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ORIGINAL ARTICLE

Fate of ileorectal anastomosis for treating Crohn's disease in the era of biologics: Results from a French retrospective multicentre cohort study

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Abstract

Aim: The rate of surgical recurrence following ileorectal anastomosis (IRA) in patients with Crohn's disease (CD) remains poorly understood. Most studies were conducted before the advent of biologics. Our aim was to assess the fate of IRA in patients with CD during the biologics era and identify risk factors for endoscopic, clinical, and surgical recurrence.

Methods: This retrospective multicentre cohort study included patients with CD who underwent IRA between 2006 and 2022. The association of patient characteristics and postoperative measures with each type of postoperative recurrence and need for a definitive stoma was investigated using the chi-square test or Fisher's exact test.

Results: During a median follow-up period of 60 months, the rates of endoscopic, clinical, and surgical postoperative recurrence were 70%, 59%, and 35%, respectively. The rate of perianal lesions was higher in patients who underwent a definitive stoma (70% vs. 35%, $p=0.007$) and with endoscopic (50% vs. 25%, $p=0.038$), clinical (54% vs. 24%, $p=0.006$), and surgical (63% vs. 34%, $p=0.015$) recurrence. The incidence of residual microscopic disease at the rectal margin was higher in patients with endoscopic recurrence ($p=0.047$). Biologics were identified as protective factors against the need for a definitive stoma ($p=0.044$).

Conclusion: IRA is a good treatment option for extensive colitis in patients with CD. However, its consideration should be weighed in the presence of perianal lesions, which have been shown to be a risk factor for delayed proctectomy.

KEYWORDS

Crohn's disease, postoperative recurrence, surgery

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INTRODUCTION

One-third of patients with Crohn's disease (CD) have colonic involvement, and this location remains broadly stable over time [1]. Crohn's colitis is a distinct clinical condition [2], with a lower incidence of surgical resection when compared to the cases with ileal involvement [3]. The main surgical indications include CD-related complications, resistance to medical therapy, and colon cancer or dysplasia [4]. Surgical indications must be carefully considered because of the functional outcomes and risk of total proctocolectomy with permanent ileostomy. When surgery is indicated, segmental resection is the preferred option because of better functional results than with total colectomy [4] and the lower risk of definitive ileostomy [5]. Total colectomy with ileorectal anastomosis (IRA) is considered an effective treatment option for extended refractory chronic Crohn's colitis [6].

In addition to refractory chronic Crohn's colitis, 5%–10% patients with CD develop acute severe colitis requiring surgical treatment [7]. In this case, emergency subtotal colectomy with ileostomy is performed. IRA may be considered after 3 months for selected patients with rectal sparing and without severe perianal disease or anal sphincter damage [8].

A previous series showed an 83% clinical recurrence rate 10 years after IRA and an acceptable secondary proctectomy rate in 15% of patients [9]. Most studies were monocentric, older than 20 years, and conducted entirely before the advent of biologics [10–18]. Moreover, the rate of repeat IRA or secondary proctectomy followed by rectal amputation or ileal pouch–anal anastomosis (IPAA) remains poorly understood.

Therefore, our study aimed to assess the fate of IRA for treating CD during the biologics era and identify risk factors for endoscopic, clinical, and surgical recurrence.

METHODS

Study population

Data of adult patients with a history of colectomy and IRA for treating CD between January 2006 and December 2022 were retrospectively reviewed. Patients were recruited from seven French tertiary centres belonging to the “GETAID surgery” group (Groupe d'Etude Thérapeutique des Affections Inflammatoires du tube Digestif) that specializes in inflammatory bowel disease management. The analyses were carried out using anonymized data. The study was approved by the institutional review board of all the participating centres.

We evaluated general characteristics (age, sex, body mass index [BMI], preoperative anaemia, nutritional status), CD characteristics (familial history of CD, smoking status, perianal lesions, age at diagnosis, age at surgery, extraintestinal manifestations), behaviour and location of CD according to the Montreal classification [19], delay between CD diagnosis and surgery, number of preoperative biologics or immunosuppressor (IS) lines, postoperative prophylactic treatment (started prior to any lesion development), indications

What does this paper add to the literature?

