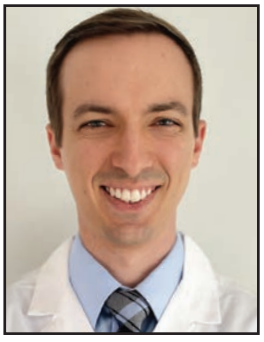
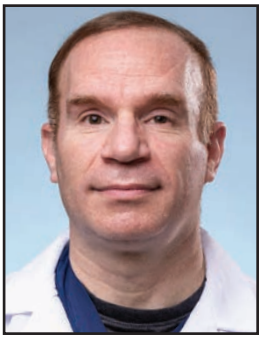
Douglas G. Adler MD, FACG, AGAF, FASGE, Series Editor

Endoscopic Management of Small Intestinal and Colorectal Anastomotic Strictures



Michael B. Andrews



Douglas G. Adler

INTRODUCTION

Small intestinal and colorectal anastomotic strictures are often difficult-to-treat post-surgical adverse events. Surgical re-intervention was previously first-line therapy, but advancements in endoscopic techniques have made endoscopy the first-line treatment approach. This review will assess the efficacy and adverse events of the currently available endoscopic management techniques for the treatment of small intestine and colorectal anastomotic strictures.

Small Intestinal Anastomotic Strictures

Etiology

Small intestinal anastomotic strictures are post-surgical adverse events following small bowel resection for malignant or benign conditions including perforation, ischemia, and Crohn's disease.[1] Surgical resection is required in 50-80% of patients with Crohn's disease within the first 10 years of diagnosis, and approximately one-third of patients will require at least a second surgery due to development of an anastomotic stricture.[2,3]

Risk Factors

Risk factors for anastomotic complications have been studied extensively in patients with Crohn's disease and show an increased risk with pre-operative poor nutritional status, weight loss, steroid use, and longer duration of disease.[4] However, more studies are needed to identify the patient risk factors specifically for small bowel anastomotic stricture development.

Choy et al. performed a meta-analysis comparing surgical anastomotic closure techniques among 1,125 patients which showed no difference in anastomotic stricture rates between hand-sewn and linearly stapled anastomoses.[5]

Clinical Manifestations

Patients commonly present with obstructive

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symptoms including abdominal pain, distention, bloating, nausea, and/or vomiting.[6]

Endoscopic Balloon Dilation

Technique

Endoscopic balloon dilation (EBD) is most commonly performed using inflatable through-the-scope (TTS) balloon dilators available in various lengths (3-8cm) and diameters (6-20mm).[2,3,7,8] The balloon dilator is positioned across the stricture with or without guidewire assistance followed by inflation using a handheld device to inject saline or contrast.[7] The main challenge using EBD to treat small intestinal anastomotic strictures compared to more proximal anastomotic strictures is reaching the stricture, which often requires push enteroscopy or balloon-assisted enteroscopy.[8]

Efficacy

Clinical success rates for EBD for small intestinal anastomotic strictures across multiple studies range from 44-89% following a mean of approximately two sessions.[2,3,9,10] Ding et al. performed a retrospective cohort study of 54 patients with Crohn's disease-related anastomotic strictures and observed a decrease in repeat EBD with escalation of medical therapy, strictures <40mm long, and shorter disease duration at the time of initial EBD.[2] Hassan et al. and Ferreira-Silva et al. reported similar improved outcomes (higher success rates with decreased need for surgical re-intervention) when anastomotic strictures were <40mm long.[3,10] Unfortunately, stricture recurrence remains a problem following EBD, occurring in 46-62% of patients and requiring use of other endoscopic therapies or surgical re-intervention.[3,10]

Adverse Events

Perforation was the most frequent adverse event with Ding et al. reporting perforation in 1.85% (1/54) of patients and 0.6% (1/151) of procedures whereas Hassan et al. reported perforation in 3.7% (13/347) of patients and 1.9% (13/695) of procedures.[2,3]

