Operative Management of Perianal Crohn's Disease



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KEYWORDS

- Crohn's disease Perianal abscess Perianal fistula Anal fissure Anal skin tag
- Anal stenosis

KEY POINTS

- Discussion of preoperative care and patient selection for surgical management of perianal Crohn's disease.
- Review of surgical options for perianal fistulas in Crohn's disease and the technique to accomplish these surgeries.
- Review of clinical presentation, surgical options, and surgical techniques for the management of anal fissures, anal skin tags, and anal stenosis in Crohn's disease.

NATURE OF THE PROBLEM

Perianal Crohn's disease is a challenging aspect of Crohn's disease for both patients and the physicians and care teams managing these patients. Its quality of life impacts on the patient, the difficulty of successful treatment, and the high recurrence rate has led perianal Crohn's disease to be a notoriously unwelcome diagnosis. It also results in significant decreases in quality of life for patients due to pain, ongoing symptoms, sexual dysfunction, and fecal incontinence. Although most perianal disease presents with luminal Crohn's disease it can on occasion present before any other manifestation, making the diagnosis tricky. Many of the manifestations listed below have had advances in treatment options whereas some have had the same "do no harm" philosophy for decades.

MANAGEMENT

Abscesses and Fistulas

Clinical presentation

Perianal fistulas are likely the first thing most would associate with perianal Crohn's disease. Incidence of perianal fistulas is 12% to 33% in patients with Crohn's disease;

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showing increasing incidence with increase in the number of years with the disease. ^{2–4} The first symptom of a fistula is often an abscess. Patients will report pain and swelling in the perianal region, sometimes worse, before a bowel movement. Systemic symptoms can accompany this pain such as fatigue, malaise, and fever. The abscess may spontaneously rupture on its own, but many will seek medical treatment to have the abscess drained. Nonhealing wounds and continued leakage of purulence, blood, or even stool are common complaints of a fistula.

The most common classification of fistulas is the Parks classification, which defines the fistula based on the relationship to the anal sphincter complex. The descriptions are superficial, intersphincteric, transsphincteric, suprasphincteric, and extrasphincteric.⁵

Medical or pharmacologic management

For treatment of perianal Crohn's disease, it would be negligent to not discuss the utmost importance a multidisciplinary approach gives to the chances of successful treatment. Management of the intraluminal inflammation present will increase the likelihood for sustained perianal disease treatment. Antibiotics have been a popular treatment choice, particularly ciprofloxacin and metronidazole. However, with the advancement in biologic therapy, TNF- α inhibitors, with or without antibiotics, have shown to be an effective strategy in treatment of fistulizing Crohn's disease. The American Gastroenterological Association recommends against the use of antibiotics alone if no abscess is present. Use of biologics in patients with perianal Crohn's disease can make a profound impact for the patient. 51% of patients may have spontaneous closure of fistulas with biologics alone. Randomized controlled trials such as CHOICE, ACCENT II and PISA II have shown improvements such as decreased drainage, fistula closure, surgical closure success and improved Quality of Life with biologics. $^{8-11}$

Abscess

Treatment of active infection has paramount importance for both patient comfort as well as inflammation mitigation. A patient presenting with the signs of an acute abscess, such as swelling, erythema, pain and fluctuance should undergo an excision and drainage of the infection. Complex or deep fistulas may benefit from CT imaging to ensure all areas of infection are located for drainage. Simple abscesses may be drainable as a bedside or clinic procedure with local anesthetic. We recommend drainage of complex fistulas in the operating room to allow for adequate comfort and compliance of the patient during exploration. Care should be taken to inspect the deep postanal space either by radiographic imaging or intraoperative aspiration. Should purulence be noted in this space, it should be fully opened by partial division of the anal coccygeal ligament. Complex fistulas, or recurrent abscesses, are likely to benefit from seton placement. Noncutting setons, such as a vessel loop, are used for patients with Crohn's disease to decrease recurrent abscess formation or development of new fistula tracts.

