

Transoral Mucosal Excision Sutured Gastroplasty: A Pilot Study for GERD and Obesity With Two-Year Follow-Up

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Abstract

Introduction. An outpatient transoral endoscopic procedure for gastroesophageal reflux disease (GERD) and obesity would be appealing if safe, effective, and durable. We present the first in human experience with a new system. **Methods.** Eight patients with GERD (3) and obesity (5) were selected according to a preapproved study protocol. All GERD patients had preprocedure manometry and pH monitoring to document GERD as well as quality of life and symptom questionnaires. Obese patients (body mass index >35) underwent a psychological evaluation and tests for comorbidities. Under general anesthesia, a procedure was performed at the gastroesophageal junction including mucosal excision, suturing of the excision beds for apposition, and suture knotting. **Results.** One patient with micrognathia could not undergo the required preprocedural passage of a 60 F dilator and was excluded. The first 2 GERD patients had incomplete procedures due to instrument malfunction. The subsequent 5 subjects had a successfully completed procedure. Four patients were treated for obesity and had an average excess weight loss of 30.3% at 2-year follow-up. Of these patients, one had an 8-mm outlet at the end of the procedure recognized on video review—a correctable error—and another vomited multiple times postoperatively and loosened the gastroplasty sutures. The treated GERD patient had resolution of reflux-related symptoms and is off all antisecretory medications at 2-year follow-up. Her DeMeester score was 8.9 at 24 months. **Conclusion.** The initial human clinical experience showed promising results for effective and safe GERD and obesity therapy.

Keywords

esophageal surgery, flexible endoscopy, gastric surgery, NOTES, interventional endoscopy

Introduction

GERD

Gastroesophageal reflux disease (GERD) affects an estimated 19 million people in the United States, which results in a direct cost of \$9.3 billion for treatments per year.^{1 (1)} The management of GERD has gained increasing attention during the past 2 decades due to a high prevalence in Western societies, a better understanding of the pathophysiology, new potent antisecretory drug therapies, the advent of minimally invasive surgery, and new transoral endoscopic procedures. Patients with early disease normally experience episodes of esophageal acid exposure shortly after meals.

An outpatient endoscopic procedure that would alter the gastroesophageal junction (GEJ) barrier to prevent acid reflux would be appealing to patients and physicians alike. In this study, an endoluminal gastroplication procedure

was studied, with the intent to demonstrate safety, symptom relief, increased lower esophageal sphincter pressure, and normalization of pH monitoring results.

Obesity

Approximately two thirds of individuals living in the United States are overweight, and of those, almost half are obese.² Obesity is associated with increases in the

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Table 1. Schedule of Tests.

Form Name	Baseline	Procedure	Day 1 Postop Phone Call	2 Weeks ± 4 Days	1 Month ± 1 Week	3 Months ± 2 Weeks	6 Months ± 1 Month	12 Months ± 1 Month	24 Months ± 1 Month
GERD symptoms	X				X	X	X	X	X
GERD medications	X				X	X	X	X	X
Quality of life (GERD-HRQL)	X				X	X	X	X	X
Esophageal assessment									
Endoscopy	X						X	X	X
Manometry	X					X		X	X
pH monitoring	X					X		X	X
Procedure		X							
Adverse event		X							
Postprocedure adverse events			X	X	X	X	X	X	X

Abbreviations: GERD, gastroesophageal reflux disease; HRQL, health-related quality of life.

prevalence of type 2 diabetes, hyperlipidemia, hypertension, obstructive sleep apnea, heart disease, stroke, asthma, back and lower extremity weight-bearing degenerative joint problems, several forms of cancer, and depression. For example, obese men have a 5.5 times greater risk of becoming diabetic.³ In comparison with a normal-weight individual, a 25-year-old morbidly obese man has a 22% reduction in lifespan, representing a loss of 12 years of life.⁴

However, as with all operative procedures, bariatric surgery is associated with morbidity and mortality. Operative mortality (30 days) is approximately 0.1% for restrictive procedures, 0.5% for gastric bypass, and 1.1% for biliopancreatic diversion or duodenal switch.⁵ In addition, increasing cost, postoperative pain, hospital stay, and other morbidities associated with surgery make this a difficult choice. Hence, effective endosurgical therapy for the treatment of obesity would be both cost-effective and highly beneficial.

