Uma Mahadevan MD, Series Editor
**guildconference.com**

# Managing Perianal Fistula

Adam Truong

Miguel Regueiro

Amy L. Lightner

**Perianal fistulas are major sources of morbidity worldwide which often require a protracted treatment course. Most simple fistulas can be managed with fistulotomy, but surgeons should remain conservative as any amount of sphincter division may result in incontinence. Management of complex fistulas are nuanced and imaging modalities may be utilized for preoperative planning. In cases of perianal Crohn's disease, medical and surgical treatments are evolving, but often require prerequisite sepsis control through seton placement. In this report, we review the range of classic and novel treatment strategies for perianal fistulas.**

## INTRODUCTION

Perianal fistula(s), anorectal fistula(s), or fistula(s)-in-ano are synonymous terms for a common anorectal disorder with an incidence of 70-96,000 cases per year amongst Americans and approximately 1.0-2.3 per 10,000 people in the European Union, although the diagnosis of perianal abscesses is likely underdiagnosed.[1-4] A perianal fistula is a chronic abnormal communication between the rectum/anus and the perianal skin through an epithelialized tunnel. In this chapter, we describe the diagnosis and classification of perianal fistulas, and review the wide range of traditional and novel treatment strategies.

Adam Truong MD, Miguel Regueiro MD, Amy L. Lightner MD, FACS Digestive Disease Institute, Division of Colorectal Surgery Cleveland Clinic, Cleveland, OH

Dr. Lightner has the following disclosures: consultant to Ossium, Takeda and Mesoblast. Dr. Regueiro has the following disclosures: advisory Board and Consultant for Abbvie, Janssen, UCB, Takeda, Pfizer, Miraca Labs, Amgen, Celgene, Seres, Allergan, Genentech, Gilead, Salix, Prometheus, Lilly, TARGET Pharma Solutions, ALFASIGMA, S.p.A., Bristol Meyer Squibb (BMS) Dr. Truong has no disclosures.

### Pathophysiology

Over 90% of perianal fistulas are cryptoglandular in origin, meaning they develop as a sequela of an anorectal abscess.[5] The proportion of patients with a clinically significant anorectal abscess who subsequently develop a fistula ranges between 20-40%, even after surgical incision and drainage.[6-10] The exact pathophysiology for the formation of a perianal abscess is still unknown, but the prevailing hypothesis is that it results from the infiltration of enteric microorganisms into perianal gland channels causing inflammation and obstruction that

*(continued on page 18)*

(continued from page 11)

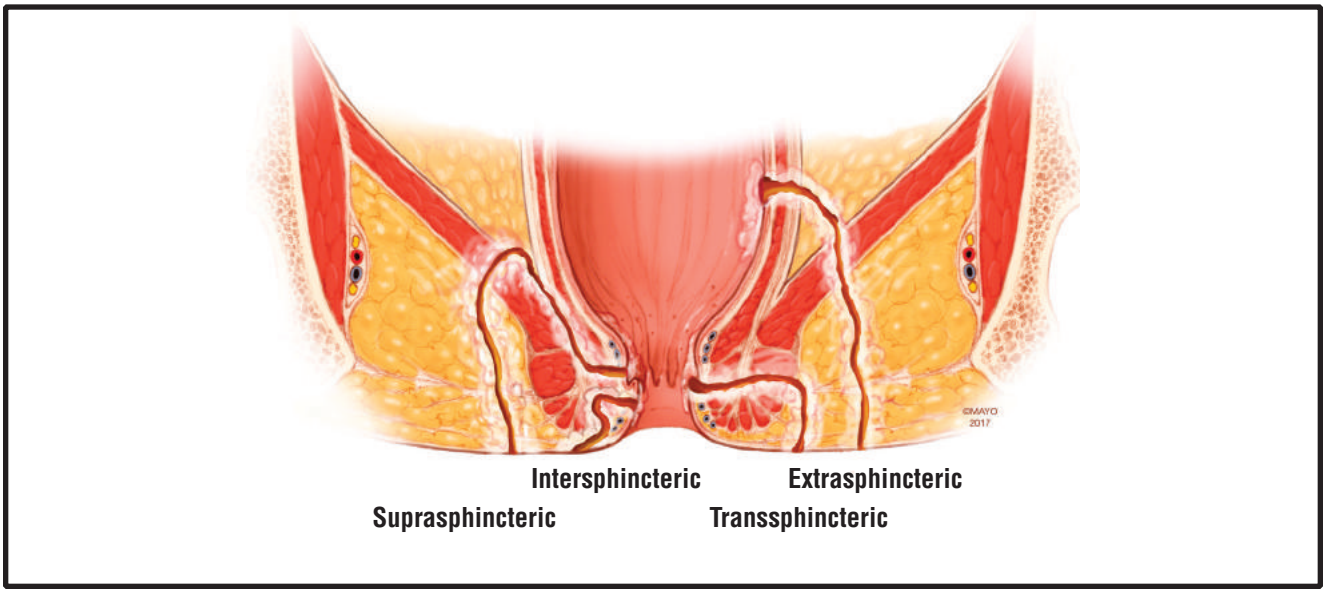


**Figure 1. Perianal Fistula Tracts.**
**Illustration of Parks' classification in the coronal plane**

perpetuate further bacterial growth.[11] The infection spreads outward through soft tissue until it finds an exit through the skin surface; accordingly, anorectal abscess and perianal fistula should be considered on the same pathogenic spectrum.

Alternatively, fistulas may occur from non-cryptoglandular causes such as penetrating perineal trauma, malignancy, ischemia, or chronic inflammation such as inflammatory bowel disease. Tissue healing is a complex molecular process involving inflammatory cytokines, mesenchymal cell activity (from epithelial-mesenchymal transition), extracellular matrix building/alteration, vascularity, oxygen, and hospitable healing environments.[11] Perturbations of any of these factors may predispose the patient to formation of these non-cryptoglandular fistulas. Consistent evaluation and reevaluation of these risk factors in cases of non-healing or recurrence are necessary to achieve effective and lasting fistula remission.