Fistulas

Preoperative/preprocedure planning. Proper patient selection for surgical correction is a key element in successful treatment of fistulizing perianal Crohn's disease. Judicious use of noncutting setons in these patients in combination with biological treatment can help decrease ongoing inflammation and even complete healing. Use of biologics and a seton has shown success in complete closure of fistulas at a higher rate than biologics alone and sometimes equal to surgical intervention. ^{12,13} Seton removal can be considered once inflammation and ongoing drainage have subsided

and medical therapy is stable. In some patients, this may be the adequate therapy for closure. Many patients will have ongoing fistula symptoms and may need to be counseled on definitive surgical management options, which are described below. Continued, indefinite use of a seton is also a consideration for patients who find the symptoms more manageable with a seton and don't desire surgery or don't obtain disease guiescence required for surgical intervention to be successful. However, PISA I did show patients with seton placement alone have a high rate of reintervention, and this approach is inferior to the use of biologics or biologics followed by surgical closure.8 Patient's may need repeat incision and drainage or repeat seton placement if the seton inadvertently becomes discontinued, new abscess develops, or a branching fistula forms. Fig. 1 shows a patient with multiple abscesses who had seton placement in multiple fistula tracts but still developed a recurrent abscess when one of the setons fell out. Surgical intervention with ongoing active inflammation is ill-advised because of the high complication and recurrence rates. However, if the patient is a candidate for surgical intervention, doing so sooner rather than later seems to be associated with increased success. Laland and colleagues showed that success was associated with surgical intervention within 52 weeks from the start of biologics, and success for PISA II patients occurred with as little as 6 to 10 weeks of prior biologic therapy. 1,11 For complex branching fistulas, preoperative MRI may help distinguish and locate the various fistula tracts.

Once the decision for surgical intervention has been made, the next consideration is which surgical procedure to perform. Multiple surgeries have been described for perianal fistulas, and all are employable for patients with Crohn's disease. Overall success of each of these procedures is lower in Crohn's disease patients than the general population and multiple factors need to be considered for each patient. Considerations should include length of fistula tract, degree of sphincter involvement, prior surgeries, baseline continence, health of anal and rectal tissues, success rates, and surgeon experience. With multiple procedures, varying results, and complications to consider, each surgical intervention for perianal Crohn's disease must be decided upon a case by case basis and with shared decision-making with the patient. Specific procedures are covered separately below.

Prep & patient positioning. Multiple positions are acceptable for surgical intervention on perianal fistulas and/or abscesses. Considerations include fistula anatomy, body habitus, comorbidities, patient limb mobility, comfort of the anesthesiologist,

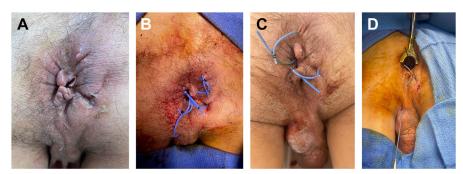


Fig. 1. (A) Young male with Crohn's disease presents with symptoms of multiple chronic fistulas and above is preoperative exam. (B) Shows his exam after setons were placed. Seton fell out and a recurrent abscess developed as shown in (C). Exam under anesthesia was performed and fistula tract is shown in (D).

equipment availability, and surgeon preference. Jackknife prone is an excellent choice for most perianal fistula procedures, but left lateral and lithotomy are also common choices. No bowel prep is routinely needed, though some surgeons may have a preference for mechanical bowel prep for complex fistulas. Preoperative antibiotics are also not necessary.

Procedural approach

Fistulotomy Fistulotomy involves the opening of the entire epithelialized tract to allow healing by secondary intention. This procedure often has the highest success rates reported but also has a risk of incontinence as partial sphincter division may be required. Simple fistulas involving less than a third of the sphincter muscle in a patient with normal baseline continence and excluding anterior fistulas in females are the best candidates for fistulotomy. The initial success rates are as high as 80% with recurrence rates up to 15%. ^{6,14} Owing to the risk of fecal incontinence, which is higher in Crohn's disease patients, caution is advised.

