



13

Anal Fissure

Kim C. Lu and Daniel O. Herzig

Key Concepts

- An acute anal fissure (symptoms <6 weeks) is likely to heal (87%) with dietary modification and supportive care.
- In a chronic anal fissure (symptoms >6 weeks), topical nitroglycerin or calcium channel blockers are slightly better than placebo in inducing healing.
- Injection of botulinum toxin into the internal anal sphincter can heal fissures refractory to topical ointments; though this is not as effective as lateral internal anal sphincterotomy.
- Lateral internal anal sphincterotomy is the most effective therapy in healing fissures; there is an increased risk, however, of fecal incontinence.
- For anal fissures associated with decreased anal sphincter tone, a dermal advancement flap is a reasonable option.

Definition/Clinical Presentation

An anal fissure is a tear in the epithelial lining of the distal anal canal [1]. While this is likely an extremely common condition, it is difficult to know exactly how common. Many people assume this is a hemorrhoidal problem and initially avoid formal evaluation. Further, many fissures will resolve without intervention. Nevertheless, persistent anal pain and bleeding eventually push many patients to seek medical attention. In one single colon and rectal surgery clinic, anal fissures resulted in more than 1200 office visits over a 5-year period [2].

Fissures can be classified as acute vs. chronic and typical vs. atypical. Acute fissures cause bright red bleeding with bowel movements and sharp, burning, tearing anal pain or

spasm that can last for hours after the bowel movement. Physical findings include a linear separation of the anoderm, at times visible with just separation of the buttocks (Figure 13-1). Often, elevated anal resting pressures are appreciated on digital rectal examination. If tolerated by the patient, the suspected diagnosis can be confirmed by visualizing the break in the anoderm with office anoscopy after using an anesthetic lubricant. If only one area can be examined, the posterior midline should be evaluated first, as it is the site of up to 90% of typical anal fissures. The remaining minority of typical fissures are found in the anterior midline [3]. Acute fissures generally resolve within 4–6 weeks of appropriate management; chronic fissures are therefore defined as those producing symptoms beyond 6–8 weeks. Chronic fissures have additional physical findings of an external sentinel tag at the external apex, exposed internal sphincter muscle, and a hypertrophied anal papilla at the internal apex (Figure 13-2).

Typical fissures are usually located in the posterior or anterior midline, have the characteristic findings described above, and are not associated with other diseases. In contrast, atypical fissures can occur anywhere in the anal canal (Figure 13-3), can have a wide variety of findings, and can tend to be associated with other diseases, including malignancy, Crohn's disease, human immunodeficiency virus (HIV) infection, syphilis, and tuberculosis (Figure 13-4).

Pathogenesis

Despite the common nature of this long-standing problem, the exact etiology remains uncertain. Many have described onset of a fissure after the passage of a large, hard stool or anal trauma.

By a mechanical theory, the occurrence in the posterior midline might be because the anorectal angle creates the greatest stress at this location [4]. Sphincter hypertonicity has been frequently described in early reports of the disease

Electronic supplementary material: The online version of this chapter (doi:10.1007/978-3-319-25970-3_13) contains supplementary material, which is available to authorized users.



FIGURE 13-1. Acute fissure with clear edges and no signs of chronicity of sphincter hypertrophy. Courtesy of Dr. Richard P. Billingham, MD.



FIGURE 13-2. Chronic fissure with external sentinel tag, internal hypertrophied papilla, and thickened internal anal sphincter muscle.

and has been documented by manometry in multiple studies [5, 6]. It is not clear, however, if the elevated pressures are a cause of the disease or an effect [7].

A second common theory is relative ischemia of the posterior midline. This area of the anal canal has been shown to be relatively ischemic by both arteriographic studies and laser Doppler flowmetry [8, 9]. The theories of hypertonicity and ischemia may be related to some extent, particularly in that hypertonicity may aggravate the relative ischemia.

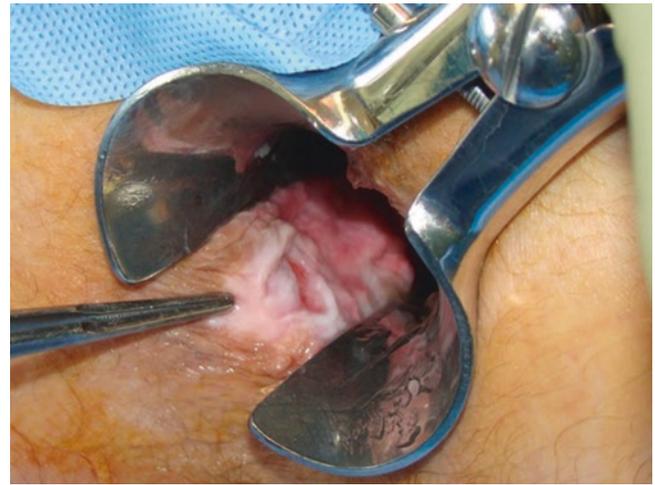


FIGURE 13-3. Atypical fissure with skin changes, broad base, and lateral location. Courtesy of Sam Atallah, MD.

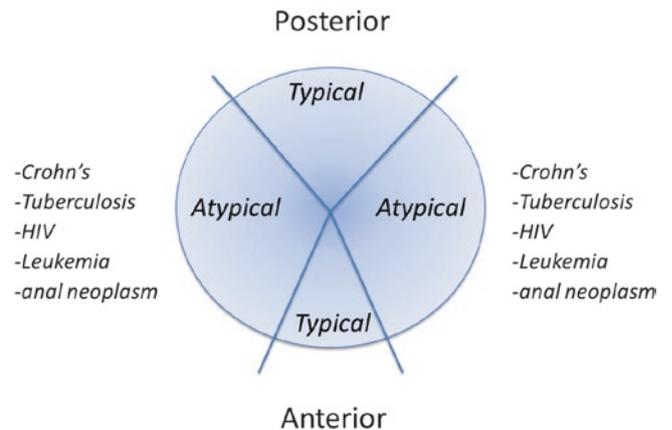


FIGURE 13-4. Type of fissure by location.

