18)	9/42 (21.43)	0.223	1.81 (0.82–4.03)
Stapled	263/310 (84.84)	230/268 (85.82)	33/42 (78.57)	0.223	0.61 (0.27–1.37)
Hand-sewn					
One layer	23/47 (48.94)	18/38 (47.37)	5/9 (55.56)	0.882	1.11 (0.27–4.54)
Two-layer	24/47 (51.06)	20/38 (52.63)	4/9 (44.44)	0.477	0.60 (0.24–2.53)
Anastomotic configuration					
End- to-end	28/310 (9.03)	25/268 (9.33)	3/42 (7.14)	0.646	0.96 (0.31–3.00)
End-to-side	30/310 (9.68)	27/268 (10.07)	3/42 (7.14)	0.550	0.96 (0.31–3.00)
Side-to-side	252/310 (81.29)	216/268 (80.60)	36/42 (85.71)	0.429	1.44 (0.58–3.62)
Anastomotic orientation					
Isoperistaltic	57/310 (18.39)	51/268 (19.03)	6/42 (14.29)	0.461	1.41 (0.56–3.53)
Anti-peristaltic	253/310 (81.61)	217/268 (80.97)	36/42 (85.71)	0.461	0.82 (0.34–1.96)
Decision after resection					
Anastomosis w/o diversion	292 (86.65)	252 (88.11)	40 (78.43)	0.061	0.49 (0.23–1.05)
Diverted anastomosis	18 (5.34)	15 (5.24)	3 (5.88)	0.852	1.13 (0.31–4.06)
End ileostomy, intra abdominal stump	7 (2.08)	5 (1.75)	2 (3.92)	0.316	2.29 (0.43–12/22)
End ileostomy, subcutaneous stump	13 (3.86)	11 (3.85)	2 (3.92)	0.979	1.02 (0.22–4.76)
End ileostomy, mucous fistula	7 (2.08)	3 (1.05)	4 (7.84)	0.002	8.03 (1.70–37.96)
Postoperative antibiotics	169 (50.15)	130 (45.45)	39 (76.47)	0.000	3.90 (1.92–7.90)

Univariate comparative analysis of intraoperative characteristics between groups. Categorical variables described as percentages whereas numerical variables were described as mean or median (accordingly) with their range. Normality of each numerical variable was evaluated visually and with the Kolmogorov-Smirnov test. Chi square or Fisher exact tests, as appropriate, for the comparison of categorical variables, and the Student's T or Fisher's exact test for continuous variables. OR with respective 95% CI also calculated.

sis. Lastly, regarding management of the colonic stump in patients without primary anastomosis, POC patients presented a higher proportion of ileostomy and colonic mucous fistula.

Postoperative outcomes

Postoperative variables are listed in Table 3. Patients from the POC group had significantly longer hospitalization stay (19.54 vs. 5.48 days, $P < .001$), higher rates of readmissions to hospital (35.29% vs. 4.20%, $P < .001$), reoperations (66.67% vs.

1.75, $P < .001$) and mortality (7.84 vs. 0, $P < 0.001$) within 30 days of the index operation.

In total, 16 patients (5.16%) presented anastomotic leakage after surgery, for which most required reoperation.

Multivariate analysis

Table 4 describes the results of multivariable analysis. Smoking (OR = 2.99, $P = .040$) and intraoperative complications (OR=8.43, $P = .034$) were independently associated with the occurrence of major postoperative complications.

Table 3 – Postoperative variables.

Variables	All patients N = 337 (100%)	NPOC N = 286 (84.87%)	POC N = 51 (15.13%)	P value	OR (95% CI)
Hospitalization length in days (median, 95% CI)	8.03 (2–81)	6.01 (2–35)	19.54 (6–81)	0.000	
Readmission to hospital	30 (8.90)	12 (4.20)	18 (35.29)	0.000	12.45 (5.13–30.23)
Reoperation	39 (11.57)	5 (1.75)	34 (66.67)	0.000	112.40 (23.98–526.85)
Mortality	4 (1.19)	0	4 (7.84)	0.000	

Univariate comparative analysis of postoperative characteristics between groups. Categorical variables described as percentages whereas numerical variables were described as mean or median (accordingly) with their range. Normality of each numerical variable was evaluated visually and with the Kolmogorov-Smirnov test. Chi square or Fisher exact tests, as appropriate, for the comparison of categorical variables, and the Student's T or Fisher's exact test for continuous variables. OR with respective 95% CI also calculated.