Technique

- Identification of fistula tract
 - Use a lacrimal duct probe placed through the external opening of the fistula tract and allow it to follow through to the internal opening.
 - This technique should not require force
 - Should the probe not run easily, switch to a smaller size
- Inspection of sphincter
 - Palpate the area of muscle distal to the probe by placing a finger on the skin and rolling it over the fistula probe
 - Consider the thickness of the muscle that will be opened
 - Palpate the length of the anal canal by placing a finger into the rectum and identifying the puborectalis muscle, the location of the internal fistula opening, and the end of the sphincter muscle
 - Consider the percentage of the length of the sphincter muscle that is involved
 - Identify the intershincteric groove by palpation
 - Consider the anatomic description of the fistula.
- Decision to proceed with fistulotomy
 - Taking the exam finding and patient history into account, decide if it is safe to proceed with fistulotomy without a high rate of incontinence
- Opening of fistula tract
 - Cautery is used to incise all tissue on top of the lacrimal probe
- Destruction of epithelialized tissue
 - Curettage the tract with a curette or sponge
- Marsupialization
 - The authors do not routinely marsupialize the wound edges but in cases of deep tracts, such as in obese patients, it is considered on a case by case basis
 - 3-0 Chromic or vicryl in a running fashion from the apex to the external opening on both sides
- Ensure hemostasis
 - o Judicious use of cautery or hemostatic agents

Ligation of intersphincteric fistula tract The ligation of intersphincteric fistula tract (LIFT) procedure involves identification and division of the fistula tract in the intersphincteric grove. An advantage of this procedure is limited damage to the anal sphincter muscle. Additionally, recurrences may occur with shorter intersphincteric

fistulas instead of long transphincteric fistulas. Initial healing occurred in 9 out of 15 Crohn's disease patients studied by Gingold and colleagues, though 1 patient did eventually redevelop symptoms at the fistula site, and 3 patients developed a new fistula. ¹⁵ All fistula tracts that healed were in the lateral position, and the surgery was proceeded by seton placement. Importantly, although it a small study, no patients experienced incontinence. These success rates have been reproduced in Crohn's disease patients. ¹⁶ Smoking is associated with decreased healing. ¹⁶ Postoperative MRI, also considered as radiological healing, has been associated with the lack of future recurrence. ^{11,17}

When compared directly to endorectal advancement flaps, van Praag and colleagues showed a higher clinical healing rate for LIFT (89% vs 60%); however, radiologic healing and recurrence were similar. This study found an incontinence rate of 15.8%.

Technique

- Identification of fistula tract
 - o Should a seton be in place, it is first replaced with a lacrimal duct probe
- Identification of intersphincteric groove by palpation
- Transverse or curvilinear incision is made over the intersphincteric groove
- Skin retractors can be used, such as rakes, or self-retaining retractors, such as a lone star device, but the authors find it often unnecessary
- A small right angle or hemostat can be used to spread in the intersphincteric groove until the fistula tract is identified and isolated
- A small right angle is used to pass 2 ties (3–0 vicryl for example) around the fistula tract; the probe is then removed. The ties are tied down on the proximal and distal sides with a centimeter of space between the 2
- Ligation of the fistula tract can be performed with scissors between the 2 ties. If length permits, a small section can be removed between the 2 ties.
- Curettage of external opening, or even a partial fistulotomy of the external tract, before sphincter involvement, can be done
- The LIFT incision can be closed with interrupted sutures or left open if small

Endorectal Advancement Flap This procedure involves covering the fistula tract with healthy rectal mucosa from above the fistula opening. This procedure also involves limited interaction with the anal sphincter muscles, but the dissection is easiest in uncompromised planes with no inflammation and can be difficult in Crohn's disease patients. Despite that conceptually the sphincter muscle should not be damaged in this procedure, the incontinence rate is reported to be 10% to 20%. ^{18,19} Full closure happens in 60% to 64% of patients with Crohn's Disease (CD) with an 18% to 19% recurrence rate, compared to 80% success in cryptoglandular abscesses. ^{18–20}

Technique

- Internal fistula tract opening is identified by probing the tract with a lacrimal duct probe
- Elevation of the submucosal plan with lidocaine with epinephrine to improve hemostasis
- U-shaped incision with a wide base is made in the mucosa with the base of the U
 just distal to the internal opening
- The flap is then raised using sharp dissection, such as Metzenbaum scissors or Electrocautery, taking care not to damage the sphincter muscle
 - Do not thin the flap
 - Include the entire submucosa