## Anatomy

To understand the diagnosis and treatment options for perianal fistulizing disease, a thorough understanding of the anal sphincter complex anatomy is essential. The external anal sphincter is under voluntary control and is composed of striated muscle continuous with the puborectalis and levator ani muscles. It lays superficial, external, and "cups" the internal anal sphincter which is composed of involuntarily controlled smooth muscle, comprising 85% of the resting anal tone.[12] The internal sphincter smooth muscle is continuous with the circular smooth muscle of the rectum. Rectal distension causes involuntary relaxation of the internal anal sphincter, also known as the rectoanal inhibitory reflex, followed by a reflexive contraction of the external anal sphincter preventing accidental release of rectal contents. Fecal continence is maintained by both the internal and external anal sphincters and their autonomic interaction.

A perianal fistula is the pathologic communication between the anal canal and the skin through a narrow tunnel lined by an epithelial surface. These most commonly originate at the level of the dentate line where the squamocolumnar junction and 4-10 anal glands reside (Figure 1). The Parks' classification system is the most widely used classification system for anal fistulas, defining the fistula anatomy based on the relationship to the anal sphincter complex (Table 1).[5] While the true prevalence of each fistula type is unknown and likely varies across countries, the vast majority of fistulas are of the intersphincteric and transsphincteric varieties. Suprasphincteric

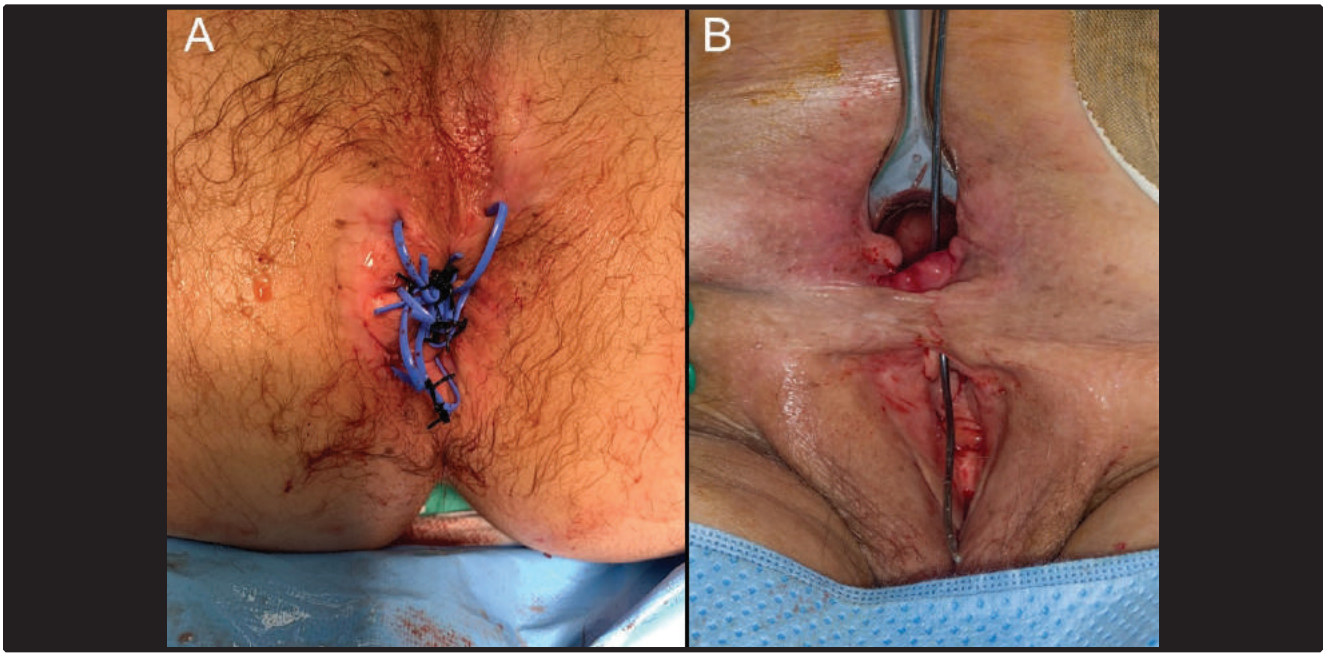


**Figure 2. Complex Fistulas.**
**Examples of complex perianal fistulas include those with A) multiple openings or B) vaginal involvement.**

and extrasphincteric fistulas are most often associated with non-cryptoglandular etiologies. The modified Parks' classification system adapts the Parks' classification and includes the addition of submucosal fistulas which are superficial and do not traverse any sphincter muscle. Division of these fistulas pose no risk of incontinence.

Goodsall's rule offers some guidance to the path of the fistula. The rule states that the external opening of the fistula tract located anterior to a transverse line drawn across the anus travels in a direct straight path to the anal canal/rectum. In contrast, if the external opening is posterior to the transverse anal line, the fistulous path may be curved or unpredictable. Awareness of these tendencies are critical for treatment planning.

## Epidemiology

Most perianal abscesses are diagnosed during the 4-5th decade of life and are more common in men.[4] Independent predictors of fistulization after perianal abscess formation are female gender, age between 41-60 years, diabetes mellitus, and ischiorectal or intersphincteric location of the initial abscess.[10,16] There is minimal data to suggest that anal-receptive intercourse, poor hygiene, and obesity are associated with abscess formation.

