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SPECIAL REPORT



Gastroesophageal reflux disease: indications for antireflux surgery, outcomes, and side effects

Francisco Schlottmann^{a,b}, Sofia Bertona^a, Fernando A.M. Herbella^c and Marco G. Patti^d

^aDepartment of Surgery, Hospital Alemán of Buenos Aires, Buenos Aires, Argentina; ^bDepartment of Surgery, University of Illinois at Chicago, Chicago, IL, USA; ^cDepartment of Surgery, Escola Paulista de Medicina, São Paulo, Brazil; ^dDepartment of Surgery, University of Virginia, Charlottesville, VA, USA

ABSTRACT

Introduction: Gastroesophageal reflux disease (GERD) is a frequent digestive disorder that presents with a broad spectrum of symptoms. Global consensus on which patients should be selected for anti-reflux surgery is lacking.

Areas covered: This evidence-based review will analyze current indications for anti-reflux surgery, outcomes of the operation, and potential side effects.

Expert commentary: Treatment of GERD has three main purposes: control symptoms, improve quality of life, and prevent potential serious complications such as bleeding, esophageal stenosis, Barrett's esophagus, and esophageal adenocarcinoma. Although medical therapy is effective in the majority of patients, some might require anti-reflux surgery in order to achieve these goals. Adequate patient selection for anti-reflux surgery is critical to obtain optimal outcomes. Most patients undergoing a fundoplication have adequate long-term symptomatic relief. However, potential side effects of anti-reflux surgery should also be discussed with patients to help manage expectations from the operation.

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KEYWORDS

Gastroesophageal reflux disease; hiatal hernia; anti-reflux surgery; fundoplication; outcomes; side effects

1. Introduction

Gastroesophageal reflux disease (GERD) is a condition resulting from reflux of stomach contents into the esophagus causing troublesome symptoms and/or complications [1]. GERD is a frequent digestive disorder worldwide, especially in developed countries. For instance, it is estimated that 20% of the population in the United States is affected by GERD, and its prevalence is increasing over the years mostly due to the epidemic of obesity [2]. Direct health care costs related to GERD are approximately \$10 billion per year only in the U.S., with medical therapy being the largest contributor to these expenses (nearly \$6 billion) [3,4].

Heartburn, regurgitation, and dysphagia are considered typical symptoms of GERD. However, many patients affected by GERD can present with extraesophageal symptoms such as cough, wheezing, asthma, chest pain, hoarseness, and/or dental erosions [5]. Lifestyle modifications and medical therapy are effective in the majority of patients with GERD. Pharmacologic agents for the treatment of GERD include non-absorbable agents (antacids and alginate formulations), histamine-2 receptor antagonists, proton pump inhibitors (PPIs), potassium channel acid blockers (P-CABs), prokinetic agents, and inhibitors of transient lower esophageal sphincter relaxations [6]. PPIs remain the dominant treatment, but long-term therapy still requires follow-up and reevaluation for potential adverse effects [7].

Treatment of GERD has three main purposes: control symptoms, improve patients' quality of life, and prevent complications such as bleeding, esophageal stenosis, Barrett's esophagus, and esophageal adenocarcinoma. Some patients with GERD will indeed require anti-reflux surgery in order to achieve these goals [8,9]. The aim of this study was to analyze current indications for anti-reflux surgery, outcomes of the operation, and potential side effects.

2. Indications for anti-reflux surgery

Selecting patients for anti-reflux surgery is indeed challenging. In 2019, a group of international experts (gastroenterologists, surgeons, and physiologists) published the ICARUS guidelines (International consensus regarding preoperative examinations and clinical characteristics assessment to select adult patients for anti-reflux surgery) in order to guide patient selection for anti-reflux surgery [10]. Unfortunately, global consensus was reached for few statements, and the authors concluded that referring a patient for fundoplication has to be an informed decision process, based on both positive and negative supporting findings.

Based on current guidelines, evidence, and our clinical experience, we believe that an anti-reflux surgery should be considered in the following cases:

Article highlights

- GERD is a frequent digestive disorder, and its prevalence is increasing over the years, mostly due to the epidemic of obesity.
- Lifestyle modifications and medical therapy are effective in the majority of patients with GERD.
- The presence of typical symptoms with good response to medication is a strong positive predictor of success after anti-reflux surgery.
- An anti-reflux operation is a very good alternative for patients with symptoms related to the large volume of reflux contents (i.e. regurgitation).
- Symptomatic patients with a large hiatal hernia should be strongly considered for fundoplication.
- Anti-reflux surgery should be discussed with symptomatic patients with poor adherence to medical treatment or refusal to long-term medical therapy.
- Symptomatic patients with Barrett's esophagus are good candidates for anti-reflux surgery.
- Minimally invasive fundoplication is the procedure of choice for the surgical treatment of GERD.
- A properly executed operation that respects key technical elements is critical to achieve optimal outcomes.
- Side effects such as dysphagia, gas-related symptoms, or diarrhea might, albeit rarely, occur after the operation.

