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Review Article

Endoscopic management of gastroesophageal reflux disease in 2012: What works and what doesn't

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Abstract

Gastroesophageal reflux disease results primarily from the loss of an effective antireflux barrier, which forms a mechanical barrier against the retrograde movement of gastric contents. Multiple devices have been developed for the endoscopic treatment of GERD, using approaches such as sewing, transmural fasteners, endoscopic staplers, and thermal treatment. Devices that are currently commercially available for the endoscopic treatment of GERD in the US include: EndoCinch; EsophyX; Stretta. This article will highlight the endoscopic therapy of gastroesophageal reflux disease with focus on Stretta and EsophyX.

Key words

Endoluminal radiofrequency ablative technology, gastroesophageal reflux disease, fundoplication, stretta procedure

Introduction

Gastroesophageal reflux disease (GERD) results primarily from the loss of an effective antireflux barrier, which forms a mechanical barrier against the retrograde movement of gastric contents. Multiple devices have been developed for the endoscopic treatment of GERD, using approaches such as sewing, transmural fasteners, endoscopic staplers, and thermal treatment. Other devices that have been developed involve injection or implantation of foreign materials but are not commercially available. Devices that are currently commercially available for the endoscopic treatment of GERD in the US include: EndoCinch (C. R. Bard, Inc., Murray Hill, NJ); EsophyX (EndoGastric Solutions, Redwood City, CA); Stretta (Mederi Therapeutics, Greenwich, CT). The SRS endoscopic stapling system (MediGus Ltd., Tel Aviv, Israel) is currently under study. Devices that are no longer or never became commercially available for the treatment of GERD include: Endoscopic Suturing Device (ESD) (Cook Medical Inc., Bloomington, IN); NDO Plicator (NDO Surgical Inc., Mansfield, MA); Syntheon AntiReflux Device (ARD) (Syntheon, Miami, FL); His-Wiz Device (Olympus, Tokyo, Japan); Enteryx procedure (Boston Scientific, Natick, MA); Gatekeeper Reflux Repair System (Medtronic, Minneapolis, MN); Durasphere GR (Carbon Medical Technologies, Inc., St. Paul, MN). Since the long-term data with Endocinch have not been promising, we will not discuss this technology and we will focus on Stretta and EsophyX.

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Stretta

Application of controlled radiofrequency (RF) energy to the lower esophageal sphincter region (Stretta procedure) induces collagen contraction and has been shown to have therapeutic benefits in patients with GERD.[1] Stretta appears to reduce postprandial transient lower esophageal sphincter relaxations, may decrease esophageal acid sensitivity, and may improve gastroparesis. The four-channel radiofrequency (RF) generator and catheter system delivers pure sine-wave energy. Each needle tip incorporates a thermocouple that automatically modulates power output to maintain a desired target (muscle) tissue temperature. Maintaining lesion temperatures below 100°C minimizes the collateral tissue damage due to vaporization and high impedance values. Temperature is similarly monitored with a thermocouple at each needle base, and power delivery ceases if the mucosal temperature exceeds 47°C.

The RF catheter is passed by mouth and positioned 1 cm above the z-line according to the distance measured during endoscopy. The four needle electrodes are deployed to a preset

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length of 5.5 mm and RF delivery commenced. Additional lesion sets are created by rotating and changing the linear position of the catheter so as to create several rings of lesions 1 cm above and below cardia.

One randomized trial included 64 patients who were assigned to RF treatment or a sham procedure.[2] At six months, those who had undergone the RF procedure were significantly more likely to experience a >50 percent improvement in heartburn-related quality-of-life (HRQL) scores compared with sham treated patients (61 versus 30%) and were more likely to be without daily heartburn symptoms (61 versus 33%). The groups had similar median acid exposure times, though acid exposure time was significantly improved when responders (>30% decrease in heartburn score) were compared with non-responders.

In a second trial, 36 patients were assigned to a single session RF procedure (12 patients), a sham procedure (12 patients), or RF treatment with a repeat RF treatment if GERD health-related quality of life (HRQL) was not 75% improved after four months (12 patients, 10 of whom underwent a second RF procedure).[3] Patients who underwent RF procedures had greater improvements in HRQL scores at 12 months than patients who underwent sham therapy, and patients in the double RF group showed a greater improvement than patients who underwent a single treatment. In the single RF group two patients (17%) normalized their HRQL scores, in the double RF group seven patients (58%) normalized, and in the sham group no patients normalized. Similar findings were noted with regard to the number of patients no longer requiring GERD medications.

