

Endoscopic Closure of Gastrointestinal Leaks

Gottumukkala Subba Raju, MD, FRCP, FACC, FASGE¹

Surgery has been the mainstay of therapy in patients with gastrointestinal perforations. This paradigm started to shift with the development of techniques for endoscopic closure of gastrointestinal perforations. A detailed review of the literature on this subject, along with a commentary on practical aspects in the management of patients with gastrointestinal leaks, is provided here.

SUPPLEMENTARY MATERIAL is linked to the online version of the paper at <http://www.nature.com/ajg>.

 Video content online

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INTRODUCTION

Although interest in endoscopic closure began in the early 1990s with the first description of clip closure of gastric perforation, natural orifice transluminal endoscopic surgery (NOTES) has provided the much-needed impetus for development of this field (1,2). A review of the various closure devices and their role in endoscopic closure of gastrointestinal perforations, followed by a commentary on practical aspects of endoscopic management of gastrointestinal perforations is presented here.

REVIEW METHODOLOGY

A MEDLINE search of English language publications related to endoscopic closure of gastrointestinal perforations was carried out from 1966 to June 2008 by using the keywords “endoclip” and “suturing.” Reference lists from relevant manuscripts were also inspected to identify additional applicable articles missed by the above search strategy. The role of stents and glues is not reviewed in this article.

DEVICES

Clips

Clips are widely used for mechanical hemostasis; recently, their role in endoscopic closure of perforations has been explored (3,4). Five different designs of clips are available: (i) QuickClip2 (Olympus Corp., Melville, NY) is a rotatable clip device that is ready for use immediately after taking out of the package unlike its predecessor that required loading of clips on a reusable applicator (**Supplementary Video 1**).

(ii) TriClip (Cook Medical Inc., Winston-Salem, NC) is a tri-pronged single-use clip device with a flushing mechanism designed to orient on the target site without the need for rotation of the prongs (**Supplementary Video 2**). (iii) Resolution Clip (Boston Scientific, Natick, MA) has the ability to reopen up to five times before final deployment, thus offering a second chance to realign the clip for better tissue approximation if necessary (**Supplementary Video 3**). (iv) InScope Multiclip Applier (Ethicon Endosurgical Inc., Cincinnati, OH) has the ability to deliver four clips, 1:1 rotation to align the jaw openings across the defect and reopening of the clip if necessary (**Supplementary Video 4**). (v) Over-the-scope clip (Ovesco Endoscopy, Tuebingen, Germany) is a nitinol clip loaded at the tip of the endoscope that can capture small perforations and compress the lesions until healing (5).

Sutures

Suture closure devices are in the pre-clinical phase of evaluation.

- (1) *T-tags* (Ethicon Endo-Surgery, Cincinnati, OH): A 19-gauge hollow needle loaded with a metal T-tag and a thread is inserted through the endoscope channel. After puncturing the tissue a few millimeters away from the edge of the perforation, the T-tag is ejected beyond the wall. Another T-tag is placed on the opposite side of the perforation. Subsequently, the threads are tied together with a locking cinch.
- (2) *Purse string modified T-tags* (Cook Endoscopy, Winston-Salem, NC): A “purse string” T-tag along with a metal ring at the midpoint of the T bar allows

¹Department of Gastroenterology, Hepatology, and Nutrition - Unit 1466, The University of Texas MD Anderson Cancer Center, Houston, Texas, USA.

Correspondence: Gottumukkala Subba Raju, MD, FRCP, FACC, FASGE, Department of Gastroenterology, Hepatology, and Nutrition, Unit 1466, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, Texas 77030-4009, USA. E-mail: gsraju@mdanderson.org

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the fasteners to be deployed sequentially on the same suture around a gastrotomy site for closure (6).