Nevertheless, tears in the anoderm undoubtedly occur with a great deal of frequency, whether from a large stool, anorectal intercourse, or instrumentation for surgical procedures, and the evolution to a chronic fissure is likely only seen in a minority of these instances. Furthermore, fissures can occur in the absence of any trauma or constipation.

Nonoperative Treatment

Healing Rates in Acute Anal Fissure

Practice parameters from the American Society of Colon and Rectal Surgeons state that conservative therapy is safe, has few side effects, and should usually be the first step in therapy [10]. Jensen reported a randomized trial done in patients with acute anal fissure. The control group in this trial was instructed to take 10 g of unprocessed bran twice daily and use a warm sitz bath for 15 min twice daily and after bowel

movements, if possible. Overall, 91% of patients were able to follow the study protocol. In that control group, the fissure healing rate was 87% [11].

Healing Rates in Chronic Anal Fissure

A more frequent problem for the surgeon is the patient who has had symptoms for several weeks and has failed an initial approach similar to that described by Jensen. In these patients, spontaneous healing rates are likely to be seen in only a minority of patients. A recent Cochrane review of the nonoperative treatment of anal fissure analyzed over 70 randomized trials of chronic anal fissure [12]. Unlike the acute fissure population, the healing rate in the combined placebo group is 35.5%.

Because internal anal sphincter hypertonicity is related to anal fissure, initial nonoperative treatment is targeted to alleviate internal anal sphincter activity through two topical agents, nitroglycerin and diltiazem, and one injectable agent, botulinum toxin A.

Topical

Nitroglycerin

Nitric oxide was reported to be the neurotransmitter mediating relaxation of the internal anal sphincter in the early 1990's [13]. Topical application of 0.2% glyceryl trinitrate ointment (GTN) was subsequently found to result in relaxation of the anal sphincter by manometric studies [14]. A landmark randomized trial was reported in 1997. That showed a healing rate of 68% with GTN treatment, compared with 8% in the placebo group [15]. The recent Cochrane analysis of 18 trials (four including children), however, showed a healing rate of 48.9% with GTN treatment, compared to 35.5% in the placebo or control group. With longer-term follow-up, recurrence varied from 51 to 67% [12].

The most common side effect of topical GTN treatment is headache, at a reported rate of 27% in the pooled analysis and may be as high as 50% [16]. While often minor and temporary, it may lead to discontinuation of therapy in 10–20% of patients [17–19]. In one prospective randomized trial comparing endoanal application vs. perianal application, endoanal application of 0.4% nitroglycerin bid was associated with decreased frequency and severity of headaches [20]. A second potential drawback to topical GTN is tachyphylaxis, which does not respond to escalations in dose or frequency.

There is was not an FDA-approved indication for nitroglycerin in the United States until 2011. The topical form of nitroglycerin was initially supplied as a 2% ointment. To achieve a 0.2% concentration, the prescription often needs to be filled at a compounding pharmacy. Jonas et al. reported that after application of 0.2% GTN, the reduction in mean anal resting pressure lasted only about 2 h, which may

explain some of the treatment failures seen with GTN [16]. In 2011, the FDA approved Rectiv (0.4% nitroglycerin) which is applied endoanally bid for 6–8 weeks. At 24-week follow-up, there was a 77% healing rate [20].

Calcium Channel Blockers

Both diltiazem and nifedipine have been described either orally or topically to cause relaxation of the smooth muscle of the internal anal sphincter. Oral and topical nifedipine have been shown to lower mean resting anal pressure [21]. Similarly, diltiazem has been shown to decrease mean resting anal pressure, although the effect is greater with topical diltiazem [22, 23]. Since studies done with calcium channel blockers have more variability with respect to the medication, dosages, and routes, it is difficult to pool data for analysis. Multiple small trials suggest healing rates equivalent to GTN with fewer side effects [24, 25]. Neither diltiazem nor nifedipine are FDA approved for the treatment of anal fissure. There is no topical formulation available in the United States, so a compounding pharmacy needs to make a topical gel from an oral formulation.

Botulinum Toxin Type A

Botulinum toxins are a family of neuroparalytic proteins synthesized by *Clostridium botulinum*. They inhibit the release of acetylcholine at the neuromuscular junction [26, 27]. These agents can be used to induce a local paralysis that lasts for several months, depending upon the subtype used. The toxins are labeled A through G, according to immunologic specificity, with type A being most commonly used in the United States. Botulinum toxins are Food and Drug Administration approved for treatment of certain spastic disorders, but not anal fissures. They have been used off-label in other disorders, including chronic anal fissures. There is no uniformly recommended dose or site of injection. Botulinum toxin type A is supplied as a powder in 100-unit single-patient-use vials. Once reconstituted, any remaining solution after use must be discarded. Relaxation of the muscle occurs within days and lasts for 2–4 months. This has the theoretical advantage of allowing fissure healing while avoiding permanent fecal incontinence.

After the initial report in 1994, various methods of injection, including injection into the internal or external sphincter, at single or multiple sites, and in various doses, have been described [28]. In one small study of 50 patients with posterior anal fissures, patients were randomized to anterior vs. posterior internal anal sphincter injections. Those injected in the anterior internal anal sphincter were significantly more likely to heal [29].

Botulinum toxin injections of the internal anal sphincter have been compared with placebo, as well as other treatments, with mixed results. In a widely referenced, early, double-blind, placebo-controlled randomized crossover trial

of 30 patients, botulinum toxin A injection was found to be superior to saline injection, with a healing rate of 73% with Botox, compared to 13% with placebo ($p=0.003$) [30].

