original article

Indicators for early surgery in patients with intra-abdominal fistulizing Crohn's disease

Ghada N. Enani,[a] Sarah S. Al Ghamdi,[b] Reem L. Mimish,[c] Ali Farsi,[c] Nadeem Shafique Butt,[d] Nouf Akeel[a]

From the [a]Department of Surgery, King Abdulaziz University, Jeddah, Saudi Arabia; [b]Department of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia; [c]Department of Radiology, King Abdulaziz University, Jeddah, Saudi Arabia; [d]Faculty of Medicine Rabigh, King Abdulaziz University, Jeddah, Saudi Arabia

Correspondence: Dr. Ghada N. Enani, Department of Surgery, King Abdulaziz University, Jeddah, Saudi Arabia, gnenani@kau.edu.sa ORCID: https://orcid.org/0000-0003-4379-0543

Citation: Enani GN, Al Ghamdi SS, Mimish RL, Farsi A, Butt NS. Indicators for Early Surgery in Patients with Intra-Abdominal Fistulizing Crohn's Disease. Ann Saudi Med 2025; 45(3): 182-189. DOI: 10.5144/0256-4947.2025.182

Received: February 11, 2025

Accepted: May 10, 2025

Published: June 5, 2025

Funding: None.

BACKGROUND: The management of intra-abdominal fistulizing Crohn's disease involves surgical resection and biologic therapy. The criteria for choosing one therapy over the other are debated.

OBJECTIVES: Identify factors influencing the choice of early surgical intervention over biologic therapy.

DESIGN: Retrospective

SETTING: Single center, tertiary training and research hospital

PATIENTS AND METHODS: We analyzed adult patients with Crohn's disease who had intra-abdominal fistulas and were followed for three years. Baseline data were collected from medical records, and imaging studies assessed the fistula type, number, affected segment length, and presence of strictures and abscesses. Multivariable logistic regression analysis was used to identify predictors for surgical intervention.

MAIN OUTCOME MEASURES: Factors that led to early surgical intervention in patients with intra-abdominal fistulizing Crohn's disease.

SAMPLE SIZE: 73 patients

RESULTS: Seventy-three patients met the inclusion criteria: 27 (37.0%) in the nonsurgical group and 46 (63.0%) in the surgical group. Early surgical intervention was done if patients had bloating or constipation (P=.018), extensive disease segments (P<.001), and no prior biologic treatment (0.015). In the multivariate analysis, early surgical intervention was indicated for enterocutaneous fistulas (odds ratio [OR]: 8.20, 95% confidence interval [CI]: 1.25-53.80, P=.03), abscesses (OR: 5.18, 95% CI: 1.03-26.12, P=.046), and strictures (OR: 6.08, 95% CI: 1.26-29.25, P=.024). Nonsurgical fistula treatment resulted in complications in 55% of patients, 48% of them requiring surgical resections, whereas biologic treatment achieved a 40.7% fistula healing rate.

CONCLUSIONS: Findings associated with Crohn's fistulas, including enterocutaneous fistulas, extensive disease segments, strictures, and abscesses, are associated with a higher likelihood of early surgical intervention and may suggest potential ineffectiveness of biologic therapies.

LIMITATIONS: This was a retrospective analysis of a single center with a small sample size, which may involve a degree of recall bias when data are collected, thus reducing the reliability of the results.

CONFLICT OF INTEREST: None.

Crohn's disease (CD) is a chronic inflammatory bowel disease characterized by inflammatory, stricturing, and penetrating phenotypes, all of which result in transmural bowel damage. Around 20-40% of patients with CD present with a penetrating phenotype,[1-3] and 50% of patients with a disease course of 20 years will have fistulizing disease.[4] In Saudi Arabia, 25.4% of patients diagnosed with CD have penetrating disease.[5] These patients may develop deep abscesses and intra-abdominal fistulas, including enterocutaneous, entero-enteric, entero-vesical, and entero-vaginal fistulas.[1-3]

