
Subject: Endoscopic Anti-Reflux Procedures
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INSTRUCTIONS FOR USE

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Endoscopic anti-reflux procedures for the treatment or management of gastroesophageal reflux disease (GERD) are considered experimental, investigational or unproven and not medically necessary. Procedures that are considered experimental, investigational or unproven and not medically necessary include, but are not limited to, the following:

- Stretta[®] System
 - EndoCinch[™] or Bard[™] Endoscopic Suturing System (BESS)
 - Endoscopic Plication[™] System
 - EsophyX[™] System
 - Gatekeeper[™] Reflux Repair System
 - plexiglas or polymethylmethacrylate (PMMA) implantation
 - Syntheon ARD Plicator
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General Background

Gastroesophageal reflux disease (GERD) is defined as symptoms or mucosal damage produced by the abnormal reflux of gastric contents into the esophagus (DeVault, et al., 2005). Approximately 44% of the United States population experience gastroesophageal symptoms at least once a month; 14% have weekly symptoms, and 7% have daily symptoms (Finks, et al., 2007).

The most common symptoms of GERD are heartburn, a sensation of substernal burning pain, and regurgitation of swallowed food. Other esophageal complaints may include a sensation of a foreign body in the posterior pharynx or excessive salivation. Difficulty, inability or pain with swallowing, bleeding, anemia, and weight loss are considered alarm symptoms. These alarm symptoms (e.g., malignancy, esophageal stricture) may suggest complicated disease and might require further evaluation (Finks, et al., 2007).

A trial of empirical therapy with typical reflux symptoms is appropriate for patients who do not present with alarm symptoms or other indications for endoscopy. A good response to empirical therapy is considered diagnostic of GERD and has accuracy comparable to that of 24-hour esophageal hydrogen ion concentration (ph) monitoring. Other testing used in the diagnosis of GERD includes endoscopy, barium esophagram, and manometry (Finks, et al., 2007).

The goals of therapy for GERD patients are relief of symptoms and long-term disease control. Patients with significant esophagitis or other complications will require mucosal healing. Treatment of GERD may include lifestyle modification (e.g., smoking cessation, weight loss, diet restrictions), medical therapy, including over-the-counter antacids and alginates to treat milder forms of GERD and prokinetic agents (e.g., Reglan). H₂ receptor antagonists (H₂RA) are proven to be effective in numerous placebo-controlled trials. Proton pump inhibitors (PPIs) are the most effective medical therapy for GERD, with 80% of the patients experiencing symptom relief and esophageal healing. Several large, controlled trials have demonstrated the superiority of PPIs over H₂RAs in terms of esophageal healing and symptom relief. Most patients can be managed effectively with PPIs, although the therapy is lifelong (Finks, et al., 2007).

Anti-reflux surgery may be an option for patients who have failed pharmacotherapy or for those who choose not to continue on medication therapy for the long term. Patients with persistent symptoms despite maximal therapy (e.g., volume reflux, regurgitation) may consider anti-reflux surgery. Additionally, anti-reflux surgery may be considered in patients with complications of GERD such as strictures, laryngotracheal aspiration or Barrett's Esophagus. An open or laparoscopic Nissen fundoplication may be considered for patients who have an abnormal ambulatory pH test, have normal esophageal motility studies, and have responded, at least partially, to PPI therapy. Long-term outcome from surgery shows symptom relief maintained in 85%–90% of patients in most case series with at least five years of follow-up. Reoperative rates range from 3%–8% (Finks, et al., 2007).

Endoscopic Therapies

Several endoscopic or endoluminal therapies for treating GERD have been developed as alternatives to anti-reflux surgery or pharmacological therapy. Endoscopic, or endoluminal, therapies for GERD are designed to alter structures at the gastroesophageal junction to prevent reflux of gastric contents. Endoscopic therapies are limited in their use to patients with esophageal symptoms, hiatal hernia < 2 cm, esophagitis grade II or lower, and no evidence of Barrett's Esophagus. Most of the data on endoscopic procedures comes from open-label trials with follow-up of a year or less. Case series have demonstrated improvement in GERD symptoms and quality of life (QOL) scores, but none of the devices normalizes esophageal acid exposure. Long-term, controlled clinical trials are needed before endoscopic therapies for the treatment of GERD can be assessed (Finks, et al., 2007).