Trials have compared botulinum toxin injection with lateral internal sphincterotomy for fissures refractory to topical medical management. Arroyo et al. reported a randomized controlled trial of 80 patients and showed healing rates of 92.5% for the lateral internal sphincterotomy group, compared with 45% in the botulinum toxin group. They concluded, however, that botulinum toxin was still their preference in patients over 50 or at risk for incontinence due to a higher but not statistically significant incidence of incontinence after sphincterotomy [31]. Other small studies support the finding of higher number of treatment failures, but fewer complications in the botulinum toxin group [32, 33]. In a recent meta-analysis of seven randomized controlled trials, comparing botulinum toxin injection with lateral internal anal sphincterotomy, the healing and recurrence rates were worse with botulinum toxin [34]. In a recent randomized prospective trial comparing lateral internal sphincterotomy with Botox injection/topical diltiazem, 1-year healing rates were far superior with lateral internal anal sphincterotomy (94% vs. 65%) [35].

There is limited data regarding the long-term effectiveness of botulinum toxin. In one retrospective review of 411 patients who failed topical diltiazem, patients were treated with 100 units of botulinum toxin A and underwent fissurectomy under general anesthesia. 74% were healed at 2-year follow-up. Of note, the botulinum toxin was injected into the intersphincteric space.

Operative Treatment

Anal Dilatation

One of the earliest forms of treatment was anal dilatation, first described in 1829, and studied later in various trials for anal fissure [36, 37]. While extensively studied, there is considerable variability in the technique and a wide range of reported outcomes. Few well-controlled studies exist. The recent Cochrane review included an analysis of seven randomized controlled trials, comparing manual anal stretch to internal sphincterotomy [38]. They demonstrated that dilatation was not more effective than sphincterotomy and had a higher rate of incontinence (OR = 4.03, 95% CI = 2.04–7.46). A more standardized and objective method of anal stretch, balloon dilatation, has been reported. Renzi et al. evaluated the use of balloon dilatation compared to lateral internal sphincterotomy in a prospective randomized trial [39]. Healing rates were high in both groups, and there was no difference between the groups. After 24 months of follow-up, however, incontinence was zero in the balloon dilatation group, compared to 16% in the lateral internal sphincterotomy

group ($p < 0.0001$). While manual dilatation is no longer indicated for anal fissure, balloon dilatation may be one alternative.

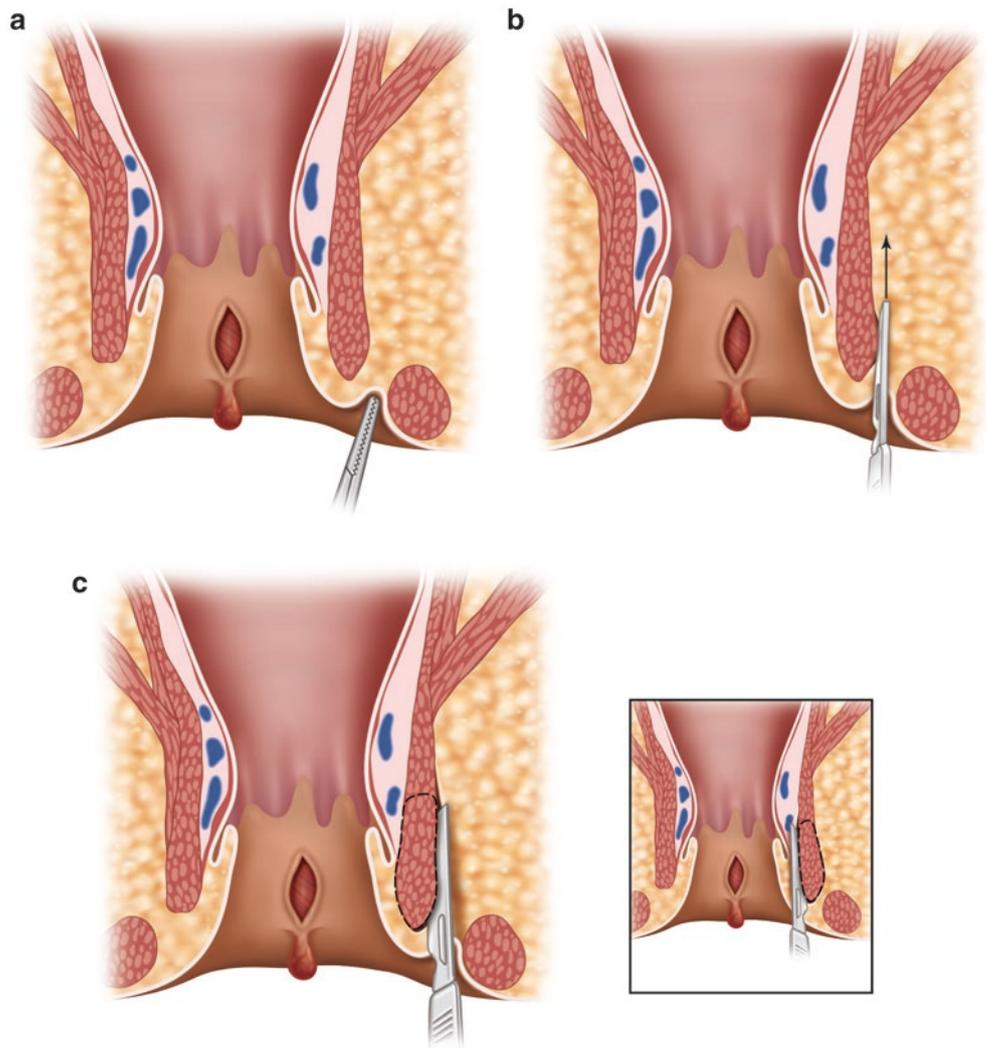
Anal Sphincterotomy (Technique)

While also described in various forms since the early 1800's, isolated division of the internal anal sphincter muscle (sphincterotomy) was first described by Eisenhammer in the 1950's [40]. His technique of posterior internal sphincterotomy at the site of the fissure led to a posterior midline "gutter" or "keyhole" deformity, leading to fecal soiling in 30–40% of patients. Notaras described a simple modification: performing the sphincterotomy laterally, which eliminated this problem [41]. Since then, lateral internal anal sphincterotomy has become the main surgical intervention for failure of medical management. The procedure can be done under local anesthesia, as an outpatient. The variations currently include open vs. closed technique and conservative vs. traditional sphincterotomy. The closed technique is performed by inserting the scalpel blade in the intersphincteric groove and then turning it medially to break the fibers of the internal sphincter (Figure 13-5). The open technique is done through a radial incision overlying the intersphincteric groove. After dissecting the internal anal sphincter away from the anoderm, the distal internal anal sphincter is divided under direct vision (Figure 13-6). Division was originally described to the dentate line, but recent reports describe a more conservative approach, either with division of the muscle to the fissure apex or with division just until the band of hypertrophied muscle is released.