2.1. Heartburn as the main symptom with good response to medical therapy

Contrary to the common belief that patients with poor response to PPIs are good candidates for surgery, the presence of typical symptoms with good response to medication is a strong positive predictor of success after anti-reflux surgery. For instance, a previous study showed that three factors were predictive of a successful outcome after a fundoplication: abnormal 24-h pH score, a typical primary symptom, and a clinical response to acid suppression therapy [11]. Similarly, another study demonstrated that preoperative response to acid reducing medications, presence of typical symptoms, and body mass index <35 kg/m² were relevant predictive factors of success after laparoscopic fundoplication [12]. Therefore, patients with heartburn as the main symptom who respond adequately to PPIs are excellent candidates for anti-reflux surgery (this is the only Grade A recommendation of the aforementioned ICARUS guidelines) [10].

2.2. Regurgitation as the main symptom

We should be aware that PPI therapy alters the pH of the gastric juice but does not eliminate the occurrence of gastroesophageal reflux episodes. Reflux episodes increase during the postprandial period irrespective of PPI therapy (patients on PPI mostly having nonacid reflux episodes and patients off PPI mostly having acid reflux episodes) [13]. For this reason, while patients on PPI often present symptomatic relief of their heartburn (intrinsically related to the acidity of the reflux episodes), regurgitation might persist. In contrast to medical therapy, a fundoplication restores the lower esophageal sphincter function and abolishes reflux of all gastric content into the esophagus. Therefore, an anti-reflux operation is a very good alternative for patients with symptoms related to the large volume of reflux contents (i.e. regurgitation), regardless of the response pattern to PPI therapy.

2.3. GERD symptoms and large hiatal hernia

The presence of hiatal hernia is not commonly discussed in guidelines as a relevant factor for considering or not anti-reflux surgery. Type I sliding hiatal hernias are a common finding in the general population and can even be asymptomatic. Repair of a small type I hernia in the absence of gastroesophageal reflux disease or in patients who respond satisfactorily to PPIs is probably not necessary [14]. However, patients with a large hiatal hernia often have GERD symptoms and are more likely to remain symptomatic despite medical therapy, mostly because of a low compliance of the gastroesophageal junction and an increased number of reflux episodes in the supine position [15].

A recent study investigated how the size of a hiatal hernia affected the esophageal function, reflux profile, and degree of mucosa injury. Increasing size of a hiatal hernia was associated with decreased pressure of the lower esophageal sphincter and weaker peristalsis on high-resolution manometry. Ambulatory pH monitoring showed that patients with larger hernias had more acid reflux in both the distal and proximal esophagus, and endoscopy revealed more severe esophagitis in those with large hernias. In addition, 50% of the patients with a hiatal hernia >5 cm had Barrett's esophagus [16].

Overall, symptomatic patients with a large hiatal hernia (>3 cm) have more severe reflux episodes and a higher risk of GERD complications (i.e. severe esophagitis and/or Barrett's esophagus). Non-surgical management with medical therapy can still be considered in asymptomatic or oligosymptomatic patients with large hiatal hernia (especially frail or elderly patients). However, as medication is not capable of fixing a severely altered gastroesophageal junction anatomy, symptomatic patients with large hiatal hernia should be strongly considered for anti-reflux surgery.

2.4. Poor adherence to medical therapy

Adherence to medication should be investigated in patients with poor response to PPIs. Although long-term PPI prescribing is very common in general practice, only a minority of patients request their prescriptions regularly [17]. Main factors determining whether or not patients take the medication are the presence or severity of symptoms, desire to remain in personal control, fear of side-effects, and lack of knowledge about the drugs [17]. A previous study showed that a large proportion of patients without need of long-term treatment use PPI for an unnecessary extended period, and half of the patients use PPI on-demand or intermittently [18]. Therefore, anti-reflux surgery should at least be discussed with symptomatic patients with poor adherence to medical treatment.