A nonrandomized, prospective, multicenter study included 118 patients who all received RF treatment for GERD.[4] Follow-up information was available for 94 patients (80 percent) at 12 months. Significant improvements were observed in the median heartburn, GERD, and satisfaction scores, and on the mental and physical components of the Medical Outcomes Study Short Form-36 (SF-36). The proportion of patients requiring proton pump inhibitors fell from 88 to 30%. Esophageal acid exposure improved significantly (from 10 to 6%).

The Vanderbuilt group stratified patients to either endoscopic therapy or laparoscopic fundoplication.[5] Patients were offered RF treatment if they did not have a hiatal hernia greater than 2 cm, had a lower esophageal pressure of at least 8 mmHg, and did not have Barrett's esophagus. At six months, the quality of life scores were similar in both groups and both groups were satisfied with their procedures (89% of RF treated patients and 96% of fundoplication patients). Fifty-eight percent of RF patients and 97% of fundoplication patients were off of PPI and an additional 31% of RF patients had reduced their PPI dose significantly. In a non-randomized cohort of 32 patients referred to a surgical practice who underwent RF treatment with an average follow-up of 53 months, 19 patients (59%) subsequently required anti-reflux surgery. Those not undergoing surgery showed a significant improvement in their GERD satisfaction scores from 3.1 to 1.5, but had significantly lower pre-procedure heartburn scores (2.4) than those who proceeded to surgery. The Stretta procedure was effective in reducing symptoms in 40 percent of patients.

RF treatment was also effective in improving GERD in selected obese patients (BMI>30). Obese patients are often not ideal candidates for fundoplication and are at increased risk of failure after antireflux surgery. In an Emory University retrospective study of 12 consecutive obese patients (mean body mass index 38.6) with GERD undergoing Stretta with a mean follow-up of 1.5 years, there were less patients on PPI medications after the procedure than before (45% versus 81%, P=0.1).[6]

Transoral incisionless fundoplication

Transoral incisionless fundoplication (TIF) with the EsophyX device has been reported to be effective in creating a continent gastro-esophageal valve and resulting in good functional outcomes, as measured by pH impedance in patients with GERD. Restoration of the incompetent antireflux barrier is possible by longitudinal and rotational advancement of the gastric fundus about the lower esophagus, creating an esophago-gastric fundoplication. The TIF technique enables the creation of a full-thickness esophago-gastric fundoplication with fixation extending longitudinally up to 3.5 cm above the Z-line and rotationally more than 270 degrees around the esophagus. A key element of the technique involves rotating the fundus around the esophagus with a tissue mold during gastric desufflation. Anatomic considerations and use of the device's tissue invaginator to push the esophagus caudally are important to ensure safe positioning of the plications below the diaphragm.[7]

In order to assess the structural changes of the gastro-esophageal junction (GEJ) following TIF, the Pittsburg group used the functional lumen imaging probe (FLIP) that employs impedance planimetry to measure the geometry of a distensible organ.[8] Two different approaches (TIF1.0 and 2.0) using the EsophyX™ device were performed in six and five animals, respectively. Three dogs underwent a sham procedure. FLIP measurements were performed pre- and post-procedure and at 2-week follow-up. Upper endoscopy, manometry, and 48-h pH testing were also performed at each time point. FLIP was also performed in ten patients before and 3 months after TIF. Following TIF procedures, there was a significant decrease in cross-sectional area (CSA) of GEJ compared to baseline; however, the CSA of both groups returned to baseline at 2-week follow-up. The FLIP results were supported with pH testing and correlated highly with both measures of GEJ structural integrity (LES and cardia circumference). Following TIF in humans, there was a decrease in GEJ distensibility compared to baseline that persisted to the 3-month evaluation. They

concluded that FLIP may measure and display changes in tissue distensibility at the GEJ and its results correlate with established methods of testing and evaluation of outcomes after transoral or laparoscopic antireflux surgery. FLIP correlated highly with LESP and cardia circumference, and these findings were supported with pH testing.

An Italian study aimed to assess the long-term effect of TIF in patients with symptomatic GERD.[9] The investigators performed the TIF 2.0 fundoplication in 42 consecutive patients who were all studied with GERD-HRQL and GERD-QUAL questionnaires, upper gastrointestinal (GI) endoscopy, esophageal manometry, and 24 h pH impedance before and at 6, 12, and 24 months after TIF. There were 26 patients with complete 24-month follow-up; 11 (42.3%) completely stopped PPI therapy, 7 (26.9%) more than halved it, and 8 (30.8%) were taking the same dose as before the procedure. Hiatal hernia and ineffective esophageal motility seemed to raise the risk of recurrence of symptoms (P=0.02 and P<0.001, respectively). The number of fasteners deployed during TIF was the only factor predictive of successful outcome (P=0.018).

