




Biological therapy prior to repeat ileocolic resection in Crohn's disease can reduce the postoperative complication rate

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Abstract

Background The aim of this study was to assess the effect of preoperative biologic therapy on the surgical outcome of Crohn's disease (CD) patients undergoing repeat ileocolic resection.

Methods This was a retrospective analysis of all CD patients who underwent repeat ileocolic resection at Cleveland Clinic Florida between January 2011 and April 2021. Patients were divided into two groups: treatment biologic therapy prior to surgery and controls.

Results Sixty-five patients (31 males, median age 54 [range 23–82] years) were included in the study. Twenty nine (44.6%) were treated with biologic therapy prior to repeat ileocolic resection. No demographic differences were found between the biologic therapy and control groups. In addition, no differences were found in mean time from index ileocolic resection ($p=0.9$), indication for surgery ($p=0.11$), and preoperative albumin ($p=0.69$). The majority of patients (57; 87.7%) were operated on laparoscopically, and mean overall operation time was 225 (SD 49.27) min. Overall, the postoperative complication rate was 43.1% (28 patients) and median length of stay was 5 (range 2–21) days. Postoperative complications were more common in the control group, compared to the biologic therapy group (55.6 vs 27.5%; $p=0.04$). Conversion rate (35.7 vs 20.7%; $p=0.24$), operation time (223 vs 219 min; $p=0.75$), length of stay (5.2 vs 5.9 days; $p=0.4$), and readmission (16.6 vs 11.1%; $p=0.72$) were similar between the two groups. Multivariate analysis of risk factors for postoperative complications showed that biologic treatment was correlated with a lower risk (HR -0.28 , CI 95% -0.5596 to -0.01898 , $p=0.03$).

Conclusions Patients treated with biologic therapy for CD who underwent repeat ileocolic resection had fewer postoperative complications.

Keywords Crohn's disease · Postoperative complications · Repeat ileocolic resection

Introduction

The management of inflammatory bowel disease (IBD) has undergone significant changes in the last few decades. The introduction of novel medical treatments, aimed at suppressing the exaggerated inflammatory response seen in patients suffering from IBD, has widened the therapeutic options available for this chronic disease [1]. Despite the significant

advances in medical therapy, more than 70% of patients suffering from Crohn's disease (CD) still require surgical intervention during the course of their disease, and almost half of these patients will require an additional intervention during their lifetime [2].

Operative outcomes of CD patients tend to be worse than patients with other intestinal diseases, with a relatively higher complication rate [3]. There have been multiple investigations in recent years, demonstrating that preoperative factors, such as malnourishment [4] and chronic steroid use [5], are directly correlated with a higher risk for postoperative morbidity, along with disease severity and surgical timing [6]. Other medications, including biologic therapy, were in the epicenter of many studies in recent decades to determine whether they play a role in determining postoperative outcomes in CD. The effect of anti-tumor necrosis factor (TNF) alpha on the immune system led to a concern

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that it may negatively impact wound healing and intestinal anastomosis, thereby increasing postoperative morbidity [7]. Although the initial studies demonstrated a tendency toward higher complication rates in CD patients treated with biologics [8], more recent studies including several meta-analyses showed no significant effects on the postoperative outcome [9]. However, the vast majority of these studies were retrospective and with a relatively small number of patients, adding to the uncertainty many surgeons experience when they plan a surgical intervention in CD patients.

Repeat ileocolic resection for recurrent CD can be complex and carries a significant risk for postoperative complications when compared to primary resection [10]. There are several postulated causes for the increased morbidity in repeat ileocolic resections, mainly disease severity and adhesions from the previous intervention. In addition, an open surgical approach is often used in these cases, although several studies have already demonstrated that a laparoscopic approach is feasible in repeat surgical interventions [10, 11].

In recent years, several studies have examined the need for repeat surgical procedures in the biologic therapy era, suggesting that novel treatments may reduce the need for or delay repeat surgery [12]. Conversely, there is evidence that biologic therapy may increase the risk of postoperative complications, resulting in an increased risk for surgical recurrence and need for repeat surgery [13–15]. Therefore, it is crucial to identify interventions that might minimize this risk.

In this study, we aimed to assess the effect of preoperative treatment with biologic medications in CD patients undergoing repeat ileocolic resection in a large tertiary referral center, to aid in the decision-making in these complex cases.

