

# MINIMALLY INVASIVE PROCEDURES FOR GASTROESOPHAGEAL REFLUX DISEASE (GERD)

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## COVERAGE RATIONALE

The following are unproven and not medically necessary for treating gastroesophageal reflux disease (GERD) due to insufficient evidence of efficacy:

- [Endoscopic therapies](#)
- [Injection or implantation techniques](#)
- [LINX Reflux Management System](#)

Endoluminal therapy with GERDx™ is investigational, unproven and not medically necessary for treating GERD as it has not received U.S. Food and Drug Administration (FDA) approval.

See the Medical Policy titled [Bariatric Surgery](#) for information regarding endoscopic therapies for the treatment of obesity.

## APPLICABLE CODES

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Coverage Determination Guidelines may apply.

CPT Code	Description
43210	Esophagogastroduodenoscopy, flexible, transoral; with esophagogastric fundoplasty, partial or complete, includes duodenoscopy when performed
43284	Laparoscopy, surgical, esophageal sphincter augmentation procedure, placement of sphincter augmentation device (i.e., magnetic band), including cruroplasty when performed
43257	Esophagogastroduodenoscopy, flexible, transoral; with delivery of thermal energy to the muscle of lower esophageal sphincter and/or gastric cardia, for treatment of gastroesophageal reflux disease
43289	Unlisted laparoscopy procedure, esophagus
43499	Unlisted procedure, esophagus
43999	Unlisted procedure, stomach

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## DESCRIPTION OF SERVICES

Gastroesophageal reflux disease (GERD) is a condition that is characterized by either a weak or dysfunctional lower esophageal sphincter (LES) that results in partially digested food from the stomach to flow back into the esophagus, a process known as reflux. Persistent GERD may lead to esophageal damage or other serious conditions, such as severe esophagitis, strictures, Barrett's metaplasia, and adenocarcinoma of the esophagus.

Initial treatment of GERD usually involves over-the-counter (OTC) antacids, OTC histamine-2-receptor antagonists (H<sub>2</sub>RAs; also called H<sub>2</sub> blockers), and proton pump inhibitors (PPI). Daily use of proton pump inhibitors (PPI) is generally effective in the treatment of the majority of patients with GERD; however, up to 40% have persisting symptoms (Weitzendorfer et al., 2018). For individuals who wish to discontinue use of these medications due to concern of long term side effects or for individuals whose GERD is refractory to pharmacologic treatment, an open or laparoscopic Nissen fundoplication may be considered. However, some individuals may not be suitable candidates given the invasiveness and risks associated with surgery. As a result, minimally invasive procedures, including endoscopic or endoluminal therapies and laparoscopic approaches, have been proposed as alternative treatment methods to improve the function of the LES, with the objective of eliminating symptoms, healing esophagitis, preventing recurrence of symptoms or progression of disease, and reducing the need for lifelong pharmacologic therapy.

Minimally invasive approaches proposed in the treatment of GERD, include the following:

- Radiofrequency energy: The Stretta procedure administers radiofrequency (RF) energy via endoscopic needles placed in the tissues surrounding the lower esophageal sphincter. The RF energy heats this neighboring tissue, creating thermal lesions. Submucosal scarring forms as the lesions heal, causing shrinkage and tightening around the LES. The mechanism of action is believed to be related to decreased sensitivity to acid, decreased compliance of the LES or increased pressure of the LES (Stephanidis et al., 2017).
- Endoscopic plication or suturing:
  - The Bard EndoCinch and the Endoscopic Suturing Device (ESD) involves endoscopic suturing, allows for the placement of proximal to the LES, and the NDO Endoscopic Plication System, also known as the NDO Plicator System, places a full-thickness transmural plication near the gastroesophageal junction under direct endoscopic visualization.
  - EsophyX is an endoluminal therapeutic option that uses a trans-oral and fastener deploying device. It is inserted orally within a thin, flexible tube and deployed inside the stomach to create a full thickness plication of the stomach fundus at the GE junction, thereby resembling an endoscopic fundoplication. The current TIF 2.0 technique (the initial TIF 1.0 technique is no longer recommended) generates a physiological valve via fasteners placed on the far posterior and anterior sides of the lesser curvature, with additional fasteners placed 1–3 cm proximal to the GE junction (Stephanidis et al., 2017).
  - GERDx™ (G-SURG) is an endoscopic full-thickness plication device that uses hydraulic elements for controlling.
  - The Medigus Ultrasonic Surgical Endostapler (MUSE™ system, Medigus) is an endoscopic stapling device for transoral partial fundoplication. According to the manufacturer's website, as the MUSE system contains the surgical stapler, microvisual, and ultrasonic capabilities, it allows a single physician to complete the procedure.
- Injection or implantation techniques include the following:
  - The Plexiglas® (polymethylmethacrylate [PMMA]) procedure involves injection of an inert polymer material into the submucosa of the proximal LES zone to provide bulking support to the sphincter and decrease transient relaxation of the lower esophageal sphincter (tLESRs).
  - Another bulking agent, pyrolytic carbon-coated beads (Durasphere®), is being evaluated for treatment of GERD.
  - The LINX™ Reflux Management System is an implant that consists of a ring that fits around the esophagus and is intended to prevent reflux of bile and acid from the stomach into the esophagus. According to the company website, the LINX system is a small flexible band of interlinked titanium beads with magnetic cores. The magnetic attraction is intended to help the LES resist opening to gastric pressures, preventing reflux from the stomach into the esophagus. A surgeon uses a laparoscopic incision to implant the device around the patient's esophagus just above the stomach while the patient is under general anesthesia.

## CLINICAL EVIDENCE

### **Radiofrequency Energy (Stretta System)**

Noar et al. (2017) prospectively assessed and compared patient-reported outcomes in 18 patients refractory to laparoscopic Nissen fundoplication (LNF) and 81 patients with gastrointestinal reflux disease (GERD) refractory to medical management that all underwent Stretta during 10-year follow-up. Patient-reported outcomes measured were GERD-HRQL (health-related quality of life), patient satisfaction scores, and daily medication requirements. The refractory LNF subset demonstrated median improvements in GERD-HRQL, satisfaction, and medication use at all follow-up time points ≥6 months to 10 years, which was significant from a baseline of both on- and off-medications ( $p < 0.05$ ). Specifically at 10 years, median GERD-HRQL decreased from 36 to 7 ( $p < 0.001$ ), satisfaction increased from

1 to 4 ( $p < 0.001$ ), and medication score decreased from 7 to 6 ( $p = 0.040$ ). Nine patients decreased medication use by half at 10 years. No significant differences existed between refractory LNF and standard refractory GERD subsets at any follow-up time point  $\geq 6$  months to 10 years ( $p > 0.05$ ) after Stretta. At 10 years, no significant differences were noted between refractory LNF and standard Stretta subsets regarding medication use ( $p = 0.088$ ), patient satisfaction ( $p = 0.573$ ), and GERD-HRQL ( $p = 0.075$ ). Stretta procedures were completed without difficulty or significant intraoperative or long-term adverse events. The authors concluded that within a small cohort of refractory LNF patients, Stretta resulted in sustained improvement over 10 years with equivalent outcomes to non-LNF standard Stretta patients. Study limitations include non-randomization and small patient population.

Kalapala et al. (2017) reported short-outcomes (3 months) from a prospective randomized study comparing the Stretta treatment with controls receiving proton pump inhibitors (PPIs). Patients ( $n = 20$ ) with symptoms of heartburn, regurgitation, abnormal esophageal acid exposure ( $\geq 4\%$ ), and endoscopically confirmed esophagitis were included into the study. The primary measure was improvement in quality of life (QOL) and decrease in the frequency and severity of GERD symptoms. The mean age of the patients was 39 ( $\pm 15$ ) years and controls were 34 ( $\pm 11$ ) years. Three months after Stretta, 80% reported improvement in QOL compared to 40% in the control group. At the end of 3 months, significant ( $p < 0.05$ ) improvement in GERD symptom score for heartburn, regurgitation, chest pain, and cough compared with the control group was observed. After Stretta treatment, 60% of the patients were free of PPIs whereas there was no change in the control group. Almost 80% of the patients on Stretta treatment were satisfied with the treatment compared to 30% of the patients in the control group. Randomized controlled trials with larger patient populations and longer follow-up periods are needed to further assess Stretta.

In a single center cohort study, Dughera et al. (2014) assessed the durability of the Stretta procedure for patients with GERD with 4 to 8 year follow-up results. Of the original 86 patients, 26 reached the 8-year follow-up end point. All patients underwent clinical evaluation by upper endoscopy, oesophageal pressure, and pH studies. Median LES pressure did not show significant amelioration at 4 and 8 years and mean oesophageal acid exposure significantly improved at 4 years ( $P=0.001$ ) but returned to baseline values after 8 years. The authors conclude that the results of their follow-up study from 4 to 8 years sustain the concept that Stretta might represent a viable treatment option for selected patients with symptomatic mild to moderate GERD. They suggest that these results need to be confirmed in larger cohorts of patients, and could ultimately result in a reasonable recommendation for younger GERD sufferers as a "bridge therapy" between the continuous medical treatment and the optimal timing for laparoscopic fundoplication.

Noar et al. (2014) prospectively assessed the long-term safety, efficacy, and durability of response to radiofrequency treatment of the lower esophageal sphincter (Stretta) in 217 patients with medically refractory GERD. There was no control arm in this study. The primary outcome measure (normalization of GERD-health-related quality of life (GERD-HRQL) in 70% or greater of patients at 10 years) was achieved in 72% of patients (95% confidence interval 65–79). For secondary outcomes, a 50% or greater reduction in PPI use occurred in 64% of patients, (41% eliminating PPIs entirely), and a 60% or greater increase in satisfaction occurred in 54% of patients. Both secondary endpoints were achieved. The most common side effect was short-term chest pain (50%). Preexisting Barrett's metaplasia regressed in 85% of biopsied patients. No cases of esophageal cancer occurred. The authors concluded that In this single-group evaluation of 217 patients before and after Stretta, GERD-HRQL scores, satisfaction, and PPI use significantly improved and results were immediate and durable at 10 years.