The surgical group from UC Irvine reported their initial experience with 10 patients undergoing TIF in patients with prior esophageal and gastric surgery.[10] To assess their results, they used RAND-36 and Visual Analog Scale symptom scores that were collected at pre- and postoperative appointments for a mean of 9.2 months. The mean procedure time was 68 minutes. There were no intra-operative or postoperative complications. Patients with prior pancreatico-duodenectomy had reduced working space due to prior distal gastrectomy and required additional insufflation due to lack of pyloric resistance. The patient with prior fundoplication required additional time and force for fastener penetration of the resultant scar from the partially disrupted fundoplication. All patients were discharged within 23 hours of the procedure. Regarding medication use, three (38%) patients reported complete cessation of pharmaceuticals and four (50%) stated a reduced dosage and/or frequency whereas one (13%) still required her preoperative medical regimen. Similarly, patients' responses for symptomatic control showed four (50%) having complete control, three (38%) with partial control, and one (13%) reporting no change in symptom control. The mean RAND-36 scores were 71.4 pre-procedure and 76.3 post-procedure (P=0.18). The mean VAS scores were 0.55 pre-procedure and 0.41 post-procedure (P=0.20). There were no late complications.

The Boston Medical Center thoracic surgery group reported their initial experience with TIF.[11] Over a 24-month period, 46 patients (mean age, 49 years; 50% female) underwent 48 TIF procedures under general anesthesia. Two surgeons participated in all cases; one served as the endoscopist, and the other performed the partial fundoplication. Heartburn severity was measured using the GERD health-related quality of life (GERD-HRQL) instrument (best score=0, worst score=45), which included an additional question assessing overall satisfaction. Preoperatively, 33 (72%) of 46 patients had small (<3 cm) hiatal hernias, and none had undergone any previous anti-reflux procedures. Preoperative workup included manometry and barium esophagogram, with pH testing reserved for patients with atypical symptoms or typical symptoms and a lack of response to proton-pump inhibitors. The mean procedure time was 83 minutes (range, 36-180 minutes). The mean procedure time decreased after the first 5 cases from 122 to 78 minutes (P=.001). Mean length of stay was 1.3 days. One patient was readmitted with aspiration pneumonia. Three patients had minor complications (1 had minor bleeding from a suture site and 2 had urinary retention). There were no peri-operative deaths. Mean follow-up was 140 days. The mean GERD-HRQL scores improved significantly (23 vs 7; P<.001). There were 22 patients with follow-up greater than 90 days (mean follow-up, 240 days). GERD-HRQL scores remained significantly improved for these patients (23 vs 8; P=.001). Four patients from the entire group (8.6%) had no improvement, in 3 instances due to breakdown of the wrap. Two patients were treated with repeat endoscopic fundoplication and 1 was treated with laparoscopic Nissen fundoplication, and all had a significant improvement in symptoms after reoperation.

The use of laparoscopic hiatal hernia repair (HHR) can augment the use of transoral fundoplication without introducing the side effects of laparoscopic fundoplication. A retrospective community-based study evaluated the safety and symptomatic outcomes of the TIF procedure with or without HHR in patients with GERD.[12] Forty-eight patients underwent TIF using EsophyX in 3 community hospitals; those who presented with a hiatal hernia 3 cm or more in the greatest transverse diameter underwent laparoscopic HHR before TIF. Forty-two patients completed follow-up assessment at a median of 6 (range 1–11) months. Laparoscopic HHR was performed in 18 (43%) patients before TIF. There were no long-term postoperative complications. GERD-health related quality of life scores indicated heartburn elimination in 63% of patients. The need for daily proton pump inhibitor (PPI) therapy was eliminated in 76% of patients. Atypical symptom relief measured by the median reflux symptom index score reduction was significant (5 [0–47] vs 22 [2– 42] on PPIs, P<.001).

A GI physiology group from Modena, Italy assessed reflux parameters before and after EsophyX or laparoscopic fundoplication and their relationship with symptoms in patients with refractory GERD.[13] In an open-label study, they prospectively enrolled patients with heartburn/regurgitation that were persisting despite high-dose PPI therapy. Impedance-pH monitoring was performed on PPI therapy before intervention and off PPI therapy 3 months after intervention. Ten patients chose to undergo EsophyX while ten chose laparoscopic fundoplication, and their baseline characteristics were comparable. Distal and proximal reflux

events were significantly reduced post-operatively in the surgical but not in the endoscopic group and the median values were significantly lower in the former than in the latter. The esophageal acid exposure time was normal in 50% of cases after EsophyX and in 100% of cases after surgery (P=0.033); the number of distal refluxes was normal in 20% and 90% of cases (P=0.005) and the number of proximal refluxes was normal in 40% and 100% of cases (P=0.011), respectively. A positive persisting symptom-reflux association was found post-operatively in 6/10 patients in the EsophyX group and in 0/10 patients in the surgical group (P=0.011). The authors concluded that, in patients with refractory GERD, EsophyX is significantly less effective than laparoscopic fundoplication in improving reflux parameters and accordingly, in inducing symptom remission.

