Clinical Practice Guideline for the Management of Anal Fissures

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The American Society of Colon and Rectal Surgeons is dedicated to ensuring high-quality patient care by advancing the science, prevention, and management of disorders and diseases of the colon, rectum, and anus. The Clinical Practice Guidelines Committee is composed of society members who are chosen because they have demonstrated expertise in the specialty of colon and rectal surgery. This committee was created to lead international efforts in defining quality care for conditions related to the colon, rectum, and anus. This is accompanied by developing clinical practice guidelines based on the best available evidence. These guidelines are inclusive, and not prescriptive. Their purpose is to provide information based on which decisions can be made, rather than to dictate a specific form of treatment. These guidelines are intended for the use of all practitioners, health care workers, and patients who desire information about the management of the conditions addressed by the topics covered in these guidelines. It should be recognized that these guidelines should not be deemed inclusive of all proper methods of care or exclusive of methods of care reasonably directed toward obtaining the same results. The ultimate judgment regarding the propriety of any specific procedure must be made by the physician in light of all the circumstances presented by the individual patient.

STATEMENT OF THE PROBLEM

The term *anal fissure* most commonly refers to a longitudinal tear within the anal canal, one that typically extends from the dentate line toward the anal verge. This benign anorectal ailment is quite common, although there have been virtually no published[1] population-level data describing its incidence. Constipation and diarrhea are frequent antecedent historical features. The primary symptom associated with anal fissures is anal pain, which is often provoked by defecation and may last for several hours following defecation. Anorectal bleeding may also be associated with fissures, and, when this symptom is present, it can contribute to a misdiagnosis of symptomatic hemorrhoids. In up to 90% of cases, the anal fissure is located within the posterior midline of the anal canal. Fissures are located in the anterior midline in as many as 25% of female patients and in as many as 8% of male subjects. In 3% of patients, fissures can be located at posterior and anterior positions simultaneously. Fissures located at lateral locations within the anal canal, and multiple fissures, are considered to be atypical and require careful evaluation because of their association with such diseases as HIV infection, Crohn's disease, syphilis, tuberculosis, and hematologic malignancies.

Acute fissures, defined as symptoms present for fewer than 8 weeks, will appear as a longitudinal tear. Fissures of a longer duration will manifest one or more stigmata of chronicity, including a hypertrophied anal papilla at the proximal aspect of the fissure, a sentinel tag at the distal aspect of the fissure, and exposed internal anal sphincter muscle within the base of the fissure.

METHODOLOGY

These guidelines were built on the last set of the American Society of Colon and Rectal Surgeons practice parameters for treatment of fissure-in-ano published in 2004. An organized search of MEDLINE, PubMed, EMBASE, and the Cochrane Database of Collected Reviews was performed from October 2015 through March 2016. Retrieved publications were limited to the English language, but no limits on year of publication were applied. The search strategies were based on the concepts "anal fissure" and "fissure-in-ano" as primary search terms. Searches were also performed based on various treatments for anal fissures, including "anal fissure AND nitroglycerin," "anal fissure AND nitrates," "anal fissure AND diltiazem," "anal fissure AND nifedipine," "anal fissure AND fiber," "anal fissure AND botulinum," "anal fissure AND sphincterotomy," and "anal fissure AND flap."

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Directed searches of the embedded references from the primary articles were also performed in certain circumstances. Prospective, randomized, controlled trials and meta-analyses were given preference in developing these guidelines. The final grade of recommendation was performed using the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) system (Table 1).[2]

RECOMMENDATIONS

1. **Nonoperative treatment of acute anal fissures continues to be safe, has few side effects, and should typically be the first-line treatment. Grade of Recommendation: Strong recommendation based on moderate-quality evidence, 1B.**

Almost half of all patients who have acute anal fissure will resolve their symptoms with nonoperative measures such as sitz baths and the use of psyllium fiber or other bulking agents, with or without the addition of topical anesthetics or topical steroids.[1,3–7] These interventions are well tolerated, with minimal to no side effects. Treatment with sitz baths and fiber supplementation is associated with a superior degree of pain relief in comparison with topical anesthetics and topical hydrocortisone.[3] In addition, maintenance therapy with fiber is associated with lower rates of fissure recurrence compared with placebo.[6] There are no data supporting one type of fiber in comparison with another.

