J Gastrointest Surg (2010) 14 (Suppl 1):S121–S126
DOI 10.1007/s11605-009-1027-z

DEMEESTER FESTSCHRIFT

Initial Experience with New Intraluminal Devices for GERD Barrett's Esophagus and Obesity

Charles J. Filipi · Rudolf J. Stadlhuber

Received: 15 July 2009 / Accepted: 25 August 2009 / Published online: 24 September 2009

Abstract
Background Transoral intraluminal surgery is less painful. However, endoscopic antireflux procedures have been unsuccessful, endoscopic foregut mucosal excision procedures are often difficult to perform, and endoscopic intraluminal suturing is both imprecise and too shallow. We have endeavored to correct these deficiencies and report here new devices for GERD, obesity, and Barrett's mucosal excision.
Method A retrospective review of ex vivo and in vivo animal experiments using sharp blade mucosal excision for esophageal and gastric mucosa and a suturing device with transverse needles designed to full thickness penetrate the gastric wall were completed. A total of 338 excisions were performed in 134 ex vivo tissue experiments and in 119 in vivo attempts. Suture needle testing was performed in ex vivo human stomachs and porcine stomachs and in in vivo canine and baboon stomachs.
Results One excision perforation (0.9%) occurred in a live animal. Satisfactory mucosal excision depth for the Barrett's device was reproducible. Progressive suture actuation reliability improved from 83% during ex vivo testing to 96.7% in in vivo experiments.
Conclusion The results demonstrate feasibility, reliability, and safety for gastric and esophageal mucosal excision. Suturing reliability improved and further studies will be performed to finalize the instrument designs, the operative techniques, and the other device applications.

Keywords Mucosa · GERD · Barrett's esophagus · Obesity · Endoscopy · Excision

Introduction

Laparoscopy, a surgical milestone within the past two decades has irreversibly changed the surgical paradigm. In combination with sophisticated engineering and advanced endoscopic techniques, surgeons are now able to perform more complex endoluminal procedures. At Creighton University, we have focused on transoral procedures for Barrett's mucosa, gastroesophageal reflux disease (GERD), and obesity. The unique excision technique and suture management used is also applicable for post gastric bypass pouch and outlet reduction, gastric sleeve revision, esophageal perforation closure, and colon polyp excision.

The endoscopic techniques published to date for GERD can be categorized in three major groups. Techniques applying radiofrequency to the lower esophageal sphincter,[1] approaches injecting or implanting biopolymers at the GEJ,[2,3] and devices that perform endoluminal sewing or plicating at the gastro esophageal junction.[4–8] However, none of these devices/techniques have become the standard of care.[9]

Based on the excellent weight loss results observed with restrictive procedures such as adjustable gastric banding, a transoral endoscopic outpatient intraluminal restrictive

Financial Support: SafeStitch Medical Inc., 4400 Biscayne Blvd, Suite 670, Miami, FL 33137

C. J. Filipi (✉) · R. J. Stadlhuber
Department of Surgery, Creighton University School of Medicine,
601 N 30th Street, # 3700,
Omaha, NE 68131, USA
e-mail: cjfilipi@creighton.edu

procedure that could be effectively revised after several years is expected to be appealing to patients and surgeons alike. Investigations of intraluminal restrictive techniques for obesity are ongoing but durability of effect is in question.[10,11]

Numerous mucosal ablation and excision methods for Barrett's esophagus have been devised; ablation techniques include photodynamic therapy, ultrasonic ablation, Argon beam coagulation, radiofrequency ablation, cryotherapy ablation, and bipolar electrocoagulation.[12–15] The primary excision technique is endoscopic mucosal resection (EMR) which is limited by cautery margins, specimen disorientation, and small size. Both EMR and the ablation methods are designed to remove the Barrett's epithelium and to treat either high-grade dysplasia or early noninvasive adenocarcinoma.

Mucosal excision has been shown to be relatively safe with a bleeding rate of 8% and a perforation rate of less than 1%.[16] However, this form of therapy often provides a piece meal removal of the tissue, or cancer if present, and the tissue specimens cannot be oriented for pathologic inspection; thus, accurate lateral margins are unattainable. More importantly, the technique is time consuming and difficult to perform. A device that would reliably, rapidly, and safely remove mucosa and muscularis mucosa with a low incidence of complication would be attractive.

Durability of effect for endoluminal GERD and obesity procedures is lacking, and our intention is to create sufficient scar formation to prevent tissue separation over time. The main focus of our initial laboratory work was feasibility, safety, quality, and reliability of mucosal excision and suture needle actuation. Here, we report the results of this effort and a new device for Barrett's mucosal excision.

