The role of endoscopy in patients with anorectal disorders

This is one of series of statements discussing the use of GI endoscopy in common clinical situations. The Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy (ASGE) prepared this text. In preparing this guideline, a search of the medical literature was performed by using PubMed. Studies or reports that described fewer than 10 patients were excluded from analysis if multiple series with more than 10 patients addressing the same issue were available. Additional references were obtained from the bibliographies of the identified articles and from recommendations of expert consultants. Guidelines for appropriate use of endoscopy are based on a critical review of the available data and expert consensus at the time the guidelines are drafted. Further controlled clinical studies may be needed to clarify aspects of this guideline. This guideline may be revised as necessary to account for changes in technology, new data, or other aspects of clinical practice. The recommendations are based on reviewed studies and were graded on the strength of the supporting evidence (Table 1).[1] The strength of individual recommendations is based on both the aggregate evidence quality and an assessment of the anticipated benefits and harms. Weaker recommendations are indicated by phrases such as "we suggest," whereas stronger recommendations are typically stated as "we recommend."

This guideline is intended to be an educational device to provide information that may assist endoscopists in providing care to patients. This guideline is not a rule and should not be construed as establishing a legal standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment. Clinical decisions in any particular case involve a complex analysis of the patient's condition and available courses of action. Therefore, clinical considerations may lead an endoscopist to take a course of action that varies from these guidelines.

Symptoms related to anorectal disorders are common among patients presenting to gastroenterologists and are sometimes challenging to manage. Some require the combined effort of both gastroenterologists and surgeons. Although it is beyond the scope of this article to discuss all abnormalities, common problems are reviewed. This document is a revision of a previous American Society for Gastrointestinal Endoscopy (ASGE)[2] guideline and discusses the role of endoscopy in patients with anorectal disorders, including chronic radiation proctopathy, anal fissures, internal hemorrhoids and fecal incontinence. Additional information about the role of endoscopy in the evaluation of patients with perianal disease in inflammatory bowel disease is described in another ASGE guideline.[3]

CHRONIC RADIATION PROCTOPATHY

Among patients receiving prostate irradiation, the rectum is the most common segment of the GI tract that is affected, with chronic radiation-induced injury occurring in up to 20% of patients.[4,5] The term *radiation proctitis* is a misnomer because there is no inflammatory component found on the biopsy sample, but there is the presence of ischemic endarteritis of the submucosal arterioles and submucosal fibrosis. Chronic radiation proctopathy can occur from 9 months to 30 years after pelvic radiation injury, although patients typically present within 2 years after radiation.[6] Symptoms may include hematochezia, tenesmus, diarrhea, and defecatory urgency, whereas the endoscopic appearance ranges from diffuse, friable angioectatic lesions to frank ulceration. Approximately 95% of mild radiation-induced proctopathy is temporary and self-limited, and up to 5% of patients experience symptoms that are refractory to conservative management. Treatment of radiation proctopathy that is found incidentally on endoscopy is not usually indicated unless there are signs (eg, anemia) or symptoms that affect the patient's overall health status or quality of life because mild proctopathy will spontaneously resolve in the majority of patients. Complications of radiation proctopathy include anemia, rectal strictures, rectovesical fistula formation,[7] and increased risk of colorectal cancer.[8-10]

Treatment

A variety of treatments have been described for the management of chronic radiation proctopathy, including oral therapy (eg, 5-aminosalicylates, metronidazole, antioxidants), topical formalin application, rectal instillation therapy (eg, hydrocortisone, sucralfate, 5-aminosalicylates, short-chain fatty acids, metronidazole), thermal therapy (eg, argon plasma coagulation, heater probe,[11] laser), and hyperbaric oxygen.[12] There are no large randomized, controlled studies of the management of chronic radiation

TABLE 1. GRADE system for rating the quality of evidence for guidelines

Quality of evidence	Definition	Symbol
High quality	Further research is very unlikely to change our confidence in the estimate of effect.	⊕⊕⊕⊕
Moderate quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.	⊕⊕⊕○
Low quality	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.	⊕⊕○○
Very low quality	Any estimate of effect is very uncertain.	⊕○○○