Outcomes Between Closed and Open Anal Sphincterotomy

From the Cochrane Library, a systematic review on the operative procedures for anal fissures was updated in 2011 [38]. The techniques of open and closed sphincterotomy have been compared in multiple reports, including five randomized studies that met inclusion criteria for the Cochrane analysis [42–46]. Combined, these reports show no difference in either persistence of fissure or incontinence with the two techniques. A prospective cohort study evaluated 140 consecutive patients undergoing open or closed sphincterotomy with postoperative endosonography [47]. Postoperative endoanal ultrasounds showed that open sphincterotomy was associated with a significantly higher proportion of complete sphincterotomies. The rate of incontinence and treatment failure was not different between the open and closed groups, but there was a strongly significant increase in incontinence scores ($p < 0.001$) and decrease in recurrence rates ($p < 0.001$) with increasing length of sphincterotomy.

FIGURE 13-5. Closed lateral sphincterotomy. (a) Location of the intersphincteric groove. (b) Insertion of the knife blade in the intersphincteric plane. (c) Lateral to medial division of the internal anal sphincter (*inset*: medial to lateral division of the muscle).



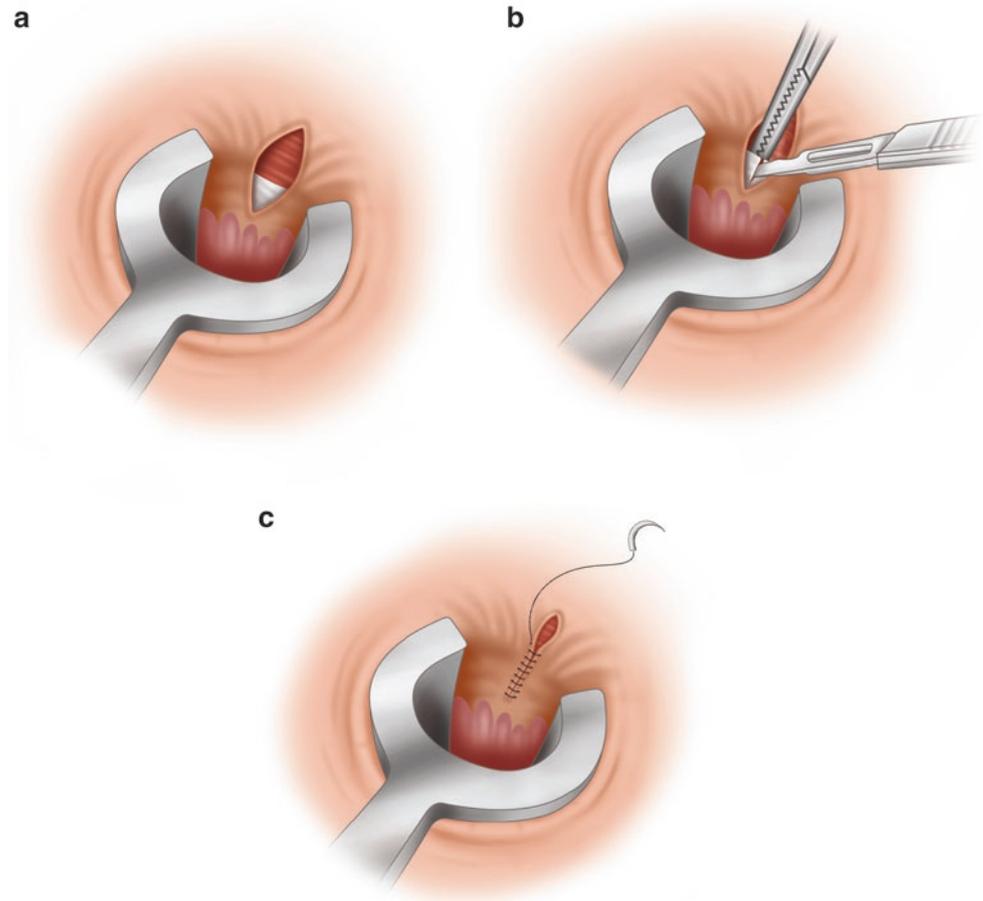
Extent of Sphincterotomy

The decision regarding the extent of sphincterotomy performed in the operating room is a controversial topic. Excessive division increases the risk of incontinence, yet inadequate division increases the risk of persistence or recurrence. While many texts describe division to the dentate line, recent studies have examined a more conservative sphincterotomy. Mentis et al. prospectively randomized 76 patients with chronic anal fissure to lateral internal sphincterotomy to the dentate line or to the apex of the fissure [48]. Treatment failure was zero in the traditional group, and 13% in the conservative group after 1 year of follow-up, with most of the treatment failures occurring after 2 months. There was no statistically significant difference in the postoperative incontinence scores between the two treatment groups. There was, however, an increase in the postoperative incontinence score in the traditional group; this study may have been underpowered to detect a possible difference. In a similar manner, Elsebae et al. prospectively randomized 92 patients to sphincterotomy to the dentate line (traditional) or sphincter-

otomy to the apex of the fissure (conservative) [49]. Treatment failure was zero in the traditional group and 4% in the conservative group ($p=NS$); persistent incontinence was 4% in the traditional group and 0% in the conservative group ($p=NS$). The follow-up period, however, was only 18 weeks. In an even more recent study, Magdy et al. randomized 150 patients to traditional sphincterotomy, V-Y advancement flap, or conservative sphincterotomy+V-Y advancement flap. The healing rates were 84% in the traditional group and 94% in the conservative division/advancement flap group. The incontinence rates were 14% vs. 2%, respectively. The low healing rates with traditional sphincterotomy, however, are a bit hard to believe [50].

