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REVIEW

Management and Treatment of Perianal Fistulizing Crohn's Disease

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Abstract: Perianal fistulizing Crohn's disease is a severe and disabling phenotype of Crohn's disease, affecting up to one-third of Crohn's patients. This phenotype can result in significant quality of life impairment in quality of life due to chronic pain, persistent perianal drainage, and the risk of fecal incontinence. The presence of a perianal fistula indicates a more aggressive disease course, often requiring more frequent and coordinated care. Optimal management relies on a multidisciplinary team, including gastroenterologists, colorectal surgeons, and radiologists, to address the complex interplay of medical and surgical needs. Medical therapy achieves durable remission in only about one-third of patients, necessitating surgical intervention for the majority, with patients arriving to the operating room with more advanced disease activity and longer duration of immunosuppression. For patients with refractory disease, mesenchymal stem cell (MSC) therapy has emerged as a promising option, with clinical remission rates of approximately 50–80% at 6–12 months and a favorable safety profile, notably without increasing the risk of incontinence compared to conventional surgery. However, there is no approved MSC product currently available for clinical use. Given the complexity and morbidity of fistulizing perianal Crohn's disease, a multidisciplinary approach focused on individualized, evidence-based therapy is essential for optimizing outcomes.

Keywords: perianal Crohn's disease, perianal fistula, mesenchymal stem cell therapy, perianal surgery

Introduction

Crohn's disease (CD) is a phenotype of inflammatory bowel disease (IBD) known for its chronic nature and transmural involvement in the gastrointestinal tract. For unknown reasons, the incidence and prevalence of CD continue to increase globally underscoring the need for ongoing research to improve understanding and treatment of this disease. Pathognomonic transmural inflammation observed in CD can result in a penetrating phenotype throughout the gastrointestinal tract, the most common location being perianal.[1] Perianal disease can also include non-fistulizing disease such as hemorrhoids and perianal skin tags that are present in 2–6% of CD patients.[2,3] Far more common, however, is penetrating involvement; perianal abscesses occur in up to 80% of CD patients which often lead to a perianal fistula development.[4] In 8.6% of the overall CD population, a perianal fistula is the initial presenting manifestation and can precede intestinal symptoms.[5] If not the initial presentation, at least 26% of patients would develop perianal fistulas within the first two decades after diagnosis of disease,[6–9] especially if the patient had colorectal involvement.[1] Unfortunately, these patients are at significant risk of morbidity secondary to pain, persistent drainage, recurrent perianal sepsis, and increased incontinence, all of which contribute to a poor quality of life.[10,11]

The presence of perianal fistulizing disease indicates a more aggressive phenotype of CD,[12] which requires frequent access to medical care, incurring increased costs to the patient and the medical system.[11,13] Medical treatment includes immunosuppressive regimens that come with significant potential side effect profiles. Despite undergoing medical therapy, more than 90% of patients undergo multiple surgical interventions that increase the risk of fecal incontinence.[6] Regardless of a range of applied strategies, the overall recurrence after initial healing was known to remain high at 37–44%.[14] A recent 2025 prospective study utilized a coordinated multidisciplinary protocol which

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included early use of biologics, regular surgical review, and proactive maintenance. They reported clinical healing in 39% of patients after one year and 84% after two years. Radiologic remission was seen in 25% at 22 months, and relapse among those healed was rare (7% at 23 months), showing that lasting remission is possible with an optimized treatment plan.[15] Therefore, the optimal care of patients with perianal fistulizing CD integrates a team of gastroenterologists, surgeons, and radiologists who actively work towards improving treatment of this debilitating disease.[11,16] This review aims to describe the management and role of multidisciplinary therapy in treating patients with perianal fistulizing CD (PFCD).