Adapted from Guyatt et al.[1]

proctopathy, and most of the data are based on case series and small trials.[13]

Medical therapy. Several medical therapies are briefly described here. In one prospective case series of 14 patients, rectal sucralfate suspension relieved symptoms in 11 patients over a mean follow-up of 6 months.[14] Sucralfate enemas (2 g twice daily) have been found to be superior to the combination of oral sulfasalazine and steroid enemas in controlling symptoms (94% vs 53%, $P < .05$) in a prospective, randomized trial of 37 patients.[15] In a case series of 26 patients with moderate to severe radiation proctopathy, sucralfate suspension twice daily was associated with a good symptom response in 77% by 4 weeks and 92% by 16 weeks.[16] 5-Aminosalicylic acid enemas failed to improve symptoms or the endoscopic appearance of the rectal mucosa in a prospective, open-label trial.[17] Similarly, treatment with butyric acid enemas failed to result in significant improvements in symptom, endoscopic, and histologic scores in a randomized, double-blind, placebo-controlled, crossover trial in 12 patients.[18] In a randomized, double-blind, crossover trial of 120 patients, hyperbaric oxygen treatment was associated with an absolute risk reduction for nonhealing of 32% (number needed to treat = 3) and enhanced bowel-specific quality of life.[19] In a Cochrane review, significant improvement was seen in healing of radiation proctopathy with hyperbaric oxygen treatment ($P = .02$).[20] In a open-label pilot study of 20 patients using a combination of vitamin E (400 IU 3 times daily) and vitamin C (500 IU 3 times daily), there was a significant symptomatic improvement in bleeding, diarrhea, and urgency.[21]

Endoscopic therapy. Endoscopic therapy for radiation proctopathy includes thermal coagulation therapy and topical formalin application. The neodymium yttrium aluminum garnet laser has been effectively used in the treatment of radiation proctopathy and delivers a deeper tissue effect than the argon and potassium titanyl phosphate lasers. A median of 3 treatment sessions (range 1-9) is usually needed to obtain an optimal clinical response.[22-26] However, laser treatments are expensive and the equipment is not widely available.

Argon plasma coagulation (APC) has become the predominant endoscopic therapy for chronic radiation proctopathy because of its advantages over laser treatment, including lower cost, portability, and the ability to apply noncontact thermal therapy in tangential locations. APC is associated with reduced rectal bleeding in 80% to 90% of cases of radiation proctopathy and may improve the other troublesome symptoms of diarrhea and urgency.[27] Typically, 1 to 3 treatment sessions are required to achieve bleeding control with power settings of 25 to 60 W and flow rates of 0.5 to 2.5 L/min.[28] In a prospective study of 56 patients, all patients with mild proctopathy (n = 27) and 79% of those with severe disease (n = 29) had cessation of rectal bleeding and/or no recurrence of anemia ($P < .05$).[6] During a mean follow-up of 17.9 months (range 6-33 months), 34 of 38 patients (90%) remained in clinical remission. Recurrence of rectal bleeding was higher in those using anticoagulants or aspirin ($P = .02$). Reported complications include rectal stenosis[29] and fistulae[30] in a minority of patients. Colonic explosions have been reported in patients who receive only an enema bowel preparation before APC.[31] In patients with cardiac pacemakers and defibrillators, caution and recommendations are the same as for the other endoscopic electrocautery systems.[32]

Dilute (eg, 2%-10%) formalin topical treatment of radiation proctopathy has been applied either through a rigid proctoscope or instilled into the rectum. Complete clinical responses range from 63% to 100%.[33-36] In a retrospective analysis of 100 patients with a mean follow-up of 18 months, 10% formalin was applied by using a 16-inch cotton tip applicator passed through a proctoscope in the office setting.[37] Cessation of bleeding occurred in 93% of patients after an average of 3.5 formalin applications at 2- to 4-week intervals. Approximately 1% of these patients experienced anal pain and spasm or transient dizziness. Complications, including anal stenosis, mucosal ulceration, and mild fecal incontinence have been reported.[38-40] Radiofrequency ablation using an endoscopically directed focal ablation device and endoscopic cryotherapy have also been described in small case series.[41,42] Overall, con-

sidering the superficial nature of injury and wide availability of APC and topical formalin, these methods are practical first-line approaches to the endoscopic management of chronic radiation proctopathy. Relative contraindications for endoscopic therapy include evidence of malignant recurrence, stenosis, and fistulae. All thermal treatment methods may create symptomatic ulceration (including pain and bleeding), which can require months to resolve.

