

Laparoscopic surgery for gastroesophageal reflux disease: Nissen, Toupet or anterior fundoplication

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Abstract: Gastroesophageal reflux disease (GERD) is one of the most frequent upper gastrointestinal disorders worldwide. It is defined as a chronic condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications. A review of literature has been performed to evaluate the adequate preoperative diagnostic workup, indications to anti-reflux surgery, and surgical outcomes. To establish a correct indication, objective diagnosis of GERD with endoscopy, 24-hour impedance-pH monitoring and esophageal manometry is needed. A careful preoperative selection of patients is the first critical step to reduce the risk of side effects and failure of laparoscopic anti-reflux surgery (LARS). Laparoscopic 360° fundoplication (LTF) is the gold standard surgical treatment for GERD. Relief of heartburn and regurgitation is achieved by 80–90% of patients at 10 years follow-up. Partial fundoplications (anterior and posterior) guarantee similar outcomes in terms of symptom control with a lower risk of postoperative dysphagia. However, at the long-term follow-up, partial fundoplications are associated with an increased number of recurrent reflux episodes at 24-hour pH monitoring when compared to 360° fundoplication. More studies are needed to compare the different types of fundoplication in the long-term follow-up period.

Keywords: Gastroesophageal reflux disease (GERD); laparoscopic 360° fundoplication (LTF); partial anterior fundoplication; partial posterior fundoplication; 24-hour ambulatory pH-monitoring

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Introduction

Gastroesophageal reflux disease (GERD) is defined as a chronic condition which develops when the reflux of stomach contents causes troublesome symptoms and/ or complications (1). GERD is one of the most common gastrointestinal disorders worldwide; the estimated prevalence of patients experiencing at least weekly heartburn or regurgitation in the Western world ranges from 10% to 30% (2). However, the real prevalence of the disease is probably higher than reported, because patients with milder symptoms use over-the-counter remedies instead of consulting health care providers.

The goals of GERD treatment are the control of

symptoms, prevention of GERD complications and improvement in patients' health-related quality of life. GERD treatment relies on lifestyle and diet modification, acid-suppressive medical therapy and laparoscopic anti-reflux surgery (LARS). The American College of Gastroenterology recommends lifestyle interventions, such as smoking cessation, head of the bed elevation, avoidance of potentially triggering foods and weight loss as the first therapeutic approaches for GERD (3). However, the level of evidence is low, and to date there is no evidence to support these modifications as primary GERD treatment (4).

Proton Pump Inhibitors (PPI) are the mainstay of medical therapy for GERD. These medications are the

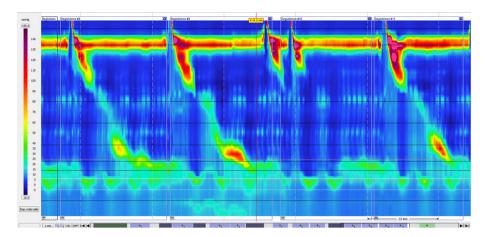


Figure 1 High-resolution manometry showing hypotonic lower esophageal sphincter and impaired esophageal motility.

most effective medical treatment for GERD, relieving heartburn and healing erosive esophagitis in the majority of patients. However, they have several drawbacks. First, long-term continuative PPI therapy is needed to maintain healing of esophagitis over time. Secondly, PPI are less effective in patients with regurgitation, and response rates to PPI are even lower in patients with atypical symptoms (5). Finally, the long-term use of PPI is associated with higher risks of community-acquired infections, hip fractures and osteoporosis (6-8).

In a metanalysis of seven randomized controlled trials (RCTs) comparing medical therapy to LARS for GERD, Rickenbacher *et al.* found that surgery was more effective than medical treatment in improving symptoms and health-related quality of life in the short to medium follow-up (9). In addition, several studies confirmed these results also in the long-term follow-up (10-13).