The techniques of division to the dentate line or to the fissure apex have objective definitions, yet many surgeons approach the sphincterotomy as a more subjective task. The band of hypertrophied internal anal sphincter muscle may or may not relate to either of these two landmarks. While division of the hypertrophied muscle segment is subjective, a subsequent report from Mentis et al. attempted to compare this method by creating a sphincterotomy that achieves an

FIGURE 13-6. Open lateral internal sphincterotomy. (a) Radial skin incision distal to the dentate line exposing the intersphincteric groove. (b) Elevation and division of the internal sphincter. (c) Primary wound closure.



anal caliber of 30 mm. They prospectively compared this technique to division to the apex of the fissure [51]. Their findings showed the average anal caliber was greater in the group that underwent division to the apex, the incontinence rates were higher, and there was no significant difference in treatment failure.

Fissurectomy

The hallmark of chronic fissure is the triad of a hypertrophied internal sphincter, a hypertrophied anal papilla, and an external sentinel tag. Excision of the papilla and tag, or complete fissurectomy, is optional, but particularly useful if the fissure edges appear rolled and epithelialized, as this may promote faster wound healing. Renewed interest in fissurectomy (unroofing of superficial tract extending caudad from fissure) as primary treatment of the fissure has recently been reported [52].

Results of Sphincterotomy

In addition to these randomized controlled trials, a myriad of additional nonrandomized reports are available, describing a

wide range of results from lateral internal sphincterotomy. While most reports cite low rates of treatment failure, the incontinence rate is widely variable and is as high as 30–40% [53, 54]. With a multimodal approach designed to minimize the risk of permanent incontinence, the trend is clearly moving away from lateral internal sphincterotomy and toward more medical therapy and/or botulinum toxin. It is not clear whether or not this strategy will be the most effective long-term solution with respect to morbidity, costs, and patient satisfaction. The disease, however, is largely measured by the subjective experience of the patient, who is ultimately the best judge of which treatment is worth pursuing and which risks are worth taking. Floyd et al. reported that with multiple options offered to patients, the ultimate time to healing is prolonged, but 72% of patients can avoid operative treatment, and 97% of patients can be healed [55].

In a similar report with a median follow-up of 47 months, Lysy et al. reported results from their approach of escalating from topical agents, to botulinum toxin, to sphincterotomy [56]. Like the cohort described by Floyd, 71% of patients resolved without lateral sphincterotomy. They also noted that the low rate of sphincterotomy came at the price of increased recurrences before complete healing, and a longer time spent in treatment.

Fissures Without Anal Hypertonicity

Treatments directed at relaxation of the anal sphincter, either pharmacologically or surgically, presume that relief of anal hypertonicity will lead to healing. A subset of patients with fissure, however, will not demonstrate hypertonicity, and hypotonicity may actually be found. Giordano et al. recently reported results from their prospective study of simple cutaneous advancement flap in 51 patients over a 6-year period for all patients, regardless of anal tone [57]. They found the procedure to be well tolerated, with a 98% treatment success rate. Nyam and colleagues evaluated 21 patients with fissures and below normal anal pressures. In this group, an island advancement flap resulted in complete healing and no incontinence in all patients [58]. A 2002 report from St. Mark's noted favorable results with advancement flaps for fissures with hypotonicity in a small series, with successful treatment in 7/8 patients with a median follow-up of 7 months [59]. While this technique might not be useful for all patients with refractory fissures, it holds particular promise in addressing the fissure in the setting of a hypotonic anus. Video 13-1 demonstrates the

technique of an anal flap. While the video portrays anal stenosis, the technical points of the procedure are well demonstrated.

Crohn's Disease

Fissures are commonly seen in people with Crohn's disease, affecting approximately 30% of patients [60, 61]. When they occur, they tend to be in more atypical locations, deeper, and associated with other pathology, especially fistula. These fissures have atypical appearance as well, often creating deep ulcerations, and potentially creating significant deformity. As with other manifestations of Crohn's, it is reasonable to intervene only as complications dictate. Some authors have reported acceptable outcomes from interventions in these patients [62, 63], but caution should be the rule, and sphincter salvage is prudent. Multidisciplinary care is crucial in addressing anorectal disease in the patient with Crohn's, as appropriate medical management of the disease may lead to resolution of the anorectal disorders in 50% or more of these cases [64, 65].

