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Review Article

The use of OverStitch™ for the treatment of intestinal perforation, fistulas and leaks

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A B S T R A C T

Gastrointestinal perforations, leaks and fistulas may complicate endoscopic and surgical procedures. Surgical repair is associated with significant morbidity. Therapeutic endoscopic tools and techniques have included the application of tissue sealants, clip closure, and stent placement. Endoscopic suturing is a rapidly evolving minimally invasive technique. The OverStitch™ (Apollo Endosurgery, USA) is currently the only available endoscopic suturing system. Although technically more difficult than clip closure, endoscopic suturing allows closure of larger defects. In some settings, outcomes similar to surgical management with less morbidity may be achieved. This review describes the OverStitch™ endoscopic suturing system and the published literature regarding its use for perforations, leaks and fistulas.

Keywords: Fistula; Leaks; Perforation

Introduction

Gastrointestinal (GI) leaks and fistulas may complicate GI surgical procedures including intestinal resections and bariatric procedures. GI perforations are a common complication of endoscopic procedures. These conditions may also develop due to infection, inflammation or increased intestinal pressure unrelated to a post-procedural complication. Etiologies of perforation, leaks and fistula are listed in Table 1.

Surgical repair is often complex and associated with increased anesthesia risks and significant morbidity.[1] The clinical presentation varies with the size and location of the lesion. Fistula may involve communication between the intestinal tract and nearly any other location (entero-cutaneous, entero-atmospheric, entero-bronchial, entero-enteric, etc).[2] Common presenting symptoms include fever, pain, cough, malnourishment, and diarrhea.

Definition of Perforation, Leaks and Fistula

- Perforation: Acute full thickness defect of the GI tract
- Leak: Disruption in a surgical anastomosis or closure resulting in fluid egress and accumulation
- Fistula: Abnormal communication between two epithelialized surfaces

Table 1 Causes of Intestinal Perforations, Leaks and Fistula

Endoscopy: EGD, colonoscopy, EUS, ERCP
Endoscopic treatment of intestinal bleeding
Endoscopic treatment of stricture or achalasia: Bougie, balloon, POEM
Endoscopic tissue resection: EMR, ESD
Foreign body
Posts-surgical anastomotic leaks
Marginal ulcers
Boerhaave syndrome
Trauma
Malignancy
IBD
Diverticulitis
Radiation therapy
Intestinal ischemia

EGD, esophagogastroduodenoscopy; EUS, endoscopic ultrasound; ERCP, endoscopic retrograde cholangiopancreatography; POEM, peroral endoscopic myotomy; EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection; IBD, inflammatory bowel disease.

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Endoscopic versus Surgical Approach to Repair

The basic principles of fistula, perforation and leak management include identification of the site of the leak or fistula, drainage of leaked contents and disruption of the flow of intestinal fluids across the fistula or leak with diversion or closure. The decision between an endoscopic versus surgical approach depends on the size and chronicity of the leak or fistula, the location and endoscopic accessibility and the ability to drain associated contamination (Fig. 1). Endoscopic management requires diversion, closure, or a combination of both. A summary of currently available endoscopic tools for closure of GI leaks and fistulas is presented in Table 2.

Perforation/leaks associated with peritoneal contamination typically require surgical management. A multidisciplinary approach that includes surgery, interventional radiology and gastroenterology is required for these complex patients. A comprehensive approach to management that includes bowel rest, fluid and electrolyte management, nutritional support including total parenteral nutrition, antibiotic therapy and drainage of collections and abscesses, along with management of the primary site of leak, fistula or perforation is required. A recent case series demonstrated successful closure of full thickness intestinal perforation with associated peritoneal contamination managed with the OverStitch™ endoscopic suturing device in 3 patients.[3]

