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Surgical Anti-Reflux Options Beyond Fundoplication

Dan Azagury[1] · **John Morton**[1]

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Abstract
Purpose of Review This paper provides an overview of current and future surgical interventions available for the management of gastroesophageal reflux disease (GERD) beyond the well established and recognized fundoplication. Review the current indications and outcomes of these surgical procedures.
Recent Findings Fundoplication has been a cornerstone of the surgical management of GERD. However, other effective surgical options exist and can be considered based on prior interventions as well as patient, anatomical or other factors. These options are intended to address some of the shortcomings or potential complications of fundoplication such as symptom recurrence, dysphagia, or gas bloating, for example.
Summary Alternative procedures to fundoplication include magnetic sphincter augmentation, electrical stimulation and Roux-en-Y gastric bypass. The indication for surgical management remains failure of or inability to tolerate medical therapy.

Keywords GERD · Fundoplication · Magnetic sphincter augmentation · Gastric bypass · LES electrical stimulation (EndoStim)

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✉ John Morton
morton@stanford.edu

Dan Azagury
dazagury@stanford.edu

[1] Section of Bariatric and Minimally Invasive Surgery, Stanford University School of Medicine, 300 Pasteur Drive, H3680A, Stanford, CA 94305-5655, USA

Introduction

Nissen and Rossetti first reported and described the fundoplication as a treatment for gastroesophageal reflux disease (GERD) more than a half century ago, in 1959 [1]. In 1991, Bernard Dallemagne revolutionized the procedure and reported the first laparoscopic Nissen fundoplication (LNF) [2]. Twenty-five years later, this procedure remains a cornerstone of surgical management of GERD. LNF has demonstrated its overall long-term safety and efficacy; however, some shortcomings exist with the procedure. These include recurrence, dysphagia, gas-bloating or the inability to belch. Other effective surgical options exist and can be considered on the basis of patient, anatomical or other factors. They include magnetic sphincter augmentation, electrical stimulation and Roux-en-Y gastric bypass. This article will review the current indications and outcomes of these surgical procedures.

Magnetic Sphincter Augmentation (LINX)

The magnetic sphincter augmentation (MSA) device is an FDA-approved device (LINX Reflux Management System, Torax Medical, Shoreview, MN, USA). It was specifically designed to provide an alternative to LNF. It was devised to dynamically increase the lower esophageal pressure and consists of a chain of magnetized beads placed laparoscopically around the gastroesophageal junction (GEJ). The magnetic attractive forces between beads augment the pressure circumferentially around the GEJ. Esophageal peristaltic contractions usually produce 40 to 100 mmHg of pressure that allow the food bolus to overcome the force of the device and to pass the GEJ normally. In a similar way, while gastric refluxate will not have sufficient pressure to overcome the augmented barrier, emesis will generate enough force to do so and allow patients to vomit if needed.

The device was approved by the FDA based on the 1-year results of a multi-center trial involving 100 patients [3]. Subsequent 3-year results demonstrated that 64% of patients achieved either resolution or >50% reduction of acid exposure. Ninety-three percent of patients were able to reduce their proton pump inhibitor (PPI) use by at least 50%, and the prevalence of esophagitis decreased from 40% to 12% ($p < 0.001$). Patient satisfaction was 94%, as compared to 13% preoperatively, and all but 2 patients maintained their ability to vomit. Of note, cruroplasty was performed in 34% of patients [4•].

The 5-year results of this same trial have recently been published [5]. Of the initial 100 patients, 85 were available for follow-up. The study consisted of clinical assessment and questionnaires as well as endoscopy (in 82 patients). A reduction of 50% or more in the average daily dose of PPIs occurred in 89.4% of patients (76 of 85 patients) compared to 93% at the one-year mark. Of the 40 patients with preoperative esophagitis, 34 underwent follow-up endoscopy, and among them, 8 still had esophagitis at 5 years, as compared with 12 (of 100) at the 1-year mark. Among the 8 patients with ongoing esophagitis, 6 patients were classified as grade A and the other patients as grade B. Five patients developed de novo esophagitis over the 5 years of follow-up.

In this cohort, postoperative dysphagia occurred in 68% of patients in the early postoperative setting, in 11% at 1 year and in 5% at 5 years (vs. 6% preoperatively). Nineteen patients required endoscopic dilation during the first year. Device removal occurred in 7 patients in total over the 5-year period. Severe and persistent dysphagia was rare but led to the early removal of the device (≤3 months) in 3 patients. In a fourth patient, the device was removed because of dysphagia at 5 years. In the 3 other patients, two removals occurred at the second year due to intermittent vomiting and persistent reflux symptoms, respectively, while the last device was removed in year 3 because of persistent chest pain. Interestingly, 3 of these 7 patients subsequently underwent a Nissen fundoplication.