Although surgical rates have decreased with the earlier use of biologic therapy, surgery still plays an important role in managing CD, particularly in patients with stenotic and penetrating phenotypes.[6] In these scenarios, early surgical intervention may be recommended, as bowel damage is present and irreversible, reducing the efficacy of biologics.[1,7] Choosing between surgical and medical treatments for intra-abdominal fistula in CD remains challenging, with the optimal approach yet to be determined.[8,9] The rate of internal fistula closure in patients with CD varies across studies, but it is higher with asymptomatic single fistulas.[8-10]

Most patients with intra-abdominal fistulizing CD typically undergo surgical resection but may start biologic therapy beforehand.[4] Undue delay in the use of biologics may lead to more complicated and extensive resections, ultimately hindering effective disease control.[11,12]

In this study, we aimed to examine and study the factors associated with early surgical intervention over medical therapy and vice versa in patients with intra-abdominal fistulizing CD.

PATIENTS AND METHODS

Data collection

In this retrospective study, we analyzed all patients diagnosed with intra-abdominal fistulizing CD at a tertiary academic hospital from 2005 to 2021. Data were obtained from a prospectively compiled database known as the Saudi Inflammatory Bowel Disease Information System at King Abdulaziz University Hospital (KAUH). The study was approved by the Research Ethics Board Committee at KAUH (NBCE registration No: HA-02-J-008).

The inclusion criteria were as follows: adult patients aged >18 years, clinically diagnosed with CD and confirmed to have an intra-abdominal fistula by computed tomography enterography (CTE) or magnetic resonance enterography (MRE) as verified and reported by an abdominal radiologist. Patients were excluded if they were aged <18 years, had no diagnosis of CD, had no radiological evidence of internal fistula on CTE or MRE, or were lost to follow up within three years of their diagnosis.

For the study, imaging studies were reread and evaluated for the following radiological indicators of CD: type and number of fistulae, length of disease segment, stricture with pre-stenotic dilatation (defined as a narrowing of 50% or more of the intestine lumen), and presence of an abscess. Both protocols involve bowel distension using >900 mL oral neutral or biphasic enteric contrast agents in divided doses over 45–60 minutes before the study. This was followed by contrast-enhanced imaging—CTE with iodinated contrast during the enteric phase, and MRE with gadolinium. Intra-abdominal fistulae were classified clinically into two groups: those which formed an internal connection between two bowel layers or segments, and those that occured between the intestine and other organs, such as entero-vesical, rectovaginal, or abdominal wall fistula.[1-3]

Data collected included the following: age, gender, nutritional assessment (albumin, body mass index), C-reactive protein (CRP) level, smoking history, duration of illness, duration of fistula diagnosis (from index imaging), concurrent steroid treatment, and history of biologic treatment (adalimumab, infliximab, and vedolizumab). All images were reviewed by a radiologist to identify the radiological characteristics of all patients, including type of fistula (ileocolic, ileo-ileal, enterocutaneous, ileo-vesical, rectovesical), number of fistulas found on imaging, associated abscesses, phlegmon, strictures, and length of diseased segment.

The treatment approach was determined through a retrospective review of outpatient and inpatient records for all study patients. Patients who underwent surgery within a year of being diagnosed with fistulizing CD, as indicated by imaging, were classified as having received "early" surgical intervention.[13]

The effectiveness of biologic therapy for intra-abdominal fistulas was assessed by monitoring patients for at least three years after diagnosis via initial imaging. We evaluated the need for surgery, ostomy requirements, resolution of the fistula (indicated by the absence of the fistula tract on post-therapy imaging), and complications (such as obstruction, perforation, and abscess). Follow-up imaging (CTE or MRE) was performed at one year and three years post diagnosis for those receiving therapy. Illness duration was categorized into four groups: less than a year, 1-3 years, 4-8 years, and more than 8 years.