Methods

Testing was performed in ex vivo porcine, canine, baboon, and human tissue.

A dilator-shaped device (SafeStitch Medical Inc.) was used to perform excision and suture placement (Fig. 1). The 60 F flexible instrument has a distal integrated excision and suture capsule, while a standard small caliber transnasal endoscope introduced through the device shaft is used for direct visualization. The 5-cm long rigid distal capsule contains the excision blade, vertical anchor needles for tissue holding and Adrenalin injection, and two circular needles each connected to a separate 2.0 Prolene suture running through the device (Figs. 2 and 3). Two sets of two full-thickness sutures and a mucosal excision down to the level of the muscularis propria on the anterior and the posterior stomach wall are used for each stage of the

Figure 1 The 60 F dilator-shaped endoluminal gastroplasty device.

gastroplasty. After correct positioning of the device with the endoscope in retroflexion, the gastric wall is pulled into the trough with 500 mm/Hg negative pressure. The two three-quarter-circle needles are actuated to rotate 360° through the captured tissue. The tissue is then injected with 5 cm^3 of 1:200,000 adrenalin solution to create tissue swelling for hemostasis and a safe cut in the correct gastric wall layer (Fig. 4). The second suture excision cycle is performed by advancing the device into the correct position and repeating the sequence. The sutures are then tied and cut with a flexible endoscopic device resulting in a full-thickness stomach wall apposition. The vertical gastroplasty line is approximately 6 cm long and a result of three subsequent overlapping stages forming the neo-esophagus with pouch and restrictive outlet (Fig. 5). Attention was paid to excision and excision overlap safety and reliability for both the one stage GERD gastroplasty and the three-stage obesity gastroplasty line.

Esophageal mucosal resection using a new flexible endoscopic device (SafeStitch Medical Inc.) was performed. Preliminary ex vivo studies were carried out with porcine, canine baboon, and human esophagi. These experiments allowed us to determine the correct excision technique and device characteristics necessary for consistent strip endoscopic mucosal resection.

The instrument consists of a flexible shaft (Fig. 6) with an integrated distal excision capsule. A standard small

Figure 2 5 cm long rigid distal excision and suture capsule with transnasal endoscope in a retroflexed position. The guillotine excision blade is half way advanced and visible within the excision trough.

caliber transnasal endoscope is introduced into the device for visual orientation (Figs. 7 and 8). The excision capsule is 5 cm long and is rigid (Fig. 9). The device is mounted on the endoscope, and the rounded distal flexible tip allows safe introduction of the device through the oropharynx. The resection window is 2.8 cm long, 1.3 cm wide, and 0.4 cm deep and is positioned by endoscopic visualization. After device positioning the endoscope is retracted into the device shaft. Two suction channels pull the mucosa into the capsule and vertical anchor needles help fix the tissue in position. To assure the correct cutting depth and hemostasis a 1:200,000 Adrenaline solution is injected with a longitudinal injection needle placed above the bottom of the trough (Fig. 9). The injectate further separates the muscularis mucosa from the muscularis propria thus increasing the "target space." The multifunctional device handle provides longitudinal-injection-needle placement with

Figure 3 Capsule with flexible transition that allows introduction through the oro- and hypopharynx.

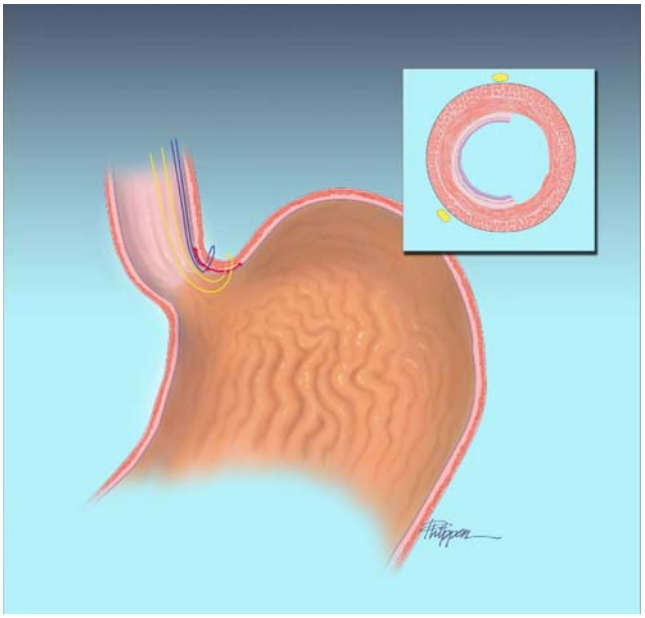

Figure 4 Step 1 gastroplasty for GERD at GEJ with excision pattern including 180° of the distal esophagus.