Table 4 – Multivariate analysis.

Variables	OR	Standard Error	P value	95% CI
Smoking	2.99	1.605	0.040	1.05– 8.56
Preoperative Anemia	1.43	0.710	0.476	0.54–3.79
Urgency setting	0.69	0.377	0.497	0.236–2.015
Surgery for complications of the disease	1.69	1.455	0.544	0.31–9.15
Preoperative albumin level	0.57	0.205	0.120	0.29–1.16
Operative time	1.00	0.002	0.236	0.99–1.01
Intraoperative complications	8.43	8.472	0.034	1.18–60.44
Primary anastomosis	1.08	0.626	0.895	0.35–3.37
Need for postoperative antibiotics	1.08	0.626	0.895	0.35–3.37

Multivariable analysis using a logistic regression model including all the variables compared with a p value of less than 0.05 and those variables considered clinically significant by the investigators. A p value below 0.05 was considered statistically significant, using postoperative major complications as dependent variable.

Discussion

This study presents a large group of patients operated on for primary ileocecal CD and comprises one of the first international multicenter experiences about surgical treatment of patients with CD from different Latin America countries. In the multivariable analysis, smoking and intraoperative complications were independently associated with higher rates of postoperative morbidity.

Because postoperative morbidity after resection is still a major problem in the management of CD (especially when compared to other intestinal problems),¹³ several recent studies have aimed to determine specific factors that could potentially affect postoperative outcomes. Certain risk factors for major complications have been extensively described, such as smoking,¹⁴ preoperative anemia,^{15,16} urgent procedures,^{14,17} penetrating disease,^{5,15,17–20} hypoalbuminemia,^{20–22} and previous exposure to steroids.^{14,18,19,23} Our study presented similar findings in the univariate analysis, where smoking, preoperative anemia, urgent surgery and complicated disease (stenotic or penetrating) were more frequently observed in patients with postoperative complications.

In addition, previous exposure to biological agents has been the object of endless debate regarding its possible association with worse postoperative outcomes. Although some studies have identified a correlation between preoperative anti-TNF agents and higher rate of postoperative complications,^{16,23–25} a large meta-analysis based on information from 18 non-randomized studies failed to find an association between infliximab and total complications.²⁷ Furthermore, the prospective multicentric PUCCINI trial²⁸ evaluated postoperative morbidity in IBD patients exposed to biologics and likewise could not demonstrate an association between these drugs and worse postoperative outcomes. Overall rates of infections (18.1% vs. 20.2%, $P = .469$) and surgical site infections (12.0% vs. 12.6%, $P = .889$) were similar in patients previously exposed to anti-TNF agents and those unexposed. In the multivariable analysis, current exposure to these agents was not associated with overall infections (OR, 1.050; 95% CI, 0.716–1.535) or surgical site infection (OR, 1.249; 95% CI, 0.793–1.960). Detectable concentrations of anti-TNF agents were not associated with infectious complications. In our study,

preoperative exposure to biologics was observed in 52.94% of patients with major postoperative complications and 53.5% of those without morbidity ($P = .942$); these findings are compatible with most retrospective studies and the aforementioned prospective PUCCINI trial. Guidelines still do not present specific formal recommendations regarding preoperative use of biologics,²⁹ and more cause-effect relationship studies are warranted.

Few studies have investigated intraoperative factors in ileocecal resections due to CD and their possible relation with postoperative complications. Our study found that prolonged operative time and intraoperative complications negatively impacted postoperative morbidity, whereas a primary anastomosis seemed to work as a protective factor. A possible reason for this finding is that surgeons, facing patients in worse conditions or requiring more complex procedures, could be less eager to perform a primary anastomosis (selection bias). Postoperative antibiotics were also more needed in patients with complications, which could be partially explained by the fact that this group faced more complex surgery, with longer operative time and more complicated disease.

In our study, the presence of postoperative major complications had a major impact on other postoperative indicators, including prolonged hospitalization as well as higher rates of reoperations, readmissions and mortality. This highlights the interest in defining preoperative risk factors for these events, with special interest in modifiable characteristics, such as smoking or delayed surgical indication.