ANAL FISSURE

An anal fissure is a tear in the anal mucosa below the dentate line, characterized by pain and bleeding with defecation. Anal fissures are also associated with Crohn's disease, although the most common causes are local trauma from hard stool, hypertension of the internal anal sphincter, multiparity, or previous surgery.[43] Fissures usually arise in the posterior midline, but may also be seen in the anterior midline in 19%,[44] and ischemia is involved in the pathogenesis.[45,46] Diagnosis is suggested by the history with characteristic symptoms of a "tearing" pain associated with bowel movements. Endoscopy should be considered when the diagnosis is in doubt, if bleeding occurs, to rule out associated inflammatory bowel disease and for patients due for a screening colonoscopy. However, temporarily deferring colonoscopy until after initial treatment of the anal fissure may help to avoid the discomfort associated with bowel preparation and colonoscopy in these patients. Anal fissures are best visualized with the patient lying on his or her side in the knee-to-chest position and by distracting the buttocks. Although acute fissures appear as a laceration, chronic fissures appear as linear white-based lesions with horizontally oriented fibers, typically associated with an external skin tag (sentinel tag) and hypertrophied anal papillae.

Nonsurgical Treatment

If constipation is present, acute fissures should be managed conservatively with stool softeners, fiber, fluids, and lubricants such as mineral oil and flaxseed oil. For chronic anal fissures, initial medical therapy is typically recommended except for fissures associated with an abscess or fistula. However, a Cochrane review concluded that medical therapy in adults is far less effective than surgery.[47] Medical therapies that have been used include fiber supplementation, topical therapy (ie, mineral oil, anesthetics, nitroglycerin, calcium channel blockers), corticosteroids, calcium channel blockers, and botulinum toxin injection.[48] Although a meta-analysis of topical nitroglycerin demonstrated significant benefit in healing compared with placebo (odds ratio for fissure persistence = 0.55), side effects (especially headaches, with an odds ratio = 4.09) were common.[49] Moreover, a subgroup analysis that excluded studies with low placebo response rates showed no significant benefit of nitroglycerin. Nitroglycerin has to

be compounded for application, usually as a 0.2% ointment.

Calcium channel blockers, nifedipine, and diltiazem have been studied in different studies, administered both orally and topically (0.2%-0.3% nifedipine and 2% diltiazem). In a Cochrane review analysis, there was no significant difference in efficacy compared with glyceryl trinitrate.[47] Calcium channel blockers have shown fewer side effects than topical nitrates[50] and have been found to be superior to topical lidocaine and hydrocortisone.[51,52] A randomized study of 50 patients comparing topical with oral diltiazem showed topical to be more effective.[53] In a randomized, controlled trial comparing oral nifedipine and lateral anal sphincterotomy with tailored sphincterotomy, lateral anal sphincterotomy was associated with significantly better fissure healing rates ($P < .001$ at 16 weeks) and less recurrence ($P = .003$) than nifedipine.[54] There are no studies available that assess recurrence rates after 1 year. Given the limitations of oral and topical therapy, there has been considerable interest in botulinum toxin injection for chronic anal fissures. Botulinum toxin induces muscle relaxation by inhibiting the release of acetylcholine and is used in several spastic disorders. Reported healing rates with botulinum toxin injection vary widely, ranging from 37% to 92%.[55-58] The internal anal sphincter is palpated and, using a 27-gauge needle, a total of 20 U of botulinum toxin A is injected in divided doses in either side of the fissure.[58] When botulinum toxin was compared with nitroglycerin, botulinum toxin was more effective in fissure healing than nitroglycerin (92%-96% vs 60%-70%, respectively).[55,57] Repeat injection may be beneficial in initial nonresponders or after relapse. Temporary, mild fecal incontinence and perianal thrombosis have been reported.[59] Long-term benefits and complications are unknown at this point.

