




Risk Factors for Anastomotic Leakage Following Total or Subtotal Colectomy

J. Ocaña¹  P. Pastor-Peinado¹ P. Abadía¹ A. Ballester¹ D. Ramos¹ JC. García-Pérez¹
JM. Fernández-Cebrián¹ J. Die¹

¹Department of General and Digestive Surgery, Division of Coloproctology, Ramón y Cajal University Hospital, Madrid, Spain.

Address for correspondence J. Ocaña, MD, Department of General and Digestive Surgery, Ramón y Cajal University Hospital, Ctra. Colmenar Viejo, Km 9.100-28034, Madrid, Spain (e-mail: jocajim@gmail.com).

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Abstract

Introduction A higher rate of anastomotic leakage (AL) is reported after ileosigmoid anastomosis (ISA) or ileorectal anastomosis (IRA) in total or subtotal colectomy (TSC) compared with colonic or colorectal anastomosis. The main aim of the present study was to assess potential risk factors for AL after ISA or IRA and to investigate determinants of morbidity.

Methods We identified 180 consecutive patients in a prospective referral, single center database, in which 83 of the patients underwent TSC with ISA or IRA. Data regarding the clinical characteristics, surgical treatment, and outcome were assessed to determine their association with the cumulative incidence of AL and surgical morbidity.

Results Ileosigmoid anastomosis was performed in 51 of the patients (61.5%) and IRA in 32 patients (38.6%). The cumulative incidence of AL was 15.6% (13 of 83 patients). A higher AL rate was found in patients under 50 years-old ($p = 0.038$), in the elective-laparoscopic approach subgroup ($p = 0.049$), and patients in the inflammatory bowel disease (IBD) subgroup ($p = 0.009$). Furthermore, 14 patients (16.9%) had morbidity classified as Clavien-Dindo \geq IIIA.

Discussion A relatively high incidence of AL after TSC was observed in a relatively safe surgical procedure. Our findings suggest that the risk of AL may be higher in IBD patients. According to our results, identifying risk factors prior to surgery may improve short-term outcomes.

Keywords

- ▶ total or subtotal colectomy
- ▶ ileorectal anastomosis
- ▶ ileosigmoid anastomosis
- ▶ anastomotic leakage

Introduction

Ileorectal anastomosis (IRA) and ileosigmoid anastomosis (ISA) following total or subtotal colectomy (TSC) are mainly performed in inflammatory bowel disease (IBD)—Crohn's disease, ulcerative colitis, and indeterminate colitis—familial adenomatous polyposis or colonic polyposis syndromes, and colorectal cancer (CRC). Less frequently, TSC is performed in cases of refractory constipation and ischemic colitis.^{1–3}

Anastomotic leakage (AL) is a significant complication, associated with increased mortality, reoperation, and derivative morbidity^{4,5} and is also related to poor long-term outcomes in oncological resections.^{6–8} Even though IRA and ISA are anatomically easy to perform—pelvic dissection is not mandatory, there is no tension at the anastomosis, and a blood supply is theoretically ensured—a higher risk of AL is reported after IRA or ISA (6.5–21%)^{4,5,9} when compared with colonic or colorectal anastomosis, which has a lower AL rate,

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mainly under 15%.^{4,10,11} Regardless of the indication,¹² similar AL rates are seen after TSC in IBD (4–12%),^{13,14} polyposis (20%)¹⁵ and colon cancer (6–21%).^{4,16} Reducing AL rates might improve short and long term as well as functional outcomes after IRA or ISA. There is not enough evidence of determining factors for AL following colectomy with IRA or ISA. The main aim of the present study was to assess the potential risk factors for AL after ISA or IRA and to investigate determinants of morbidity.