- Excise the internal opening from the flap
- Close the internal opening with interrupted suture
- The flap is then pulled to the edge for the cut mucosa and should not be under significant tension. If it does not reach easily, more tissue should be elevated
- Absorbable suture is used to secure the flap in an interrupted fashion, leaving enough room for drainage of hematoma or fluid under the flap, which could compromise the flap

Diversion For Crohn's disease patients who continue to have symptoms prohibitive of a good quality of life because of perianal disease, diversion could be a welcomed help. Patients with failure of biologics to improve intraluminal inflammation may achieve better inflammatory control with an ileostomy, which may open the door for fistula intervention and healing, while diverted. Temporary fecal diversion may be needed in up to 50% of the patients with perianal CD.²¹ In a recent metanalysis by Jew and colleagues, 61% of patients had symptom improvement with diversion.²² Initial healing of perianal disease may occur in up to 56% and often within the first year.²¹ The concern with fecal diversion has long been the possibility of permanent ostomy. This is still a concern, even in this biologic era as successful restoration of intestinal continuity was found to only be 16.6% to 21% in meta-analysis.²¹⁻²³ Patients may decide to keep the ostomy out of preference; lack of disease response or disease progression can lead to proctectomy. Proctectomy and permanent ostomy would be the last option for control of perianal disease. Need for proctectomy after diversion occurs in 34% to 42% of patients despite increased use in biologics. 22-24 Some studies suggest that the use of biologics, and the earlier the fecal diversion is done before failure of all biologic options, the more likely a patient may be to have the ostomy reversed. 21,22,24,25

Additional Considerations Another challenging situation is the fistulizing perianal disease in a patient with an ileo pouch-anal anastomosis (IPAA). A stricture or fistula in a Crohn's patient with an IPAA can be diagnostically complex to determine if this finding is due to technical complication or inflammation from Crohn's disease. A multidisciplinary approach is required. A fistula forming directly from the anastomosis is likely technical, but a fistula arising more distal, from the anus, is more likely to be fistulizing Crohn's disease. Similar thoughts may be applied to the timing of the complication with the earlier complications favoring surgical etiologies. Initial management would be to initiate biological therapy and observe for a response.

Surgical intervention is a daunting task. The Cleveland clinic recently reported on a series of 91 such patients. In this retrospective study, 68% healed with perioperative medical management. Although several patients had multiple surgeries, there was a 59.3% healing rate for those who underwent surgery. The individual surgical success was as follows: fistulotomy (56.7%), advancement flap (33.3%), fistula plug (33.3%), redo-pouch (28.6%), seton + fistulotomy (25%), episoproctomy (20%), seton placement (12.1%) Mesenchymal stem cells (MSCs) (0%), and gracilis flap (100%).²⁶ 18.7% had diversion during treatment options with a 58.8% closure rate and overall pouch failure rate was 12.1%.²⁶ Another interesting finding was that patients who had seton placement at any point were actually less likely to heal.²⁶ Although the high volume experience of this institution must be considered, the results are overall encouraging for this population group.

Emerging Therapies and Emerging Treatment

Although fistula plugs, fibrin glue, laser ablation, and video assisted treatment have been discussed for more than a decade, they have failed to muster sustained enthusiasm owing to varied or low success rates, often barely above 50%.^{27,28} The low morbidity of these procedures does sometimes make them a tempting option for Crohn's disease patients.