Diagnosis

History

Patients with perianal fistula will often present with symptoms or a history of perianal pain, drainage, incontinence, or signs of pelvic sepsis. A complete history should include any abdominal pain, diarrhea, hematochezia, fever, fatigue, or weight changes.[16]

Physical Exam

The abdomen should be palpated to assess for any abdominal or pelvic tenderness. Next, the perianal region should be inspected for skin tags, fissures, or hemorrhoidal tissue. Careful external palpation should investigate any potential external openings of a perianal fistula. Evidence of active sepsis with purulent discharge or chronic sepsis with induration should be noted. A digital rectal exam should be performed to evaluate anal tone and assess for anal canal irregularities. Proctoscopy is used to confirm anal canal inflammation, distal proctitis, and visualization of perianal fistula tract openings.[16]

Ancillary Studies

Once diagnosed, the fistula anatomy must be identified and characterized to guide management. An exam under anesthesia (EUA) or imaging modalities such as an endoanal ultrasound (EUS) or pelvic magnetic resonance imaging (MRI) are comparable in diagnostic accuracy when defining the fistula anatomy.[17–20] Recent meta-analyses show that while pelvic MRI remains the golden standard due to superior spatial resolution, and given lack of radiation, is preferred for serial imaging.[21] Is Of note, the diagnostic accuracy approaches 100% when combining the pelvic MRI and EUA findings.[20]

Although clinical assessment and imaging remain the gold standard for diagnosis, fecal calprotectin levels may further distinguish PFCD origin from cryptoglandular fistulas.[22,23] Prospective studies demonstrate a significantly higher level of fecal calprotectin levels, with cutoffs around 110–150 μg/g, in patients with PFCD.[22–24] However, given that it primarily reflects intestinal mucosal inflammation, it may not reliably differentiate isolated perianal CD in the absence of luminal disease nor provide information on fistula complexity or severity.[25,26]

Anatomic Classification (Park's and TOpClass Classification)

Perianal fistulas are classified based on their anatomical location and complexity as low or high, and simple or complex. A low perianal fistula originates distal to the dentate line, whereas a high perianal fistula originates proximally to the dentate line. Simple fistulas are typically low-lying, non-tender, less than 30% of external anal sphincter involvement, and characterized by a single external opening. They do not have evidence of abscess, rectovaginal involvement or anorectal stricture.[7,27,28] Complex fistulas include those that are high in locations, have multiple external openings, with associated abscess, rectovaginal fistula, anorectal stricture, or have concurrent active rectal disease.[27,28] Given the severity of the disease, all PFCD cases are, by definition, considered complex fistulas.

The advanced imaging described previously, namely pelvic MRI, is essential for accurate delineation of anatomy, identification of multiple tracts, and detection of occult abscesses. The Parks classification describes the perianal fistulas in relation to the anal sphincter complex, particularly the external anal sphincter. The location of the fistula can be categorized as intersphincteric, transsphincteric, suprasphincteric, and extrasphincteric[28,29] (Table 1).

Table 1 The Parks Classification of Perianal Fistula

Anatomy	Description	Rate of Occurrence
Intersphincteric	Crosses the internal sphincter and exits through the perianal skin. Does not penetrate the external sphincter.	20-45%
Transsphincteric	Penetrates external sphincter below the level of puborectalis muscle and exits within the ischiorectal fossa.	30-60%
Suprasphincteric	The tract courses over the puborectalis, descends through the ischiorectal fossa, and exits at the perianal skin.	20%
Extrasphincteric	Passes from the perineal skin, through the ischiorectal fossa and levator muscles, into the rectum, lying entirely outside the external sphincter complex.	2-5%

Table 2 The TOpClass Classification by Geldolf Et al

Class	Description	Subclassification	Treatment Goal
I	Minimal disease with mild symptoms and low disease burden		Medical therapy aimed at preventing disease progression
II	Chronic symptomatic perianal disease	2a: Suitable for repair 2b: Suitable for symptom control 2c: Progressive disease	2a: Fistula closure 2b: Disease and symptom control 2c: Disease and symptom control by diversion
III	Severe, refractory disease		Requires proctectomy
IV	Persistent perineal symptoms following proctectomy	Subclassified by treatment goal	Repair or symptom control