Endoscopic therapy for GERD is less invasive than anti-reflux surgery and is generally performed in the outpatient setting. The proposed endoscopic techniques include the delivery of radiofrequency energy to the gastroesophageal junction, injection or implantation of agents into the cardia or distal esophagus, and suture plication of the proximal stomach (Falk, et al., 2006a).

Radiofrequency Energy: Radiofrequency energy for the treatment of GERD requires a special single-use catheter and radiofrequency energy generator (Stretta[®] System, (formerly Curon Medical Inc., Fremont, CA). The procedure is generally performed using standard conscious sedation but has required general anesthesia in some patients. The possible mechanisms of action that result from radiofrequency energy are scarring or neurolysis at, or near, the gastroesophageal junction. This procedure is commonly referred to as the Stretta procedure (Falk, et al., 2006a).

Suturing: There are two basic techniques designed to place sutures or staples at the cardia, including submucosal stitching devices and deep transmural plicating devices. Both techniques create pleats or plications of tissue just beneath the gastroesophageal junction. Sedation required for this technique varies as does procedure time. Examples of suturing/plication devices include the EndoCinch[™] or Bard Endoscopic Suturing System (BESS) (Bard Endoscopic Technologies, Billerica, MA); the full-thickness NDO Surgical Endoscopic Plication[™] System (NDO Surgical, Inc., Mansfield, MA); and the Syntheon ARD Plicator (Syntheon, Miami, FL) (Falk, et al., 2006a).

A new endoluminal fundoplication (ELF) technique that utilizes a transoral and fastener-deploying technique is the EsophyX[™] System (EndoGastric Solutions, Inc., Redmond, WA). Preclinical testing reports that the EsophyX System is safe, but long-term safety and efficacy studies are still needed (Cadiere, et al., 2007).

Injection of Bulking Agents: Bulking agents are substances injected under endoscopic guidance into the esophageal wall at the level of the esophagogastric junction to impede reflux (American Society for

Gastrointestinal Endoscopy [ASGE]), 2004). In the 2006 American Gastroenterological Association (AGA) technical review on the use of endoscopic therapy for GERD, the authors reported that “there are no longer any devices that require injection of bulking agents or implantation of a bioprosthesis in the lower esophageal sphincter zone” (Falk, et al., 2006a). Implantable products/devices include:

- expandable hydrogel prosthesis (Gatekeeper™ Reflux Repair System; Medtronic, Inc., Minneapolis, MN). It has been reported that the device was withdrawn in late 2005 before U.S. Food and Drug Administration (FDA) approval (Falk, et al., 2006a).
- ethylene vinyl alcohol copolymer with tantalum dissolved in dimethyl sulfoxide (Enteryx™; Boston Scientific Corp, Natick, MA). Although FDA approved for GERD in April 2003, in October 2005 the FDA issued Advice for Patients with Enteryx for Gastroesophageal Reflux Disease, stating Boston Scientific has recalled all Enteryx Procedure Kits and Enteryx Single Pack Injectors because of reports that improper injection procedures can lead to serious patient injury or death (FDA, 2005).
- plexiglas polymethylmethacrylate microspheres (PMMA). This agent is not commercially available in the United States (Falk, et al., 2006a). Per the manufacturer Website (Artes Medical Inc., San Diego, CA), they are in preclinical development of ArteFlux™ for the treatment of GERD. ArteFlux consists of a combination of PMMA microspheres suspended in purified bovine collagen.

