

Current Surgical Treatment of Gastro-oesophageal Reflux Disease

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Abstract

Gastro-oesophageal reflux disease (GORD) is a disorder caused by lower oesophageal sphincter (LOS) dysfunction. Local anatomical abnormalities such as a hiatal hernia can predispose to this condition, leading to the characteristic hypotonia or shortening of the LOS. Smoking, alcohol, obesity and pregnancy also predispose patients to GORD. The most significant factor in the development of GORD is transient LOS relaxation (TLOSR). TLOSR typically lasts for 10–45 seconds and is unrelated to swallowing. Barium oesophagram, upper gastrointestinal endoscopy, pH monitoring and oesophageal manometry remain the key elements in the diagnostic work-up of GORD. Medical management of GORD is aimed at treating the predisposing factors using lifestyle modification (weight loss, smoking, alcohol cessation and avoidance of predisposing foods, etc.) and medications (i.e. antacids or proton pump inhibitors). Surgical intervention is aimed at restoration of LOS function (i.e. fundoplication). Recently, endoluminal therapy has been employed in the treatment of GORD with promising short-term results.

Keywords

Gastro-oesophageal reflux disease, Barrett's oesophagus, Nissen fundoplication, transoral incisionless fundoplication, endoscopic antireflux procedure

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Pathophysiology of Gastro-oesophageal Reflux Disease

When properly functioning, the lower oesophageal sphincter (LOS) is a physiological, rather than an anatomical, structure located slightly cephalad to the gastro-oesophageal junction that prevents reflux of gastric contents into the oesophagus.¹ Hypotonia, shortening of the LOS and hiatal hernia predispose to gastro-oesophageal reflux disease (GORD). Sliding (type I) hiatal hernia is the most common hiatal hernia associated with this condition (see *Figures 1* and *2*). However, the presence of a hiatal hernia does not accurately reflect the occurrence of reflux disease.² Other predisposing factors include obesity, smoking, alcohol intake and pregnancy.

Normal LOS resting pressures range from 10 to 30mmHg higher than the gastric pressure. A physiological short relaxation phase ranges from two to eight seconds. Transient LOS relaxation (TLOSR) lasts longer (10–45 seconds), is unrelated to swallowing and is the most significant factor in developing GORD. TLOSR is triggered by the belch reflex and occurs between three and eight times per hour in patients with GORD.^{3,4}

Clinical Presentation

Upper mid-abdominal pain or 'heartburn' is the most common symptom of GORD. Dysphagia, regurgitation and globus are other gastrointestinal (GI) symptoms associated with GORD. The development of dysphagia may represent an oesophageal stricture. Endoscopic evaluation is mandatory to exclude the presence of a

mechanical obstruction. The impact of acid reflux can extend beyond the GI tract and may affect the pulmonary system.

Misdiagnosing GORD with asthma or recurrent chest infections is not uncommon as GORD can present with respiratory symptoms including altered voice, anosmia, asthma, cough or recurrent respiratory tract and sinus infections.⁵ These are referred to as atypical symptoms of GORD, laryngopharyngeal reflux (LPR) or laryngo-oesophageal reflux disease (LORD). Prior positive response to proton pump inhibitor (PPI) therapy is the most useful predictor for the relief of reflux-related respiratory symptoms following antireflux procedure (ARP).⁶

Diagnostic Evaluations

The anatomy of the oesophagus and the proximal stomach and the presence or absence of a hiatal hernia can typically be demonstrated by obtaining a barium oesophagram.⁷

Oesophagogastroduodenoscopy (EGD) helps to confirm the diagnosis of GORD by documenting active oesophagitis or Barrett's oesophagus. EGD allows for endoscopic sampling of Barrett's oesophagus to assess for dysplasia as well as excluding other disease processes, i.e. tumours. Thus, any surgical intervention must be preceded by an upper endoscopy.⁸