Surgical Treatment

Surgery has been superior to medical therapy in recent studies,[60-65] with high healing and low relapse rates. Lateral internal sphincterotomy involves incising the internal anal sphincter through the skin of the lateral aspect of the anus, away from the anterior and posterior midline to reduce sphincter tone. Mean healing/improvement rates are reported at 95%, with a mean rate of incontinence of 9.3%.[66] Even with higher rates of incontinence, overall improvement in quality of life has been reported.[67]

INTERNAL HEMORRHOIDS

Hemorrhoids are common, with more than 75% of persons in the United States reporting symptomatic hemorrhoids at some point during their life.[68] Approximately 30% of patients with hemorrhoids seek medical care.[69] There are multiple factors associated with hemorrhoid formation, including degeneration of supporting tissue of the anal canal fibrovascular cushions and decreased ve-

nous return. These factors are exacerbated by increased abdominal pressure and inadequate intake of soluble fiber and water.[70] Hemorrhoids are classified as either external or internal depending on their presence below or above the dentate line, respectively. The Goligher classification of internal hemorrhoids has 4 degrees.[71] In the first degree, the hemorrhoids bleed but do not prolapse. Second-degree internal hemorrhoids prolapse but spontaneously reduce. Third-degree hemorrhoids prolapse and require manual reduction, and fourth-degree hemorrhoids prolapse but cannot be reduced. Typical presenting symptoms include rectal pain, itching, prolapse, and bleeding, and about 20% may have concomitant fissures. Diagnosis is made by inspection of the perineum, digital rectal examination, and office anoscopy. Endoscopic evaluation for colorectal cancer should be performed depending on the clinical situation (eg, patient age, symptoms, previous evaluation, and family history). Internal hemorrhoids are best viewed by anoscopy or if flexible endoscopy is being performed, on retroflexion.

Treatment

Medical management suffices for most patients with symptomatic internal hemorrhoids; the type of treatment is dictated by the severity of symptoms and degree of prolapse. Detailed medical management is beyond the scope of this document. The use of fiber shows a consistent beneficial effect for relieving overall symptoms and bleeding in the treatment of symptomatic hemorrhoids.[72,73] Other nonsurgical options for hemorrhoid treatment include sclerotherapy,[74] rubber band ligation (RBL),[75] infrared photocoagulation,[76] electrocoagulation,[77] cryotherapy,[78] and low-voltage direct current.[79] Sclerotherapy, which can be performed through an anoscope, is effective for first- and second-degree hemorrhoids, although rare complications include mucosal necrosis, abscess, prostatitis, erectile dysfunction, and portal pyemia.[80] RBL is an effective procedure and can be performed with either flexible or rigid endoscopes. Although it is easier to do multiple ligations with flexible endoscopes, discomfort and cost are reportedly higher.[81] Suction band ligation was noted to be superior to forceps ligation with respect to pain and intraprocedure bleeding in a randomized study of 100 patients.[82] In a study of 45 patients with chronic rectal bleeding secondary to second- and third-degree internal hemorrhoids randomized to RBL or bipolar coagulation therapy, success was higher with RBL (92% vs 62%, $P < .05$) with a similar safety profile.[83] Recurrent symptoms were similar at 1 year. Experts caution against RBL of internal hemorrhoids in sedated patients because significant pain caused by errant band placement too close to or below the dentate line can occur. Usually, no more than 3 hemorrhoidal groups are banded in 1 session,[84,85] although some experts advocate placing only 1 band at a time to minimize symptoms. Hemorrhoidal disease requiring the placement of 4 or more bands was associated with

a trend toward higher failure rates and a greater need for subsequent operative hemorrhoidectomy.[86]

Surgical treatments (eg, open or closed hemorrhoidectomy, stapled hemorrhoidopexy, and Doppler-guided vascular pedicle ligation) are the treatments of choice for all fourth-degree hemorrhoids, strangulated hemorrhoids, and those that have not been successfully treated by other forms of therapy. RBL is the treatment of choice for mild rectal mucosal prolapse and bleeding in first-, second-, and selected third-degree hemorrhoids when medical treatments fail. Surgical treatment should be reserved for patients with very large third- and fourth-degree hemorrhoids or patients in whom RBL failed.[87]