Since this is one of the first multicenter Latin American studies about the surgical treatment of CD patients, it provides an interesting overview of surgery-related characteristics. Initially, the overall 51% rate of laparoscopic procedures seems low in the era of minimally invasive techniques. However, in other studies, the percentage of laparoscopic cases is below 60%.^{5,14–26,30} This could be due to the fact that the main indications for surgery in patients with CD are disease-related complications, such as long fibrotic stenosis, internal or external fistulae, and inflammatory masses, which may limit surgical approach options.

Overall, the rate of primary anastomosis was high in our cohort of patients, and the most common type and configuration of the anastomoses created (stapled, side-to-side) are

compatible with the recommendations of international guidelines.²⁹ Even though there is no consensus on the management of the colon stump when a primary anastomosis is not performed, the tendency for exteriorization as a double-loop stoma or mucous fistula instead of an intra-abdominal stump (which was observed in patients with complications) can be explained by the fact that patients in poor general condition might be at risk of colon stump leakage and consequent septic complications.

Our study is associated with certain inherent limitations, such as its retrospective nature and the low number of patients with complications. Furthermore, practices may vary among medical centers, and the surgeons' experience and expertise were not evaluated in detail (some cases may have been performed by junior surgeons, others by senior staff members, and some by residents with assistance). Minimally invasive resections were performed in 60% of cases, which reflects the general reality of our continent in colorectal surgery. We also did not analyze possible differences between hospitals, as some study centers included fewer patients than others, and this was not the main purpose of our analysis. Also, the groups were not considered fully homogeneous, as some variables differed between patients with and without associated morbidity. Another limitation is that no specific sample calculation was possible, and we worked with a convenience sample.

On the other hand, the main strength of our study is that it represents the very first solid international multicenter analysis of postoperative outcomes from Latin America, which may assist in surgical management of CD in our region.

In summary, smoking and the presence of intraoperative complications were identified as predictors of major postoperative complications after ileocecal resections in CD and may have an important impact on different postoperative indicators. This international study focuses efforts on gathering more experience in the surgical management of CD in Latin America. Further prospective research aimed at identifying preoperative risk factors for postoperative complications is warranted in order to properly optimize patients for ileocecal resections in our region.

Conflict of interest

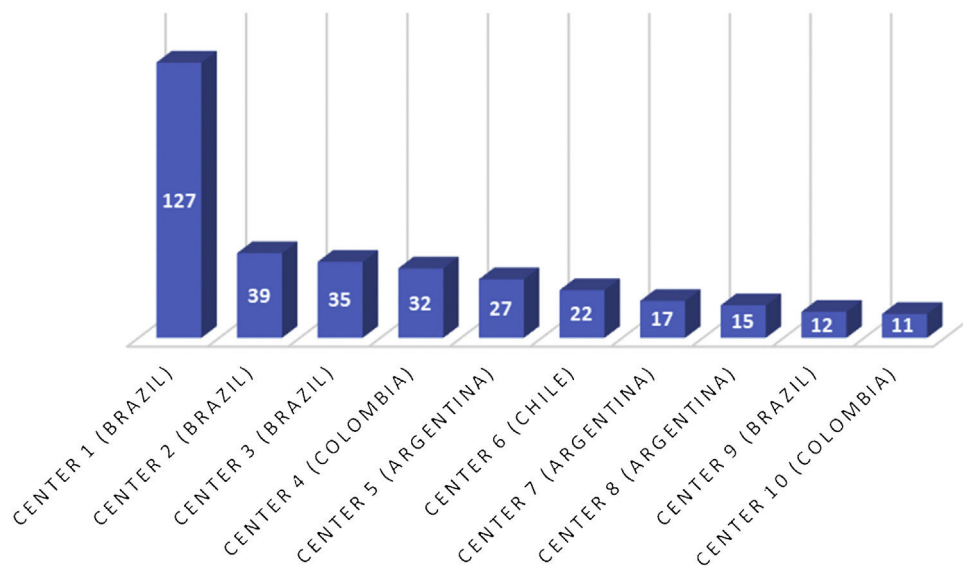
The authors declare no conflict of interest.

Funding

This study has not been funded.