Excision of mucosa followed by apposition of the excision beds will result in a durable plication. In an abstract this was demonstrated, and it is evident from open and laparoscopic surgery that raw or open gastric edges do fuse with suture reinforcement, as in anastomoses. We have demonstrated in canines that sufficient and durable fibrosis is placed to alter GEJ compliance and to create a durable 6 mm in diameter outlet along the lesser curvature.⁶ The gastroplasty line must also remain intact as any opening will increase and remove the restrictive nature of the procedure. In addition, a distal 1 cm opening must be secure to provide a relative obstruction to the rapid intake of food. We have demonstrated in the animal laboratory that this is possible.⁷ The purpose of this pilot project was to demonstrate feasibility and safety of the procedure and if possible preliminary effectiveness.

Methods

After hospital ethics committee and National Regulatory Agency protocol approval, patients were screened for

study eligibility, and then GERD patients were administered a symptom scoring questionnaire, the GERD-HRQL (health-related quality of life). They underwent upper endoscopy to rule out a hiatal hernia larger than 2 cm and other contraindicating pathology before manometry and pH monitoring testing. The DeMeester score was determined and patients with a normal score or a score more than 50 were excluded. The schedule of tests is shown in Table 1.

For obesity patients, the following tests were performed: Impact of Weight on Quality of Life Questionnaire (IWQOL), a symptom questionnaire, medication usage, a psychological evaluation, body weight and height, a *Helicobacter pylori* test, a UGI series, assessment of comorbidities including an A1c level, blood pressure, a sleep apnea questionnaire, and serum lipids. This was followed by upper endoscopy. Table 2 shows the scheduled tests.

Safety was evaluated by monitoring the incidence of adverse events. The following is a list of possible adverse events: esophageal perforation, gastrointestinal bleeding requiring transfusion, gastric perforation, aspiration, cardiac events, pneumothorax, or bacteremia.

Operative Technique

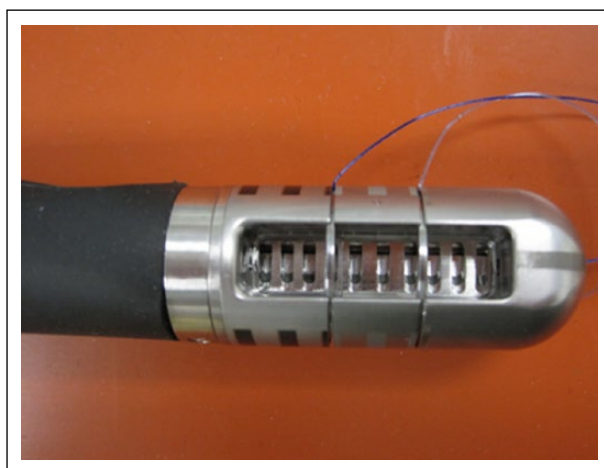
Initially, the patients were placed in the supine position after intubation and initiation of general anesthesia. Upper endoscopy was performed followed by Savary guidewire esophageal dilation with a 60 F Savary dilator. Instrument insertion of the excision device (Figure 1) was difficult but possible in the first patient; however, the device and other malfunctions occurred.

In the second patient, we found the supine and left lateral decubitus position difficult because the fundus of the stomach could not be captured correctly for excisions. We tried then used the right lateral decubitus position which allowed tissue capture of the proximal greater curvature such that injection and excision could be consistently performed. However, the suture device

Table 2. Schedule of Tests.

Form Name	Baseline	Procedure	2 Weeks	1 Month	3 Months	6 Months	12 Months	24 Months
H&P	X							
Medications	X		X	X	X	X	X	X
UGI symptoms	X		X	X	X	X	X	X
Body weight	X		X	X	X	X	X	X
Stool guiac			X					
UGI series	X		X		X			
Assessment of comorbidities								
Blood pressure	X	X	X	X	X	X	X	X
Fasting blood glucose	X	X		X	X	X	X	X
Hb A1C	X	X		X	X	X	X	X
<i>Helicobacter pylori</i> breath test	X							
Lipid profile	X				X	X	X	X
IWQOL questionnaire	X			X	X	X	X	X
Procedure		X						
Endoscopy		X				X	X	X
Adverse events		X						
Postprocedure adverse events			X	X	X	X	X	X
Standard psychological evaluation	X							

Abbreviation: IWQOL, Impact of Weight on Quality of Life Questionnaire.

**Figure 1.** The excision device with the blade.**Figure 2.** The suture device with suture needles and attached sutures.

(Figure 2) malfunctioned and this procedure was terminated as well.