To address clinical and research challenges in PFCD, the international TOpClass consortium developed a classification system that integrates anatomical and clinical features with an evidence-based, patient-centered management approach. The TOpClass system represents an important advancement by aligning treatment strategies with patient goals and disease severity, considering factors such as symptoms, disease activity, and anatomical complexity to guide suitability for fistula repair. This framework emphasizes shared decision-making, acknowledging that symptom control rather than complete fistula healing may often be the most realistic therapeutic goal. The classification includes four categories: Class I (minimal disease), II (chronic symptomatic disease), III (severe refractory disease), and IV (post-proctectomy symptoms)[30] (Table 2).

Goals of Treatment

The treatment of PFCD focuses on resolving symptoms of drainage or sepsis without compromising continence. The European Crohn's and Colitis Organization (ECCO) defines healing as the combination of clinical and radiographic improvement, specifically the absence of drainage upon external palpation and no abscess greater than 2 cm in any two of three dimensions on pelvic MRI.[31] Healing outcomes may vary as some patients achieve partial response, with over 50% reduction in drainage yet persistent evidence of a tract; others may show no improvement at all. It is important to align management with the patient's personal goals. Patients who remain asymptomatic despite a persistent tract often do not require active treatment. For some individuals, simply reducing drainage enough to stop using pads is satisfactory, while others may seek complete eradication of the tract.[16]

Medical Treatment

Antibiotic Therapy

Before the landmark infliximab trial in PFCD,[32] antibiotics were the only medical therapy available. Although high-quality efficacy data is limited, oral antibiotics have long been used to manage symptoms, though they rarely lead to complete remission. A small randomized controlled trial found no significant difference in treatment response between ciprofloxacin 500 mg twice daily and metronidazole 500 mg twice daily. However, ciprofloxacin was associated with symptom improvement in up to 40% of patients.[33]

When used as adjunctive therapy, antibiotics have demonstrated efficacy when combined with immunomodulators or biologic agents.[34] In a prospective open-label trial involving 52 patients, rates of fistula closure were compared between antibiotic monotherapy (ciprofloxacin and/or metronidazole) and combination therapy with azathioprine plus antibiotics. The combination group achieved a significantly higher clinical response rate than the antibiotics-alone group (48% vs 15%, $P = 0.03$).[35] Similarly, a prospective, double-blind, placebo-controlled study of 24 patients compared combination therapy with ciprofloxacin and infliximab to infliximab monotherapy. The results suggested that the combination was more effective than infliximab alone (OR = 2.37, 95% CI: 0.94–5.98, $P = 0.07$).[36] Based on these findings, the American Gastroenterological Association (AGA) guidelines for the medical management of PFCD recommend the use of biologic therapy in combination with antibiotics, rather than biologic monotherapy, for the induction of fistula remission.[37]

Thiopurines

Thiopurines, such as azathioprine and 6-mercaptopurine (6-MP), are frequently utilized in the management of PFCD, although prospective data supporting their efficacy remain limited. A 1995 meta-analysis that included five studies evaluating the response of CD-PAF to azathioprine or 6-MP demonstrated that these agents significantly improved fistula symptoms and healing compared with placebo (odds ratio 4.44; 95% CI, 2.20–12.60).[38] However, thiopurines generally show only limited effects on fistula response, with low rates of complete closure and a high likelihood of recurrence after treatment is discontinued. Consequently, they are likely most effective as adjunctive therapy alongside anti-TNF agents.[34]