- (3) *Eagle Claw VIII (Olympus Corporation, Tokyo, Japan)*: This is an over-the-endoscope suturing device with two opposing jaws that move simultaneously, one fixing the target tissue and another holding a curved needle to deliver the suture through the tissue. After needle penetration through both edges of perforation with the closure of jaws, it can detach and lock into the suture unit cartridge, thus completing a suture in one single motion (7).
- (4) *Purse string-suturing device (LSI Solutions, Victor, NY)*: This prototype device utilizes vacuum to draw the gastric wall into a small suction chamber in which a 3-mm cutting blade can also be used to create an incision. After the sutures have been deployed, another device is used to tighten and secure the purse string with a titanium knot (8).
- (5) *Flexible endostitch (Covidien, North Haven, CT)*: The jaws of the flexible Endostitch hold a double-ended, sharp needle attached to a suture. Opening and closing the jaws toggles the needle back and forth with the needle passing through tissue to create a running suture with barbs to engage with the tissue (9).
- (6) *Plicator (NDO Surgical Inc., Mansfield, MA)*: This is a large-caliber device that is inserted over a Savory wire into the stomach, with a port for a small-caliber endoscope to observe the closure. After the device is positioned, the jaws are opened to bring the perforation edges within the jaws of the device. Firing the device delivers pledgeted transmural suture bundles to close the defect (10).

Staples

Staple closure similar to the surgical staple closure can also be accomplished with a computer-mediated, electromechanically powered cutting and stapling device delivered on a flexible working shaft, the flexible stapler (Power Medical Interventions, Langhorne, PA) (11).

EXPERIMENTAL EVIDENCE

Endoscopic closure of gastric, colonic, and esophageal perforations has been investigated extensively to study the closure of portals of entry into body cavities and to develop techniques for the management of tumors and perforations that can arise during removal of such lesions.

Esophageal perforation closure

In a randomized trial, endoscopic clip closure of a 2-cm esophageal perforation in a porcine model resulted in significantly better healing and less periesophageal adhesions compared with endoluminal suture closure and thoracoscopic repair (12).

Gastric perforation closure

Initially clips were used for gastrotomy closure (2,13,14). Since then a number of tissue approximation devices (T-tags, purse string-suturing device, resolution clips, Eagle Claw VII, flexible stapler, and flexible endostitch) have been shown to be successful in gastrotomy closure (15–23).

Both direct clip approximation of the edges of gastrotomy and clip closure of the self-approximating submucosal tunnel have been shown to be effective in the closure of gastrotomy for NOTES (24).

Endoscopic closure of gastrotomy (or gastric perforation) can be achieved with the following techniques (9):

- (a) *Parallel closure of all the gastric wall layers* (similar to standard surgical suture closure) using the Eagle Claw VIII and the endostitch.
- (b) *Inverted closure with serosa-to-serosa apposition* using the flexible stapler and Resolution clips.
- (c) *Everted closure with mucosa-to-mucosa apposition* using the T-tags, purse string modified T-tags, and the purse string-suturing device.

Both parallel and inverted closures provide superior closure compared with everted closure. The resolution clips, Eagle Claw VIII, flexible endostitch, and flexible stapler devices produce closure comparable with surgical closure. Suture closure with T-tags, purse string modified T-tags, and the purse string-suturing device resulted in inferior closures (9).

Colon perforation closure

A porcine colon model was used to study endoscopic clip and suture closure of colon perforations, with special reference to healing of perforation by methylene blue dye leak test under water, prevention of peritonitis, pericolic and paracolic abscesses, and adhesions (7,25–32).

Partial thickness clip approximation of a 2-cm linear perforation of the colon resulted in excellent healing of perforation at 1 week (25). A leak-proof sealing of 5-cm linear and 2-cm circular perforation could also be achieved with clips (26,31). Clip closure of colon perforation reduces the risk of peritonitis and adhesion development (28). An over-the-scope clip device could also be used to close small perforations of the colon (5).

Sutures have been shown to be successful in the closure of gaping perforations with everted edges where clips fail (7,29). Endoscopic closure of colon perforation is comparable to surgical closure in the prevention of peritonitis and is superior to surgery in the prevention of peritoneal adhesions (32).

The role of endoscopic full-thickness colon resection followed by closure of the mural defect is currently being investigated in our animal laboratory.

CLINICAL EVIDENCE

Clinical evidence on endoluminal closure of perforations is limited to case reports and case series. There are no randomized controlled clinical studies in this area.