Arts et al. (2012) conducted a double-blind randomized cross-over study of Stretta and sham treatment. Patients underwent two upper gastrointestinal endoscopies with 3 months interval, during which active or sham Stretta treatment was performed in a randomized double-blind manner. In all, 22 GERD patients (17 females, mean age  $47 \pm 12$  years) participated in the study; 11 in each group. Initial sham treatment did not affect any of the parameters studied. Three months after initial Stretta procedure, no changes were observed in esophageal acid exposure and lower esophageal sphincter (LES) pressure. In contrast, symptom score was significantly improved and gastro-esophageal junction (GEJ) compliance was significantly decreased. Administration of sildenafil, an esophageal smooth muscle relaxant, normalized GEJ compliance to pre-Stretta level, arguing against GEJ fibrosis as the underlying mechanism. The authors concluded that Stretta improved GERD symptoms and decreased GEJ compliance. According to the authors, the limitation of this study was reflux evaluation did not include impedance monitoring. The study was also limited by a small patient population, short follow-up, and lack of comparison to other surgical alternatives.

In a RCT, 36 patients were randomized into three groups. In group A, 12 patients underwent a single session Stretta procedure (Aziz et al., 2010). In group B, 12 patients underwent a sham Stretta procedure (mirror of the active procedure in all aspects except there was no deployment of the electrodes). In group C, 12 patients underwent a single Stretta treatment followed by repeat Stretta if GERD health-related quality of life (HRQL) was not 75% improved after 4 months. At 12 months, the mean HRQL scores of patients no longer on medications, the lower esophageal sphincter (LES) basal pressure, the 24-hr pH scores, and the PPI daily dose consumption were significantly improved from baseline in both Stretta groups. The double Stretta was numerically but not significantly better than the single Stretta for mean HRQL, mean 24 h pH, mean LES pressure, and PPI use. Seven patients in the double Stretta treatment group reported normal HRQL scores at 12 months compared with 2 patients in the single-

treatment group. The sham group patients had a small but statistically significant decrease in their daily PPI dosages and mean HRQL scores. The investigators concluded that the Stretta procedure significantly reduced HRQL associated with GERD, use of PPI drugs, esophageal acid exposure, LES pressure, and grade of esophagitis compared with the sham procedure. The double Stretta therapy had numerically superior outcomes for most parameters and a significantly more frequent normalization of HRQL scores compared with the single Stretta group. According to the investigators, the Stretta procedure is partially effective for the treatment of GERD symptoms. Double Stretta therapy has better efficacy than single therapy, but has greater side effects. The investigators also noted that antireflux surgery (fundoplication) has a higher success rate than that of Stretta. Furthermore, a more prolonged effect is found with antireflux surgery. The conclusions of this study are limited by small sample size and lack of comparison to other surgical alternatives.

In another RCT, Coron et al. (2008) compared radiofrequency and a PPI in PPI-dependent patients. Patients were randomly allocated to either RF or PPI regimen alone. The primary endpoint, evaluated at 6-months, was defined as the possibility for the patient to stop or to decrease PPI use to <50% of the effective dose required at baseline. In the radiofrequency group, 18/20 patients stopped (n=3) or decreased (n=15) PPI use compared to eight of 16 in the PPI group. None of the control patients could stop PPI. HR-QOL scores were not significantly different between groups. No significant change in oesophageal acid exposure (OAE) was noted between baseline and 6-months after radiofrequency treatment. The investigators concluded that in a majority of patients, PPI therapy cannot be completely stopped. Furthermore, the efficacy of RF does not seem to be related to a decrease in OAE.

In a controlled trial, Jeansonne et al. (2009) compared the effectiveness of endoscopic full-thickness plication (FTP) and endoscopic radiofrequency treatments for patients with GERD. Follow-up data was obtained for 63 patients (mean follow-up was 6 months). Outcome measures included comparison of medication use, symptom scores, and pH values at baseline and follow-up. In the RF group, patients with moderate to severe heartburn decreased from 55% to 22%, and PPI use decreased from 84% to 50%. Decreases were also seen for dysphagia, voice symptoms, and cough. The pH values were unchanged. In the FTP group, patients with moderate to severe heartburn decreased from 53% to 43%, and PPI use decreased from 95% to 43%. Percentage of time that the pH was less than 4 decreased from 10.0% to 6.1%. Decreases were also seen for regurgitation, voice symptoms, and dysphagia. According to the investigators, RF and FTP both resulted in a decrease in both PPI use and in scores for voice symptoms and dysphagia. In addition, RF resulted in decreased heartburn and cough, while FTP resulted in the most dramatic reduction in regurgitation. The investigators concluded that both procedures are effective, providing symptomatic relief and reduction in PPI use. For patients whose chief complaint is regurgitation, FTP may be the preferred procedure. Study limitations included lack of randomization, small sample size, and short follow-up.

Fass et al. (2017) conducted a systematic review and meta-analysis of randomized controlled and cohort studies to determine the efficacy of the Stretta procedure in treating patients with GERD. Twenty-eight studies (4 RCTs, 23 cohort studies, and 1 registry) representing 2468 unique Stretta patients were included in the meta-analysis. The (unweighted) mean follow-up time for the 28 studies was 25.4 [14.0, 36.7] months. The pooled results showed that the Stretta reduced (improved) the health-related quality of life score by -14.6 [-16.48, -12.73] ( $P < 0.001$ ). Stretta also reduced (improved) the pooled heartburn standardized score by -1.53 [-1.97, -1.09] ( $P < 0.001$ ). After Stretta treatment, only 49% of the patients using proton pump inhibitors (PPIs) at baseline required PPIs at follow-up ( $P < 0.001$ ). The Stretta treatment reduced the incidence of erosive esophagitis by 24% ( $P < 0.001$ ) and reduced esophageal acid exposure by a mean of -3.01 [-3.72, -2.30] ( $P < 0.001$ ). Lower esophageal sphincter (LES) basal pressure was increased post Stretta therapy by a mean of 1.73 [-0.29, 3.74] mmHg ( $P = \text{NS}$ ). The authors concluded that the Stretta procedure significantly improves subjective and objective clinical endpoints, except LES basal pressure, and therefore should be considered as a viable alternative in managing GERD. Longer-term outcomes are needed to further evaluate the Stretta procedure.

Numerous non-randomized and non-comparative cohort studies evaluated radiofrequency energy for the treatment of GERD (Dughera et al., 2011; Liu et al., 2011; White et al., 2009; Dundon et al., 2008; Noar and Lotfi-Emran et al., 2007; Reymunde and Santiago, 2007; Lutfi et al., 2005). The body of evidence is of low quality due to overall weaknesses in study design, including lack of comparison groups, lack of randomization, short follow-up periods, and small patient populations.

Torquati et al. (2007) conducted an evidence-based systematic review of the literature of FDA-approved modalities of endoluminal treatment of GERD. Study authors concluded that the methodological quality of most of the included studies was average. The authors stated that there is grade 1b (individual randomized trial) and 2b (individual cohort study) evidence demonstrating that the Stretta procedure is effective in reducing GERD symptoms at short- and mid-term follow-up. However, in the majority of the studies analyzed, the procedure did not significantly reduce acid exposure in the distal esophagus.

The National Institute for Health and Care Excellence (NICE) guideline on endoscopic radiofrequency ablation for GERD considers the evidence on this procedure to be adequate in the short and medium term but there is uncertainty



about longer-term outcomes. With regard to efficacy, there is evidence of symptomatic relief but objective evidence on reduction of reflux is inconclusive (NICE, 2013).

## **Endoscopic Plication or Suturing**

### ***EndoCinch***

No new well-designed clinical trials evaluating the EndoCinch were identified.

Schwartz et al. (2007) conducted a single-center, double-blind, randomized, sham-controlled trial of endoscopic gastroplication by the Endocinch suturing system in 60 patients. Patients with GERD were randomly assigned to three endoscopic gastroplications (n=20), a sham procedure (n=20) or observation (n=20). The research nurse and patients in the active and sham groups were blinded to the procedure assignment. After 3 months, open-label active treatment was offered to all patients. At 3 months, the percentage of patients who had reduced drug use by  $\geq 50\%$  was greater in the active treatment group (65%) than in the sham (25%) or observation groups (0%). The active treatment effects on PPI use, symptoms and quality of life persisted after 6 and 12 months of open-label follow-up (n=41), but 29% of patients were retreated in this period. The investigators concluded that endoscopic gastroplication, using the Endocinch device, reduced acid-inhibitory drug use, improved GERD symptoms, and improved the quality of life at 3 months compared with a sham procedure with durable effects up to 12 months. However, the reduction in oesophageal acid exposure was not significantly different between treatment and sham groups.

In a randomized, placebo controlled study by Montgomery et al. (2006), 46 patients with GERD requiring regular use of PPIs were enrolled to evaluate the effects of the EndoCinch plication technique. Patients were randomized to the EndoCinch plication technique or a sham procedure. Reflux-specific symptoms and use of PPIs (total intake, as well as number of patients not taking PPIs) significantly improved in the treatment group compared with the sham control group at 3 months of follow-up. Gastro-esophageal endoscopy showed that 71% and 67% of sutures remained at 3 and 12 months, respectively. The authors concluded that although some short-term positive effects were achieved, there were no significant differences between the treatment and control groups after 12 months. Additionally, the lack of reduction of esophageal acid exposure suggests that the EndoCinch plication technique is not recommended for use in clinical practice. Researchers suggest that the lack of long-term effects is primarily due to detachment of the sutures in about 30% of patients.