Preoperative assessment of GERD

Clinical bistory

The clinical diagnosis of GERD is based on the presence of typical symptoms such as heartburn and regurgitation, and on a favorable response to a trial of empiric medical therapy with PPI, the so-called "PPI trial" (3). However, many studies demonstrated that a GERD diagnosis based on symptoms alone was not reliable. Several other diseases, such as irritable bowel syndrome, gallstone disease and coronary artery disease could be misdiagnosed as GERD (14-16). For instance, Patti *et al.* performed functional esophageal tests on 822 consecutive patients with a clinical diagnosis of GERD and found that 30% of patients had normal reflux scores. Moreover, the incidence of heartburn and regurgitation, and the use of acid-reducing medications were similar between patients with or without pathologic reflux (14).

Also, in a metanalysis of 12 studies, Numans *et al.* showed that PPI trial, compared to 24-hour pH monitoring, had a sensitivity of 78% but a specificity of only 54% (17). Therefore, clinical diagnosis of GERD based on symptoms and response to PPI trial is not sufficient before considering LARS, and objective documentation of GERD is required.

Endoscopy

It is generally performed at the clinical presentation in case of persistent GERD symptoms despite appropriate medical therapy or in cases with warning signs (dysphagia, unintentional weight loss, hematemesis) (3,18). The presence of erosive esophagitis, peptic strictures, or Barrett's esophagus (BE) is diagnostic for GERD with a specificity of 95% (19). However, up to one-quarter of patients with abnormal reflux does not present any mucosal damage at endoscopy (20,21). Upper endoscopy is performed in all patients before LARS, in order to exclude other diagnoses such as esophageal cancer and eosinophilic esophagitis.

Esophageal manometry

Esophageal manometry, performed with conventional water-perfused catheters or more recently with a high-resolution solid-state catheter, is of limited importance in the primary diagnosis of GERD, but its strength lies in the clinical evaluation of oesophageal motility (*Figure 1*).

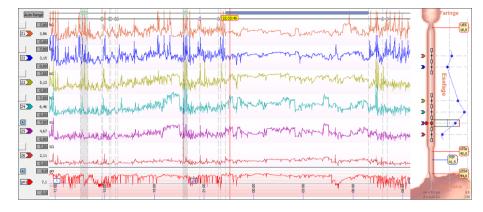


Figure 2 Twenty-four-hour impedance-pH monitoring showing a pathologic reflux.

It provides information regarding the functions of the lower esophageal sphincter (LES) and the esophageal body motility. Manometric findings of defective LES can be seen in up to 60% of GERD patients, and the degree of impaired esophageal motility seems to increase with the severity of erosive esophagitis (22).

The main purpose of preoperative esophageal manometry is to rule out the presence of primary esophageal motility disorders, such as achalasia, that would be contraindications to LARS. Moreover, esophageal manometry is required to correctly place the esophageal pH monitoring probe (5 cm above the LES) (23).

Ambulatory 24-bour impedance-pH monitoring

Ambulatory 24-hour impedance-pH monitoring is considered the gold standard for diagnosing GERD because it quantifies the number of reflux episodes and their correlation with symptoms, using the symptom index (SI) or the symptom association probability (SAP) (24,25) (*Figure 2*). It allows the characterization of the refluxate based on pH (into acid, weakly acidic and weakly alkaline reflux) and type of the refluxate (liquid, gaseous, mixed).

The current most common indications for this test are: patients with typical symptoms refractory to PPI therapy, patients with atypical symptoms and evaluation of endoscopy-negative patients with GERD symptoms (26).

Barium swallow

It is not a diagnostic test for GERD because it has low diagnostic sensitivity and specificity (respectively 40% and 85%) (27). However, it provides information about the

length and diameter of the esophagus, and regarding the presence and size of a hiatal hernia. In the case of findings of large hiatal hernia, additional investigations such as computed tomography or magnetic resonance can be performed preoperatively for more accurate sizing (28).

Indications

When the diagnosis of GERD is objectively confirmed, indications to LARS are: (I) patients with typical symptoms and successful medical management; (II) patients with inadequate symptom control despite adequate medical therapy; (III) patients with GERD complications (i.e., BE, peptic strictures); (IV) patients with extra-esophageal symptoms that are related to GERD (29).

Patients with typical symptoms and successful response to PPI are the best candidates to LARS. Patients might choose to undergo surgery despite adequate symptom control for several reasons, including the need of taking lifelong medications, especially in younger patients, poor compliance or the presence of side effects associated with medical treatment, and the cost of prolonged medical therapy.