Esophageal leaks

A recent review on endoscopic treatment of esophageal leaks provides comprehensive information on this subject (33). Endoclips have been shown to be successful in the closure of esophageal perforations from Boerhaave's syndrome (34); iatrogenic perforations such as those after dilation of esophageal stricture (35), achalasia cardia (36), and anastomotic stricture of esophagojejunostomy (37); endoscopic mucosal resection (38); post-operative esophageal leakage (35,39,40); perforations after ingestion of foreign bodies, such as fish bone (41) and metal curtain hook (42); and empyema (43).

The clips are successful in the closure of esophageal perforations varying from a few millimeters to 2 cm. Multiple clips are required to close larger perforations. Some cases require two or three separate sessions for closure (39). Experience with endoscopic suturing of esophageal perforations and fistulas is limited (44).

Fresh perforations heal within a week of clip application, whereas fistulas require 2–3 weeks to heal. In a pooled analysis of 11 articles and 17 patients, the median healing time after clip application was 18 days (range 6–26 days). Only the duration of perforation was a significant predictor of closure time (45).

Fresh perforations heal quickly with clip closure alone. Chronic fistula benefit from clearance of mediastinal and peritoneal infection with debridement and drainage before clip closure (46).

Gastroduodenal leaks

Binmoeller *et al.* (1) described the first successful endoluminal closure of a 0.5-cm gastric perforation with three clips after snare polypectomy of a pedunculated leiomyoma. Since then a number of reports have described successful outcome after clip closure of perforations. These include gastric perforations after endoscopic mucosal resection of gastric neoplasia (47), clip closure of duodenal perforations resulting from insertion of an endoscopic ultrasound scope (48), resection of duodenal carcinoids and ampullary adenomas, and biliary sphincterotomy (49,50) and migrated biliary stent (51), and clip closure of jejunal perforation after balloon dilation (**Supplementary Video 5**) (52).

The type of clip closure depends on the size of the gastric perforation. Simple clip approximation of the edges is sufficient for closing small gastric perforations. An omental patch closure may be required for large (25 mm) perforations (53).

Endoscopic clip closure of gastric perforations results in an excellent outcome (54,55). In a recent study, 115 of 117 patients with gastric perforations during EMR that were closed successfully with clips recovered fully, and the outcome of the patients was similar to those without a perforation (54,55).

Colon leaks

Two different mechanisms of injury lead to colonoscopic perforations. Mechanical injury during retroflexion maneuver of the endoscope in a small rectum or during the negotiation of a sigmoid colon with a colonoscope that is fixed by adhesions, or

excessively redundant and thermal injury during endoscopic mucosal resection or endoscopic submucosal dissection could result in colorectal perforations. Limited case studies have reported successful closure of these different types of colonoscopic perforations (56–63). Endoloops have also been used to close iatrogenic colon perforation (64).

Magdeburg *et al.* reported management of iatrogenic colon perforation in 30 patients (2004–2006). Twenty-seven perforations were closed with clips: 25 patients were discharged from the hospital after 3.5 days and two patients with failed clip closure required surgery. Five patients underwent surgery. The length of hospitalization was shorter after endoscopic closure compared with surgical closure (3.5 vs. 12.2 days) (65).

In addition to perforation closure, clip closure has been reported to be successful in the closure of chronic fistulas such as the gastric–colocutaneous fistula after the removal of PEG (66), colo-vesical fistula after diverticulitis (67), fecal fistula complicating appendicular abscess (68), and colocutaneous fistula after colectomy or necrotizing pancreatitis (**Supplementary Video 6**) (69–71).

PRACTICAL ENDOSCOPIC MANAGEMENT OF GI PERFORATIONS

On the basis of a thorough review of the published literature on endoscopic management of gastrointestinal perforations, extensive review of all the videos on this subject at the ASGE Learning Center, and personal reflections on the experience gained from the animal experiments, I have made an attempt to put things into perspective on this subject.