In a RCT, endoluminal gastroplasty (EndoCinch) was compared with polymer injection (Enteryx). The study included 51 patients dependent on PPI therapy. Twenty-six patients were assigned to EndoCinch treatment, 23 patients received Enteryx implantation, and 2 patients dropped out before applying endoscopic therapy. At 6 months, PPI therapy could be stopped or dosage was reduced by  $\geq 50\%$  in 20 of 26 EndoCinch-treated patients and in 20 of 23 patients treated by Enteryx. The authors concluded that EndoCinch and Enteryx seem to be equally successful in the treatment of GERD by significantly reducing the PPI dosages, and also improving symptoms of patients (Domagk et al., 2006). Conclusions regarding long-term health outcomes could not be made based on the short-term follow-up duration of this study.

Torquati et al. (2007) conducted a systematic review of endoluminal therapies for GERD, including EndoCinch. The authors identified evidence demonstrating that EndoCinch plication is effective in reducing GERD symptoms in the short term. However, they noted that the procedure does not significantly reduce the acid exposure in the distal esophagus.

Other clinical trials for EndoCinch are limited to observational case series that do not allow for conclusions about durability and long term effectiveness (Paulssen and Lindsetmo, 2008; Ozawa et al., 2009).

### ***Endoscopic Plicator or Suturing***

De Moura et al. (2018) evaluated long-term results of 47 patients non-responsive to PPIs who underwent endoluminal plication (n=26) or polymer injection (n=21) for the treatment of GERD. The number of patients with no response to endoscopic treatment with reintroduction of PPIs increased in time for both techniques. There was symptomatic improvement up to 12 months, with progressive loss of this trending up to 60 months for both procedures. Health-related quality of life score (GERD-HRQL) demonstrated total response in both procedures at 1, 3, 6 and 12 months. The 60-month analysis showed an increased number of patients with no response in both groups. The quality of life assessment (SF-36) showed benefit in polymer injection up to 3 months and showed a higher rate of complications. There were no deaths. There was healing of esophagitis at 3 months in 45% of patients in polymer injection and 40% in endoluminal plication. There was no improvement in manometric or pH findings. The authors concluded that endoscopic therapies were ineffective in controlling GERD in the long term.

In a randomized, single-blind, prospective, multicenter trial by Rothstein et al. (2006), 159 patients were selected to either undergo endoscopic full-thickness restructuring of the gastric cardia with transmural suture (n=78) or a sham procedure (n=81) to determine the effectiveness of endoscopic full-thickness plication for the treatment of GERD. Group assignments were revealed following the 3-month evaluation. By intention-to-treat analysis, at 3 months, the

proportion of patients achieving  $\geq 50\%$  improvement in GERD-HRQL score was significantly greater in the active group compared with the sham group. Complete cessation of PPI therapy was higher among patients in the active group than in the sham group. However, the median percent time that  $\text{pH} < 4$  was not significantly improved between the active and sham group. Between-group analysis revealed the active therapy was superior to sham treatment in improving the median percent time that the  $\text{pH}$  value was  $< 4$ . The authors concluded that endoscopic full-thickness plication was effective in reducing GERD symptoms and PPI use compared with a sham procedure. Additional studies are needed to evaluate the durability of endoscopic full-thickness plication for the treatment of GERD.

In a RCT, Antoniou et al. (2012) evaluated the effectiveness of endoscopic plication and laparoscopic fundoplication in terms of QOL and symptom control. A total of 60 patients with documented GERD were randomly assigned to undergo either endoscopic plication or laparoscopic fundoplication. QOL scores and symptom grading were recorded before treatment and at 3- and 12-months of follow-up. Twenty-nine patients from the endoscopic group and 27 patients from the operative group were available at follow-up. QOL scores showed a substantial and similar increase for both groups after treatment. Symptoms of heartburn, regurgitation, and asthma were significantly improved in the endoscopic group, whereas laparoscopic fundoplication was more effective in controlling symptoms of heartburn and regurgitation compared to the endoscopic procedure. The authors concluded that endoscopic plication and laparoscopic fundoplication resulted in significant symptom improvement with similar QOL scores in a selected patient population with GERD, whereas operative treatment was more effective in the relief of heartburn and regurgitation at the expense of higher short-term dysphagia rates. Small sample size and lack of long-term follow-up limit the validity of these conclusions.

### **GERDx™**

Weitzendorfer et al. (2018) assessed the clinical safety and efficiency of the GERDx™ device by evaluating clinical parameters, reflux symptom scores, and quality of life (QoL) in a prospective one-arm trial. Patients ( $n=40$ ) with at least one typical reflux symptom despite treatment with a PPI for  $> 6$  months, pathologic esophageal acid exposure, hiatal hernia of size  $< 2$  cm, and endoscopic Hill grade II-III were included. Evaluation of Gastrointestinal Quality of Life Index (GIQLI), symptom scores, esophageal manometry, and impedance-pH-monitoring were performed at baseline and at 3 months after surgery. Four out of forty patients experienced postoperative complications requiring intervention. Seven of forty patients were subjected to laparoscopic fundoplication 3 months after endoscopic plication due to persistent symptoms and were lost to further follow-up. Thirty out of forty patients were available at 3-month follow-up. There was an improvement of the GIQLI score, from a mean of  $92.45 \pm 18.47$  to  $112.03 \pm 13.11$  ( $p < 0.001$ ). The general reflux-specific score increased from a mean of  $49.84 \pm 24.83$  to  $23.93 \pm 15.63$  ( $p < 0.001$ ), and the DeMeester score from a mean of  $46.48 \pm 30.83$  to  $20.03 \pm 23.62$  ( $p < 0.001$ ). There was no significant change in manometric data after intervention. Three of thirty patients continued daily antireflux medication. The authors concluded that endoscopic plication with the GERDx™ device reduced distal acid exposure of the esophagus, reflux-related symptoms, and improved GIQLI scores with minimal side effects in a selected cohort of patients and may be a safe alternative in the treatment of GERD. Randomized clinical trials with larger patient populations and longer follow-up periods are needed to further assess GERDx.

### **MUSE™**

Kim et al. (2016) reported long-term outcomes from the Zacherl et al. (2015) MUSE study using the Medigus Ultrasonic Surgical Endostapler (MUSE™). Efficacy and safety data for 37 patients were analyzed at baseline, 6 months, and 4 years post-procedure. In one center (IU), efficacy and safety data were evaluated at baseline, 6 months post-procedure, and then annually up to 4 years. No new complications have been reported in our long-term analysis. The proportions of patients who remained off daily PPI were 83.8 % (31/37) at 6 months and 69.4 % (25/36) at 4 years post-procedure. GERD-Health Related Quality of Life (HRQL) scores (off PPI) were significantly decreased from baseline to 6 months and 4 years post-procedure. The daily dosage of GERD medications, measured as omeprazole equivalents (mean  $\pm$  SD, mg), decreased from  $66.1 \pm 33.2$  at baseline to  $10.8 \pm 15.9$  at 6 months and  $12.8 \pm 19.4$  at 4 years post-procedure ( $P < 0.01$ ). The authors conclude that the MUSE™ stapling device appears to be safe and effective in improving symptom scores as well as reducing PPI use in patients with GERD and that the results appeared to be equal to or better than those of the other devices for endoluminal GERD therapy. Future studies with larger patient series, sham control group, and greater number of staples are awaited to further evaluate MUSE.

Zacherl et al. (2015) reported 6-month outcomes from a multi-center prospective trial using the MUSE™ for the treatment of GERD ( $N=69$ ; 3 lost to follow-up). Six months after the procedure, the GERD-HRQL score improved by  $>50\%$  off PPI in 73% (48/66) of patients (95% CI 60–83%). Forty-two patients (64.6%) were no longer using daily PPI medication. Of the 23 patients who continued to take PPI following the procedure, 13 (56.5%) reported a  $\geq 50\%$  reduction in dose. The mean percent of total time with esophageal  $\text{pH} < 4.0$  decreased from baseline to 6 months ( $P < 0.001$ ). Common adverse events were peri-operative chest discomfort and sore throat. Two severe adverse events requiring intervention occurred in the first 24 subjects, no further esophageal injury or leaks were reported in the remaining 48 enrolled subjects. Early experience with the device necessitated procedure and device changes to

improve safety, with improved results in the later portion of the study. Continued assessment of durability and safety are ongoing in a three-year follow-up study of this patient group.

In a review of the techniques and outcomes of TIF (EsophyX and MUSE™) in the treatment of GERD, Testoni et al. (2016) recommend that the long-term efficacy of the MUSE technique needs to be further assessed through randomized controlled trials to establish its role in the management of GERD. Preoperative anatomical and functional findings and technical procedural aspects that will help select patients and predict a successful outcome still need to be identified.

In a review of endoscopic management of GERD, Nabi and Reddy (2016) note that certain drawbacks with endoscopic anti-reflux modalities (EARMs) are noteworthy. First, these devices have been tried in select patients with minimal esophageal inflammation and small hiatal hernia. Second, although symptom response is reasonably good, objective data (like Esophageal acid exposure time [EAET]) are less impressive. The current literature suggests that EARMs do reduce EAET, but often do not normalize the same. Normalization of EAET is no doubt a difficult goal to achieve, but cannot be ignored due to potential long-term consequences like Barrett's esophagus and esophageal adenocarcinoma. Similarly, the need of PPI use is reduced but not eliminated completely in substantial proportion of patients undergoing endoscopic therapy. Lastly, long-term data with some of the recently introduced EARMs are not sufficient and comparative studies between different endoscopic modalities are lacking. Therefore, according to the authors, the best EARM is not known. Other clinical trials regarding endoscopic plicator or suturing are limited to observational case series that do not allow for conclusions about durability and long-term effectiveness (Birk et al., 2009; von Renteln et al., 2009).