Statistical analysis

Comparative analyses between the surgical and nonsurgical groups were performed using Chi-square tests, Fisher's exact tests, and t-tests. Fisher's exact tests were specifically used for categorical data with small sample sizes. Descriptive analyses were conducted to summarize long-term follow-up data and clinical outcomes for nonsurgical patients. Multivariable logistic regression analysis was used to identify predictors for early surgical intervention, with odds ratios (ORs) calculated to estimate the likelihood of surgical intervention based on radiological findings. A *P* value of less than .05 was considered statistically significant. All statistical analyses were conducted withIBM SPSS Statistics for Windows, Version 26.0 (Armonk, NY: IBM Corp.).

RESULTS

Patient demographics and baseline clinical characteristics

A total of 73 patients were included, 27 (37.0%) in the nonsurgical group and 46 (63.0%) in the surgical group. The mean age was similar between groups (31.3 vs. 29.5 years, *P*=.504), with males comprising the majority (48, 65.8%). Bloating and constipation were significantly more common in the nonsurgical group than in the surgical group (37.0% vs. 10.9%, respectively, *P*=.018) (**Table 1**). There were more patients with a symptom of fistula leakage in the surgical group than in the nonsurgical group (19.6% vs. 3.7%, respectively), but this was not statistically significant (*P*=.121). The presence

Table 1. Demographics and baseline clinical characteristics of patients with Crohn's disease with intra-abdominal fistulas.

		Nonsurgical group	Surgical group	Total	*P* value
Total n (%)		27 (37.0)	46 (63.0)	73 (100)	
Age, mean (SD)		31.3 (11.5)	29.5 (10.2)	30.2 (10.6)	.504[a]
Gender	Female	9 (33.3)	16 (34.8)	25 (34.2)	1.000[b]
	Male	18 (66.7)	30 (65.2)	48 (65.8)	
History of surgical resection	No	20 (74.1)	28 (60.9)	48 (65.8)	.372[b]
	Yes	7 (25.9)	18 (39.1)	25 (34.2)	
Duration of Crohn's disease	<1 year	6 (22.2)	22 (47.8)	28 (38.4)	.111[b]
	1-3 years	13 (48.1)	12 (26.1)	25 (34.2)	
	4-8 years	6 (22.2)	7 (15.2)	13 (17.8)	
	>8 years	2 (7.4)	5 (10.9)	7 (9.6)	
Preoperative albumin level (g/dL), mean (SD)		29.6 (9.4)	29.0 (9.1)	29.2 (9.1)	.826[a]
Preoperative CRP Level (mg/L), mean (SD)		68.0 (56.3)	59.9 (53.6)	62.3 (54.0)	.622[a]
Symptoms (abdominal pain)	No	4 (14.8)	13 (28.3)	17 (23.3)	.305[b]
	Yes	23 (85.2)	33 (71.7)	56 (76.7)	
Symptom: bloating/ constipation	No	17 (63.0)	41 (89.1)	58 (79.5)	.018[b]
	Yes	10 (37.0)	5 (10.9)	15 (20.5)	
Symptom: diarrhea	No	25 (92.6)	43 (93.5)	68 (93.2)	1.000[b]
	Yes	2 (7.4)	3 (6.5)	5 (6.8)	
Symptom: fistula leakage	No	26 (96.3)	37 (80.4)	63 (86.3)	.121[b]
	Yes	1 (3.7)	9 (19.6)	10 (13.7)	
Presence of perianal disease	No	21 (77.8)	39 (84.8)	60 (82.2)	.661[b]
	Yes	6 (22.2)	7 (15.2)	13 (17.8)	

Values are number (%) unless otherwise indicated. CRP: C-reactive protein.

[a]Independent samples T-test. [b]Chi-square test (Yates continuity correction).

of perianal fistula, a history of surgical resection, and preoperative albumin and CRP levels were comparable between groups (**Table 1**).

Medication characteristics

A significantly higher proportion of non-surgical patients had a history of biologic use than surgical patients (85.2% vs. 54.3%, *P*=.015), and 5-ASA use was also more common in the non-surgical group (25.9% vs. 4.3%, *P*=.019). Although not statistically significant, immunomodulator use (azathioprine) was more frequent in the non-surgical group (51.9% vs. 34.8%, *P*=.236). Among biologic agents, infliximab and adalimumab were more commonly used, with no significant differences in their distribution between groups. Notably, shorter biologic treatment duration (<1 year) was associated with early surgical intervention (*P*=.016), whereas longer durations (1–3 years and 3–8 years) were significantly associated with non-surgical treatment (P=.001 and *P*=.019, respectively). Preoperative steroid use did not differ significantly between groups. (**Table 2**).

