

Gastroesophageal reflux disease: A review of surgical decision making

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Abstract

Gastroesophageal reflux disease (GERD) is a very common disorder with increasing prevalence. It is estimated that up to 20%-25% of Americans experience symptoms of GERD weekly. Excessive reflux of acidic often with alkaline bile salt gastric and duodenal

contents results in a multitude of symptoms for the patient including heartburn, regurgitation, cough, and dysphagia. There are also associated complications of GERD including erosive esophagitis, Barrett's esophagus, stricture and adenocarcinoma of the esophagus. While first line treatments for GERD involve mainly lifestyle and non-surgical therapies, surgical interventions have proven to be effective in appropriate circumstances. Anti-reflux operations are aimed at creating an effective barrier to reflux at the gastroesophageal junction and thus attempt to improve physiologic and mechanical issues that may be involved in the pathogenesis of GERD. The decision for surgical intervention in the treatment of GERD, moreover, requires an objective confirmation of the diagnosis. Confirmation is achieved using various preoperative evaluations including: ambulatory pH monitoring, esophageal manometry, upper endoscopy (esophagogastroduodenoscopy) and barium swallow. Upon confirmation of the diagnosis and with appropriate patient criteria met, an anti-reflux operation is a good alternative to prolonged medical therapy. Currently, minimally invasive gastroesophageal fundoplication is the gold standard for surgical intervention of GERD. Our review outlines the many factors that are involved in surgical decision-making. We will review the prominent features that reflect appropriate anti-reflux surgery and present suggestions that are pertinent to surgical practices, based on evidence-based studies.

Key words: Gastroesophageal reflux disease; Decision-making; Fundoplication

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Core tip: Gastroesophageal reflux disease (GERD) is a common disorder with increasing prevalence. Excessive reflux of acidic gastric contents has a multitude of symptoms for the suffering patient including heartburn, regurgitation, cough, and dysphagia. Surgical interven-

tion is often necessary in those who fail medical therapy, are non-compliant or wish to discontinue long-term medical therapy, have complications secondary to GERD, or present with extra-esophageal symptoms. There are various types of anti-reflux operations that are successful in treating GERD. Laparoscopic fundoplication is the gold standard for surgical treatment. Robotic Nissen fundoplication is also advantageous with good outcomes.

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INTRODUCTION

The prevalence of gastroesophageal reflux disease (GERD) in the United States has appreciably increased in the last few decades, making it one of the most common chronic diseases^[1]. It is estimated that up to 20%-25% of Americans experience symptoms of GERD weekly^[2]. Interestingly, most patients that present to their primary care doctor with typical GERD symptoms, such as heartburn and regurgitation, never undergo formal diagnostic evaluation and are managed with non-surgical therapy such as proton pump inhibitors (PPI) long-term^[3]. In accordance with the American Gastroenterological Association and the American College of Gastroenterology, patients with symptoms suggestive of GERD should undergo an 8-wk empiric treatment regimen with a PPI^[4]. Non-responders should undergo esophagogastroduodenoscopy (EGD) as well as esophageal pH monitoring if EGD reveals no abnormalities^[4]. On the other hand, patients with extraesophageal symptoms are much more difficult to diagnose and should undergo pH monitoring sooner in the diagnostic algorithm^[5]. Unremitting GERD can result in complications including esophagitis with scarring and stricture formation, Barrett's esophagus and cancer, specifically adenocarcinoma. These types of symptoms may often require daily medication, which can be a significant adverse impact on the patients' quality of life^[6].

PATHOPHYSIOLOGY AND SYMPTOMATOLOGY

In simple terms, GERD results from failure of the distal esophageal reflux barrier^[7,8]. During normal physiologic swallowing, relaxation of the lower esophageal sphincter (LES) and crura occur which in turn allow the food bolus to enter the stomach. Furthermore, the LES and crura relax during belching to allow gas venting. If the LES relaxes separately from initiation of a swallow, these

relaxations are termed transient lower esophageal relaxations (TLESRs)^[7,8]. It has been shown that abnormal TLESRs result in an enlarged cross sectional area at the gastro-esophageal junction resulting in increased reflux of gastric contents and gas. These TLESRs are rather important as they likely result in 90% of reflux episodes^[7,9]. Hiatal hernias appear to increase the degree of reflux during TLESRs. In patients with severe reflux esophagitis, a hypotensive LES seems to be the etiology rather than abnormal TLESRs^[7,10]. If the LES pressure is < 10 mmHg, reflux tends to occur with more frequency. If the LES pressure is < 4 mmHg, however, free reflux occurs^[7,11,12].