Self-Expandable Metal Stents

Technique

Self-expandable metal stents (SEMS) are composed of metal mesh which can be covered with overlying silicone or plastic to resist tumor or tissue ingrowth.[11] SEMS for small intestinal use are either uncovered (UCSEMS) or partially covered (PCSEMS).[11] These include the uncovered Wallstent and Wallflex stents (Boston Scientific, Natick, Massachusetts, United States) and the uncovered or partially covered Hanarostents (M.I. Tech, Seoul, Korea) available in various diameters (20-22mm) and lengths (60-170mm).[11,12] SEMS work by exerting constant radial force against the anastomotic stricture until removal during a subsequent endoscopic procedure.[11]

Efficacy

Branche et al. and Das et al. published case series with a combined 26 patients, all having anastomotic stricture lengths <6cm treated with the partially-covered Hanarostent, and observed clinical success rates of 100% and 81%, respectively.[12,13] However, Branche et al. noted recurrence in 33% of patients at six-month follow-up.[12] Ferreira-Silva et al. reported clinical success rates of 36-100% in 71 total patients across case reports and series.[10]

Adverse Events

Migration was the most reported adverse event seen in as many as 15.8% (3/19) of patients in Das et al.'s case series using PCSEMS.[10,12,13] It is important to understand stent migration is not always a true adverse event and instead may occur following stricture resolution as there is no stenosis to anchor the stent in place. Nonetheless, anchoring techniques have been used to reduce migration rates including endoscopic suturing and TTS or over-the-scope (OTS) clips attaching the stent to adjacent mucosa.[14] In a case series of seven patients, Senol. et al. described successful use of TTS clips to affix jejunal SEMS with a 0% migration rate.[14]

Lumen-Apposing Metal Stents

Technique

The AXIOS stent (Boston Scientific, Natick MA, United States) is the only commercially available lumen-apposing metal stent (LAMS) in the United States and was originally designed with FDA approval for draining pancreatic fluid collections.[15,16] However, LAMS are commonly used in an off-label manner for the treatment of luminal strictures, including small intestinal anastomotic strictures.[15]

LAMS are 8-15mm long with diameters of 6, 8, 10, 15, and 20mm.[15,16] LAMS are deployed across the anastomotic stricture using a guidewire under a combination of endoscopic and fluoroscopic visualization.[15]

The AXIOS catheter is often not long enough to reach distal small intestinal anastomotic strictures. Ferrell et al. reported a modified technique to assist in reaching distal small intestinal anastomotic strictures.[17] The AXIOS stent was deployed into sterile water followed by twisting the ends in opposite directions and backloading the stent into the distal end of the working channels of a colonoscope and double-balloon enteroscope.[17] Once the stricture was reached, the stent was manually deployed using biopsy forceps. In general, LAMS are deployed across strictures within reach of an upper endoscope, which includes duodenal and proximal jejunal strictures.

Efficacy

Ferrell et al. utilized the modified technique described above to reach distant small intestinal anastomotic strictures in two patients with strictures <1cm long that were previously refractory to EBD.[17] Both patients remained asymptomatic without signs of stricture recurrence at three-month follow-up.[17] Axelrad et al. reported a case with successful use of LAMS in a patient with a 1cm small intestinal anastomotic stricture refractory to EBD.[18] The stent was removed after 60 days, and the patient remained asymptomatic without signs of stricture recurrence at 90-day follow-up.[18]

Adverse Events

Neither Ferrell et al. nor Axelrad et al. reported adverse events in the three cases.[17,18]