Advanced Therapies

Infliximab

The introduction of advanced therapies has significantly advanced the medical management of perianal CD. Infliximab, the first anti-TNFα monoclonal antibody approved for the treatment of CD, remains the cornerstone of therapy for PFCD.[34] Infliximab has been shown to induce fistula closure in approximately 55% of patients within 3 months; however, initial studies observed sustained response at one year in only about 36%.[39,40] While long-term remission rates remain below 50%, maintenance therapy with infliximab has been associated with reduced rates of hospitalization and surgical intervention in patients with perianal CD.[41] Despite the initial study by Present et al did not find a difference in outcomes between 5 mg/kg and 10 mg/kg, several studies have suggested higher serum levels of infliximab are associated with healing of PFCD.[42–45] A study found that infliximab levels greater than or equal to 10.1 mcg/mL may be associated with higher rates of response.[46] When evaluating for radiological improvement, an MRI study found that infliximab was highly successful at treating the surrounding inflammation of fistula tracts, however did not obliterate the tract.[47] Similarly, another study utilizing endoanal ultrasonography visualized the persistent fistula tracts, although inflammation and drainage were healed or improved.[48]

Adalimumab and Certolizumab

Although randomized controlled trials specifically evaluating adalimumab and certolizumab for perianal CD are lacking, subgroup analyses from larger clinical trials suggest these agents have moderate efficacy in promoting fistula healing. In the CHARM trial, patients treated with adalimumab achieved higher rates of fistula remission compared to placebo at both week 26 (30% vs 13%) and week 56 (33% vs 13%).[49] Similarly, the CHOICE trial reported that approximately 40% of patients experienced complete fistula healing from baseline, with sustained benefit observed over a two-year period.[50] Data from the PRECiSE 2 trial showed a 36% remission rate at 26 weeks among patients with perianal disease for certolizumab.[51]

Vedolizumab

Vedolizumab is an anti-integrin therapy designed to be gut selective. It is approved for moderate-to-severe CD, although data on its effectiveness in PFCD is limited. Data on vedolizumab's effect on fistula healing comes from a subgroup analysis of the GEMINI 2 trial, which showed a 33% probability of fistula closure at 52 weeks. Notably, the study population consisted of patients who had failed prior anti-TNF therapy, indicating that vedolizumab may be effective even in treatment-refractory cases.[52] Recent systematic reviews and meta-analyses, concluded that vedolizumab is not superior to placebo for either the induction or maintenance of fistula response. The certainty of evidence supporting its efficacy was rated as very low to moderate, given the most recent ENTERPRISE Phase IV trial that evaluated two IV regimens was underpowered due to early termination.[53,54]

Ustekinumab

Ustekinumab, an interleukin-12/23 antagonist, has been approved for the treatment of moderate to severe CD.[34] A subgroup analysis of the initial UNITI clinical trials demonstrated higher rates of fistula healing and response among ustekinumab-treated patients compared with placebo. At week 22, 47% of patients receiving ustekinumab achieved fistula healing compared with 30% in the placebo group (P = 0.33).[55] By week 44, fistula response was observed in 80% of patients treated with ustekinumab versus 46% in the placebo group (P = 0.64). The relatively high placebo response rate may be attributed to the fact that the placebo group received an induction dose of ustekinumab.[56] Although fistula responses at 6 and 12 months were 44% and 53.9%, respectively, the rate of complete fistula closure remained low at 17%, likely reflecting that most participants had previously failed at least one other biologic therapy.[57,58]

Mesenchymal Stem Cell Treatment

Mesenchymal stem cells (MSCs), found in many tissue types including adipose tissue and bone marrow, have gained considerable attention as a therapeutic option for various inflammatory and degenerative diseases, including graft-versus-host disease, systemic lupus erythematosus, myocardial infarction, multiple sclerosis, and CD.[59–63] These cells can be obtained either from the patient's own tissue (autologous) or from donor sources (allogeneic). MSCs possess anti-inflammatory and immunomodulatory functions, enabling them to home to sites of inflammation or tissue injury, where they promote an anti-inflammatory environment by regulating T cell activity and influencing cytokine production, ultimately aiding tissue repair.[64]