Radiological characteristics

Enterocutaneous fistulas were significantly more common in the surgical group than in the nonsurgical group (43.5% vs. 7.4%, respectively, *P*=.003), whereas ileo-ileal fistulas were more common in the nonsurgical group than in the surgical group (66.7% vs. 37.0%, respectively, *P*=.027) (**Table 3**). The presence of ileo-vesical and ileocolic fistulas was similar in both groups. The length of the affected bowel segment, with fistulas and associated inflammation, was categorized as short (<6 cm), medium (6-10 cm), or long (>10 cm). Most patients in the nonsurgical group had short- and medium-segment diseased bowel. In contrast, most patients with long-segment diseased bowel underwent early surgical intervention. The number of fistulas, associated stricture, and associated abscesses were comparable between study groups (**Table 3**).

Follow-up

In the nonsurgical group, 55% developed complications and fistula closure failure. Of those patients, 48% underwent surgical resections and all had stoma. Specific complications during the follow-up period included perforation in 26.7% of patients, obstruction in 40%, abscess in 46.7%, and phlegmon in 20%. Other complications observed during follow-up were recur-

Table 2. Clinical characteristics and medication history of patients with Crohn's disease with intra-abdominal fistulas in Surgical vs. Non-Surgical groups.

		Nonsurgical group	Surgical group	Total	*P* value
Total n (%)		27 (37.0)	46 (63.0)	73	
History of biologic use	Yes	23 (85.2)	25 (54.3)	48 (65.8)	.015[a]
	No	4 (14.8)	21 (45.7)	25 (34.2)	
History of immunomodulator use (Azathioprine)	Yes	14 (51.9)	16 (34.8)	30 (41.1)	.236[a]
	No	13 (48.1)	30 (65.2)	43 (58.9)	
History of 5-ASA use	Yes	7 (25.9)	2 (4.3)	9 (12.3)	.019[a]
	No	20 (74.1)	44 (95.7)	64 (87.7)	
Type of biologic used	Infliximab	11 (40.7)	11 (23.9)	22 (30.1)	.212[a]
	Adalimumab	12 (44.4)	14 (30.4)	26 (35.6)	.34[a]
	Vedolizumab	0 (0.0)	1 (2.2)	1 (1.4)	1.000[a]
Duration of biologic treatment	<1 year	0 (0.0)	11 (23.9)	11 (15.1)	.016[a]
	1-3 years	12 (44.4)	4 (8.7)	16 (21.9)	.001[a]
	3-8 years	7 (25.9)	2 (4.3)	9 (12.3)	.019[a]
Preoperative steroid use	Yes	17 (63.0)	24 (52.2)	41 (56.2)	.514[a]
	No	10 (37.0)	22 (47.8)	32 (43.8)	

Values are number (%) unless otherwise indicated.

[a]Independent samples T-test

Table 3. Radiological characteristics of patients with Crohn's disease with intra-abdominal fistulas.

		Nonsurgical group	Surgical group	Total	*P* value
Total n (%)		27 (37.0)	46 (63.0)	73 (100)	
Type of fistula	Ileocolic	19 (70.4)	29 (63.0)	48 (65.8)	.703[a]
	Enterocutaneous	2 (7.4)	20 (43.5)	22 (30.1)	.003[a]
	Ileo-ileal	18 (66.7)	17 (37.0)	35 (47.9)	.027[a]
	Ileo-vesical	5 (18.5)	3 (6.5)	8 (11.0)	.232[a]
Number of fistulas	1	10 (37.0)	17 (37.0)	27 (37.0)	.551[a]
	2	9 (33.3)	21 (45.7)	30 (41.1)	
	3	2 (7.4)	3 (6.5)	5 (6.8)	
	>3	6 (22.2)	5 (10.9)	11 (15.1)	
Other CTE finding	Stricture	15 (55.6)	33 (71.7)	48 (65.8)	.250[a]
	Abscess	6 (22.2)	21 (45.7)	27 (37.0)	.080[a]
Diseased segment length	<6 cm	9 (33.3)	5 (10.9)	14 (19.2)	<.001[a]
	6-10 cm	13 (48.1)	4 (8.7)	17 (23.3)	
	>10 cm	5 (18.5)	37 (80.4)	42 (57.5)	