Biodegradable Stents

Technique

Biodegradable stents (BDS) were designed to treat esophageal strictures but have been used off-label for treatment of other luminal strictures, including small intestinal anastomotic strictures.[19,20] The SX-ELLA BDS (ELLA-CS, Hradec Kralove, Czech Republic) is the only commercially available BDS but is not approved for use in the United States. BDS range in diameter (18-25mm) and length (60-135mm) with flared ends (23-27mm wide) designed to reduce stent migration.[10,19,20] BDS are constructed of synthetic polymers which supply radial force against the stricture for 4-6 weeks before degrading and fragmenting over the next 6-24 weeks, after which they spontaneously pass.[10,19]

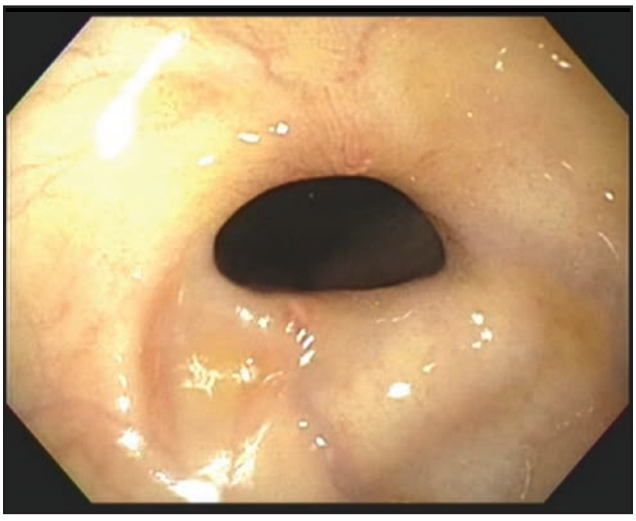

Figure 1. Moderate colonic anastomotic stricture showing circumferential fibrosis

BDS require assembly prior to placement. These devices are advanced across a stricture using a guidewire under endoscopic and/or fluoroscopic visualization.[19,20] Positioning of the stent is facilitated by locating the radiopaque ends of the stent with fluoroscopy.[19] The main limitation to using BDS for small intestinal anastomotic strictures is the potential inability of the BDS delivery system to reach distal strictures.[19]

Efficacy

Rejchrt et al. performed a case series with 11 patients including 8 who had small intestinal anastomotic strictures treated with BDS.[19] All patients underwent EBD prior to stent placement.[19] 62.5% (5/8) of patients were asymptomatic at follow-up ranging from 12-26 months, and complete BDS degradation was noted at a mean of four months.[19]

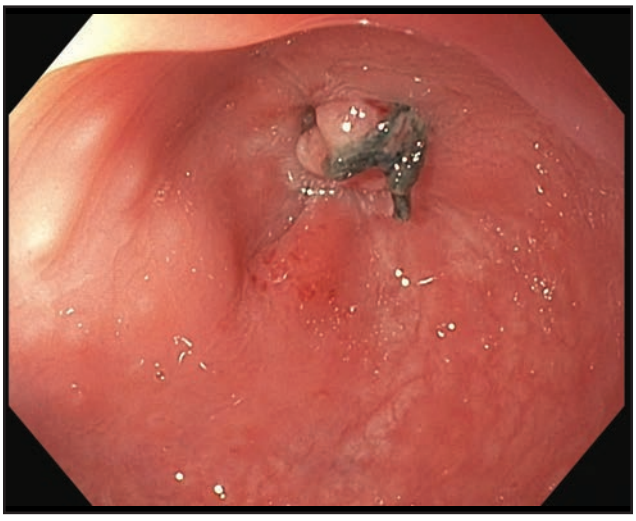

Figure 2a. Severe colonic anastomotic stricture with visible suture material and a pinhole lumen