The local administration of MSCs directly into fistula tracts has emerged as a promising therapeutic approach. The earliest reported case in 2003 described successful closure of a refractory rectovaginal fistula following injection of autologous adipose-derived MSCs.[65] This breakthrough prompted numerous clinical trials (phases I through III) exploring the safety and effectiveness of MSC therapy for PFCD. These studies have utilized both autologous and allogeneic MSCs derived from bone marrow or adipose tissue, delivered in varying doses and either as single or multiple injections.[66–68]

The landmark Phase III randomized, placebo-controlled clinical trial, ADMIRE-CD, enrolled 212 refractory perianal fistulizing CD patients and demonstrated significantly higher fistula healing rates at six months with MSC treatment compared to placebo (51% vs 36%, p=0.021), with sustained benefits observed at one year (56% vs 39%, p=0.010). Follow-up studies revealed continued healing at two and three years, findings that contributed to updated clinical guidelines endorsing MSC use for complex perianal fistulas.[69,70]

Subsequent phase IB/IIA trials extended investigation to more complicated cases previously excluded from trials, such as patients with anal canal involvement, moderate proctitis, multiple internal fistula openings, vaginal fistulas, and pouch-related fistulas.[71,72] Despite these challenges, MSC treatment achieved healing rates up to 83%, outperforming control groups.[71] Pediatric studies have also shown favorable safety and efficacy outcomes, with no serious adverse events linked to MSC administration.[73]

Nevertheless, the results have not been universally positive. The larger ADMIRE II trial, which randomized 569 patients, did not demonstrate a significant benefit of MSC therapy over placebo. Thus, a biologics license application (BLA) was never submitted to the Food and Drug Administration (FDA) for approval. This, combined with considerable

cost and logistical complexities involved in MSC delivery resulted in pulling the approved MSC product from the European market, significantly impairing broad clinical utilization.[74]

Hyperbaric Oxygen Therapy

Hyperbaric oxygen therapy (HBOT) has been proposed as a potential adjunctive treatment for patients with ulcerative colitis and CD. The therapy involves breathing 100% oxygen at pressures higher than normal atmospheric levels. This state of hyperoxygenation and controlled oxidative stress has been shown to produce anti-inflammatory effects, promote stem cell mobilization, and enhance the expression of growth factors.[75]

A systematic review of observational studies reports that HBOT has shown complete healing of PFCD of 47.64% (95% CI: 22.05–74.54) while 34.29% (17.33–56.50) demonstrated partial healing.[76] The HOT-TOPIC trial, a prospective interventional cohort study, evaluated 20 patients with therapy-refractory perianal fistulizing CD who underwent 40 sessions of HBOT. The study demonstrated significant clinical and radiological improvements at 16 weeks, with sustained therapeutic responses observed at the one-year follow-up.[77] This growing evidence supports that HBOT may be a useful adjunctive treatment in therapy-refractive perianal CD.

Surgical Treatment

Up to 90% of patients with perianal CD will undergo at least one surgical procedure, with many requiring multiple interventions due to the refractory nature of the condition. Surgical options are often limited by the risk of impaired wound healing and fecal incontinence. Given these challenges, particularly in cases involving anal canal disease or proctitis, most surgeons adopt a conservative approach, typically using seton placement to control perianal sepsis while minimizing complications.

Incision and Drainage

The most frequently performed surgical procedure for perianal CD is incision and drainage (I&D) of a perianal abscess or undrained fistula.[78] While small, asymptomatic abscesses (<1 cm) identified on imaging may be managed medically, symptomatic abscesses require I&D to control perianal sepsis.[79–81] Although many abscesses are associated with underlying fistula tracts, some occur independently. Current guidelines recommend against actively probing for a fistula during abscess drainage when no tract is clearly identified, as this may risk the inadvertent creation of a false passage or internal opening. When a fistula is evident, management should be individualized. A lay-open fistulotomy is appropriate for simple, low, subcutaneous fistulas. On the other hand, seton placement is preferred for tracts involving the sphincter complex to minimize tissue injury and preserve continence.[28]