simultaneous controlled injection. The desired cutting depth through the first third of the submucosa assures complete removal of Barrett's mucosa and submucosal glands while decreasing the potential for stricture formation. A guillotine blade resects the mucosa (Fig. 9). Mucosal excision is performed with a single proximal-to-distal pushing movement of the blade. After the mucosectomy is complete, the device is removed from the esophagus with the specimen within the capsule. The specimen can be easily orientated for the pathologist and sent for histological analysis.

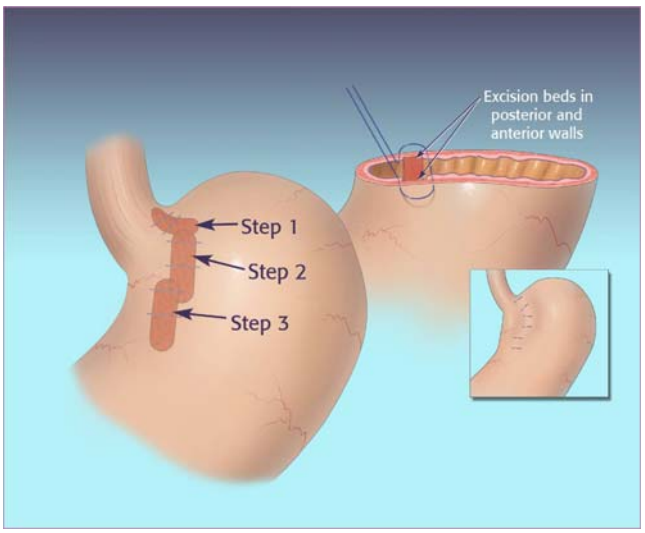

Figure 5 Schematic description of a three-step vertical gastroplasty with excision overlap and full-thickness sutures placement.

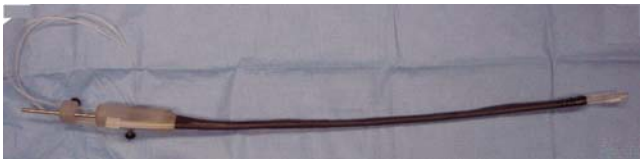

Figure 6 Barrett's excision device with flexible shaft, excision capsule, and multifunctional handle.

Results

Gastric mucosal excisions were most often within the submucosal layer and in-vivo testing submucosal excision depth was present in 98% of specimens. Only successful tissue injection with subsequent tissue swelling ensures a safe overlap excision. In ex vivo experiments focusing on excision overlap we provoked full-wall excision (n=6). As a result, we modified the injection needle positions to achieve more reliable submucosal injection when partially overlapping previously excised areas. The new injection needle positions allowed consistent fluid bolster application and successful excision overlap in 99.1% of in vivo experiments. In the latest gastroplasty excision and suture device, suture needle actuation reliability increased from 83% in ex vivo experiments to 96.7% during in vivo procedures.

The first nonsurvival canine and porcine esophageal mucosa excision experiments were promising in terms of safety. The device could be introduced without trauma in both canine and porcine models, and six mucosal excisions were performed without bleeding. Easy 1-mm target cautery mark localization and accurate capsule placement was proven. No perforations occurred and none of the in vivo esophagi, after removal, showed evidence of excision penetration to the muscularis propria level.

Figure 7 A transnasal endoscope is advanced through the tip of the device and retroflexed within the stomach for proper device positioning.

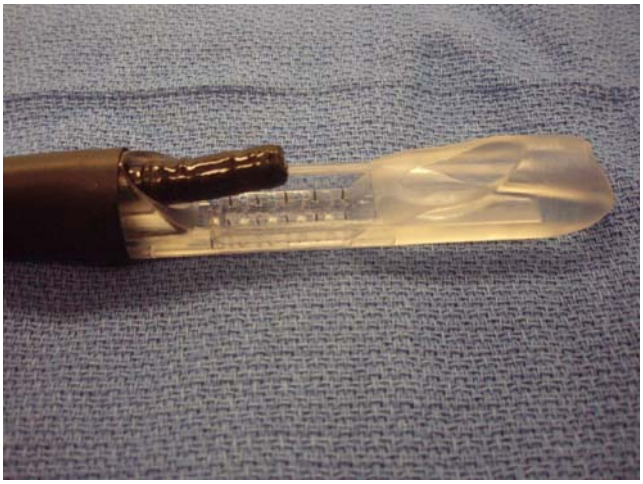

Figure 8 The antegrade position provides visualization of the distended target area.