Materials and methods

A retrospective chart review of an Institutional Review Board (IRB)-approved prospectively maintained database at Cleveland Clinic Florida was performed. Patients were identified after we retrospectively reviewed the medical charts of all CD patients included in the database who underwent ileocolic resection during the study period (January 2011–April 2021). All adult patients with a previous ileocolic resection were included in our cohort for final analysis. Patients who underwent emergency surgical interventions and those treated for causes other than CD were excluded. The cohort was divided into two groups: patients treated with biologic therapy prior to surgery (biologic therapy group) and patients referred to surgery without prior biologic treatment (control group). We included adult patients treated with biologics up to 1 month prior to surgery. This is with previous studies, and is consistent with our standard practice. Due to the retrospective nature of the

study and the heterogeneous patient population referred to our institute from other centers, we were unable to evaluate the specific reasons for which some patients were treated with biologics prior to surgery and some were not.

Patient demographics, clinical, operative, and postoperative data were reviewed and analyzed. Thirty-day postoperative complications were classified and analyzed according to the Clavien–Dindo classification [16]. This study was approved by our institutional IRB.

Statistical analysis

Data were compared using Fisher's exact test and the χ^2 test to evaluate differences between categorical variables including 30-day postoperative complications and postoperative complications based on the Clavien–Dindo score. Student's *t* test was applied to compare continuous variables. Multivariate logistic regression analysis was performed to assess possible risk factors for postoperative complications. A confidence interval of 95% with *p* value of <0.05 was considered significant. The statistical analysis was performed using SAS/STAT for Windows version 9.4 (Statistical Analysis System Corp., NC, USA).

Results

Overall, 65 of 230 (28.2%) CD patients who underwent ileocolic resection underwent repeat ileocolic resection for CD during the study period. Thirty-one patients (47.7%) were male and the mean age was 54 (range 23–82) years. The median body mass index (BMI) was 23.3 (range 16.4–32.4) kg/m². The most common indication for repeat surgical intervention was anastomotic stricture (*n* = 58; 89.2%). The median time from the index ileocolic resection to the repeat surgery was 12 (range 1–53) years.

Twenty-nine patients (44.6%) were treated with biologic therapy prior to the repeat ileocolic resection. Seven patients were treated with Adalimumab, 9 with Certolizumab, 7 with Infliximab, 5 with Ustekinumab, and 1 with Vedolizumab. No demographic differences were found between the two groups in terms of sex (*p* = 0.8), age (*p* = 0.33), median American Society of Anesthesiologists (ASA) class (*p* = 0.56), and BMI (*p* = 0.94). In addition, no differences were found in mean time between the first and repeat ileocolic resections (*p* = 0.9), indication for surgery (*p* = 0.11), preoperative serum albumin level (*p* = 0.69), and Montreal Classification. Patients' demographics and clinical data for the two groups are detailed in Table 1.

Fifty-seven patients (89.2%) underwent repeat ileocolic resection using a laparoscopic approach, and 16 (28%) required conversion to open surgery. The main indications for conversion were significant adhesions and inflammation

Table 1 Patients' demographics and perioperative data

	Biologic therapy group <i>n</i> /mean/median (%/SD) <i>n</i> = 29	Control group <i>n</i> /mean/median (%/SD) <i>n</i> = 36	<i>P</i> value
Sex (M/F) (<i>n</i> , %)	14 (48.3)/15 (51.7)	16 (44.5)/20 (55.5)	0.8
Age (years), median (range)	54 (25–82)	54 (23–78)	0.33
ASA class, median (range)	2 (1–3)	2 (1–4)	0.56
Smoking (<i>n</i> , %)	5 (17.2)	1 (2.7)	0.08
BMI (<i>n</i> , %)	23.5 (4.1)	23.4 (3.9)	0.94
Time interval between index and repeat ileocolic resection (years)	14.3	14	0.9
Previous surgery surgical approach (Lap/Open) (<i>n</i> , %)	19 (65.5)/10 (34.5)	21 (58.3)/15 (41.7)	0.61
Indication for surgery (<i>n</i> , %)			0.11
Stricture	28 (96.5)	30 (83.3)	
Fistula and/or abscess	1 (3.5)	6 (16.7)	0.69
Preoperative albumin	4 (0.4)	3.9 (0.3)	0.69
Montreal classification (<i>n</i> , %)			
Age at diagnosis (years)			0.44
A1 (≤ 16)	1 (3.5)	3 (8.3)	
A2 (17–40)	26 (89.6)	28 (77.8)	
A3 (> 40)	2 (6.9)	5 (13.9)	
Behavior			0.11
B2—Stricture	28 (86.2)	30 (63.8)	
B3—Penetrating	1 (13.8)	6 (36.2)	
Location			0.09
L3—Ileocolic	27 (93.1)	27 (75)	
L3 + L4—Ileocolic + upper gastrointestinal	2 (6.9)	9 (25)	