### **EsophyX™ System (Transoral Incisionless Fundoplication [TIF])**

Trad et al. (2018) reported 5-year outcomes from the previously described TEMPO clinical trial (TIF 2.0). A total of 63 patients with chronic GERD refractory to PPI therapy, absent or  $\leq 2$  cm hiatal hernia, and abnormal esophageal acid exposure were randomized to the TIF group or PPI group. Following the 6-month evaluation, all patients in the PPI group elected for crossover to TIF. Of 63 patients, 60 were available at 1 year, 52 at 3 years, and 44 at 5 years for evaluation. Troublesome regurgitation was eliminated in 88% of patients at 1 year, 90% at 3 years, and 86% at 5 years. Resolution of troublesome atypical symptoms was achieved in 82% of patients at 1 year, 88% at 3 years, and 80% at 5 years. No serious adverse events occurred. There were 3 reoperations by the end of the 5-year follow-up. At the 5-year follow-up, 34% of patients were on daily PPI therapy as compared with 100% of patients at screening. The total GERD Health-related quality-of-life score improved by decreasing from 22.2 to 6.8 at 5 years ( $P < .001$ ). The authors concluded that in this patient population, the TIF 2.0 procedure provided safe and sustained long-term elimination of troublesome GERD symptoms. Study limitations include small patient population and non-randomization to another endoscopic procedure for GERD.

Ebright et al. (2017) reported follow-up data on endoscopic fundoplication performed on 80 patients. Although symptoms and satisfaction improved significantly over a mean follow-up period of 24 months, approximately 30% of patients continued to take PPIs. Future studies are needed to focus on longer-term durability and comparisons with laparoscopic techniques.

Stefanidis et al. (2017a) evaluated the long-term benefit of TIF using the EsophyX device ( $n=45$ ) for the management of GERD responsive to medical therapy. After a median follow up period of 59 months (36-75) the median GERD-HRQL scores improved significantly from 27 (2-45) at baseline to 4 (0-26) ( $P < 0.001$ ) in the 44 patients completing the study. Heartburn was eliminated in 12 out of the 21 patients included (57.1%), regurgitation was eliminated in 15 out of the 17 patients included (88.2%) and finally chest pain was eliminated in 5 patients out of the six patients included (83.3%). Overall, 32 patients out of the 44 patients (72.7%) that completed the study follow up reported elimination of their main symptom, without the need for PPI administration. Furthermore, six more patients (13.6%), five with heartburn, and one with regurgitation reported half PPI dose taken for  $< 50\%$  of the preceding follow up period (occasional PPI usage), while six more patients (four with heartburn, one with regurgitation, and one with chest pain) reported full or half PPI dose taken for more than 50% of the preceding follow up period (daily PPI usage). Randomized clinical trials are needed to validate these results in comparison with other treatments for GERD.

Trad et al. (2017) reported 3-year outcomes from the TEMPO trial (TIF 2.0). A total of 63 patients with chronic GERD refractory to PPI therapy, absent or  $\leq 2$  cm hiatal hernia, and abnormal esophageal acid exposure were randomized to the TIF group or PPI group. Following the 6-month evaluation, all patients in the PPI group elected for crossover to TIF. At 3-year follow-up, elimination of troublesome regurgitation and all atypical symptoms was reported by 90% (37/41) and 88% (42/48) of patients, respectively. The mean Reflux Symptom Index score improved from 22.2 (9.2) on PPIs at screening to 4 (7.1) off PPIs 3 years post-TF,  $p < 0.0001$ . The mean total % time pH  $< 4$  improved from 10.5 (3.5) to 7.8 (5.7),  $p = 0.0283$ . Esophagitis was healed in 86% (19/22) of patients. At the end of study, 71% (37/52) of patients had discontinued PPI therapy. All outcome measures remained stable between 1-, 2-, and 3-year follow-ups. Study limitations include small patient population and non-randomization to another endoscopic procedure for GERD.

In a double-blind sham-controlled study in patients with moderate to severe GERD who were chronic PPI users, Håkansson et al. (2015) evaluated the TIF2 procedure (using the EsophyX device) versus sham (upper GI endoscopy). Patients (n=44) were randomized into the two groups. The primary effectiveness endpoint was the proportion of patients in clinical remission after 6-month follow-up. Secondary outcomes were: PPI consumption, esophageal acid exposure, reduction in Quality of Life in Reflux and Dyspepsia and Gastrointestinal Symptom Rating Scale scores and healing of reflux esophagitis. The time (average days) in remission offered by the TIF2 procedure (197) was significantly longer compared to those submitted to the sham intervention (107),  $P < 0.001$ . After 6 months 13/22 (59%) of the chronic GERD patients remained in clinical remission after the active intervention. Likewise, the secondary outcome measures were all in favor of the TIF2 procedure. No safety issues were raised. Although the authors concluded that the TIF2 procedure is effective in chronic PPI-dependent GERD patients, the study was limited by small patient population and short follow-up period.

Rinsma et al. (2015) conducted a randomized controlled trial to evaluate the effect of endoscopic fundoplication and PPI therapy on baseline impedance and heartburn severity in GERD patients. Forty-seven GERD patients randomized to endoscopic fundoplication (n = 32) or PPI therapy (n = 15), and 29 healthy controls were included. Before randomization and 6 months after treatment, baseline impedance was obtained during 24-h pH-impedance monitoring. Heartburn severity was evaluated using the GERD-HRQL questionnaire. Before treatment, baseline impedance in GERD patients was lower than in healthy controls ( $p < 0.001$ ). Antireflux therapy increased baseline impedance (from 1498 [IQR 951-2472] to 2393 [IQR 1353-3027]  $\Omega$ ,  $p = 0.001$ ), however it only led to a partial recovery when compared to healthy controls (2393 [IQR 1353-3027] vs 2983 [2335-3810]  $\Omega$ ,  $p < 0.01$ ). The effect of both treatment options was not significantly different ( $p = 0.13$ ) despite the increased number of non-acid reflux events in the PPI group. No correlation was found between baseline impedance and GERD symptoms before or after treatment.

Testoni et al. (2015) evaluated 50 patients with GERD who underwent TIF 2.0. All underwent GERD-HRQL and GERD-QUAL questionnaires, upper GI endoscopy, esophageal manometry, and 24-h pH-impedance before and 6, 12, and 24 months after TIF, and subsequent yearly clinical re-evaluation. Patients were followed for up to six years (mean 52.7  $\pm$  19.7 months). In all, 83.7, 79.6, 87.8, and 84.4% of patients stopped or halved the PPI therapy 6, 12, 24, and 36 months after TIF. Three-year figure remained stable up to 6 years. Symptom scores off PPI were significantly lower at 6, 12, 24, and 36 months. At 6 months, Hill's grade I of the newly created valve persisted in all pre-procedure Hill's grade I patients, in 66.7% of grade II and 58.3% of grade III. This figure remained substantially unchanged at 12 and 24 months. Impedance monitoring indicated significantly fewer total and acid refluxes after treatment ( $p = 0.01$ ). Factors predicting good outcomes were pre-procedure Hill's grade I-II, no hiatal hernia or hernia  $\leq 2$  cm ( $p = 0.03$ ), absence of ineffective esophageal motility ( $p < 0.0001$ ), and number of fasteners deployed ( $p = 0.01$ ).

In a prospective, sham-controlled trial, Hunter et al. (2015) aimed to determine if TIF reduced troublesome regurgitation to a greater extent than PPIs in patients with GERD. Patients with GERD, taking daily PPIs, and hiatal hernias  $\leq 2$  cm were randomly assigned to groups that underwent TF and then received 6 months of placebo (n=87), or sham surgery and 6 months of once- or twice-daily omeprazole (controls, n = 42). Patients were blinded to therapy during follow-up period and reassessed at 2, 12, and 26 weeks. At 6 months, patients underwent 48-hour esophageal pH monitoring and esophagogastroduodenoscopy. By intention-to-treat analysis, TF eliminated troublesome regurgitation in a larger proportion of patients (67%) than PPIs (45%) ( $P=.023$ ). A larger proportion of controls had no response at 3 months (36%) than subjects that received TF (11%;  $P=.004$ ). Control of esophageal pH improved after TF (mean 9.3% before and 6.3% after;  $P < .001$ ), but not after sham surgery (mean 8.6% before and 8.9% after). Subjects from both groups who completed the protocol had similar reductions in GERD symptom scores. Severe complications were rare (3 subjects receiving TF and 1 receiving the sham surgery). Based on evaluation 6 months after the procedure, the authors concluded that TF was an effective treatment for patients with GERD symptoms, particularly in those with persistent regurgitation despite PPI therapy. Short follow-up period and smaller control group were limitations of this study.

Witteaman et al. (2015) conducted a randomized controlled trial of TIF vs. PPIs for the treatment of GERD in 60 patients who opted for endoscopic option versus lifelong dependence on PPIs. A total of 60 patients (TIF n=40, PPI n=20, mean body mass index 26 kg/m<sup>2</sup>, 37 male) were included. At 6 months, GERD symptoms were more improved in the TIF group compared with the PPI group ( $P<0.001$ ), with a similar improvement of distal esophageal acid exposure ( $P=0.228$ ) compared with baseline. The pH normalization for TIF group and PPI group was 50% and 63%, respectively. All patients allocated for PPI treatment opted for crossover. At 12 months, quality of life remained improved after TIF compared with baseline ( $P<0.05$ ), but no improvement in esophageal acid exposure compared with baseline was found ( $P=0.171$ ) and normalization of pH was accomplished in only 29% in conjunction with deteriorated valve appearances at endoscopy and resumption of PPIs in 61%. Although TIF resulted in an improved GERD-related quality of life and produced a short-term improvement of the antireflux barrier in a selected group of GERD patients, no long-term objective reflux control was achieved.

Richter et al. (2018) conducted a systematic review and meta-analysis of randomized controlled trials to directly compare TIF and laparoscopic Nissen fundoplication (LNF). Included were 7 trials comprising 1128 patients. The



authors found LNF to have the greatest ability to improve physiologic parameters of GERD, including increased LES pressure and decreased percent time pH <4. Although TIF produced the largest increase in health-related quality of life, this could be due to the shorter follow-up time of patients treated with TIF vs LNF or PPIs. TIF is a minimally invasive endoscopic procedure, yet based on evaluation of benefits vs risks, the authors do not recommend it as a long-term alternative to PPI or LNF treatment of GERD.