Values are number (%). CTE: computed tomography enterography.

[a]Chi-square test (Yates continuity correction)

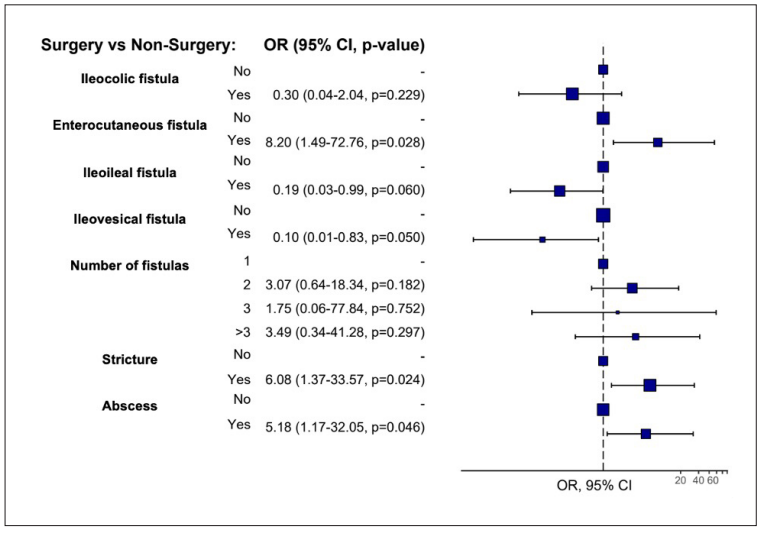

Figure 1. Forest plot of adjusted odds ratios from multivariate logistic regression analysis of predictors for failure of biologic therapy in patients with Crohn's disease with intra-abdominal fistulas. The illustrated the odds ratios (OR) with 95% confidence intervals (CI) and *P* values.

rence of internal fistula in 13.3% of patients and death in 6.7%. The risk of surgical resection or recurrence after diagnosis of fistula was 33.3% after 3 years and 14.8% after 5 years. Notably, 40.7% of patients had evidence of internal fistula healing with resolution of symptoms seen on follow-up imaging.

Multivariable logistic regression analysis

The predictors of failure of biologic therapy were shown in **Figure 1**. The presence of ileocolic fistula was not significantly associated with early surgery (OR: 0.30, 95% CI: 0.04-2.04, *P*=.229). In contrast, enterocutaneous fistula demonstrated a significant association with early surgical intervention (OR: 8.20, 95% CI: 1.49-72.76, *P*=.028). The presence of an ileo-ileal fistula was marginally associated with a decreased likelihood of surgery (OR: 0.19, 95% CI: 0.03-0.99, *P*=.060). Additionally, ileo-vesical fistula showed a statistically significant protective effect against surgery (OR: 0.10, 95% CI: 0.01-0.83, *P*=.050). Although the number of fistulae and the presence of an ileocolic fistula trended toward reduced odds of surgery, these findings were not statistically significant.

Regarding radiological finding, CT-detected strictures were significantly associated with early surgical intervention (OR: 6.08, 95% CI: 1.37-33.57, *P*=.024).

Similarly, the presence of an abscess on CT was significantly linked with increased odds of early surgery (OR: 5.18, 95% CI: 1.17-32.05, *P*=.046).