The most accurate and reliable test of oesophageal physiology is oesophageal manometry. LOS resting pressures normally range from

Figure 1: Large Hiatal Hernia

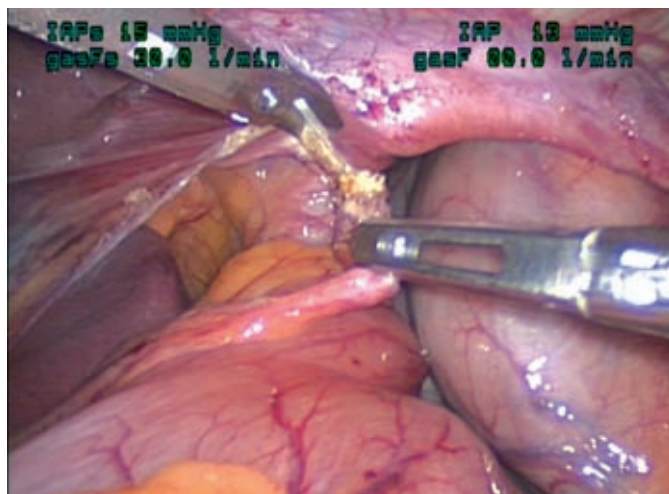
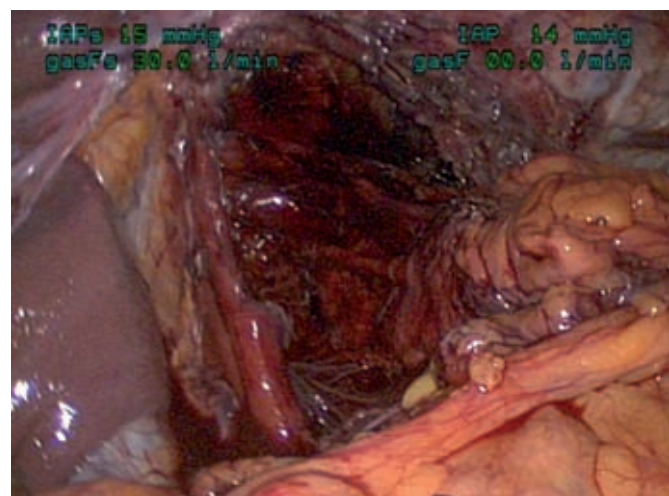


Figure 2: Large Hiatal Hernia After Mobilisation Obtaining 4cm of Intra-abdominal Oesophagus



10 to 30mmHg higher than the gastric pressure. GORD is more commonly encountered with LOS resting pressures less than 6mmHg and/or sphincter length of less than 2cm.⁹

Continuous pH monitoring is considered the gold standard for the diagnosis of GORD. The most commonly performed test to measure oesophageal pH is the single-channel pH probe. This involves placing a pH-sensitive catheter transnasally with the tip positioned proximal to the LOS when the patient is off antireflux medications. The patient continues normal diet and activity while pH measurements are obtained continuously for 24 hours. A composite DeMeester score is calculated using the total time with pH <4, the upright time with pH <4, the supine time with pH <4, the total number of episodes of pH <4, the number of episodes lasting longer than five minutes and the longest episode.¹⁰ Although the DeMeester scores are not standardised, a composite of more than 14.7 is generally considered abnormal. Over the last few years the Bravo capsule, which is placed endoscopically and does not require a catheter, has been implemented.