MSC has been the most promising emerging therapy of the last few years. The treatment is not readily available to all patients, and the techniques are not well standardized. Injection of allogenic MSC into the fistula tract has had a success rate of 50% to 67%, and this does include some more difficult fistulas such as rectovaginal and ileo pouch fistulas. ^{29,30} Patients may still have improvement of symptoms even if complete healing does not take place. ²⁹ Autologous MSCs have been used as an injection into the tract with a mucosal advancement flap or applied to fistula plugs (STOMP). These studies have shown success rates of up to 80% to 91% at 6 month with nearly no adverse events. ^{31–33}

FISSURES AND ULCERS Clinical Presentation

Anal fissures in Crohn's disease are typically broad based and deep with undermined edges.³ In contrast to the idiopathic fissures, which are commonly in the midline, fissures associated with Crohn's disease may be located anywhere around the anal canal and are often multiple in nature. Clinical presentation is more commonly painless bleeding rather than the typical painful fissures, which present secondary to other etiologies.³ Fissures may be acute or chronic with chronicity typically defined by persistence beyond 6 weeks and other clinical features, such as sentinel pile, hypertrophied anal papilla, or cyanotic hue to the surrounding skin.³⁴

Anal canal ulcers in the setting of Crohn's disease are almost always associated with luminal rectal inflammation. These ulcerations can result in the development of strictures, fistulas, or abscesses. Presenting symptoms are commonly related to the sequela of the ulcer.

Medical and Pharmacologic Management

Standard medical management of anal fissures includes fiber-supplementation and sitz baths. There are little data to support the use of topical agents such as topical glycerol trinitrate, isosorbide dinitrate, diltiazem, or botulinum toxin injection for anal fissures in the setting of Crohn's disease. The etiology of Crohn's disease fissures is thought to result from ulcerations secondary to the Crohn's disease process and not related to hypertrophy or spasm of the internal sphincter, which is why treatments aimed at relaxing the anal sphincter are avoided. This is also why multidisciplinary management with gastroenterology is paramount as optimization of the underlying Crohn's disease will most likely help this symptom.

SKIN TAGS Clinical Presentation

Skin tags are considered secondary lesions, which results because of complications from primary lesions such as fissures and ulcers. There are 2 types of skin tags described. The first type results from healed anal fissures or ulcers and appears as large, edematous, hard, cyanotic skin tags. These skin tags often coexist with intestinal inflammation. The second type referred to as "elephant ear" tags are flat, soft, and can be broad or narrow.

Preoperative and Preprocedure Planning

Some controversy exists regarding the excision of skin tags and hemorrhoids in patients with inflammatory bowel disease. Several recent studies have investigated

the link between excisional hemorrhoidectomy or skin tag excision and the need for proctectomy in patients with Crohn's disease. They have concluded that the link is likely related to the natural course of perianal Crohn's disease and not a direct result of having undergone the procedure. This finding indicates that, in appropriately selected patients without evidence of luminal rectal inflammation, skin tag excision is safe. Surgical excision of the large, firm cyanotic tags is ill-advised because of the potential for poor wound healing and management should include treatment of the intestinal disease. The soft, painless "elephant ear" tags can be safely excised if they cause problems with maintenance of perianal hygiene, and there is no evidence of rectal inflammation.

Prep and Patient Positioning

Skin tag removal requires no bowel preparation or perioperative antibiotics. The procedure can be performed using local anesthetic in the clinic setting or in the operating room under general or regional anesthesia. Typical positioning is prone jackknife position, lithotomy, or lateral decubitus. Similar to other perianal procedures, in the setting of Crohn's disease, it is imperative to rule out active rectal inflammation before operating.

Procedural Approach

Skin tag removal

Technique

- Anoscopy to evaluate for anorectal inflammation
- Excision
 - Methods include
 - Sharp excision
 - Suture ligation
 - Electrocautery
 - Cryoablation
 - Laser
- Leave wound open to heal by secondary intention or close with absorbable suture

Recovery & rehabilitation

Recovery after skin tag removal is similar to the above perianal surgeries. Patients should require minimal pain medications and are encouraged to take warm baths, keeping the surgical area clean and dry. Return to usual activity is rapid.

STRICTURES

Clinical Presentation

Strictures are another secondary lesion that can result as complications from ulcerations, abscesses, fissures, and/or fistulas. Anorectal strictures should raise suspicion for malignancy and require biopsy to rule out cancer. They may be short (<2 cm) and annular or long and tubular. Many patients are asymptomatic, but some may present with incontinence, urgency, frequency, tenesmus, change in stool caliber, or difficulty with defecation. Although many patients are asymptomatic, when strictures result in symptoms, it can be particularly morbid for patients and result in decreased quality of life.

