Introduction

Historically, surgical management of gastrointestinal fistula was the sole option, but it is associated with high morbidity and mortality [1]. Medical management has emerged as an important adjunct, and more recently interventional radiology has taken a prominent role in the management of these complex patients [2]. As flexible endoscopic technology has improved and new endoscopic devices have been developed, endoscopists are expanding their role in the management of gastrointestinal fistula. Endoscopically deployable stents, endoscopic suturing devices, through-the-scope and over-the-scope clips, sealants, fistula plugs and vacuum sponges are among the technologies being used to treat fistulas. These allow many patients to avoid surgical fistula repair. We will review the emerging role of endoscopy in the management of gastrointestinal fistula.

Definition and Classification

Fistulas can be internal or external. External fistulas involve a communication between the gastrointestinal tract and skin; internal fistulas connect the gastrointestinal tract to the peritoneal space, retroperitoneal space, thorax or another internal organ [3].

Fistulas are classified by etiology, anatomy (origin and ending site), and output (low <500 ml/day, or high >500 ml/day) [4]. End fistulas are distinguished from lateral (side) fistulas. End fistulas have complete loss of continuity of the gastrointestinal tract beyond the fistula and require surgical repair. Complex fistulas are multiple connected fistulas arising from different organs.

Etiology

The majority of fistulas occur after surgical procedures (75-85%) [4]. Rate of fistulization or leak varies dramatically among surgical procedures: pancreaticoduodenectomy (5-8%), liver transplantation (2-9%), cholecystoduodenostomy (5-19%), total gastrectomy (0-28%), esophagectomy (2%), elective colectomy (5%), laparoscopic Roux-en-Y gastric bypass (RYGB) (2-5%), open RYGB (2-3%), and sleeve gastrectomy (5%) [5,6]. The remaining 15-25% of fistulas form without surgical intervention. Inflammatory bowel disease, divertic-
ulosis, malignancy, and radiation therapy are associated with fistula formation. Trauma such as gunshot wound, stab wound, or blunt trauma can also lead to fistulas [4].

**Endoscopic management**

**Localization**

Localization of the fistula orifice may be challenging. Imaging can be helpful. Fistula with a drain in place can be localized using contrast and methylene blue. If an external drain is in place, it can be submerged under water. Carbon dioxide insufflated through the endoscope should produce bubbles from the drain. Next, methylene blue and radiopaque contrast can be injected into the drain with endoscopic and fluoroscopic visualization of the fistula tract and opening. The anatomy of the gastrointestinal tract surrounding the fistula os is an important determinant of optimal therapy for fistula closure. Stents, for example, are not likely to be effective for treatment of a fistula in a recessed area such as the blind portion of the Roux limb.

**Sealants**

Fibrin sealant, a biodegradable compound, has been used in surgery for attachment of skin grafts, colostomy closure, hemostasis, and even for preventing gastrointestinal fistula [7]. Fibrin sealant may block passage of gastrointestinal contents through the fistula, and promote cellular migration, angiogenesis and tissue repair via fibroblast and keratinocyte growth.

Endoscopic application of fibrin sealant can be performed via a catheter. Once granulation tissue that has formed over the opening of the fistula has been excoriated, argon plasma coagulation APC should be used to ablate the tissue surrounding the fistula os. Endoscopic application of fibrin can be performed using double-lumen catheters. However, rapid-exchange catheters are unsuitable, as they may allow leakage inside the instrument channel. If these are used, the more viscous component should be inserted through the catheter’s larger diameter lumen. Care must be taken when applying fibrin sealant, as the two components have different viscosities and will pass through the catheter at different rates. Varying amounts of adhesive will be necessary, depending on the size of the fistula. Multiple applications are sometimes required.

Large prospective trials of fibrin sealant are necessary to confirm its usefulness in the treatment of gastrointestinal fistula. Further research could elucidate which fistula types are most amenable to treatment with fibrin sealant. At this point, endoscopic treatment of gastrointestinal fistula with fibrin sealant appears to be safe and effective.

**Stent Placement**

Endoscopic placement of self-expanding stents allows exclusion of gastrointestinal contents from the fistula, and allows healing while enteral nutrition is resumed [8]. Covered self-expanding metal stents (SEMS) and self-expanding plastic stents (SEPS) have been studied for treatment of fistula.

After endoscopic identification of the fistula os, and fluoroscopic confirmation, the stent is deployed to exclude the fistula. In the esophagus, the stent should be deployed below the upper esophageal sphincter to avoid inducing globus. The distal end should not impact the enteral wall. Once deployed, the stent position can be
adjusted with forceps, and stents can be clipped or sutured into place [9]. After 8 weeks, stent removal can become challenging. When stents cannot be removed with forceps due to tissue ingrowth, APC may be needed to fulgurate tissue to facilitate stent removal. Placement of SEPS within metal stents for one week can induce necrosis of tissue ingrowth and ease subsequent stent removal [5]. Other complications of stent placement include pain, occlusion, migration, perforation, bleeding, aspiration and inadequate exclusion of the defect. Esophageal stents may be complicated by tracheoesophageal fistula and esophageal reflux [10].