Methods

Patients

All consecutive patients who underwent ISA or IRA following TSC between January 2013 and December 2019 were retrospectively identified from the prospective database of a tertiary referral center in the Ramón y Cajal University Hospital, Madrid, Spain. In case of missing data, patients' records were reviewed. We defined ISA as an anastomosis higher than promontory level, and anastomosis below this level was considered as IRA. The main indications for colectomy in eligible patients were CRC, IBD, polyposis syndromes, and refractory constipation. We defined AL as a defect in the integrity of the intestinal wall at the anastomotic site leading to a communication of the intra- and extraluminal, or to a pelvic abscess adjacent to the anastomosis, according to the definition set by the International Study Group of Rectal Cancer.^{17,18} When the AL required no active therapeutic intervention, they were classified as grade A. When the AL required active therapeutic intervention (such as antibiotics and percutaneous drainage), but was manageable without relaparotomy, they were classified as grade B. The AL requiring reintervention were classified as grade C. There was a postoperative follow-up of 90 days. Postoperative morbidity and mortality were considered within 90 days after surgery. The Clavien-Dindo classification of morbidity was used to grade postoperative complications.¹⁹ Readmission was considered within 90 days in those patients who presented surgical-associated morbidity, excluding other diagnosis. Patients under 18-years-old, terminal ileostomy after TSC, and two-stage procedure (IRA or ISA with diverting ileostomy) were excluded. The anastomosis was performed according to the surgeon's preference. Demographic and clinical data were collected from each patient, including age, gender, physical status according to the American Society of Anesthesiologists' (ASA) classification, presence of cardiovascular disease, diabetes mellitus, chronic kidney failure, or other underlying diseases, planning of operation (emergent/elective), and preoperative total proteins. Surgical approach, operative variables, and type of anastomosis (handsewn or stapler) were also collected.

Statistical Analysis

The results are reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.²⁰ Continuous variables were reported as the median and interquartile range, whereas categorical variables were reported as the number of patients and percentage. A univariate analysis was performed to assess

the association between dependent variables (AL and postoperative morbidity) and independent variables (ISA or IRA, patients' and surgical data): continuous variables and discrete variables were analyzed by the U Mann-Whitney test and the χ^2 test, respectively. Statistical significance was indicated by a p -value < 0.05 (2-tailed test). The IBM SPSS Statistics for Windows, Version 22.0 software (IBM, CorpArmonk, NY, USA) was used for the analyses.

Results

Of the 180 patients identified in the database (**►Fig. 1**), 92 were excluded as they did not have bowel reconstruction with ISA or IRA, and another 5 patients already had diverting stoma. The remaining 83 patients were included and assessed in the study. Demographic characteristics and preoperative data according to AL are shown in **►Table 1**. The cumulative incidence of AL was 15.6% (13 of 83), with 1 patient having grade A, 1 patient grade B, and 11 patients grade C. A higher rate of AL was found in patients under 50 years-old ($p = 0.038$). Surprisingly, no comorbidities were found to be correlated with AL in the univariate analysis. The main indication for surgery was colon cancer ($n = 63$; 75.9%). Colonic polyposis ($n = 3$; 3.6%), IBD ($n = 15$; 18.1%), and refractory constipation ($n = 2$, 2.4%) were other reasons for surgery. Whereas the AL rate was significantly higher in the IBD group ($p = 0.009$), no significant AL rate differences were found in the emergent surgery group (25% vs 13.4%; $p = 0.27$).

All surgical data is shown in **►Table 2**. Ileosigmoid anastomosis was performed in 51 patients (61.5%), and IRA was used in 32 patients (38.6%). No significant differences in AL rate ($p = 0.21$) were found between IRA and ISA. The anastomosis technique (handsewn vs. stapler, 10.3% vs. 18%) and the type of anastomosis were also found not to be predictors of AL, with $p = 0.31$ and $p = 0.57$ respectively. Laparoscopic surgery was performed in 19 of the 83 patients (22.9%). In the elective surgery subgroup, laparoscopic approach had higher AL rate than open surgery (27.8% vs. 8.2%), with $p = 0.049$.

Surgical morbidity according to patient and surgical data is shown in **►Table 3**. Of the 83 patients, 38 (45.8%) had no surgical complications within 90 days postoperatively (**►Table 4**). None of the assessed potential predictors of morbidity were found to be significant. Fourteen patients (16.9%) had morbidity classified as Clavien-Dindo \geq IIIA (moderate-severe). The distribution of exposures according to AL grade was assessed (**►Table 3**), and no potential predictors were found to be statistically significant. There weren't any deaths within 90 days after surgery. Only 2 patients were readmitted (2.4%) in the follow-up.