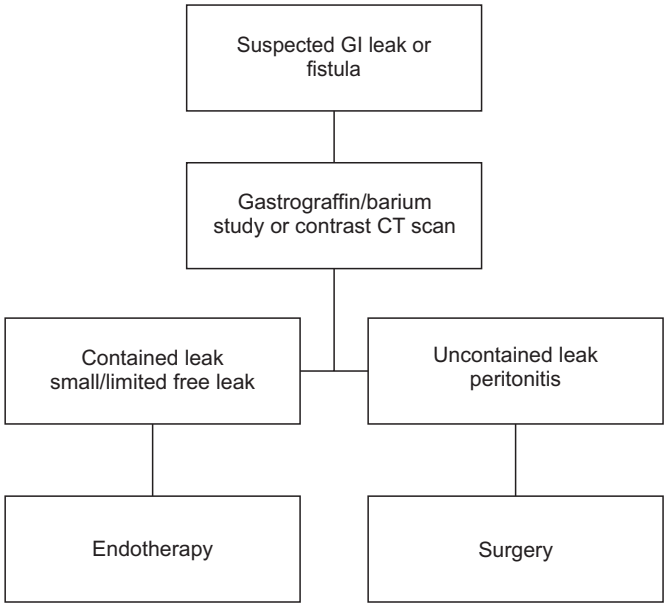

Fig. 1. Management approach to gastrointestinal (GI) leaks and fistula. CT, computed tomography.

Table 2 Endoscopic Tools for the Management of Gastrointestinal Perforations, Leaks and Fistula

Diversion	Closure
Fully covered metal self-expanding stents - Risk of migration may be reduced with endoscopic stent suturing - Stents require endoscopic removal (typically within 2–3 months) to prevent the stent from embedding or eroding in the intestinal wall	1. Over-the-scope clip - Difficult to maneuver - Not suitable for friable tissue 2. Hemostatic clips - Limited efficacy 3. Tissue adhesives - Typically, an adjunct therapy 4. Suturing device: OverStitch™

Endoscopic Suturing Device: OverStitch™

Several endoscopic suturing devices have been described over the past decade, including the EndoCinch (C. R. Bard, Murray Hill, NJ, USA),[4–6] T-bars (Cook Medical, Bloomington, IN, USA),[7] and Eagle Claw devices,[8] but each had limitations that prevented widespread use.[9] The OverStitch™ (Apollo Endosurgery, Austin, TX, USA) is currently the only U.S. Food and Drug Administration-approved endoscopic suturing device. The current device overcomes many of the limitations of prior devices.[10] It has been increasingly used to anchor stents within the GI lumen,[11] perform closure of perforations,[11] leaks, and fistulas, in addition to closure of mucosectomy after peroral endoscopic myotomy (POEM),[12,13] Natural Orifice Transluminal Endoscopic Surgery defect closures,[14] and perform primary and revision bariatric procedures.[15,16] This review will focus on endoscopic suturing with the OverStitch™ platform in the management of GI perforations, leaks and fistula.

The OverStitch™ System

The OverStitch™ system is a disposable single-use, single operator, endoscopic suturing device that allows placement of running and interrupted full-thickness sutures using either permanent non-absorbable (2-0 and 3-0 polypropylene) or absorbable (2-0 and 3-0 polydioxanone) suture material. This device requires a double channel therapeutic endoscope.[17]

Components of the OverStitch™ Device

1. End cap
2. Needle driver
3. Needle driver handle
4. Anchor exchange catheter
5. Cinch device
6. Overtube
7. Helix cork screw catheter to assist with tissue apposition

The end cap of the OverStitch™ device is mounted on the distal tip of the double channel endoscope. The end cap includes a suture arm which moves in an arc-like fashion, and the anchor exchange channel which approximates with the endoscopes therapeutic channel (Fig. 2).

The suture arm is connected and controlled by a hand lever which is attached near the endoscope channel ports. The suture material is attached to a pointed tissue anchor that is passed through the operating channel. Tissue approximation and suture placement may be facilitated by an optional tissue-retracting helix catheter or grasping forceps. After suturing is completed, a cinching device is utilized to secure the sutures. The OverStitch™ Endoscopic Suturing System allows interrupted or continuous stitches without needing to remove the device (Fig. 3). The device can be reloaded with a new needle multiple times, without removing the endoscope.