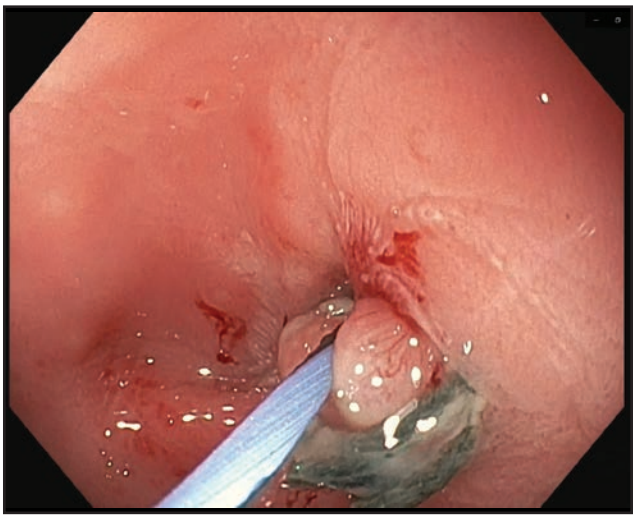

Figure 2b. Guidewire placement across the stricture prior to LAMS placement

Adverse Events

Rejchrt et al. reported stent migration in 37.5% (3/8) of patients.[19] No other adverse events were reported.[19]

Colorectal Anastomotic Strictures

Etiology

Colorectal anastomotic strictures may result following partial or complete colonic and/or rectal resection. (Figure 1) Common indications for resection include malignant or benign conditions including diverticulitis, inflammatory bowel disease, perforations, and ischemic bowel.[21] Post-operative colorectal anastomotic strictures occur in 2-30% of patients.[21,22,23,24] Jain et al. noted most colorectal anastomotic strictures are diagnosed within one year of surgery.[24]

Risk Factors

Patients are at increased risk of developing colorectal anastomotic strictures if they are male, smoke tobacco, underwent neoadjuvant or adjuvant radiation therapy, or experienced perioperative anastomotic leakage.[22,24,25] Anastomotic leaks increase the risk for anastomotic stricture formation by promoting local inflammation with resultant fibrosis and stenosis.[24] Risk factors for anastomotic leakage include male sex, diabetes, obesity, kidney disease, cardiovascular disease, radiation therapy, smoking, heavy alcohol use (>35 drinks/week) and the use of immunosuppressive medications such as steroids.[26]

Slesser et al. performed a meta-analysis of 10 randomized controlled trials with 1,969 patients examining the risk for colorectal anastomotic strictures among different surgical anastomotic closure techniques.[27] They reported no difference in colorectal anastomotic stricture rates between hand-sewing, stapling, or using compression rings to create anastomoses.[27] One surgical technique shown to reduce risk of colorectal anastomotic strictures is mobilization of the splenic flexure which was observed by Surek et al. in a retrospective cohort study of 375 patients.[28]

Clinical Manifestations

Patients may experience abdominal pain, bloating, distention, nausea, vomiting, constipation, and/or weight loss.[29] While symptoms often occur within the first year following surgery, there have been reports of onset as early as one month after surgery and as late as 12 years after surgery.[24]

Endoscopic Balloon Dilation

Technique

EBD is first-line therapy for treating colorectal anastomotic strictures using the same techniques described previously for small intestinal anastomotic strictures.[8,23,30] Most colorectal anastomotic strictures are reachable with standard colonoscopes, but, rarely, strictures may require push enteroscopy or balloon-assisted enteroscopy in

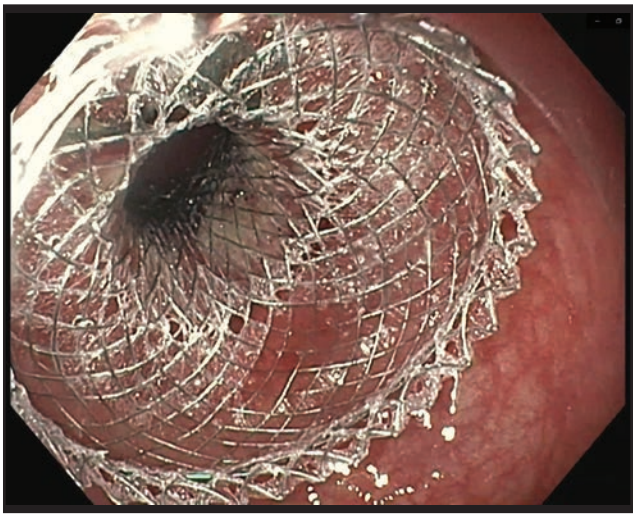

Figure 2c. LAMS placed across stricture to good effect

certain cases such as patients with tortuous colons.[8] Klag et al. cautioned dilation beyond 25mm due to a perceived increased risk of perforation.[8]

