Endoscopic management of esophageal strictures

Douglas G. Adler, MD, FACP, AGAF, FASGE,1 Ali A. Siddiqui, MD, FACP2

Salt Lake City, Utah; Philadelphia, Pennsylvania, USA

GRAPHICAL ABSTRACT

Esophageal strictures remain a commonly encountered clinical entity. These strictures arise because of a wide variety of benign and malignant conditions. Dysphagia, the most common symptom, occurs when a stricture causes greater than 50% of the esophageal lumen to be obstructed as a result of benign or malignant disease. From a treatment point of view, some esophageal strictures are readily treated via minimally invasive and low-risk means, whereas others can be refractory and recalcitrant to the most aggressive endoscopic therapies. In this article we review the current state of the endoscopic management of esophageal strictures and primarily focus on evidence presented in well-constructed studies published to date.

BENIGN ESOPHAGEAL STRICTURES

Peptic strictures

Peptic strictures, so named because of their association with acid reflux, are common. Acid suppression combined with esophageal dilation (either with a through-the-scope [TTS] balloon or a bougie) are the mainstay of treatment for these lesions, and most respond well to therapy. Both types of dilators relieve dysphagia, but treatment effect may be more durable with TTS dilators.1 Proton pump inhibitor therapy has been shown to reduce the need for dilations overall.2 Steroids can also be injected into peptic strictures.3 A randomized, placebo-controlled trial of intralesional steroid injection in refractory esophageal peptic strictures showed that this treatment resulted in the need for fewer dilations and increased the time between dilations overall.4

Schatzki rings

Schatzki rings are benign, fibrous rings that are most commonly located in the lower esophagus and are strongly associated with the presence of a hiatal hernia, suggesting acid exposure as a possible cause5 (Fig. 1). Schatzki rings have also been linked to eosinophilic esophagitis (EoE).6 Many Schatzki rings are asymptomatic, but dysphagia is a common complaint in patients harboring these lesions. Acid suppression alone may help a significant number of patients with symptomatic Schatzki rings, possibly treating concomitant EoE as well.7

Esophageal dilation is a long-established treatment for Schatzki rings and can be performed with a TTS balloon or a bougie dilator. These devices were believed to be equally effective in a randomized prospective study of 251 patients undergoing dilation with both kinds of devices without a statistically significant difference in outcomes.8 In patients with rings that are recalcitrant to dilation alone, incisional therapy with a needle-knife or other

Abbreviations: EoE, eosinophilic esophagitis; FCSEM, fully covered self-expanding metal stent; SEMS, self-expanding metal stents; SEPS, self-expanding plastic stents; TTS, through-the-scope.

DISCLOSURE: The following authors disclosed financial relationships relevant to this publication: D. G. Adler: Consultant for Boston Scientific and Merit Endotek; A. A. Siddiqui: Consultant for Boston Scientific.

Copyright © 2017 by the American Society for Gastrointestinal Endoscopy

0016-5107/536.00

http://dx.doi.org/10.1016/j.gie.2017.03.004

(footnotes continued on last page of article)
device can be considered. Additional techniques to disrupt a Schatzki ring, including jumbo biopsy forceps bites, argon plasma coagulation, and endoscopic scissors, can be considered as well, although data supporting these measures are extremely scarce. We recommend dilation of Schatzki rings as first-line therapy with other more aggressive therapies held out for patients with chronic or refractory symptoms.

Eosinophilic esophagitis
A full discussion of the diagnosis and management of EoE is beyond this review, but a few salient points about the management of strictures related to EoE are warranted. Findings suggestive of EoE are commonly encountered in patients with dysphagia who present for upper endoscopy, and patients with EoE often complain of dysphagia (Fig. 2). Most patients with EoE can have marked improvement in their symptoms via medical treatment, usually with proton pump inhibitors, topical (swallowed) steroids (fluticasone, budesonide), or other medications. Patients with persistent symptoms despite medical therapy, significant esophageal strictures, and dysphagia may warrant endoscopic therapy, usually via endoscopic dilation. Endoscopic dilation, performed via TTS balloons or bougie dilators, can produce significant improvement in dysphagia symptoms and often needs to be repeated periodically. Dilatation in patients with EoE has been associated with an increased risk of perforation and should be performed with significant care (ie, careful stepwise increase in balloon size, endoscopic evaluation after dilation, etc).

