

ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

Section Editor: Prateek Sharma, MD

Endoscopic Therapies for Gastroesophageal Reflux Disease



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G&H What are the most common endoscopic procedures used for the treatment of gastroesophageal reflux disease?

MD Currently, the available endoscopic therapies for gastroesophageal reflux disease (GERD) are transoral incisionless fundoplication (TIF2, eg, EsophyX device), radiofrequency energy application (Stretta), and novel emerging therapies such as antireflux mucosal ablation using argon plasma coagulation and antireflux mucosal resection. TIF can be performed by itself, or if there is a large hiatal hernia (>2 cm), the procedure can be performed in conjunction with a surgeon, reducing the hiatal hernia. This is known as combined TIF and hiatal hernia repair (cTIF). There are other options that may not be available in North America, one of which is plication therapy, or gastric plication using the GERDx device, approved in Europe. Recently, a randomized sham-controlled trial showed safety and efficacy of this device at 12 months.

G&H What has the latest research shown regarding the efficacy and safety of these procedures for the treatment of GERD?

MD In general, there are high-quality data for TIF2 with the EsophyX device. At least 5 randomized controlled trials (RCTs) and several retrospective studies have shown that in the short term it works very well with significant reduction in GERD symptoms as well as a high rate of discontinuation of proton pump inhibitor (PPI) medication. The TEMPO trial has 5-year data showing that the efficacy was sustainable in 86% of patients who underwent endoscopic antireflux TIF. Results of a large-scale

multicenter trial evaluating cTIF (NCT04795934) will be available in a few years and may increase understanding of whether endoscopic antireflux therapy, in conjunction with surgery, is as good as the current gold standard of care, which is laparoscopic Nissen fundoplication. Data on the Stretta procedure have been relatively hit or miss owing to several issues with the technology or reimbursement. However, retrospective reports of radiofrequency energy application have shown a sustainable impact over 10 years in a subgroup of patients. At least 4 RCTs, most of them published before 2012, show that the modality works well in the short term (approximately 12 months of follow-up). In general, for both TIF2 and Stretta, short-term data show efficacy, decrease in GERD symptom scores, and decrease in PPI usage; however, robust long-term data are lacking, and that is one of the big caveats of these therapies.

G&H What are some of the benefits and challenges associated with endoscopic therapies compared with the use of PPIs or surgery?

MD With PPIs, the main challenge is the growing amount of literature pointing toward some type of side effect or adverse event associated with long-term use, be it the impact on the kidneys, cognitive decline, increased risk of enteric infection or *Clostridioides difficile* infection, pneumonia, and so forth. This increases patients' perspectives on taking a medication long term, even though a recent RCT showed no significant association with most adverse events when PPIs are used over 3 to 5 years. However, more high-quality prospective data are needed to confirm any true causation in the long term. For most

patients with GERD, the condition affects quality of life for the life of the patient. Many patients are not comfortable with having to take a medication, which may not provide substantial relief, for the rest of their lives. Thus, GERD patients experience a lot of anxiety because of the possibility of side effects and the implications of

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long-term therapy. On the other hand, some patients may be intolerant to these medications, and a substantial proportion do not have 50% relief in symptoms after taking higher doses of medications. That brings surgery and other therapies forward.

Currently, surgical antireflux therapies are considered the standard of management with the hope of achieving curative remission; however, surgery being selective in nature is offered to a minority of patients with GERD. Unfortunately, data show that under the best circumstances nearly 35% of patients may have recurrence of reflux disease after laparoscopic fundoplication. Another caveat is that any repeated surgery is challenging for disrupted fundoplication or slipped fundoplication with hernia, which is not uncommon after a few years. Fundoplication also may be associated with complications, such as gas-bloat syndrome, bloating, diarrhea, and dysphagia.