Efficacy

Hong et al. noted clinical success rates of 88-100% using EBD with recurrence rates of 30-88%.[21] Clifford et al. performed a systematic review including ten studies with 380 patients treated with EBD which showed clinical success rates of 80.6-100% after a mean range of 1-3 dilation sessions.[22] Araujo et al.'s case series of 24 patients and Di Giorgio et al.'s prospective cohort study of 30 patients observed clinical success in 91.7% and 100% of patients following a mean of 2.3 and 2.6 dilation sessions, respectively.[23,30]

Despite initial clinical success rates that are high, stricture recurrence is common after EBD. Biraima et al., in a retrospective cohort study of 76 patients, found that 49% of patients required more than two dilation sessions to achieve clinical success, and stricture recurrence occurred in 11% of patients at 12 months, 22% of patients at 24 months, and 25% of patients at 60 months. [31]

Thomas-Gibson et al. performed a retrospective cohort study of 53 patients with Crohn's disease related colorectal anastomotic strictures and observed initial success in 82% of patients.[32] However, long-term clinical success (remaining asymptomatic after six months) was observed in only 42% of patients at mean follow-up of 21 months.[32] 58% of patients required another surgery within a median of 4.9 months following EBD.[32]

Adverse Events

Perforation was reported in 1.18% (6/509) of patients across multiple studies.[22,31,32] Other infrequently reported adverse events included minor bleeding and fever.[22]

Self-Expandable Metal Stents

Technique

SEMS for colorectal use were originally designed for, and continue to be used for, treatment of malignant large bowel obstruction.[21] Because these stents were intended to either be left in place as a palliative device or to be removed by surgery, they are only available as UCSEMS in the United States. Epithelization of these stents commonly occurred but was not considered an adverse event.[21] As their use expanded to include treatment of benign strictures, including colorectal anastomotic strictures, fully covered (FCSEMS) colorectal stents were manufactured which reduced epithelialization and made stent removal feasible, but these are not available in the United States.[21]

Commercially available SEMS include Wallflex colonic stents (Boston Scientific, Natick MA, United States) available in various diameters (22-25mm) and lengths (60-120mm).[11] The colonic Z-stent and Evolution stents (Cook Medical, Winston-Salem, NC) are also available in various lengths (40-120mm) with a 25mm diameter.[11] Stent placement near the dentate line should be avoided to reduce the risk of tenesmus and pain.[33]

Efficacy

Clinical success rates using SEMS ranged from 25-70% across three case studies with a combined 48 patients.[21,33,34] Caruso et al. performed a case series of 16 patients in Italy and observed a significant difference (p-value 0.035) in clinical success rates between patients treated with smaller FCSEMS 20-22mm in diameter (17%) compared to larger FCSEMS 24-26mm in diameter (80%).[34]

Adverse Events

Stent migration was the most common adverse event reported among the 48 patients.[21,33,34] Caruso et al.

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and Lamazza et al. treated anastomotic stricture patients with FCSEMS and noted stent migration in 19% and 37.5% of patients, respectively.[33,34] Hong et al. and Lamazza et al. treated patients with UCSEMS and noted stent migration in 17% and 0% of patients, respectively.[21,33] Hong et al. also noted UCSEMS epithelialization in 17% of patients with a median follow-up time of 16.7 months.[21] Other reported adverse events included pain and minor bleeding without any reports of perforation.[21,33,34]

Lumen-Apposing Metal Stents

Technique

Using the previously described technique, LAMS can be used in an off-label manner to treat short (<1-1.5cm long) colorectal anastomotic strictures.[35,36] (Figure 2) Pre-stent or in-stent dilation may be utilized at the discretion of the operator.