Adverse Events

Madan et al. (2006) summarized the adverse events of endoluminal therapies for the treatment of GERD. The FDA Manufacturer and User Facility Device Experience data base (MAUDE) was searched to examine all voluntary adverse events reported on emerging endoluminal therapies. The adverse events were divided into three categories: radiofrequency ablation, injection, and suture. A total of 50 adverse events were reported on four specific therapies. Half of the complications were a result of injection-based therapy, and 44% of the complications were found to result in radiofrequency ablation-based therapy. A total of eight deaths were reported (i.e., five in the injection group and three in the radiofrequency ablation group). Sixty-four percent of the adverse events resulted in hospitalizations, and 10% of the patients required surgery.

U.S. Food and Drug Administration (FDA)

The Stretta System (FDA, 2000a), EndoCinch or Bard Endoscopic Suturing System (FDA, 2000b), NDO Surgical Endoscopic Plication System (FDA, 2003), EsophyX System (FDA, 2007) have been approved through the 510(k) premarket notification process. The Syntheon ARD Plicator, Gatekeeper Reflux Repair System, and PMMA or ArteFlux are not FDA-approved devices.

Literature Review

Radiofrequency Energy (Stretta Procedure): In a prospective study, Noar et al. (2007) reported on data from a series of 109 consecutive drug-refractory GERD patients treated with the Stretta procedure who reached four-year follow-up assessment. Heartburn scores, total heartburn scores, and patient satisfaction improved ($p < 0.001$). Medication usage decreased from 100% in patients who were on twice-daily PPI therapy at baseline to 75% of patients showing elimination of medications, or only as-needed use of antacids/over-the-counter PPIs, at 48 months ($p < 0.005$). The authors reported no serious complications related to the procedure. The authors stated the limitations of this study are the lack of a comparative group and no long-term pH or motility studies. Similar findings were reported in a prospective study of 83 patients by Reymunde et al. (2007).

Lutfi et al. (2005) reported on data from their three-year experience with the Stretta procedure. GERD was documented by a positive 24-hour pH study. Patients were excluded from the study for the following: a hiatal hernia > 3 cm, a lower esophageal sphincter (LES) pressure < 8mm Hg, Barrett’s esophagus, active grade 3 or 4 esophagitis, American Society of Anesthesiologist 4, age < 18 years, and pregnancy. Patients were mailed SF-12 health status questionnaires and GERD-specific quality of life questionnaires, questions about satisfaction with Stretta and medication use. Seventy-seven patients with follow-up times > six months qualified for the study. Follow-up surveys were completed by 61 patients. Sixty-one percent of the patients were satisfied with the procedure. There were no long-term procedure-related complications. Twenty-six patients were completely off PPI at follow-up. There were 39 responder

patients who were taking $\leq 50\%$ of their original dosage or were completely taken off their medications. Twenty-two patients who remained on the same preoperative dosage or reduced their original dose by 50% were considered nonresponders, including eight patients who underwent Nissen fundoplication. The overall satisfaction rate was 73%. Ninety-five percent of the responders were satisfied, while only 41% of the nonresponders were satisfied and said they would have the procedure again. Twenty-four patients who completed the questionnaires agreed to undergo the 24-hour pH study, including 18 responders and six nonresponders. There was an improvement in distal acid exposure for those patients who had the 24-hour pH study ($7.8 \pm 2.6\%$ to 5.1 ± 3.3 ; $p=0.001$). The authors stated the limitations of this study are the small number of patients responding and the small number of patients who agreed to come back for the 24-hour pH study. Furthermore, the authors stated longer term studies with more complete follow-up are needed to fully assess the role of Stretta in the management of GERD.