The most common symptom of GERD is heartburn, which is said to be caused by the stimulation and activation of mucosal chemoreceptors in the distal esophagus^[3]. Other typical esophageal symptoms include regurgitation which, in addition to heartburn, reflect dysfunction of the reflux barrier. Extra-esophageal symptoms include cough, asthma, and chest pain. Additional testing, including combined impedance/pH monitoring, should be performed if GERD is thought to be the cause of any atypical symptom and/or the patient has been on long-term medical treatment and surgery is being considered^[8,13,14].

MANAGEMENT OF GERD

Surgical vs medical management of GERD

Medical options for patients with GERD include antacids, histamine-receptor antagonists or PPI therapy^[4]. Studies comparing medical management of GERD to surgical therapy have shown that anti-reflux operations are an effective alternative to medical treatments, even for patients with good symptom control on pharmacologic therapy^[15].

Furthermore, fundoplication results show significantly less acidic content and increased LES pressure compared to medical treatment alone. Fundoplication is associated with a high level of patient satisfaction and improved quality of life in patients with chronic GERD. According to the guidelines written by the American Society for Gastrointestinal and Endoscopic Surgeons (SAGES), surgical procedures for GERD are curative in 85%-93% of cases^[16]. In review of a meta-analysis comparing open vs laparoscopic surgery, a total of 16.2% of the patients in the open group and 14.7% in the laparoscopic group used acid suppression drugs post-operatively^[17]. As advancements in the field of laparoscopy have been made, minimal invasive operations have been established as the gold standard in the surgical treatment of this condition^[8].

Indications for anti-reflux surgery

The most frequent indication for anti-reflux operations symptoms refractory to pharmacological therapy^[18]. It is critical, however, to have physiological testing showing pathological acid reflux exists. SAGES guidelines suggest

that surgical intervention may be appropriate in patients who have failed medical management, decide for surgery despite successful medical management, have complications of GERD such as Barrett's esophagus and/or peptic stricture, have medical complications attributable to a large hiatal hernia, or have "atypical" symptoms such as asthma, hoarseness, cough, chest pain, dental erosions or aspiration and reflux documented on 24 h pH monitoring^[16]. It is important to note, however, that operative intervention to alleviate GERD should be performed after the diagnosis of GERD has been objectively confirmed and should only be considered in individuals who meet the aforementioned criteria. In the subset of patients who do indeed respond to pharmacologic therapy but are either unable or unwilling to take daily medication, anti-reflux surgery will likely prove quite beneficial. It has been estimated that up to 40% of patients do not respond to PPI therapy^[4]. There have been studies showing poor resolution of reflux symptoms after surgery in patients who do not respond to acid reducing medications. An eleven year follow-up study reported response and lack of response to acid reducing medications were associated with 77.1% and 56.0% success rates of laparoscopic Nissen fundoplication (LNF) respectively^[19]. Despite the potential of suboptimal results, failure of pharmacologic therapy in the treatment of GERD still remains an operative indication. In one study reviewing long-term outcomes after anti-reflux surgery, at 69 mo, the majority of patients maintained improvement or resolution of heartburn (90%), regurgitation (92%), and dysphagia (75%) when compared to before laparoscopic reflux surgery. The results were less satisfactory in patients with extraesophageal symptoms such as hoarseness (69%) and cough (69%)^[20]. Few absolute contraindications to an anti-reflux exist except the presence of esophageal cancer or Barrett's mucosa with untreated high-grade dysplasia. A long-term outcome 5-year follow-up study evaluating anti-reflux surgery in patients with Barrett's esophagus that included patients with low-grade dysplasia, short and long-segment Barrett's showed reflux symptoms were absent in 67 of 85 patients (79%) after surgery^[21]. In regards to resolution of Barrett's, low-grade dysplasia regressed to nondysplastic Barrett's in 7 of 16 (44%), and intestinal metaplasia regressed to cardiac mucosa in 9 of 63 (14%). High-grade dysplasia and adenocarcinoma were prevented in all 97 patients^[21].