In this large multicentre cohort study, the rate of surgical recurrence was 35% at 60 months after IRA for CD. Abdominoperineal rectal amputation was the most frequently performed procedure. Perianal lesions were identified as a risk factor for delayed proctectomy, whereas prophylactic biologics were found to be protective factors.

for colectomy (refractory CD, colonic dysplasia, severe acute colitis), type of surgical approach for colectomy and IRA (open or laparoscopic), type of anastomosis (handsewn or stapled), number of patients requiring diverting ileostomy, severe postoperative morbidity within 90 days of surgery (classified according to the Clavien–Dindo classification [CDC]) [20], endoscopic recurrence (classified according to the Rutgeerts score) [21], and clinical and surgical recurrence.

We pathologically evaluated the presence of epithelioid granuloma, length of small bowel resection when required, and residual microscopic disease (on the ileal or rectal side or both) with positive histological margins. Despite our efforts, it was not possible to assess the precise location of epithelioid granulomas in the small bowel or colon using this database.

Defining variable

Poor nutritional status was defined as a BMI <17 kg/m² or 10% weight loss within 6 months, albumin level <35 g/L, or prealbumin level <0.21 g/L.

Severe postoperative complications were defined as those classified as CDC stage III or higher (defined as complications requiring local or general anaesthesia, such as reoperation, or interventional procedures, including endoscopic or radiological drainage).

Endoscopic recurrence was defined as a Rutgeerts score ≥2, when available, or by the presence of active CD lesions on rectosigmoidoscopy (classified according to the dominant anastomotic side of recurrence [ileal or rectal]). Clinical recurrence was defined by gastrointestinal symptoms requiring introduction or intensification of medical therapy. Surgical recurrence was defined as the requirement for resection of the IRA and thus warranting a redo IRA, proctectomy with IPAA, or abdominoperineal resection with permanent ileostomy. Other small bowel resections (distant to IRA) or surgical procedures for treating anoperineal diseases were not considered as surgical recurrence.

Statistical analysis

Descriptive statistics are presented as mean (standard deviation [SD]) or median (interquartile range [IQR]) in cases of skewed distribution for quantitative variables and as frequency (percentage) for categorical variables. Normality of distribution was assessed

using the Shapiro–Wilk test. Among the 85 patients included, some had missing follow-up data for specific types of recurrence, but these patients were not systematically the same—for example, patients with missing data for endoscopic or clinical recurrence were not always the same. To maximize statistical power, we included all patients with data pertaining to at least one recurrence in the analysis.

The association of patient characteristics and postoperative measures with each type of postoperative recurrence and need for a definitive stoma was investigated using the chi-square test (or Fisher's exact test in cases of expected value <5). All statistical tests were conducted at a two-tailed α -level of 0.05 using SAS software version 9.4 (SAS Institute, Cary, NC, USA).

RESULTS

Baseline characteristics

A total of 85 patients with CD who underwent IRA were included in this study; 27 (31.8%) were men. The patient characteristics are summarized in Table 1. The median follow-up period after IRA was 60 months (IQR: 36–108). Most patients (68/85, 80%) had no gastrointestinal resection before IRA.

CD characteristics

The median age at colectomy was 35 years (IQR, 26–45 years). The mean period between CD diagnosis and surgery was 10.4 (SD, 7.4) years. Most patients were treated with antitumour necrosis factor α therapy (67/82; 81.7%) and were smokers (57/82; 69.5%) during colectomy and IRA. The mean number of treatment lines (biologics or IS) before colectomy was four (SD, 2.2; Table 1).

Perianal lesions were detected at the time of surgery in 34 of 84 patients (40.5%). The rate of perianal lesions was significantly higher in patients with endoscopic (50% vs. 25%, $p=0.038$), clinical (54% vs. 24%, $p=0.006$), and surgical (63% vs. 34%, $p=0.015$) recurrence (Table 2) and in those who underwent a definitive stoma (70% vs. 35%, $p=0.007$; Table 3).

The CD location at the time of surgery (Table 1) was L2 (colonic) in 38 patients (44.7%) and L3 (ileocolonic) in 41 (48%). CD behaviour at the time of surgery was B1 (nonstricturing–nonpenetrating) in 28 patients (32.9%), B2 (stricturing) in 29 (34%), and B3 (penetrating) in 28 (32.9%; Table 1). Neither CD location nor behaviour was associated with postoperative recurrence (Table 2). Therefore, ileitis was not a risk factor for postoperative recurrence.