In a review article, Zagol and Mikami (2011) evaluated transoral fundoplication devices (included EndoCinch, NDO Plicator, Esophyx, and Stretta) for GERD that have been commercially available within the last 5 years. Both blinded and unblinded randomized studies were evaluated. Reviews of all studies with greater than 20 patients were evaluated to assess the efficacy and safety of transoral fundoplication devices. These endoluminal devices were primary matched against sham procedures. The EndoCinch and Stretta procedures were the only devices compared to laparoscopic fundoplication, the current standard for surgical management of GERD. The authors concluded that endoluminal treatment of GERD has been shown to be safe and effective in recent studies. However, the authors indicated that more RCTs need to be carried out to determine if endoluminal therapies will be a durable option for patients with GERD.

In a retrospective study, Trad et al. (2012) evaluated the safety, symptom resolution, patient satisfaction, and medication use 1-2 years after TIF in patients with GERD and/or laryngopharyngeal reflux (LPR) symptoms. Thirty-four patients with a confirmed diagnosis of GERD symptoms that were inadequately controlled by antisecretory medications, and who were either dissatisfied with their current therapy or not willing to continue taking medication, underwent TIF using Esophyx. Follow-up assessments were completed in 28 patients. At a median 14-months follow-up, 82% (23/28) of patients were off daily PPIs (64% completely off PPIs), and 68% (19/28) were satisfied with their current health condition compared to 4% before TIF. Median GERD Health-Related Quality of Life scores were significantly reduced to 4 (0-25) from 26 (0-45) before TIF ( $P < 0.001$ ). Heartburn was eliminated in 65% (17/26) and improved by >50% in 86% (24/28) of patients. Regurgitation was eliminated in 80% (16/20) of patients. Atypical LPR symptoms such as hoarseness, coughing, and throat clearing were eliminated in 63% (17/27) of patients as measured by Reflux Symptom Index scores. Small patient population, retrospective analysis, and non-randomization are study limitations.

Bell and Freeman (2011) retrospectively evaluated the efficacy and safety of a rotational/longitudinal esophagogastric transoral incisionless fundoplication (TIF) in 37 patients on antisecretory medication, and with proven gastroesophageal reflux and limited hiatal hernia. Five patients were re-operations for failed laparoscopic fundoplication. The authors concluded that rotational/longitudinal esophagogastric fundoplication using the Esophyx device significantly improved symptomatic and objective outcomes in over 70% of patients at median 6-month follow-up. According to the authors, limitations of this study include its retrospective study design an incomplete data set for all patients, and the short 6-month duration of follow-up.

In a retrospective study, Barnes et al. (2011) evaluated clinical outcomes in 110 consecutive GERD patients who underwent TIF. At a median 7-month follow-up, typical and atypical symptom scores were normalized in 75% to 80% of patients and PPIs were completely discontinued by 93% of patients. According to the authors, these results supported the safety and efficacy of TIF. However, the retrospective study design, the lack of a control group, and the short term follow up limits the validity of these study results.

In a review of the evidence for techniques and outcomes for TIF in the treatment of GERD, Testoni et al. (2016) reported that based on their analysis, the overall complication rates for TIF with the Esophyx<sup>®</sup> device range from 3% to 10%. Major complications arose rarely and were bleeding, mucosal tears or perforation requiring endoscopic intervention or surgery, pneumothorax, and mediastinal abscesses. Bleeding requiring transfusions has been reported in about 3%-5% of cases. Mediastinal abscesses have been reported in less than 2% of cases. No procedure-related deaths have occurred. Concerning outcomes, their findings show that the patient selection is one determinant in achieving clinical success. The operator's experience is also key in the success, noting that in the majority of included studies, the procedure was done early in the operator's learning curve. From a technical point of view, in the authors' opinion, the number of fasteners deployed and the rotational technique were associated with a better outcome; a larger number of fasteners increased by four folds the success rate. Other factors associated with a higher rate of unsuccessful results include Hill grades III and IV, hiatal hernia larger than 2 cm, and ineffective esophageal motility. An impaired esophageal clearance may induce epithelial sensitization and reflux-related symptoms, even in presence of a low-volume reflux. The authors conclude that long-term efficacy of TIF needs to be further assessed; mainly for the MUSE<sup>™</sup> technique through randomized controlled trials. However, the role of TIF in the management of GERD still needs to occur for both procedures. Preoperative anatomical and functional findings and technical procedural aspects that will help select patients and predict a successful outcome still need to be identified, as well.

Huang et al. (2017) performed a systematic review with meta-analysis of studies evaluating the role of TIF in GERD. Only randomized controlled trials evaluating the efficacy of TIF, and prospective observational studies reporting outcomes after TIF were included. The authors identified that the total number of refluxes was reduced after TIF

compared with the PPIs/sham group. The esophageal acid exposure time and acid reflux episodes after TIF were not significantly improved. PPI usage increased with time and most of the patients resumed PPIs treatment at reduced dosage during the long-term follow-up. The total satisfaction rate after TIF was about 69.15 % in 6 months. The incidence of severe adverse events consisting of gastrointestinal perforation and bleeding was 2.4 %. The authors concluded that TIF has comparable short-term patient satisfaction as an alternative intervention to GERD-related symptoms. Long-term results showed decreased efficacy with time and patients often resumed PPIs at reduced doses.

Other clinical trials for EsophyX are limited to observational case series that do not allow for conclusions about durability and long-term effectiveness (Narsule et al., 2012; Testoni et al., 2012; Frazzoni et al., 2011; Hoppo et al., 2010; Repici et al., 2010; Demyttenaere et al., 2010; Testoni et al., 2010).

## **Polymer Injection and Implantation Techniques**

### ***Plexiglas and Durasphere***

No new studies that provide substantial new evidence regarding polymer injection and implantation techniques were identified.

In a nonrandomized uncontrolled study, Ganz et al. (2009) assessed the long-term safety and effectiveness of Durasphere (Carbon Medical Technologies), an injectable bulking agent, in the treatment of mild to moderate GERD. Nine patients completed the 12-month trial. There were no adverse events. The procedure was well tolerated with minimal patient discomfort and no dysphagia. At 12 months, 70% of patients discontinued all antacid medication completely and 90% of patients reduced PPI use by greater than 50%. There were no reports of esophagitis (at 12 months), erosion, ulceration, or sloughing of material at any injection site. The Durasphere material did not appear to migrate. The authors concluded that Durasphere appears to be a promising new injectable bulking agent for the treatment of mild to moderate GERD, with demonstrable efficacy and no significant adverse events in a small cohort of patients. Study limitations include nonrandomized study design without a control group and small number of subjects.

Chen et al. (2009) conducted a systematic review that included 33 studies examining 7 endoscopic procedures (Stretta procedure, Bard EndoCinch, Wilson-Cook Endoscopic Suturing Device, NDO Plicator, Enteryx, Gatekeeper Reflux Repair System and Plexiglas) Of the three procedures that were compared with sham controls (Stretta procedure, Bard EndoCinch and Enteryx), patient outcomes in the treatment group were either as good as, or significantly better than, those of control patients in terms of heartburn symptoms, QOL, and medication usage. However, for the two procedures that were compared with the laparoscopic fundoplication (Stretta) procedure and the Bard EndoCinch device, outcomes for patients in the endoscopic group were conflicting. Some patients in the endoscopic group experienced comparable outcomes as patients undergoing the laparoscopic approach, while others experienced inferior outcomes. The authors concluded that there is insufficient evidence to determine the safety and efficacy of endoscopic procedures for GERD, particularly over the long term (Chen et al., 2009).

### ***LINX Reflux Management System***

Louie et al. (2018) reported one-year results from a mandated post-approval multicenter, prospective study of 200 patients with pathologic acid reflux confirmed by esophageal pH testing, who underwent magnetic sphincter augmentation (MSA). Predefined clinical outcomes were assessed at the annual visit including a validated, disease-specific questionnaire, esophagogastroduodenoscopy (EGD) and esophageal pH monitoring, and use of proton pump inhibitors. At 1 year, the mean total acid exposure time decreased from 10.0% at baseline to 3.6%, and 74.4% of patients had normal esophageal acid exposure time (% time pH<4 ≤5.3%). GERD Health-Related Quality of Life scores improved from a median score of 26.0 at baseline to 4.0 at 1 year, with 84% of patients meeting the predefined success criteria of at least a 50% reduction in total GERD Health-Related Quality of Life score compared with baseline. The device removal rate at 1 year was 2.5%. There was a report of one erosion, and no serious adverse events were reported. Although the authors conclude that safety and effectiveness of MSA has been demonstrated outside of an investigational setting to further confirm it as treatment for GERD, study limitations include non-randomization and short follow-up period.

Saino, et al. (2015) completed the 5-year follow-up from a prospective, multicenter study which evaluated the safety and efficacy of the MSAD. Prior to MSAD placement, patients (n=44) had abnormal esophageal acid and symptoms poorly controlled by proton pump inhibitors (PPIs). Patients served as their own control, which allowed comparison between baseline and postoperative measurements to determine individual treatment effect. 33 patients completed the 5-year follow-up. Mean total percentage of time with pH <4 was 11.9% at baseline and 4.6% at 5 years (P < .001), with 85% of patients achieving pH normalization or at least a 50% reduction. Mean total GERD-HRQL score improved significantly from 25.7 to 2.9 (P < .001) when comparing baseline and 5 years, and 93.9% of patients had at least a 50% reduction in total score compared with baseline. Complete discontinuation of PPIs was achieved by 87.8% of patients. No complications occurred in the long term, including no device erosions or migrations at any point. Based on long-term reduction in esophageal acid, symptom improvement, and no late complications, the authors concluded

that this study shows the relative safety and efficacy of magnetic sphincter augmentation for GERD. The study was limited by small patient population and no control arm.