Prevent perforation

Caution is required during the insertion of an endoscope in patients with cervical spondylosis or stiff neck to avoid cervical esophageal perforation. The risk of rectal perforation during retroflexion of the endoscope in patients with a small rectum could be avoided by examining the rectum after slow deflation of the rectum instead of the retroflexion maneuver, or by using a thinner caliber upper endoscope if retroflexion is absolutely necessary. Sigmoid colon perforation could be precipitated by the use of excessive force during the insertion of an endoscope through a colon that is either fixed by adhesions or is redundant. Limiting the mechanical force during endoscope insertion or trying alternatives such as the use of a smaller caliber endoscope, use of stiffeners or overtubes, or the use of a double-balloon endoscope could avoid this complication. Spillage of luminal microbial soup through a perforation can precipitate the septic shock; hence, *it is critical and preferable to avoid elective endoscopy, especially any therapy with a risk of perforation, in a patient with debris in the lumen until it is cleared and cleaned out.* For example, a clean esophagus is critical before dilation, especially in patients with achalasia. A poorly prepared colon can lead to fecal contamination of

peritoneal cavity, if perforation were to occur; hence, a clean colon is critical.

Perforations from balloon dilation of the strictures could be limited by starting with a smaller dilator; gradually increasing the size of dilator; limiting the use of excessive force during bougie dilation; and closely observing the dilation site through the balloon for deep extension of tears.

Before endoscopic resection of the polyp, dry up the endoscopic field in the operating segment to prevent escape of luminal contents through the perforation, if it were to happen. Applying a snare on the stalk of a pedunculated polyp away from the wall and tenting it up before cautery could limit transmural burn and perforation. Injection of ample amount of submucosal fluid and separating the lesion from the muscularis propria is critical to prevent thermal injury to the muscle. In addition, piece-meal resection of large polyps may limit deeper injury to the muscle compared with the large en-bloc resections. Consider surgery if the risk of perforation is high during endoscopic removal of large lesions.

As carbon dioxide gets absorbed quickly by the body compared with air (72,73), use of carbon dioxide infusion for endoscopy may be beneficial in patients undergoing endoscopic procedures at a high risk for perforation.

Diagnosis of perforation. Perforations from mechanical trauma are clinically obvious either during or immediately after the procedure, whereas those from cautery damage may take a few hours or a day to develop. Act immediately if a patient complains of pain by examining the patient and do not brush off the complaint as trivial due to gas. Delay in the diagnosis is associated with a poor outcome. As perforations of the gastrointestinal tract are rare, it is difficult to recognize it on endoscopy for the novices. This could be improved by watching videos on endoscopic submucosal dissection to identify small perforations. In addition, development of abdominal pain, abdominal distension that cannot be decompressed, and sudden deterioration of vital signs due to tension pneumoperitoneum or tension pneumothorax should raise an alarm about a gastrointestinal perforation. Contrary to traditional teaching, endoscopy is safe to diagnose esophageal perforations and should be undertaken, if necessary, after a negative CT scan or esophagogram to exclude the diagnosis.

Immediate endoscopic management

Immediately after the recognition of an iatrogenic perforation during endoscopy, check for tension pneumoperitoneum or pneumothorax and consider immediate decompression with a wide-bore needle puncture. Currently, endoscopic clips are the only devices available in the market for closure of perforations, whereas suturing and stapling devices are not available for clinical use. Clips can be used to close perforations of less than 2 cm size. There are no data in the literature on endoscopic closure of iatrogenic perforations in patients who

return to the emergency room after discharge from the endoscopy unit. Endoscopic management of such patients should be considered as part of an investigational protocol in close collaboration with surgeons.

Endoscopic clip closure of perforation involves a technique that is quite different from the one that is used for mechanical hemostasis, as described below. One could learn this art by attempting to close mucosal defects after endoscopic mucosal resection in clinical practice, by attending hands-on-courses on this technique, or during the investigation of the endoscopic closure of colon perforations in the animal laboratory (as I have done). Clip closure of perforations is not for the novice with no prior experience in the use of clips. It is critical for both the endoscopist and his assistant to be conversant with the use of clips before undertaking endoscopic closure of perforations.

Attention to the details as outlined below is critical for successful clip closure of perforations.