2. **Anal fissures may be treated with topical nitrates, although side effects may limit their efficacy. Grade of Recommendation: Strong recommendation based on high-quality evidence, 1A.**

Topical nitric oxide donors are associated with healing in approximately 50% of chronic anal fissures.[8] Based on a pooled analysis of studies, this represents a 13.5% improvement in the absolute rate of healing and a 38% relative improvement in the rate of healing compared with placebo or lidocaine alone.[9] Dose escalation does not improve healing rates, but escalating doses are associated with an increased incidence of medication side effects.[10,11]

The principal side effect with this medication is headaches, occurring in at least 30% of treated patients and being nearly ubiquitous in some reports.[8,12] This adverse effect is dose related and leads to the cessation of therapy in up to 20% of patients.[13] In addition, up to 50% of patients treated with this medication experience recurrent fissures, a significantly higher percentage than observed with surgical treatment.[9] Nonresponders to topical nitrates should, in general, be considered either for botulinum toxin therapy or for a surgical sphincterotomy.

TABLE 1. The GRADE system grading recommendations

	Description	*Benefit vs risk and burdens*	*Methodological quality of supporting evidence*	*Implications*
1A	Strong recommendation, High-quality evidence	Benefits clearly outweigh risk and burdens or vice versa	RCTs without important limitations or overwhelming evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1B	Strong recommendation, Moderate-quality evidence	Benefits clearly outweigh risk and burdens or vice versa	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1C	Strong recommendation, Low- or very-low-quality evidence	Benefits clearly outweigh risk and burdens or vice versa	Observational studies or case series	Strong recommendation but may change when higher-quality evidence becomes available
2A	Weak recommendation, High-quality evidence	Benefits closely balanced with risks and burdens	RCTs without important limitations or overwhelming evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2B	Weak recommendations, Moderate-quality evidence	Benefits closely balanced with risks and burdens	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2C	Weak recommendation, Low- or very-low-quality evidence	Uncertainty in the estimates of benefits, risks, and burden; benefits, risks, and burden may be closely balanced	Observational studies or case series	Very weak recommendations; other alternatives may be equally reasonable

GRADE = Grades of Recommendation, Assessment, Development, and Evaluation; RCT = randomized controlled trial.
Adapted from Guyatt G, Gutermen D, Baumann MH, et al. Grading strength of recommendations and quality of evidence in clinical guidelines: report from an American College of Chest Physicians Task Force. *Chest*. 2006;129:174–181.[2] Used with permission.

3. Compared with topical nitrates, the use of calcium channel blockers for chronic anal fissures has a similar efficacy, with a superior side effect profile, and can be used as first-line treatment. Grade of Recommendation: Strong recommendation based on high-quality evidence, 1A.

Topical calcium channel blockers (typically diltiazem or nifedipine) have been associated with healing rates of anal fissures of 65% to 95%.[14] Side effects, particularly headaches, are significantly less frequent than experienced with topical nitrates.[12,14–16] Although superior rates of healing for chronic anal fissures are described,[12,15] it should be noted that this trend is not unanimously reported, leading to pooled analyses that have not been able to confirm a clear advantage in healing with this class of medications in comparison with topical nitrates.[9,16,17] There are data to suggest that the cure rate associated with topical calcium channel blockers is increased with increasing frequency of daily application.[18]

A single randomized controlled trial demonstrated that topical diltiazem was equivalent to botulinum toxin in terms of healing and pain relief after 3 months of treatment.[19]

Anal fissures may also be treated with *oral* calcium channel blockers. Direct comparison of oral and topical nifedipine found similar rates of healing and pain relief.[20] Given the higher incidence of systemic effects associated with oral calcium channel blockers, topical delivery is preferred.

4. Botulinum toxin has similar results compared with topical therapies as first-line therapy for chronic anal fissures, and modest improvement in healing rates as second-line therapy following treatment with topical therapies. Grade of Recommendation: Strong recommendation based on low- and very-low-quality evidence, 1C.