In a randomized study, GERD patients received radiofrequency energy delivery to the gastroesophageal junction ($n=35$) or to a sham procedure ($n=29$). Principal outcomes were reflux symptoms and quality of life. Secondary outcomes were medication use and esophageal acid exposure. After six months, interested sham patients crossed over to active treatment. Results at six months indicate active treatment significantly and substantially improved patients' heartburn symptoms and quality of life. More active (61%) versus sham (33%) patients were without daily heartburn symptoms and more had a $> 50\%$ improvement in their GERD quality of life score (61% versus 30%). Symptom improvements persisted at 12 months after treatment. At six months, there were no differences in daily medication use after a medication withdrawal protocol or in esophageal acid exposure times. There were no perforations or deaths. The authors stated, "This procedure represents a new option for selected symptomatic GERD patients who are intolerant of, or desire an alternative to, traditional medical therapies" (Corley, et al., 2003).

In a multicenter study, researchers evaluated GERD symptoms, patient satisfaction, and antisecretory drug use in 558 patients treated with the Stretta procedure. Mean follow-up was eight months. After treatment, onset of GERD relief was less than two months (68.7%) or 2–6 months (14.6%). The median drug requirement improved from PPIs twice daily to antacids as needed. The percentage of patients with satisfactory GERD control, absent or mild, improved from 26.3% at baseline, on drugs, to 77.0% after Stretta. Median baseline symptom control on drugs was 50%, compared to 90% at follow-up. Baseline patient satisfaction on drugs was 23.2%, compared to 86.5% at follow-up. Authors contend these results support the use of the Stretta procedure for patients with GERD, particularly those with inadequate control of symptoms on medical therapy (Wolfsen, et al., 2002).

A prospective study of 94 patients evaluated the Stretta procedure. At 12 months' follow-up, PPI requirement fell from 88.1% to 30% of patients. Also at 12 months, GERD symptom scores, patient satisfaction score, SF-36, and esophageal acid exposure by 24-hour pH improved significantly (Triadafilopoulos, et al., 2002).

A comparative study evaluated the short-term results of the radiofrequency treatment of the gastroesophageal junction known as the Stretta procedure versus laparoscopic fundoplication (LF) in patients with GERD. Patients were offered the Stretta procedure ($n=65$) if they had documented GERD and did not have a hiatal hernia larger than 2 cm, LES pressure less than 8 mmHg, or Barrett's esophagus. Patients with larger hiatal hernias, LES pressure less than 8 mmHg, or Barrett's were offered LF ($n=75$). Preoperative esophageal acid exposure time was higher in the LF group. Preoperative LES pressure was higher in the Stretta group. There was an equal magnitude of improvement between pre- and postoperative quality of life and SF-12 scores between Stretta and LF patients. Both groups were highly satisfied with their procedure. The authors concluded that patients undergoing Stretta have improved GERD symptoms and quality of life comparable to LF and believe the Stretta procedure is an effective alternative to LF in well-selected patients (Richards, et al., 2003).

Suturing (EndoCinch Suturing System): In a randomized sham-controlled trial, Schwartz et al. (2007) reported on endoscopic gastroplication by the EndoCinch suturing system. A total of sixty patients with GERD were randomly assigned to three endoscopic gastroplications ($n=20$), a sham procedure ($n=20$) or observation ($n=20$). The primary outcome measures were PPI use and GERD symptoms. The secondary measure was 24-hour esophageal acid exposure. Follow-up assessments were performed at three, six, and 12 months. At three 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%) ($p < 0.02$). GERD symptoms improved more in the active group than in the sham group ($p < 0.01$). Esophageal acid exposure was modestly decreased after active treatment ($p < 0.02$) but was not significantly greater than after the sham procedure ($p = 0.61$). The active treatment effects on PPI use and symptoms persisted after six and 12 months of open-label follow-up ($n = 41$), but 29% of patients were re-treated in this period. The authors stated, "Widespread use of the endoscopic suturing device should probably be avoided until the technique is improved and efficacy on objective end points has been proved in a sham-controlled fashion" (Schwartz, et al., 2007).