Endoscopic suturing of perforations in the gastrointestinal tract

OverStitch™ suturing has been shown in animal models to achieve good results in the closure of full thickness perforation.[18] Rajan et al[18] performed full-thickness gastric biopsy with gastric muscularis propria resection in twelve domestic pigs utilizing a submucosal endoscopy technique with the creation of a mucosal

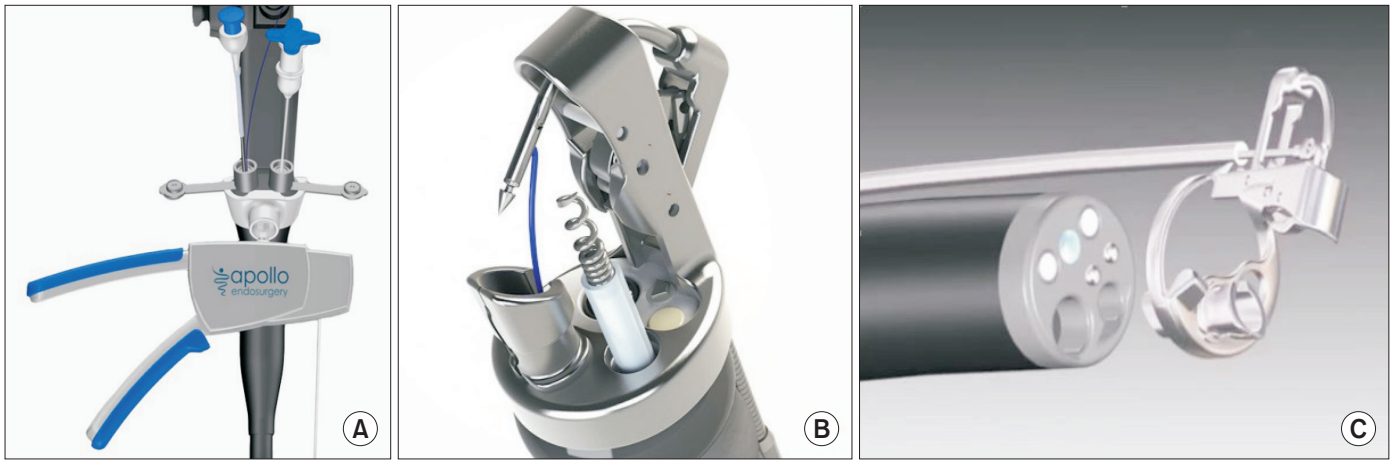

Fig. 2. (A–C) OverStitch™ (Apollo Endosurgery, USA) device with the helix catheter. Image was reused with permission from Apollo Endosurgery.