Barrett's Oesophagus

Barrett's oesophagus, intestinal metaplasia of the lower oesophagus, is a pre-malignant condition that might progress to adenocarcinoma. Frequently, patients with Barrett's oesophagus have GORD symptoms

that are difficult to control with medical therapy. There is little evidence that the natural history of Barrett's is affected by PPI use. Oelschlager et al.¹¹ reported excellent control of reflux and associated symptoms after ARP in patients with Barrett's oesophagus. More importantly, complete regression was demonstrated in 34 of 106 patients (32%) with this histological abnormality and in 55% of those with short segments (< 3cm) of Barrett's oesophagus. Hofstetter et al.¹² observed low-grade dysplasia regression to non-dysplastic Barrett's in seven of 16 patients (44%), while in nine of 63 (14%) intestinal metaplasia regressed to cardiac mucosa. Additionally, Bowers et al.¹³ reported a regression rate of 59% (13 of 22) of patients with short segments of Barrett's oesophagus. Given the increasing body of evidence suggesting the beneficial impact of ARP on the natural behaviour of Barrett's oesophagus and the risk of oesophageal cancer, surgical therapy should be strongly considered for patients with Barrett's oesophagus. However, it is clear that Barrett's oesophagus with high-grade dysplasia should not be treated with ARP, but instead requires oesophageal resection.

Management

Patient satisfaction with ARP has been well documented in the surgical literature with alleviation of symptoms in 88–95% of patients.^{14,15} These excellent results include patients with complicated GORD, such as those with large hiatal hernias, refractory oesophagitis and peptic strictures. Objective pH monitoring demonstrated excellent control of oesophageal acidification more than five years after ARP.¹⁵ A randomised, multicentre trial with five-year follow-up demonstrated that ARP is more effective than PPIs in controlling GORD symptoms.^{15–19}

A randomised trial with 10-year follow-up compared ARP with medical therapy (omeprazole), and demonstrated that surgical patients had improved relief of symptoms.¹⁹ Proponents of medical therapy argue that 60% of patients in the surgical group were taking antacids on a regular basis and should therefore be considered treatment failures. However, the liberal use of antacids in medical practice today makes medication use an unreliable outcome measure of ARP. Further flaws in this argument are illustrated by the fact that up to 75% of patients who take such medications after

Misdiagnosing gastro-oesophageal reflux disease (GORD) with asthma or recurrent chest infections is not uncommon as GORD can present with respiratory symptoms including altered voice, anosmia, asthma, cough or recurrent respiratory tract and sinus infections.

Nissen fundoplication have normal 24-hour pH results. Oelschlager's study from the University of Washington demonstrated symptomatic improvement in 93% of patients at six years after surgery, and more than 50% of the remaining patients had a normal 24-hour pH study.¹¹

Techniques of Fundoplication

The most commonly performed ARP is the 360° Nissen fundoplication (see Figure 3). The risk of post-operative dysphagia

has raised the discussion of total versus partial fundoplication. Proponents of the Nissen acknowledge that the wrap needs to be 'floppy' to minimise post-operative dysphagia. The floppy Nissen fundoplication is safe and effective, even in patients suffering from defective oesophageal peristalsis. Proponents of total fundoplication importantly note the decreased effectiveness of a partial fundoplication in controlling reflux.¹⁸

Two partial fundoplications in practice are the 180° anterior Dor fundoplication (see *Figure 4*) and the 270° posterior Toupet fundoplication. Fibbe et al.²⁰ compared laparoscopic Nissen and Toupet fundoplications in 200 patients with proven oesophageal motility disorders and found no difference in post-operative recurrence of reflux. Similarly, Laws et al.²¹ found no clear advantage of one wrap over the other in their prospective, randomised study comparing the use of these two fundoplications in patients with abnormal oesophageal motility. Moreover, in a meta-analysis of nine prospective randomised trials including open and laparoscopic Nissen versus Toupet fundoplications in 793 patients, no statistical difference was found in new-onset dysphagia or recurrence of reflux.²² Currently, partial fundoplication is implemented in patients with scleroderma and post-myotomy achalsia.²³