ASA American Society of Anesthesiologists, *BMI* Body mass index

(15 patients), and in one case, conversion was performed due to a large phlegmonous bowel segment that could not be extracted through a small incision. Further evidence to the complexity of these surgical procedures can be seen in the median operation time of the entire cohort, which was 220 (range 116–386) minutes. In 19 patients (29.2%), a fistula was resected during the repeat surgical intervention, and an intra-abdominal abscess was seen and drained intraoperatively in 5 patients (7.7%). The median estimated intraoperative blood loss was 100 (range 0–1000) ml and 2 patients required intraoperative blood transfusion.

The overall postoperative complication rate was 43.1% (28 patients) and the mean length of stay was 5 (range 2–21) days. Three patients (4.6%) were diagnosed with an anastomotic leak, 2 of whom required a reoperation. Eight patients (12.3%) suffered from major postoperative complications (Clavien–Dindo score \geq III). One patient required postoperative blood transfusions due to a significant decrease in hemoglobin levels following surgery. Nine patients (13.8%) were readmitted due to postoperative complications.

Comparison of the adverse events between the two groups demonstrated a significantly higher rate of postoperative complications in the control group compared to the biologic

therapy group (55.6 vs 27.5%; $p=0.04$). The use of biologics prior to the ileocolic resection was significantly associated with a reduction in the risk of complications compared to the control group (OR 0.3, CI 95% 0.107–0.867; $p=0.02$). Complications related to infection were similar between the two groups (20.6 vs 13.9%; $p=0.52$). The conversion rate (35.7 vs 20.7%; $p=0.24$), mean operative time (223 vs 219 min; $p=0.75$), mean length of stay (5.2 vs 5.9 days; $p=0.4$), and readmission rate (13.7 vs 13.8%; $p=0.99$) were similar between the two groups (Table 2).

Twenty-two patients (33.8%) were treated with steroids prior to repeat ileocolic resection. Analysis of the main postoperative outcomes between patients treated with steroids prior to the repeat surgical intervention showed no differences in the postoperative complication rate (36.3 vs 46.5%; $p=0.59$), conversion to open surgery (36.3 vs 22.8%; $p=0.39$), or length of stay (5.4 vs 5.7 days, $p=0.68$). A tendency toward a longer operative time in the steroid groups was also noted (235 vs 214 min; $p=0.09$), although it was not statistically significant. A comparison of postoperative outcomes between patients treated with steroids preoperatively and patients not on steroids prior to surgery is provided in Table 3.

Table 2 Surgical outcomes of patients treated with biologics prior to surgery and controls

	Biologic therapy group <i>n</i> /mean (%/SD)	Control group <i>n</i> /mean (%)	<i>P</i> value
Conversion to open surgery	10/28 (35.7)	6/29 (20.7)	0.24
Operation time (minutes)	223 (±61)	219 (±38)	0.75
Postoperative complications	8 (27.5)	20 (55.6)	0.04
Infectious complications	6 (20.6)	5 (13.9)	0.52
Major complications (Clavien–Dindo ≥ 3)	4 (13.7)	4 (11.1)	0.71
Length of stay (days) (SD)	5.2 (±2.2)	5.9 (±3.3)	0.4
Readmission	4 (13.7)	5 (13.8)	0.99

Table 3 Surgical outcomes of patients treated with Steroids prior to surgery and controls

	Steroid therapy Group <i>n</i> /mean (%/ SD) <i>n</i> = 22	Control Group <i>n</i> /mean/ (%/ SD) <i>n</i> = 43	<i>P</i> value
Conversion from laparoscopic to open surgery	8/22 (36.3%)	8/35 (22.8)	0.39
Operation time (minutes)	235 (±62.1)	214 (±40.7)	0.09
Postoperative complications	8 (36.3)	20 (46.5)	0.59
Major complications (Clavien–Dindo ≥ 3)	2 (9.1)	6 (13.9)	0.7
Length of stay (days)	5.4 (±2.5)	5.7 (±3.1)	0.68
Readmission	3 (13.6)	6 (13.9)	0.99