Efficacy

Xu et al. described successful use of LAMS with in-stent dilation to treat a <1cm long malignant colorectal anastomotic stricture previously refractory to EBD.[35] The LAMS remained patent at six months, and the patient remained asymptomatic at 14-month follow-up, the last follow-up prior to the case report's publication.[35]

Kankotia et al. performed a retrospective cohort study of 29 patients comparing EBD (N=18) and LAMS (N=11) for treatment of benign colorectal anastomotic strictures.[36] They observed no significant difference in clinical success (EBD 66.7% vs. LAMS 81.8%; p-value 0.67) or stricture recurrence (EBD 33.3% vs. LAMS 11.1%; p-value 0.35), but the trend favored LAMS overall.[36]

Adverse Events

The most common adverse event reported by Kankotia et al. was LAMS migration seen in 46% (5/11) of patients.[36] However, stent migration is not always a true adverse event and may instead be a surrogate marker of stricture resolution. There were no reports of perforation, bleeding, or pain in the LAMS group.[36]

Biodegradable Stents

Technique

BDS have been used outside the United States in an off-label manner to treat colorectal anastomotic strictures via the previously described technique.[37,38]

Efficacy

Repici et al. and Janik et al. performed case series with a combined 14 anastomotic stricture patients treated with BDS following pre-stent dilation.[37,38] Repici et al. observed a less-than-ideal clinical success rate of 45% (5 of 11 patients) whereas Janik et al. observed clinical success in 100% (3/3) of patients with stent degradation noted at 4-5 months.[37,38]

Adverse Events

Janik et al. reported no adverse events.[38] Repici et al. noted BDS migration in 36% (4/11) within two weeks.[37] No other adverse events were reported.[37]

Endoscopic Incisional Therapy

Technique

Endoscopic incisional therapy (EIT) is a commonly utilized modality to treat esophageal strictures and has been successfully used to treat colorectal anastomotic strictures.[22,39,40] Multiple radial incisions of operator-dependent length and depth are made around the stricture with or without excision of the fibrosed mucosal tissue in-between incisions.[40] Operators have an array of instruments available to create the incisions including sphincterotomes, needle knives, insulation-tip (IT) knives or other endoscopic submucosal dissection (ESD) knives, and even polypectomy snares with argon plasma coagulation (APC) as seen in one study.[40]

Efficacy

Clifford et al. performed a systematic review including three retrospective cohort studies with a combined 455 patients treated with EIT which showed clinical success rates ranging from 71.4-100%.[22] Jain et al. performed a meta-analysis with 186 patients treated with EIT alone or in combination with other modalities such as EBD or steroid injection.[40] 95.5% of patients treated with EIT alone achieved clinical success with stricture recurrence in 2.8% of patients.[40] 87.8% of patients treated with combined EIT and EBD achieved clinical success with stricture recurrence in 12.5% of patients.[40] 91.2% of patients treated

with combined EIT and steroid injection achieved clinical success.[40]

Adverse Events

Jain et al. reported pain in 3.8% (7/186) of patients.[40] Clifford et al. did not report any adverse events among their 455 patients.[22]

CONCLUSION

Small intestinal and colorectal anastomotic strictures pose a significant clinical challenge, and endoscopic management techniques continue to advance providing many solutions, each with varying efficacies and associated adverse events. For both small intestinal and colorectal anastomotic strictures, endoscopic balloon dilation remains first-line therapy but is hindered by high recurrence rates. Stenting with SEMS, LAMS, or BDS serves as another treatment option while endoscopic incisional therapy is another solution for small bowel and colorectal anastomotic strictures. ■

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