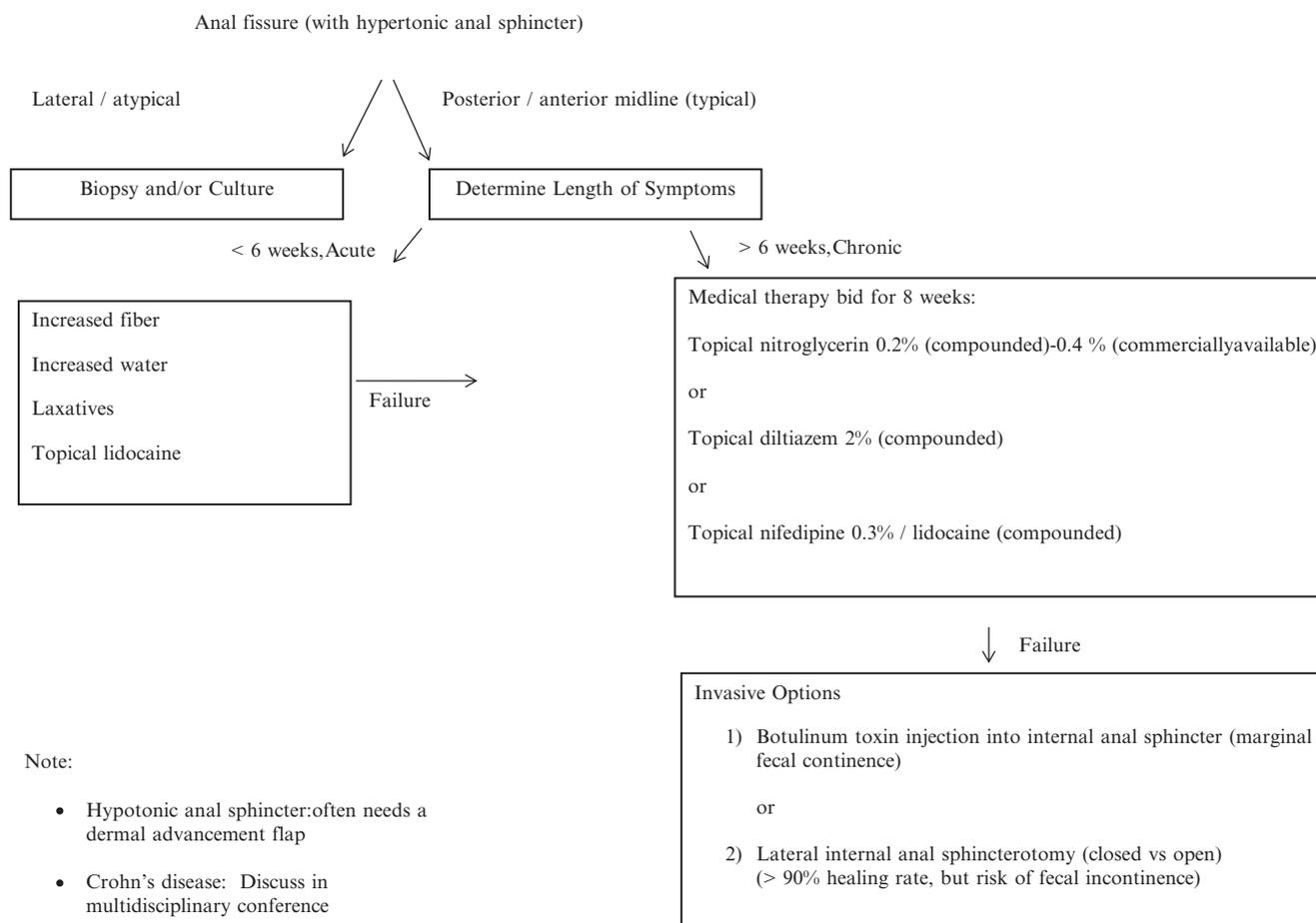


FIGURE 13-7. Treatment algorithm for anal fissure.

Human Immunodeficiency Virus

HIV-related anal disease includes both typical fissures and anorectal ulcers, which can appear as deep, broad-based, or cavitating lesions. Poor sphincter tone and function is a more frequent finding than the hypertonicity that accompanies typical, non-HIV-related fissures. Small studies have reported successful treatment of typical fissures, and the medical treatment of HIV continues to improve [66, 67]. Concerns about delayed wound healing and increased infectious complications, however, remain.

Conclusions

Anal fissure is a common disorder that is effectively treated and prevented with conservative measures in its acute form. Chronic fissures usually require medical therapy that can be effective in a small majority of patients. Initial therapy includes bulking agents, control of constipation, and topical medications to relax the internal anal sphincter. Botulinum toxin and lateral internal sphincterotomy can both be considered for treatment of refractory anal fissures, and the popularity of botulinum toxin is increasing. Sphincterotomy remains an effective operation, with a very high rate of resolution of symptoms, but at the price of some risk of permanent incontinence. A suggested treatment algorithm is provided in Figure 13-7.