2.5. Refusal to long-term medical therapy

Some patients (especially young patients) refuse a strategy with life-long medication use due to quality-of-life considerations, anticipated high expenses, or concerns about the accumulated risk of side effects. Patients with poor adherence to medical therapy are also more likely to refuse long-term medical therapy. The REFLUX trial has demonstrated that

a laparoscopic anti-reflux operation is a cost-effective alternative to continued medical treatment over five years [19]. A recent study also showed that anti-reflux surgery was less expensive and more effective over PPI medication after 9 years of follow-up [20]. Thus, offering an anti-reflux operation to a patient refusing long-term medical therapy is a reasonable alternative.

2.6. Side effects of medical treatment

PPIs were clinically introduced more than 30 years ago and have since proven to be effective and safe [21]. Adverse effects, however, may occur especially in patients with extended use. Adverse outcomes unrelated to acid inhibition include allergic reactions, acute interstitial nephritis, chronic kidney disease, cardiac events, dementia, and drug interactions; adverse effects due to acid inhibition include electrolyte abnormalities, nutrient deficiencies, gastrointestinal infections, pneumonia, osteoporosis/fractures, and small intestinal bacterial overgrowth [22–24].

Although most side effects might be association and not causation, physicians should discuss the risks and benefits of PPIs with their patients. In addition, potential adverse effects related to acid suppression therapy should be monitored. Nevertheless, current evidence linking PPI use to long-term adverse consequences remains weak.

2.7. Barrett's esophagus

Barrett's esophagus (BE) is defined as the presence of at least 1 cm of metaplastic columnar epithelium replacing the stratified squamous epithelium normally lining the distal esophagus. Currently, the presence of intestinal metaplasia (columnar epithelium with goblet cells) is also needed for the diagnosis of BE [25]. Around 10–15% of the patients with GERD will eventually develop BE, which is the strongest risk factor for esophageal adenocarcinoma [26].

Several studies have tried to determine the value of anti-reflux surgery in the setting of BE with conflicting results [27–30]. The American College of Gastroenterology states: 'Anti-reflux surgery should not be considered as an antineoplastic measure in the setting of BE. Therefore, the indications for this procedure in BE patients are the same as those in general GERD patients' [25]. However, a fundoplication might be rational for patients with BE due to the following reasons: (a) biliary reflux plays an important role in the pathophysiology of BE and PPIs do not impede biliary reflux; (b) large hiatal hernias and severe esophageal motility disorders (i.e. hypotonic sphincter and hypomotility) are often present in patients with BE; and (c) elimination of symptoms with medical therapy does not guarantee adequate reflux control due to the reduced sensitivity of the metaplastic epithelium.

In patients with BE and low-grade dysplasia, both close endoscopic surveillance and radiofrequency ablation (RFA) are valid. In patients with high-grade dysplasia, RFA is mandatory [31]. After complete endoscopic eradication of BE, a fundoplication might help reduce recurrence rates of BE [32].

Although the indication for anti-reflux surgery in patients with BE remains debatable, a fundoplication should at least be considered on a case-by-case basis in symptomatic patients because it effectively controls GERD symptoms.

3. Outcomes of anti-reflux surgery

Studies with long-term follow-up have shown good results after anti-reflux surgery. Dallemagne and colleagues reported that at 10 years, almost 90% of the patients were free of significant reflux, and quality of life scores were still significantly better than preoperative scores of patients under medical therapy [33]. Another study with a mean follow-up of 11 years after laparoscopic fundoplication showed that the vast majority of patients had their symptoms resolved or significantly improved, 93.3% of the patients would have the procedure again, and 70% were off daily anti-reflux medications [34]. Laparoscopic fundoplication durability at 20 years was also analyzed, with 94% of patients reporting only occasional or fewer reflux symptoms and 90% satisfied with their choice of surgery [35]. Successful long-term outcomes have also been shown in studies using objective measurements of GERD with pH monitoring [36].

Laparoscopic anti-reflux surgery is indeed effective for enhancing physiological factors related to GERD, including LES pressure and esophageal acid exposure [37]. A meta-analysis comparing medical and surgical treatment in patients with GERD reported that heartburn and regurgitation were significantly less frequent after surgical intervention. Although a proportion of patients still needed anti-reflux medication after LARS, most patients were highly satisfied with the operation [38]. A recent study analyzed long-term clinical outcomes after LARS and found a statistically significant reduction of GERD symptoms compared to the preoperative period. LARS was associated with an overall satisfaction rate of 86% at long-term follow-up [39]. Many studies have also found long-term reduction in the use of PPIs following anti-reflux surgery [40,41].

4. Factors associated with poor outcomes

4.1. Technical failures

Technical elements of the operation such as malformation of the wrap or inadequate crural closure are common causes of failure [42,43]. The standardization of the following key technical steps is recommended to achieve optimal surgical outcomes.