Other factors associated with anorectal abscesses and fistulas include chronic systemic inflammation such as inflammatory bowel disease (IBD), immunocompromised states such as human immunodeficiency virus, and tobacco use.[17,18] Crohn's disease (CD) is a well-known risk factor for the development of perianal disease and patients with active rectal disease are at greatest risk. Hellers, et al. estimated that 15% of those with ileocolonic CD with rectal involvement had perianal fistulas, compared with 41% with rectal-sparing colonic involvement, and 92% with both colon and rectal involvement.[19,20] Younger age of CD onset and African-American race or Hispanic ethnicity also increase the risk of perianal CD.[21,22]

## Diagnosis

### *CLINICAL PRESENTATION*

Frequently, a detailed history and physical examination is sufficient to diagnose an anorectal abscess. Perianal pain, swelling, erythema, and tenderness are common symptoms that occur rapidly over the course of several days to weeks. Fever is not often reported by patients.

**Table 1. Modified Parks' Classification**

| | Type | Origin | Path | Frequency[13-15] |
|---|---|---|---|---|
| **Simple** | Submucosal | Dentate line | Submucosal, superficial to the internal and external anal sphincters | 15% |
| | Intersphincteric | Dentate line | Between the internal and external anal sphincters towards the skin | 24-70% |
| **Simple if low/ Complex if high** | Transsphincteric | Dentate line | Through the internal and external anal sphincters towards the skin | 23-58% |
| **Complex** | Suprasphincteric | Dentate line | Between the internal and external anal sphincters superiorly, travelling through the puborectalis then exiting back through the levator ani towards the skin | 2-3% |
| | Extrasphincteric | Rectum | Through the levator ani towards the skin | 1-5% |

An indurated fluctuant tender mass is seen on visual examination in a superficial abscess. A digital rectal exam often elucidates the diagnosis and clarifies the abscess location but is often not tolerated by patients without sedation or anesthesia. The differential diagnosis includes a thrombosed external hemorrhoid, fissure, pilonidal disease or hidradenitis, venereal disease, CD, or anal cancer. In these cases, inquiring about trauma or high-risk sexual practices and a thorough review of systems is paramount. A patient's bowel habits and practices, anal sphincter function, previous anorectal surgery, and comorbidities are also key for surgical planning.

Patients with perianal fistula following treatment of anorectal abscess will typically report perianal swelling and foul-smelling drainage. The induration and pain often wax and wane as abscesses bloom then drain through the fistula. Fistulas are classified as "simple" or "complex". A simple fistula is low (submucosal, intersphincteric, and low transsphincteric) with minimal internal anal sphincter involvement and has a single fistula opening. A complex fistula is high (high transsphincteric, extrasphincteric, or suprasphincteric), has multiple external openings, or exits anteriorly as a rectovaginal fistula (Figure 2). Further, complex fistulas are associated with non-cryptogenic causes such as CD or malignancy.[23]

Patients with spontaneous fistula following resolution of a remote anorectal abscess or recurrent fistula following treatment should undergo workup of non-cryptogenic causes. Throughout the process of diagnosis and treatment of anorectal abscesses and fistulas, revisiting and questioning the etiology is important to avoid misdiagnosis.

### *IMAGING*

Most abscesses and fistulas are diagnosed by a history and physical and do not typically require imaging.[24] Further detail about potential secondary abscesses or fistula tracts can be investigated during treatment and instrumentation. In cases of complicated fistulas, imaging may be useful to define anatomy and determine sphincter involvement.

A fistulogram may be helpful to evaluate a surgical reference in high transsphincteric,

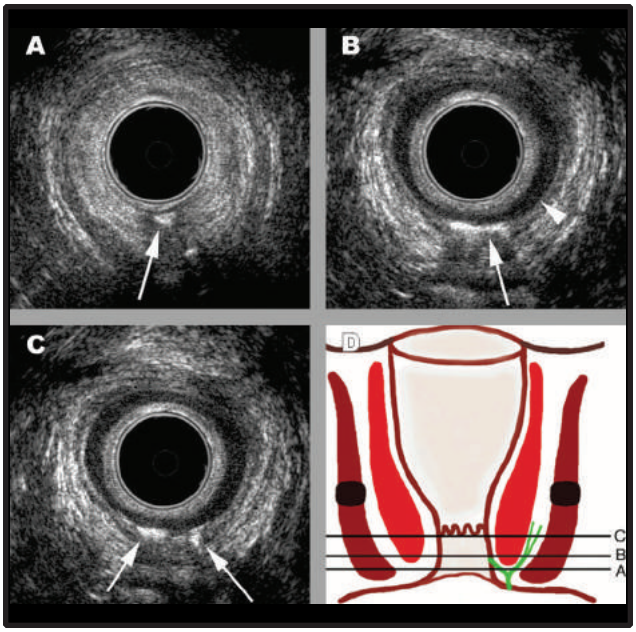


**Figure 3. Endoanal Ultrasound.**
**Endoanal ultrasound image of an intersphincteric fistula with complex tract aided by hydrogen peroxide administration. A) the fistula (arrow) extends below the level of the internal anal sphincter (arrow) and B) upwards into the intersphincteric plane. C) The fistula tract is seen branching within the intersphincteric plane. D) A drawing in the coronal plane with horizontal lines corresponding to the levels of the ultrasound images and the green showing the fistula extent. Reprinted with permission.[28]**

suprasphincteric, or extrasphincteric fistulas and may identify secondary tracts. A fistulogram is performed by inserting an 8-French foley catheter into the external fistula opening, occluding the opening with the balloon and then injecting the tract with contrast under pressure. A balloon with radiopaque fluid within the anus helps mark the puborectalis muscle and assists in determination of anal canal length. While studies report the ability to identify 75% of internal fistula openings and 92% of secondary tracts, [25] it can be technically difficult to perform, complicated to interpret, and requires expertise. We do not routinely employ fistulography.