Appendix 1. Number of patients per center

NUMBER OF PATIENTS OPERATED PER CENTER



REFERENCES

- Thoreson R, Cullen J. Pathophysiology of inflammatory bowel disease: an overview. *Surg Clin North Am*. 2007;87(3):575-85. <http://dx.doi.org/10.1016/j.suc.2007.03.001>.
- Rungoe C, Langholz E, Andersson M, Basit S, Nielsen NM, Wohlfahrt J, Jess T. Changes in medical treatment and surgery rates in inflammatory bowel disease: a nationwide cohort study 1979-2011. *Gut*. 2014;63(10):1607-16. <http://dx.doi.org/10.1136/gutjnl-2013-305607>.
- Kotze P, Underwood FE, Mourao AO, Ferraz JGP, Saad-Hossne R, Toro M, et al. Progression of inflammatory bowel diseases throughout latin america and the caribbean: a systematic review. *Clin Gastroenterol Hepatol*. 2020;18:304-12.
- Kirchhoff P, Clavien PA, Hahnloser D. Complications in colorectal surgery: risk factors and preventive strategies. *Patient Saf Surg*. 2010;4(1):5. <http://dx.doi.org/10.1186/1754-9493-4-5>.
- Bellolio F, Cohen Z, Macrae HM, O'Connor BI, Huang H, Victor JC, McLeod RS. Outcomes following surgery for perforating Crohn's disease. *Br J Surg*. 2013;100(10):1344-8. <http://dx.doi.org/10.1002/bjs.9212>.
- Farmer RG, Hawk WA, Turnbull RB. Indications for surgery in Crohn's disease: analysis of 500 cases. *Gastroenterology*. 1976;71(2):245-50.
- Yamamoto-Furusho J, Parra-Holguin N, Julio-Baños F, Puentes F, López R, Bosques-Padilla F, et al. Clinical differentiation of inflammatory bowel disease (IBD) in Latin America and the Caribbean. *Medicine*. 2022;101(3):e28624. <http://dx.doi.org/10.1097/MD.00000000000028624>.
- Surgical IBD LATAM Consortium. Earlier surgery is associated to reduced postoperative morbidity in ileocaecal Crohn's disease: results from SURGICROHN - LATAM study. *Dig Liver Dis*. 2022. <http://dx.doi.org/10.1016/j.dld.2022.09.011>. ISSN 1590-8658.
- Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg*. 2004;240(2):205-13. <http://dx.doi.org/10.1097/01.sla.0000133083.54934.ae>.
- Bemelman WA, Warusavitarne J, Sampietro GM, Serclova Z, Zmora O, Luglio G, et al. ECCO-ESCP consensus on surgery for Crohn's disease. *J Crohns Colitis*. 2018;12(1):1-16. <http://dx.doi.org/10.1093/ecco-icc/jjx061>.
- Maruyama BY, Ma C, Panaccione R, Kotze PG. Early laparoscopic ileal resection for localized ileocaecal Crohn's disease: hard sell or a revolutionary new norm? *Inflamm Intest Dis*. 2022;7(1):13-20. <http://dx.doi.org/10.1159/000515959>.
- Rosenthal R, Hoffmann H, Clavien PA, Bucher HC, Dell-Kuster S. Definition and Classification of Intraoperative Complications (CLASSIC): Delphi Study and pilot evaluation. *World J Surg*. 2015;39(7):1663-71. <http://dx.doi.org/10.1007/s00268-015-3003-y>.
- Larson DW, Abd El Aziz MA, Perry W, Behm KT, Shawki S, Mandrekar J, Mathis KL, Grass F. Surgical resection for Crohn's and cancer: a comparison of disease-specific risk factors and outcomes. *Dig Surg*. 2021;38(2):120-7. <http://dx.doi.org/10.1159/000511909>.
- Neary PM, Aiello AC, Stocchi L, Shawki S, Hull T, Steele SR, et al. High-risk ileocolic anastomoses for Crohn's disease: when is diversion indicated? *J Crohns Colitis*. 2019;13(7):856-63. <http://dx.doi.org/10.1093/ecco-icc/jjz004>.
- Yamamoto T, Spinelli A, Suzuki Y, Saad-Hossne R, Teixeira FV, Carvalho de Albuquerque I, 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. <http://dx.doi.org/10.1177/2050640615600116>.
- Brouquet A, Maggiori L, Zerbib P, Lefevre JH, Denost Q, Germain A, et al. Anti-TNF therapy is associated with an increased risk of postoperative morbidity after surgery for ileocolonic Crohn disease. *Ann Surg*. 2018;267(2):221-8. <http://dx.doi.org/10.1097/SLA.0000000000002017>.