Pill-injury esophageal strictures
It has long been established that certain medications, usually in pill form, can produce esophageal inflammation and a resulting stricture. Pill injuries can arise when medications produce a direct chemical burn to the esophageal mucosa. Pills can have slow or delayed transit through the esophagus in patients with underlying esophageal stenosis and poor motility and in patients taking medications while in the recumbent position or when lying supine. Even normal structures that extrinsically compress the esophagus (ie, the aortic arch or vertebral bodies) can impede passage of a pill, resulting in an injury and an associated stricture. Antibiotics, potassium supplements, quinidine, bisphosphonates, and many other medications can cause pill injury and associated strictures. In general, pill-induced injury rarely results in chronic stricture formation. Withdrawal of the offending medication and/or institution of procedures to ensure passage of the pill combined with acid-blocking medications such as proton pump inhibitors typically produce clinical resolution of symptoms.

Caustic strictures
Caustic (aka corrosive) strictures, most commonly because of ingestion of concentrated alkali solutions (lye), can be among the most difficult to treat. These strictures can be long-segment and/or multifocal in nature, have a complex geometry and architecture, may not allow standard upper endoscope passage, and are usually associated with a concomitant motility disorder because of injury to deeper tissue layers at the time of the initial chemical burn. Much of the literature on this topic is case-based, with few controlled or prospective studies performed, and treatment is often individualized and based on patient preference and physician experience, because the literature offers few firm guidelines. Endoscopic dilations are the standard of care, with many patients requiring frequent dilations.

Corticosteroids have been evaluated often as treatment options for patients with caustic strictures. An 18-year, prospective study of 60 pediatric patients with caustic strictures treated with systemic corticosteroids published in the New England Journal of Medicine failed to demonstrate a benefit, with the authors noting that the development of a caustic stricture was most commonly related to the severity of the original injury. Conversely, a study of 36 pediatric
patients with caustic injuries compared the use of prednisone with dexamethasone and found that those treated with dexamethasone had improved outcomes and required fewer dilations, somewhat conflicting with their other study. More recent data are still unclear as to the long-term value of steroids in this situation. Mitomycin-C is a topical antineoplastic antibiotic that can inhibit DNA synthesis. Topical mitomycin-C has been evaluated in several studies of patients with caustic strictures with promising results, mostly in pediatric patients. Long-term data on this treatment are lacking, and patients still typically require endoscopic dilations to achieve improvement or resolution of dysphagia. If endoscopic treatments fail, dysphagia becomes intractable, or perforation occurs, patients may need to undergo a colonic interposition or other forms of resection and reconstruction. These are invasive procedures and carry significant long-term risks of failure and adverse events. In 1 large study of caustic injuries, late adverse events occurred in half of the patients after colonic interposition for corrosive injuries and accounted for half of the so-called failures.

**Anastomotic strictures**

**Nonstent therapies.** Anastomotic strictures most commonly occur after esophagectomy for esophageal cancer but can also occur after surgery, including repair of esophageal congenital abnormalities such as esophageal atresia or after esophageal perforations or thoracic trauma (Fig. 3). Anastomotic strictures are often recalcitrant to therapy with a high rate of restenosis because there is typically some component of ischemia and fibrosis to the stricture. This situation may be further complicated by the presence of sutures, fistulas, and/or staples at the level of the stenosis.

Dilation, either with TTS balloons or bougies, is often the starting point of therapy in patients with symptomatic anastomotic strictures. Dilation alone tends to be effective in producing short-term results; some patients derive long-term results, whereas others require more-aggressive interventions. Some carefully selected patients can be taught to self-dilate with a bougie. Other approaches have historically included steroid injection, the use of a needle-knife to try to disrupt fibrotic bands, or a combination of these methods. In single-arm studies, these techniques are usually found to have some benefit. Prospective studies comparing these techniques are few in number.

A prospective, multicenter, double-blind trial of endoscopic corticosteroid injections combined with dilation in 60 patients with anastomotic strictures found that steroid injections did not prolong the dysphagia-free period over dilation alone. This may reflect the fact that many of these strictures have very little inflammatory component, and, as such, corticosteroids may not be the appropriate agent to use in this setting.

Savary bougienage was compared with electrocautery incision in a prospective, multicenter study of 62 patients by Hordijk et al. Patients were compared at 1, 3, and 6 months after the first treatment. No patients had major adverse events, and overall these 2 modalities were found to be equally effective. In contrast to the use of steroid injection, both of these techniques are able to physically disrupt fibrotic tissue, which may explain the effectiveness seen in both treatment arms. In our experience, nonstent-based therapies often produce less than ideal results, and many patients undergo esophageal stent placement for anastomotic strictures.