Preoperative considerations

Preoperative objectives should identify the proper patients for anti-reflux surgery after appropriately evaluating symptoms and diagnostic studies. Proper selection of patients optimizes outcomes. Initial evaluation must include a thorough history and physical exam. It is important for the surgeon to focus on the duration of symptoms, type of reflux symptoms and causation/temporal relationship of symptoms. Studies have shown that patients with typical symptoms, in comparison to

those with atypical symptoms, have a better response to fundoplication. A 10-year follow-up study reported 85% percent of patients with typical symptoms had a successful outcome after LNF, compared to only 41% with atypical symptoms^[19]. Furthermore, patients who experience exaggerated symptoms when supine rather than standing tend to have better outcomes after fundoplication as well. In the supine position, transient lower esophageal relaxation periods increase. Studies have shown that fundoplication reduces TLRSR frequency by 50% and thus decrease reflux events^[22,23]. After a detailed history and physical examination is performed, important preoperative studies to consider are: (1) Upper endoscopy (EGD): Endoscopy has a high specificity (95%) for diagnosing GERD as the operator can note visual and histopathologic changes of the esophageal mucosa. Moreover, the operator is able to take biopsies of the mucosa that are essential in ruling out other etiologies or complications of reflux. Biopsies of the mucosa are necessary to diagnose and exclude other non-reflux esophageal disorders such as eosinophil esophagitis, *Helicobacter pylori*, Barrett's esophagus or esophageal cancer. As stated previously, if high-grade dysplasia or esophageal cancer is noted on endoscopy, the surgeon cannot perform anti-reflux surgery. If, however, low-grade dysplasia or intestinal metaplasia is noted, the surgeon should proceed with the procedure as studies have shown resolution and regression to cardiac mucosa. Despite its' high specificity, endoscopy lacks sensitivity in the diagnosis of GERD as up to half of patients with GERD will have normal endoscopic findings^[24]. EGD is also useful to visualize the presence of a hiatal hernia. If a hiatal hernia is discovered pre-operatively, the surgeon must repair the hiatal hernia prior to performing the wrap; (2) pH monitoring: As stated previously, non-responders to pharmacologic therapy should undergo EGD as well as esophageal pH monitoring. pH monitoring can be a very valuable tool to objectively establish a diagnosis of GERD and is the gold standard for pathologic acid reflux^[25]. A 24-h or 48-h intra-esophageal study can be done to evaluate the patient's pH levels during daily life, and thus assess reflux patterns as well as determining the patients' ability and frequency of clearing acid. Multiple devices are available for use in pH monitoring. Two specific devices include a 24 h transnasal catheter placement and BRAVO wireless esophageal pH probe monitoring, both of which have been proven effective to accurately diagnose GERD^[5]. It is necessary that the patient discontinue his/her acid suppression medication for a minimum of 1 wk for the pH monitoring to be accurate. If the patient is unable to stop the medication, referral for an impedance test should be done^[26]. Most studies have shown an elevated DeMeester score indicates pathological reflux. Impedance testing can distinguish between acidic and nonacidic reflux. Impedance testing, however, is prone to interpretational error so it is not optimal^[27]; (3) Esophageal manometry is used to identify dysmotility of the esophagus, for example, achalasia. Some surgeons

will determine the type of surgery necessary for the patient based on their manometry results (Nissen vs partial). However, there is overwhelming data showing even with poor motor function of the esophagus, a Nissen fundoplication provides the best results by effective blockade of reflux, which is most likely, the cause of poor dysmotility^[28,29]. Our group has shown that compared to patients with good motor function, patients with poor motor function tend to have longer short-term dysphagia, yet at the 3-mo follow-up period, both groups behaved similarly; and (4) Barium swallow: Perhaps not useful to all surgeons, a barium swallow can help to better understand the anatomy of esophagus and stomach. A barium swallow can prove valuable in patients with various anatomical abnormalities such as a shortened esophagus or hiatal hernias. Hiatal hernias affect the competence of the LES, in turn, impeding the ability to clear acid in the esophagus. It is prudent that the surgeon recognizes hiatal hernias preoperatively as it is necessary to repair them during any anti-reflux operation. A barium swallow study can also determine if the patient has esophageal dysmotility. For example, the diagnosis of achalasia is supported by barium swallow findings including dilation of the esophagus, a narrow esophago-gastric junction with "bird-beak" appearance, aperistalsis, and poor emptying of barium^[30].

SURGICAL TECHNIQUES USED TO TREAT GERD

Laparoscopic vs open technique for GERD

A laparoscopic, transabdominal approach is preferred for the vast majority of patients undergoing anti-reflux surgery. Rarely, transthoracic and open abdominal approaches are required and may be considered for patients undergoing revision of their former anti-reflux operations^[31]. However, reoperation surgery typically can be performed laparoscopically. Perioperative morbidity was found to be significantly lower (65%) after laparoscopic compared with open fundoplication^[32]. Laparoscopic fundoplication is associated with longer operative times but shorter hospital stays^[17]. In turn, conversion rates to open surgery were less than 5%^[17]. Laparoscopic fundoplication is preferred over open surgery because it is associated with shorter hospital stay, decreased pain, postoperative wound infections and abdominal wall hernia formation^[17]. Additionally, using the laparoscopic approach, surgeons have the advantage of seeing all the hiatal structures in a magnified fashion. In a 10-year randomized trial comparing LNF to conventional Nissen fundoplication (CNF or open technique), it was noted that twice as many patients required reoperation after CNF, including a much higher number of incisional hernia corrections. The 10-year effectiveness of LNF and CNF is comparable in terms of improvement of GERD symptoms, PPI use, quality of life, and objective reflux control seen on impedance studies. Thus, the long-term results from this trial