Techniques of clip closure of perforations (personal reflections) are as follows:

- Keep the clip close to the end of the endoscope with the clip and the endoscope acting as a single unit.
- Positioning the wide-open clip across the defect at 90° to the defect.
- Gently push the clip-endoscope unit as one unit while applying gentle suction to collapse the lumen so that as much tissue away from the edge of perforation as possible could be grasped while slowly closing the clip.
- Confirm satisfactory clip closure of the perforation with approximation of the edges before deployment of the clip.
- Be patient while applying a clip because a clip misplaced to one edge of the perforation could lead to difficulty in applying additional clips for satisfactory closure.
- Place additional clips from top-to-bottom in linear perforations or left-to-right in circular perforations after satisfactory application of the first clip, which is the most critical component of closure.
- Suction and decompress the lumen before withdrawal of the endoscope.

Stents may be a better option in perforations or fistulas larger than 2 cm and in defects with everted edges because current clips (with wingspan <2 cm) fail to close such defects, and also in patients with a leak occurring in the setting of a malignant lesion because clips tend to tear through cancerous tissue and fail to keep the edges of perforation approximated. Drainage of infection before closing the defect is critical because clips may tear through edematous tissue, resulting in failure of closure. Use of rotatable clips or a cap-fitted endoscope may be useful in closing defects in the esophagus, especially if an en-face approach to the defect is unsuccessful (40).

Post-endoscopic perforation closure management

It is critical to involve a surgeon right from the beginning in the management of the patients after endoscopic closure

of perforations because of the surgeon's extensive experience in the management in this area. Both bowel rest and broad-spectrum intravenous antibiotics are critical for healing of the perforation after endoluminal closure. Patients with esophageal perforation may benefit from minimizing the gastroesophageal reflux by elevating the head end of the bed. Intermittent tube suction of luminal secretions keeps the lumen collapsed and limits the escape of luminal contents through any smaller defects after clip closure. Parenteral nutrition should be considered in patients with leaks that take more than a few days to heal. All patients should be closely monitored for signs of peritoneal irritation in close collaboration with the surgeons. Oral intake could be resumed as soon as the pain and fever resolve, appetite and bowel function return, and laboratory signs of inflammation such as leucocytosis and elevated CRP return to normalcy. In patients with an esophageal perforation, an esophagogram is undertaken before the resumption of oral intake.

In summary, data on endoluminal closure of gastrointestinal perforations are encouraging. With proper training in endoluminal closure of perforations and endoscopists working in close collaboration with surgeons, patients with gastrointestinal perforations and leaks could be managed better.

CONFLICT OF INTEREST

Guarantor of the article: Gottumukkala Subba Raju, MD, FRCP, FACP, FASGE.

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Videos 1–4 (reproduced with permission from Elsevier) from Raju GS, Kattenbach T, Soetikno R. Endoscopic mechanical hemostasis of GI arterial bleeding (with videos). *Gastrointest Endosc* 2007; 66:774–85. Video 5 (reproduced with permission from Elsevier) from Groce JR, Raju GS, Hewlett A, Zwischenberger JB. Endoscopic clip closure of a gastric staple-line dehiscence (with video). *Gastrointest Endosc* 2007; 65:321–2. Video 6 (reproduced with permission from Elsevier) from Mummati RR, Groce JR, Raju GS, Gomez G. Endoscopic management of colocutaneous fistula in a morbidly obese woman (with video). *Gastrointest Endosc* 2008; 67:1207–8. Videos 1–6 (reproduced with permission from ASGE). Portions of these videos were presented at the ASGE Video Forum 2007 as part of emerging options in the management of postoperative leaks (http://daveproject.org/ViewFilms.cfm?Film_id=603). I dedicate this work to my mentors, who taught me endoscopy.

Study Highlights

WHAT IS CURRENT KNOWLEDGE

- ✓ Surgery is required in the management of most patients with gastrointestinal leaks, although patients with a contained leak can be managed by non-surgical methods.

WHAT IS NEW HERE

- ✓ Endoscopic closure of gastrointestinal leaks is feasible.
- ✓ Close collaboration with surgeons is critical in the management of patients after endoscopic closure of perforations.
- ✓ Training in endoscopic closure of perforations is needed.

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