Preoperative or Preprocedure Planning

Most patients have minimal or no symptoms and do not require treatment. First-line therapy for symptomatic strictures is nonsurgical management with diet, fiber-supplementation, and stool softeners. Strictures with symptoms that are refractory

to lifestyle modification are managed with dilation. Options for dilation include selfdilation with single finger, Hegar's dilators, or coaxial balloons. Most patients will require repeat dilations.^{3,41} Symptomatic strictures refractory to dilation therapy may require procedures, such as anoplasty or even proctectomy.³⁴

Prep & Patient Positioning

Dilation of anal strictures is an outpatient procedure that can be performed in the clinic or in the operating room with the aid of anesthesia. No bowel preparation or perioperative antibiotics are indicated.

Procedural Approach

Anal stricture dilation

Technique

- Anoscopy to evaluate for anorectal luminal inflammation
- Dilate
 - Lubricate and insert dilator^a to halfway point
 - ∘ Turn 360°
 - Remove
 - Repeat with next size dilator

Recovery & rehabilitation

Recovery after anal stricture is minimal. Patients may return to normal activity within hours. Patients should continue their fiber supplementation and avoid constipation. Many patients require repeat dilations and the time between dilations can be variable.

SUMMARY

The perianal manifestations of Crohn's disease including abscesses, fistulas, fissures, ulcers, skin tags, and strictures can be significant quality of life limiting-diagnoses. The frustrating nature of the symptoms in patients can lead to an increasing pressure to act surgically on these diagnoses. Therefore, it is important to maintain proper patient selection and treat intraluminal disease before initiating surgical treatment. Surgical management of perianal fistulas includes fistulotomy, LIFT, endorectal advancement flap, and diversion in select cases. Anal fissures should be treated with optimization of medical therapy for the underlying Crohn's disease. Skin tags can be excised if they are not associated with active inflammation. Surgical management of symptomatic strictures includes dilation. All of the aforementioned surgical therapies for perianal Crohn's disease follow the same general principles: control of sepsis, control of anorectal symptoms, minimization of complications, and avoidance of proctectomy.

CLINICS CARE POINTS

- Choice of surgical management for perianal fistulas in will depend on patient, disease, and surgeon factors.
- Despite advancement in biologic treatment options, permanent ostomy is a possibility for patient with perianal Crohn's disease.

^a Alternative options include finger dilation or balloon dilation.

- Skin tags may be excised in the absence of rectal inflammation when they interfere with maintenance of perianal hygiene.
- Most anal strictures in Crohn's disease are asymptomatic. When symptomatic and without
 active inflammation, the surgical therapy of choice is dilation. Refractory cases may
 require proctectomy.

DISCLOSURES

The authors have nothing to disclose.