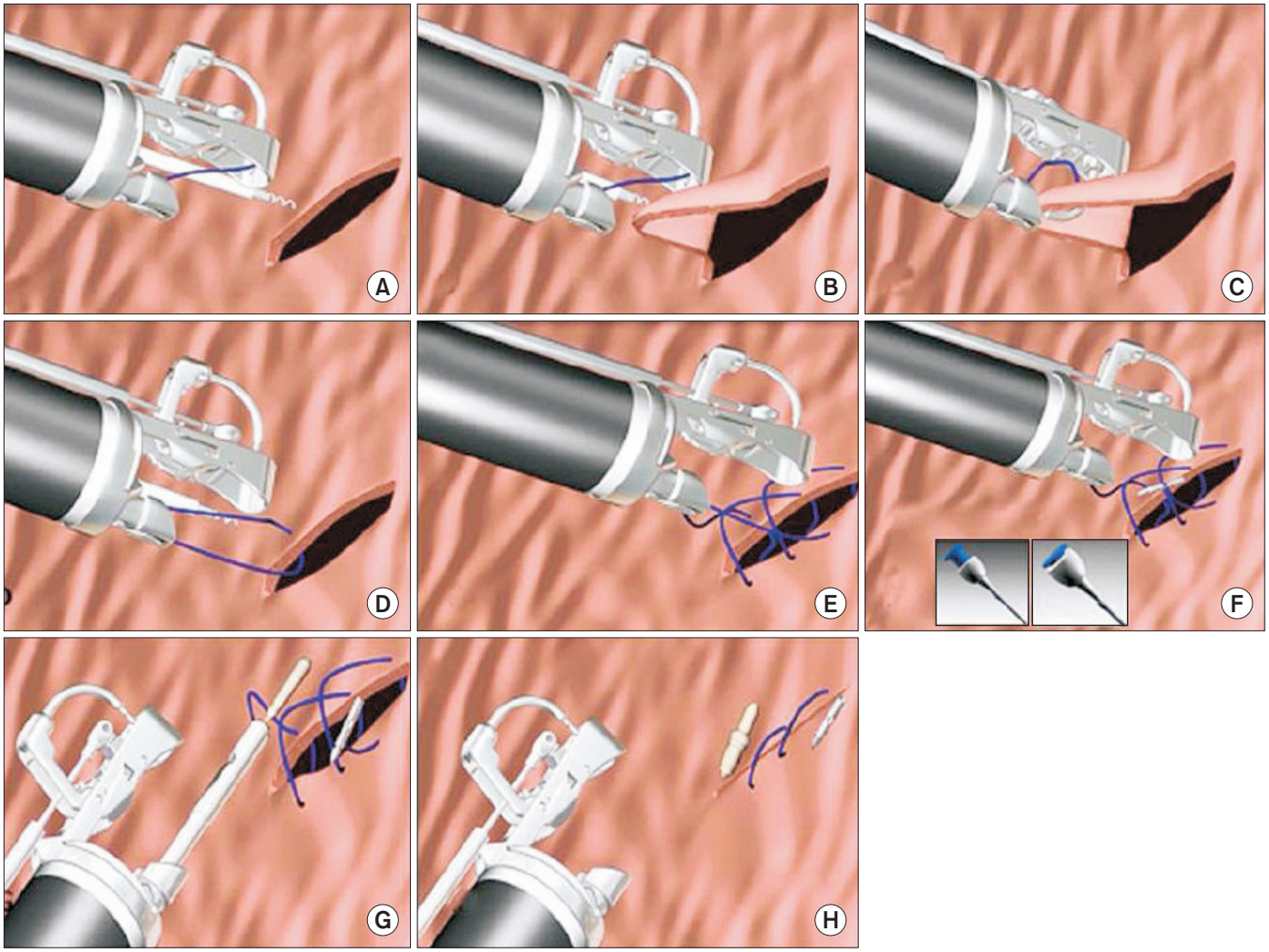

Fig. 3. Steps involved in placing endoscopic sutures. (A) Grasp the tissue using tissue helix. (B) Retract the tissue into the needle path. (C) Drive the needle through the tissue. (D) Open the arm and release the tissue. (E) Repeat stich as needed. (F) Press the blue button to release the needle (T-fastener). (G) Tighten and cinch. (H) Repeat as needed. Reproduced from the article of Stavropoulos et al (*World J Gastrointest Endosc*. 2015;7:777-89)[31] in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license.

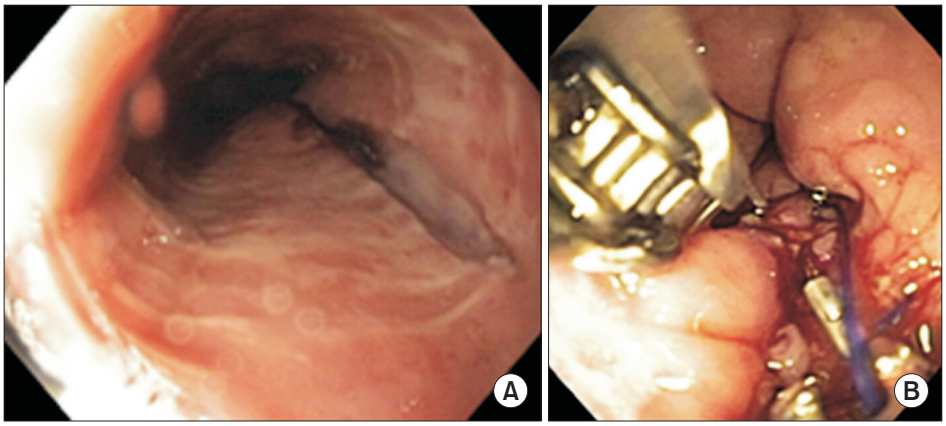

Fig. 4. (A) Endoscopic view of esophageal perforation after food impaction. (B) Subsequent closure with endoscopic suturing. Reprodu ced from the article of Henderson et al (*Gastrointest Endosc*. 2014;80:535-7)[20] with permission.