References

- Herzig DO, Lu KC. Anal fissure. *Surg Clin North Am*. 2010;90:33–44.
- Ricciardi R, Dykes S, Madoff R. Anal fissure. In: Beck DE, Roberts P, Saclarides TK, Senagore AJ, Stamos MJ, Wexner SD, editors. *The ASCRS textbook of colon and rectal surgery*. 2nd ed. New York, NY: Springer; 2011. p. 203–18.
- Hoexter B. Anal fissure. In: Fazio VW, Church J, Delaney CP, editors. *Current therapy in colon and rectal surgery*. 2nd ed. Philadelphia, PA: Elsevier Mosby; 2005. p. 19–22.
- Perry GG. Fissure in ano—a complication of anusitis. *South Med J*. 1962;55:955–7.
- Farouk R, Duthie GS, MacGregor AB, Bartolo DC. Sustained internal sphincter hypertonia in patients with chronic anal fissure. *Dis Colon Rectum*. 1994;37:424–9.
- Nothmann BJ, Schuster MM. Internal anal sphincter derangement with anal fissures. *Gastroenterology*. 1974;67:216–20.
- Gibbons CP, Read NW. Anal hypertonia in fissures: cause or effect? *Br J Surg*. 1986;73:443–5.
- Klosterhalfen B, Vogel P, Rixen H, Mittermayer C. Topography of the inferior rectal artery: a possible cause of chronic, primary anal fissure. *Dis Colon Rectum*. 1989;32:43–52.
- Schouten WR, Briel JW, Auwerda JJ, De Graaf EJ. Ischaemic nature of anal fissure. *Br J Surg*. 1996;83:63–5.
- Perry WB, Dykes SL, Buie WD, Rafferty JF. Standards Practice Task Force of the American Society of C, Rectal S. Practice parameters for the management of anal fissures (3rd revision). *Dis Colon Rectum*. 2010;53:1110–5.
- Jensen SL. Treatment of first episodes of acute anal fissure: prospective randomised study of lignocaine ointment versus hydrocortisone ointment or warm sitz baths plus bran. *Br Med J*. 1986;292:1167–9.
- Nelson RL, Thomas K, Morgan J, Jones A. Non surgical therapy for anal fissure. *Cochrane Database Syst Rev*. 2012; (2): CD003431.
- O’Kelly T, Brading A, Mortensen N. Nerve mediated relaxation of the human internal anal sphincter: the role of nitric oxide. *Gut*. 1993;34:689–93.
- Loder PB, Kamm MA, Nicholls RJ, Phillips RK. ‘Reversible chemical sphincterotomy’ by local application of glyceryl trinitrate. *Br J Surg*. 1994;81:1386–9.
- Lund JN, Scholefield JH. A randomised, prospective, double-blind, placebo-controlled trial of glyceryl trinitrate ointment in treatment of anal fissure. *Lancet*. 1997;349:11–4.
- Jonas M, Barrett DA, Shaw PN, Scholefield JH. Systemic levels of glyceryl trinitrate following topical application to the anoderm do not correlate with the measured reduction in anal pressure. *Br J Surg*. 2001;88:1613–6.
- Brisinda G, Maria G, Bentivoglio AR, Cassetta E, Gui D, Albanese A. A comparison of injections of botulinum toxin and topical nitroglycerin ointment for the treatment of chronic anal fissure. *N Engl J Med*. 1999;341:65–9.
- Lund JN, Armitage NC, Scholefield JH. Use of glyceryl trinitrate ointment in the treatment of anal fissure. *Br J Surg*. 1996;83:776–7.
- Watson SJ, Kamm MA, Nicholls RJ, Phillips RK. Topical glyceryl trinitrate in the treatment of chronic anal fissure. *Br J Surg*. 1996;83:771–5.
- Perez-Legaz J, Arroyo A, Moya P, Ruiz-Tovar J, Frangi A, Candela F, et al. Perianal versus endoanal application of glyceryl trinitrate 0.4% ointment in the treatment of chronic anal fissure: results of a randomized controlled trial. Is this the solution to the headaches? *Dis Colon Rectum*. 2012;55:893–9.
- Chrysos E, Xynos E, Tzovaras G, Zoras OJ, Tsiaoussis J, Vassilakis SJ. Effect of nifedipine on rectoanal motility. *Dis Colon Rectum*. 1996;39:212–6.
- Carapeti EA, Kamm MA, Phillips RK. Topical diltiazem and bethanechol decrease anal sphincter pressure and heal anal fissures without side effects. *Dis Colon Rectum*. 2000;43:1359–62.
- Jonas M, Neal KR, Abercrombie JF, Scholefield JH. A randomized trial of oral vs. topical diltiazem for chronic anal fissures. *Dis Colon Rectum*. 2001;44:1074–8.
- Bielecki K, Kolodziejczak M. A prospective randomized trial of diltiazem and glyceryltrinitrate ointment in the treatment of chronic anal fissure. *Colorectal Dis*. 2003;5:256–7.
- Kocher HM, Steward M, Leather AJ, Cullen PT. Randomized clinical trial assessing the side-effects of glyceryl trinitrate and diltiazem hydrochloride in the treatment of chronic anal fissure. *Br J Surg*. 2002;89:413–7.
- Cheng CM, Chen JS, Patel RP. Unlabeled uses of botulinum toxins: a review, part 1. *Am J Health Syst Pharm*. 2006;63:145–52.
- Tjandra JJ. Ambulatory haemorrhoidectomy - has the time come? *ANZ J Surg*. 2005;75:183.
- Gui D, Cassetta E, Anastasio G, Bentivoglio AR, Maria G, Albanese A. Botulinum toxin for chronic anal fissure. *Lancet*. 1994;344:1127–8.

