Techniques in Gastrointestinal Endoscopy 17 (2015) 141–150

Contents lists available at ScienceDirect

Techniques in Gastrointestinal Endoscopy

journal homepage: www.techgiendoscopy.com/locate/tgie

Closure of transmural defects in the gastrointestinal tract by methods other than clips and sutures

Juliana Yang, MD, David Lee, MD, MPH, Deepak Agrawal, MD, MPH*

Department of Medicine, Division of Digestive and Liver Diseases, University of Texas Southwestern Medical Center, POB1, 520P, 5323 Harry Hines Blvd, Dallas, Texas 75390

ARTICLE INFO

Article history:
Received 26 April 2015
Accepted 15 June 2015

Keywords:
Closure
Transmural defect
Fistula
Perforation
Tissue adhesives
Fistula plugs
Endoluminal vacuum therapy
AMPLATZER Septal Occluder
T-tag tissue apposition system

ABSTRACT

Traditionally, the mainstay of therapy for transmural defects of the gastrointestinal tract has been surgical repair. However, in recent years, the spectrum of novel and innovative therapies available for the repair of such defects has been rapidly increasing, and patients now have a variety of nonsurgical options available to them for specific indications. In this article, we review the devices and techniques, other than clips and sutures, which have been developed for the closure of transmural defects. In this review, we include some well-known and commonly available interventions, such as tissue adhesives and endoscopic band ligation, as well as novel combinations of common techniques, such as the "clutching rose stems" technique and endoloop and endoclip closure. Additionally, we include a review of various innovative devices that have been explored, such as the AMPLATZER Septal Occluder, endoluminal vacuum therapy, and the T-tag tissue apposition system. Such devices and techniques represent a dynamic area of development currently, with many showing promising early results in treatment of transmural gastrointestinal defects. With further refinement, these devices and techniques may enter mainstream therapeutic use in the future.

1. Definition and causes

Transmural gastrointestinal (GI) defect is defined as a complete GI mucosal perforation resulting in a nonphysiological connection between the GI lumen and outermost layer of the GI wall due to natural, pathogenic, or iatrogenic causes. The greatest concern is the spillage of bacteria-laden GI contents into the sterile abdominal or thoracic cavity that may result in serious systemic inflammation and infection.

Depending on the onset, perforations are classified as acute or chronic. *Acute* perforations are often unexpected and iatrogenic (eg, perforation during endoscopic dilation or polypectomy). It is reported that the incidence of iatrogenic endoscopic perforation is between 0.01% and 0.6% for diagnostic and between 0.6% and 5.5% for therapeutic endoscopies [1-5]. As we explore and expand the frontiers of endoscopic therapeutic options with techniques such as endoscopic mucosal resection (EMR), endoscopic submucosal dissection (ESD), peroral endoscopic myotomy, endoscopic full-thickness resection (EFTR), and others, the incidence of iatrogenic perforation is bound to increase [3,6-9]. Anastomotic leaks may complicate 5%-30% of esophageal anastomoses [10,11] and 5%-15% of rectal anastomoses [12,13]. However, not all iatrogenic acute transmural defects are complications of the procedures. For example, endoscopic access from within the GI lumen to other structures or organs is established during placement of percutaneous enteral feeding tubes or endoscopic drainage of extraluminal cysts or abscesses. Acute perforations can be pathogenic in cases such as perforation of a diverticulum or a severely dilated colon.

Chronic transmural defects occur when inflammation extends across the GI wall causing destruction of the tissue, resulting in fistula formation with connection of GI lumen to either skin or other lumen. Examples include fistulae in Crohn's disease and tracheoesophageal fistulae (TEFs) in esophageal malignancy. Owing to chronic inflammatory changes and scar tissue around the defect, intraluminal contents do not usually leak into surrounding structures such as the mediastinum or the peritoneum. Chronic cutaneous fistulae may develop at the site of external tube drainage, such as the formation of a gastrocutaneous fistula after removal of a gastric feeding tube or a pancreatocutaneous fistula after removal of tubes for drainage of pancreatic fluid collections.

2. Management of transmural defects

Until a few years ago, surgical repair had been the mainstay of treatment of transmural defects, especially perforations and leaks.

The author reports no direct financial interests that might pose a conflict of interest in connection with the submitted manuscript.

* Corresponding author.
E-mail address: deepak_ag@yahoo.com (D. Agrawal).

http://dx.doi.org/10.1016/j.tgie.2015.06.005
0049-0172/

However, surgical repair is associated with definite morbidity and mortality risks. With improvements in endoscopic technology—more flexible endoscopes, larger working channels, and innovative accessories—endoscopic methods of closure of transmural defects are being developed.

Through-the-scope clips were the first commonly used method for closure of leaks and perforations. Since then, several devices and methods have been described such as ligation by endoloops and rubber bands, endoscopic suturing, sealing with fibrin glue (FG) or cyanoacrylate glue (CG), self-expanding metal stents, and more recently, over-the-scope-clipping device [4,6,14-16]. In this review, we discuss few novel techniques, other than clips and sutures (which have been reviewed in other articles) that can be used for closure of transmural defects.