flap. The resultant offset mucosal entry site was closed with endoscopic suturing. At the end of 2 weeks, animals had a repeat endoscopy and necropsy which demonstrated the absence of ulceration at both the mucosal entry sites and the muscularis propria resection sites with complete healing of the serosa in all animals. Pauli et al[19] demonstrated in a human (treat-and-resect) colon model in 4 patients undergoing elective colectomy with subsequent histologic examination of the endoscopic suturing results in post-colectomy specimen. They found that OverStitch™ permitted safe and effective suturing at a sub-serosal depth without iatrogenic injury to adjacent structures. In addition, OverStitch™ has been successfully utilized in the closure of iatrogenic endoscopic perforations (Fig. 4).[20]

With widespread performance of endoscopic mucosal resection (EMR) and dissemination of endoscopic submucosal dissection (ESD), there is a need for additional minimally invasive methods to manage large iatrogenic perforations. Traditionally clips have been utilized.[21,22] A retrospective study of 12 patients showed that closure of large post-ESD defects with the OverStitch™ endoscopic suturing device is technically feasible and can avoid hospitalization.[12] Twelve ESD sites with a mean size of 42.5 ± 14.8 mm, located in the colon, rectum, and stomach with perforation underwent immediate suturing repair. The mean suturing time was 10.0 ± 5.8 minutes and successful closure without additional complication was achieved in all patients.[12] OverStitch™ case has also been utilized for the closure of full thickness esophagotomy defects which developed during POEM procedures.[13,23]

Endoscopic suturing for the treatment of fistula and leaks

Successful closure of GI fistulae using endoscopic suturing (some after failed attempts with clips) and tissue adhesives has been reported over the past 5 years.[24–27] Fistula recurrence may develop following endoscopic suturing and additional data regarding long-term outcomes is needed. As with each intervention, careful selection of lesions for endoscopic therapy as part of a multidisciplinary team is required.[28] Epithelialized chronic fistula tracts may be very resistant to closure and be predisposed to recurrence after initial closure. Preparation of the tract with tissue cautery (often with argon plasma coagulation) at the perimeter of the fistula has been advocated. The fistula tract and edges may also be abraded with a brush to de-epithelialize the tissue, and promote tissue adherence. Running interrupted sutures are usually performed in two to three layers. Repeat treatment may be required.

With chronic fistulae, percutaneous catheters placed by radiology to drain the cavities/fluid collections are typically recommended. A technique utilizing a submucosal dissection and snare cautery to resect the fistulous tract, followed by closure, has been reported.[29]

Occasionally after removal of a percutaneous endoscopic gastrostomy (PEG) tube, the stoma remains open, resulting in a gastrocutaneous fistula. Kantsevoy and Thuluvath[27] reported closure of such a fistula with OverStitch™ endoscopic suturing. Subsequent reports detailed successful closure of widened PEG stoma.[24,26]

Entero-bronchial fistula are notoriously difficult to close, and may require use of both enteric and bronchial stents. Catalano et al[2] reported successful closure in 6 patients, with 2 patients with endo-bronchial fistula requiring 3 to 4 sessions. All patients were able to resume oral feeding within 7 to 14 days. OverStitch™ has also been used to close a chronic esophago-pleural fistula that developed due to Boerhaave syndrome.[25] Tuyama et al[30] retrospectively evaluated 11 patients which underwent full thickness suturing in comparison to 22 patients who had superficial suturing for endoscopic repair of gastro-gastric fistula after Roux-en-Y gastric bypass. OverStitch™ full thickness suturing was found to be superior to suction based superficial suturing, with successful closure in 45% versus 22% of cases.