Some trials have compared MSA to either LNF or Toupet fundoplication. In a matched, non-randomized comparison of 50 patients, LNF and MSA were equivalent at 1 year in terms of PPI use, dysphagia, symptomatic GERD resolution and GERD-related quality of life. Gas-bloating was more frequent in the LNF group (10 vs. 0 cases) [6]. A similar study compared 103 patients undergoing Toupet fundoplication with 138 patients undergoing MSA over at least 1 year, and conclusions were similar. Patients in both groups had similar GERD-related quality of life, PPI use, gas-related symptoms and dysphagia [7].

The most feared complication regarding MSA is esophageal erosion. In a pooled analysis of the first 1000 cases, the device removal rate was reported as 3.4%, and erosions were reported in 0.1% of cases [8]. A recent study with a relatively high follow-up rate focused on device removal. Of 164 patients followed for a median of 4 years, 11 required removal (6.7%), including 2 patients with esophageal erosion (1.2%). The median duration of therapy prior to removal was 20 months and ranged between 11 and 47 months. The two erosions occurred at 12 and 19 months after implantation and were treated laparoscopically [9•]. Based on recent small publications, it appears that of approximately 5500 devices that have been placed worldwide thus far, 190 have been removed, and 11 erosions (0.2%) have occurred [10, 11].

Laparoscopic Roux-en-Y Gastric Bypass

The prevalence of obesity in the USA reached 37.7% in 2014 [12]. There is also a clear association between increasing BMI and reflux symptoms, suggesting that obese patients may be relatively more likely to seek treatment for GERD [13]. When it comes to surgical management of GERD, obesity has been shown to be a major risk factor for the failure of standard approaches such as LNF. In a retrospective study, the recurrence rate of reflux after LNF was 4.5% in patients with body mass index (BMI) < 25 kg/m^2 and 31% in patients with BMI > 30 kg/m^2, a greater than sixfold increase [14]. Obese patients are therefore a distinct population in both gastroenterological and surgical GERD clinics who are likely not well served by LNF. A survey of 92 surgeons showed that 35% would rather chose to do nothing rather than subject these patients to a fundoplication [15].

The Roux-en-Y gastric bypass (RYGB) was first described by Mason and Ito nearly 50 years ago [16]. They described improvements in the technique that would reduce the presence of acid in the proximal stomach, including a small proximal gastric pouch; according to the authors, "Renewed emphasis on a very small fundic segment will mean even fewer parietal cells and this should further decrease the incidence of stoma ulcer". In 1982, a series of six morbidly obese patients with symptomatic reflux esophagitis and hiatal hernia was described. They were treated with RYGB, which led to successful symptom resolution in all 6 cases [17]. The procedure, now performed laparoscopically (LRYGB), creates a very small gastric pouch along the lesser curve that separates most of the acid producing cells from the distal esophagus. A Roux limb (60–150 cm) is brought up and anastomosed to the pouch, and a Y reconstruction is performed distally, approximately 40–60 cm from the ligament of Treitz, preventing bile reflux into the distal esophagus.

Until recently, the effectiveness of RYGB on GERD had mostly been assessed by preoperative and postoperative symptom questionnaires. In a cohort of 152 patients, these questionnaires demonstrated a significant decrease in heartburn (87 to 22%, $p < 0.001$) as well as in the use of PPI and H2 blockers (44 to 9%, $p < 0.001$ and 60 to 10%, $p < 0.01$; respectively) [18]. Another study of 239 patients showed similar results with symptom improvement in 89% of patients at 3 months and 94% at 9 months. GERD-related medication use

decreased from 30% of patients preoperatively to 3% at 3 months and 5% at 9 months postoperatively [19]. A couple of studies included pH data in small cohorts. A comparison of 6 patients after LNF and 6 after laparoscopic Roux-en-Y gastric bypass (LRYGB) demonstrated a highly significant decrease in mean DeMeester score in both cohorts, from 64.3 to 2.8 in the LNF group and from 34.7 to 5.7 in the LRYGB group [20]. In another study of 20 patients who had undergone LRYGB, the percentage of time spent with pH < 4 was 10.7 ± 6.7 before and 1.6 ± 1.2 after LRYGB ($p < 0.001$) [21].

The level of evidence in favor of RYGB for the treatment of GERD has been lately strengthened. A recent publication reported 3-year follow-up results of a prospective trial including objective data on 55 patients. The study included preoperative and postoperative GERD symptoms, endoscopic appearance and, most importantly, 24-h pH probe results. These metrics were obtained preoperatively and at 6 months and 3 years postoperatively. This study included only morbidly obese patients, and results were extremely favorable: reflux symptoms improved at both 6 months and 3 years, and the incidence of esophagitis decreased from 45% at baseline to 32% at 6 months and 19% at 3 years. DeMeester scores decreased from 28.6 at baseline to 9.4 at 6 months and 1.2 at 3 years ($p < 0.001$). Of note, these procedures were performed in an open fashion and included a silastic ring [22•].