Discussion

In the present study of risk factors for AL and morbidity following TSC with ISA or IRA, the overall AL rate was 15.6%. No mortality event was recorded within 90 days postoperatively, which is similar to previous reports, with a mortality rate under 5%^{9,16} in recently published series. The mortality

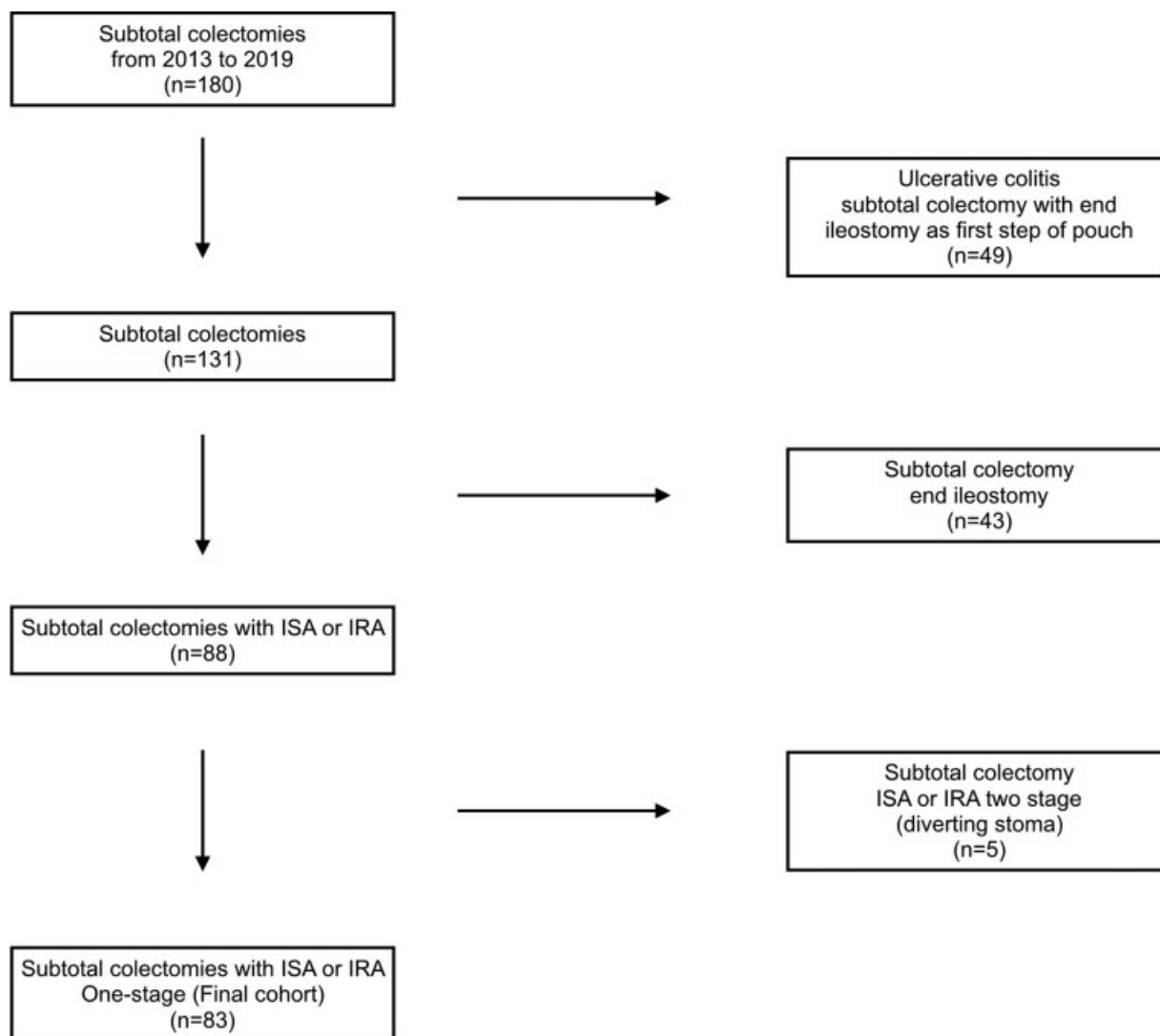


Fig. 1 Flowchart of selection.