Montgomery et al. (2006) reported data from 46 patients enrolled in a single-center, randomized, sham-controlled trial of EndoCinch plications. There was no difference in the use of PPIs between the sham and the EndoCinch groups at six weeks or 12 months, whereas at three months, there was a significant reduction in the use of PPIs in the treatment group compared to controls ($p < 0.05$). Compared to baseline, there was a significant improvement in QOL as assessed by the gastrointestinal symptom rating scale (GSRS) at six weeks, as well as at three and 12 months post-procedure in both groups. At three months (but not at six weeks and 12 months), there was a significant difference in GSRS scores between the groups, favoring the treatment group versus the control group. Similarly to the sham group, the EndoCinch treatment group had no significant changes in esophageal acid exposure, as indicated by pH monitoring at three and 12 months, in any of the groups.

Chen et al. (2005) reported results of a prospective, multicenter trial with two-year follow-up of 85 patients who were treated with endoluminal gastroplication (ELGP) using the EndoCinch device for GERD. Inclusion criteria were three or more heartburn or regurgitation episodes per week, $> 4.2\%$ time in 24 hours with esophageal pH < 4 , and dependency on antisecretory medications. Exclusion criteria were the presence of varices, achalasia, aperistalsis, or previous gastric resection. Patients underwent manometry, 24-hour pH monitoring, and symptom severity scoring before and after the procedure. Patient diaries were used to assess medication use and to estimate annual medication cost. The authors concluded that ELGP is safe and effective for the long-term control of GERD symptoms. The procedure also appears to reduce esophageal acid exposure substantially for at least six months. Antisecretory medications were significantly decreased after ELGP, resulting in a large reduction in annual drug costs. Seven patients experienced adverse events (i.e., oozing at suture site, melena, bronchospasm, dysphagia, and hypoxemia from sedation). The authors stated patients with classic GERD symptoms who are responsive to antisecretory medications are good candidates for ELGP if an alternative to long-term medical therapy or surgery is being considered. Additional studies will be needed to evaluate whether the procedure should be routinely offered to patients who fail medical therapy or who have other unfavorable parameters.

Schiefke et al. (2005) prospectively evaluated the long-term outcome after EndoCinch. A total of 70 patients were interviewed using a standard questionnaire regarding their symptoms and medications prior to and 18 months after EndoCinch. Follow-up included endoscopy, 24-hour pH monitoring, and esophageal manometry. No major short- or long-term complications post-procedure were reported. At 18 months after procedure, 56/70 patients were considered treatment failures, as their heartburn symptoms did not improve, or PPI medication exceeded 50% of the initial dose. Endoscopy showed all sutures in situ in 12/70 patients, while no remaining sutures were detected in 18/70 patients. The authors summarized that EndoCinch was shown to be safe but not as effective as expected after 18 months of follow-up. The loss of plications was reported in the majority of patients which led to treatment failure.

A study of 87 consecutive patients compared transoral endoluminal gastroplasty (EG) by the Bard EndoCinch device and laparoscopic anti-reflux surgery (LAS) (Chadalavada, et al., 2004). Overall, 66% of patients were satisfied with EG as compared to 93% after LAS. Postoperative PPI/motility agent use was 32% for EG and 13% for LAS. Three EG patients subsequently had LAS within six months of the procedure. These researchers believe LAS offers a greater reduction in medication use than EG, as well as more durable patient satisfaction and that the benefits of EG may include short-term symptomatic improvement while considering definitive surgical management.

An evaluation was conducted to determine any benefit of the Endocinch technique in 22 patients seen up to 12 months post-procedure (Mahmood, et al., 2003). Heartburn symptom scores and regurgitation scores were reduced. Mean (standard error of mean) pH DeMeester acid score was reduced at three

months post-procedure. Percentage upright acid exposure and number of reflux episodes were also reduced significantly. Use of PPIs was reduced by 64% at 12 months post-procedure. All quality of life assessments showed significant improvement. The authors concluded that the Endocinch procedure is an effective and safe outpatient procedure that offers GERD patients significant improvement in symptomatology and reduced requirements for PPIs over at least a one-year period.

