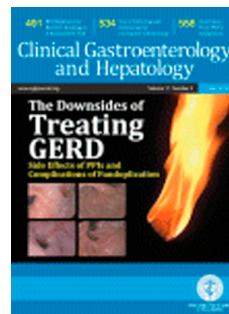


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Steven Park, Russell Weg, Vivek Kaul



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## **10 THINGS EVERY GASTROENTEROLOGIST SHOULD KNOW ABOUT ANTI-REFLUX SURGERY!**

Steven Park<sup>1</sup>, Russell Weg<sup>2</sup>, Vivek Kaul<sup>2</sup>

<sup>1</sup>Department of Internal Medicine, University of Rochester Medical Center, Rochester, NY

<sup>2</sup>Division of Gastroenterology & Hepatology, University of Rochester Medical Center, Rochester, NY

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### **Corresponding Author:**

Vivek Kaul, MD, FACG, FASGE, AGAF

Segal-Watson Professor of Medicine

Division of Gastroenterology & Hepatology

University of Rochester Medical Center & Strong Memorial Hospital

Ph: 585 275 4711

Fax: 585 276 0101

email: [Vivek\\_Kaul@urmc.rochester.edu](mailto:Vivek_Kaul@urmc.rochester.edu)

## **10 THINGS EVERY GASTROENTEROLOGIST SHOULD KNOW ABOUT ANTI-REFLUX SURGERY!**

Gastroesophageal reflux disease (GERD) was the most frequent outpatient gastroenterology diagnosis in 2009 with almost 9 million visits.[1] The mainstay of medical treatment for GERD are proton pump inhibitors (PPIs) which stop gastric acid production by irreversibly binding the proton pump in the parietal cells of the stomach. Up to 40% of patients with typical GERD symptoms are refractory to standard PPI therapy.[2] In cases of PPI-refractory GERD (or PPI intolerance), anti-reflux surgery is an effective alternative therapeutic option.

To aid in clinical decision making, we present a practical list of 10 things every gastroenterologist should know when considering anti-reflux surgery for their patient:

1. *The pathogenesis of GERD involves a dynamic interplay between the lower esophageal sphincter (LES) and pressure changes that promote reflux.*

The LES is a zone of high pressure located in the lower esophagus (figure 1). This zone consists of the intrinsic musculature of the distal esophagus, sling fibers of the gastric cardia and the crural diaphragm that together maintain tonic contraction and augment pressure. The diaphragm is an extraintestinal component of the esophagogastric junction (EGJ) that envelops the esophagus at the LES. Intact diaphragmatic crura augments the pressure at the LES, which is vital in preventing reflux of gastric contents.[3] Hiatal hernia, a pathologic displacement of the esophagus relative the diaphragm, compromises the LES's ability to withstand the transdiaphragmatic pressure gradient and is a key contributor to GERD. The LES competency determines the volume

of gastric refluxate entering the esophagus; the clearance of esophageal acid determines the duration of esophageal acid exposure (EAE).

GERD occurs when the intra-gastric pressure overcomes this high-pressure LES zone. This can occur by several mechanisms:

- a) Transient lower esophageal sphincter relaxation (t-LESR) is an important physiologic response to gastric distension by food and air and permits belching. However, over-distension of the stomach, via excess ingestion, increases the frequency of t-LESRs and predisposes to GERD.
- b) A hypotensive LES, often associated with a hiatal hernia and loss of the diaphragmatic “pinch,” compromises the mechanical barrier and results in increased reflux.
- c) The hiatal hernia itself contributes to GERD by increasing the frequency of t-LESRs and creating an “acid pocket” at the hernia sac that easily refluxes into the distal esophagus.[4]

Other factors contributing to GERD include medications, esophageal and systemic diseases (e.g. achalasia, scleroderma), obesity, pregnancy and delayed gastric emptying.

**2. *Anti-reflux surgery aims to increase basal LES pressure and decrease t-LESR frequency and magnitude to reduce reflux.***

Fundoplication is the primary form of laparoscopic anti-reflux surgery (LARS). There are several forms of fundoplication available (Nissen, Toupet, Dor, etc.), all of which address the anatomical factors that contribute to gastroesophageal reflux (GER)[5]. These include: (1) intra-abdominal re-positioning of the distal esophagus (i.e. reduction

of the hiatal hernia), (2) establishing the crural closure, (3) creating the fundoplication, and (4) ensuring the patency of a one-way valve (figure 2). These modifications aid in establishing an adequate intra-abdominal length of esophagus, increasing the basal LES pressure, decreasing the frequency of t-LESRs and inhibiting complete LES relaxation, all of which help reduce GER.