Discussion

Laboratory results have demonstrated gastric and esophageal mucosal excision feasibility and safety. Intraluminal gastric automated suture placement reliability was established but further device revisions are needed for both excision and suturing before proceeding to human trials.

The appeal of an outpatient transoral endoscopic obesity procedure has led to multiple investigations of endoscopic treatments. Deviere and Moreno have published pilot human studies using a transoral device to create a vertical gastroplasty.[10,11] The device named transoral gastroplasty (Satiety, Palo Alto, CA) contains a stapler body with two jaws and a septum with retraction wire to orient the stomach tissue for capture and stapling. Suction pulls tissue from the anterior and posterior walls of the stomach into the device and the stapler is closed and fired. Three rows of 11

Figure 9 The 5-cm long rigid excision capsule with vertical anchor needles, suction ports, guillotine excision blade, and a longitudinal injection needle.

titanium staples create a transmural staple line connecting the anterior and posterior stomach. The continuity of the gastroplasty line, especially at the proximal aspect of the neo-esophagus, is a requirement as a single gap will increase emptying, resulting in the loss of the pouch and volume restriction. This complication was seen by Deviere et al. as staple line gaps were visible endoscopically or on barium swallow in 13 of 21 patients (~62%).[11]

Maish et al. compared the depth of invasion accuracy of endoscopic ultrasound (EUS) using a 7.5- and a 12-MHz probe and EMR findings in surgically resected esophageal specimens.[17] Ultrasound and EMR findings concurred in only one of seven patients. In two patients, the EUS understaged the tumor depth, and in two patients, the EUS overstaged the depth of invasion. In their study, the accuracy of EUS to determine intramucosal from submucosal tumor invasion was 20%. Final pathologic examination confirmed that the EMR specimen had accurately determined the depth of tumor invasion in all seven lesions. Two patients had complete removal of a visible cancer by EMR, but after resection, an additional adenocarcinoma was found within the Barrett's segment that had not been previously detected. One of these patients had a 16-cm segment of Barrett's mucosa, but the other had a short tongue of Barrett's mucosa.[17] These findings demonstrate the importance of clean excision margins and widespread excision. Occult esophageal adenocarcinoma biopsy error rates in patients with previous diagnosed high-grade dysplasia or adenocarcinoma are as high as 43%.[18]

The largest endoscopic resection study for high-grade intraepithelial neoplasia and mucosal adenocarcinoma achieved a complete response in 96.6% of 349 patients and a mean follow-up of 63.6±23.1 months. The technique used was the "suck-and-cut" technique with a ligation device or cap.[19] Confirmatory studies are needed.

Endoscopic mucosal resection is an important staging and therapeutic tool for a select group of patients with Barrett's esophagus. However, current limitations of EMR include lateral and depth margin coagulation artifacts, absence of specimen orientation, and small specimen size.

Further device modifications would make endoscopic mucosal resection of colonic lesions possible. Many colon polyps are sessile,[20] and a snare EMR technique is being used. A cold blade device with mucosal injection and a big resection window would provide accurate histologic margins and avoid piecemeal resections. Access to the transverse and right colon will require design changes. Bleeding is always a concern with mucosal excision but immediate Adrenaline solution injection or cautery is possible with the current mucosal excision device.

Additional procedures amenable to the devices described are post-gastric bypass pouch and outlet reduction. Both conditions are becoming more common as more gastric bypass operations are performed. Mucosal excision with full-thickness suturing is more likely to succeed than the other endoscopic techniques being currently employed. Tissue stretching can be altered by significant scar formation. Macrophages, the precursors of fibroblasts which make collagen, come from the blood stream, and the blood supply of the stomach is excellent throughout. Stimulation of this pathway and prevention of re-epithelialization after mucosal excision is necessary.

Finally, esophageal perforations are being successfully managed with stents and fibrin glue but occasional mediastinal leakage continues. Immediate full-thickness suture placement in the transverse plane for a longitudinal tear could be advantageous. Currently available suturing devices for the esophagus place sutures longitudinally. The suture mucosal excision device will be modified to a suture-only approach and would be applicable for esophageal, gastric, and colonic perforations.