Endoscopic therapy offers multipurpose benefits as a definitive therapy, bridge therapy, or in conjunction with or after surgical therapy for recurrence of symptoms in selective cases. It can be offered to patients with the understanding that the impact may be less durable (eg, 3-5 years), but the complication rate is low compared with that of surgery. Even temporary discontinuation of antireflux therapy, including PPIs or histamine 2 blockers, is a substantial relief for the patient. Cost-effectiveness studies comparing endoscopic therapy with surgery and lifelong PPI therapy have shown a benefit toward endoscopic therapy. Another benefit is that patients who have had an endoscopic therapy and experience recurrence of symptoms could undergo the endoscopic therapy again. Finally, perioperative mortality and morbidity are low

with endoscopic therapy compared with surgical therapy. The challenge with current endoscopic antireflux therapy is that it is not advisable in the patient with a substantial hiatal hernia. Prior data examining endoscopic therapies included only patients who had a small hiatal hernia (<2 cm), mild or no esophagitis (Los Angeles Classification grade A or B), absence of esophageal motility disorder, and long-term PPI therapy or resistant GERD. Endoscopic therapy is not considered for patients with a large hiatal hernia (>2 cm) because of risk of failure. However, cTIF currently under investigation (NCT04795934) could address this issue and perhaps avoid postoperative complications associated with the current standard of care for surgical management of GERD. In addition, cTIF may provide similar durable efficacy as surgical fundoplication and could be repeated in the future if there is recurrence of symptoms compared with revision surgical fundoplication.

G&H When should patients with GERD be considered for an endoscopic therapy?

MD Currently, per the clinical trials, endoscopic antireflux therapy is indicated for patients with confirmed GERD who have a hiatal hernia of less than 2 cm, who want to discontinue PPI or any medical therapy or have intolerance to medical therapy, and who have a history of Barrett esophagus and/or concurrent dysplasia. Patients who are not surgical candidates or prefer minimally invasive endoscopic therapy are also eligible. Patients who have a hernia larger than 2 cm and patients with underlying or coexisting conditions (eg, esophageal motility disorders) are not eligible. Increasing data have demonstrated that eventually with cTIF, gastroenterologists will be able to offer endoscopic therapy to a larger subset of patients.

G&H How do you decide which endoscopic approach to use among the currently available options?

MD The decision to use an endoscopic approach starts with a discussion with the patient and a review of their underlying anatomic changes. This involves high-quality upper endoscopy with measurements of the hiatus and antireflux barrier using the available grading tools. These include Hill grading to assess the hiatus, as well as the American Foregut Society grading, which was published September 2022 in a white paper. The measurement of flap valve integrity and hiatal hernia is integral in deciding what therapy to offer to the patient.

When a patient has a 2-cm or smaller hernia, per available data, the endoscopic antireflux therapy option to offer is TIF2 because that has robust data of benefit.

When TIF2 is not available, and the patient is not a good surgical candidate, the Stretta radiofrequency device (if available and patient reimbursement is possible) can be pursued. Other options for patients with no substantial hiatal hernia, such as endoscopic antireflux mucosal ablation using hybrid argon plasma coagulation and band mucosectomy, could also be considered by gastroenterologists able to perform the procedures. Currently, these therapies are not designated for GERD, and there are no long-term data to show durable benefit.

G&H What do the recently updated guidelines on GERD management recommend for the use of an endoscopic therapy?

MD The current guidelines from the American College of Gastroenterology and American Gastroenterological Association, as well as the surgical societies, recognize the role of endoscopic antireflux therapies, and they also acknowledge that this role is still evolving. This is important because currently the standard of care for GERD management is still surgical fundoplication. The ongoing multicenter trial on cTIF (NCT04795934) may show

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data in favor or against endoscopic antireflux therapies. Having said that, endoscopic antireflux therapy could still be considered in patients who want to avoid invasive surgery, understand the benefits and limitations of the therapy, and are otherwise candidates for endoscopic antireflux therapy or TIF2, if they have a small hiatal hernia.

G&H In what other instances might an endoscopic approach for GERD be considered?

MD That is a good question, and this area is changing rapidly. Patients with sleeve gastrectomy could be considered one of the special populations in which the role of endoscopic antireflux therapy could be explored. Results of a meta-analysis of several studies have shown that these individuals are at high risk for new-onset GERD. In fact, Barrett esophagus, a long-term complication of GERD, could develop in these patients as early as 3 to 5 years after surgery. In the population who had anatomic alteration of the stomach and are having a significant amount of reflux, performing another surgery, especially when the stomach

size has been reduced, could be challenging. The second population for which the role of endoscopic antireflux therapy can be explored is patients who experience new GERD after peroral endoscopic myotomy for management of achalasia. Finally, it could be worth exploring use of endoscopic antireflux therapy in individuals with scleroderma or gastroparesis who have a significant amount of reflux. These patients unfortunately must rely on medications without substantial benefit because they have some form of anatomic modification or a functional problem that cannot be overcome by medication alone. Surgeons are hesitant to perform any form of surgery in these patients because they may develop more difficulty swallowing. Endoscopic antireflux therapy may not provide a sustained, durable benefit in these situations; however, it may ameliorate a proportion of symptoms and reduce the medication burden for these patients.