rate might be higher in emergent surgery.²¹ The range of AL after IRA or ISA is widely variable depending of the study design.^{5,22,23} The occurrence of AL in the present study was similar to the findings reported by Segelman et al., who found an AL rate of 13.2% after TSC with ISA or IRA, reporting a significantly lower AL rate (7%) in two-stage procedures (loop ileostomy); Duclos et al. also reported a significant AL rate of 7%. It might be due to a high rate of two-stage procedures (20%), whereas in a nationwide register study, an AL rate of 13.4% was reported following TSC in colon cancer.⁴ Even though including two-stage procedures had improved our final results, we decided in the study design to exclude those patients to avoid potential bias in the risk factors for AL detection. In previous published reports of emergent TSC in obstructed left colon cancer, an incredible low AL rate was reported, under 10%.²⁴⁻²⁶ The heterogeneity of AL in the literature might be due to a discrepancy in the definition of AL. In our study, we adopted the definition set by the International Study Group of Rectal Cancer¹⁷ to be able to compare our results with those previously reported by others who use the same definition.¹⁶

The impact of the anastomosis (ISA or ISA) on AL is controversial. Segelman et al.¹⁶ did not find any statistical difference in one of the most recent studies (XX). In our study, there was no difference in the rate of AL between ISA and IRA, showing that the height of the anastomosis might not have a critical relevance. The difference between ISA and IRA was assessed in elective surgery, and no statistical differences were found. Even though the operation records were difficult to analyze when trying to identify which vessels were preserved, anastomosis involving the distal segment of the small bowel often has sufficient blood supply. On the other hand, in benign diseases, the superior rectal artery can be preserved, allowing sufficient blood perfusion to the anastomosis. It is still unclear if there is an impact of high ligation of the inferior mesenteric artery in the AL rate.²⁷⁻³⁰ Likewise, the impact of the perfusion of the distal part of ISA or IRA in the AL rate is also controversial.

A great number of studies have been published about risk factors for AL after colectomy,^{4,10,11,28-30} but the majority are focused on colorectal cancer patients. The results of IRA or ISA after TSC are mixed with other anastomosis sites, and

Table 1 Baseline and preoperative data, and anastomosis leakage

	Anastomosis leakage		
	Non- anastomosis leakage n (%)	Anastomosis leakage n (%)	p-value OR (CI95%)
Age, median (range)	66 (28–82)	61 (39–80)	0.49
Age: 50y			0.038 4.23 (1.13–9.83)
Age ≥ 50y	61 (88.4)	8 (11.6)	
Age < 50y	9 (64.3)	5 (37.5)	
Gender			0.48
Male	50 (80.6)	8 (13.8)	
Female	20 (80)	5 (20)	
ASA			0.10
I	23 (74.2)	8 (25.8)	
II	37 (92.5)	3 (7.5)	
III	9 (81.8)	2 (18.2)	
Cardiovascular disease	13 (92.2)	1 (7.1)	0.29
Chronic kidney disease	8 (83.1)	1 (16.9)	0.94
Diabetes mellitus	9 (90)	1 (10)	0.58
Reason for surgery			0,048
Cancer	56 (88.9)	7 (11.1)	
Colonic polyposis	3 (100)	0	
IBD	9 (60)	6 (40)	
Constipation	2 (100)	0	
Reason for surgery			0.009 3.88 (1.52–9.90)
IBD	9 (60)	6 (40)	
Non IBD	61 (89,7)	7 (10.3)	
Planning of operation			0.27
Elective	58 (86.6)	9 (13.4)	
Emergent	12 (75)	4 (25)	
Preoperative hemoglobin (mg/dL) median (range)	12.7 (9.8–17.2)	14 (12.2–17.4)	0.14
Preoperative total proteins (g/dL)	6.05 (4–7.5)	6.45 (4.5–8.3)	0.42

Abbreviations: ASA, American Society of Anesthesiologists; CI, confidence interval; IBD, inflammatory bowel disease.

the reported results are hardly clear and conclusive. In contrast to previous studies, we have not found any association between AL rates and the ASA score, gender, diabetes mellitus, and other comorbidities.^{4,10,29,31–33} The absence of this association may be explained due to an important percentage of AL having occurred in IBD patients, who most often corresponded to young patients without other comorbidities. Therefore, in elderly patients who underwent emergent TSC in obstructed or perforated colon cancer, ileostomy was preferably performed. In our study, we found patients under 50-years-old as predictors of AL ($p = 0.038$). This may be because young IBD patients who underwent TSC might have a poorer clinical situation. Furthermore, young patients who presented emergent TSC were more eligible to

primary anastomosis, with the assumption of higher risk of AL, thus avoiding stoma creation.