A meta-analysis of 7 studies utilizing SEMS and SEPS for treatment of leaks after bariatric surgery reported a pooled proportion for leak closure of 87.8% [11]. Only 9% of patients required surgical revision. Pooled proportion for stent migration was 16.9%. Endoscopic stent placement appears to be safe and effective for treatment of gastrointestinal fistula and leak. Further studies with novel stent types are ongoing.

Endoscopic Suturing

Novel suturing devices have made endoscopic apposition of tissue possible. Intraluminal closure of gastrointestinal fistulas is one potential use of these devices. However, procedural complexity and the need for specialized technical skill have limited its adoption.

Sutured fistula closure is especially applicable in the treatment of fistulas that develop after bariatric surgery. After RYGB, patients can develop fistulas between the surgically-created gastric pouch and the defunctionalized gastric remnant. This can result in reflux of acid into the pouch, causing gastroesophageal reflux or marginal ulceration [12]. Return of weight may also occur as food is diverted into the gastric remnant. Chronic gastrogastric fistula occurs more commonly with the open approach, when the pouch is contiguous with the excluded stomach [6].

The newer Apollo OverStitch™ (Apollo Endosurgery, Austin, TX), which creates full-thickness plications, showed early success in an abstract presented by Watson et al, achieving durable closure in 3/7 gastrogastric fistulae [13]. No complications were noted. This technique is promising as morbidity and cost are far lower than surgical revision. Further research is ongoing to determine closure rates after full-thickness sutured fistula closure.

Endoscopic Clips

Endoscopic clips are available in various shapes and sizes; they can be deployed through-the-scope (TTS) or over-the-scope (OTS). TTS clips are used primarily for hemostasis in the management of gastrointestinal bleeding, but have been studied for multiple other uses in the gastrointestinal tract [14,15].

TTS clips are composed of two arms which achieve a 10-12 mm wide span when open. The clips are placed across the fistula opening under endoscopic guidance and deployed in a configuration perpendicular to defect’s long axis to approximate its edges. Multiple clips can be deployed sequentially from the edges to the center. Thermal ablation or scraping around the defect prior to apposition results in more durable closure [16].

To overcome the limitations of TTS clips, the over-the-scope clip (OTSC) (Ovesco Endoscopy AG, Tübingen, Germany), is larger in size and applies higher force. The OTSC is mounted on a plastic cap, which is secured to endoscope tip. The tissue surrounding the fistula os is suctioned into a cap at the endoscope tip, and the nitinol OTSC is deployed [17]. The arms of the OTSC appose and trap all tissue that lies between. Their
larger size and additional force application permits the closure of larger mucosal defects than TTS clips. Unlike TTS clips, the OTSC can perform full-thickness apposition [18]. A twin grasper accessory is available [17]. It appears that the OTSC is more effective at closing acute gastrointestinal fistula and leak rather than chronic fistula, which generally involves chronic fibrotic changes and scarring. Further research is necessary to understand the types of fistula most responsive to the OTSC, and to compare it to other treatments for gastrointestinal fistula.

**Fistula plug**

The Surgisis AFP plug™ (Cook Biotech, West Lafayette, IN) is made from acellular fibrogenic matrix, preventing inflammatory foreign-body reaction. This device was developed for treatment of anorectal fistula, and has performed better than fibrin sealant in that role [19, 20]. Endoscopic insertion for treatment of gastrocutaneous fistula begins with fluoroscopic localization of the fistula tract with contrast injection. A guidewire is inserted into the external fistula os and advanced through the fistula tract under fluoroscopic guidance until it visualized endoscopically. The end of the wire is grasped with a snare and pulled out through the mouth. The fistula tract can be abraded over the guidewire until bleeding occurs. Next, a snare is attached to the guidewire and passed through the fistula to the outside. The snare is used to grasp the narrower end of the fistula plug, which is pulled into the fistula tract and released. Multiple plugs may be needed to occlude large-bore fistulas.

**Vacuum closure**

Vacuum-assisted sponge closure is an emerging technique that has demonstrated effectiveness in closure of postsurgical fistula. The device comprises an open-cell sponge and a tube attached to external vacuum suction. The suction improves perfusion and removes secretions, while the sponge induces formation of granulation tissue [21]. A standard feeding tube is inserted transnasally, then externalized through the mouth. The sponge, which has been cut to a smaller size than the fistula cavity, is sutured to the tip of the feeding tube. Endoscopic forceps are used to grasp the sponge, and the endoscope is advanced to the internal fistula os. The sponge is placed within the fistula tract. The feeding tube is connected to continuous vacuum suction. The sponge should be changed every three to four days.

**Conclusion**

Gastrointestinal fistula is a common occurrence after surgery. Surgical revision is associated with high morbidity. Patients with fistula may already have concurrent infection, nutritional deficiency, or organ failure, making revision surgery more difficult. Despite the inherent challenges in this patient population, endoscopic therapies for fistula have demonstrated safety and efficacy. These techniques can be used alone, but are even more effective when used in combination. Further research is ongoing to determine which fistula types are most suitable for a specific endoscopic therapy. As evidence builds for the efficacy of these endoscopic techniques relative to surgical management, gastroenterologists will play an expanding role in the treatment of gastrointestinal fistula.

**References**