DISCUSSION

In this study, we aimed to determine factors that lead to early versus late surgical intervention. Most patients with a long diseased segment in our cohort were offered early surgical intervention rather than biologic therapy. This could be due to the higher disease burden in patients with a long diseased segment that may not be as responsive to biologic therapy, resulting in treatment with surgery upfront. The coexistence of an abscess or stricture was found to be a predictor of biologic therapy failure, whereas the number of fistulas and duration of CD did not affect the outcomes of biologic therapy. In the presence of abscesses or strictures with an internal fistula, the data are conflicting, with some studies showing a preference for surgical intervention[13] and others a preference for medical intervention.[14] However, having multiple fistulas and concomitant strictures were more likely to require surgical resection.[14]

The most common type of fistula found in both groups was ileocolonic, which is consistent with the current literature.[13,15,16] Our data showed that patients with ileo-vesical fistulas were less likely to require early surgical intervention. Studies have shown that the likelihood of opting for surgical resection in patients with entero-vesical fistula is not statistically significant.[13,17] One study revealed that 35% of patients achieved remission without surgical intervention.[18] Although patients with entero-vesical fistulas are more likely to develop urinary tract infections, potentially delaying the start of biologic therapy, our study's retrospective design prevented us from identifying the exact reasons for nonsurgical resections in these patients. One possibility is that they had complex multi-segment disease, which could make surgeons less enthusiastic about the surgical option.

The healing rate with biologic therapy has varied across studies. The failure rate with biologic therapy varies between 41-77%.[8,10] Older studies did not show a significant effect of infliximab on internal fistula healing, although these studies did not assess the effect of new biologics on the healing rate.[14,18,19] Our study included patients treated with newer biologic agents such as ustekinumab and vedolizumab and revealed a 55% failure rate. The rate of surgery to treat intra-abdominal fistulae varied among studies. In some studies, it was shown to be lower in patients treated with an anti-tumor necrosis factor agent.[13,17] However, in one previous analysis, the cumulative risk for surgery after diagnosis of an internal fistula was found to be 38% at one year, 52% after three years, and 58.7% after five years.[15] Another study found that 43.6% of patients treated with a biologic required surgical resection over a 3.5-year follow-up period.8 Biologics have previously been shown to have an impressive initial response; however, most patients ultimately require surgical intervention because of inadequate healing or complications, including stenosis or abscess formation.[20] In our cohort, the fistula healing rate with biologics was 37% after three years. This finding indicates a need for larger prospective studies on the effect of newer agents on fistula healing in CD. It also raises the question of whether the integration of timely biologics with appropriately scheduled surgery could produce a synergistic effect that enhances patient outcomes.

Recent advancements in biologic therapies, particularly with novel agents such as ustekinumab (IL-12/IL-23 inhibitor) and vedolizumab (integrin inhibitor), offer promising therapeutic alternatives for patients who fail initial anti-TNF therapies.[21] These biologics target different inflammatory pathways that may provide efficacy in fistulizing CD, especially in patients who are refractory to conventional treatments. Ustekinumab, in particular, has demonstrated potential in reducing fistula-related complications and improving clinical outcomes in patients with refractory disease,[22] while Vedolizumab may provide benefits by modulating gut-specific inflammation.[23] Both biologics offer distinct mechanisms of action that override some of the limitations seen with anti-TNF therapy, suggesting that early introduction or combination approaches could potentially optimize outcomes for patients with complex fistulizing disease.

Our cohort revealed early onset of intra-abdominal fistula in patients who were newly diagnosed with CD, with 38.4% of them developing intra-abdominal fistulas within the first year. A Canadian study also noted earlier onset of internal fistulas in patients with early-onset CD.[24] We found that longer biologic therapy duration reduced the likelihood of surgical intervention, as patients responding well to treatment tended to remain on the therapy longer, whereas non-responders were more often referred for surgery.