lend level 1 support to the use of LNF as the surgical procedure of choice for GERD^[33]. Regardless of the type of fundoplication performed, the aim of the operation is the same: Re-create and restore the normal physiologic functionality of the LES, reconstruction of the hiatus when necessary and repair of any hiatal hernia if present.

Partial vs total fundoplication

In the United States, in comparison to Europe, a 360° fundoplication is the most common anti-reflux operation performed. European surgeons, however, favor a partial fundoplication operation. Many prospective, randomized, controlled studies have evaluated both 360° and 270° fundoplication procedures and have shown similar short- and long-term efficacy^[34,35]. Despite these findings, proponents of the Nissen fundoplication argue its superiority over the partial fundoplication. Advocates for the partial fundoplication argue that their patients have fewer symptoms of bloating and retain their ability to vomit. In one randomized control study, there were noted to be a higher rate of postoperative dysphagia, flatulence, and bloating in total fundoplication as compared to partial fundoplication^[36]. There were not, however, significant differences between the two modalities in the continuing postoperative incidence of heartburn, esophagitis or persistent acid reflux. A similar proportion of patients experiencing excellent long-term outcomes were seen in both partial and Nissen fundoplication^[34,36]. Another study reported at 10 years, 89.5% patients who had undergone laparoscopic fundoplication were free of significant reflux (93.3% after Nissen, 81.8% after Toupet). Thus, Nissen patients did better than Toupet patients, although the difference was not statistically significant^[34].

Anterior (Dor) vs Nissen fundoplication

Prospective, randomized controlled studies comparing 120-degree anterior fundoplication vs Nissen fundoplication showed anterior fundoplication to be associated with less postoperative dysphagia, 74% in the Nissen group and 95% in the anterior fundoplication group after 24 mo follow up^[36]. However, this technique was shown to be less effective for controlling reflux over time. In addition, more patients required reoperations for reflux control after anterior fundoplication^[37].

Toupet vs Nissen fundoplication

There have been several randomized control studies comparing Toupet fundoplication to Nissen fundoplication. Studies have shown lower rates of post-operative dysphagia after a Toupet fundoplication when compared to results after a Nissen fundoplication - around 8.5% vs 13.5% respectively^[38]. There were no differences, however, in the percentage of patients affected by heartburn comparing the two procedures^[38]. Regarding the operative technique, recent findings have shown that the length of the wrap is important when performing a Toupet fundoplication. For example, a 3.0 cm Toupet vs 1.5 cm Toupet proved to better control reflux. The

Table 1 Comparison of advantages and disadvantages in different types of funduplications

	Advantages	Disadvantages
Nissen fundoplication	Very effective in controlling reflux over long periods of time	Increased flatulence, bloating and dysphagia
Anterior (Dor) fundoplication	Less postoperative dysphagia	Recurrent symptoms over time requiring more reoperations
Toupet fundoplication	Less postoperative dysphagia	Surgeons need to be mindful of length of wrap as it determines quality of reflux control

length of the wrap in a Nissen fundoplication, however, did not influence reflux control, rather mild dysphagia rates were higher for the 3.0 cm wrap (8.8%) compared to the 1.5 cm wrap (21.2%) at the 12-mo follow up^[39]. Five years after the operation, mild dysphagia rates in the Nissen fundoplication groups were equivocal, 9.7% in the 1.5 cm wrap and 7% in the 3.0 cm wrap^[39]. More level 1 evidence with longer follow up periods is required to determine whether Nissen fundoplication is superior to Toupet fundoplication in terms of patient outcomes (Table 1).

Use of robotic surgery in treating GERD

The use of robotic surgery for managing GERD has been shown to be a viable and safe option, with similar outcomes when compared to laparoscopy after one year follow up. Robot-assisted LNF is comparable to traditional laparoscopy in terms of complications, mortality and length of hospital stay. Robotic Nissen fundoplication is advantageous as the surgeon has improved ergonomics, visualization, comfort, and autonomy. The only disadvantages seen with robotic assisted surgeries were reported to have longer surgical times (131.3 min vs 91.1 min laparoscopically), and generally higher costs when compared to laparoscopic surgery^[40].