Step 1: Division of the gastrohepatic ligament starting above the caudate lobe of the liver toward the right crus, which should then be separated from the esophagus with blunt maneuvers. The posterior vagus nerve is identified at this point. The right crus is dissected all the way down toward the junction with the left crus.

Step 2: Division of the phrenoesophageal membrane above the esophagus, and identification of the anterior vagus which should be left attached to the esophageal wall. The left pillar of the crus is separated from the esophagus and dissected bluntly downward toward the junction with the right crus.

Step 3: Division of the upper short gastric vessels starting from a point midway along the greater curvature of the stomach. This will allow performing a tension-free fundoplication afterward.

Step 4: Creation of a window between the gastric fundus, esophagus, and diaphragmatic crura, and placement of Penrose drain around the esophagus. Retracting the esophagus away from the hiatus with the Penrose drain will help perform mediastinal dissection in order to obtain at least 3 cm of esophagus below the diaphragm.

Step 5: Closure of the diaphragmatic crura with interrupted non-absorbable sutures (e.g. 2-0 silk or polyester). The esophagogastric junction is a complex anti-reflux barrier whose integrity relies on both the intrinsic lower esophageal sphincter (LES) and the extrinsic crura diaphragm. Some studies suggest that while the fundoplication reinforces the LES, the diaphragm closure is critical for restoring the EGJ competency and preventing hiatal hernia recurrence [44–49].

Reinforcement of the hiatus with a mesh has been promoted to further reduce recurrence rates [50,51]. Current evidence, however, does not support the systematic use of prosthesis [52]. Mesh reinforcement of the hiatus might be useful in selected cases such as large paraesophageal hernias with poor quality of the crura (usually elderly patients) or redo operations [53].

Step 6: Wrap construction. There are two main types of fundoplication during an anti-reflux operation: total 360° fundoplication (Nissen fundoplication) or partial posterior 240° fundoplication (Toupet fundoplication). As both types of fundoplication are similarly effective for controlling abnormal reflux [54,55], the choice of the type of the wrap should be based on the surgeon's own training and experience. In patients with severely impaired esophageal motility identified in the preoperative esophageal manometry, a partial fundoplication is preferred (Figure 1).

The Hill repair reestablishes the gastroesophageal flap valve and anchors the gastroesophageal junction to the

preaortic fascia. This procedure is often added to the fundoplication to decrease recurrence rates and has shown long-term durability and successful outcomes [56–58]

Overall, a proper surgical technique is critical for obtaining optimal outcomes. In addition, minimally invasive surgery should always be encouraged due to numerous advantages such as shorter hospital stay, lower morbidity and mortality, and lower costs for the healthcare system as compared to the conventional approach [59]. Finally, an anti-reflux operation should be performed by a specialized foregut surgeon and preferably at a high-volume center [60].

4.2. Incomplete diagnostic work-up

The diagnosis of GERD solely based on symptoms is often wrong because the clinical presentation is heterogenous and symptoms overlap with other gastrointestinal disorders [61,62]. In fact, a previous study showed that when the diagnosis of GERD is based exclusively on the presence of heartburn and regurgitation, around one-third of patients have normal esophageal acid exposure [63]. As previously established by a panel of expert gastroenterologists and surgeons, the diagnostic work-up before an anti-reflux operation should include: upper endoscopy, barium esophagram, esophageal manometry, and pH monitoring. In selected cases, a gastric emptying study is also needed [64].

The ambulatory pH monitoring is the gold standard for the diagnosis of GERD because it objectively establishes pathologic acid exposure and correlates specific symptoms with episodes of gastroesophageal reflux. An abnormal pH monitoring is not an indication for anti-reflux surgery *per se*, but rather confirms that the patient has GERD and establishes a correlation with symptoms.

Esophageal manometry is critical to rule out primary esophageal motility disorders, such as achalasia, which can present with similar symptoms to GERD (i.e. heartburn, dysphagia,