Endoluminal Therapy

Recent interest in the development of endoluminal therapy has led to new alternatives in the treatment of GORD. These treatment modalities are reserved for patients who suffer from a dysfunctional LOS but with no hiatal hernia. Therapy is performed transorally, via upper endoscopy. There are three principal types of endoluminal treatment of GORD. First, radiofrequency energy delivered to the LOS theoretically adds bulk to the LOS and changes the sphincter's compliance. Although the mechanism of action has not been fully established, it is presumably due to neurolysis and the abolishment of neuromodulated LOS relaxation. With the Stretta catheter (Curon Medical, Sunnyvale, CA, USA), radiofrequency energy is generated by a four-channel radiofrequency generator, which delivers 465kHz/2–5W per channel/80V through four nickel–titanium needle electrodes. Multiple prospective non-randomised studies with short-term results (up to two years) demonstrated promising results. Triadafilopoulos et al.²⁴ confirmed improved quality of life scores, decreased oesophageal acid exposure, decreased median DeMeester scores (from 40.0 to 26.4; $p < 0.009$) and 70% of patients off PPIs at 12 months. Additional data on long-term follow-up, including the incidence and natural history of oesophagitis in these patients, are needed to establish the utility of this procedure.

A second endoscopic therapy for GORD involves the creation of a mechanical barrier at the gastro-oesophageal junction (GOJ). Enteryx (Boston Scientific, Natick, MA) is an ethylene vinyl alcohol co-polymer that was endoscopically injected within the submucosa or muscular layers of the oesophageal wall 1–2mm proximal to the Z-line. This technique was discontinued by the company due to excessive complications.²⁵ The Gatekeeper Reflux Repair System (Medtronic, Tolochenaz, Switzerland) entails the submucosal placement of a polyacrylonitrile-based hydrogel prosthesis (1.5x18mm) above the GOJ. In a prospective, non-randomised study of 68 patients with a six-month follow-up, quality of life was improved, median LOS pressure was increased (from 8.8 to 13.8mmHg; $p < 0.01$) and 70.4% of the prostheses were still in place

Figure 3: Nissen (360° Wrap) and Diaphragmatic Repair with Biologic Mesh

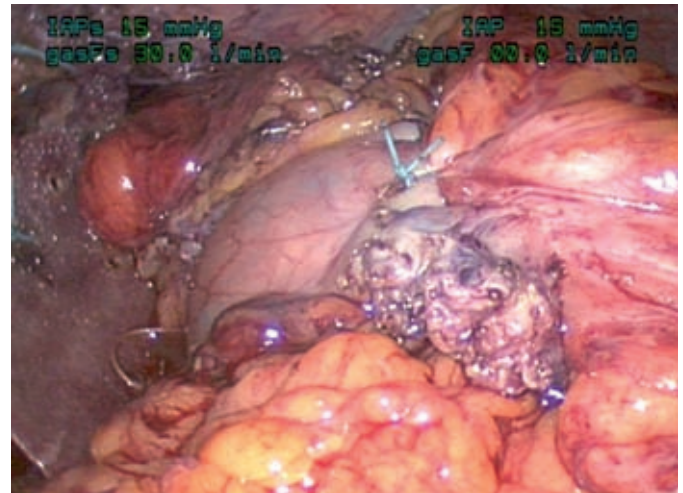
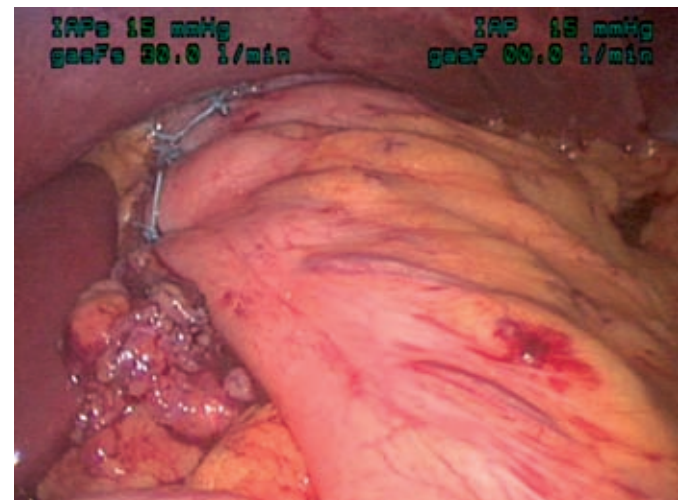


Figure 4: Dor (180° Wrap) Anterior Fundoplication



at six months.²⁶ Concerns remain about the durability and safety of the implants, leaving the long-term utility of the procedure a question for further study.