### **3. Current guidelines regarding indications for anti-reflux surgery are limited and suboptimal.**

The guidelines published by the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) and the American College of Gastroenterology (ACG) agree to recommend surgical options for GERD for the following reasons:[6, 7]

- a) Desire to discontinue medical therapy (i.e., expense, quality of life, side effects).
- b) Non-compliance with medical therapy.
- c) Failed medical management (i.e. persistent symptoms, peptic stricture, esophagitis refractory to medical therapy).

Current guidelines fall short in determining appropriate patients who would benefit most from surgery. For instance, the recommendation that a desire to discontinue PPI therapy is a suitable indication for anti-reflux surgery fails to recognize that 62% of patients end up back on PPI within 9 years.[8] Furthermore, indicating that those patients who “failed medical management” would benefit from surgery neglects the fact that the patients who respond best to anti-reflux surgery are those who have responded well to PPI therapy in the first place.[9] Lack of a specific, robust and practical guidance for gastroenterologists as referring providers puts patients at risk of both exposure to unnecessary surgery or, conversely, withholding measures that may significantly improve

their disease and symptoms. Therefore, when considering anti-reflux surgery, patient selection and education about realistic expectations post-surgery is of paramount importance.

**4. A comprehensive preoperative evaluation is critical in selecting the most appropriate surgical candidates to optimize outcomes and minimize complications.**

Appropriate preoperative evaluation will alter the diagnosis or modify the original operative plan in approximately 30% of patients.[10] In order to optimize outcomes, each candidate should receive an objective evaluation of symptoms prior to considering surgery.[11] EGD with biopsy should be performed to evaluate for erosive esophagitis or strictures and to assess for Barrett's esophagus, dysplasia or cancer. A 24-hr esophageal pH-metry can be used when endoscopic evidence of GER is lacking to assess for acid reflux.[12] A barium swallow may help delineate challenging anatomy by assessing esophageal length and degree of hiatal hernia. Esophageal manometry with impedance testing is advocated by some experts to uncover an impaired esophageal pump, which may modify the surgical procedure to a partial fundoplication. Manometry will also reveal relative or absolute contraindications to surgery in up to 7% of patients, such as absent esophageal contractility (i.e. achalasia, scleroderma) where surgery can result in pseudo-obstruction.[10] Ultimately, the surgical decision making should incorporate comprehensive clinical and objective data.

Favorable outcomes and satisfaction after anti-reflux surgery are seen in patients who have a good response to PPIs and are compliant with medical therapy.[9] Careful consideration should be given to PPI non-responders to exclude alternative etiologies as well as patients with atypical GERD symptoms (i.e., asthma, chronic cough, laryngitis,

hoarseness, otitis media) who tend to benefit less with anti-reflux surgery. PPI failure can be a result of increased genetic propensity for PPI metabolism or “GER” symptoms may be a forme fruste of functional bowel disorder, functional dyspepsia, delayed gastric emptying, untreated *Helicobacter Pylori* infection, achalasia, eosinophilic esophagitis or pill esophagitis.[13]

**5. *Long-term efficacy of anti-reflux surgery is limited, and many patients end up back on PPI therapy post-operatively after a variable period of time.***

82.6% of patients resume their original PPI prescription within 15 years.[14] By the same token, since PPIs are frequently prescribed for diseases other than GERD (i.e. peptic ulcer disease, gastritis, dyspepsia), the fact that patients resume PPI does NOT always indicate that surgery has failed. Physicians and patients should not always expect discontinuation of PPI use after surgery and the desire to be able to come off of PPI as an indication for surgery should be broached with caution. Again, attempts to secure an accurate GER diagnosis and patient education are key to a successful outcome.

**6. *Anti-reflux surgery has no significant impact on the progression of Barrett’s esophagus (BE) to esophageal adenocarcinoma; endoscopic ablation of dysplastic BE is still recommended.***

Chronic esophageal exposure to refluxed gastroduodenal acid and/or bile is a critical factor (among several others) in the development of Barrett’s esophagus (BE).[15] In contrast with PPI therapy, which only serves to limit acid production, anti-reflux surgery creates a mechanical valve at the EGJ that reduces *all* forms of reflux, thus theoretically reducing the risk of BE related dysplasia/neoplasia.