G&H When is an endoscopic approach to treatment not appropriate?

MD The currently existing endoscopic therapies are not targeting hiatal hernias larger than 2 cm. Unfortunately, most patients with GERD have some form of weakness in the antireflux barrier, mainly their hiatus. This creates a problem in terms of ongoing reflux. Because existing TIF technology includes reduction of small hiatal hernias only, patients with large hernias (>2 cm) must undergo hernia correction first, before any other form of endoscopic therapy.

G&H Why are endoscopic therapies for GERD underutilized?

MD There could be several reasons. Multiple endoscopic therapies and instruments have come forth, and then become extinct owing to lack of robust data on long-term efficacy. While medications have been overutilized, physicians as well as patients may not be aware of other options. With the advent of incisionless endoscopic interventions, the field of endoscopic antireflux therapies is evolving. However, currently, there is no standard-of-care endoscopic therapy for GERD. Consequently, many general gastroenterologists may not perform this type of therapy or perform follow-up of patients with possible complications or symptom recurrence in the short term after this therapy and may not know how to manage these patients. This is a challenge. I am hopeful that as knowledge of endoscopic therapies increases and guidelines support their use, more gastroenterologists and patients will consider such therapies as TIF2. In the past 5 years, more patients have been undergoing TIF2 therapy than there were 5 years earlier.

G&H Why are the recently updated guidelines on GERD management worthwhile for nongastroenterologists as well as gastroenterologists?

MD Knowledge regarding all the available options is very important for gastroenterologists as well as nongastroenterologists because nongastroenterologists see patients with GERD more often than gastroenterologists. These patients present to the gastroenterologist when reflux is not controlled, or they have coexisting conditions. At that point, approximately 75% of patients have already tried medications for reflux and may have already had side effects or a complication. Thus, education of nongastroenterologists is important. Failing to discuss all available options is a disservice to the patient. Many patients do not experience substantial relief in symptoms and yet continue to take medication, which predisposes them to a variety of complications related to the medication. Like with antibiotic stewardship, a discussion about PPI stewardship to minimize unnecessary medication utilization is necessary.

G&H Are you and your colleagues looking at any specific issues in the guidelines that are being developed?

MD We are looking at the role of endoscopic antireflux therapies in adults as well as the pediatric population. Through a consensus panel, we are systematically reviewing evidence (by the Grading of Recommendations Assessment, Development, and Evaluation criteria) to grade evidence and make recommendations using experts and a panel of different stakeholders that includes patient advocates. Our goal is to understand what the evidence recommends and where research should move toward in the future regarding the positioning of various therapies, including medications, lifestyle interventions, endoscopic therapies, and surgery, in the management of GERD.

G&H What might future research on endoscopic interventions for GERD evaluate?

MD Future research should not focus only on patients with small hiatal hernias but should develop strategies to correct the antireflux barrier and help a wider group of patients. At the same time, endoscopic therapies should be feasible in the way colonoscopy with polyp resection

is for all gastroenterologists. According to a large-scale survey study by Delshad and colleagues published in 2020, 1 in 3 individuals in North America may experience GERD and half of them take medications, including PPIs. In addition, many of the individuals surveyed did not have substantial relief in symptoms. Many of these patients could be a target for endoscopic antireflux therapy, especially patients with true acid reflux who are at risk for long-term side effects from medications affecting quality of life. This therapy will be useful to reduce not only the number of medications being overutilized, but also the impact of unnecessary surgery for some patients. Overall, future research should focus on routine management of GERD with therapies that can be easily applicable at a grassroots level and reproducible for any general gastroenterologist. Development of more options for special populations (eg, patients who had sleeve gastrectomy, patients with anatomic issues) also will be good for patient care.

Disclosures

Dr Desai has no relevant conflicts of interest to disclose.

Suggested Reading

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