

ADVANCES IN ENDOSCOPY

Current Developments in Diagnostic and Therapeutic Endoscopy

Section Editor: Todd H. Baron, MD

Endoscopic Approaches for the Treatment of Gastroesophageal Reflux Disease



Ronnie Fass, MD

Professor of Medicine, Case Western Reserve University
 Medical Director, Digestive Health Center
 Director, Division of Gastroenterology and Hepatology
 Head, Esophageal and Swallowing Center
 MetroHealth Medical Center
 Cleveland, Ohio

G&H When should endoscopic therapy, rather than surgical therapy, be considered for the treatment of gastroesophageal reflux disease?

RF Endoscopic therapy for the treatment of gastroesophageal reflux disease (GERD) has been in a great position for the last decade because fewer patients are interested in chronic medical therapy with proton pump inhibitors (PPIs) due to the potential for adverse events. Similarly, more patients are looking for alternatives to antireflux surgery because of concerns about potential short- and long-term complications. Candidates for endoscopic therapy are those who exhibit typical symptoms of GERD, such as heartburn and regurgitation, and have low-grade erosive esophagitis (Los Angeles Grades A and B), endoscopy negative with abnormal esophageal acid exposure, a hiatal hernia smaller than 3 cm in size, and at least a partial response to PPI treatment. Patients with poor compliance with medical therapy, a desire to discontinue medical therapy, or a preference for nonmedical, nonsurgical therapy who are not interested in anti-reflux surgery and who meet the aforementioned criteria should be considered for endoscopic therapy for GERD.

G&H What endoscopic therapies are available for the treatment of GERD?

RF The currently used endoscopic therapies include an endoscopic radiofrequency ablation procedure (Stretta,

Restech), the transoral incisionless fundoplication (TIF, EndoGastric Solutions) procedure, and the Medigus Ultrasonic Surgical Endostapler (MUSE, Medigus) procedure.

G&H How are these procedures performed?

RF The Stretta procedure uses an endoluminal approach to deliver low-power, temperature-controlled, radiofrequency energy into the gastroesophageal junction. A 4-channel radiofrequency generator and an esophageal catheter with a bougie tip with an expanded basket are used to deploy 4 needle electrodes. The TIF procedure employs the Esophyx Z device to create an anterior full-thickness fundoplication, constructing a valve 3 to 5 cm in length and 200 to 300 degrees in circumference. The MUSE procedure also creates an anterior full-thickness fundoplication using a modified endoscope that incorporates a miniature camera, an ultrasound probe, and a stapler on its tip.

G&H How effective are endoscopic approaches compared with the use of PPIs or surgical therapy?

RF Not many studies have compared the efficacy of endoscopic procedures to PPIs or surgical fundoplication. In a randomized, small sample trial, the TIF procedure was compared to PPI therapy and was shown to control

patients' GERD symptoms and provide similar improvement in esophageal acid exposure in the short term (6 months). However, at 12 months, the TIF procedure normalized esophageal acid exposure in only 29% of the patients, and 61% of patients returned to PPIs. In a larger randomized, controlled trial, the TIF procedure was compared to PPI therapy in patients with GERD. Although both groups experienced a similar reduction in GERD-related symptoms, patients in the TIF group demonstrated a significantly better control of regurgitation.

The MUSE procedure was compared to laparoscopic fundoplication in a very small number of patients. Those in the MUSE group had a longer procedure time and lengthier stay in the hospital. Additionally, more patients used PPIs and fewer reported improvement in GERD health-related quality of life at 6 months post-procedure than did patients in the laparoscopic fundoplication group.

When compared with antireflux surgery, the Stretta procedure showed similar control of GERD symptoms and reduction in PPI use, but had less effect on improving the typical GERD symptoms and had a higher rate of repeat intervention after 3 years.

G&H What are the main benefits and challenges associated with treating GERD via an endoscopic approach?