A multicenter trial evaluated plication in 64 patients treated with a transoral, flexible endoscopic suturing (Filipi, et al., 2001). Eleven patients required repeat procedure for suboptimal results, and ten patients withdrew. In 47 patients with complete follow-up, gastroesophageal reflux symptoms improved. Twenty-four-hour pH monitoring at three and six months indicated improvement in 24 patients studied.

Plication (NDO Surgical Endoscopic Plication System): In a prospective study, Pleskow et al. (2007) evaluated the long-term safety and durability of effect for endoscopic full-thickness plication for the treatment of GERD. Twenty-nine patients completed the 12-month and 36-month follow-up. All procedure-related adverse events occurred acutely, and no new events were observed during extended follow-up. At 36-months post-procedure, 57% (16/28) of baseline PPI-dependent patients remained off daily PPI therapy. Treatment effect remained stable from 12–36 months, with 21/29 patients off daily PPI at 12 months compared to 17/29 patients at 36 months. Median GERD–Health Related Quality of Life (HRQL) scores remained significantly improved at 36 months versus baseline off meds scores (8 versus 19, $p < 0.001$). In addition, the proportion of patients achieving $\geq 50\%$ improvement in GERD-HRQL score was consistent from 12 months (59%) to 36 months (55%). No long-term procedural adverse effects were reported. The authors reported that the limitations of this study are the small number of patients, lack of a comparative sham group, and no patients had complex GERD.

In a randomized, prospective multicenter trial, Rothstein et al. (2006) examined the effectiveness of endoscopic full-thickness plication for the treatment of GERD in comparison with a sham procedure. Patients with symptomatic GERD requiring maintenance PPI therapy were entered into the trial. A total of 78 patients were randomly assigned to undergo endoscopic full-thickness restructuring of the gastric cardia with transmural suture, while 81 patients underwent a sham procedure. Group assignments were revealed following the three-month evaluation. The primary end point was greater than or equal to 50% improvement in GERD HRQL score. Secondary end points included medication use and esophageal acid exposure. By intention-to-treat analysis, at three months, the proportion of patients achieving greater than or equal to 50% improvement in GERD-HRQL score was significantly greater in the active group (56%) compared to the sham group (18.5%; $p < 0.001$). Complete cessation of PPI therapy was higher among patients in the active group than in the sham group by intention-to-treat analysis (50% versus 24%; $p = 0.002$). The percent reduction in median percent time pH less than four was significantly improved within the active group versus baseline (7 versus 10, 18%, $p < 0.001$) but not in the sham group (10 versus 9, -3%, $p = 0.686$). Between-group analysis revealed the active therapy to be superior to the sham in improving median percent time pH less than 4 ($p = 0.010$). Twenty-four patients randomized in the study were lost to follow-up or excluded from further study because they were ruled ineligible by entry criteria. The authors stated, “Further studies, including those with longer term follow-up, will help clarify the role of this promising procedure across a broader range of patients with GERD” (Rothstein, et al., 2006).

In a multicenter trial, 64 patients underwent plication to assess the safety and efficacy of endoscopic full-thickness plication. At six months after plication, PPI therapy had been eliminated in 74% of previously medication-dependent patients. Authors believe this study showed that a single full-thickness plication placed at the gastroesophageal junction reduced symptoms, medication use, and esophageal acid exposure associated with GERD. Fifty-seven patients completed the 12-month study follow-up (Pleskow, et al., 2005). After one year, improvements were sustained in the GERD-specific quality of life questionnaires, and there was a reduction in PPI dependence. No new adverse events were reported. The limitation to this study is the lack of a sham treatment group for comparisons of outcomes. The authors stated the procedure is durable at one year and may be a viable treatment option for patients who require chronic antisecretory treatment (Pleskow, et al., 2004).