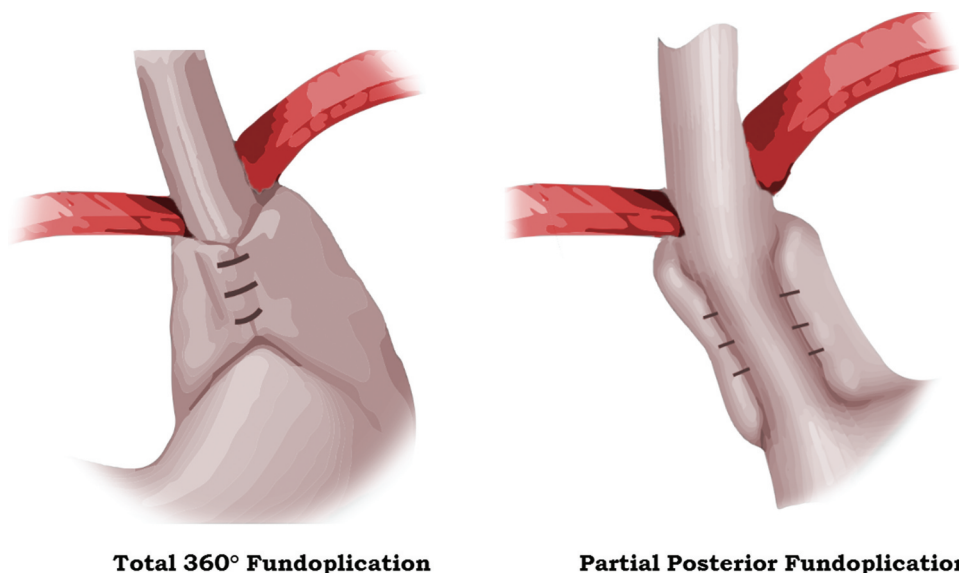


Figure 1. Total 'Nissen' fundoplication and partial 'Toupet' fundoplication.

and regurgitation). Motility disorders caused by GERD are also commonly seen such as ineffective esophageal motility, distal esophageal spasm, or hypercontractile esophagus. Absent peristalsis can also be detected in patients with severe reflux symptoms [65,66]. The identification of any of these manometric patterns can help tailoring the operation, especially on whether to perform a total or partial fundoplication (i.e. partial fundoplication is preferred in patients with severe esophageal dysmotility).

The EndoFLIP is a novel diagnostic tool that generates a 3D image of the esophageal lumen using high-resolution impedance planimetry. This technology measures pressure, diameter, and volume changes within the esophagus, offering detailed insights into its functionality and motility. The EndoFLIP can be used preoperatively for diagnosis, intraoperatively for guidance, and/or postoperatively to assess response to therapy [67,68]. During the operation, it can assist surgeons in adjusting the tension of the fundoplication by providing real-time measurements of esophageal distensibility and pressure. A tailored fundoplication based on the patient's esophageal anatomy, distensibility, and motility could potentially improve surgical outcomes [69,70].

4.3. Obesity

Patients undergoing anti-reflux surgery should have a body mass index $<35 \text{ kg/m}^2$. Patients with morbid obesity have significantly increased intra-abdominal pressure due to deposition of abdominal fat. In fact, the altered transdiaphragmatic pressure gradient due to an increased abdominal pressure is the main pathophysiologic factor of GERD in these patients [71]. As the fundoplication acts mainly at the gastroesophageal barrier, it is more likely to fail in obese individuals. A Roux-en-Y gastric bypass is ideal in this scenario because it provokes substantial weight loss and is an excellent anti-reflux operation: the acid reflux is prevented due to the few parietal cells in the small gastric pouch, and the biliary reflux is avoided because of the Roux-en-Y loop configuration.

5. Adverse events of anti-reflux surgery

An antireflux surgery is a safe operation when performed by experienced surgeons. Acute postoperative complications are very uncommon but may include gastrointestinal visceral perforation (mainly esophagus or stomach), pneumothorax, bleeding, and splenic injury [72]. Late postoperative complications or side effects occur more frequently and might cause patients' dissatisfaction despite adequate control of reflux symptoms.

Dysphagia: Patients might suffer from some degree of transient dysphagia in the initial weeks following a fundoplication. Long-term dysphagia, however, is rare and should raise concern for a technical problem (e.g. tight wrap, long wrap $>2.5 \text{ cm}$) and/or wrap performed with the body of the stomach rather than the fundus). The use of a bougie inside the esophagus while performing the fundoplication decreases the incidence of long-term dysphagia [73]. Persistent dysphagia after fundoplication should be initially treated with endoscopic dilatations [74].

Esophageal dilations should start with small balloon diameters (i.e. 10 mm) and gradually increase them over sessions to minimize the risk of complications. Multiple dilation sessions might be required with a success ranging from 50% to 67% [75,76]. A redo operation might be needed in cases of refractory dysphagia. These patients should undergo a thorough diagnostic work-up to understand the pathophysiology involved in the onset of the dysphagia. Redo anti-reflux surgery is associated with significantly higher morbidity, and thereby an extensive surgical planning is recommended [77].