RF Presently, endoscopic procedures have a unique position in GERD management. There is a marked decline in the number of surgical funduplications performed annually in the United States at a time when more patients are interested in alternatives to chronic PPI treatment. The main benefit of endoscopic therapy is that it provides patients who cannot or do not wish to take chronic PPI treatment with a therapeutic option besides surgical intervention. Additional benefits are that these endoscopic approaches are outpatient procedures, are less expensive than surgical intervention, are relatively safe, are effective at controlling GERD symptoms, and can improve health-related quality of life.

The current challenges of endoscopic therapy include durability of the intervention, a lack of normalization of esophageal acid exposure in most patients, and a limited effect on healing erosive esophagitis as well as lower esophageal sphincter basal pressure. Candidates for endoscopic therapy are carefully selected and need to meet rigorous inclusion criteria. Endoscopic therapy should be performed by expert endoscopists who routinely perform the procedures, with surgery as backup. Lastly, reimbursement of endoscopic therapy has been a great challenge and has somewhat limited the use of these procedures in clinical practice.

G&H What are the most common adverse events associated with endoscopic therapy? How can complications be managed or prevented?

RF The complication rate of the TIF procedure ranges between 3% and 10%. Major complications are uncommon and may include bleeding, perforation, pneumothorax, mediastinal abscess, and mucosal tear. Additional side effects include dysphagia, chest pain, sore throat, and bloating. Reports of complications after the MUSE procedure have been limited to very few studies. Major complications may affect approximately 6% of patients and include pneumothorax, esophageal leak, pneumomediastinum, and bleeding. Minor adverse events may affect up to 22% of patients and include dysphagia, chest pain, and sore throat. Adverse events of the Stretta procedure occur at a rate of approximately 1% and include mucosal lacerations, erosions, prolonged gastroparesis, bleeding, pleural effusion, pneumonia, and mediastinal inflammation.

Although complications from gastrointestinal procedures, including endoscopic therapy, are many times inevitable, steps should be taken to reduce them and improve their outcome. Careful patient selection is pivotal to improve clinical outcome and minimize adverse events. Operators of the procedure should be well trained, highly experienced, provided with all the equipment and staff needed to perform the procedure, and have sufficient patient volume to ensure performance of the technique on a regular basis. Major adverse events should be identified early, and proper therapy should be instituted as soon as possible. Endoscopic or surgical interventions may be needed in a very small subset of patients.

G&H How common is symptom recurrence, and are repeat interventions likely, with endoscopic therapy?

RF Very few studies have prospectively investigated different data points that evaluated symptom recurrence over time, preventing clinicians from better assessing the durability of the procedures. In addition, symptomatic response may decrease over time following endoscopic intervention without necessarily complete symptom recurrence. Of the patients undergoing the TIF procedure, after 1 year, between 15% and 58% reported having GERD symptoms. In the case of the MUSE procedure, approximately 27% of patients demonstrated GERD symptoms 2 years postprocedure. With the Stretta procedure, which has the longest follow-up evaluation (>10 years), up to 42% of the patients demonstrated GERD symptoms.

For both the TIF and the MUSE procedures, recurrence of symptoms is either managed conservatively with medical therapy or with surgical fundoplication. In the case of the Stretta procedure, symptom recurrence may also be treated with endoscopic intervention.

G&H In whom are these endoscopic approaches contraindicated?

RF Endoscopic therapy should be avoided in morbidly obese patients; those who have scleroderma, a history of esophageal or gastric surgery, a major esophageal motor disorder (eg, achalasia, jackhammer esophagus, absent contractility, distal esophageal spasm, and esophagogastric junction outflow obstruction), an esophageal stricture, Barrett esophagus, or esophageal or gastric varices; and in pregnant or lactating women. There is a paucity of information about the value of endoscopic therapy in patients with atypical or extraesophageal presentations of GERD.

G&H Have any cost-effectiveness studies been performed regarding the use of endoscopic approaches for GERD?