Indication for colectomy

Surgery was indicated for patients with colonic stenosis (28/85, 32.9%), colitis refractory to medical therapy (25/85, 29.4%), severe

TABLE 1 Patient characteristics.

Characteristics	N	Values
Age, year, median [Q1–Q3]	85	–
At diagnosis		23 [18; 33]
At surgery		35 [26; 45]
Sex, n (%)	85	–
Female		58 (68)
Male		27 (32)
Body mass index, kg/m ² , mean (SD)	81	21.5 (4.7)
Haemoglobin, g/L, median [Q1–Q3]	52	10.4 [9.2; 12.4]
Albumin, g/L, median [Q1–Q3]	38	30 [24; 33]
Prealbumin, g/L, median [Q1–Q3]	26	0.2 [0.1; 0.3]
Familial history of CD, n (%)	70	13 (19)
Smoking status, n (%)		
At surgery	82	25 (30)
At recurrence	70	14 (20)
APL, n (%)	84	34 (40)
Extraintestinal manifestations, n (%)	83	22 (26)
Behaviour of CD*, n (%)	85	
B1		28 (33%)
B2		29 (34%)
B3		28 (33%)
Location of CD*, n (%)	85	
L2		38 (45)
L3		41 (48)
L4		6 (7)
Delay between CD diagnosis and surgery, year, mean (SD)	85	10.4 (7.4)
Preoperative treatments, n (%)		
Aminosalicylate	52	38 (73)
Steroids	69	58 (84)
Azathioprine	71	61 (86)
Methotrexate	58	29 (50)
Antitumour necrosis factor	82	67 (82)
Infliximab	71	58 (82)
Adalimumab	67	51 (76)
Certolizumab	46	11 (24)
Vedolizumab	42	11 (26)
Ustekinumab	43	14 (33)
Number of preoperative treatment lines, n, median [Q1–Q3]	85	4 [3; 6]
Postoperative prophylactic biologics treatment, n (%)	62	30 (48)
Indications for colectomy, n (%)	85	
Refractory CD		25 (29)
Stenosis		28 (33)
Fistula		11 (13)
Cancer		4 (5)

(Continues)

TABLE 1 (Continued)

Characteristics	N	Values
Severe acute colitis		17 (20)
Surgical approach, n (%)	85	
Open		38 (45)
Laparoscopy		47 (55)
Type of anastomosis, n (%)	75	
Handsewn		41 (55)
Stapled		34 (45)
Temporary diverting ileostomy, n (%)	77	24 (31)
Severe postoperative morbidity CDC score >3, n (%)	85	10 (12)
Postoperative recurrence, n (%)		
Endoscopic	81	57 (70)
Clinical	83	49 (59)
Surgical	78	27 (35)
Epithelioid granuloma, n (%)	83	39 (46)
Length of small bowel resection, cm, median [Q1–Q3]	56	15 [5.5; 20]
Residual microscopic disease, n (%)		
Ileal margin	82 81	15 (18)
Rectal margin		33 (41)
Type of surgery for surgical recurrence, n (%)	27	
Proctectomy and definitive ileostomy		18 (67)
Redo ileorectal anastomosis		7 (26)
Ileal pouch–anal anastomosis		2 (7)

Abbreviations: APL, anoperineal lesions; CD, Crohn's disease; CDC, Clavien–Dindo classification; Q, quartile; SD, standard deviation.

*According to the Montreal classification.

acute colitis (17/85, 20%), fistulas (11/85, 12.9%), and colonic cancer (4/85, 4.7%). The postoperative recurrence rate was influenced by the surgical indications. Of the 72 patients who underwent IRA for colitis refractory to medical therapy, 51 (71%) experienced endoscopic, clinical, or surgical recurrence. Among the 80 patients who underwent IRA for stenosis, 32 (40%) had endoscopic, clinical, or surgical recurrence. The postoperative clinical recurrence rate was higher when colectomy was indicated for colitis refractory to medical therapy (41% vs. 15%) and lower when colectomy was indicated for stenosis (22% vs. 50%; Table 2).