Computed tomography may assist in perianal abscess characterization but is of minimal value for fistulas given its inadequate soft tissue contrast resolution.[23,25] Pelvic magnetic resonance imaging (MRI) provides improved diagnostic accuracy for fistulas but has limited resolution for determining internal fistula openings and cannot discern the dentate line.[25,26] Its strength lies in the cross-sectional evaluation of the pelvic floor. Endoanal ultrasound is a safe, rapid, and well-tolerated examination of the pelvic floor and sphincter anatomy and allows for 3D image reconstruction. Routine use of hydrogen peroxide improves ultrasound accuracy through tiny air bubble generation, changing the fistula tract from hypoechoic to hyperechoic and enhancing contrast (Figure 3).[27, 28]

A prospective evaluation of endoanal ultrasound and MRI utility found that MRI was able to detect all abscesses and 4/5 fistulas in cases of simple perirectal infection.[29] Among complicated cases (multiple recurrences or IBD-associated) 6/7 abscesses, 12/14 fistulas, but only 75% of internal fistula openings were identified. In a blinded prospective study by Schwartz, et al. endoanal ultrasound, MRI, and surgical examination were compared and all were at least 85% accurate for assessment of perianal fistulas, but accuracy increased to 100% when any two methods were combined.[30] In situations where MRI or endoanal ultrasound are not accessible, transperineal ultrasound is a cheap, non-invasive, and rapid tool with comparable accuracy to endoanal ultrasound for abscess and fistula detection, but provides lower resolution of the anal sphincter and cannot perform 3D reconstruction.[31] While neither pelvic MRI nor endoanal ultrasound is perfect, we advocate for the use of an imaging modality when dealing with complicated fistulas.

## Treatment

In cases of a perianal abscess or fistula with associated abscess, surgical incision and drainage should be performed within 24 hours to limit the risk of deep infection or sepsis, particularly in patients with diabetes or who are immunocompromised. Abscess aspiration is not recommended given its 41% failure rate.[32] Incisions should be left open to heal by secondary intention, and additional antibiotics after sufficient drainage have not been shown to affect abscess healing or recurrence rate.[33] The use of post-drainage antibiotics for prevention of fistula formation is debated. One placebo-controlled randomized trial from 2011 showed no effect of 10 days of amoxicillin-clavulanic acid on rates of fistula formation[34] but another more

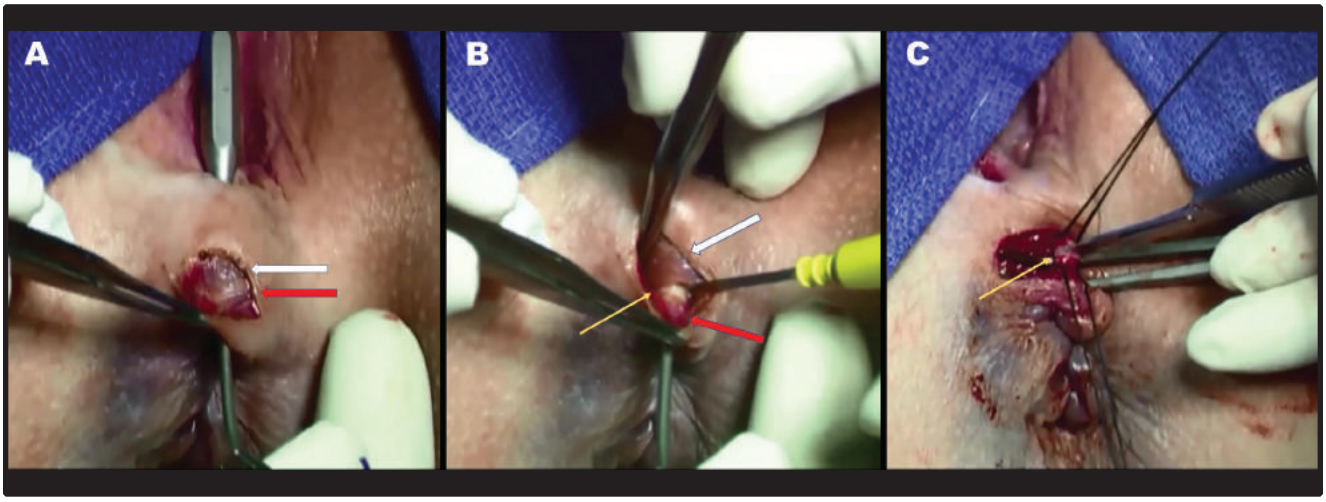


**Figure 4. Ligation of the Intersphincteric Fistula Tract.**
**Rectovaginal fistula treated with LIFT technique. A) A fistula probe spans the fistula tract with external anal sphincter (white arrow) distinct from the paler internal anal sphincter (red arrow). B) Dissection reveals the fistula tract (yellow arrow) which is C) isolated, suture-ligated, and divided with a scalpel. Images provided by Dr. Phillip Fleshner, MD.**

recent single-blind randomized trial showed that 7 days of oral metronidazole and ciprofloxacin after abscess drainage yielded a protective effect against fistula development, with an odds ratio of 0.37 (95% CI 0.2-0.7).[35] It is our practice to omit adjuvant antibiotics.

In determining the optimal treatment for perianal fistulas, it is best to first classify the fistula anatomically and determine whether the fistula is "simple" or "complex" as defined in the previous section, DIAGNOSIS – *CLINICAL PRESENTATION*. Both diagnosis and treatment are best accomplished with an anorectal exam under anesthesia, and preoperative imaging is recommended in cases of suspected or confirmed complex fistulas or recurrent fistulas. The primary goal of the initial exploration is to define the fistula and control sepsis by placing a non-cutting seton. A seton prevents recurrent abscesses and may be kept long term (months to years) without negative consequences, allowing for sepsis or unfavorable clinical factors such as active proctitis to quiesce before attempted fistula repair.[36] Cutting setons are not recommended due to their risk of sphincter damage and anal deformation.