Table 4 Multivariate analysis of demographic and perioperative factors as risk factors for postoperative complications in CD patients undergoing repeat ileocolic resection

Factor	Standard error	95% confidence interval	<i>P</i> value
Time from previous surgery (years)	0.006389	−0.004645 to 0.02098	0.20
Preoperative steroids	0.1497	−0.2684 to 0.3320	0.83
Preoperative biologics	0.1348	−0.5596 to −0.01898	0.03

Multivariate analysis aimed to identify risk factors for postoperative complications and demonstrated that biologic therapy prior to surgery was correlated with a lower risk for postoperative morbidity (OR −0.28, 95%CI −0.5596 to −0.01898, $p=0.03$). Multivariate analysis of demographic and perioperative factors is detailed in Table 4.

Discussion

We found that patients treated with biologic agents were less likely to experience postoperative complications. In addition, our analysis showed that preoperative biologic treatment was the only factor significantly associated with a lower risk for postoperative morbidity. When we performed

an analysis specifically for infectious complications, we found similar rates in both groups.

Biologic medications for CD were first approved in the 1990s, starting with Infliximab, which works by binding to TNF- α , a pro-inflammatory cytokine produced by macrophages and monocytes during acute inflammation, thus inhibiting the inflammatory activity by preventing TNF- α from binding to its receptor on the cell membrane [17, 18]. Infliximab laid the ground for the approval of several other medications from the same class (Anti-TNF) including Adalimumab and Certolizumab. In the last decade, another class of biologic medications, leukocyte adhesion molecule inhibitors, were introduced as possible treatments for IBD patients. These include Vedolizumab and Ustekinumab, monoclonal antibodies that inhibits inflammatory cells from binding to inflammatory sites, thus reducing the inflammatory response. Although these medications work in different ways, their aim is similar and they all reduce inflammation significantly [19, 20].

The role of biologic treatment in the surgical management of CD patients has been controversial in recent years. One of the first series published on the subject from the Mayo clinic analyzed the postoperative outcomes of 52 patients treated with Infliximab prior to surgery and showed no association between biologic therapy and an increased risk of complications [21]. Although these initial results were encouraging, subsequent retrospective studies reported conflicting results, where biologic therapy was found to be associated with an

increased rate of postoperative morbidity, longer hospitalization, and higher readmission rates following surgery [22, 23]. In addition, high serum levels of biologic medications were found to be correlated to a higher rate of postoperative infectious complications and readmissions [24], while other studies found no such correlation [25, 26]. Furthermore, a multicenter prospective study (PUCCINI trial) that included 17 referral centers and approximately 1000 patients, showed that detectable levels of anti-TNF alpha were not correlated to an increased tendency for postoperative complications and morbidity [27]. Several recent meta-analyses have addressed this issue and demonstrated a slightly higher tendency for infectious postoperative complications associated with preoperative anti-TNF therapy [28]. Conversely, analysis of newer medications such as Ustekinumab and Vedolizumab failed to demonstrate any similar correlation [9, 29]. However, it is important to remember that the majority of the published literature is retrospective in nature and often combines ulcerative colitis patients with CD patients in the same analysis.

Repeat ileocolic resection in patients with CD can be complex, not only due to surgical adhesions from the previous surgery, but also due to the nature of the disease that often manifests with significant inflammation and penetration to adjacent tissues. Surprisingly, although almost half of patients suffering from CD will require repeat surgical intervention, the literature on patients with surgical recurrence is limited. A large, recently published series examined the correlation between repeat surgical intervention and the surgical approach used, demonstrating that laparoscopy was feasible and that biologic therapy prior to surgery did correlate with higher rates of conversion to open surgery [10]. In our study, biologic therapy had no effect on the conversion rate, and although the majority of laparoscopic interventions were feasible, the conversion to open surgery rate was relatively high, almost exclusively due to significant inflammation and adhesions. Another recent study, by Johnston et al. [30], demonstrated an increased risk of anastomotic leakage in patients undergoing repeat ileocolic resection. A small-scale study by Brouquet et al. [31] also demonstrated that repeat surgery carries a substantial rate of postoperative morbidity. The authors noted that none of the patients who were previously treated with anti-TNF suffered from major complications following surgery, but only 8 patients were analyzed. Finally, in a nationwide study from Italy that included 258 patients who underwent repeat surgery for CD, the authors found that postoperative complications were more prevalent than in patients undergoing primary surgery, and that they occurred in about one-third of patients. The study also analyzed the role of preoperative biologic and steroid use for postoperative morbidity but showed no correlation [32].