Seton Placement

The placement of a non-cutting loosely tied seton is a widely accepted and effective approach for managing complex perianal fistulas in CD, primarily to control ongoing sepsis and prevent its recurrence.[82–86] Typically, a nonabsorbable suture or vessel loop is passed through the fistula tract and loosely secured, allowing continuous drainage and keeping the tract open. Setons are often most effective when combined with medical therapy. One randomized controlled trial demonstrated improved fistula healing at 3 months when a seton was placed prior to initiating infliximab, compared to infliximab alone.[87]

A major challenge with seton use is determining the optimal timing for removal. Prolonged placement can lead to epithelialization of the tract, resulting in chronic fistulization. However, early removal carries a high risk of recurrence, with local sepsis recurring in up to 70% of cases and fistula recurrence rates reaching 80% at ten years.[6,82,88] Therefore, setons are best used as an adjunct during the induction of biologic therapy or as a temporary measure to control sepsis before more definitive surgical management, particularly in the absence of anal canal disease or proctitis. When active inflammation or proctitis is present, seton removal offers minimal benefit due to the near-certain risk of recurrent sepsis.[16] The PISA trial, a multicenter randomized controlled study, directly compared three treatment strategies for high PFCD; chronic seton drainage, anti-TNF therapy, and surgical closure following anti-TNF induction. The primary

outcome was the cumulative number of patients requiring fistula-related reinterventions at 1.5 years. The study found that chronic seton drainage alone was associated with the highest rate of reinterventions compared with the other treatment arms. Therefore, chronic seton drainage should not be used as monotherapy. Rather, anti-TNF therapy and surgical closure following medical induction appear more effective in reducing the need for further fistula-related procedures.[89]

Fistulotomy

Fistulotomy is rarely indicated in perianal CD due to the common presence of proctitis, anal canal involvement, diarrhea from proximal disease, and the risk of incontinence from sphincter disruption. However, in carefully selected patients, with a low-lying fistula that does not involve the sphincter complex and in the absence of anal canal disease or proctitis, simple fistulotomy can achieve healing rates of 80 to 100%.[9] In contrast, the presence of active proctocolitis significantly reduces healing rates to around 27% and increases the risk of poor wound healing and incontinence.[90] In such cases, the preferred approach is seton placement combined with optimized medical therapy.[87] Fistulotomy should be avoided when more than one-third of the sphincter is involved, as over 50% of these patients may experience some degree of incontinence.[91]

Fibrin Glue and Fistula Plug

Fibrin glue and bioprosthetic fistula plugs are sphincter-preserving interventions often considered in high-risk patients with PFCD. While both techniques avoid disruption of the sphincter complex, their long-term efficacy remains limited.

Fibrin glue, composed of fibrinogen and thrombin, is injected into the fistula tract to form a clot intended to seal and close the tract. Although early series reported promising outcomes, larger studies have yielded more limited results.[92,93] A multicenter randomized controlled trial involving 12 sites demonstrated clinical remission in 38% of patients at 8 weeks, compared to 16% in the observation group ($p = 0.04$). However, this study did not assess radiographic healing and lacked long-term follow-up.[94] The ECCO guidelines highlight that while fibrin glue is a sphincter-sparing option with favorable safety profile, it should not be isolated treatment and be considered an adjunct to medical therapy, such as an anti-TNF agent.[95] Other medical and surgical strategies should be prioritized given that a retrospective series demonstrated a worrisome cumulative incidence of PFCD related surgery within 5 years for 54% of patients treated with fibrin glue.[96,97]