No difference was identified in relation to AL when using handsewn or stapler anastomosis, which was similar to the findings of a Cochrane review and a recent meta-analysis showing no superiority of either technique.^{34,35} The types of stapler anastomosis (circular vs. linear) and anastomosis placement were also assessed, and no association with AL was found. It is still unclear if anastomosis placement might be associated with AL.^{34,35} In our study, we found the laparoscopic approach in elective surgery as a predictor to AL ($p = 0.049$). No difference has been reported between laparoscopic and open colectomies in colon cancer and IBD.^{36,37} Furthermore, our findings might be explained by

Table 2 Operative data and anastomosis leakage

	Anastomosis leakage		
	Non-anastomosis leakage n (%)	Anastomosis leakage n (%)	p-value OR (CI95%)
Surgical approach			0.16
Open	56 (87.5)	8 (12.5)	
Laparoscopic	14 (73.7)	5 (26.3)	
Anastomosis			0.21
IRA	25 (78.1)	7 (21.9)	
ISA	45 (88.2)	6 (11.8)	
Anastomosis technique			0.31
Stapler	44 (81.5)	10 (18.5)	
Handsewn	26 (89.7)	3 (10.3)	
Type of anastomosis			0.57
End-to-side	2 (66.7)	1 (33.3)	
Side-to-side	44 (83)	9 (17)	
Side-to-end	24 (88.9)	3 (11.7)	
Type of stapler			0.89
Linear	26 (81.3)	6 (18.8)	
Circular	19 (82.6)	4 (17.4)	
Planning of operation			
Elective			
Open	45 (91.8)	4 (8.2)	0,049
Laparoscopic	13 (72.2)	5 (27.8)	4.32 (1.01–18.49)
IRA	22 (78.6)	6 (21.4)	0.10
ISA	36 (92.3)	3 (7.7)	
Emergent			
Open	11 (73.3)	4 (26.7)	0.44
Laparoscopic	1 (100)	0	
IRA	3 (75)	1 (25)	1.0
ISA	9 (75)	3 (25)	

Abbreviations: IRA, ileorectal anastomosis; ISA, ileosigmoid anastomosis.

the difficulty of proper placement of the small bowel over the distal stump in the laparoscopic approach. Often, the small bowel can be rotated, and it may produce insufficient perfusion or increased tension over the anastomosis. Further studies are needed to assess the potential impact factor of ISA or IRA in the laparoscopic approach on the AL rate.

In our study, we found higher AL rates in IBD patients when compared with other indications ($p = 0.009$; OR: 3.88). Although Nakamura et al. reported no differences in morbidity according to the underlying disease,¹² some authors found a high rate of morbidity in IBD patients, from 20 to 32%.^{5,13,14,27} Segelman et al. used two-stage procedures in IBD patients more often than in the other indications.¹⁶ Further studies about AL risk in total or subtotal colectomies with IRA or ISA in IBD patients are needed to stratify the risk of AL and other postoperative complications. If a high risk of

AL is estimated, two-stage surgery (loop ileostomy) may be performed, as it has been shown to be a protective factor against AL.¹⁶ Further studies are necessary regarding the value of indocyanine green to prevent AL, improving the assessment of the rectal stump's blood supply.

Overall, the morbidity was 45.8%, including medical and surgical postoperative morbidity within 90 days. No statistical differences were found in the severity of morbidity according to underlying diseases or other surgical data. Duclos et al. reported a lower morbidity rate of 19.5%.⁹ Even in emergency colectomy, lower rates were reported (15%), with a high mortality rate of 9.7%.²¹ This heterogeneity of the reported morbidity rates shows the importance of reporting the results in detail so they can be accurately assessed. In the present report, cases of AL after IRA or ISA were often clinically severe (grade C). The same findings are