Operative data, diversion ileostomy, and postoperative complications

A laparoscopic approach was used in 47 patients (55.3%). Colectomy and IRA were performed during the same surgical procedure in most patients (57/85, 67%). Stapled anastomoses were performed in 34 of 75 patients (45.3%). Diversion ileostomy was performed in 24 of 77 patients (31.1%). The rate of postoperative

surgical recurrence and the risk of undergoing a definitive stoma was significantly higher when diverting ileostomy was performed (43% vs. 21% and 69% vs. 21%; $p=0.003$ and $p<0.001$, respectively; Table 2). Unfortunately, despite our best efforts, it was not possible in this database to assess the precise reason for diverting ileostomy, such as an intraoperative positive “air leak test” and severe associated rectitis and others.

A total of 20 of 75 patients (26%) underwent terminal ileal resection with a mean (SD) ileal length of 19.4 (20.4) cm. A total of 10 of 85 patients (11.8%) experienced severe postoperative complications.

Pathology

Granulomas were detected in 38 of 83 patients (45.8%); however, the presence of granulomas did not correlate with endoscopic, clinical, or surgical recurrence. The incidence of granulomas was insignificantly higher in patients who underwent a definitive stoma (60% vs. 36%; $p=0.067$). Residual microscopic disease was detected in the ileal margin of 15 of 82 patients (18.2%) and at the rectal margin of 33 of 81 patients (40.7%). Residual microscopic disease at the ileal margin was not associated with a higher rate of recurrence. The rate of residual microscopic disease at the rectal margin was significantly higher in patients with endoscopic recurrence (47% vs. 23%, $p=0.047$).

Postoperative prophylactic treatment

A total of 62 of 82 patients (75.6%) received postoperative prophylactic treatment with biologics ($n=30$, 48%) or an IS ($n=32$, 52%). The mean time to reintroduce postoperative prophylactic treatment was 4.4 (SD, 5.3) months. No effect of postoperative prophylactic treatment was observed with biologics or IS on endoscopic ($p=0.062$), clinical ($p=0.17$), and surgical ($p=0.071$) recurrence. However, biologics were identified as protective factors against the need for a definitive stoma ($p=0.044$; Table 3).

Postoperative recurrence

Endoscopic recurrence was detected in 57 of 81 patients (70.4%); however, Rutgeerts scores were available for only 25 patients (Table 1). The mean delay in endoscopic recurrence after surgery was 21 (SD, 21.1) months. In 33 of 55 patients (60%), endoscopic recurrence was in the small bowel and in the rectum in 22 (40%). A total of 49 of 83 patients (59%) experienced clinical recurrence at a median of 12 months (IQR, 6–22). A total of 27 of 77 patients (35.1%) experienced surgical recurrence at a median of 30 months (IQR, 18–83). Abdominoperineal resection of the rectum with permanent ileostomy was the most frequently performed procedure (18/27, 66.7%), followed by a redo IRA (7/27, 25.9%) and proctectomy with IPAA (2/27, 7.4%). Surgical recurrence was indicated for

TABLE 2 Patient characteristics according to the type of recurrence.