REFERENCES

- 1. Laland M, François M, D'Amico F, et al. Identification of the optimal medical and surgical management for patients with perianal fistulising Crohn's disease. Colorectal Dis 2023;25(1):75–82.
- 2. Park SH, Aniwan S, Scott Harmsen W, et al. Update on the natural course of fistulizing perianal Crohn's disease in a population-based cohort. Inflamm Bowel Dis 2019;25(6):1054–60.
- 3. Sandborn WJ, Fazio VW, Feagan BG, et al. AGA technical review on perianal Crohn's disease. Gastroenterology 2003;125(5):1508–30.
- 4. Schwartz DA, Loftus EV, Tremaine WJ, et al. The natural history of fistulizing Crohn's disease in Olmsted County, Minnesota. Gastroenterology 2002;122(4):875–80.
- 5. Parks AG, Gordon PH, Hardcastle JD. A classification of fistula-in-ano. Br J Surg 1976;63(1):1–12.
- 6. Williams JL, Shaffer VO. Modern management of perianal Crohn's disease: a review. Am Surg 2021;87(9):1361–7.
- Feuerstein JD, Ho EY, Shmidt E, et al. AGA clinical practice guidelines on the medical management of moderate to severe luminal and perianal fistulizing Crohn's disease. Gastroenterology 2021;160(7):2496–508.
- 8. Wasmann KA, de Groof EJ, Stellingwerf ME, et al. Treatment of perianal fistulas in Crohn's disease, seton versus anti-TNF versus surgical closure following anti-TNF [PISA]: a randomised controlled trial. J Crohns Colitis 2020;14(8):1049–56.
- Lichtiger S, Binion DG, Wolf DC, et al. The CHOICE trial: adalimumab demonstrates safety, fistula healing, improved quality of life and increased work productivity in patients with Crohn's disease who failed prior infliximab therapy. Aliment Pharmacol Ther 2010;32(10):1228–39.
- Papamichael K, Vande Casteele N, Jeyarajah J, et al. Higher postinduction infliximab concentrations are associated with improved clinical outcomes in fistulizing Crohn's disease: an ACCENT-II post hoc analysis. Am J Gastroenterol 2021; 116(5):1007–14.
- 11. Meima-van Praag EM, Becker MAJ, van Rijn KL, et al. Short-term anti-TNF therapy with surgical closure versus anti-TNF therapy alone for Crohn's perianal fistulas (PISA-II): long-term outcomes of an international, multicentre patient preference, randomised controlled trial. EClinicalMedicine 2023;61:102045.
- 12. Regueiro M, Mardini H. Treatment of perianal fistulizing Crohn's disease with infliximab alone or as an adjunct to exam under anesthesia with seton placement. Inflamm Bowel Dis 2003;9(2):98–103.
- 13. Abramowitz L, Brochard C, Pigot F, et al. Surgical closure, mainly with glue injection and anti-tumour necrosis factor α, in fistulizing perianal Crohn's disease: a multicentre randomized controlled trial. Colorectal Dis 2022;24(2):210–9.

- 14. Parian AM, Obi M, Fleshner P, et al. Management of perianal Crohn's disease. Am J Gastroenterol 2023;118(8):1323–31.
- 15. Gingold DS, Murrell ZA, Fleshner PR. A prospective evaluation of the ligation of the intersphincteric tract procedure for complex anal fistula in patients with Crohn's disease. Ann Surg 2014;260(6):1057–61.
- 16. Wood T, Truong A, Mujukian A, et al. Increasing experience with the LIFT procedure in Crohn's disease patients with complex anal fistula. Tech Coloproctol 2022; 26(3):205–12.
- Meima-van Praag EM, van Rijn KL, Monraats MA, et al. Magnetic resonance imaging after ligation of the intersphincteric fistula tract for high perianal fistulas in Crohn's disease: a retrospective cohort study. Colorectal Dis 2021;23(1):169–77.
- 18. van Praag EM, Stellingwerf ME, van der Bilt JDW, et al. Ligation of the intersphincteric fistula tract and endorectal advancement flap for high perianal fistulas in Crohn's disease: a retrospective cohort study. J Crohns Colitis 2020;14(6): 757–63.
- 19. Soltani A, Kaiser AM. Endorectal advancement flap for cryptoglandular or Crohn's fistula-in-ano. Dis Colon Rectum 2010;53(4):486–95.
- Stellingwerf ME, van Praag EM, Tozer PJ, et al. Systematic review and metaanalysis of endorectal advancement flap and ligation of the intersphincteric fistula tract for cryptoglandular and Crohn's high perianal fistulas. BJS Open 2019;3(3): 231–41.
- 21. McCurdy JD, Reid J, Yanofsky R, et al. Fecal diversion for perianal Crohn disease in the era of biologic therapies: a multicenter study. Inflamm Bowel Dis 2022; 28(2):226–33.
- 22. Jew M, Meserve J, Eisenstein S, et al. Temporary faecal diversion for refractory perianal and/or distal colonic Crohn's disease in the biologic era: an updated systematic review with meta-analysis. J Crohns Colitis 2024;18(3):375–91.
- 23. Singh S, Ding NS, Mathis KL, et al. Systematic review with meta-analysis: faecal diversion for management of perianal Crohn's disease. Aliment Pharmacol Ther 2015;42(7):783–92.
- 24. Hain E, Maggiori L, Orville M, et al. Diverting stoma for refractory ano-perineal Crohn's disease: is it really useful in the anti-TNF era? A multivariate analysis in 74 consecutive patients. J Crohns Colitis 2019;13(5):572–7.
- 25. Coscia M, Gentilini L, Laureti S, et al. Risk of permanent stoma in extensive Crohn's colitis: the impact of biological drugs. Colorectal Dis 2013;15(9):1115–22.
- 26. Otero-Piñeiro AM, Hull T, Holubar S, et al. Surgical options for the treatment of perianal and anovaginal fistulas in the setting of ileoanal pouch Crohn's disease: experience of a tertiary center. J Gastrointest Surg 2023;27(12):2867–75.
- 27. O'Riordan JM, Datta I, Johnston C, et al. A systematic review of the anal fistula plug for patients with Crohn's and non-Crohn's related fistula-in-ano. Dis Colon Rectum 2012;55(3):351–8.
- 28. Alam A, Lin F, Fathallah N, et al. FiLaC(®) and Crohn's disease perianal fistulas: a pilot study of 20 consecutive patients. Tech Coloproctol 2020;24(1):75–8.
- 29. Lightner AL, Reese JS, Ream J, et al. A phase IB/IIA study of ex vivo expanded allogeneic bone marrow-derived mesenchymal stem cells for the treatment of rectovaginal fistulizing Crohn's disease. Surgery 2024;175(2):242–9.
- 30. Reenaers C, Gillard RP, Coimbra C, et al. Clinical and MRI evolution after local injection of bone marrow-derived mesenchymal stem cells in perianal fistulae in Crohn's disease: results from a prospective monocentric study. J Crohns Colitis 2023;17(5):728–37.