Technology Assessments/Reviews

Torquati et al. (2007) conducted an evidence-based review of the literature of FDA-approved modalities of endoluminal treatment of GERD. Sixteen studies met the inclusion criteria, representing 787 patients. The studies were categorized according to the guidelines for levels of evidence and grades of

recommendation supplied by the Oxford Centre for Evidence-Based Medicine. The authors concluded, "The methodological quality of most of the included studies was average; four studies were grade 1b (individual randomized trial), 10 were grade 2b (individual cohort study), and two were grade 3b (individual case-control study). There is grade 1b and 2b evidence demonstrating the EndoCinch plication is effective in reducing GERD symptoms at short-term follow up. However, in the majority of the studies analyzed, the procedure does not significantly reduce the acid exposure in the distal esophagus. The majority of the studies with long-term outcome showed disappointing outcomes, probably due to suture loss in the majority of patients. There is grade 1b and 2b 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 reduce significantly the acid exposure in the distal esophagus. There is grade 1b and 2b evidence demonstrating that full-thickness plication is effective in reducing GERD symptoms, and acid exposure in the distal esophagus" (Torquati, et al., 2007).

In a review of endotherapy for GERD, the author concluded that the target population for GERD endotherapy currently consists of PPI-dependent GERD patients who have < 2 cm or no sliding hiatal hernia and without severe esophagitis or Barrett's esophagus. The Stretta procedure and the NDO plicator have been analyzed in sham-controlled studies. Safety of these procedures has been reported, but serious morbidity, including rare mortality has been reported. The author concluded that additional comparative, long-term studies are needed to determine the role of endoscopic procedures (Triadafilopoulos, 2007).

In 2005, the Agency for Healthcare Research and Quality issued a report on the Comparative Effectiveness of Management Strategies for GERD. The authors concluded, "The quality, quantity, and consistency of studies on the endoscopic approaches to treatment of GERD are inferior to those of medical or surgical therapy, which can be expected since endoscopic approaches are new developments and data are evolving. At present, their efficacy compared with continued (or intensified) medical therapy is unclear. Sham controlled trials have demonstrated that some of the benefits of these procedures observed in the uncontrolled trials may not be directly attributable to the interventions, thus underscoring the need for additional sham-controlled trials. Although these devices are already commercially available, their long term efficacy and safety have not yet been established" (Ip, et al., 2005).

In 2005, the National Institute for Clinical Excellence (NICE) issued an interventional procedure guidance document titled Endoluminal Gastroplication for GERD, reporting that the current evidence suggests that there are no major safety concerns associated with endoluminal gastroplication for GERD. However, evidence of efficacy is not adequate for this procedure to be used without special arrangements for consent and for audit or research.

In 2004, NICE issued an interventional procedure guidance document titled Endoscopic Injection of Bulking Agents for GERD. The authors report that the current evidence on the safety and efficacy of endoscopic injection of bulking agents for GERD does not appear adequate for this procedure to be used without special arrangements for consent and for audit or research.

Blue Cross/Blue Shield Technology Evaluation Center (TEC) Technology Assessment (2004) evaluated available evidence to determine the effect of endoscopic technologies on health outcomes, such as relief of symptoms, prevention of long-term complications, and adverse events. It was summarized that the procedures have not been compared to Nissen fundoplication in controlled trials, and the risks and benefits of the procedures compared to Nissen fundoplication are not established. The evidence does not permit conclusions on whether endoscopic suturing, radiofrequency energy delivery, or implantation of inert polymers for treatment of GERD improves health outcomes or is as beneficial as established alternatives. Therefore, it was concluded that endoscopic suturing, radiofrequency energy delivery, or implantation of inert polymers for treatment of GERD do not meet the TEC criteria.

In 2004, the Canadian Coordinating Office for Health Technology Assessment (CCOHTA) issued an assessment on endoscope-based treatments for GERD, stating the technologies are promising, but their place in healthcare is not established.