	Endoscopic recurrence			Clinical recurrence			Surgical recurrence		
	No (n = 24)	Yes (n = 57)	p-value	No (n = 50)	Yes (n = 27)	p-value	No (n = 57)	Yes (n = 20)	p-value
Smoking at surgery	5/21 (24)	20/56 (36)	0.32	7/30 (23)	18/49 (37)	0.21	12/47 (26)	11/27 (41)	0.17
Colectomy at age >40 years	8/24 (33)	19/57 (33)	0.99	14/34 (41)	15/49 (31)	0.32	20/50 (40)	7/27 (26)	0.22
Location of CD*									
L2	10/24 (42)	26/57 (46)	0.56	16/34 (47)	21/49 (43)	0.54	22/50 (44)	11/27 (41)	0.77
L3	11/24 (46)	28/57 (49)		17/34 (50)	23/49 (47)		25/50 (50)	13/27 (48)	
L3+L4	3/24 (12)	3/57 (5)		1/34 (3)	5/49 (10)		3/50 (6)	3/27 (11)	
Phenotype of CD*									
B1	9/24 (37)	18/57 (32)	0.29	11/34 (32)	16/49 (33)	0.72	18/50 (36)	8/27 (30)	0.56
B2	10/24 (42)	17/57 (30)		13/34 (38)	15/49 (31)		16/50 (32)	7/27 (26)	
B3	5/24 (21)	22/57 (39)		10/34 (29)	18/49 (37)		16/50 (32)	12/27 (44)	
Anoperineal lesions	6/24 (25)	28/56 (50)	0.038	8/34 (24)	26/48 (54)	0.006	17/50 (34)	17/27 (63)	0.015
Severe postoperative morbidity	1/24 (4)	8/57 (14)	0.27	3/34 (9)	7/49 (14)	0.52	9/50 (18)	1/27 (4)	0.90
Severe acute colitis	4/24 (17)	13/57 (23)	0.54	6/34 (18)	16/42 (38)	0.59	12/50 (24)	5/27 (19)	0.58
Type of anastomosis									
Handsewn	10/24 (42)	27/47 (57)	0.21	13/31 (42)	26/42 (62)	0.091	24/47 (51)	12/21 (57)	0.64
Stapled	14/24 (58)	20/47 (43)		18/31 (58)	16/42 (38)		23/47 (49)	9/21 (43)	
Granuloma	13/23 (57)	25/56 (45)	0.34	14/33 (42)	24/48 (50)	0.50	18/49 (37)	14/26 (54)	0.15
MRD on rectal margin	5/22 (23)	26/55 (47)	0.047	11/32 (34)	21/47 (45)	0.36	30/58 (52)	10/25 (40)	0.89
MRD on ileal margin	3/23 (13)	10/56 (18)	0.99	4/33 (12)	9/47 (19)	0.40	8/49 (16)	4/25 (16)	0.99
Postoperative prophylactic biologics	4/15 (27)	25/46 (54)	0.062	9/24 (38)	21/38 (55)	0.17	22/38 (58)	7/21 (33)	0.071
Indications for surgery									
Resistance to medical therapy	6/24 (25)	18/57 (32)	0.32	5/34 (15)	20/49 (41)	0.042	10/50 (20)	13/27 (48)	0.08
Stenosis	11/24 (46)	16/57 (28)		17/34 (50)	11/49 (22)		20/50 (40)	5/27 (19)	
Fistula	1/24 (4)	9/57 (16)		4/34 (12)	6/49 (12)		6/50 (12)	4/27 (15)	
Cancer	2/24 (8)	2/57 (4)		2/34 (6)	2/49 (4)		2/50 (4)	1/27 (4)	
Severe acute colitis	4/24 (17)	12/57 (21)		6/34 (18)	10/49 (20)		12/50 (24)	4/27 (15)	

Note: Data are expressed as number (percentage). Values in bold are statistically significant.

Abbreviations: CD, Crohn's disease; MRD, microscopic residual disease.

*According to the Montreal classification.

CD recurrence at the anastomotic site (17/26, 65%) or development of severe anoperineal lesions (9/26, 35%). At the end of the follow-up period, permanent ileostomy was avoided in 67 patients (78.8%).

DISCUSSION

With a median follow-up period of 60 months, the rates of endoscopic, clinical, and surgical postoperative recurrence after IRA for treating CD in this multicentre retrospective study were 70%, 59%, and 35%, respectively. We observed a direct association between the presence of perianal lesions at the time of colectomy and endoscopic, clinical, and surgical recurrence of CD and the need for a definitive stoma. Moreover, residual microscopic disease at the rectal

margin was significantly more common in patients with endoscopic recurrence (47% vs. 23%; $p=0.047$).

In this study, we confirmed that total colectomy with IRA is the gold standard treatment for extensive CD colitis with a spared rectum. Despite a surgical recurrence rate of 35%, nearly 80% of patients avoided definitive ileostomy at the 5-year follow-up.

The 59% clinical recurrence rate at 5 years observed in our study was in line with that of other older studies. For example, more than 20 years ago, Cattani et al. reported a 58% clinical recurrence rate at 60 months in a bicentric retrospective study of 118 patients examined between 1980 and 1997 [9]. However, at that time, patients were treated less often and less effectively postoperatively; 75.6% patients in our study received prophylactic postoperative treatment (biologics, 48%; IS, 52%), compared to 51.7% in the study by Cattani et al. (azathioprine, 23%; aminosalicilate, 29%).