**Stent-based therapies.** The advent of esophageal self-expanding metal stents (SEMSs), especially fully covered SEMSs (FCSEMSs), gave endoscopists a treatment approach that was potentially more durable, more...
aggressive, and potentially removable (in the case of FCSEMSs). Although stents are usually deployed over a guidewire under fluoroscopic guidance, more acute placement is required in proximal malignant strictures; in these cases the stent can be placed under both endoscopic and fluoroscopic guidance. Stents can potentially relieve dysphagia and treat the underlying stricture simultaneously. Self-expanding plastic stents (SEPSs) have been used in this context but are now largely obsolete despite significant data showing their effectiveness. SEPSs have a cumbersome assembly process and a large-diameter delivery catheter when compared with SEMSs, and, as such, SEPSs are no longer in widespread use.

Despite the appeal of these devices, results have been less than ideal in clinical trials, and the available literature on these devices is largely retrospective. A large multicenter study of outcomes of esophageal SEMSs in patients with benign esophageal diseases included 13 patients with anastomotic strictures who underwent a total of 23 procedures. Only 3 of 13 patients (23%) had treatment success, defined as durable relief of symptoms after stent removal. A study of 23 patients with adverse events of esophagectomy treated with stents found that those patients with strictures had only a 27% success rate, further demonstrating how difficult these strictures are to treat. Lumen-apposing metal stents can be used in an off-label manner to treat anastomotic structures (Fig. 4). Biodegradable stents are available outside of the United States and have been used to treat anastomotic strictures in several case reports, but overall the literature on biodegradable stents in this context is too small from which to draw any conclusions.

MALIGNANT ESOPHAGEAL STRICTURES

Malignant dysphagia is defined as difficulty in swallowing as a result of partially or completely obstructed esophageal lumen because of cancer (Fig. 5). Greater than 50% of patients with esophageal carcinoma present with locally advanced stage or distant metastases with tumor-related symptoms. These patients often present with dysphagia, which increases as the disease progresses. Surgical resection or curative chemoradiotherapy is often not feasible in these patients as a result of severe comorbidities and/or metastatic disease. Therapy of dysphagia is required mainly under 2 circumstances: for those with metastatic disease and for those with locally advanced disease who are undergoing neoadjuvant chemoradiotherapy before curative surgery.

The goals of therapy are to relieve symptoms of dysphagia, maintain oral intake, retard or halt weight loss, decrease hospital stay, and improve quality of life. Endoscopic therapies used to treat malignant dysphagia in patients with esophageal carcinoma include bougie (Savary-Gilliard) or balloon dilators, thermal energy (Nd-YAG laser, argon beam coagulation), laser-induced photodynamic damage with singlet oxygen to destroy tumor cells (photodynamic therapy), and esophageal stents. Dilation produces short-lived benefits in patients with malignant dysphagia. Lasers, although effective, are rarely used to treat malignant dysphagia anymore. Photodynamic therapy and argon plasma coagulation are likewise rarely used in this context.

Esophageal stents

Esophageal stents are one of the primary means used to relieve dysphagia in patients with unresectable esophageal carcinoma and in those with a short life expectancy. Other malignant conditions where patients benefit from stent placement include extrinsic compression from lung cancer, mediastinal cancer, or metastatic disease.

The main advantages of stent therapy include successful insertion of the device in almost all cases, rapid (24-48 hours) relief of dysphagia, a low rate of major adverse events, and an acceptable cost of treatment.
Disadvantages of stent therapy are reocurrence of dysphagia in up to one-third of patients and stent-related adverse events, including pain, bleeding, and fistula formation. Although most stents are placed in the mid or distal esophagus across the gastroesophageal junction, insertion in the proximal esophagus is now considered equally effective, provided the lesion is located away from upper esophageal sphincter by more than approximately 2 cm; some patients, however, warrant stent placement above this level. The characteristics of the stent selected are based on tumor length, tumor bulk, tumor location, and configuration of the obstructive stricture. No single stent type or design is believed to be ideal, and treatment should be individualized. After assessment by an upper endoscopy, the stent is deployed with its ends extending beyond the margin of growth by at least 2 cm on each side (if possible) to prevent tumor overgrowth.

Esophageal SEMSs have now evolved to be the predominant modality to treat malignant esophageal strictures. Current SEMSs consist of a nitinol wire design (which can be braided or laser-cut), which allows them to conform to the anatomic configuration of the tumor. Most SEMSs that are currently used have a partial or full covering that reduces tumor ingrowth, although these coatings may increase migration rates.

Although the polyester Polyflex (Boston Scientific Endoscopy, Nantucket, Mass) stent is the only available SEPS, its use in malignant dysphagia is uncommon because of a wide stent deployment catheter diameter, a cumbersome assembly and operation, and a high stent migration rate. Although still commercially available, these devices are in limited use at this time.