Professional Societies/Organizations

The American Gastroenterological Association (AGA) Institute Position Statement on the Use of Endoscopic Therapy for GERD states, "Most studies of endoscopic therapy have only limited follow-up information of a relatively small number of patients. Thus, the durability of these technologies beyond 1–2 years remains unclear. Short-term and long-term safety issues are unresolved, but serious adverse events led to the voluntary withdrawal of Enteryx by the manufacturer in September 2005 and suspension of the Gatekeeper clinical program in late 2005. The economics of all techniques for the patient, practitioner, and society are unknown. While newer devices and improvements in endoscopic anti-reflux techniques may yield better and more durable treatment outcomes, current data suggest that there are no definite indications for endoscopic therapy for GERD at this time. Both practitioners and patients need to be aware of the limitations in the evidence that exist with these devices at present" (Falk, et al., 2006b).

In 2005, the American College of Gastroenterology updated their 1999 Practice Guidelines for GERD. The committee recommendations state endoscopic therapy controls symptoms in selected patients with well-documented GERD. The techniques seem to improve reflux symptoms, although significant changes in lower esophageal pressure have not been documented. Less than 35% of the patients have demonstrated normalization of their intraesophageal acid exposure, which is measured by ambulatory pH testing. The available published manuscripts and abstracts leave many issues unresolved, including long-term durability, safety and efficacy of endoscopic therapies performed outside of clinical trials with efficacy in atypical presentations of GERD, among others.

American Society for Gastrointestinal Endoscopy (ASGE) Technology Assessment (2002) states there are no published sham-controlled trials among the endoscopic anti-reflux therapies. There are no published comparative trials evaluating the endoscopic anti-reflux therapies versus medical or surgical treatments. There is no established standardized training protocol and no credentialing or privileging guidelines regarding the adoption of endoscopic reflux therapies. The ASGE Technology Assessment concludes that a variety of endoscopic or endoluminal approaches are FDA approved and available or under development to treat GERD, and initial uncontrolled results are favorable; however, comparative and longer-term efficacy and safety data are needed.

Summary

There are several proposed modalities to treat gastroesophageal reflux disease (GERD) (i.e., medications, endoscopic therapies, surgery). For patients who have severe GERD, laparoscopic fundoplication remains the procedure of choice. Endoscopic therapy studies for the treatment of GERD have been prospective but generally not randomized or controlled. Patient selection criteria need to be optimized. Comparative studies between the different endoscopic therapies are needed. Large, well-designed, controlled trials showing long-term safety and efficacy outcomes are lacking.

Coding/Billing Information

Note: This list of codes may not be all-inclusive.

Experimental/Investigational/Unproven/Not medically necessary:

| CPT* Codes | Description |
|--------------------|---|
| 43201 [†] | Esophagoscopy, rigid or flexible; with directed submucosal injection(s), any substance |
| 43236 [†] | Upper gastrointestinal endoscopy including esophagus, stomach, and either the duodenum and/or jejunum as appropriate; with directed submucosal injection(s), any substance |
| 43257 | Upper gastrointestinal endoscopy including esophagus, stomach, and either the duodenum and/or jejunum as appropriate; with delivery of thermal energy to the muscle of lower esophageal sphincter and/or gastric cardia, for treatment of gastroesophageal reflux disease |
| 0133T | Upper gastrointestinal endoscopy, including esophagus, stomach, and either the duodenum and/or jejunum as appropriate, with injection of implant material into and along the muscle of the lower esophageal sphincter (eg, for treatment of |

| | |
|--|---|
| | gastroesophageal reflux disease) (Code deleted 6/30/07) |
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†Note: Experimental, investigational or unproven and not medically necessary when used to report endoscopic anti-reflux procedures performed for the treatment or management of gastroesophageal reflux disease (GERD)/esophageal reflux.

| HCPCS Codes | Description |
|-------------|---|
| C9724 | Endoscopic full-thickness placcation in the gastric cardia using endoscopic placcation system (EPS); includes endoscopy |

| ICD-9-CM Diagnosis Codes | Description |
|--------------------------|--------------------|
| 530.11 | Reflux esophagitis |
| 530.81 | Esophageal reflux |
| | All other codes |

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