Conclusion

Overall, given the potential risks of novel endoscopic techniques for the management of GERD, there is an imperative need for well designed trials that are randomized prospective, sham-controlled, reproducible, long-term and adequately powered. Vigilance on the emerging data with endoscopic therapies and juxtaposition of such data to the ones from other options for GERD, such as medical and surgical therapies, are recommended as follows: (1) select the best candidates for fundoplication or endoscopic therapy, (2) availability of a well qualified laparoscopic surgeon and endoscopist, (3) long-term surgical and endoscopic therapy outcomes, (4) problems with redo surgery (in patients after fundoplication), (5) management of regurgitation and extraesophageal symptoms.

A stringent definition of symptoms and measurement of discontinuation, rather than reduction, of antisecretory medications would strengthen future studies. With the new modes of plication using TIF showing promise, continued improvement in endoluminal radiofrequency ablative technology and continuing research to break new ground, the future looks promising in spite of significant setbacks. The process of establishing endoluminal technology to control GERD is in its infancy, but a strong study design from the outset will move its growth with greater speed and efficiency.[14]

References

1. Triadafilopoulos G, Dibaise JK, Nostrant TT, Stollman NH, Anderson PK, Edmundowicz SA, *et al.* Radiofrequency energy delivery to the gastroesophageal junction for the treatment of GERD. Gastrointest Endosc 2001;53:407-15.
2. Corley DA, Katz P, Wo JM, Stefan A, Patti M, Rothstein R, *et al.* Improvement of gastroesophageal reflux symptoms after radiofrequency energy: A randomized, sham-controlled trial. Gastroenterology 2003;125:668-75.
3. Aziz AM, El-Khayat HR, Sadek A, Mattar SG, McNulty G, Kongkam P, *et al.* A prospective randomized trial of sham, single-dose Stretta, and double-dose Stretta for the treatment of gastroesophageal reflux disease. Surg Endosc 2010;24:818-25.
4. Triadafilopoulos G, DiBaise JK, Nostrant TT, Stollman NH, Anderson PK, Wolfe MM, *et al.* Stretta procedure for the treatment of GERD: 6 and 12 month follow-up of the U.S. open label trial. Gastrointest Endosc 2002;55:149-56.
5. Richards WO, Houston HL, Torquati A, Khaitan L, Holzman MD, Sharp KW. Paradigm shift in the management of gastroesophageal reflux disease. Ann Surg 2003;237:638-47.
6. White B, Jeansonne LO, Cook M, Chavarriaga LF, Goldenberg EA, Davis SS, *et al.* Use of endoluminal antireflux therapies for obese patients with GERD. Obes Surg 2009;19:783-7.
7. Bell RC, Cadière GB. Transoral rotational esophagogastric fundoplication: Technical, anatomical, and safety considerations. Surg Endosc 2011;25:2387-99.
8. Hoppo T, McMahon BP, Witteman BP, Kraemer SJ, O'Rourke RW, Gravesen F, *et al.* Functional lumen imaging probe to assess geometric changes in the esophagogastric junction following endolumenal fundoplication. J Gastrointest Surg 2011;15:1112-20.
9. Testoni PA, Vailati C, Testoni S, Corsetti M. Transoral incisionless fundoplication (TIF 2.0) with EsophyX for gastroesophageal reflux disease: Long-term results and findings affecting outcome. Surg Endosc 2011 Dec 15. [Epub ahead of print].
10. Nguyen A, Vo T, Nguyen XM, Smith BR, Reavis KM. Transoral incisionless fundoplication: Initial experience in patients referred to an integrated academic institution. Am Surg 2011;77:1386-9
11. Narsule CK, Burch MA, Ebright MI, Hess DT, Rivas R Jr, Daly BD, *et al.* Endoscopic fundoplication for the treatment of gastroesophageal reflux disease: Initial experience. J Thorac Cardiovasc Surg 2012;143:228-34.
12. Ihde GM, Besancon K, Deljkich E. Short-term safety and symptomatic outcomes of transoral incisionless fundoplication with or without hiatal hernia repair in patients with chronic gastroesophageal reflux disease. Am J Surg 2011;202:740-6.
13. Frazzoni M, Conigliaro R, Manta R, Melotti G. Reflux parameters as modified by EsophyX or laparoscopic fundoplication in refractory GERD. Aliment Pharmacol Ther 2011;34:67-75.
14. Jafri SM, Arora G, Triadafilopoulos G. What is left of the endoscopic antireflux devices? Curr Opin Gastroenterol 2009;25:352-7.

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