Several randomized trials have evaluated the use of uncovered SEMSs for palliation of malignant strictures. Knyrim et al performed 1 of the sentinel randomized trials that provided evidence that SEMSs were advantageous in the palliation of malignant dysphagia compared with plastic prosthesis. In their study, 42 patients were randomized to either a conventional plastic prosthesis or an uncovered SEMS. Although dysphagia and quality of life scores had similar degrees of improvement and comparable reintervention rates, adverse events were significantly less in the SEMS group versus the plastic prostheses group. Despite the initial higher costs of SEMSs, metal stents were still more cost-effective over the long term as a result of decreased hospitalization stay and absence of fatal adverse events. Selinger et al evaluated 137 patients with progressive dysphagia. Relief of dysphagia occurred in 94% of patients. Chest pain was seen in 14% of patients, and perforation as a result of stent deployment occurred in 5.8% of cases. A comparative study randomized 101 patients using SEPS or uncovered SEMSs and showed similar efficacy for palliation of dysphagia. However, SEPSs were associated with higher failure of stent placement and greater migration rate compared with SEMSs. Insertion was believed to be technically more difficult, and dilation had to be performed more frequently.

When deciding on the characteristics of metal stents, partially covered SEMSs are superior to uncovered SEMSs for palliation of malignant dysphagia using chemotherapy/radiotherapy/brachytherapy in unresectable esophageal cancers and are most commonly reserved for this setting. Initial relief of dysphagia and migration rates between the 2 SEMS types are similar. Recurrent dysphagia as a result of tumor ingrowth is significantly higher with uncovered SEMSs. No differences in performance status and survival were noted between the 2 groups. Retrospective series have shown an increased rate of stent migration, bleeding, and fistulization in patients treated with previous chemoradiation who had uncovered SEMSs.

In patients with locally advanced cancer, Siddiqui et al showed that FCSEMSs were safe and effective to improve dysphagia and allowed for oral nutrition during neoadjuvant therapy. Although stent migration was high (31%), this was not associated with injury or harm to the patient and usually represented a positive response to neoadjuvant therapy.

Antimigration features of SEMSs include the following: (1) increased diameter of the stent flares, (2) no covering of the proximal and distal ends of the metal mesh to allow some degree of localized tissue ingrowth to help fix the stent in place, (3) addition of struts to the outer stent covering that then act as anchoring devices, and (4) specialized shapes (especially of the flanges) to minimize migration. Despite these design modifications, studies show that these covered stents frequently migrate. It should be noted that migration of a FCSEMS is not always a bad thing per se, because migration after neoadjuvant therapy for esophageal cancer may indicate a reduction in tumor burden and a clinical response to treatment. Most migrated stents can be easily removed endoscopically. In rare cases, a stent that has migrated below
A high-grade stricture may be difficult or impossible to remove. In patients with FCSEMs or those receiving chemoradiotherapy where there is higher risk of migration, endoscopic suturing or over-the-scope clips have been demonstrated to effectively reduce the migration rate.76

Polymeric biodegradable stents and drug-eluding stents are commercially available in certain countries and may enter the U.S. market in the future. Although they have potential advantages over currently used metal stents for a range of clinical applications, more robust research is required in establishing the role of these devices in clinical practice.

**Adverse events related to esophageal SEMSs.** The adverse event rate in patients receiving esophageal stents is 30% to 35%; the adverse event rate increases with a longer stent indwelling time. There may be a myriad of short-term adverse events, which include stent expansion resulting in increased postprocedural dysphagia, retrosternal pain, stent migration, tracheal compression in stenting of the proximal esophageal tumors, and esophageal bleeding. The most common long-term adverse events include recurrent dysphagia and fistula formation. Stent-related esophageal perforation is rare.

Development of retrosternal pain after stent insertion may occur in up to 60% of cases. The pain usually lasts for 3 to 10 days, with most patients requiring analgesics. Our practice is to supply all patients with a short-term supply of pain medications after esophageal stent placement. We also recommend administering proton pump inhibitors (if the stent crosses the gastroesophageal junction), antiemetics, and nonsteroidal anti-inflammatory drugs to reduce discomfort. Prolonged pain may require narcotic use.27 Removal of stents as a result of severe pain is required in only 5% to 14% of cases.76-80

Recurrence dysphagia may develop in almost one-third of patients. In cases of tumor overgrowth or ingrowth, placement of a second stent is effective to restore luminal patency in most cases.71,86 Blockage of a stent because of impacted food is typically managed by endoscopic stent clearance. Another rare late adverse event is spontaneous stent fracture with collapse.83,84

Formation of an esophagorespiratory fistula usually occurs several months after stent placement. The radial forces of the stent can result in pressure necrosis, usually next to the proximal or distal flanges of the stent. Fistulas of this type can sometimes be treated via stents, clips, sutures, or a combination thereof but in practice may be recalcitrant to all endoscopic therapies.