A fistulotomy involves incising the fistula and debriding the epithelialized tract. Incontinence rates range from 0-64% and increases with greater division of the external anal sphincter. Thus, surgeons should remain conservative.[37] A fistulotomy should still be considered the gold-standard approach given that the majority of cryptoglandular fistulas are not complicated and involve a minimal amount of sphincter. In a single-center study of 675 patients with fistulas involving less than one third of the external anal sphincter by preoperative MRI, fistula healing was achieved in 98% of patients after a single fistulotomy, and in 2% after repeat fistulotomy, without any change in continence scores.[38]

For certain circumstances or complex fistulas, a variety of sphincter-preserving operations are available. Endorectal advancement flap is performed by mobilizing a rectal tissue flap of mucosa and submucosa to cover the fistula's internal opening, leaving the sphincter complex intact. This can only be performed on single tracts in the absence of proctitis with success rates ranging from 45-93%.[39] The procedure for ligation of the intersphincteric fistula tract (LIFT) was first described by Rojanasakul, et al. in 2007 as a sphincter preserving procedure with 94% effectiveness.[40] The technique involves the ligation and removal of the fistula pathway through the intersphincteric space (Figure 4). The majority of reports on this topic are retrospective small series.

In studies including patients with transphincteric fistulas exclusively, healing rates range from 61-100%.[41-44] Mushaya, et al. compared LIFT to an anorectal advancement flap in the treatment of cryptogenic complex transphincteric fistulas and found similar recurrence rates (8%), but LIFT allowed patients to return to normal activities one week earlier.[45]

Other sphincter preserving techniques include the insertion of a fistula plug or fibrin glue injections. An anal fistula plug is made of lyophilized porcine intestinal submucosa and is meant to provide a scaffold for host fibroblasts to promote healing after implantation into the fistula tract. Fibrin glue promotes clot development which induces fibrinolysis and tissue-healing processes. Success rates of both vary widely in the literature and follow-up studies of both techniques have failed to replicate initial success,[46,47] Usage of both of these techniques have largely fallen out of favor due to poor efficacy.

## Complex Fistula Treatment

The treatment of complex anorectal fistulas is nuanced and challenging. Routine use of imaging, including endoanal ultrasound and pelvic MRI, is advised for the majority of suprasphincteric and extrasphincteric fistulas. Anorectal manometry is useful as an assessment of baseline function or when addressing a high transsphincteric fistula. Fistulotomy with sphincteroplasty is a surgical option which attempts to reconstruct incised sphincter muscle to reduce the risk of incontinence. Recent studies on its usage in complex perianal fistulas have shown promise, but no randomized trials exist.[48-50] Careful patient selection to avoid patients with any sphincter involvement must be exercised to prevent incontinence.

The body of literature surrounding medical and surgical treatment of Crohn's-related perianal fistulas has grown significantly over the past decade. The cornerstone of effective fistula management has been concomitant medical and surgical therapy.[51] Anti-tumor necrosis factor alpha (anti-TNF) therapy [i.e. infliximab (IFX) or adalimumab (ADA)] is considered the most effective class of medical therapy, inducing complete fistula healing in 55% of patients receiving IFX and 60% receiving ADA.[52,53] The use of ciprofloxacin has been trialed as monotherapy, and when given in combination with ADA has been shown to improve symptoms and fistula healing rates by 24%.[51,54,55] Despite these promising results, anti-TNFs and antibiotic therapy are most efficacious after surgical management of abscesses and sepsis through seton placement.[56,57]

Even in CD, fistulas are most often treated with fistulotomy provided the anal sphincter complex is not significantly involved. Previously discussed sphincter-sparing surgical options are also efficacious but should only be attempted in the absence of proctitis.[58-61] An emerging tool for fistula management in perianal CD is the injection of mesenchymal stem cells (MSCs). The recently completed ADMIRE-CD phase III clinical trial utilized allogeneic expanded adipose-derived MSCs (Cx601-darvadstrocel) in which 120 million MSCs were injected around the internal fistula opening and peri-fistula tissue along tract walls.[62] A total of 212 patients received Cx601 or saline placebo and the trial found that significantly more patients achieved both clinical closure of external fistula openings and absence of collections on imaging in the experimental arm.[63] These results were redemonstrated at 52-weeks, with 59% in the Cx601 group maintaining clinical remission.[62] Recently, the phase-1 STOMP trial also studied the application of autologous MSCs on a fistula plug.[64] Twelve patients with cryptoglandular fistulas were treated with 83% success at six months. The advent of novel stem cell technology in the treatment of complicated perianal fistulas shows promise alongside improving medical and surgical therapy.

Fecal diversion and proctectomy are aggressive but effective last-resort treatment options for refractory perianal fistulizing disease, particularly in CD. Galandiuk and colleagues report 62% of patients with perianal CD will require fecal diversion at some point in their life.[65] For patients requiring temporary fecal diversion, over 40% ultimately require proctectomy.[66] Thus, a comprehensive discussion setting expectations with patients is recommended early after diagnosis.

In cases of fistulas associated with malignancy or involving other pelvic organs, a multidisciplinary approach is recommended. Consideration of tissue viability and potential radiation effects is particularly important in cases requiring reconstruction.

## CONCLUSION

Perianal fistulizing disease is a major source of morbidity and its diagnosis and treatment are challenging. Vigilance should be exercised to avoid misdiagnosis of non-cryptoglandular fistulas, particularly in cases of recurrent, non-healing, or complicated fistulas. In these cases, use of multiple imaging modalities allows a more thorough understanding of anatomy, yet nothing replaces early examination under anesthesia as the gold-standard for both diagnosis and therapy. The highest priorities when treating perianal fistulizing disease are determining whether the fistula is simple or complicated and controlling sepsis. Fistulotomy is an effective treatment for most simple fistulas, even Crohn's-related fistulas, but surgeons should remain conservative as any anal sphincter division risks incontinence. Patients with complicated fistulas or Crohn's disease should be evaluated with a multidisciplinary approach to optimize medical and surgical interventions. Emerging stem cell therapies are minimally-invasive, sphincter-preserving, and offer promising results. ■

### Acknowledgements

Thank you, Dr. Phillip Fleshner, MD for sharing your expertise with the LIFT procedure.