Ganz et al. (2016) reported the 5-year follow-up evaluation of patients who received a magnetic sphincter augmentation (MSA) device for GERD. The original prospective study at 14 centers in the United States and the Netherlands was conducted on 100 adults with GERD for 6 months or more, who were partially responsive to daily proton pump inhibitors (PPIs) and had evidence of pathologic esophageal acid exposure. At baseline, the median GERD-HRQL scores were 27 in patients not taking PPIs and 11 in patients on PPIs; 5 years after device placement this score decreased to 4. All patients used PPIs at baseline; this value decreased to 15.3% at 5 years. Moderate or severe regurgitation occurred in 57% of subjects at baseline, but only 1.2% at 5 years. All patients reported the ability to belch and vomit if needed. Bothersome dysphagia was present in 5% at baseline and in 6% at 5 years. Bothersome gas-bloat was present in 52% at baseline and decreased to 8.3% at 5 years. The authors concluded that MSA provides significant and sustained control of reflux, with minimal side effects or complications, which in their opinion validates the long-term safety and efficacy of MSA for patients with GERD.

Lipham et al. (2012) conducted a case series of antireflux surgery with a Magnetic Sphincter Augmentation Device (MSAD). MSAD is used to restore the competency of the lower esophageal sphincter with a device rather than a tissue fundoplication. The aim of the study was to examine the safety profile of the MSAD in the first 1000 implanted patients. The author compiled data from multiple sources starting in July 1, 2013. The analysis included intra/perioperative complications, hospital readmissions, procedure-related interventions, reoperations, and device malfunctions leading to injury or inability to complete the procedure. Approximately 1000 patients worldwide have been implanted with the MSAD, at 82 institutions with median implant duration of 274 days. The author concluded that the safety analysis of the first 1000 patients treated with MSAD for gastroesophageal reflux disease confirms the safety of this device and the implantation technique. The preliminary and positive results of this study are hampered by lack of an adequate control or comparator group, and lack of randomization and blinding.

Ganz et al. (2013) conducted a nonrandomized uncontrolled study (n=100; 52% men; median age, 53 years, range 18-75) in patients with a history of GERD for at least 6 months and who had experienced a partial response to PPI treatment. The primary outcomes were normalization of esophageal acid exposure or a  $\geq 50\%$  reduction in acid exposure at 1 year of follow-up. Secondary outcomes were 50% reduction in the QOL score compared with the score without PPIs at baseline. The esophageal sphincter device was implanted using standard laparoscopy by surgeons with experience with fundoplication. Normalization of or at least a 50% reduction in esophageal acid exposure was achieved in 64% of all patients (64/100). Secondary outcomes of a 50% reduction in the QOL score compared with the score without PPI at baseline was achieved in 92% of all patients (92/100). Post-hoc analysis demonstrated a reduction of  $\geq 50\%$  in the average daily dose of PPI was observed in 93% of all patients (93/100). Six patients experienced serious adverse effects, 4 of whom required removal of the device. In 3 patients, the device was removed at various time points following implantation because of persistent dysphagia. The most frequently reported adverse effect was dysphagia occurring in 68% of all patients. At 1 year, 11% of patients reported persistent and ongoing dysphagia. The preliminary and positive results of this study are hampered by the poor quality design, which includes lack of an adequate control or comparator group, and lack of randomization and blinding.

Bonavina et al. (2010) conducted 1- and 2-year evaluations of a feasibility trial to assess the safety and efficacy of a laparoscopically implanted sphincter augmentation device (LINX Reflux Management System) in 44 patients with GERD. Complete cessation of PPI use was reported by 90% of patients at 1 year and by 86% of patients at 2 years. One device was laparoscopically explanted for persistent dysphagia without disruption of the anatomy or function of the cardia. There were no device migrations, erosions, or induced mucosal injuries. At 1 and 2 years, 77% and 90% of patients, respectively, had a normal esophageal acid exposure. According to the authors, the new laparoscopically implanted sphincter augmentation device eliminates GERD symptoms without creating undue side effects and is effective at 1 and 2 years of follow-up. Further research with a larger patient population is needed to confirm these preliminary results and determine the clinical relevance of these findings.

As a follow-up to the Bonavina et al. (2010) study, Lipham et al. (2012) evaluated 44 patients who underwent a laparoscopic surgical procedure for placement of the LINX System. Each patient's baseline GERD status served as the control for post implant evaluations. For esophageal acid exposure, the mean total % time pH < 4 was reduced from 11.9% at baseline to 3.8% at 3 years, with 80% of patients achieving pH normalization. At  $\geq 4$  years, 100% of the patients had improved QOL measures for GERD, and 80% had complete cessation of the use of PPIs. There have been no reports of long-term device-related complications such as migration or erosion. The authors concluded that sphincter augmentation with the LINX Reflux Management System provided long-term clinical benefits with no safety issues. According to the authors, patients with inadequate symptom control with acid suppression therapy may benefit from treatment with sphincter augmentation. Limitations of the study include the lack of controls and a small sample size.

Bonavina et al. (2008) conducted a multi-center feasibility trial to evaluate safety and efficacy of a magnetic sphincter augmentation (MSA) device. Over a 1-year period, 38 out of 41 enrolled patients underwent implantation of this device. The mean follow-up was 209 days. At 3 months post-operatively, 89% of patients were no longer taking anti-reflux medications and 79% of patients had a normal 24-hr pH test. Mild dysphagia occurred in 45% of patients. No migrations or erosions of the device occurred. The authors concluded that laparoscopic implant of the MSA device is safe and well tolerated. It requires minimal surgical dissection and a short learning curve compared to the conventional Nissen fundoplication. The small study population limits the validity of the conclusion of this study.

In an observational cohort study, Asti et al. (2016) compared the quality of life in patients undergoing laparoscopic Toupet fundoplication (LTF) versus LINX. Consecutive patients undergoing LTF or LINX over the same time period were compared by using the propensity score full matching method and generalized estimating equation. Of 238 eligible patients, 103 underwent an LTF and 135 a LINX procedure. All patients had a minimum 1-year follow-up. Over time, patients in both groups had similar GERDHRQL scores (odds ratio [OR] 1.04, confidence interval [CI] 0.89–1.27; P=0.578), PPI use (OR 1.18, CI 0.81–1.70; P=0.388), gas related symptoms (OR 0.69, CI 0.21–2.28; P=0.542), dysphagia (OR 0.62, CI 0.26–1.30; P=0.241), and reoperation-free probability (stratified log-rank test=0.556). In 2 concurrent cohorts of patients with early stage GERD undergoing LTF or LINX and matched by propensity score analysis, health related quality of life significantly improved and GERD-HRQL scores had a similar decreasing trend over time up to 7 years of follow-up. Based on these findings, the authors concluded that LTF and LINX provide similar disease-specific quality of life over time in patients with early stage GERD.

In a retrospective review, Warren et al. (2018) analyzed factors influencing the outcome of MSA for chronic GERD. A pivotal trial (N = 99) and the authors' prospectively maintained esophageal database (N = 71). A priori outcomes were defined as excellent (GERD-HRQL <5, no PPI, no esophagitis), good (GERD-HRQL 6-15, no PPI, grade A esophagitis), fair (GERD-HRQL 16 to 25, PPI use, grade B esophagitis), and poor (GERD-HRQL >25, PPI use, grade C/D esophagitis). Univariable and multivariable logistic regression analyses were performed to determine predictors of achieving an excellent/good outcome. A total of 170 patients underwent MSA with a median age of 53 years, [43-60] and a median BMI of 27 (IQR = 24-30). At baseline, 93.5% of patients experienced typical symptoms and 69% atypical symptoms. At univariable analysis, excellent/good outcomes were negatively impacted by BMI, preoperative LES residual pressure, Hill grade, and hiatal hernia. At multivariable analysis, BMI >35 (OR = 0.05, 0.003-0.78, p = 0.03), structurally defective LES (OR = 0.37, 0.13-0.99, p = 0.05), and preoperative LES residual pressure (OR = 0.89, 0.80-0.98, p = 0.02) were independent negative predictors of excellent/good outcome. The authors' conclusion is that Magnetic sphincter augmentation results in excellent/good outcomes in most patients but a higher BMI, structurally defective sphincter, and elevated LES residual pressure may prevent this goal. The authors' conclusion is that a higher BMI, structurally defective sphincter, and elevated LES residual pressure may prevent optimal treatment with MSA.

Aiolfi et al. (2018) conducted a systematic review and meta-analysis of early results of MSA versus fundoplication for the treatment of GERD. Seven observational cohort studies, published between 2014 and 2017, matched the inclusion criteria. Overall, 1211 patients, 686 MSA and 525 LF, were included. Postoperative morbidity ranged from 0 to 3% in the MSA group and from 0 to 7% in the LF group, and there was no mortality. Dysphagia requiring endoscopic dilatation occurred in 9.3% and 6.6% of patients respectively (OR = 1.56, 95% CI = 0.61-3.95, p = 0.119). The pooled OR of gas/bloat symptoms, ability to vomit, and ability to belch were 0.39 (95% CI 0.25-0.61; p < 0.001), 10.10 (95% CI 5.33-19.15; p < 0.001), and 5.53 (95% CI 3.73-8.19; p < 0.001), respectively. The postoperative GERD-HRQL was similar (p = 0.101). The pooled OR of PPI suspension, endoscopic dilatation, and reoperation were similar in the two patients groups (p = 0.548, p = 0.119, p = 0.183, respectively). The authors concluded that both anti-reflux procedures are safe and effective up to 1-year follow-up. PPI suspension rate, dysphagia requiring endoscopic dilatation, and disease-related quality of life are similar in the two patient groups. MSA is associated with less gas/bloat symptoms and increased ability to vomit and belch. Study limitations include the exclusion of randomized controlled trials, and short follow-up periods of the included studies.