This study is the first to investigate the clinical and radiological features of intra-abdominal fistulas in patients with CD in Saudi Arabia. With a three-year follow-up period, we assessed the success rate of biologic treatments on fistula healing. Despite the valuable insights provided by this study, several limitations should be acknowledged. Data were sourced from a single tertiary referral institution. The study also has a small sample size hindering the ability to reach

statistical power. Another important limitation is that some patients with aggressive disease were directed to surgery from the start without a trial of biologics, which could have influenced outcomes. Measuring adherence was further complicated by patients receiving treatment at multiple centers, and we lacked disease severity indices at diagnosis. Some imaging data from external facilities were also unavailable, possibly leading to underreporting of fistula cases. Socioeconomic factors, such as lack of insurance, may have contributed to high complication rates in the nonsurgical group due to missed biologic doses. These limitations highlight the need for multicenter prospective studies with standardized protocols to improve biologic therapy monitoring and adherence tracking, along with better follow-up data to improve understanding of long-term outcomes and guide treatment decisions for intra-abdominal fistulizing CD.

CONCLUSION

Early surgical intervention in the management of intra-abdominal CD was indicated in cases where patients presented with enterocutaneous fistula, intra-abdominal abscess, strictures, and were not receiving biologic therapy. This research highlights the differences in clinical characteristics and treatment options between patients with CD who have intra-abdominal fistulas. Certain fistula types, such as enterocutaneous fistulas, as well as extensive disease segments, strictures, and abscesses, may indicate potential failure of biologic therapies. The nonsurgical cohort experienced significant complications, underscoring the need for careful monitoring. These findings enhance our understanding of treatment variables in intra-abdominal fistulizing CD and emphasize the importance of personalized management strategies. Future studies should focus on determining the best timing for surgical intervention. Furthermore, more studies are needed to examine the impact of biological dosages compliance and the effect of different biologic therapy on fistula closure. The challenge remains in developing tailored recommendations for individual patients.

Disclosure

The authors report no propriety or commercial interest in any product mentioned or concept discussed in this article.