### References

1. Davis BR, Kasten KR. Anorectal abscess and fistula. Steele SR, Hull TL, Read TE, Saclarides TJ, Senagore AJ, Whitlow CB, eds. The ASCRS Textbook of Colon and Rectal Surgery. 3rd ed. New York: *Springer*; 2016. Vol 1: 215-44.
2. Nelson R. Anorectal abscess fistula: what do we know?. *Surg Clin North Am*. 2002;82(6):1139-vi. doi:10.1016/s0039-6109(02)00063-4
3. Abcarian H. Anorectal infection: abscess-fistula. *Clin Colon Rectal Surg*. 2011;24(1):14-21. doi:10.1055/s-0031-1272819
4. Zanotti C, Martinez-Puente C, Pascual I, Pascual M, Herreros D, García-Olmo D. An assessment of the incidence of fistula-in-ano in four countries of the European Union. *Int J Colorectal Dis*. 2007;22(12):1459-1462. doi:10.1007/s00384-007-0334-7
5. Parks AG. Pathogenesis and treatment of fistuila-in-ano. *Br Med J*. 1961;1(5224):463-469. doi:10.1136/bmj.1.5224.463
6. Vasilevsky CA, Gordon PH. The incidence of recurrent abscesses or fistula-in-ano following anorectal suppuration. *Dis Colon Rectum*. 1984;27(2):126-130. doi:10.1007/BF02553995
7. Khalil OM, Al Ozaibi L, Kaiyasah HM, Hejazi NA. Incidence and risk factors affecting development of perianal fistulas after drainage of perianal abscesses. *Dubai Med J*. 2021; 4:43-46. Doi:10.1159/000513277
8. Lohsiriwat V, Yodying H, Lohsiriwat D. Incidence and factors influencing the development of fistula-in-ano after incision and drainage of perianal abscesses. *J Med Assoc Thai*. 2010;93(1):61-65.
9. Henrichsen S, Christiansen J. Incidence of fistula-in-ano complicating anorectal sepsis: a prospective study. *Br J Surg*. 1986;73(5):371-372. doi:10.1002/bjs.1800730515
10. Sahnan K, Askari A, Adegbola SO, et al. Natural history of anorectal sepsis. *Br J Surg*. 2017;104(13):1857-1865. doi:10.1002/bjs.10614
11. Włodarczyk M, Włodarczyk J, Sobolewska-Włodarczyk A, Trzciński R, Dziki Ł, Fichna J. Current concepts in the pathogenesis of cryptoglandular perianal fistula. *J Int Med Res*. 2021;49(2):300060520986669. doi:10.1177/0300060520986669
12. Morris J, Spencer JA, Ambrose NS. MR imaging classification of perianal fistulas and its implications for patient management. *Radiographics*. 2000;20(3):623-637. doi:10.1148/radiographics.20.3.g00mc15623
13. Rosa G, Lolli P, Piccinelli D, Mazzola F, Bonomo S. Fistula in ano: anatomoclinical aspects, surgical therapy and results in 844 patients. *Tech Coloproctol*. 2006;10(3):215-221. doi:10.1007/s10151-006-0282-1
14. Original modified parks Rosa G, Rossi C, Gagni G, Sannini I (1979) Fistole anali – Attuali orientamenti di terapia chirurgica. Piccin, Padua, pp 55–56
15. Parks AG, Gordon PH, Hardcastle JD. A classification of fistula-in-ano. *Br J Surg*. 1976;63(1):1-12. doi:10.1002/bjs.1800630102
16. Hamadani A, Haigh PI, Liu IL, Abbas MA. Who is at risk for developing chronic anal fistula or recurrent anal sepsis after initial perianal abscess?. *Dis Colon Rectum*. 2009;52(2):217-221. doi:10.1007/DCR.0b013e31819a5c52
17. Wei PL, Keller JJ, Kuo LJ, Lin HC. Increased risk of diabetes following perianal abscess: a population-based follow-up study. *Int J Colorectal Dis*. 2013;28(2):235-240. doi:10.1007/s00384-012-1519-2
18. Devaraj B, Khabassi S, Cosman BC. Recent smoking is a risk factor for anal abscess and fistula. *Dis Colon Rectum*. 2011;54(6):681-685. doi:10.1007/DCR.0b013e31820e7c7a
19. Sheedy SP, Bruining DH, Dozois EJ, Faubion WA, Fletcher JG. MR Imaging of Perianal Crohn Disease. *Radiology*. 2017;282(3):628-645. doi:10.1148/radiol.2016151491
20. Hellers G, Bergstrand O, Ewerth S, Holmström B. Occurrence and outcome after primary treatment of anal fistulae in Crohn's disease. *Gut*. 1980;21(6):525-527. doi:10.1136/gut.21.6.525
21. Tang LY, Rawsthorne P, Bernstein CN. Are perineal and luminal fistulas associated in Crohn's disease? A population-based study. *Clin Gastroenterol Hepatol*. 2006;4(9):1130-1134. doi:10.1016/j.cgh.2006.06.021
22. Nguyen GC, Torres EA, Regueiro M, et al. Inflammatory bowel disease characteristics among African Americans,

*(continued on page 26)*

*(continued from page 24)*

Hispanics, and non-Hispanic Whites: characterization of a large North American cohort. *Am J Gastroenterol*. 2006;101(5):1012-1023. doi:10.1111/j.1572-0241.2006.00504.x