The majority of published studies evaluating the use of botulinum toxin involve comparisons with topical agents such as nitroglycerin.[19,21] From these studies, botulinum toxin is associated with a modest (37%–43%), but consistently reported improvement in healing rates of anal fissures, which is almost uniformly defined in the literature as resolution of anal pain. These studies, as well as those comparing botulinum toxin with topical nitroglycerin and surgical sphincterotomy, have several limitations; a variety of dosages, as well as variations in the number of injections and injection sites prevent generalizations from published studies.

A Cochrane review[22] suggested that botulinum toxin was only marginally superior to placebo, but with few treatment-associated adverse events.

Several prospective studies[23,24] suggest that, in direct comparison with 0.2% to 1% topical nitroglycerin and 0.2% topical nifedipine, botulinum toxin (20–60 units) provides healing rates ranging from 18% to 71% within 9 weeks of treatment, with results comparable to or slightly better than topical therapies. A recent double-blind randomized trial[19] comparing 2% diltiazem with 20 units of botulinum toxin demonstrated that, after 3 months, both treatment arms were associated with a 43% healing rate. The botulinum toxin group experienced a higher rate of reduction in pain scores as defined as a minimum reduction in discomfort of 50% (82% vs 78%). Although one multicenter randomized study performed in 2014 suggested that botulinum toxin is more effective than topical nitroglycerin,[24] with improved rates of healing and with lower recurrence rates at 1 year (28% vs 50%), the majority of prospective and retrospective studies suggest equivalent outcomes, with the exception that the cost of botulinum toxin is higher. A meta-analysis[25] from 2008, which predates several of these aforementioned studies, concluded that botulinum toxin is as effective as nitroglycerin but that it may be associated with a lower incidence of adverse events.

The use of topical nitroglycerin in conjunction with botulinum toxin has been suggested to improve healing and symptoms in patients with chronic anal fissure, although the literature is limited in demonstrating a consistent improvement in either healing or recurrence rates.[26,27] Small retrospective studies[28,29] evaluating botulinum toxin as second-line therapy following unsuccessful treatment with topical nitroglycerin have suggested improved symptomatic relief and avoidance of surgical sphincterotomy at short-term follow-up.

A Cochrane review[9] from 2012 found no clear trend between dose, preparation, or injection site of botulinum toxin and associated healing rates.

5. Lateral internal sphincterotomy is associated with consistently superior healing rates compared with medical therapy for chronic anal fissure and thus may be offered in select patients without first confirming failure of pharmacological treatment. Grade of Recommendation: Strong recommendation based on high-quality evidence, 1A.

Multiple randomized trials have confirmed the superiority of lateral internal sphincterotomy (LIS) compared with topical nitrates, calcium channel blockers, or botulinum toxin, with healing rates of 88% to 100%, and with fecal incontinence rates ranging from 8% to 30%, all based on follow-up intervals of up to 6 years.[30–41] One reason for the superior results associated with LIS may be the poor compliance associated with long-term medical therapy, an observation that was confirmed by a recent Cochrane review comparing surgical and nonsurgical therapies for anal fissures.[9] Given the poor treatment compliance and the higher rate of persistent fissures with nonoperative management, quality of life has also been reported as sig-

nificantly improved in patients undergoing LIS. Because long-term fecal continence and quality of life are preserved in the vast majority of patients following LIS,[34,42–44] operative management with LIS can safely be offered as first-line therapy for chronic anal fissures in patients with no underlying fecal incontinence of any degree; in most cases this would exclude LIS as first-line therapy for patients such as women with prior obstetrical injuries, patients with IBD, and patients who have undergone previous anorectal operations or who have a documented anal sphincter injury.

Although LIS for chronic anal fissure is not typically performed in women of child-bearing age, there are no long-term data regarding the risk of subsequent fecal incontinence in this population, with or without an obstetric injury. A prospective comparative study including 31 consecutive women who underwent tailored LIS for chronic anal fissure showed various degrees of postoperative fecal incontinence in 52% (16/31) of patients at a mean follow-up of 4.7 months.[45] Fifty-five percent of women had previous vaginal deliveries and no patients had preoperative fecal incontinence. Continence scores significantly correlated with the extent of sphincter division, and the proportion of patients with a continence score of 0 was significantly greater in patients in whom sphincter division was less than 25%, which for women in this study corresponded to <1 cm of muscle transection.