29. Maria G, Brisinda G, Bentivoglio AR, Cassetta E, Gui D, Albanese A. Influence of botulinum toxin site of injections on healing rate in patients with chronic anal fissure. *Am J Surg*. 2000;179:46–50.
30. Maria G, Cassetta E, Gui D, Brisinda G, Bentivoglio AR, Albanese A. A comparison of botulinum toxin and saline for the treatment of chronic anal fissure. *N Engl J Med*. 1998;338:217–20.
31. Arroyo A, Perez F, Serrano P, Candela F, Lacueva J, Calpena R. Surgical versus chemical (botulinum toxin) sphincterotomy for chronic anal fissure: long-term results of a prospective randomized clinical and manometric study. *Am J Surg*. 2005;189:429–34.
32. Iswariah H, Stephens J, Rieger N, Rodda D, Hewett P. Randomized prospective controlled trial of lateral internal sphincterotomy versus injection of botulinum toxin for the treatment of idiopathic fissure in ano. *ANZ J Surg*. 2005;75:553–5.
33. Menten BB, Irkorucu O, Akin M, Leventoglu S, Tatlicioglu E. Comparison of botulinum toxin injection and lateral internal sphincterotomy for the treatment of chronic anal fissure. *Dis Colon Rectum*. 2003;46:232–7.
34. Chen HL, Woo XB, Wang HS, Lin YJ, Luo HX, Chen YH, et al. Botulinum toxin injection versus lateral internal sphincterotomy for chronic anal fissure: a meta-analysis of randomized control trials. *Tech Coloproctol*. 2014;18:693–8.
35. Gandomkar H, Zeinoddini A, Heidari R, Amoli HA. Partial lateral internal sphincterotomy versus combined botulinum toxin A injection and topical diltiazem in the treatment of chronic anal fissure: a randomized clinical trial. *Dis Colon Rectum*. 2015;58:228–34.
36. Saad AM, Omer A. Surgical treatment of chronic fissure-in-ano: a prospective randomised study. *East Afr Med J*. 1992;69:613–5.
37. Steele SR, Madoff RD. Systematic review: the treatment of anal fissure. *Aliment Pharmacol Ther*. 2006;24:247–57.
38. Nelson RL, Chattopadhyay A, Brooks W, Platt I, Paavana T, Earl S. Operative procedures for fissure in ano. *Cochrane Database Syst Rev*. 2011; (11): CD002199.
39. Renzi A, Izzo D, Di Sarno G, Talento P, Torelli F, Izzo G, et al. Clinical, manometric, and ultrasonographic results of pneumatic balloon dilatation vs. lateral internal sphincterotomy for chronic anal fissure: a prospective, randomized, controlled trial. *Dis Colon Rectum*. 2008;51:121–7.
40. Eisenhammer S. The evaluation of the internal anal sphincterotomy operation with special reference to anal fissure. *Surg Gynecol Obstet*. 1959;109:583–90.
41. Notaras MJ. Lateral subcutaneous sphincterotomy for anal fissure--a new technique. *Proc R Soc Med*. 1969;62:713.
42. Arroyo A, Perez F, Serrano P, Candela F, Calpena R. Open versus closed lateral sphincterotomy performed as an outpatient procedure under local anesthesia for chronic anal fissure: prospective randomized study of clinical and manometric longterm results. *J Am Coll Surg*. 2004;199:361–7.
43. Filingeri V, Gravante G. A prospective randomized trial between subcutaneous lateral internal sphincterotomy with radiofrequency bistoury and conventional parks' operation in the treatment of anal fissures. *Eur Rev Med Pharmacol Sci*. 2005;9:175–8.
44. Boulos PB, Araujo JG. Adequate internal sphincterotomy for chronic anal fissure: subcutaneous or open technique? *Br J Surg*. 1984;71:360–2.
45. Kortbeek JB, Langevin JM, Khoo RE, Heine JA. Chronic fissure-in-ano: a randomized study comparing open and subcutaneous lateral internal sphincterotomy. *Dis Colon Rectum*. 1992;35:835–7.
46. Wiley M, Day P, Rieger N, Stephens J, Moore J. Open vs. closed lateral internal sphincterotomy for idiopathic fissure-in-ano: a prospective, randomized, controlled trial. *Dis Colon Rectum*. 2004;47:847–52.
47. Garcia-Granero E, Sanahuja A, Garcia-Botello SA, Faiz O, Esclapez P, Espi A, et al. The ideal lateral internal sphincterotomy: clinical and endosonographic evaluation following open and closed internal anal sphincterotomy. *Colorectal Dis*. 2009;11:502–7.
48. Menten BB, Ege B, Leventoglu S, Oguz M, Karadag A. Extent of lateral internal sphincterotomy: up to the dentate line or up to the fissure apex? *Dis Colon Rectum*. 2005;48:365–70.
49. 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;31:2052–7.
50. Magdy A, El Nakeeb A, el Fouda Y, Youssef M, Farid M. Comparative study of conventional lateral internal sphincterotomy, V-Y anoplasty, and tailored lateral internal sphincterotomy with V-Y anoplasty in the treatment of chronic anal fissure. *J Gastrointest Surg*. 2012;16:1955–62.
51. Menten BB, Guner MK, Leventoglu S, Akyurek N. Fine-tuning of the extent of lateral internal sphincterotomy: spasm-controlled vs. up to the fissure apex. *Dis Colon Rectum*. 2008;51:128–33.
52. Pelta AE, Davis KG, Armstrong DN. Subcutaneous fissurotomy: a novel procedure for chronic fissure-in-ano. a review of 109 cases. *Dis Colon Rectum*. 2007;50:1662–7.
53. Garcia-Aguilar J, Belmonte C, Wong WD, Lowry AC, Madoff RD. Open vs. closed sphincterotomy for chronic anal fissure: long-term results. *Dis Colon Rectum*. 1996;39:440–3.
54. Madoff RD, Fleshman JW. AGA technical review on the diagnosis and care of patients with anal fissure. *Gastroenterology*. 2003;124:235–45.
55. Floyd ND, Kondylis L, Kondylis PD, Reilly JC. Chronic anal fissure: 1994 and a decade later--are we doing better? *Am J Surg*. 2006;191:344–8.
56. Lysy J, Israeli E, Levy S, Rozentzweig G, Strauss-Liviatan N, Goldin E. Long-term results of "chemical sphincterotomy" for chronic anal fissure: a prospective study. *Dis Colon Rectum*. 2006;49:858–64.
57. Giordano P, Gravante G, Grondona P, Ruggiero B, Porrett T, Lunniss PJ. Simple cutaneous advancement flap anoplasty for resistant chronic anal fissure: a prospective study. *World J Surg*. 2009;33:1058–63.
58. Nyam DC, Wilson RG, Stewart KJ, Farouk R, Bartolo DC. Island advancement flaps in the management of anal fissures. *Br J Surg*. 1995;82:326–8.
59. Kenefick NJ, Gee AS, Durdey P. Treatment of resistant anal fissure with advancement anoplasty. *Colorectal Dis*. 2002;4:463–6.

60. Sangwan YP, Schoetz Jr DJ, Murray JJ, Roberts PL, Collier JA. Perianal Crohn's disease. Results of local surgical treatment. *Dis Colon Rectum*. 1996;39:529-35.
61. Platell C, Mackay J, Collopy B, Fink R, Ryan P, Woods R. Anal pathology in patients with Crohn's disease. *ANZ J Surg*. 1996;66:5-9.
62. Wolkomir AF, Luchtefeld MA. Surgery for symptomatic hemorrhoids and anal fissures in Crohn's disease. *Dis Colon Rectum*. 1993;36:545-7.
63. Fleshner PR, Schoetz Jr DJ, Roberts PL, Murray JJ, Collier JA, Veidenheimer MC. Anal fissure in Crohn's disease: a plea for aggressive management. *Dis Colon Rectum*. 1995;38:1137-43.
64. Ouraghi A, Nieuviarts S, Mougenel JL, Allez M, Barthet M, Carbonnel F, et al. Infliximab therapy for Crohn's disease anoperineal lesions. *Gastroenterol Clin Biol*. 2001;25:949-56.
65. Sweeney JL, Ritchie JK, Nicholls RJ. Anal fissure in Crohn's disease. *Br J Surg*. 1988;75:56-7.
66. Viamonte M, Dailey TH, Gottesman L. Ulcerative disease of the anorectum in the HIV+ patient. *Dis Colon Rectum*. 1993;36:801-5.
67. Weiss EG, Wexner SD. Surgery for anal lesions in HIV-infected patients. *Ann Med*. 1995;27:467-75.