Table 3 Baseline data and operative characteristics in surgical morbidity

	Surgical morbidity n (%)		p-value	Clavien-Dindo scale n (%)							p-value	Leakage grade n (%)			Readmission n (%)		p-value	
	No	Yes		I	II	IIIA	IIIB	IV	A	B		C	No	Yes				
Age			0.350														0.38	
≤ 50 y	39 (56.5)	30 (43.5)		5 (7.2)	15 (21.7)	3 (4.3)	6 (8.7)	0		1 (12.5)	0			7 (87.5)	66 (97.1)	2 (2.9)		
> 50 y	6 (42.9)	8 (57.1)		1 (7.1)	1 (7.1)	0	4 (28.6)	1 (7.1)		0	1 (20)	4 (80)			14 (100)	0		
Gender			0.79														0.339	224
Male	32 (55.2)	26 (44.8)		4 (6.9)	11 (19)	3 (5.2)	5 (8.6)	1 (1.7)		1 (12.5)	1 (12.5)	6 (75)			55 (96.5)	2 (3.5)		
Female	13 (52.2)	12 (48.8)		2 (8)	5 (20)	0	5 (20)	0		0	0	5 (100)			25 (100)	0		
ASA			0.621														0.274	253
I	15 (48.4)	16 (51.6)		2 (6.5)	7 (22.6)	0	5 (16.1)	1 (3.2)		0	1 (12.5)	7 (87.5)			31 (100)	0		
II	24 (60)	16 (40)		4 (10)	6 (15)	2 (5)	4 (10)	0		0	0	3 (100)			38 (97.4)	1 (2.6)		
III	6 (54.5)	5 (45.5)		0	2 (18.2)	1 (9.1)	1 (9.1)	0		1 (50)	0	1 (50)			10 (90.9)	1 (9.1)		
CV-D			0.728														0.677	0.403
Yes	7 (50)	7 (50)		0	5 (35.7)	0	1 (7.1)	0		0	0	1 (100)			13 (100)	0		
No	38 (55.1)	31 (44.9)		6 (8.7)	11 (15.9)	3 (4.3)	9 (13)	1 (1.4)		1 (8.3)	1 (8.3)	10 (83.3)			67 (97.1)	2 (2.9)		
CKD			0.52														0.840	0.579
Yes	4 (66.7)	2 (33.3)		0	1 (16.7)	0	1 (16.7)	0		0	0	1 (100)			6 (100)	0		
No	41 (53.2)	36 (46.8)		6 (7.8)	15 (19.5)	3 (3.9)	9 (11.7)	1 (1.3)		1 (8.3)	1 (8.3)	10 (83.3)			74 (97.7)	2 (2.6)		
DM			0.694														0.840	0.184
Yes	6 (60)	4 (40)		0	2 (20)	0	1 (10)	0		0	0	1 (100)			9 (90)	1 (10)		
No	39 (53.4)	34 (46.6)		6 (8.2)	14 (19.2)	3 (4.1)	9 (12.3)	1 (1.4)		1 (8.3)	1 (8.3)	10 (83.3)			71 (98.6)	1 (1.4)		
Reason for surgery			0.516														0.540	0.769
Cancer	37 (58.7)	26 (41.3)		5 (7.9)	12 (19)	3 (4.8)	4 (6.3)	0		1 (14.3)	0	6 (85.7)			60 (96.8)	2 (3.2)		
Colonic polyposis	1 (33.3)	2 (66.7)		1 (33.3)	1 (33.3)	0	0	0							3 (100)	0		
IBD	6 (40)	9 (60)		0	3 (20)	0	5 (33.3)	1 (6.7)		0	1 (16.7)	5 (83.3)			15 (100)	0		
Constipation	1 (50)	1 (50)		0	0	0	1 (50)	0							2 (100)	0		
Planning of operation			0.350														0.443	0.327
Elective	38 (56.7)	29 (43.3)		5 (7.5)	12 (17.9)	3 (4.5)	6 (9)	1 (1.5)		1 (11.1)	1 (11.1)	7 (77.8)			65 (98.5)	1 (1.5)		
Emergent	7 (43.8)	9 (56.3)		1 (6.3)	4 (25)	0	4 (25)	0		0	0	4 (100)			15 (93.8)	1 (6.3)		
Surgical approach			0.714														0.234	0.30
Open	34 (53.1)	30 (46.9)		6 (9.4)	12 (18.8)	3 (4.7)	7 (10.9)	0		1 (12.5)	0	7 (87.5)			61 (96.8)	2 (3.2)		
Laparoscopic	11 (57.9)	8 (42.1)		0	4 (21.1)	0	3 (15.8)	1 (5.3)		0	1 (20)	4 (80)			19 (100)	0		
Anastomosis			0.541														0.248	0.723
IRA	16 (50)	16 (50)		6 (9.4)	12 (18.8)	1 (3.1)	4 (12.5)	1 (3.1)		1 (14.3)	1 (14.3)	5 (71.4)			30 (96.8)	1 (3.2)		