6. **Of all surgical options, lateral internal sphincterotomy is the treatment of choice for chronic anal fissures. Grade of Recommendation: Strong recommendation based on high-quality evidence, 1A.**

LIS remains the surgical treatment of choice for chronic anal fissures.[46] Multiple studies[3,47–50] and a recent Cochrane review[46] show that LIS is superior to uncontrolled manual anal dilation, yielding superior healing rates with less incontinence. Controlled pneumatic balloon dilation has shown promise in one small series,[51] although this treatment has not been investigated enough to serve as a standard therapy. LIS has been compared with fissurectomy in 2 randomized trials including a total of 112 patients, with superior healing rates with LIS and with equivalent incontinence rates.[52,53] The addition of topical nitric oxide donors[54] or botulinum toxin[55–57] improves the results of fissurectomy in nonrandomized series; however, this combined approach has not been directly compared with LIS.

7. **Open and closed techniques of lateral internal sphincterotomy yield similar results and either technique may be used. Grade of Recommendation: Strong recommendation based on high-quality evidence, 1A.**

Multiple, well-designed comparative studies have concluded that there are no significant differences in outcomes between properly performed open and closed surgical sphincterotomies.[58–62] A Cochrane analysis also confirmed this finding,[45] reporting a Peto OR (with 95% CI) for fissure persistence of 1.00 (0.4–2.48) and an OR of 0.87 (0.41–1.83) for incontinence to flatus. In one recent prospective, randomized study of 136 patients, open sphincterotomy was associated with significantly higher postoperative pain scores and a 4.4% delayed healing rate of the surgical site at 1-year follow-up.[63]

8. **Lateral internal sphincterotomy tailored to the length of the fissure yields equivalent to worse healing rates with less incontinence compared with traditional lateral internal sphincterotomy extending to the dentate line. Grade of Recommendation: Weak recommendation based on moderate-quality evidence, 2B.**

"Tailored" sphincterotomy, defined as sphincterotomy to the apex of the fissure, has been proposed in an effort to reduce the rate of fecal incontinence following conventional LIS, the latter being defined as transecting sphincter muscle as far proximally as the dentate line. Three randomized trials of conventional versus tailored sphincterotomy showed statistically superior fissure healing rates in the traditional arm; 2 studies reported worse fecal continence scores in the traditional arm,[64,65] whereas one did not.[66] Regardless of LIS technique, these studies demonstrated a low incidence of fecal incontinence.

In an attempt to decrease the risk of fecal incontinence after LIS, a so-called calibrated sphincterotomy has also been reported, which involves transecting sphincter muscle to achieve a predetermined diameter of the anal canal. One randomized, controlled trial compared calibrated LIS with conventional LIS to achieve a 30-mm aperture of the anal canal.[67] Although healing was equivalent, early (7 and 28 days) postoperative fecal incontinence scores were significantly higher in the tailored LIS group. In a recent prospective observational study from Brazil using clinical and 3-dimensional sonographic evaluation in women status post-LIS, the safe extent of sphincter transection was less than 25% of the total internal anal sphincter length, which in this study corresponded to a sphincterotomy length of less than 1 cm.[68]

9. **Short-term outcomes of repeat LIS for recurrent anal fissure have shown good healing rates with a low risk of fecal incontinence. Grade of Recommendation: Weak recommendation based on low-quality evidence, 2C.**

Only one study has evaluated the outcomes of repeat LIS for recurrent chronic anal fissures. Fifty-five patients underwent repeat contralateral tailored LIS and showed a 98% healing rate and a 4% minor fecal incontinence rate at a 12.5-month mean follow-up.[69] Larger studies with longer follow-up intervals are required on this topic.

10. **Anocutaneous flap is a safe surgical alternative in the management of chronic anal fissure, with inferior healing rates and with a decreased risk of fecal incontinence compared**

with LIS. Grade of Recommendation: Weak recommendation based on moderate-quality evidence, 2B.