Historically, LARS was advocated mainly for GERD patients with failed medical therapy. During the last decades, however, indications to LARS have evolved (30). Campos *et al.* performed a multivariate analysis on 199 consecutive patients undergoing laparoscopic 360° fundoplication (LTF). Three preoperative factors were statistically significant predictors of success after LARS: abnormal pH monitoring score, the presence of typical symptoms, and the favorable response to acid suppressive therapy (31). Comparable results were reported by Davis *et al.* in a review of 13 RCT assessing

Page 4 of 9

Annals of Laparoscopic and Endoscopic Surgery, 2019



Figure 3 Laparoscopic 360° fundoplication.

outcomes of LARS. They concluded that the presence of a large hiatal hernia, lack of response to preoperative acidreducing medications, the presence of atypical symptoms and overweight were associated with significantly lower success rates after laparoscopic fundoplication (32).

A careful selection of patients is mandatory in case of symptoms unresponsive to PPI before considering LARS. Traditionally, failure of medical therapy was attributed to the presence of residual reflux, either acid or non-acidic (33). More recently, the Rome IV classification recognized two separate functional esophageal disorders, functional heartburn and reflux hypersensitivity, that overlap with GERD and are considered to be responsible for the lack of response to treatment despite adequate medical therapy in the majority of PPI non-responder patients (5,34,35). Understanding the reasons beneath medical failure is essential to address patients to specific individualized treatment properly.

The role of LARS in patients with BE is controversial because the evidence is very limited. Only a few small retrospective studies have been published to date regarding the outcomes of laparoscopic fundoplication in patients with BE, showing a good symptom control rate (36-39). Also, these studies showed a not negligible rate of BE regression, ranging from14 to 52%, after LARS (40). In their recently published guidelines, the British Society of Gastroenterology concluded that LARS was not superior to acid-reducing medications in the prevention of BE neoplastic progression; surgery can be offered to highly symptomatic BE patients with poor response to PPI (41).

Surgical treatment for GERD

Laparoscopic fundoplication is the procedure of choice for the surgical treatment of GERD. The surgical procedure results in an increased LES tone and reduced backflow of gastric contents to the esophagus.

The following technical steps in performing a laparoscopic fundoplication have been standardized: (I) opening of the phreno-esophageal ligament, with preservation of the anterior vagus nerve; (II) dissection of both crura; (III) mobilization of the distal esophagus to allow at least 3 cm of esophagus in the abdominal cavity; (IV) eventual short gastric vessel division; (V) posterior crural repair; (VI) wrap creation (42).

Laparoscopic 360° fundoplication (LTF)

LTF is the standard procedure for the surgical treatment of GERD. A 360° short and floppy wrap is created by bringing the right and left portion of the gastric fundus around the distal esophagus (42) (*Figure 3*). Compared to conventional (open) 360° fundoplication, the laparoscopic approach allows similar perioperative and long-term outcomes with lower postoperative morbidity and mortality rates (43-47). Several studies demonstrated that LTF is highly effective in reflux control over time, relieving heartburn and regurgitation in about 80–90% of patients at 10 and 20 years follow-up (46,48-51).

Two major causes of patients' dissatisfaction with LTF are dysphagia and gas-bloat syndrome. Transient dysphagia is frequently experienced by patients submitted to LTF in the early postoperative period, while long-term dysphagia is rare.

In order to reduce the incidence of these side-effects, several potential technical factors were evaluated. The use of a calibration bougie while performing the fundoplication was associated with decreased postoperative dysphagia rate (52). Routine short gastric vessel division was suggested by some authors to achieve a tension-free wrap. However, several RCTs showed no differences in postoperative dysphagia rate for patients submitted to routine short gastric vessels division during LTF (53-55). Therefore selective short gastric vessels division is required only in selected cases when the gastric fundus cannot be wrapped around the esophagus without tension (29).