Gas-related symptoms: Bloating, inability to belch, early satiety, and flatulence may occur after a fundoplication [78,79]. It is unclear why some patients develop gas-related symptoms after anti-reflux surgery and others do not [80]. Inability of the surgically modified gastroesophageal junction to relax in response to gastric distention, aerophagia (relatively common among patients with severe GERD), and vagus nerve injury are potential pathophysiologic factors. Dietary modifications (i.e. avoidance of gas-producing foods and carbonated beverages), eating slower to avoid aerophagia, gas-reducing agents (i.e. simethicone), and prokinetic medications can help. However, patients should be aware of these possible side effects to help manage expectations from surgery.

Vagus nerve injury: The vagus nerve can be unintentionally injured if it is not properly identified during the procedure (e.g. large hiatal hernia, adhesions, poor visibility of the anatomy in the gastroesophageal junction, anatomical variations of the vagus nerve, and inexperienced surgeon). Postoperative gastric emptying is significantly delayed in patients with vagus nerve injury, and patients might suffer from nausea, vomiting, and/or bloating [81].

Diarrhea: Although postoperative diarrhea is relatively common, its pathophysiology is not yet fully understood. Post-fundoplication enhanced gastric emptying contributing to a more rapid gut transit, inadvertent vagotomy, dietary modifications after fundoplication (e.g. liquid and bland diets) and/or exacerbation of underlying irritable bowel syndrome are potential causes [72,82]. Antimotility drugs, antibiotics for small intestinal bacterial overgrowth, and cholestyramine can be empirically used in these patients.

6. Other treatments for GERD

6.1. Magnetic sphincter augmentation device

The magnetic sphincter augmentation (MSA) device (i.e. LINX) consists of a flexible ring created with titanium beads with a magnetized core that is placed around the LES. The magnetic force restores the LES barrier function preventing the passage of stomach contents into the esophagus [83]. The LINX procedure is currently approved for GERD patients with indications for anti-reflux surgery, normal esophageal motility, BMI $< 35 \text{ Kg/m}^2$, no previous foregut surgery, and hiatal hernia $<3 \text{ cm}$. Multiple studies have shown that LINX is an effective treatment modality with most patients achieving symptom relief and improvement in quality of life. Dysphagia, however, is relatively common after the procedure and requires device removal in some patients [84,85]. Albeit rare, serious complications such as esophageal erosion and/or device migration can also occur [86].

6.2. Endoscopic procedures

Multiple endoscopic therapies are currently available for the management of GERD. Although these techniques are indeed less invasive than anti-reflux surgery, the strict patient selection for endoscopic procedures somehow limits their use. In general, patients should not have severe esophagitis (LA grade C/D), esophageal strictures, and/or large hiatal hernia (>3 cm).

6.2.1. Endoscopic radiofrequency ablation of the lower esophageal sphincter

The endoscopic radiofrequency ablation of the LES (i.e. Stretta procedure) consists in delivering radiofrequency energy above and below the Z-line, ultimately causing decreased compliance and distensibility of the LES [87]. Previous research has proven that the procedure improves GERD Health-Related Quality of Life (GERD-HRQL) scores, reduces heartburn symptoms, and reduces esophagitis rates. [88]. A significant reduction in medication use was also seen in short- and long-term studies [89,90]. A meta-analysis comparing Stretta to sham treatment, however, showed that Stretta did not improve objective GERD outcomes [91]. Due to heterogenous results in different studies, the procedure is not yet endorsed by the American College of Gastroenterology [92].

6.2.2. Transoral incisionless fundoplication

The transoral incisionless fundoplication (TIF) procedure relies on restoring the angle of His and reinforcing the gastroesophageal valve function by the creation of an endoscopic 270° fundoplication (plication formed by full-thickness apposition of the gastric fundus to the distal esophagus with non-absorbable sutures).

A previous randomized study with 5 years follow-up showed that the procedure provides long-term and durable relief of GERD symptoms, improvement in quality of life, and reduction of medication utilization [93]. A recent-analysis also demonstrated substantial improvements in quality of life and pH scores after TIF procedure with a 2.4% adverse event rate consisting of perforation and bleeding [94]. Another study also showed avoidance of daily use of PPIs in the vast majority of patients (30% of patients off PPIs at 6 years) [95]

6.2.3. Anti-reflux mucosectomy

Anti-reflux mucosectomy (ARMS) is a novel endoscopic procedure first reported in 2014 which involves the resection of the mucosa of the cardia and gastroesophageal junction. This technique generates constriction of the LES by scar formation during mucosal healing. Several studies have shown successful outcomes after the procedure [96–98]. A recent study has demonstrated a relatively high weighted pool proportion of patient satisfaction and a significant improvement in GERD-HRQL. There was also a significant decrease in the use of PPIs and in the DeMeester score after ARMS [99]. Complications such as stricture, perforation, or bleeding might occur after the procedure. Dysphagia is the most common side effect, and it can usually be treated with endoscopic dilatation [100,101].