**Cryotherapy**

Endoscopic spray cryotherapy with low-pressure liquid nitrogen is a novel method for the treatment of malignant dysphagia by debulking advanced esophageal tumors (Fig. 6). This form of cryotherapy can effectively snap-freeze the tissue. The thawing process after freezing causes oxidative cell death (reperfusion injury) and results in immediate cell death while preserving the underlying tissue architecture and extracellular matrix, debulking the tumor, and causing limited long-term scarring.79 In a 2014 case study, a 63-year-old patient with esophageal squamous cell carcinoma with recurrent disease developed dysphagia as a result of tumor ingrowth at the ends of a previously placed metal stent. Liquid nitrogen cryotherapy was used to recanalize the lumen of the metal stent successfully.86 Cash et al77 reported the use of liquid nitrogen cryotherapy for recurrent esophageal squamous cell cancer, showing a relief of symptomatic dysphagia and disease-free survival at the 2-year follow-up. Literature on cryotherapy remains limited, although the technology is widely available.

**Other therapies for palliation of malignant dysphagia**

Several thermal tumor ablation treatments are available for palliation of malignant dysphagia. Argon plasma coagulation has been widely used to debulk tumors and thereby relieve obstruction and dysphagia. In a study with 83 esophageal cancer patients, argon plasma coagulation achieved recanalization, permitting passage of normal food in 48 patients (58%) after 1 session and an additional 22 patients (84%) after 2 sessions.88 High-power Nd:YAG laser can provide palliation of dysphagia by coagulating and vaporizing malignant tissue with endoscopic control. Palliation, with ingestion of a soft diet, can be achieved in most patients for about 4 to 6 weeks.88 The least-expensive endoscopic technique for esophageal cancer ablation is the chemical method of injecting absolute alcohol as a sclerosant during endoscopy. However, experience with this is limited, and damage to normal tissue and perforations have been reported.89 Although photodynamic therapy can be safely used for palliation of cancers that cause complete obstruction of the

**Figure 6.** Spray cryotherapy was applied in a palliative manner to an esophageal cancer that caused a stricture and was producing malignant dysphagia.
esophageal lumen, it has major problems that include retention of photofrin in the skin for about 6 weeks after injection, leading to severe photosensitivity.91

CONCLUSION

Esophageal strictures, both benign and malignant, remain commonly encountered clinical entities. A variety of endoscopic therapies is available to treat these strictures, although even in the current era there are relatively few prospective and/or randomized studies available to compare different techniques and clinical outcomes, and most of the available literature is based on retrospective data. Although we have made great strides in some areas (treatment of Schatzki rings and malignant strictures), some esophageal strictures (such as refractory benign strictures) continue to defy our most aggressive interventions. Future research should focus on complex or difficult strictures with well-constructed studies comparing different modalities in an effort to identify ideal treatment algorithms.

REFERENCES


1. True statements regarding anastomotic strictures
   a. usually have long-lasting response to dilation using bougies
   b. May respond to injections of mitomycin-C
   c. Have a significant inflammatory component and respond to systemic steroids
   d. Savary dilation is as effective as electocautery incision to disrupt the stricture

2. The most common long-term adverse events of stent placement for malignancy include
   a. perforation
   b. bleeding
   c. recurrent dysphagia
   d. fistula formation

True or False

3. Self-expanding metal stents are preferred over self-expanding plastic stents for the management of difficult strictures.

4. Schatzki rings that recur despite multiple dilations are best treated by injecting steroids.

5. During neoadjuvant chemo-radiation, stents frequently migrate as the tumor shrinks.

6. Stents for upper esophageal tumors work best if the lesion is at least 2cm below the UES.

7. Self-expanding metal stents provide excellent clinical results in the management of difficult benign strictures

8. If a Schatzki ring is identified during an endoscopy for intermittent dysphagia, there is no need to do random esophageal biopsies to exclude eosinophilic esophagitis.

9. Covered esophageal stents reduces tumor ingrowth but increases chances of stent migration

10. New covered stents with modifications to prevent migration rarely migrate.

11. After stent placement, up to 60% of patients develop severe chest pain that lasts 3-10 days and requires narcotics for control.