The following 5 patients all had a complete procedure although in the third patient the excisions were not in ideal position. With the subsequent patients the mucosal excisions were in satisfactory position and the procedure was performed as follows.

The excision device was introduced into the proximal stomach and the stomach was insufflated after a 6 mm endoscope was introduced through the device (Supplemental Data Figure S1; available online at <http://SRI.sagepub.com/supplemental>). After excision device positioning, a vacuum was applied and tissue was pulled into the excision device trough. A 4.2% hypertonic saline (HTS) and 1:100 000 adrenaline solution was injected and the vacuum was discontinued. The tissue

escaped the capsule trough (Supplemental Data Figure S2) and the cushion was inspected for position, length, height, and width. If satisfactory the cushion was recaptured and again injected (Supplemental Data Figure S3). Excision was performed after a 60-second delay for adrenaline-mediated vasoconstriction. The vacuum was discontinued, the stomach was reinsufflated and the mucosa visualized in the bottom of the trough (Figure 3). A small elevating platform at the bottom of the trough was activated and the mucosal/submucosal strip was positioned (Supplemental Data Figure S4) so that it could be removed. A foreign body grasping forceps was introduced through the endoscope (Supplemental Data Figure S5) and the tissue was removed with the endoscope through the endoscope channel (Supplemental

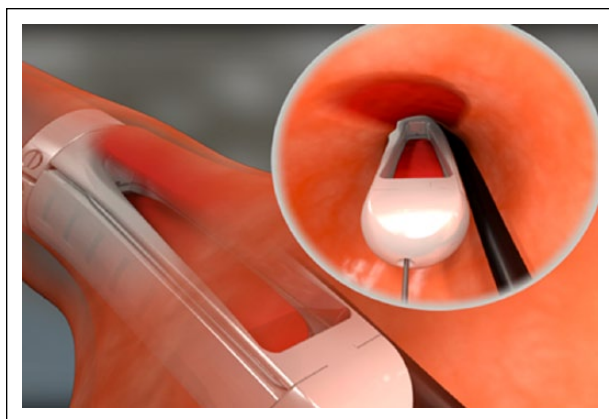


Figure 3. The mucosa submucosal strip is seen with the through.

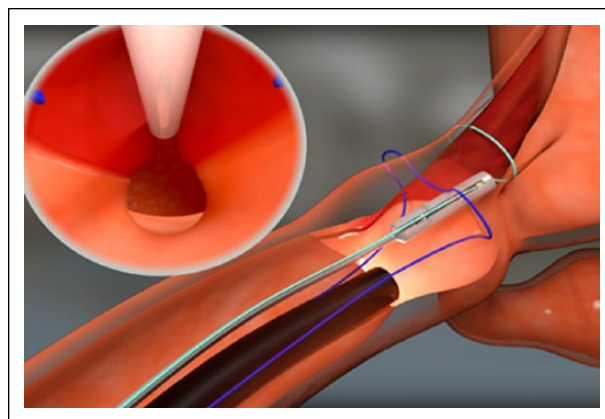


Figure 5. The endoscope monitoring tissue apposition.

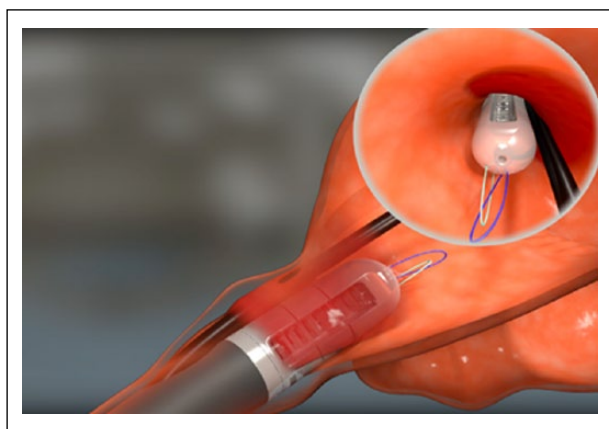


Figure 4. The suture device is positioned for the first suture cycle.

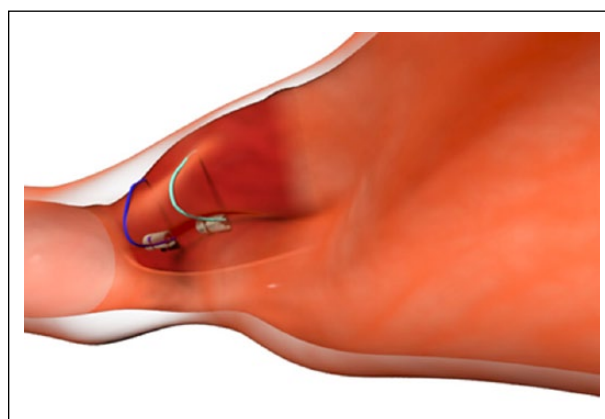


Figure 6. The GERD procedure with excisions more proximally located.