FECAL INCONTINENCE

Fecal incontinence is a common anorectal disorder with a reported prevalence of 8.3% in noninstitutionalized U.S. adults. The prevalence is similar in men and women (7.7% and 8.9%, respectively) and increases with age.[88] Because anorectal malignancy or proctitis can cause fecal incontinence, all these patients should be considered for flexible sigmoidoscopy or colonoscopy as indicated by age, family history, and previous endoscopic evaluation. The evaluation should also assess for prolapsing hemorrhoids, rectal prolapse, and rectocele. A common cause of fecal incontinence is reduced internal and/or external sphincter tone or defect or decreased rectal compliance, which can be assessed by digital rectal examination and quantified with anorectal manometry. In patients with reduced sphincter tone, endoanal US (EAUS) or magnetic resonance imaging (MRI) should be considered to evaluate the integrity of the sphincters to rule out obstetrical or other injury. A prospective study of 52 patients revealed that EAUS was superior to MRI for the diagnosis of internal anal sphincter injury and equivalent to MRI for the diagnosis of external anal sphincter injury.[89] The criterion standard in this study was a consensus based on clinical evaluation and anorectal physiologic test results. Another prospective study of 237 patients with fecal incontinence revealed a nonsignificant difference in sensitivity for EAUS versus MRI (90% vs 81%, $P = .23$) in the diagnosis of external anal sphincter defects and atrophy.[90] Although some studies showed that EAUS was helpful in predicting outcomes of sphincteroplasty[91,92] and success after surgery,[93] 1 study found that the EAUS findings did not predict clinical outcomes.[94] Evolution in the technologic and procedural aspects of EAUS (eg, 3-dimensional imaging, high-frequency probes) and MRI (eg, external and dynamically phased studies, endovaginal approaches) and future comparative clinical studies will further help to define the role of these complementary imaging modalities in fecal incontinence. Other diagnostic tests that may be informative include pudendal nerve terminal motor latency and electromyography.

RECOMMENDATIONS

1. Treatment of radiation proctopathy that is found incidentally on endoscopy is not recommended unless there are signs (eg, anemia) or symptoms that are affecting the patient's overall health status or quality of life because in the majority of patients, mild proctopathy will spontaneously resolve. ⊕◯◯◯

2. When endoscopic treatment of chronic radiation proctopathy is indicated, we suggest APC as a first-line approach. ⊕⊕◯◯ Because of cost considerations, hyperbaric oxygen therapy should be reserved as an alternative for patients in whom conventional treatment fails. ⊕⊕◯◯

3. We suggest topical formalin application as an alternative treatment for chronic radiation proctopathy. ⊕⊕◯◯

4. We suggest topical nitrate or calcium channel blocker application or botulinum toxin injection as a first line nonsurgical treatment for chronic anal fissure. ⊕⊕◯◯

5. We suggest referral for lateral internal sphincterotomy as the definitive treatment for chronic anal fissure and in patients in whom botulinum toxin injection fails. ⊕⊕◯◯

6. We suggest RBL or sclerotherapy as the initial treatment of choice for patients with first-degree internal hemorrhoids that bleed but do not prolapse when conservative management has failed. ⊕⊕◯◯

7. We recommend RBL as the initial treatment of choice for patients with chronic bleeding and/or prolapsing internal hemorrhoids of second- and third-degree in whom conservative management fails. ⊕⊕⊕◯

8. We suggest that all patients with fecal incontinence undergo flexible sigmoidoscopy or colonoscopy as indicated by their age, family history, and previous endoscopic evaluation. ⊕◯◯◯

9. We suggest EAUS or MRI as a complement to anorectal manometry for the evaluation of sphincter integrity in fecal incontinence in patients for whom the results are expected to affect management. ⊕⊕◯◯

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Abbreviations: APC, argon plasma coagulation; EAUS, endoanal US; FI, fecal incontinence; MRI, magnetic resonance imaging; RBL, rubber band ligation.

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