A retrospective multicenter case series of 122 patients undergoing endoscopic suturing for fully covered stent fixation, and/or direct therapy of perforation, fistula and leaks demonstrated an overall clinical success rate of 78.8% with a mean follow-up of 68 days. Forty patients underwent suturing for fistula closure with the majority at the site of gastrojejunal anastomosis. One-third of patients had prior unsuccessful therapy. Approximately one-half of patients underwent and an additional endoscopic therapeutic maneuver, with argon plasma coagulation (APC) ablation being the most common. Long term success was achieved in 80% of patients, with equally good results when suturing was performed as a rescue therapy. Long term success was more likely if the fistula was closed within 30 days of diagnosis (69% vs 23%; $P = 0.037$). In multivariate analysis, the only predictor of success among all cases was performance of suturing within 30 days of diagnosis (odds ratio, 4.1; 95% confidence interval, 1.26–13.2; $P = 0.02$). Fifteen patients underwent suturing, predominantly for closure of post-myotomy defects. Suturing was clinically successful in all cases except for the repair of a duodenal perforation. Twenty patients underwent suturing of anastamotic leaks after bariatric surgery (18 developing after performance of gastric sleeve), in conjunction with additional endoscopic therapy in the majority of cases (including APC, clipping, and stenting). The success rate

for the treatment of anastomotic leaks was significantly lower, at 27%. Suturing for stent anchorage, most commonly in the esophagus, was performed in 47 patients, with an indication of leak or fistula in 26. Successful stent anchoring was achieved in 37 of 40 patients.[11]

Challenges with OverStitch™

Advantages of OverStitch™ relative to prior devices include the ability to reload suture material without removal of the endoscope from the patient, reliable depth of needle penetration and the ability to use tissue grasping accessories in the adjacent working channel. Some important limitations, however, persist. The current device is only compatible with double channel therapeutic endoscopes and passage through the oropharynx through an overtube is recommended. Ongoing challenges with the current version of the OverStitch™ device include its large size, limited field of view and maneuverability. Suturing may be difficult or not possible in locations such as the gastric fundus, duodenum, and right colon.[31]

Comparative Studies

Therapeutic endoscopic tools and techniques for the treatment of intestinal perforations, leaks and fistulas include the application of tissue sealants, clip closure, and stent placement in addition to endoscopic suturing.[28,32] Hemoclips were created as a tool for endoscopic hemostasis and can provide mucosal; however, not full thickness tissue apposition. Over-the-scope clip (OTSC) are more robust devices and have been utilized for closure of perforation, leaks and fistulas, as reported in typically small case reports and series.[33–35] As noted above, given the difficulty in achieving clinical success, particularly with large and chronic fistula, leak and perforations, a combination of endoscopic therapeutic modalities may be utilized. There are limited comparative studies in patient cases between different techniques. A case control study comparing endoscopic suturing versus endoscopic clip closure of the esophageal mucosotomy at the conclusion of POEM procedures found both techniques to be equally safe and effective; however, closure time was shorter with clips (16 ± 12 minutes vs 33 ± 11 minutes; $P = 0.044$) with a trend towards lower cost with clips.[36] Stavropoulos et al[31] retrospectively compared 25 POEM mucosotomy closures with clips and 25 with suturing. No difference was found in time (8.8 minutes [6–15 minutes] vs 10.1 minutes [5–16 minutes]) or cost.

Conclusion

Endoscopic suturing is an emerging technique in the management of GI perforations, leaks and fistula. Although the device requires directed training and is more complex to use than clips, it has the capability to mimic surgical closure in a minimally invasive way. Given the currently limited data, further prospective, comparative studies are needed to define the role of endoscopic suturing devices in the management of perforations, leaks and fistulas.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