Conclusion

The GERD and obesity gastroplasty device described is the only transoral device that addresses two pathologies using one device and similar operative technique. The reported results demonstrate feasibility, reliability, and safety of this approach. The Barrett's device is the first automated mucosal excision system that also has proven reliable in obtaining correct depth mucosal specimens. Further studies for both devices will be performed to finalize design and operative techniques.

References

1. Wolfsen HC, Richards WO. The Stretta procedure for the treatment of GERD: a registry of 558 patients. J Laparoendosc Adv Surg Tech A 2002;12:395–402.
2. Devière J, Costamagna G, Neuhaus H, et al. Nonresorbable copolymer implantation for gastroesophageal reflux disease: a randomized sham-controlled multicenter trial. Gastroenterology 2005;128:532–540.
3. Cicala M, Gabbrielli A, Emerenziani S, et al. Effect of endoscopic augmentation of the lower oesophageal sphincter (Gatekeeper reflux repair system) on intraoesophageal dynamic characteristics of acid reflux. Gut 2005;54:183–186.
4. Schwartz MP, Wellink H, Gooszen HG, et al. Endoscopic gastroplication for the treatment of gastro-oesophageal reflux disease: a randomised, sham-controlled trial. Gut 2007;56:20–28.
5. Schilling D, Kiesslich R, Galle PR, et al. Endoluminal therapy of GERD with a new endoscopic suturing device. Gastrointest Endosc 2005;62:37–43.
6. Rothstein R, Filipi C, Caca K, et al. Endoscopic full-thickness plication for the treatment of gastroesophageal reflux disease: A randomized, sham-controlled trial. Gastroenterology 2006;131:704–712.

7. Cadière GB, Rajan A, Germay O, et al. Endoluminal fundoplication by a transoral device for the treatment of GERD: A feasibility study. Surg Endosc 2008;22:333–342.
8. Jobe BA, O'Rourke RW, McMahon BP, et al. Transoral endoscopic fundoplication in the treatment of gastroesophageal reflux disease: the anatomic and physiologic basis for reconstruction of the esophagogastric junction using a novel device. Ann Surg 2008;248:69–76.
9. Rothstein RI. Endoscopic therapy of gastroesophageal reflux disease: outcomes of the randomized-controlled trials done to date. J Clin Gastroenterol 2008;42:594–602.
10. Moreno C, Closset J, Dugardeyn S, et al. Transoral gastroplasty is safe, feasible, and induces significant weight loss in morbidly obese patients: results of the second human pilot study. Endoscopy 2008;40:406–413.
11. Devière J, Ojeda Valdes G, Cuevas Herrera L, et al. Safety, feasibility and weight loss after transoral gastroplasty: First human multicenter study. Surg Endosc 2008;22:589–598.
12. Overholt BF, Panjehpour M, Haydek JM. Photodynamic therapy for Barrett's esophagus: follow up in 100 patients. Gastrointest Endosc 1999;49:1–7.
13. Morino M, Rebecchi F, Giaccone C, et al. Endoscopic ablation of Barrett's esophagus using argon plasma coagulation (APC) following surgical laparoscopic fundoplication. Surg Endosc 2003;17:539–542.
14. Bowers SP, Mattear SG, Waring PJ, et al. KTP laser ablation of Barrett's esophagus after anti-reflux surgery results in long-term loss of intestinal metaplasia. Surg Endosc 2003;17:49–54.
15. Montes CG, Brandalise NA, Deliza R, et al. Antireflux surgery followed by bipolar electrocoagulation in the treatment of Barrett's esophagus. Gastrointest Endosc 1999;50:173–177.
16. Ell C, May A, Pech O, et al. Curative endoscopic resection of early esophageal adenocarcinomas (Barrett's cancer). Gastrointest Endosc 2007;65:3–10.
17. Maish MS, DeMeester SR. Endoscopic mucosal resection as a staging technique to determine the depth of invasion of esophageal adenocarcinoma. Ann Thorac Surg 2004;78:1777–1782.
18. Nigro JJ, Hagen JA, DeMeester TR, et al. Occult esophageal adenocarcinoma: extent of disease and implications for effective therapy. Ann Surg 1999;230:433–438.
19. Pech O, Behrens A, May AD, et al. Long-term results and risk factor analysis for recurrence after curative endoscopic therapy in 349 patients with high-grade intraepithelial neoplasia and mucosal adenocarcinoma in Barrett's oesophagus. Gut 2008;57(9):1200–1206.
20. Waye JD. Advanced polypectomy. Endosc Clin N Am 2005;15 (4):733–756.