- Gutierrez 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 Report*. 2019;7(3):168-75. <http://dx.doi.org/10.1093/gastro/goz010>.
- Alves A, Panis Y, Valleur P, Pocard M, Vicaute E, Valleur P. Risk factors for intra-abdominal septic complications after a first ileocaecal resection for Crohn's disease: a multivariate analysis in 161 consecutive patients. *Dis Colon Rectum*. 2006;50(3):331-6. <http://dx.doi.org/10.1007/s10350-006-0782-0>.
- Tzivanakis A, Singh JC, Guy RJ, Travis S, Mortensen NJ, George BD. Influence of risk factors on the safety of ileocolic anastomosis in Crohn's disease surgery. *Dis Colon Rectum*. 2012;55(5):558-62. <http://dx.doi.org/10.1097/DCR.0b013e318247c433>.
- Galata C, Weiss C, Hardt J, Seyfried S, Post S, Kienle P, et al. Risk factors for early postoperative complications and length of hospital stay in ileocaecal resection and right hemicolectomy for Crohn's disease: a single-center experience. *Int J Colorectal Dis*. 2018;33(7):937-45. <http://dx.doi.org/10.1007/s00384-018-3072-0>.
- Ge X, Liu H, Tang S, Wu Y, Pan Y, Liu W, et al. Preoperative hypoalbuminemia is an independent risk factor for T postoperative complications in Crohn's disease patients with normal BMI: a cohort study. *Int J Surg*. 2020;79:294-9. <http://dx.doi.org/10.1016/j.ijsu.2020.05.064>.
- Shah RS, Bachour S, Jia X, Holubar SD, Hull TL, Achkar J-P, et al. Hypoalbuminaemia, not biologic exposure, is associated with postoperative complications in Crohn's disease patients undergoing ileocolic resection. *J Crohns Colitis*. 2021;15(7):1142-51. <http://dx.doi.org/10.1093/ecco-icc/jjaa268>.
- Fumery M, Seksik P, Auzolle C, Munoz-Bongrand N, Gornet J-M, Boschetti G, et al. Postoperative complications after ileocaecal resection in Crohn's disease: a prospective study from the REMIND Group. *Am J Gastroenterol*. 2017;112(2):337-45. <http://dx.doi.org/10.1038/ajg.2016.541>.
- Morar OS, Hodgkinson JD, Thalasingam S, Koyasombat K, Purcell M, Hart AL, et al. Determining predictors for intra-abdominal septic complications following ileocolonic resection for Crohn's disease—considerations in pre-operative and perioperative optimisation techniques to improve outcome. *J Crohns Colitis*. 2015;9(6):483-91. <http://dx.doi.org/10.1093/ecco-icc/jjv051>.
- de Buck van Overstraeten A, Eshuis EJ, Vermeire S, Van Assche G, Ferrante M, D'Haens GR, et al. Short- and medium-term outcomes following primary ileocaecal resection for Crohn's disease in two specialist centers. *Br J Surg*. 2017;104(12):1713-22. <http://dx.doi.org/10.1002/bjs.10595>.
- Jouvin I, Lefevre J, Creavin B, Pitel S, Chafai N, Turet E, et al. Postoperative morbidity risks following ileocolic resection for Crohn's disease treated with anti-TNF alpha therapy: a retrospective study of 360 patients. *Inflamm Bowel Dis*. 2018;24(2):422-32. <http://dx.doi.org/10.1093/ibd/izx036>.
- Xu Y, Yang L, An P, Zhou B, Liu G. Meta-analysis: the influence of preoperative infliximab use on postoperative complications of Crohn's disease. *Inflamm Bowel Dis*. 2019;25(2):261-9. <http://dx.doi.org/10.1093/ibd/izy246>.
- Cohen B, Fleshner P, Kane S. Anti-tumor necrosis factor is not associated with postoperative infections: results from prospective cohort of ulcerative colitis and Crohn's disease patients undergoing surgery to identify risk factors for postoperative infections (PUCCINI). *Gastroenterology*. 2019;156:S-80.
- Adamina M, Bonovas S, Raine T, Spinelli A, Warusavitarne J, Armuzzi A, et al. ECCO guidelines on therapeutics in Crohn's disease: surgical treatment. *J Crohns Colitis*. 2020;14(2):155-68. <http://dx.doi.org/10.1093/ecco-icc/jjz187>.
- 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. <http://dx.doi.org/10.1097/DCR.0b013e318267c74c>.