Although LIS remains the surgical treatment of choice for chronic anal fissures, the fundamental drawback is anorectal seepage and incontinence, which are reported in 8% to 30% of patients.[2–6,70] An alternative sphincter-preserving surgical approach is an anocutaneous (dermal V-Y or house) flap, which has been described using a variety of techniques, and which has been associated with good fissure healing rates (81%–100%) and low rates of minor fecal incontinence (0%–6%).[7,71,72] In a prospective study, Giordano et al[72] reported a 98% healing rate at 2 months following the construction of a flap in 51 consecutive patients, with no recurrences or changes in continence at a median follow-up of 6 months. Patel and colleagues[73] compared the outcomes of patients undergoing flaps (n = 50) and LIS (n = 50), and at a mean follow-up of 21 months fissure healing was achieved in 96% of patients who underwent anal advancement flap and 88% of those undergoing LIS ($p = 0.27$). There was no fecal incontinence reported in either group. Larger, prospective comparative trials are still needed to better define the role of anocutaneous flaps in the treatment of anal fissures.

11. The addition of an anocutaneous flap to botulinum toxin injection or to lateral internal sphincterotomy decreases postoperative pain and allows for primary wound healing. Grade of Recommendation: Weak recommendation based on low-quality evidence, 2C.

Flap techniques for fissure coverage have the advantage of primary wound healing, faster pain relief, and potentially providing better functional results. Small, noncomparative studies have evaluated the outcomes of patients undergoing anocutaneous flap coverage with either botulinum toxin injection or LIS. A combined flap with botulinum toxin injection has shown rapid symptom relief with healing rates ranging from 86.7% to 92% at follow-up intervals up to 24 months, with negligible fecal incontinence rates.[74,75] Theodoropoulos et al[76] compared the results of 30 consecutive patients who underwent LIS plus V-Y perianal skin flap and 32 patients who previously underwent LIS alone. Significantly less postoperative pain, faster healing, and fewer soiling episodes were observed in the LIS plus flap group. Magdy et al[77] randomly allocated consecutive patients to receive LIS (n = 50), V-Y advancement flap (n = 50), or combined LIS with V-Y advancement flap (n = 50). At a 1-year follow-up, healing rates were 84%, 48%, and 94% ($p = 0.001$), recurrence rates were 4%, 22%, and 2% ($p = 0.01$), and fecal incontinence rates were 14%, 0%, and 2% ($p = 0.03$).

12. Miscellaneous causes of anal fissure: Less commonly encountered etiologies of anal fissure such as Crohn's disease, sexually transmitted diseases, and low-pressure fissures are collectively discussed below because there is a paucity of literature on these topics. Grade of Recommendation: Weak recommendation based on low-quality evidence, 2C.

Fissures in patients with Crohn's disease are treated primarily via conservative approaches, with an emphasis on Crohn's medical therapy if these fissures are felt to be a manifestation of IBD. Although scant, the literature on this subject describes IBD medical therapy for active intestinal disease, with fissures resolving in many patients who respond to medical management. More aggressive, surgical management of anal fissures should be reserved for a subset of highly selected patients without proctitis or anal canal disease.[78–81]

Treatment of fissures related to sexually transmitted diseases is determined by identifying the causative organism through biopsy of the fissure, and tailoring treatment accordingly. In particular, HIV-related anal ulceration can produce disabling symptomatology. Biopsy, viral culture, debridement, and intralesional steroid therapy are the mainstays of treatment.[82] Optimizing antiretroviral therapy can effectively ameliorate the symptomatology over a longer interval, but it is not an effective short-term strategy.

In the acute setting, low-pressure anal fissures are most commonly seen in postpartum patients. In this subset of anal fissures, procedures that alter the sphincter mechanism should be avoided in favor of more conservative medical therapy.[83] In the chronic setting, there may be benefit from treating patients who have low-pressure fissure with fissurectomy with skin advancement flap. In a study of 16 female patients with chronic low-pressure anal fissure treated with anal fissurectomy and skin advancement flap, all patients had relief of symptoms.[84]

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