RF A recent cost-effectiveness analysis evaluated medical, endoscopic, and surgical treatments for adults with GERD who require daily PPI therapy. In the base case analysis, which assumed a PPI cost of \$234 over 6 months, the Stretta procedure and laparoscopic Nissen fundoplication were the most cost-effective options over a 30-year period. If the cost of PPI therapy exceeded \$90.63 per month over 30 years, laparoscopic Nissen fundoplication became the dominant treatment option. In this model, the TIF procedure was dominated by laparoscopic Nissen fundoplication at all points in time.

G&H Are any endoscopic techniques currently in development?

RF Antireflux mucosectomy can narrow the gastric cardia opening by scar formation (up to 270 degrees). Endoscopic band ligation at the esophagogastric junction may also lead to local scarring. Other techniques that have been described in the literature include peroral endoscopic cardiac constriction with band ligations in

the greater and lesser curvature, mucosal resection followed by plication, and submucosal injection of a bio-compatible substance.

G&H What are the priorities of research in this field?

RF Durability assessment of all endoscopic procedures is still needed, especially for the TIF and MUSE techniques. The value of these procedures in patients with atypical and extraesophageal manifestations of GERD or in unique clinical scenarios, such as post-peroral endoscopic myotomy and post-sleeve gastrectomy, also requires further research.

Dr Fass serves as an advisor to Ironwood Pharmaceuticals, Takeda, and Chinoin. He has also served as a speaker for AstraZeneca, Takeda, Horizon, Cadila Pharmaceuticals, Diversatek, and Eisai, and has received research funds from Ironwood Pharmaceuticals and Salix.

Suggested Reading

Fass R. An overview of transoral incisionless fundoplication and magnetic sphincter augmentation for GERD. *Gastroenterol Hepatol (NY)*. 2017;13(1):50-52.

Fass R, Cahn F, Scotti DJ, Gregory DA. Systematic review and meta-analysis of controlled and prospective cohort efficacy studies of endoscopic radiofrequency for treatment of gastroesophageal reflux disease. *Surg Endosc*. 2017;31(12):4865-4882.

Funk LM, Zhang JY, Drosdeck JM, Melvin WS, Walker JP, Perry KA. Long-term cost-effectiveness of medical, endoscopic and surgical management of gastroesophageal reflux disease. *Surgery*. 2015;157(1):126-136.

Khan F, Maradey-Romero C, Ganocy S, Frazier R, Fass R. Utilization of surgical fundoplication for patients with gastro-oesophageal reflux disease in the USA has declined rapidly between 2009 and 2013. *Aliment Pharmacol Ther*. 2016;43(11):1124-1131.

Lipka S, Kumar A, Richter JE. No evidence for efficacy of radiofrequency ablation for treatment of gastroesophageal reflux disease: a systematic review and meta-analysis. *Clin Gastroenterol Hepatol*. 2015;13(6):1058-1067.e1.

Nabi Z, Reddy DN. Update on endoscopic approaches for the management of gastroesophageal reflux disease. *Gastroenterol Hepatol (NY)*. 2019;15(7):369-376.

Richter JE, Kumar A, Lipka S, Miladinovic B, Velanovich V. Efficacy of laparoscopic Nissen fundoplication vs transoral incisionless fundoplication or proton pump inhibitors in patients with gastroesophageal reflux disease: a systematic review and network meta-analysis. *Gastroenterology*. 2018;154(5):1298-1308.e7.

Testoni PA, Mazzoleni G, Testoni SG. Transoral incisionless fundoplication for gastro-esophageal reflux disease: techniques and outcomes. *World J Gastrointest Pharmacol Ther*. 2016;7(2):179-189.

Witteaman BP, Conchillo JM, Rinsma NF, et al. Randomized controlled trial of transoral incisionless fundoplication vs. proton pump inhibitors for treatment of gastroesophageal reflux disease. *Am J Gastroenterol*. 2015;110(4):531-542.