In our series, we found a significant rate of postoperative complications following repeat ileocolic resection for CD,

similar to the previously mentioned studies. However, unlike the previous studies, we found that postoperative morbidity was not correlated to preoperative biologic treatment, yet, in fact, it seemed that patients treated with these medications had a favorable surgical outcome. Although this finding may be explained by the increased use of newer medications such as Ustekinumab and Vedolizumab, the small cohort and mixing of patients on various medications limits any definitive conclusions. All of these medications, despite a different mechanism of action, have proven to be effective in decreasing inflammation. Although it is difficult to stratify which medications contributed most to this reduction, the cumulative effect is notable, even in a small cohort of patients. Furthermore, our institution is a large international referral center, resulting in a heterogeneous patient population. Since the study was retrospective, it is difficult to assess why some patients received biologic treatment prior to surgery and some did not. Our study has some additional limitations including the single-center analysis and the lack of medication serum levels prior to surgery.

Conclusions

Results are in line with the gathering evidence from recent years that biologic treatments for CD are associated with lower rates of postoperative complications, even in the setting of complex surgical interventions for recurrent disease. However, larger prospective studies are needed to confirm our findings.

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Declarations

Conflicts of interest The authors have no relevant conflicts of interest to declare.

Ethical and Informed Consent We have no conflict of interest to report, no funding was given for this study.

References

1. Ferrari L, Krane MK, Fichera A (2016) Inflammatory bowel disease surgery in the biologic era. *World J Gastrointest Surg* 8:363–370
2. Gardiner KR, Dasari BV (2007) Operative management of small bowel Crohn's disease. *Surg Clin North Am* 87:587–610
3. Lewis RT, Maron DJ (2010) Efficacy and complications of surgery for Crohn's disease. *Gastroenterol Hepatol (NY)* 6:587–596
4. Grass F, Pache B, Martin D, Hahnloser D, Demartines N, Hubner M (2017) Preoperative nutritional conditioning of Crohn's patients—systematic review of current evidence and practice. *Nutrients* 9:562