23. American Gastroenterological Association Clinical Practice Committee. American Gastroenterological Association medical position statement: perianal Crohn's disease. *Gastroenterology*. 2003;125(5):1503-1507. doi:10.1016/j.gastro.2003.08.024
24. Amato A, Bottini C, De Nardi P, et al. Evaluation and management of perianal abscess and anal fistula: a consensus statement developed by the Italian Society of Colorectal Surgery (SICCR). *Tech Coloproctol*. 2015;19(10):595-606. doi:10.1007/s10151-015-1365-7
25. Pomerri F, Dodi G, Pintacuda G, Amadio L, Muzzio PC. Anal endosonography and fistulography for fistula-in-ano. *Radiol Med*. 2010;115(5):771-783. doi:10.1007/s11547-010-0524-1
26. Buchanan GN, Halligan S, Williams AB, et al. Magnetic resonance imaging for primary fistula in ano. *Br J Surg*. 2003;90(7):877-881. doi:10.1002/bjs.4125
27. Felt-Bersma RJ. Endoanal ultrasound in perianal fistulas and abscesses. *Dig Liver Dis*. 2006;38(8):537-543. doi:10.1016/j.dld.2006.02.016
28. Kruskal JB, Kane RA, Morrin MM. Peroxide-enhanced anal endosonography: technique, image interpretation, and clinical applications. *Radiographics*. 2001;21 Spec No:S173-S189. doi:10.1148/radiographics.21.suppl_1.g01oc13s173
29. Zbar AP, de Souza NM, Puni R, Kmiot WA. Comparison of endoanal magnetic resonance imaging with surgical findings in perirectal sepsis. *Br J Surg*. 1998;85(1):111-114. doi:10.1046/j.1365-2168.1998.00573.x
30. Schwartz DA, Wiersema MJ, Dudiak KM, et al. A comparison of endoscopic ultrasound, magnetic resonance imaging, and exam under anesthesia for evaluation of Crohn's perianal fistulas. *Gastroenterology*. 2001;121(5):1064-1072. doi:10.1053/gast.2001.28676
31. Sharma A, Yadav P, Sahu M, Verma A. Current imaging techniques for evaluation of fistula in ano: a review. *Egypt J Radiol Nucl Med*. 2020;51(1):130.
32. Sørensen KM, Möller S, Qvist N. Needle aspiration treatment vs. incision of acute simple perianal abscess: randomized controlled study. *Int J Colorectal Dis*. 2021;36(3):581-588. doi:10.1007/s00384-021-03845-6
33. Macfie J, Harvey J. The treatment of acute superficial abscesses: a prospective clinical trial. *Br J Surg*. 1977;64(4):264-266. doi:10.1002/bjs.1800640410
34. Sözener U, Gedik E, Kessaf Aslar A, et al. Does adjuvant antibiotic treatment after drainage of anorectal abscess prevent development of anal fistulas? A randomized, placebo-controlled, double-blind, multicenter study. *Dis Colon Rectum*. 2011;54(8):923-929. doi:10.1097/DCR.0b013e31821cc1f9
35. Ghahramani L, Minaie MR, Arasteh P, et al. Antibiotic therapy for prevention of fistula in-ano after incision and drainage of simple perianal abscess: A randomized single blind clinical trial. *Surgery*. 2017;162(5):1017-1025. doi:10.1016/j.surg.2017.07.001
36. Truong A, Zaghiyan K, Fleshner P. Anorectal Crohn's Disease. *Surg Clin North Am*. 2019;99(6):1151-1162. doi:10.1016/j.suc.2019.08.012
37. Ommer A, Wenger FA, Rolfs T, Walz MK. Continence disorders after anal surgery--a relevant problem?. *Int J Colorectal Dis*. 2008;23(11):1023-1031. doi:10.1007/s00384-008-0524-y
38. Garg P. Is fistulotomy still the gold standard in present era and is it highly underutilized?: An audit of 675 operated cases. *Int J Surg*. 2018;56:26-30. doi:10.1016/j.ijsu.2018.06.009
39. Zabot GP, Cassol O, Saad-Hossne R, Bemelman W. Modern surgical strategies for perianal Crohn's disease. *World J Gastroenterol*. 2020;26(42):6572-6581. doi:10.3748/wjg.v26.i42.6572
40. Rojanasakul A, Pattanaarun J, Sahakitrungruang C, Tantiphlachiva K. Total anal sphincter saving technique for fistula-in-ano; the ligation of intersphincteric fistula tract. *J Med Assoc Thai*. 2007;90(3):581-586.
41. Vergara-Fernandez O, Espino-Urbina LA. Ligation of intersphincteric fistula tract: what is the evidence in a review?. *World J Gastroenterol*. 2013;19(40):6805-6813. doi:10.3748/wjg.v19.i40.6805
42. Liu WY, Aboulian A, Kaji AH, Kumar RR. Long-term results of ligation of intersphincteric fistula tract (LIFT) for fistula-in-ano. *Dis Colon Rectum*. 2013;56(3):343-347. doi:10.1097/DCR.0b013e318278164c
43. van Onkelen RS, Gosselink MP, Schouten WR. Is it possible to improve the outcome of transanal advancement flap repair for high transsphincteric fistulas by additional ligation of the intersphincteric fistula tract?. *Dis Colon Rectum*. 2012;55(2):163-166. doi:10.1097/DCR.0b013e31823c0f74
44. van Onkelen RS, Gosselink MP, Schouten WR. Ligation of the intersphincteric fistula tract in low transsphincteric fistulae: a new technique to avoid fistulotomy. *Colorectal Dis*. 2013;15(5):587-591. doi:10.1111/codi.12030
45. Mushaya C, Bartlett L, Schulze B, Ho YH. Ligation of intersphincteric fistula tract compared with advancement flap for complex anorectal fistulas requiring initial seton drainage. *Am J Surg*. 2012;204(3):283-289. doi:10.1016/j.amjsurg.2011.10.025
46. Limura E, Giordano P. Modern management of anal fistula. *World J Gastroenterol*. 2015;21(1):12-20. doi:10.3748/wjg.v21.i1.12
47. van Koperen PJ, Bemelman WA, Gerhards MF, et al. The anal fistula plug treatment compared with the mucosal advancement flap for cryptoglandular high transsphincteric perianal fistula: a double-blinded multicenter randomized trial. *Dis Colon Rectum*. 2011;54(4):387-393. doi:10.1007/DCR.0b013e318206043e
48. Ratto C, Litta F, Donisi L, Parello A. Fistulotomy or fistulectomy and primary sphincteroplasty for anal fistula (FIPS): a systematic review. *Tech Coloproctol*. 2015;19(7):391-400. doi:10.1007/s10151-015-1323-4
49. Ratto C, Litta F, Parello A, Zaccone G, Donisi L, De Simone V. Fistulotomy with end-to-end primary sphincteroplasty for anal fistula: results from a prospective study. *Dis Colon Rectum*. 2013;56(2):226-233. doi:10.1097/DCR.0b013e31827aab72
50. Hirschburger M, Schwandner T, Hecker A, Kierer W,