- 31. Dietz AB, Dozois EJ, Fletcher JG, et al. Autologous mesenchymal stem cells, applied in a bioabsorbable matrix, for treatment of perianal fistulas in patients with Crohn's disease. Gastroenterology 2017;153(1):59–62.e2.
- 32. Dozois EJ, Lightner AL, Dietz AB, et al. Durable response in patients with refractory fistulizing perianal Crohn's disease using autologous mesenchymal stem cells on a dissolvable matrix: results from the phase I stem cell on matrix plug trial. Dis Colon Rectum 2023;66(2):243–52.
- 33. Wainstein C, Quera R, Fluxá D, et al. Stem cell therapy in refractory perineal Crohn's disease: long-term follow-up. Colorectal Dis 2018;20(3):068–75.
- 34. Safar B, Sands D. Perianal Crohn's disease. Clin Colon Rectal Surg 2007;20(4): 282–93.
- 35. Buchmann P, Keighley MR, Allan RN, et al. Natural history of perianal Crohn's disease. ten year follow-up: a plea for conservatism. Am J Surg 1980;140(5):642–4.
- 36. Wolkomir AF, Luchtefeld MA. Surgery for symptomatic hemorrhoids and anal fissures in Crohn's disease. Dis Colon Rectum 1993;36(6):545–7.
- 37. Fleshner PR, Schoetz DJ, Roberts PL, et al. Anal fissure in Crohn's disease: a plea for aggressive management. Dis Colon Rectum 1995;38(11):1137–43.
- 38. Nelson RL, Manuel D, Gumienny C, et al. A systematic review and meta-analysis of the treatment of anal fissure. Tech Coloproctol 2017;21(8):605–25.
- 39. Elsebae MM. A study of fecal incontinence in patients with chronic anal fissure: prospective, randomized, controlled trial of the extent of internal anal sphincter division during lateral sphincterotomy. World J Surg 2007;31(10):2052–7.
- 40. McKenna NP, Lightner AL, Habermann EB, et al. Hemorrhoidectomy and excision of skin tags in IBD: harbinger of doom or simply a disease running its course? Dis Colon Rectum 2019;62(12):1505–11.
- 41. Scheurlen KM, MacLeod A, Kavalukas SL, et al. State-of-the-art surgery for Crohn's disease: part III-perianal Crohn's disease. Langenbeck's Arch Surg 2023;408(1):132.