Data Figure S6). The tissue was pinned on a cork board for inspection and measurements. This same process was repeated 2 more times with the 3 excisions placed adjacent to each creating one confluent excision bed (Supplemental Data Figure S7). Blood clots were removed and then hypertonic saline was injected along the lesser curvature to form a restrictive fibrotic ring in obese patients only.

The suture device was introduced over a guidewire and positioned for suturing within excision #3 (Figure 4). The sutures are full thickness if placed within the excision bed and partially close the GEJ at the greater curvature side. A vacuum is applied and after suture application the position of the suture device is checked (Supplemental Data Figure S8). The device is then rotated to the first excision bed and the process is repeated (Supplemental Data Figure S9). The suction is discontinued, the sutures are inspected (Supplemental Data Figure S10) and the

suture device is removed from the patient. The sutures are organized outside the patients' mouth and the distal suture strands are placed into the knotter and between the plug and sleeve (Supplemental Data Figure S11). The knotter is run over the sutures under slight tension into the esophagus and the 6 mm endoscope is introduced for visualization (Figures 5 and Supplemental Data Figure S12). The endoscope is retroflexed in the stomach as the sutures are tightened to the tissue to assure tissue apposition (Supplemental Data Figure S13). This is repeated with the more proximal suture strands and the completed GERD (Figure 6) and obesity procedures (Figure 7) are shown.

The obesity and GERD procedures differed in 2 ways. The mucosal excisions were closer to the squamocolumnar junction for GERD, and the radial separation of the 2 sets of sutures was greater for the obesity procedure. Thus, the sutured in-folding at the angle of His was larger and more distal for the obesity procedure.

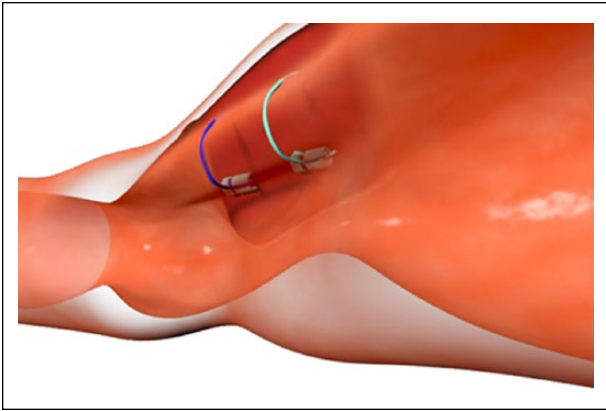


Figure 7. The obesity procedure.

Patient Results

Five GERD patients were evaluated but 2 were excluded—one because of a falsely positive pH score and the other due to a hiatal hernia larger than 2 cm. One obesity patient was excluded due to psychological issues. The first 2 patients to have a GERD procedure experienced instrument malfunction making completion of the procedures not possible. The first patient made an uneventful recovery but the second had a wrist drop that resolved with time. This was due to improper patient positioning. The third patient had micrognathia and limited neck extension making 60 F upper esophageal sphincter dilation impossible. This patient was excluded. The remaining patients had a complete procedure. These patients had the procedure performed in the right lateral decubitus position, and the instrument introduction technique was simplified by a mouth opener that made it possible to deflect the instruments into the proper plane for esophageal introduction. The mucosal excisions were uneventful but only the last 4 patients had excisions placed in what was learned to be the ideal position. During the first three procedures the excisions were difficult to place in the correct position due to redundant folds, and excision site opposition sutures were under excessive tension when tied.

Patient #4 (obese) had the excisions placed on the anterior greater curvature and the knotter was incorrectly used for the first anchor; therefore, she had only 1 of 2 anchors. Hypertonic saline was injected along the lesser curvature as described above, and although the anchor was not evident at 6 and 12 months she did have constriction of her 2 cm hiatal hernia and a 37% excess weight loss (EWL) plus normalization of her elevated baseline blood pressure at 1 year follow-up and 68% EWL at the 2-year follow-up. She had no other comorbidities.