Weinel R, Padberg W. Fistulectomy with primary sphincter reconstruction in the treatment of high transsphincteric anal fistulas. *Int J Colorectal Dis*. 2014;29(2):247-252. doi:10.1007/s00384-013-1788-4

51. Lightner AL, Ashburn JH, Brar MS, et al. Fistulizing Crohn's disease. *Curr Probl Surg*. 2020;57(11):100808. doi:10.1016/j.cpsurg.2020.100808
52. Present DH, Rutgeerts P, Targan S, et al. Infliximab for the treatment of fistulas in patients with Crohn's disease. *N Engl J Med*. 1999;340(18):1398-1405. doi:10.1056/NEJM199905063401804
53. Colombel JF, Schwartz DA, Sandborn WJ, et al. Adalimumab for the treatment of fistulas in patients with Crohn's disease. Gut. 2009;58(7):940-948. doi:10.1136/gut.2008.159251
54. Thia KT, Mahadevan U, Feagan BG, et al. Ciprofloxacin or metronidazole for the treatment of perianal fistulas in patients with Crohn's disease: a randomized, double-blind, placebo-controlled pilot study. Inflamm Bowel Dis. 2009;15(1):17-24. doi:10.1002/ibd.20608
55. Dewint P, Hansen BE, Verhey E, et al. Adalimumab combined with ciprofloxacin is superior to adalimumab monotherapy in perianal fistula closure in Crohn's disease: a randomised, double-blind, placebo controlled trial (ADAFI). *Gut*. 2014;63(2):292-299. doi:10.1136/gutjnl-2013-304488
56. Kotze PG, Albuquerque IC, da Luz Moreira A, Tonini WB, Olandoski M, Coy CS. Perianal complete remission with combined therapy (seton placement and anti-TNF agents) in Crohn's disease: a Brazilian multicenter observational study. *Arq Gastroenterol*. 2014;51(4):284-289. doi:10.1590/S0004-28032014000400004
57. 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. doi:10.1097/00054725-200303000-00003
58. van der Hagen SJ, Baeten CG, Soeters PB, Russel MG, Beets-Tan RG, van Gemert WG. Anti-TNF-alpha (infliximab) used as induction treatment in case of active proctitis in a multistep strategy followed by definitive surgery of complex anal fistulas in Crohn's disease: a preliminary report. *Dis Colon Rectum*. 2005;48(4):758-767. doi:10.1007/s10350-004-0828-0
59. Mujukian A, Truong A, Fleshner P, Zaghiyan K. Optimal Surgical Approach to Crohn's Disease Patients with a Complex Fistula. Ligation of Intersphincteric Fistula Tract (LIFT) or Rectal Advancement Flap (FLAP)? Dis Colon Rectum. 2019;62(6):e170-e171.
60. Mujukian A, Truong A, Fleshner P, Zaghiyan K. Long-term healing after complex anal fistula repair in patients with Crohn's disease. *Tech Coloproctol*. 2020;24(8):833-841. doi:10.1007/s10151-020-02238-1
61. Rozalén V, Parés D, Sanchez E, et al. Advancement Flap Technique for Anal Fistula in Patients With Crohn's Disease: A Systematic Review of the Literature. Resultados del tratamiento quirúrgico de la fístula anal en pacientes con enfermedad de Crohn mediante técnica de colgajo de avance endorrectal: revisión sistemática de la literatura. *Cir Esp*. 2017;95(10):558-565. doi:10.1016/j.ciresp.2017.09.002
62. Panés J, García-Olmo D, Van Assche G, et al. Long-term Efficacy and Safety of Stem Cell Therapy (Cx601) for Complex Perianal Fistulas in Patients With Crohn's Disease. *Gastroenterology*. 2018;154(5):1334-1342.e4. doi:10.1053/j.gastro.2017.12.020
63. Panés J, García-Olmo D, Van Assche G, et al. Expanded allogeneic adipose-derived mesenchymal stem cells (Cx601) for complex perianal fistulas in Crohn's disease: a phase 3 randomised, double-blind controlled trial. *Lancet*. 2016;388(10051):1281-1290. doi:10.1016/S0140-6736(16)31203-X
64. 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. doi:10.1053/j.gastro.2017.04.001
65. Galandiuk S, Kimberling J, Al-Mishlab TG, Stromberg AJ. Perianal Crohn disease: predictors of need for permanent diversion. *Ann Surg*. 2005;241(5):796-802. doi:10.1097/01.sla.0000161030.25860.c1
66. 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):783-792. doi:10.1111/apt.13356