	Definitive stoma		
	No (n = 57)	Yes (n = 20)	p-value
Smoking at surgery	17/54 (32)	6/20 (30)	0.90
Colectomy at age >40 years	22/57 (39)	5/20 (25)	0.27
Location of CD*			
L2	26/57 (46)	7/20 (35)	0.67
L3	27/57 (47)	11/20 (55)	
L3+L4	4/57 (7)	2/20 (10)	
Phenotype of CD*			
B1	20/57 (35)	6/20 (30)	0.64
B2	18/55 (32)	5/20 (25)	
B3	19/57 (33)	9/20 (45)	
Anoperineal lesions	20/57 (35)	14/20 (70)	0.007
Severe postoperative morbidity	9/57 (16)	1/20 (5)	0.44
Severe acute colitis	13/57 (23)	4/20 (20)	0.99
Type of anastomosis			
Handsewn	28/52 (54)	8/16 (50)	0.79
Stapled	24/52 (46)	8/16 (50)	
Granuloma	20/55 (36)	12/20 (60)	0.067
MRD on rectal margin	22/54 (40)	8/19 (42)	0.92
MRD on ileal margin	10/55 (18)	2/19 (11)	0.72
Postoperative prophylactic biologics	25/44 (57)	4/15 (27)	0.044
Indications for surgery			
Resistance to medical therapy	13/57 (23)	10/20 (50)	0.12
Stenosis	22/57 (39)	3/20 (15)	
Fistula	7/57 (12)	3/20 (15)	
Cancer	2/57 (4)	1/20 (5)	
Severe acute colitis	13/57 (23)	3/20 (15)	

Note: Data are expressed as number (percentage). Values in bold are statistically significant.

Abbreviations: CD, Crohn's disease; MRD, microscopic residual disease.

*According to the Montreal classification.

Whether biologics protect against long-term surgical recurrence remains widely debated. Postoperative prophylactic treatment in our study was not associated with a reduction in endoscopic, clinical, or surgical recurrence. Most studies evaluating CD recurrence after IRA were conducted before the era of biologics. To the best of our knowledge, only Coscia et al. have evaluated the impact of biologics and demonstrated in a retrospective study that biologics reduce the risk of undergoing a permanent stoma and are associated with an increased rate of rectal preservation after IRA [22]. Our results are in line with these findings; when patients were treated with postoperative prophylactic biologics, the rate of undergoing a definitive stoma was significantly lower (27% vs. 57%, $p=0.044$). A recent systematic review including data of 2045 patients from 37 studies observed a constant rate of clinical recurrence from 1970 to 2020, but a decreasing trend in proctectomy over time (12%–60% before 2000 and 0%–32% after 2000). Moreover, the stoma formation rate was markedly lower in studies published after compared to before 2000 (15.2% vs. 23.7%) [23].

Thus, management of postoperative recurrence in CD is complex because of the absence of a consensus on standardized definitions of clinical and endoscopic recurrence, postoperative surveillance, and treatment strategies [24]. Moreover, most risk stratifications guide treatment approaches proposed for the prevention of postoperative recurrence in patients with CD after ileocaecal resection, where lesions typically recur on the ileal side of the bowel [24–26]. In our study, 40% of the endoscopic recurrence were observed in the rectum. This high endoscopic recurrence rate on the rectal side has been reported previously [9]. To prevent the development of rectal lesions after IRA, further studies are necessary to select the best therapeutic strategies focusing on molecules with strong efficacy against colon inflammation and good safety to minimize the risk of adverse effects from prophylactic medications. In cases of associated ileitis, IRA is the only option for restoring intestinal continuity. Proctocolectomy with IPAA is contraindicated in cases of extensive Crohn's colitis associated with ileitis or anoperineal lesions

TABLE 3 Patient characteristics according to the risk of undergoing a definitive stoma.

[27]. Thus, apart from IRA, the only option is proctocolectomy with definitive ileostomy. IRA should be the preferred option for several reasons. First, patients who underwent IRA had a higher quality of life than those who underwent proctocolectomy with ileostomy [28]. Second, ileitis was not associated with an increased risk of recurrence in our study (L2 vs. L3, nonsignificant), and IRA remained a viable option in this case. Cattan et al. also showed that among patients with Crohn's colitis, those with ileal involvement at diagnosis did not have an increased risk of rectal preservation failure [9]. However, this point continues to be debated in the literature. In two studies of patients who underwent IRA for Crohn's colitis, those with ileal involvement before surgery had a higher probability of IRA failure [6, 16]. Third, besides restoring intestinal continuity, IRA avoids pelvic dissection and preserves female fertility [29], especially if surgery is performed laparoscopically [30]. Fourth, some authors have noted an increasing trend in functioning IRA and a decreasing trend in the overall rate of proctectomy and stoma formation over time, attributed to several reasons, including better management of preoperative risk factors, better postoperative monitoring, and improved treatment of septic complications [23]. The overall proctectomy rate in our study was 26% (20/77), consistent with that in other studies (0%–32%) published since 2000 [23].