Alicuben et al. (2018) reported on the worldwide experience with erosion of the MSA device. In total, 9453 devices were placed and there were 29 reported cases of erosions. The median time to presentation of an erosion was 26 months with most occurring between 1 and 4 years after placement. The risk of erosion was 0.3% at 4 years after device implantation. Most patients experienced new-onset dysphagia prompting evaluation. Devices were successfully removed in all patients most commonly via an endoscopic removal of the eroded portion followed by a delayed laparoscopic removal of the remaining beads. At a median follow-up of 58 days post-removal, there were no complications and 24 patients have returned to baseline. Four patients reported ongoing mild dysphagia. Erosion of the LINX device is an important but rare complication to recognize that has been managed via minimally invasive approaches without long-term consequences. Continued monitoring and reporting of MSA erosion will provide longer-term experience.

In a systematic review and meta-analysis of the LINX<sup>®</sup> magnetic esophageal sphincter augmentation versus Nissen fundoplication for gastroesophageal reflux disease, Skubleny et al. (2017) included randomized controlled trials, non-



randomized comparison study and case series with greater than 5 patients. Five hundred and forty-seven titles were identified through primary search, and 197 titles or abstracts were screened after removing duplicates. Meta-analysis was performed on postoperative quality of life outcomes, procedural efficacy and patient procedural satisfaction. Three primary studies identified a total of 688 patients, of whom 273 and 415 underwent Nissen fundoplication and MSA, respectively. MSA was statistically superior to LNF in preserving patient's ability to belch (95.2 vs 65.9%,  $p < 0.00001$ ) and ability to emesis (93.5 vs 49.5%,  $p < 0.0001$ ). There was no statistically significant difference between MSA and LNF in gas/bloating (26.7 vs 53.4%,  $p = 0.06$ ), postoperative dysphagia (33.9 vs 47.1%,  $p = 0.43$ ) and proton pump inhibitor (PPI) elimination (81.4 vs 81.5%,  $p = 0.68$ ). The authors' conclusion is that magnetic sphincter augmentation appears to be an effective treatment for GERD with short-term outcomes comparable to the more technically challenging and time-consuming Nissen fundoplication. Long-term comparative outcome data past 1 year are needed in order to further understand the efficacy of magnetic sphincter augmentation.

Warren et al. (2016) conducted a multi-institutional, retrospective cohort study of patients with GERD undergoing either magnetic sphincter augmentation (MSA) or Nissen fundoplication (NF). Comparisons were made at 1 year for the overall group and for a propensity-matched group. A total of 415 patients (201 MSA and 214 NF) underwent surgery. At a minimum of 1-year follow-up, 354 patients (169 MSA and 185 NF) had significant improvement in GERD-HRQL scores (pre to post: 21-3 and 19-4). MSA patients had greater ability to belch (96 vs. 69%) and vomit (95 vs. 43%) with less gas bloat (47 vs. 59%). Propensity-matched cases showed similar GERD-HRQL scores and the differences in ability to belch or vomit, and gas bloat persisted in favor of MSA. Mild dysphagia was higher for MSA (44 vs. 32%). Resumption of daily PPIs was higher for MSA (24 vs. 12,  $p=0.02$ ) with similar patient-reported satisfaction rates. The authors concluded that in appropriate candidates, MSA is a valid alternative surgical treatment for GERD management, as MSA for uncomplicated GERD achieves similar improvements in quality of life and symptomatic relief, with fewer side effects. However, the authors found that MSA had lower PPI elimination rates when compared to propensity-matched NF cases.

Warren et al. (2017) conducted a retrospective review to evaluate the manometric changes, function, and impact of magnetic sphincter augmentation (MSA) on the lower esophageal sphincter (LES). Inclusion criteria ( $n=121$ ) consisted of a confirmed diagnosis of gastroesophageal reflux disease by an abnormal esophageal pH study (body mass index  $<35\text{kg/m}^2$ , hiatal hernia  $<3\text{cm}$ , and absence of endoscopic Barrett disease). Manometric changes, pH testing, and proton pump inhibitor use were assessed preoperatively and 6 and 12 months after MSA. MSA was associated with an overall increase in the median LES resting pressure (18 pre-MSA vs 23 mm Hg post-MSA;  $P = 0.0003$ ), residual pressure (4 vs 9 mm Hg;  $P < 0.0001$ ), and distal esophageal contraction amplitude (80 vs 90 mm Hg;  $P = 0.02$ ). The percent peristalsis remained unaltered (94% vs 87%;  $P = 0.71$ ). Overall, patients with a manometrically defective LES were restored 67% of the time to a normal sphincter with MSA. Those with a structurally defective or severely defective LES improved to a normal LES in 77% and 56% of patients, respectively. Only 18% of patients with a normal preoperative manometric LES deteriorated to a lower category. The authors concluded that a manometrically defective LES can be restored to normal sphincter, whereas a normal LES remains stable. Details on the original studies were not disclosed in this abstract.

In a retrospective review, Desart et al. (2015) evaluated whether the LINX<sup>®</sup> magnetic sphincter augmentation system is a safe and effective option for patients with new gastroesophageal reflux disease following laparoscopic sleeve gastrectomy. At 2-4 weeks after the LINX procedure, all patients ( $n=7$ ) were noted to have self-reported greatly improved gastroesophageal reflux symptoms: statistically significant improved severity and frequency of their reflux, regurgitation, epigastric pain, sensation of fullness, dysphagia, and cough symptoms in their postoperative GERD symptoms compared with their preoperative evaluation. The authors concluded that the LINX<sup>®</sup> device is a safe and effective option in patients with de novo refractory gastroesophageal reflux disease after a laparoscopic sleeve gastrectomy despite appropriate weight loss. The original study was limited by small sample size and short follow-up period. In addition, there was lack of information about use of PPIs prior to or after the procedure.

Reynolds et al. (2015) conducted a retrospective analysis of 1-year outcomes of patients undergoing magnetic sphincter augmentation (MSA) with the LINX device and laparoscopic Nissen fundoplication (LF) from June 2010 to June 2013. Patients were matched using propensity scores incorporating multiple preoperative variables. Outcomes were measured by GERD Health Related Quality of Life scores, proton-pump inhibitor use, satisfaction, and complications. One hundred and seventy-nine patients met inclusion criteria, 62 MSA and 117 LNF. At 1 year after surgery, both groups had similar GERD Health Related Quality of Life scores (4.2 MSA and 4.3 LNF;  $p=0.897$ ) and proton-pump inhibitor use (17% of MSA and 8.5% of LNF;  $p=0.355$ ). Analogous GERD patients had similar control of reflux symptoms after both MSA and LNF. The inability to belch and vomit were significantly fewer with MSA, along with a significantly lower incidence of severe gas-bloat symptoms. These results support the use of MSA as first-line therapy in patients with mild to moderate GERD.

Reigler et al. (2015) evaluated the evidence for magnetic sphincter augmentation device (MSAD) and laparoscopic fundoplication (LF) in clinical practice. Two hundred forty nine patients (202 MSAD patients and 47 LF patients) had completed one-year follow-up. The LF group was older and had a greater frequency of large hiatal hernias and

Barrett's esophagus than the MSAD group ( $P < 0.001$ ). The median GERD-health related quality of life score improved from 20.0 to 3.0 after MSAD and 23.0 to 3.5 after LF. Moderate or severe regurgitation improved from 58.2 to 3.1% after MSAD and 60.0 to 13.0% after LF ( $P=0.014$ ). Discontinuation of PPIs was achieved by 81.8% of patients after MSAD and 63.0% after LF ( $P=0.009$ ). Excessive gas and abdominal bloating were reported by 10.0% of patients after MSAD and 31.9% following LF ( $P \leq 0.001$ ). Following MSAD, 91.3% of patients were able to vomit if needed, compared with 44.4% of those undergoing LF ( $P < 0.001$ ). Reoperation rate was 4.0% following MSAD and 6.4% following LF. The authors conveyed that antireflux surgery should be individualized to the characteristics of each patient, taking into consideration anatomy and propensity and tolerance of side effects. They concluded that both MSAD and LF showed significant improvements in reflux control, with similar safety and reoperation rates. In their opinion, in the treatment continuum of antireflux surgery, MSAD should be considered as a first-line surgical option in appropriately selected patients without Barrett's esophagus or a large hiatal hernia in order to avoid unnecessary dissection and preserve the patient's native gastric anatomy.

The National Institute for Health and Care Excellence (NICE) encourages further research into laparoscopic insertion of a magnetic titanium ring for GERD, including long-term outcome data and comparative trials with other anti-reflux surgery. Their recommendations do not identify any major safety concerns with this procedure (NICE, 2017). Smith et al. (2017) reported that out of a total of 3283 procedures reviewed, device removal occurred in 2.7% of cases. The most common causes of removal were dysphagia, continued reflux, and device erosion into the esophagus. Salvador et al. (2017), Parmar et al. (2017), and Lipham, et al. (2015), report similar findings.

## **Professional Societies**

### ***American Gastroenterological Association (AGA)***

In a position statement published in 2008, the AGA assigned a grade of "Insufficient" regarding the use of current and commercially available endoluminal antireflux procedures for the management of patients with an esophageal syndrome. The AGA provides no recommendation since there is insufficient evidence to recommend for or against its use (Kahrilas et al., 2008).

### ***American Society for Gastrointestinal Endoscopy (ASGE)***

In a 2015 clinical guideline on the role of endoscopy in the management of GERD, ASGE suggests that endoscopic antireflux therapy be considered for selected patients with uncomplicated GERD after careful discussion with the patient regarding potential adverse effects, benefits, and other available therapeutic options.

### ***American College of Gastroenterology (ACG)***

In 2013, the ACG published practice guidelines regarding the diagnosis and management of GERD. They state that the "usage of current endoscopic therapy or transoral incisionless fundoplication cannot be recommended as an alternative to medical or traditional surgical therapy." This recommendation is considered conditional, based on a moderate level of evidence (Katz et al., 2013).