Several preoperative patient characteristics were evaluated to determine whether they could predict the incidence of postoperative side effects. The presence of ineffective preoperative esophageal motility was investigated as a risk factor for the development of postoperative dysphagia. However, multiple RCTs and meta-analysis showed similar rates of dysphagia following 360° and partial fundoplication either with normal or defective esophageal peristalsis (56-58). To date, there is no evidence of clinical



Figure 4 Laparoscopic partial posterior fundoplication.

benefits in tailoring the fundoplication depending on manometric parameters (29). No correlation also was found between preoperative impedance-pH monitoring parameters and outcomes after LARS (59,60). Finally, the presence of preoperative delayed gastric emptying seemed to be correlated with worst functional and clinical results after LTF compared to patients with normal gastric function, probably due to lower gastric compliance to proximal gastric distension (61). However, further studies are needed to confirm the results.

Laparoscopic 360° vs. partial posterior fundoplication

Laparoscopic partial posterior fundoplication (LPPF) is considered an alternative to LTF in the treatment of GERD (*Figure 4*). Several RCTs were conducted to investigate the differences between LTF and LPPF. These studies showed minimal differences in clinical outcomes between the two procedures, that could not allow for providing definitive answers (56,62-64).

Broeders et al. performed a systematic review and meta-analysis on 7 RCTs comparing LTF (404 patients) and LPPF (388 patients). Perioperative outcomes and satisfaction with the intervention were similar for both procedures. There were no differences between the two procedures in the presence of subjective reflux recurrence, in the percentage of recurrent pathological exposure, and in the presence of esophagitis. Dysphagia and gasrelated symptoms, as well as surgical reinterventions, were more frequent in the LTF group compared to LPPF (65). This study, however, had some major limitations due to the limited methodological quality and power of the included RCTs, and to the heterogeneity in technical issues performing the procedures, such as the length of the wraps, and in outcomes definition. Moreover, the followup ranged from 12 to 60 months. Longer follow-up data are needed to confirm these results, especially because several non-randomized studies reported inferior long-term reflux control of LPPF compared to LTF (22,66). Finally, Mardani *et al.* published the long-term results of an RCT comparing open 360° versus partial posterior fundoplication, showing equally well-controlled reflux, while the differences in side effects equalized at 10 years after surgery (67).

Laparoscopic 360° vs. partial anterior fundoplication

Watson *et al.* performed a double-blind RCT in 1999 comparing 53 LTF and 54 laparoscopic partial anterior fundoplication (LPAF). Perioperative outcomes were similar in both groups (68). LPAF patients had a significantly lower incidence of dysphagia for solid food, inability to belch and increased satisfaction rate compared to LTF both at shortand long-term follow-up (68-70). However, at 14-year follow-up, patients submitted to LPAF had less effective reflux control, with an increased number of reflux episodes detected ad 24-hour pH monitoring and lower LES resting pressure at esophageal manometry compared to LTF (71).

Similar results, showing an increased rate of symptom recurrence after LPAF compared to LTF were also published by others (72-76). For instance, Baigrie *et al.* performed an RCT comparing LTF (84 patients) and LPAF (79 patients). The two surgical procedures provided comparable results in terms of symptom control, dysphagia and satisfaction rates both at short and long-term followup (77). However, at 12 years follow-up, the use of acidreducing medications was higher in LPAF patients compared to LTF (8% vs. 29%) (78).

Conclusions

GERD is one of the most frequent upper gastrointestinal disorders worldwide. Objective GERD diagnosis with endoscopy and 24-hour impedance-pH monitoring is needed before considering LARS. Further diagnostic investigations such as esophageal manometry and barium swallow provide useful information to establish correct surgical indications.

A careful preoperative selection of patients is the first critical step to reduce the risk of side effects and failure of LARS.

According to the available evidence, LTF is the surgical procedure of choice for GERD treatment. Laparoscopic partial fundoplication, either anterior or posterior, is associated with a lower incidence of dysphagia and gas

bloat syndrome, but the effects on reflux control over time are questionable. The limited quality of the studies and the lack of long-term data cannot allow drawing definitive conclusions. Therefore, the choice of the type of wrap (partial or 360°) depends on the single surgeon's experiences and preferences.

Further efforts are needed to identify preoperative prognostic factors, selecting GERD patient subgroups that could benefit from a different type of fundoplication, in order to individualize GERD treatment depending on each patient characteristics.

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Page 6 of 9

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