Patient #5 (obese) had the excisions placed correctly on the posterior side of the greater curvature and the

procedure was uncomplicated. However, on videotape review it was evident that the outlet was 8 mm in diameter (ideal is 6 mm). The patient at 24-month follow-up did lose weight and had an EBL% of 23%.

Patient #6 (obese) had a complete procedure with a satisfactory result. At 2-year follow-up she was experiencing dysphagia intermittently and had a 6 to 7 mm outlet, and her blood pressure had normalized. She had no other comorbidities. Her EWL% was 24 at 12 months and 30% at 24 months.

Patient #7 (obese) had a complete procedure but vomited repeatedly in the recovery room. Her initial chest X-ray was unremarkable but on the first postoperative day she had free air under both hemidiaphragms. Laparoscopy and simultaneous upper endoscopy showed no perforation. A nasogastric tube was left in place and she recovered and was discharged. However, on day 9 she developed vertigo with repeated vomiting and required rehospitalization. At 6-month endoscopy her gastroplasty was loose and she had no food restriction. The 12-month endoscopy showed no change and the patient had gained 9 lbs from baseline; however, the 24-month follow-up showed a return to the baseline weight. Tables 3 to 6 show the obesity patient cohort baseline information and study results.

Patient #8 (GERD) had a complete procedure and made an uneventful recovery. At 12-month follow-up she remains asymptomatic and off all antisecretory medications. Her preoperative HRQOL was 19 and the DeMeester score was 44, compared with 24-month results, which were 6 and 8.9, respectively. Her 12-month endoscopy with a 6 mm endoscope and full insufflation is shown in figure 8. No esophagitis was evident.

Discussion

The new endoluminal gastroplasty was proven to be feasible, and initial patient outcomes show that it has the potential to effectively treat GERD and obesity. During the study, we learned the proper way to insert the devices, which was simplified by the use of a mouth-opener. The right lateral decubitus position facilitated capture of the proximal greater curvature tissues for excision and suturing. Initial device problems were resolved during the study. Patients who underwent a complete procedure with excisions and sutures in the corrected position had satisfactory results with significant excess weight loss, blood pressure normalization, and acid reflux control for the GERD patient.

A number of antireflux endoscopic procedures have been introduced but only one is based on scar tissue deposition, the Stretta (Mederi Therapeutics Inc, Greenwich, CT) procedure. During this procedure, radiofrequency energy is administered to the LES, inducing fibrosis, and

Table 3. Obesity Symptoms and IWQOL Table.

Patient	Baseline		6 Months	12 Months		24 Months	
	GERD Symptoms	IWQOL ^a	GERD Symptoms	GERD Symptoms	IWQOL	GERD Symptoms	IWQOL
4	None	68		None	81	None	91
5	None	69	None	None	70		
6	None	45		Occasional dyspepsia	73	None	92
7	None	69		Occasional regurgitation	80		

Abbreviation: GERD, gastroesophageal reflux disease; IWQOL, Impact of Weight on Quality of Life Questionnaire.

^aHigher IWQOL score is improvement.

Table 4. Obesity Comorbidities Table.

Patient	Baseline			6 Months			12 Months			24 Months		
	Sleep Apnea	BP	A1C	Sleep Apnea	BP	A1C	Sleep Apnea	BP	A1C	Sleep Apnea	BP	A1C
4	No	135/100	5.5				No	115/90	5.6	No	120/80	5.2
5	No	141/100	5.8	>3× night	135/95	5.7	>3× night	150/110	5.9			
6	>3× night	142/98	5.6				>3× night	110/80	5.2	>3× night	120/82	5.1
7	>3× night	118/78	5.4				>3× night	110/70	5.6			

Abbreviation: BP, blood pressure.

Table 5. Endoscopy Results in Obesity Patients^a.

Patient	Baseline Hill Classification	Operation Result	6 Months; Gap in mm	12 Months; Gap in mm	24 Months; Gap in mm
4	Hill 3	2	0	0	0
5	Hill 3	2	0		
6	Hill 3	2	0	0	0
7	Hill 3	3	2-3	2	

^a0, not performed; 1, excisions only; 2, suture and excision not optimal; 3, suture and excision satisfactory.

Table 6. Excess Weight Loss (%EWL).