Table 1 shows the outcomes of different therapies for GERD.

Table 1. Characteristics and outcomes of studies analyzing different therapies for gastroesophageal reflux disease.

Author	Patients (n)	Median Follow-up (months)	Pre Procedure				Post Procedure					
			GERD-HRQL score	Use of PPI (%)	LES pressure (mmHg)	DeMeester Score	Median Procedure time (min)	Patient satisfaction (%)	GERD – HRQL score	Use of PPI (%)	LES pressure (mmHg)	DeMeester Score
Laparoscopic anti-reflux surgery												
Hamey* [102]	296	12	NR	100	12.1	35.3	NR	NR	NR	NR	22.4	5.1
Schwameis [103]	75	48	NR	100	14.2	36	NR	100	NR	11	NR	NR
Salvador [104]	112	240	NR	100	8	32	153	86.8	NR	26.8	NR	NR
Wang [41]	200	78	30	100	NR	52.7	NR	76	9	47.1	NR	NR
TIF												
Testoni [95]	50	52.7	20	100	8	22	69	NR	17	12.2	12	19
Witteman [105]	60	12	27.1	100	15.3	NR	33.4	NR	10.3	36	17.6	NR
MSA												
Ayazi [106]	553	10.3	33.8	NR	NR	33.9	NR	NR	7.2	6.3	NR	7.2
Bonavina [107]	465	36	22	97.8	NR	NR	43	NR	4.6	24.2	NR	NR
Stretta												
Meier [108]	140	20	12.9	100	14.8	72.9	38–75	NR	6.6	61.7	16.7	35.1
Dughera [109]	86	12	31	100	9.3	NR	50	87	20	23	NR	NR
ARMS												
Wong [97]	33	6	20.5	100	NR	20	36	NR	6	9.1	NR	NR
Wang [110]	18	24	13.4	100	NR	31.7	NR	NR	10	38.9	NR	NR

Abbreviations: GERD-HRQL: Gastroesophageal reflux disease Health-Related Quality of Life; PPI: Proton pump inhibitors; LES: Lower Esophageal Sphincter; NR: Not reported; TIF: Transoral incisionless fundoplication; MSA: Magnetic Sphincter Augmentation; ARMS: Antireflux mucosectomy.

7. Conclusion

Patient selection for anti-reflux surgery is challenging. A correct indication for surgery, a complete diagnostic work-up, and a properly executed operation are critical for a successful anti-reflux surgery. Most patients undergoing a fundoplication have adequate long-term symptomatic relief. However, potential side effects of anti-reflux surgery should also be discussed with patients to help manage expectations from the operation. Multiple endoscopic anti-reflux therapies are also currently available for a selected group of patients.

8. Expert opinion

Selecting patients for anti-reflux surgery is challenging and there is a lack of consensus among general practitioners, gastroenterologists, and surgeons on which patients should be referred for fundoplication. Indication for surgery has been traditionally based on symptom patterns and response to medical therapy. In fact, patients suffering from ‘refractory GERD’ with no response to PPIs were commonly referred to surgery. Pathophysiology of GERD is now better understood, and we know that a good response to medical therapy is actually a strong positive predictor of surgical success. Understanding how an anti-reflux operation works is key to determining which symptoms are most likely to resolve. However, indication for surgery should never be solely based on symptoms or endoscopic findings because GERD may present with a broad variety of symptoms and there is frequent

overlap with other gastrointestinal disorders (e.g. functional dyspepsia or irritable bowel syndrome). A thorough preoperative work-up including esophageal manometry and pH monitoring is always needed before the operation. Pathophysiological and clinical disease phenotypes will ultimately guide anti-reflux therapy.

Several studies have shown a decline in the use of anti-reflux surgery in the last decade. The rising prevalence of obesity might partially explain the reduced number of fundoplications. A large proportion of patients with GERD are obese, and most of these patients currently undergo bariatric surgery. However, patients and gastroenterologists concern regarding surgical outcomes and side effects might have also contributed to this decline. Poor selection of patients for surgery and non-optimal surgical results will indeed encourage underutilization of anti-reflux surgery. For this reason, surgeons with vast experience in upper gastrointestinal surgery and profound knowledge of GERD pathophysiology should take care of these complex patients.