5. Nguyen GC, Elnahas A, Jackson TD (2014) The impact of preoperative steroid use on short-term outcomes following surgery for inflammatory bowel disease. *J Crohns Colitis* 8:1661–1667
6. Yamamoto T, Allan RN, Keighley MR (2000) Risk factors for intra-abdominal sepsis after surgery in Crohn's disease. *Dis Colon Rectum* 43:1141–1145
7. Ali T, Yun L, Rubin DT (2012) Risk of post-operative complications associated with anti-TNF therapy in inflammatory bowel disease. *World J Gastroenterol* 18:197–204
8. Kopylov U, Ben-Horin S, Zmora O, Eliakim R, Katz LH (2012) Anti-tumor necrosis factor and postoperative complications in Crohn's disease: systematic review and meta-analysis. *Inflamm Bowel Dis* 18:2404–2413
9. Yung DE, Horeh N, Lightner AL et al (2018) Systematic review and meta-analysis: vedolizumab and postoperative complications in inflammatory bowel disease. *Inflamm Bowel Dis* 24:2327–2338
10. Carmichael H, Peyser D, Baratta VM et al (2021) The role of laparoscopic surgery in repeat ileocolic resection for Crohn's disease. *Colorectal Dis* 23:2075–2084
11. Celentano V, Sagias F, Flashman KG, Conti J, Khan J (2019) Laparoscopic redo ileocolic resection for Crohn's disease in patients with previous multiple laparotomies. *Scand J Surg* 108:42–48
12. Kalman TD, Everhov AH, Nordenvall C et al (2020) Decrease in primary but not in secondary abdominal surgery for Crohn's disease: nationwide cohort study, 1990–2014. *Br J Surg* 107:1529–1538
13. Riss S, Schuster I, Papay P, Mittlböck M, Stift A (2013) Repeat intestinal resections increase the risk of recurrence of Crohn's disease. *Dis Colon Rectum* 56:881–887
14. Colombo F, Frontali A, Baldi C et al (2022) Repeated surgery for recurrent Crohn's disease: does the outcome keep worsening operation after operation? A comparative study of 1224 consecutive procedures. *Updates Surg* 74:73–80
15. Leinicke JA, Dietz DW (2019) Reoperative surgery in complex Crohn's disease. *Clin Colon Rectal Surg* 2:291–299
16. Dindo D, Demartines N, Clavien PA (2004) Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 240:205–213
17. Samaan M, Campbell S, Cunningham G, Tamilarasan AG, Irving PM, McCartney S (2019) Biologic therapies for Crohn's disease: optimising the old and maximising the new. *F1000Res* 8:F1000 Faculty Rev-1210. <https://doi.org/10.12688/f1000research.18902.1>
18. Binion DG (2010) Biologic therapies for Crohn's disease: update from the 2009 ACG meeting. *Gastroenterol Hepatol (N Y)* 6(1):4–16
19. Lauro R, Mannino F, Irrera N, Squadrito F, Altavilla D, Squadrito G, Pallio G, Bitto A (2021) Pharmacogenetics of biological agents used in inflammatory bowel disease: a systematic review. *Biomedicine* 9:1748
20. Nadpara N, Reichenbach ZW, Ehrlich AC, Friedenber F (2020) Current status of medical therapy for inflammatory bowel disease: the wealth of medications. *Dig Dis Sci* 65:2769–2779
21. Colombel JF, Loftus EV Jr, Tremaine WJ et al (2004) Early post-operative complications are not increased in patients with Crohn's disease treated perioperatively with infliximab or immunosuppressive therapy. *Am J Gastroenterol* 99:878–883
22. Ahmed Ali U, Martin ST, Rao AD, Kiran RP (2014) Impact of preoperative immunosuppressive agents on postoperative outcomes in Crohn's disease. *Dis Colon Rectum* 57:663–674
23. White EC, Melmed GY, Vasiliauskas E et al (2012) Does preoperative immunosuppression influence unplanned hospital readmission after surgery in patients with Crohn's disease? *Dis Colon Rectum* 55:563–568
24. Lau C, Dubinsky M, Melmed G et al (2015) The impact of preoperative serum anti-TNFalpha therapy levels on early postoperative outcomes in inflammatory bowel disease surgery. *Ann Surg* 261(3):487–496
25. Nasir BS, Dozois EJ, Cima RR et al (2010) Perioperative anti-tumor necrosis factor therapy does not increase the rate of early postoperative complications in Crohn's disease. *J Gastrointest Surg* 14:1859–1865
26. Marchal L, D'Haens G, Van Assche G et al (2004) The risk of post-operative complications associated with infliximab therapy for Crohn's disease: a controlled cohort study. *Aliment Pharmacol Ther* 19:749–754
27. Cohen BL, Fleshner P, Kane SV et al (2019) 415a-anti-tumor necrosis factor therapy is not associated with post-operative infection: results from prospective cohort of ulcerative colitis and Crohn's disease patients undergoing surgery to identify risk factors for postoperative infection I (Puccini). *Gastroenterology* 156(6):S80
28. Yang ZP, Hong L, Wu Q, Wu KC, Fan DM (2014) Preoperative infliximab use and postoperative complications in Crohn's disease: a systematic review and meta-analysis. *Int J Surg* 12:224–230
29. Garg R, Mohan BP, Ponnada S, Regueiro M, Lightner AL, Click B (2021) Postoperative outcomes after preoperative ustekinumab exposure in patients with Crohn's disease: a systematic review and meta-analysis. *Ann Gastroenterol* 34:691–698
30. Johnston WF, Stafford C, Francone TD et al (2017) What is the risk of anastomotic leak after repeat intestinal resection in patients with Crohn's disease? *Dis Colon Rectum* 60:1299–1306
31. Brouquet A, Blanc B, Bretagnol F, Valleur P, Bouhnik Y, Panis Y (2010) Surgery for intestinal Crohn's disease recurrence. *Surgery* 148:936–946
32. Collaborative SCSocSDS (2021) National variations in perioperative assessment and surgical management of Crohn's disease: a multicentre study. *Colorectal Dis* 23:94–104

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