Patient	Baseline Weight, kg/lb/BMI	3 Month %EWL	6 Month %EWL	12 Month %EWL	24 Month %EWL
4	185/16/61	18.5	25	37	68
5	116/256/42	2	4	-0.06	23
6	154/337/61	19	20	24	30
7	98/216/39	14	9	-0.08	0

Abbreviation: BMI, body mass index.

or collagen deposition, which leads to a higher LES yield pressure and a decrease in transient LES relaxation.⁸ Long-term results proved that the Stretta procedure is effective in terms of GERD symptoms, health-related quality of life (HRQOL), and ongoing medical management.⁹⁻¹¹ Noar and Lotfi-Emram⁹ showed heartburn scores

decreased from a mean of 3.67 to 1.18 at 4-year follow-up. Medication usage also decreased significantly, and 85% of patients reduced their medication requirement by half or eliminated it completely. Reymunde and Santiago¹⁰ also reported 4-year results on the Stretta procedure. Their GERD symptom scores improved from a mean of 2.7 to

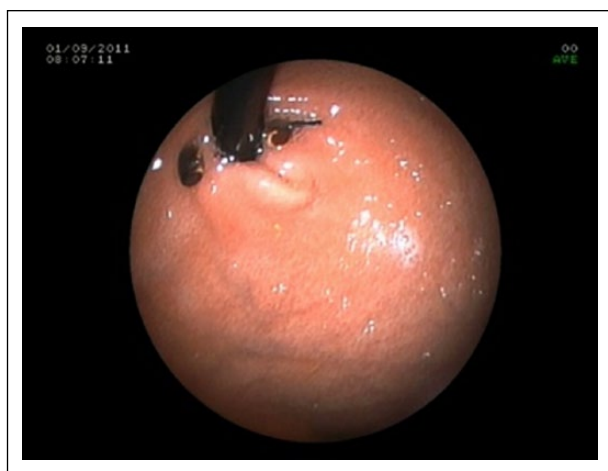


Figure 8. Patient 8's 12-month follow-up endoscopy using a 6-mm endoscope.

0.6, and 68.67% of patients showed complete resolution of symptoms. Four years after the procedure, 13.75% of the patients were on antisecretory medication. At 12-month EGD, 31.9% of the patients with grade A esophagitis at baseline healed and this remained at 4-year follow-up. The Stretta procedure demonstrates the role of fibrosis in altering the functionality of the LES. In the described gastroplasty procedure, injection of hypertonic saline and the infolding and sutured apposition of excision beds induce fibrosis as well.

Histological examinations showed that collagen deposition after Stretta takes place in the muscularis propria layer.¹² The effect of fibrosis in the esophageal wall can be described in an inorganic material analogy. The normal gastric wall is similar to a water hose that has no reinforcements in its wall. In mechanical engineering terms, the lumen wall would be described as being composed of a viscoelastic material that has a low modulus of elasticity, medium yield strength, and limited creep resistance. If you were to maintain a high water pressure on this hose, similar to a pressure created on the gastric lumen repeatedly stretching it secondary to eating, stomach overfilling, vomiting, gagging, hiccough, and heavy lifting, the lumen will expand over time. In mechanical engineering, vernacular it is known as plastic deformation caused by creep and fatigue. In this analogy, fibrosis in the submucosal layer acts as a reinforcement layer to the wall of the garden hose making it less susceptible to expansion or plastic deformation over time. In mechanical engineering terms, the scarred gastric wall would be described as also having a higher modulus of elasticity, higher yield strength, and a higher creep resistance.

The Esophyx procedure is a transoral flexible endoscopic procedure that creates a Toupet fundoplication using proprietary H fasteners. The procedure has shown

safety and efficacy in terms of symptom control and quality of life measures at 6-month follow-up.^{13,14} The Esophyx procedure (transoral incisionless fundoplication) is an endoscopic attempt at duplicating a Toupet fundoplication.

Endoscopic suturing techniques usually involve submucosal suture placement, which has limited procedure-related complications but has also led to early suture dehiscence and loss of procedural efficacy. This problem may be solved by full-thickness suturing or stapling devices that include the use of pledgets. The NDO plicator was designed to apply a full thickness pledget-reinforced U stitch near the GEJ with serosa-to-serosa apposition. Results using one¹⁵ or two¹⁶ plications failed to demonstrate a change in LES pressure, or substantial normalization of pH scores. Thus, there is still no effective endoscopic method for the control of GERD. The mucosal excision sutured gastroplasty uses a different concept whereby larger volumes of scar tissue is strategically deposited to restore LES compliance for GERD patients or create an outlet restriction for the obese.

Conclusion

Twenty-four-month patient follow-up shows promising results for the excision gastroplasty. A larger study will be conducted to more accurately determine safety and effectiveness over time.

Declaration of Conflicting Interests

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