References

1. Karl RC, Schreiber R, Boulware D, Baker S, Coppola D. Factors affecting morbidity, mortality, and survival in patients undergoing Ivor Lewis esophagogastrectomy. *Ann Surg.* 2000;231:635–43.
2. Catalano MF, Sorser SA, Henderson JB, Ali S, Enteric AA. Successful closures of enteric fistulas using the Apollo OverStitch suturing system. *Gastroenterol.* 2014;146(Suppl 1):S142–3.
3. Kumar N, Thompson CC. Management of endoscopic perforation with abdominal exploration and full-thickness sutured closure. *Gastroenterol.* 2014;146(Suppl 1):S143.
4. Mahmood Z, McMahon BP, Arfin Q, Byrne PJ, Reynolds JV, Murphy EM, et al. Endocinch therapy for gastro-oesophageal reflux disease: a one year prospective follow up. *Gut.* 2003;52:34–9.
5. Swain CP, Kadirkamanathan SS, Brown G, Gong F, Evans DF, Mills TN. Sewing at flexible endoscopy in the human gastrointestinal tract. *Gastrointest Endosc.* 1994;40:35.
6. Filipi CJ, Lehman GA, Rothstein RI, Raijman I, Stiegmann GV, Waring JP, et al. Transoral, flexible endoscopic suturing for treatment of GERD: a multicenter trial. *Gastrointest Endosc.* 2001;53:416–22.
7. Moustarah F, Talarico J, Zinc J, Gatmaitan P, Brethauer S. NOTES for the management of an intra-abdominal abscess: transcolonic peritonoscopy and abscess drainage in a canine model. *Can J Surg.* 2013;56:159–66.
8. Pham BV, Raju GS, Ahmed I, Brining D, Chung S, Cotton P, et al. Immediate endoscopic closure of colon perforation by using a prototype endoscopic suturing device: feasibility and outcome in a porcine model (with video). *Gastrointest Endosc.* 2006;64:113–9.
9. Ozawa S, Yoshida M, Kumai K, Kitajima M. New endoscopic treatments for gastroesophageal reflux disease. *Ann Thorac Cardiovasc Surg.* 2005;11:146–53.
10. ASGE Technology Committee, Banerjee S, Barth BA, Bhat YM, Desilets DJ, Gottlieb KT, et al. Endoscopic closure devices. *Gastrointest Endosc.* 2012;76:244–51.
11. Sharaiha RZ, Kumta NA, DeFilippis EM, Dimaio CJ, Gonzalez S, Gonda T, et al. A large multicenter experience with endoscopic suturing for management of gastrointestinal defects and stent anchorage in 122 patients: a retrospective review. *J Clin Gastroenterol.* 2016;50:388–92.
12. Kantsevoy SV, Bitner M, Mitrakov AA, Thuluvath PJ. Endoscopic suturing closure of large mucosal defects after endoscopic submucosal dissection is technically feasible, fast, and eliminates the need for hospitalization (with videos). *Gastrointest Endosc.* 2014;79:503–7.
13. Kurian AA, Bhayani NH, Reavis K, Dunst C, Swanström L. Endoscopic suture repair of full-thickness esophagotomy during per-oral esophageal myotomy for achalasia. *Surg Endosc.* 2013;27:3910.
14. Liu L, Chiu PW, Teoh AY, Lam CC, Ng EK, Lau JY. Endoscopic suturing is superior to endoclips for closure of gastrotomy after natural orifices translumenal endoscopic surgery (NOTES): an ex vivo study. *Surg Endosc.* 2014;28:1342–7.
15. Stier C, Chiappetta S. Endoluminal revision (OverStitch (TM), Apollo Endosurgery) of the dilated gastroenterostomy in patients with late dumping syndrome after proximal Roux-en-Y gastric bypass. *Obes Surg.* 2016;26:1978–84.
16. Gitelis M, Ujiki M, Farwell L, Linn J, Wang C, Miller K, et al. Six month outcomes in patients experiencing weight gain after gastric bypass who underwent gastrojejunal revision using an endoluminal suturing device. *Surg Endosc.* 2015;29:2133–40.
17. Watson RR, Thompson CC. Application of a novel suturing device in the GI tract. *Gastrointest Endosc.* 2011;73(Suppl):AB105.
18. Rajan E, Gostout CJ, Aimore Bonin E, Moran EA, Locke RG, Szarka LA, et al. Endoscopic full-thickness biopsy of the gastric wall with defect closure by using an endoscopic suturing device: survival porcine study. *Gastrointest Endosc.* 2012;76:1014–9.
19. Pauli EM, Delaney CP, Champagne B, Stein S, Marks JM. Safety and effectiveness of an endoscopic suturing device in a human colonic treat-and-resect model. *Surg Innov.* 2013;20:594–9.
20. Henderson JB, Sorser SA, Atia AN, Catalano MF. Repair of esophageal perforations using a novel endoscopic suturing system. *Gastrointest Endosc.* 2014;80:535–7.
21. Liaquat H, Rohn E, Rex DK. Prophylactic clip closure reduced the risk of delayed postpolypectomy hemorrhage: experience in 277 clipped large sessile or flat colorectal lesions and 247 control lesions. *Gastrointest Endosc.* 2013;77:401–7.
22. Otake Y, Saito Y, Sakamoto T, Aoki T, Nakajima T, Toyoshima N, et al. New closure technique for large mucosal defects after endoscopic submucosal dissection of colorectal tumors (with video). *Gastrointest Endosc.* 2012;75:663–7.
23. Modayil R, Friedel D, Stavropoulos SN. Endoscopic suture repair of a large mucosal perforation during peroral endoscopic myotomy for treatment of achalasia. *Gastrointest Endosc.* 2014;80:1169–70.
24. Armengol-Miro JR, Dot J, Abu-Suboh Abadia M, Masachs M, Salord JC, Armengol Bertroli J, et al. New endoscopic suturing device for closure of chronic gastrocutaneous fistula in an immunocompromised patient. *Endoscopy.* 2011;43 Suppl: E403–4.
25. Bonin EA, Wong Kee Song LM, Gostout ZS, Bingener J, Gostout CJ. Closure of a persistent esophagopleural fistula assisted by a novel endoscopic suturing system. *Endoscopy.* 2012;44 Suppl 2:E8–9.
26. Stanich PP, Sklaw B, Krishna SG. Persistent peristomal leakage from percutaneous endoscopic gastrostomy successfully treated with endoscopic suturing. *Endoscopy.* 2013;45 Suppl 2:E394.
27. Kantsevoy SV, Thuluvath PJ. Successful closure of a chronic refractory gastrocu-