Treatment of GERD is evolving, and novel anti-reflux procedures have emerged in the last two decades. Magnetic sphincter augmentation device (LINX), transoral incisionless fundoplication (TIF), radiofrequency energy application to the lower esophageal sphincter (Stretta), and anti-reflux mucosectomy (ARMS) are some of the innovative available treatment modalities for GERD. In the near future, even more endoscopic therapies will be available. Less pain, shorter hospital stays, and the absence of relatively common side effects of fundoplication (i.e. gas-related symptoms) are some

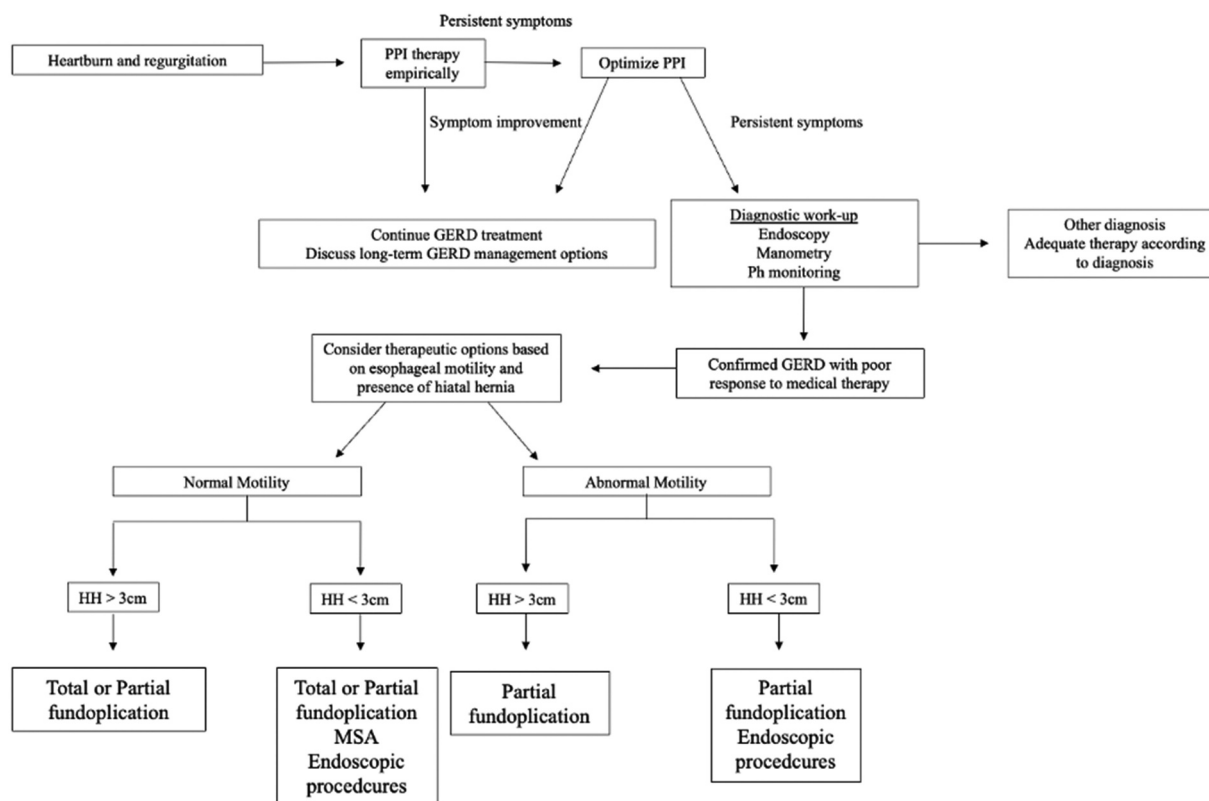


Figure 2. Algorithm for the management of gastroesophageal reflux disease (PPI: proton pump inhibitors; GERD: gastroesophageal reflux disease; HH: hiatal hernia; MSA: magnetic sphincter augmentation).

potential advantages. Also, as revisional surgery is challenging and is associated with higher morbidity, endoluminal procedures are particularly attractive for patients with prior fundoplication or bariatric surgery. Finally, these alternative therapies might fill the therapeutic gap of patients who are not effectively treated with PPIs but refuse to undergo an anti-reflux operation.

Although promising short-term effects have been reported with these novel procedures, results should be interpreted with caution given the small number of patients and significant heterogeneity among most of the studies. In addition, very few studies have shown consistent improvement in objective measurements. Fundoplication has been used to treat GERD for more than 60 years and has vastly proven safety and efficacy. Therefore, further research assessing long-term safety and feasibility is needed to embrace novel therapies in the treatment armamentarium for GERD.

An experience- and evidence-based algorithm for the management of GERD is proposed by the authors (Figure 2).

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