A recent systematic review reported no significant difference between rates of progression of dysplasia with anti-reflux surgery versus medical therapy. The incidence

of esophageal adenocarcinoma (EAC) between surgical and medical therapy groups was unchanged, 4.8 cases per 1000 patient-years [95% CI, 1.7–11.1] versus 6.5 per 1000 patient-years [95% CI, 2.6–13.8], respectively [ $P = 0.32$ ].[16] Given the lack of definitive evidence that anti-reflux surgery retards progression of BE to dysplasia/adenocarcinoma and the inherent risks of surgery, presence of BE alone should not be an indication for anti-reflux surgery. Endoscopic ablation is reserved primarily for dysplastic BE and permits a safe, well-established, highly effective and less invasive treatment option for management of dysplasia and early esophageal neoplasia in patients with BE.[17]

**7. *Laparoscopic Roux-en-Y gastric bypass surgery (LRYGB) may be the preferred “anti-reflux surgery” in morbidly obese patients.***

Obesity is associated with a 2.5 times increased risk of developing GERD due to increased intragastric pressure and anatomic disruption of the EGJ caused by high visceral fat.[18] LRYGB significantly decreases reflux symptoms (31% pre-operatively vs 5 % post-operatively), esophagitis (24% pre-operatively vs 10% post-operatively), and incidence of GERD (34% pre-operatively vs 12% post-operatively) at 39 months follow-up.[19]

It is well-established that LRYGB bestows additional health benefits of weight loss and improvement in obesity-related comorbidities including diabetes, hypertension and obstructive sleep apnea that LNF does not provide. Unfortunately, morbidity as high as 43% has been observed for LRYGB performed after a fundoplication, thus prohibiting potential health benefits in obese patients who have already undergone LNF.[18] Therefore, for patients who are morbidly obese ( $BMI > 35 \text{ kg/m}^2$ ) with PPI-refractory

GERD, LRYGB should be preferred over LNF. For patients with BMI 30-35 kg/m<sup>2</sup> and PPI-refractory GERD, the added potential of improving obesity-related comorbidities with LRYGB should be considered.

**8. *Medical therapy is more cost-effective than surgical treatment if the cost of the drug is low.***

Long term cost-efficacy studies of GERD therapy in the United States favor medical therapy when PPIs can be obtained at low cost. Markov modeling has predicted medical therapy to be cost-effective over a 30-year period when monthly PPI prescription is less than \$90 per month.[20] When the cost of PPI increased beyond \$90 a month, LNF became the most cost-effective treatment option at 5, 10, and 30 years if completed early in the disease course. Although immediate surgical complications were included in the analysis, indirect costs (i.e., loss of work productivity) were not included in the model. Further studies evaluating cost effectiveness of newer endoscopic interventions are needed.

**9. *Late complications of anti-reflux surgery are common and gastroenterologists are at the forefront of diagnosis and management.***

The success rates of laparoscopic fundoplication are variable and depend on surgical expertise, adequate preoperative evaluation and appropriate patient selection. 30-day mortality is low (<1%) and perioperative and immediate postoperative morbidity is acceptable (4.7%-17%).[21]

Late postoperative complaints are more common and are often referred back to the referring gastroenterologist for diagnosis and management. These include late-onset

dysphagia (3%-24%), recurrent heartburn (up to 62%) gas-bloat syndrome (up to 85%) and diarrhea (18%-33%).[21]

Anatomic failure of the fundoplication (figure 3) can present a unique challenge to the clinician as the symptoms and patient presentation (postoperative dysphagia, regurgitation and heartburn) can be clinically indistinct from the issues seen commonly after this surgery even in the best of circumstances.[22] Therefore, the gastroenterologist should carefully assess symptoms in a stepwise approach with upper endoscopy, barium swallow, esophageal manometry and/or ambulatory pH monitoring when appropriate and plan any interventions based on objective findings from focused testing.