Bioprosthetic plugs, constructed from bioabsorbable material, are placed within the fistula tract and secured with sutures. Small initial studies suggested high success rates, with one reporting 80% closure in a cohort of 20 patients at a median follow-up of 10 months. However, subsequent systematic reviews have reported healing rates between 55% and 58%.[98,99] Recent ECCO guidelines recommend against the use of fistula plugs in the treatment of PFCD, based on evidence from a single randomized controlled trial showing that the fistula plug was not more effective than seton removal alone.[95] Among patients with PFCD, 31.5% in the fistula plug group achieved fistula closure at Week 12 compared to 23.1% in the control group, a difference that was not statistically significant ($p = 0.45$). Adverse events were reported in 17 patients in the fistula plug group versus 8 in the control group, with no major safety concerns identified ($p = 0.07$).[100]

Endorectal Advancement Flap

Endorectal advancement flap repair is a sphincter-preserving surgical technique used for treating complex perianal fistulas, including those associated with CD. The procedure involves creating a full- or partial-thickness U-shaped flap of rectal mucosa and submucosa that includes the internal fistula opening at its base. This flap is mobilized, advanced over the internal opening, and sutured in place with absorbable suture, thereby closing the high-pressure end of the tract without compromising the external sphincter.[16]

Reported healing rates following endorectal advancement flap repair in CD vary widely, ranging from 25% to 64%.[82,101–104] A systematic review of 35 studies involving 1654 patients found an overall success rate of 64% in CD, compared to 81% in patients without underlying CD.[105] Despite these promising outcomes, the procedure carries a notable risk of postoperative incontinence. A 9% incontinence rate was reported at a median follow-up of 29 months, with additional series indicating rates as high as 10%. This risk appears to increase with repeated advancement flap procedures.[105–110]

Given the variability in outcomes and the potential for compromised continence, careful patient selection is essential. The procedure is best reserved for patients without active proctitis or significant anal stenosis, particularly those with preserved baseline continence.[107]

Ligation of Intersphincteric Tract (LIFT)

First introduced by Rojanasakul in 2007, the ligation of the intersphincteric fistula tract (LIFT) procedure is a sphincter-sparing surgical technique developed for the treatment of complex perianal fistulas.[111] The procedure involves making an incision at the intersphincteric groove, identifying the fistula tract within the intersphincteric space, ligating it at both the internal and external sphincter borders, and excising the intervening segment of the tract.[112]

Data on the use of LIFT in patients with CD remain limited. The largest reported series to date includes 23 patients from a single center, with a fistula healing rate of 48% at a median follow-up of 23 months and no reported cases of fecal incontinence, suggesting the procedure may be particularly suitable for patients without active proctitis.[113] Similarly, a separate series by Gingold et al involving 15 patients with CD demonstrated a 67% healing rate at one year, also without any incidence of incontinence. In this study, lateral fistula location and longer tract length were associated with improved long-term healing outcomes.[114] A meta-analysis confirmed this, reporting an overall success rate of 68.9% across 13 studies. The weighted overall recurrence rate was 21.9% based on 6 studies, with a subgroup analysis of studies with a minimum follow-up of 12 months showing a similar recurrence rate of 21.2%. When compared to the advancement flap, the LIFT procedure was associated with significantly lower incontinence rates (7.8% [3.3–12.4%] vs 1.6% [0.4–2.8%]).[115]

Fecal Diversion

Fecal diversion is sometimes employed as a standalone intervention or in conjunction with procedures such as advancement flap repair to promote fistula healing in PFCD. The primary rationale is to reduce intraluminal pressure at the internal fistula opening, thereby facilitating closure. While diversion often leads to significant symptomatic relief and improved quality of life, durable fistula healing without a permanent stoma remains uncommon.