Availability of data

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

REFERENCES

1. Gasche C, Scholmerich J, Brynskov J, D'Haens G, Hanauer SB, Irvine EJ, et al. A simple classification of Crohn's disease: report of the Working Party for the World Congresses of Gastroenterology, Vienna 1998. Inflamm Bowel Dis 2000;6(1):8-15.
2. Cerqueira RM, Lago PM. Clinical factors predictive of Crohn's disease complications and surgery. Eur J Gastroenterol Hepatol. 2013;25(2):129-34.
3. Cosnes J, Cattan S, Blain A, Beaugerie L, Carbonnel F, Parc R, et al. Long-term evolution of disease behavior of Crohn's disease. Inflamm Bowel Dis. 2002;8(4):244-50.
4. Sun Z, Cao L, Chen Y, Zhu W, Li Y. Long-term outcomes of intestinal penetrating Crohn's disease following successful non-operative management. Eur J Gastroenterol Hepatol. 2024;36(7):867-74.
5. Aljebreen AM, Alharbi OR, Azzam NA, Almalki AS, Alswat KA, Almadi MA. Clinical epidemiology and phenotypic characteristics of Crohn's disease in the central region of Saudi Arabia. Saudi J Gastroenterol. 2014;20(3):162-9.
6. Cosnes J, Gower–Rousseau C, Seksik P, Cortot A. Epidemiology and natural history of inflammatory bowel diseases. Gastroenterology. 2011;140(6):1785-94.
7. Thia KT, Sandborn WJ, Harmsen WS, Zinsmeister AR, Loftus EV Jr. Risk factors associated with progression to intestinal complications of Crohn's disease in a population-based cohort. Gastroenterology. 2010;139(4):1147-55.
8. Bouguen G, Huguet A, Amiot A, Viennot S, Cholet F, Nachury M, et al. Efficacy and safety of tumor necrosis factor antagonists in treatment of internal fistulizing Crohn's disease. Clin Gastroenterol Hepatol. 2020;18(3):628-36.
9. Colombel JF, Sandborn WJ, Rutgeerts P, Enns R, Hanauer SB, Panaccione R, et al. Adalimumab for maintenance of clinical response and remission in patients with Crohn's disease: the CHARM trial. Gastroenterology. 2007;132(1):52-65.
10. Kobayashi T, Hishida A, Tanaka H, Nuki Y, Bamba S, Yamada A, et al. Real-world experience of anti–tumor necrosis factor therapy for internal fistulas in Crohn's disease: a retrospective multicenter cohort study. Inflamm Bowel Dis. 2017;23(12):2245-51.
11. Iesalnieks I, Kilger A, Glaß H, Obermeier F, Agha A, Schlitt HJ. Perforating Crohn's ileitis: delay of surgery is associated with inferior postoperative outcome. Inflamm Bowel Dis. 2010;16(12):2125-30.
12. Dias CC, Portela F, Fernandes S, Ministro P, Lago P, Rosa I, et al. The timing of early therapeutic strategies has a significant impact on Crohn's disease prognosis. Dig Liver Dis. 2018;50(5):462-8.
13. Yaari S, Benson A, Aviran E, Cohain NL, Oren R, Sosna J, et al. Factors associated with surgery in patients with intra-abdominal fistulizing Crohn's disease. World J Gastroenterol. 2016;22(47):10380-7.
14. Uza N, Nakase H, Ueno S, Inoue S, Mikami S, Tamaki H, et al. The effect of medical treatment on patients with fistulizing Crohn's disease: a retrospective study. Intern Med. 2008;47(4):193-9.
15. Wang GF, Ren JA, Song LI, Jun CH, Gu GS, Wang XB, et al. Clinical characteristics of non-perianal fistulating Crohn's disease in China: a single-center experience of 184 cases. Chin Med J (Engl). 2012;125(14):2405-10.
16. Benson AA, Aviran E, Yaari S, Lev-Cohain N, Sosna J, Oren R, et al. Clinical and radiologic characteristics of intra-abdominal fistulizing Crohn's disease. Digestion. 1964;101(6):667-73.
17. Zhang W, Zhu W, Li Y, Zuo L, Wang H, Li N, et al. The respective role of medical and surgical therapy for enterovesical fistula in Crohn's disease. J Clin Gastroenterol. 2014;48(8):708-11.
18. Miehsler W, Reinisch W, Kazemi-Shirazi L, Dejaco C, Novacek G, Ferenci P, et al. Infliximab: lack of efficacy on perforating complications in Crohn's disease. Inflamm Bowel Dis. 2004;10(1):36-40.
19. Nunes J, Santos PM, Tavares L. Complete resolution of enterocolic fistulas with infliximab. BioDrugs. 2010;24 Suppl 1:28-30.
20. Poritz LS, Rowe WA, Koltun WA. Remicade® does not abolish the need for surgery in fistulizing Crohn's disease. Dis Colon Rectum. 2002;45(6):771-5.
21. Singh S, Proctor D, Scott FI, Falck-Ytter Y, Feuerstein JD. AGA Technical Review on the Medical Management of Moderate to Severe Luminal and Perianal Fistulizing Crohn's Disease. Gastroenterology. 2021 Jun;160(7):2512-2556.e9. doi: 10.1053/j.gastro.2021.04.023. PMID: 34051985.
22. Vuyyuru SK, Solitano V, Narula N, Lee MJ, MacDonald JK, McCurdy JD, et al. Pharmacological Therapies for the Management of Fistulizing Crohn's Disease: A Systematic Review and Meta-Analysis. J Crohns Colitis. 2024 Apr 23;18(4):589-603. doi: 10.1093/ecco-jcc/jjad185. PMID: 37933849.
23. Mantzaris GJ, Bressler B, Adsul S, Luo M, Colby C, Brett NRet al. Effectiveness and safety of vedolizumab and infliximab in biologic-naive patients with Crohn's disease: results from the EVOLVE study. Eur J Gastroenterol Hepatol. 2024 Mar 1;36(3):281-291. doi: 10.1097/MEG.0000000000002690. Epub 2023 Dec 27. PMID: 38179874.
24. Veloso FT, Ferreira JT, Barros L, Almeida S. Clinical outcome of Crohn's disease: analysis according to the Vienna classification and clinical activity. Inflamm Bowel Dis. 2001;7(4):306-13.