**10. Several new, less invasive surgical and endoscopic anti-reflux procedures are now FDA approved, available and appear promising.**

In the last decade, minimally invasive endoscopic and surgical anti-reflux techniques have become available. A magnetic sphincter augmentation device, commercially available as LINX Reflux Management System, was approved by the Food and Drug Administration (FDA) in 2012 for refractory GERD. With LINX, a laparoscopically placed ring of magnets encircles the EGJ to augment the LES pressure while allowing adaptation to esophageal displacement, enabling the passage of large food boluses and venting of gas. Placement of the device is quicker than fundoplication, does not alter the gastric anatomy and is more easily reversible and reproducible than fundoplication. Short term data has shown LINX to be superior to laparoscopic fundoplication in preserving the patient's ability to belch (95.2% vs 65.9%) and vomit (93.5% vs 49.5%), without a significant difference in postoperative dysphagia, gas-bloat symptoms and cessation of PPI.[23]

Two endoluminal therapies for GERD currently used in the United States are the Stretta procedure and TIF (transoral incisionless fundoplication). Stretta, FDA approved in 2000, delivers a low-power radiofrequency energy to reduce the compliance of the LES and gastric cardia. This restores the barrier function of the LES and reduces the frequency of t-LESRs. Significant improvements in health-related quality of life score, pooled heartburn scores, incidence of erosive esophagitis (by 24%) as well as the reduction of esophageal acid exposure time has been shown with Stretta.[24]

TIF, approved in 2007, aims to achieve an endoscopic fundoplication at the EGJ. TIF has been shown to improve subjective response of GERD symptoms (65.9%) when compared to PPI/sham procedure (30.48%) at 6 months.[25] Most patients resume PPIs in long-term follow-up, though at reduced doses. Adverse events occur at a rate of 2.4 % and can include perforation, bleeding, pneumothorax, severe epigastric pain and death.[25]

#### **Take Home Message:**

While most patients respond well to PPI treatment for GERD, a certain subset will require anti-reflux surgery or alternative therapy. Referring providers should be familiar with the importance of appropriate patient selection and pre-operative education, counseling and evaluation. Furthermore, gastroenterologists should be competent in the evaluation of complications that may arise postoperatively and management thereof. The best surgical results will be obtained by referring those patients who need and will benefit from surgery the most.

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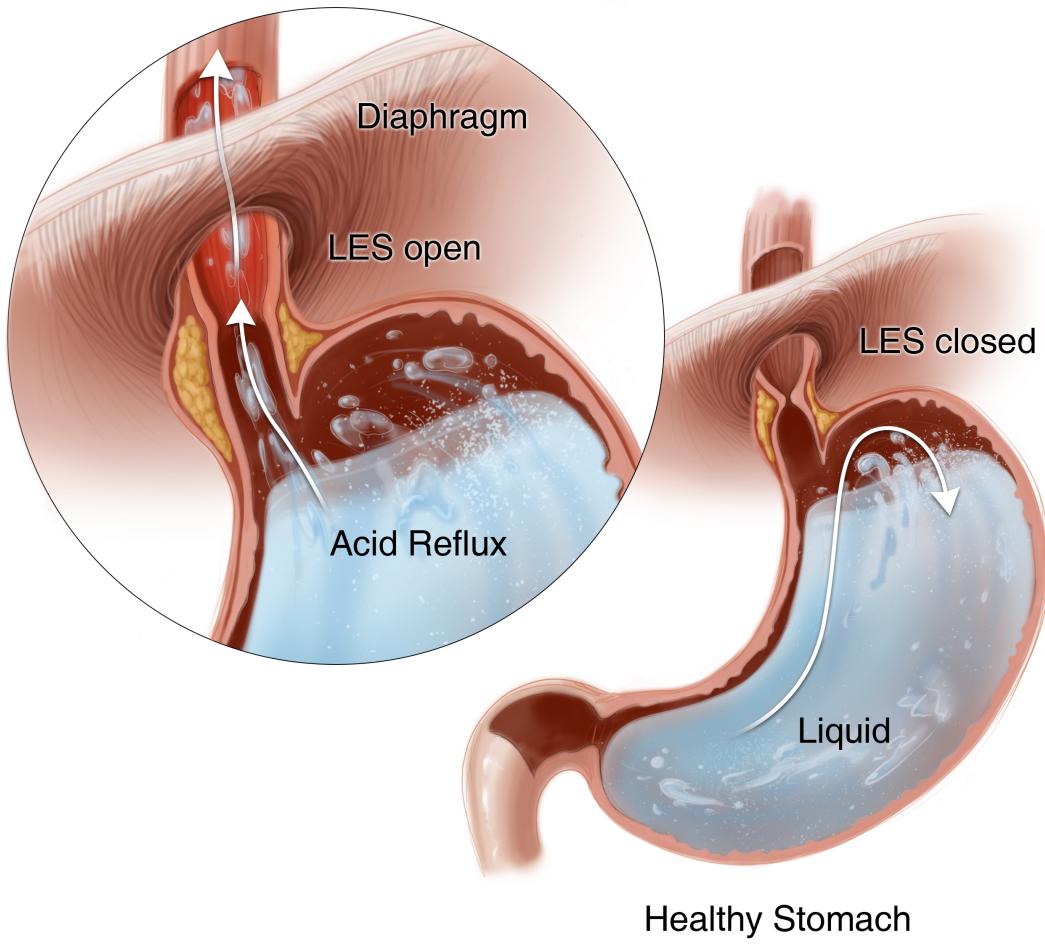
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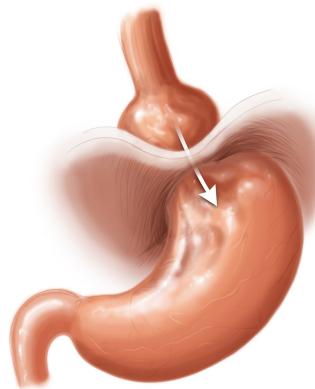
Figure 1. The lower esophageal sphincter (LES) competency determines the volume of refluxate entering the distal esophagus from the stomach.