### ***American Society of General Surgeons (ASGS)***

In 2014, the ASGS published a position statement regarding its support for the LINX procedure. ASGS states that total management of GERD will likely rely upon a combination of medical and surgical care in the current and near future. ASGS recommends that when considering a surgical procedure, the procedure will need to provide safe control of GERD with minimal side effects. The ASGS states, "Based on currently available information and the experience of their members with the procedure, they support the LINX procedure as a mechanism for controlling GERD when it is placed by properly trained laparoscopic surgeons with experience in foregut surgery and the management of GERD patients."

In April 2011, the ASGS published a position statement regarding the use of TIF stating that it supports the use of TIF in patients with symptomatic chronic GERD who are not responsive to a standard dose of PPI therapy (ASGS, 2011). The ASGS also supports its use for patients who wish to avoid lifetime drug therapy for this condition. The ASGS also supports the adoption of the procedure by trained general surgeons as a less invasive alternative to more conventional surgical techniques, stating that the preferred surgical technique should be based on the discretion and judgment of the surgeon and the patient's clinical circumstances.

In a statement regarding coverage for TIF, ASGS states that there is a sufficient body of peer reviewed literature that establishes transoral fundoplication as reasonable and medically necessary for a subset of patients who are candidates for surgical fundoplication; specifically, patients who either cannot obtain satisfactory relief from standard PPI therapy or who wish to avoid a lifetime of dependence on such medications, and present with a 2 centimeter or smaller hiatal hernia (ASGS, 2011).

## **Society of American Gastrointestinal and Endoscopic Surgeons (SAGES)**

In an updated review of endoluminal treatments for the treatment of GERD, SAGES (Stefanidis et al., 2017b) provided the following recommendations:

- Based on existing evidence, TIF can be performed with an acceptable safety risk in appropriately selected patients. The procedure leads to better control of GERD symptoms compared with PPI treatment in the short term (6 months), but appears to lose effectiveness during longer term follow-up and is associated with moderate patient satisfaction scores. Objective GERD measures improve similarly after TIF 2.0 compared with PPI. No comparative, controlled trials exist between TIF and surgical fundoplication, but preliminary evidence suggests that the latter can be used safely after TIF failure. (Level of evidence +++, strong recommendation)
- Based on existing evidence, Stretta significantly improves health related quality of life score, heartburn scores, the incidence of esophagitis, and esophageal acid exposure in patients with GERD, but does not increase lower esophageal sphincter basal pressure. In addition, it decreases the use of PPI by approximately 50%. The effectiveness of the procedure diminishes some over time, but persistent effects have been described up to 10 years after the procedure in appropriately selected patients with GERD. Stretta is more effective than PPI, but less so than fundoplication. Stretta is safe in adults and has a short learning curve. (Level of evidence +++, strong recommendation)

The SAGES Technology and Value Assessment Committee (TVAC) updated its safety and effectiveness analysis of the LINX Reflux Management System.

- Review of published studies suggests that magnetic sphincter augmentation is safe with no reported deaths and a 0.1% rate of intra/perioperative complications.
- Long-term efficacy of LINX appears good for typical GERD symptoms with reduced acid exposure, improved GERD symptoms, and freedom from PPI in 85-88% at 3-5 years.
- Dysphagia resolves in most patients and the incidence is roughly 10% at 1 year and 4% at 3 years. The need for endoscopic dilation ranges from 6-12% and the primary reason for explantation appears to be persistent dysphagia with a rate in larger series from 3-6%.
- Erosion appear to be rare, with one case reported in the 1st 1,000 patients, one additional published case report, a large series reporting 2 erosions, and several additional reports in the FDA MAUDE dataset (true number unknown, as multiple entries in this dataset may be made for each patient). Based on very limited literature, erosion can be successfully treated with explantation (Telem et al., 2017).

## **U.S. FOOD AND DRUG ADMINISTRATION (FDA)**

Several endoscopic antireflux (endoluminal) devices have received approval by the FDA for treatment of gastroesophageal reflux disease (GERD).

The Stretta System (Mederi Therapeutics) was approved in April 2000 for radiofrequency thermal ablation treatment of GERD. Additional information is available at: [http://www.accessdata.fda.gov/cdrh\\_docs/pdf10/k103017.pdf](http://www.accessdata.fda.gov/cdrh_docs/pdf10/k103017.pdf). (Accessed July 16, 2018)

The Bard EndoCinch Endoscopic Suturing System (Bard Endoscopic Technologies, Billerica, MA, a subsidiary of C.R. Bard Inc), was approved in January 2001 for endoscopic suturing in the treatment of GERD. Subsequent FDA approval was received in September 2007 for an updated version. Additional information is available at: [http://www.accessdata.fda.gov/cdrh\\_docs/pdf7/k071651.pdf](http://www.accessdata.fda.gov/cdrh_docs/pdf7/k071651.pdf). (Accessed July 16, 2018)

The NDO Surgical Endoscopic Plication System was approved in September 2007 for endoscopic suturing in the treatment of GERD in patients who require and respond to pharmacological therapy. Additional information is available at: [http://www.accessdata.fda.gov/cdrh\\_docs/pdf7/k071651.pdf](http://www.accessdata.fda.gov/cdrh_docs/pdf7/k071651.pdf). (Accessed July 16, 2018)

The current generation of EsophyX, EsophyX2, was cleared for marketing as substantially equivalent to the original EsophyX system with minor changes in November 2009 under the FDA510(k) process. The original system was cleared for marketing in September 2007 as substantially equivalent to the predicate devices NDO Surgical Endoscopic Plication System, Bard EndoCinch, and EGS StomaphyX Endoluminal Fasteners and Delivery System. According to the approval summary letter, EsophyX2 is indicated for:

- Use in transoral tissue approximation
- Full-thickness plication and ligation in the GI tract
- The treatment of symptomatic chronic gastroesophageal reflux disease in patients who require and respond to pharmacologic therapy
- Narrowing of the gastroesophageal junction
- Reduction of hiatal hernia <2 cm in patients with symptomatic chronic gastroesophageal reflux disease.

See the following websites for more information:

- [http://www.accessdata.fda.gov/cdrh\\_docs/pdf7/K071651.pdf](http://www.accessdata.fda.gov/cdrh_docs/pdf7/K071651.pdf)

- <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm?db=PMN&id=k092400>  
(Accessed July 16, 2018)

The Medigus Ultrasound Surgical Endostapler (MUSE™ System) received 510K approval on January 15, 2015 for the endoscopic placement of surgical staples in the soft tissue of the esophagus and stomach in order to create anterior partial fundoplication for treatment of symptomatic chronic GERD in patients who require and respond to pharmacological therapy. See the following website for additional information:  
[https://www.accessdata.fda.gov/cdrh\\_docs/pdf14/k143634.pdf](https://www.accessdata.fda.gov/cdrh_docs/pdf14/k143634.pdf). (Accessed July 16, 2018)

These products are Class II devices (moderate risk) deemed substantially equivalent to other endoscopic devices utilizing other procedures.

Enteryx™, a biocompatible liquid polymer, received FDA approval in 2003 through the premarket approval (PMA) process for the treatment of symptomatic GERD. However, on September 22, 2005, Boston Scientific Corporation issued a recall of Enteryx due to the device polymerizing shortly after injection into a spongy material that cannot be removed. Serious adverse events involved unrecognized transmural injections of Enteryx into structures surrounding the esophagus, potentially resulting in serious injury or death. See the following website for more information:  
<https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRes/res.cfm?id=42034>. (Accessed June 19, 2018)

Torax Medical obtained FDA PMA in March 2012 for the LINX Reflux Management System. PMA supplements have also received approval, the most recent being in March 2018: Approval for updating the precautions statement to state that use of the LINX Reflux Management System in patients with a hiatal hernia larger than 3 cm should include hiatal hernia repair to reduce the hernia to less than 3 cm and that the LINX Reflux Management System has not been evaluated in patients with an unrepaired hiatal hernia greater than 3 cm, add a hiatal hernia clinical data summary in the instructions for use, update the instructions for use section to highlight the recommendation to repair a hiatal hernia, if present, at the time of the LINX Reflux Management System implantation, and update the patient information booklet to align with the instructions for use and include 5 year clinical study results. See the following website for more information using PMA number P100049:  
<https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm>. (Accessed July 16, 2018)

Durasphere is approved by the U.S. Food and Drug Administration (FDA) as an injectable bulking agent for gastro-urology use in the treatment of adult women with stress urinary incontinence due to intrinsic sphincter deficiency. Use of this product for esophageal reflux would be considered off-label use. See the following website for more information, using PMA number P980053: <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm>.  
(Accessed July 16, 2018)

## CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Medicare does not have National Coverage Determinations (NCD) specifically for endoscopic therapies for treating gastroesophageal reflux disease (GERD). Local Coverage Determinations (LCDs) exist; refer to the LCDs for [Endoscopic Treatment of GERD, Non-Covered Category III CPT Codes, Noncovered Procedures - Endoscopic Treatment of Gastroesophageal Reflux Disease \(GERD\), Non-Covered Services, Select Minimally Invasive GERD Procedures, Services That Are Not Reasonable and Necessary, Stretta Procedure, Transoral Incisionless Fundoplication and Upper Gastrointestinal Endoscopy \(Diagnostic and Therapeutic\)](#) and [Upper Gastrointestinal Endoscopy and Visualization](#).  
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## POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
12/01/2018	<ul style="list-style-type: none"> <li>• Reorganized policy template:               <ul style="list-style-type: none"> <li>○ Simplified and relocated <i>Instructions for Use</i></li> <li>○ Removed <i>Benefit Considerations</i> section</li> </ul> </li> <li>• Simplified coverage rationale (no change to guidelines)</li> <li>• Archived previous policy version 2018T0322U</li> </ul>



## INSTRUCTIONS FOR USE

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. UnitedHealthcare Medical Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.