There are a few common requirements when endoscopy is performed for closure of transmural defects. First, there are no definite data yet, to recommend one technique over another, and the physicians should remain mindful of local expertise and technology and on-site surgical backup before attempting more challenging cases. The endoscopist may require fluoroscopy, as real-time imaging may facilitate identification and closure of transmural defects. Second, whenever possible, imaging studies should be obtained before endoscopy to determine the precise location and extent of leak. Upper GI contrast radiographies and fistulograms are preferred, as they may provide better information than the more commonly performed CT scans do. Third, carbon dioxide should be used for insufflation during endoscopy, as it is absorbed faster than room air is.

3. Tissue adhesives

Tissue adhesives are compounds that bind to tissue and have been used for hemostasis, wound closure, or fistula repair. There are 4 categories of tissue adhesives: FG, CG, polyethylene glycol polymers, and albumin-based sealants, which differ in composition and the way they are used. Of these, only FG and CG have been used in endoscopy. FG has been described for closure of chronic fistulae and anastomotic leaks, whereas CG is primarily used for treatment of bleeding gastric varices. Endoscopic use of tissue adhesives has not been approved by the U.S. Food and Drug Administration and their use to close defects after EFTR has not been studied.

4. Fibrin glue

Fibrin is the end product of the coagulation cascade and is formed when thrombin converts soluble fibrinogen to insoluble fibrin strands, which get cross-linked by Factor XIII. The basic principle of sealing a mucosal defect with fibrin is that the mixture of the 2 components (fibrinogen and thrombin) simulates the coagulation cascade in the fistulous tract while forming a matrix of fibrin. Fibrin then stimulates growth of fibroblasts, leading to scar formation, and fibrin is slowly replaced by collagen [17].

The technique of injecting FG involves endoscopic injection of fibrinogen and thrombin. If available, a double-lumen catheter is preferred, so that the 2 components meet only at the intended site (and not within the channel of the endoscope where they can aggregate). The larger lumen of the catheter should be reserved for the more viscous component. The rapid exchange or short-wire double-lumen endoscopic retrograde cholangiopancreatography (ERCP) catheters should not be used, because the sealant may leak out the sides of the catheter and damage the endoscope channel [16,18]. If a single-lumen catheter is used instead of a double-lumen probe for sealing, the catheter lumen should be flushed between the instillation of fibrinogen and thrombin. The injection of the contents should begin distally from the orifice and then moved proximally to minimize fluid retention within the tract. Multiple endoscopic procedures (average: 2-5) with repeat injections may be required to achieve complete closure.

The data on the success of FG in closing fistulae and leaks mainly come from small case series, case reports, and animal models. In a small, randomized controlled trial of 13 patients with persistent enterocutaneous fistulae, it was found that FG achieved closure of fistulae after a mean of 2 days compared with 13 days with conservative therapy ($P < 0.01$) [19]. In a retrospective series of 52 patients with GI fistulae or leaks, FG successfully closed fistulae as a sole therapy in 37% cases and as adjunct with other endoscopic modalities in 56% cases [20]. A median of 4 endoscopies per patient was needed to close the defects. However, 80% of the lesions in the colon and 50% involving the pancreas needed only 1 endoscopy, suggesting that these defects may be easier to close with FG. In a case series, FG was used in 5 patients with gastrocutaneous fistulae after gastrostomy tube removal [21]. The mean time to achieve total fistula closure was 7 days compared with 32 days in patients who were treated conservatively. Many other smaller case series or case reports have reported successful closure of enterocutaneous fistulae and gastrocutaneous fistulae after removal of feeding tubes or after bariatric surgeries [21-26] and esophageal [27] and duodenal perforations [28].

Efficacy of FG has also been studied for anal fistulae. In an RCT, patients with simple fistulae (low anal fistulae) and complex anal fistulae (high fistulae and low fistulae with compromised sphincters) were randomly assigned to either FG or conventional treatment (fistulotomy or seton insertion) [29]. The primary end point was fistula healing. No advantage was found for FG over fistulotomy for simple fistulae (50% vs 100%, $P = 0.06$), but FG healed more complex fistulae than conventional treatment did (69% vs 13%, $P = 0.003$). Another randomized trial comparing FG with observation only for patients with Crohn's disease with anal fistulae found higher closure rates in patients treated with FG (38% vs 16%, $P = 0.04$) [30].

Prophylactic application of FG has been tried to prevent anastomotic leaks in high-risk patients, for example, esophageal resection and gastric bypass [31,32]. A recent systemic review suggested that the mechanism is likely due to mechanical sealing rather than improved healing per se [33]. FG has also been tried to prevent delayed perforation following ESD of superficial duodenal adenocarcinoma [34]. In this “tissue shielding” method, the authors first endoscopically placed small pieces of polyglycolic acid (NEOVEIL; Gunze Co., Kyoto, Japan) sheet over the mucosal defect and then used FG to fix the pieces together. Polyglycolic acid is an absorbable, suture enforcement material that has also been used to prevent pancreatic fistula formation after pancreaticoduodenectomy [35,36]. In a more recent study, the tissue shielding method was used in 45 patients after ESD of gastric lesions and in 41 historical controls. There was a significant difference in the post-ESD bleeding rate between the study group and the control group (6.7% vs 22%, $P = 0.04$) [37].

5. Cyanoacrylate glue

Cyanoacrylates are a class of synthetic glues that rapidly solidify on contact with weak bases, such as water and blood. The different kinds of CGs available for medical use have been reviewed by American Society for Gastrointestinal Endoscopy [17]. CGs were initially used for skin approximation and wound closure, but they have been used off-label in the United States to treat bleeding varices and less commonly, in the closure of