Figure 2. Core principles of anti-reflux “fundoplication” surgery.

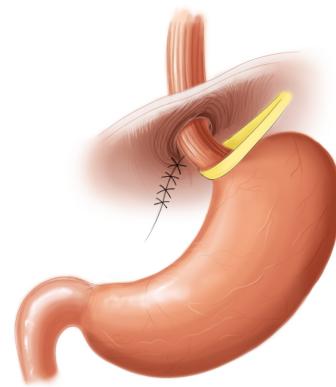
Figure 3. Anatomic failures of fundoplication

## Gastroesophageal Reflux Disease





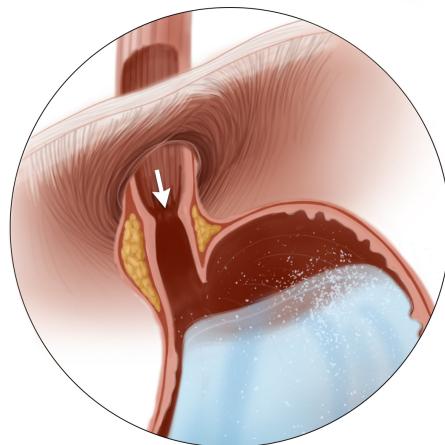
1) intra-abdominal positioning of the distal esophagus (i.e., the reduction of hiatal hernia)



2) establishing the crural closure



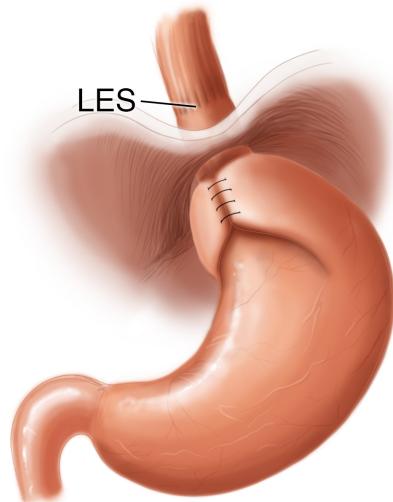
3) creating the fundoplication



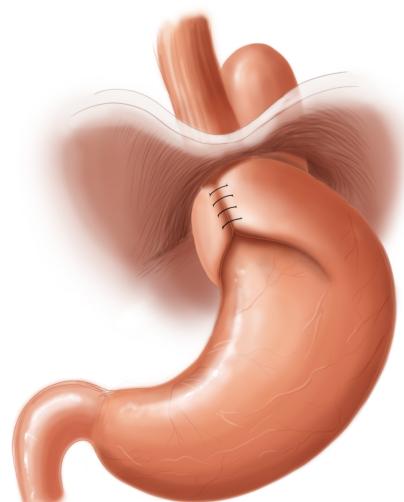
4) ensuring the patency of a one-way valve



Type IA) Herniated Fundoplication



Type IB) Slipped Nissen Fundoplication



Type II) Paraesophageal Hernia



Type III) Malpositioned Wrap