taneous fistula with a new endoscopic suturing device (with video). *Gastrointest Endosc.* 2012;75:688-90.
28. Willingham FF, Buscaglia JM. Endoscopic management of gastrointestinal leaks and fistulae. *Clin Gastroenterol Hepatol.* 2015;13:1714-21.
29. Abidi WM, Thompson CC. Endoscopic treatment of a chronic fistula by resection and sutured closure. *Gastrointest Endosc.* 2016;83:1031-2.
30. Tuyama AC, Kumar N, Aihara H, Ryan MB, Thompson CC. Endoscopic repair of gastrogastric Fistula after Roux-en-Y gastric bypass: a matched cohort study evaluating two methods of fistula closure. *Gastroenterol.* 2013;144(Suppl 1):S220.
31. Stavropoulos SN, Modayil R, Friedel D. Current applications of endoscopic suturing. *World J Gastrointest Endosc.* 2015;7:777-89.
32. Rustagi T, McCarty TR, Aslanian HR. Endoscopic treatment of gastrointestinal perforations, leaks, and fistulae. *J Clin Gastroenterol.* 2015;49:804-9.
33. Kobara H, Mori H, Fujihara S, Nishiyama N, Chiyo T, Yamada T, et al. Outcomes of gastrointestinal defect closure with an over-the-scope clip system in a multicenter experience: an analysis of a successful suction method. *World J Gastroenterol.* 2017;23:1645-56.
34. Sagara Y, Shinozaki S, Yano T, Sakamoto H, Hayashi Y, Lefor AK, et al. Use of an over-the-scope clipping device for closure of a jejuno-sigmoid fistula: a case report with long-term follow-up. *Clin J Gastroenterol.* 2016;9:369-74.
35. Mori H, Rahman A, Masaki T. Combination therapy of o ver-the-scope-clip and covered metallic stent for refractory multiple esophagobronchial fistulae and stenosis. *Dig Endosc.* 2017. doi: 10.1111/den.12840. [Epub ahead of print]
36. Pescarus R, Shlomovitz E, Sharata AM, Cassera MA, Reavis KM, Dunst CM, et al. Endoscopic suturing versus endoscopic clip closure of the mucosotomy during a per-oral endoscopic myotomy (POEM): a case-control study. *Surg Endosc.* 2016;30:2132-5.