The safety profiles and costs of LNF and LRYGB have also been compared using a large national database (University HealthSystem Consortium database). This study included 6100 LNF patients and 21,150 LRYGB patients. The two procedures were associated with a comparable length of stay (3 days) and mortality (0.05 vs. 0.1% (NS)). The total hospital costs were also nearly identical ($13,100 vs. 13,200). Surprisingly, LRYGB patients had a significantly lower in-hospital complication rate than LNF (10 vs. 7% ($p < 0.05$)) [23].

There is little doubt that LRYGB should be the primary procedure choice in patients with a BMI > 35 kg/m^2 who are operated on for GERD. In obese patients with a BMI < 35, LRYGB likely remains the first choice, but the BMI cutoff for this prioritization is somewhat unclear at present. The LRYGB procedure also affords the additional advantage over LNF of substantial improvement in other obesity-related comorbidities like diabetes and hypertension.

LES Electrical Stimulation (EndoStim)

The EndoStim™ system (EndoStim, St. Louis, MO) is an implantable electrical stimulator that delivers electrical energy to the lower esophageal sphincter (LES). This device has not been approved by the FDA and is currently only available in Europe and South America. It is mentioned briefly as it provides a novel surgical approach to GERD management, and recruitment has started in the USA for a pivotal trial. Electrical stimulation is believed to increase the resting pressure of the LES and thereby to help control reflux [24]. Two stitch electrodes are implanted laparoscopically via superficial placement into the LES muscle along the main esophageal axis with approximately 10 mm of distance maintained between the electrodes.

At this time, only two clinical trials have been published regarding this device. The first one is out of Chile and included 25 patients assessing the safety and efficacy of the device, and the two-year results have just been published. Twenty-three patients are included in the follow-up. Median 24-h esophageal acid exposure improved from 10% at baseline to 4% ($p < 0.001$), and 71% of patients demonstrated either normalization or $a \geq 50\%$ decrease in their distal esophageal acid exposure. Sixteen of the 21 patients on PPI therapy reported complete cessation of PPI use postoperatively, and only 2 patients were still using a PPI regularly at 2 years. All 21 patients reported satisfaction with their level of symptom control at 2-year follow-up as compared to 2/24 (8%) at baseline. There were no device-related serious adverse events or dysphagia reported [1, 25].

More recently, an international multicenter trial has been initiated with centers in Europe, Asia, and South America. The early results for 45 patients at 6 months of follow-up were published in 2015. Results on acid exposure are comparable to the Chilean trial, with exposure to a pH <4.0 reduced from 10.0% (IQR 7.5–12.9) to 3.8% (IQR 1.9–12.3) at 3 months ($p = 0.0027$) and to 4.4% (IQR 2.2–7.2) at 6 months ($p < 0.0001$). Of note, two serious devices or therapy-related adverse events were reported. One small bowel perforation from a laparoscopic trocar placement was identified and repaired at the time of implantation (the device was then explanted as well). One patient had asymptomatic lead erosion, identified at the six-month EGD. The device was subsequently explanted and a Toupet fundoplication performed. Four patients, who also underwent crural repair at the time of implant, reported dysphagia, which resolved in all cases without intervention. Other adverse events were mostly comprised of discomfort, nausea, hiccups, and weight loss [2].

The advantages of the EndoStim include an apparent lack of effect on esophageal motility or LES relaxation and its reversibility with minimal disruption of the local anatomy. Long-term studies are needed to determine efficacy and comparative data as compared to other surgical reflux options [26, 27].

Conclusions

Laparoscopic Nissen fundoplication remains the cornerstone of surgical GERD management. It has some known shortcomings and potential complications, however. Surgical alternatives are aimed to provide effective GERD relief while addressing some of the limitations of LNF. Magnetic sphincter augmentation provides similar outcomes to LNF while allowing patients to belch and vomit. It is also reversible and has lower rates of postoperative gas-bloating. The potential for esophageal

erosion as well as small but non-negligible removal rates are the device's major drawbacks. LRYGB offers an alternative to LNF in obese and severely obese patients in whom GERD recurrence rates after LNF are higher than in non-obese patients. LRYGB provides long-term efficacy with significant improvement in additional obesity-related comorbidities and has comparable or lower complications rates, hospital stay, and costs relative to LNF. Its role in overweight or non-severely obese patients is not yet well defined. EndoStim is an experimental device in the USA that appears to be unique in its reversibility and minimal anatomic disruption, though further data are needed to comment adequately on its safety and efficacy.

Compliance with Ethical Standards

Conflict of Interest Dan Azagury and John Morton declare no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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