The third category of endoluminal procedures employs direct, endoscopic tightening of the LOS via sewing or plication. This appears to be the most promising of the endoluminal therapies. The endoscopic suturing devices currently available include the EndoCinch (BARD Endoscopic Technologies, Billerica, MA), the ESD (Wilson-Cook Medical, Winston-Salem, NC), the Esophyx (EndoGastric Solutions, Redmond, WA) and the Full-Thickness Plicator (NDO Surgical Inc., Mansfield, MA). The major difference between the devices is the depth of suture. The Esophyx and the NDO Plicator take full-thickness sutures of gastric fundus, whereas the other endoscopic plicators utilise a partial mucosal/submucosal stitch. Partial-thickness sutures have a greater potential to pull through the tissue or migrate over time. The Esophyx and NDO Plicator system appear to have the technical advantages of a full-thickness stitch, with serosa-to-serosa approximation. With the NDO Plicator system this provides direct tightening of the LOS, possible lengthening of the LOS and favourable altering of the angle of His. Pleskow et al.²⁷ showed in a non-randomised, prospective study of 64 patients with follow-up of

12 months that mental and physical Short Form (SF)-36 scores were significantly improved. Importantly, 80% of patients had improved distal oesophageal acid exposure, as evidenced by significantly decreased DeMeester scores (from 44 to 30; $p < 0.001$). Moreover, the majority of patients (68%) were off PPIs at 12-month follow-up. A recent study evaluating the use of the NDO Plicator and Stretta procedure in the obese population found a significant overall failure rate (28%). The study demonstrated only modest reductions in moderate/severe symptoms from pre-procedure evaluations. Chest pain and cough decreased by 4 and 14%, respectively, with larger decreases in voice and dysphagia complaints (25 and 23%, respectively). PPI use decreased from 81% pre procedure to 45% post-procedure.²⁸ Similar to the NDO Plicator, the Esophyx also utilises the full-thickness stitch. An anterior partial fundoplication (270°) is created by attaching the fundus to the anterior and left lateral wall of the distal oesophagus using this full-thickness suture. Two-year follow-up of 14 of the original 19 patients demonstrated no adverse events related to the procedure, relief of heartburn in 93% and elimination of daily PPI use, hiatal hernia and oesophagitis in 71, 60 and 53%, respectively.²⁹

The NDO Plicator and Esophyx, as well as the other endoluminal therapies, need to be evaluated very carefully in randomised studies with larger study groups and long-term comparisons. Study groups remain small, and difficulties with recruiting patients for researching the endoscopic ARPs persists. Appropriate selection criteria remain stringent and up to 90% of screened potential study participants have been excluded largely due to issues with PPI use and large hiatal hernias.³⁰ This may identify a significant difficulty in the utilisation of endoluminal therapies, as patient selection may severely limit the number of potential beneficiaries of these procedures. In all probability, they will provide an alternative or

bridge therapy between pharmacological therapy and ARP, but are unlikely to replace the existing ARP.

Conclusion

GORD represents a physiological and anatomical disorder of the LOS. The diagnostic work-up includes barium oesophagram, upper gastrointestinal endoscopy, pH monitoring and oesophageal manometry. To date, in selected patients surgical ARPs represent the standard of care. Endoluminal therapies demonstrated promising short-term results in patients who suffer from GORD with no hiatal hernia. Further studies of the endoluminal approach are needed to assess its safety and efficacy, especially in high-risk patients or in cases of recurrence after surgical repair. ■

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