Residual microscopic disease at the rectal margin was a risk factor for endoscopic recurrence in our study. In a recent systematic review and meta-analysis, histological features such as plexitis, positive microscopic resection margins, and granulomas were predictors of postoperative endoscopic, clinical, and surgical recurrence [31]. McKenna et al. [32] identified an inflamed distal margin of the colon or rectum at resection as a risk factor for subsequent proctectomy and ileostomy, consistent with our histological findings. Moreover, the number of granulomas detected pathologically was almost twice as high in patients who underwent a definitive stoma (60% vs. 36%; $p=0.067$). Although this difference in granuloma incidence did not reach statistical significance, we attribute it to limited study power.

In a recent prospective multicentre study by the REMIND group including 289 ileocolic resections in patients with CD, male sex and active smoking status at surgery were identified as risk factors for postoperative endoscopic recurrence [33]. However, these results were not confirmed in the present study. When considering IRA specifically, Yamamoto et al. found in a retrospective study of 69 patients that neither sex nor smoking status influenced the proctectomy rate [12]. This suggests that mechanisms of postoperative recurrence differ between ileocolic resection and IRA.

In our study, the presence of perianal lesions correlated with the risk of endoscopic, clinical, and surgical recurrence of CD and the risk of definitive stoma formation. Some studies have also suggested an association between the presence of perianal disease and increased CD recurrence rates. Bernell et al. showed that patients with perianal disease who underwent colectomy had an increased relative risk of relapse after surgery (relative risk, 1.5; 95% confidence interval: 1.06–2.2) [10]. Salice et al. also showed

that the presence of perianal disease significantly affected CD recurrence [6]. Moreover, in cases of severe perianal lesions, it appears unreasonable to restore intestinal continuity with IRA, and the rate of surgical recurrence in this case was probably underestimated owing to the limitations of IRA indications. Despite our efforts, it was not possible to assess the type of perianal disease precisely with this database.

In this study, we observed a higher rate of postoperative surgical recurrence and risk of undergoing a definitive stoma when diverting ileostomy was performed. To the best of our knowledge, this has not been described elsewhere and reflects the severity of colitis. The indications for colectomy influenced the rate of postoperative clinical recurrence. The rate of clinical postoperative recurrence was higher, especially when colectomy was performed owing to resistance to medical therapy, and lower when colectomy was indicated for colonic stenosis.

The main limitation of this study was its retrospective nature. However, IRA is currently a rare indication for patients with CD, and a prospective study is difficult to conduct. Indeed, we intentionally limited the period of inclusion to 2006 to ensure that all participating centres had access to biologics. However, during the 17-year recruitment period, only 85 patients were included in the study. Data were extracted from seven referral centres and do not reflect the “real life experience” of a broader population of patients with CD, as the study likely included highly selected individuals. However, as we recently published [34], centralization of surgery for CD is desirable, and performing such a study outside tertiary centres specialized in inflammatory bowel disease management would be impractical.

CONCLUSION

IRA is a safe and effective option for treating extensive colitis in patients with CD, with a high rate of long-term intestinal continuity. However, its consideration should be weighed in the presence of perianal lesions, which have been shown to be risk factors for delayed proctectomy. Postoperative prophylactic biologics treatment should be encouraged, especially in cases with pejorative histological features and colectomy due to resistance to medical therapy.

AUTHOR CONTRIBUTIONS

Juba Ait Mohand: Validation; methodology; writing – original draft. **Arnaud Alves:** Methodology; writing – review and editing; validation. **Antoine Brouquet:** Methodology; validation. **Adeline Germain:** Methodology; validation. **Valerie Bridoux:** Methodology; validation. **Bertrand Trilling:** Methodology; validation. **Etienne Buscail:** Methodology; validation. **Caroline Valibouze:** Methodology; validation; supervision. **Maxime Leroy:** Methodology; formal analysis; writing – review and editing; validation. **Pierre Desreumaux:** Methodology; supervision; validation; writing – review and editing. **Philippe Zerbib:** Conceptualization; formal analysis; writing – original draft; writing – review and editing; methodology; validation; supervision.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

The study was approved by the institutional review board of all the participating centers.

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