KEY OPERATIVE STEPS IN ROBOTIC NISSEN FUNDOPLICATION

Positioning

Supine position with arms out on arm boards.

Incision and exposure

Veress technique is used to enter the abdominal cavity 13 cm subxiphoid and 5 working ports are placed under direct visualization. A Genzyme liver retractor is placed to retract the left lobe of the liver superiorly and laterally. The patient is placed in steep reverse Trendelenburg, and the robot (DaVinci Xi) is docked and the working instruments are placed.

Procedure

Dissection begins with the takedown of the gastrohepatic ligament using a vessel sealer all the way to the right crus that is clearly dissected off the esophagus. The short gastrics are then taken all the way through the angle of His until the left crus is clearly defined. Right and left crus are clearly delineated, and the esophagus is identified. A Penrose drain is placed around the esopha-

gus and the posterior vagus after clearly identifying this window. Dissection is carried into the chest, allowing for complete reduction of the esophagus, and after which the hiatus is closed using V-Loc and 3-0 silk sutures.

The fundoplication is then performed around a 56 bougie taking a distal and proximal bite of the esophagus. The bougie is then removed. Posterior pexy is then performed to the right crus with 2 sutures. An anterior pexy is performed to the right and left crus.

Penrose is removed as is the Genzyme retractor.

The robot is undocked and the ports were removed under direct visualization.

The skin is approximated using fine absorbable sutures in a subcuticular manner.

Special situations

GERD in morbidly obese patients and surgical technique: There is a direct association between obesity and gastroesophageal reflux. The prevalence of GERD is higher with people that have higher body mass index (BMI), and linearly increases with increased BMI. Some studies have shown fundoplication surgeries for morbidly obese patients to have a higher rate of failures compared to normal weight patients^[19]. Other studies, however, have showed equivalent outcomes in obese and normal weight patients^[41,42]. One of the many lifestyle alterations suggested by physicians to aid in the treatment of GERD is weight loss. Morbidly obese patients following Roux-en-Y gastric bypass (LRYGB) have improved reflux symptoms after losing weight^[43]. One prospective study quoted 94% resolution of reflux symptoms 9-mo after patients underwent LRYGB^[44]. Essentially, the LRYGB procedure helps the patient lose weight and improve reflux symptoms as well. Thus, it is the procedure of choice for many surgeons treating morbidly obese patients with GERD.

Revisional surgery for failed anti-reflux surgery

The failure rate of fundoplication ranges from 3% to 16%^[45]. Not every patient who has failed anti-reflux surgery needs reoperation. It is important for the surgeon to determine whether a physiologic or anatomic failure can be ameliorated surgically. The most common indications for reoperation are a "slipped" fundoplication or herniation of the wrap into the mediastinum^[45,46]. Laparoscopic re-operative anti-reflux surgery is a viable and safe option for patients. While it is effective, re-operative surgeries have higher complication rates compared to primary repairs such as gastric or esophageal perforation^[45]. The re-operation should be done

in the same manner as the primary fundoplication. Revisional surgery, compared to primary repair, requires longer operative times (mean duration of reoperation was 177.4), is correlated with higher conversion rates to an open approach and has higher complication rates^[47]. Patient satisfaction after revisional surgery is generally high (89%) with resolution of heartburn symptoms in almost 80% of patients and resolution of regurgitation in 85% of patients, 18 mo after surgery^[48].

CONCLUSION

GERD is a very common disorder with increasing prevalence. Excessive reflux of acidic gastric contents has a multitude of symptoms for the suffering patient including heartburn, regurgitation, cough, and dysphagia. There are also associated complications of GERD including erosive esophagitis, Barrett's esophagus, stricture and adenocarcinoma. Surgical intervention is often necessary in those who fail medical therapy, are non-compliant or wish to discontinue long-term medical therapy, have complications secondary to GERD, or present with extra-esophageal symptoms. There are various types of anti-reflux operations that have been quite successful in treating GERD and restoring competence in an otherwise incompetent LES, while at the same time repairing a potential hiatal hernia. Laparoscopic fundoplication is the gold standard for surgical treatment of severe GERD and results in approximately 95% patient satisfaction. Robotic Nissen fundoplication is also very advantageous with good outcomes. In regards to the specific type of fundoplication, the Nissen fundoplication has overall improved outcomes when compared to partial wraps. Before entertaining a surgical approach, it is important that the surgeon take all necessary preoperative measures to ensure surgery is the appropriate choice for the patient. The surgeon must also take into consideration special situations such as obese patients or those that are in need of a revisional anti-reflux procedure.

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