A large meta-analysis including 556 patients with PFCD reported that 64% achieved an early clinical response following diversion. However, only 17% of patients underwent successful restoration of bowel continuity. Among those, 27% experienced fistula recurrence requiring re-diversion or additional surgical interventions. Ultimately, 42% of patients required proctectomy, underscoring the challenges of achieving long-term, stoma-free remission through diversion alone.[116] A recent retrospective review of 132 patients with medically refractory distal CD and advanced perianal disease, temporary ileostomy led to clinical improvement and reversal in only 19%, with 65% showing no improvement and 38% ultimately requiring proctocolectomy, emphasizing that diversion is largely ineffective in achieving durable clinical response.[117]

Proctectomy

Proctectomy remains the most definitive surgical option for patients with symptomatic, nonhealing perianal CD, though it is generally reserved as a last resort. Reported rates of proctectomy for refractory perineal disease range from 8% to 40%.[118] The likelihood of requiring this procedure increases in patients with a history of multiple prior perianal surgeries, temporary fecal diversion (42%), Crohn's colitis with rectal sparing (46%), and particularly in those with proctitis (89%).[8,78,110,116]

Most patients undergo numerous medical and surgical interventions before proceeding to proctectomy with permanent ostomy creation. In a series of 87 patients, the median number of procedures attempted prior to proctectomy was 12, with a median interval of 6.3 years from initial intervention to definitive surgery.[119]

De Groof et al suggests that performing a total mesorectal excision, rather than leaving the mesorectal fat in place to fill the pelvic dead space, may enhance perineal wound healing. This benefit is thought to result from removal of pro-inflammatory mesenteric tissue.[120] Given that perineal wound complications remain a significant challenge following proctectomy in CD, patients should be thoroughly counseled on the potential risks, including wound infection, prolonged wound care needs, and the development of chronic presacral sinuses.

Predictors of Recurrence

The most significant predictors of PFCD recurrence are the presence of active colitis, proctitis, and complex fistula anatomy. Recurrence rates in patients with Crohn's colitis have been reported as high as 84–100%.[8,90,91,103] In one small case series, none of the three patients with severe colitis and perianal fistulas achieved healing despite temporary fecal diversion and biologic therapy; all ultimately required permanent stomas.[121] Similarly, a study involving 513 patients with CD demonstrated a proctectomy rate of 67% in those with proctitis, compared to only 11% in patients without macroscopic rectal involvement.[80]

Regarding modifiable risk factors, the American College of Gastroenterology guidelines continue to identify active smoking as the only modifiable factor associated with postoperative recurrence. Smokers experience higher rates of perianal complications, stricturing disease, and require more interventions or surgeries.[122] Additionally, they have a reduced response to anti-TNF therapy and more frequent need for steroids, immunosuppressants, and biologics. Evidence indicates that smoking cessation is associated with improved outcomes and lower recurrence rates.[123]

Complex fistulas are also associated with higher procedural burden and increased rates of fecal diversion.[103] In cases of chronic, non-healing fistulas, clinicians should maintain a high index of suspicion for malignant transformation. Biopsy of the fistula tract is warranted in such scenarios, as approximately half malignancies are colonic and rectal adenocarcinomas (CRC), with a distinct subtype of mucinous adenocarcinoma, and the remainder are squamous cell carcinomas of the anus (SCCA).[124,125] A recent systematic review and expert consensus identified risk factors for SCCA, including smoking, early-onset disease, complex or long-standing perianal fistulas, HIV, immunosuppression, high-risk HPV, receptive anal intercourse, active colitis, and a stricturing phenotype. These findings strongly support the need for HPV vaccination and anal cancer screening in this population.[125]

Conclusion

Definitive treatment of perianal CD remains challenging. Infliximab achieves fistula healing in only half of patients, with adalimumab and certolizumab demonstrating even lower efficacy. Surgical options such as seton placement and advancement flaps carry risks, including incontinence, and often require prolonged management. Temporary fecal diversion can provide symptom relief, but recurrence after stoma reversal is common. Emerging therapies, such as adipose-derived mesenchymal stem cells, offer encouraging results without compromising continence, though widespread adoption is still limited. Therefore, the optimal care of patients with PFCD requires a multidisciplinary approach involving gastroenterologists, surgeons, and radiologists working collaboratively to improve outcomes in this debilitating disease.

Disclosure

The authors report no conflicts of interest in this work.

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