(Continued)

Table 3 (Continued)

	Surgical morbidity n (%)		p-value	Clavien-Dindo scale n (%)							p-value	Leakage grade n (%)			p-value	Readmission n (%)		p-value
	No	Yes		I	II	IIIA	IIIB	IV	A	B		C	No	Yes				
ISA	29 (56.9)	22 (43.1)		0	10 (19.6)	2 (3.9)	6 (11.8)	0	0	6 (100)		50 (98)	1 (2)					
Anastomosis technique			0.555								0.380				0.279		0.193	
Stapler	28 (51.9)	26 (48.1)		5 (9.3)	9 (16.7)	3 (5.6)	7 (13)	1 (1.9)	1 (10)	8 (80)		52 (96.3)	2 (3.7)					
Handsewn	17 (58.6)	12 (41.4)		1 (3.4)	7 (24.1)	0	3 (10.3)	0	0	3 (100)		28 (100)	0					
Type of anastomosis			0.70								0.338				0.804		0.412	
E-S	2 (66.7)	1 (33.3)		0	0	0	1 (33.3)	0	0	1 (100)		3 (100)	0					
S-S	30 (56.6)	23 (43.4)		3 (5.7)	9 (17)	3 (5.7)	8 (15.1)	0	1 (11.1)	7 (77.8)		51 (96.2)	2 (3.8)					
S-E	13 (48.1)	14 (59.1)		3 (11.1)	7 (25.9)	0	1 (3.7)	1 (3.7)	0	3 (100)		26 (100)	0					

Abbreviations: ASA, American Society of Anesthesiologists; CV-D, cardiovascular disease; CKD, chronic kidney disease; DM, diabetes mellitus; IBD, inflammatory bowel disease; IRA, ileorectal anastomosis; ISA, ileosigmoid anastomosis; E-S, end-to-side anastomosis; S-S, side-to-side anastomosis; S-E, side-to-end anastomosis.

Table 4 Postoperative morbidity and complications

Variables	N (%)
Overall morbidity	38 (45.8)
Anastomotic leakage	13 (15.6)
Grade A	3 (3.6)
Grade B	2 (2.4)
Grade C	11 (13.2)
Management of anastomotic leakage	
Surgical	11/13 (13.2)
End ileostomy	7 (8.4)
Drainage	1 (1.2)
Diverting ileostomy	3 (3.6)
Urinary retention	1 (1.2)
Abdominal wall hematoma	1 (1.2)
Intra-abdominal abscess	1 (1.2)
Wound infection	4 (4.82)
Intra-abdominal bleeding	1 (1.2)
Lower intestinal bleeding	1 (1.2)
Gastroesophageal reflux	1 (1.2)
Supraventricular tachycardia	1 (1.2)
Wound herniation	2 (2.4)

reported after TSC by Duclos et al., 6.8% from a morbidity rate of 19.5%,⁹ and by Bakker et al., who reported a mortality rate of 13% for AL following TSC.⁴

The strength of the present study is that it is one of the largest series published in last years focused on restorative TSC. Even though a great effort has been made to correct possible bias in the study design, its retrospective nature will have introduced an element of bias. A large cohort, including various types of indications for surgery, might cause confusion, but it can help assess the impact of the pathology on the results. Possible confounders, such as two-stage procedures or delayed ISA or IRA, have been excluded from the study. The deep assess of the surgical morbidity may not have enough power in this sample. For this reason, large multicenter prospective studies should be made to determine pathology and surgical data impact on the type of morbidity. The applied definition criteria for AL may underdiagnose AL, as not all suspicions of AL were identified by a radiological examination with rectal contrast.

The global AL rate of 15.6% after TSC in this study shows a high frequency of leakage after a relatively safe surgical procedure. Our findings suggest that, in IBD patients, the risk of AL may be higher. According to our results, identifying risk factors prior to surgery may improve short-term negative outcomes.

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Conflict of Interests

The authors have no conflict of interests to declare.

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