P. Marco Fisichella
Editor

Failed Anti-Reflux Therapy

Analysis of Causes and Principles of Treatment

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To Barbara Jericho

Preface

A fundoplication is very effective in controlling the symptoms of gastroesophageal reflux disease (GERD) in most patients. However, the procedure proves ineffective in 10–15% of patients. In these patients, symptoms of GERD recur or they experience dysphagia. Some of these patients eventually need a second operation. However, the chances of success of a second operation are inferior to the outcome of primary surgery. Hence, the management of patients who fail antireflux surgery is complex, and the indications for reoperation are far from straightforward. This book will cover the comprehensive evaluation and treatment of failed antireflux therapy. Pathophysiology, diagnostic evaluation, treatment, and strategies are included and based both on evidence-based data and the experience of the contributors. Each chapter will describe a very specific aspect of the analysis of causes and principles of treatment for failed medical and surgical therapy, by a known expert. In addition, this book will outline the current diagnostic and management strategies of failures, as well as the simplified re-operative approaches with relevant technical considerations.

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West Roxbury, MA, USA P. Marco Fisichella

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History of Medical and Surgical Antireflux Therapy

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Fernando A.M. Herbella
and Ana Cristina C. Amaral

Introduction

> *Those who cannot remember the past are condemned to repeat it.*
> The Life of Reason, Volume 1, 1905
> George Santayana (1863–1952), Spaniard/American philosopher

Initial and scarce attempts to operate the esophagus have been described since the seventeenth century, mostly due to traumatic injury [1]; however, the real history of esophageal surgery is relatively young compared to other organs. According to Fogelman and Reinmiller [2], esophageal surgery was both uncommon and poorly performed prior to the nineteenth century. This may be attributed to the fact that the esophagus is a peculiar organ. It has a unique *anatomy*: (1) important organs surround the esophagus in its entire length; (2) the esophagus crosses the neck, the chest, and the abdomen; (3) it lacks a serosa and its own artery, and (4) the lymphatic drainage is abundant and erratic [3]. This leads to an exclusive surgical anatomy: (1) access routes to the esophagus may be variable and multiple; (2) oncologic margins are elusive; and (3) organs need to be prepared in order to replace it [4]. Also, the esophagus has a distinctive *physiology*: (1) it is a digestive organ without known absorptive or endocrine functions; (2) it is bounded by two sphincters; and (3) it exhibits a motility pattern only at feed and different from other digestive segments. Moreover, esophageal diagnostic tests such as esophageal function tests and even esophagoscopy are recent achievements. All this lead to unsuccessful tries and fears to operate the esophagus and consequently delay in the development of procedures even though esophageal diseases have odd characteristics too: (1) they frequently affect other organs, either through neoplastic dissemination or regurgitation of esophageal refluxed contents; (2) they mimic diseases from other organs; and (3) they bring severe suffering, e.g., gastroesophageal reflux disease (GERD) burdens quality of life in levels comparable to or greater than that observed in other chronic conditions, such as diabetes, arthritis or congestive heart failure [5].

This book focuses on the failure of antireflux therapy. The understanding that a collective and historical experience may help prevent the repetition of errors is essential. Although esophageal surgery is still in the infancy, some lessons from the past are frequently ignored and those who cannot remember the past are condemned to repeat it.

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Gastroesophageal Reflux Disease

The surgical history of GERD, or "ante-mortem digestion of the esophagus" [6] was associated for a long time with esophagitis and hiatal hernia (HH), since they were considered synonyms.

Esophagitis was firstly describe by Quincke in 1859 [7] (Fig. 1.1) but Winkelstein is usually given the credit for first describing peptic esophagitis as a new clinical entity only in 1935 [8]. Postmortem description of diaphragmatic hernias can be found in Hippocrates works, but Morgagni in 1769 described HH as it is known nowadays (Fig. 1.2). In the clinical scenario, Eppinger diagnosed the first HH in a live patient and Mayo did the first operation for this condition in 1909 [9].

The initial therapy for GERD consisted in replacing the stomach to the abdomen and repairing and tightening the esophageal hiatus. Philip Rowland Allison (1908–1974) (Fig. 1.3), a British surgeon [10], initiated the modern era of antireflux surgery. He published in 1951 [11] a series of patients that, utilizing a transthoracic approach, the stomach were reduced to the abdomen and the crural fibers were closed behind the esophagus. He believed these crural fibers functioned as a pinchcock to prevent reflux. He had good long term results with over 80% of symptoms relieve after 20 years, with 49% of radiologic recurrence of the hernia [12], a rate below paraesophageal mesh-reinforced hiatoplasty and fundoplication in modern series [13]. Latter, it was acknowledged that GERD could exist without an associated HH and Allison procedure was also carried out successfully in these patients [14]. From this time, became clear that fixing the HH and performing a hiatoplasty were essential parts of the surgical treatment for GERD. In fact, modern authors learned that the absence of a hiatoplasty leads to much worse outcomes [15]. This fact culminated with the use of prosthetic reinforcement of the hiatus to make this part of the procedure even stronger, actually not a modern idea but dating

Fig. 1.2 Joannes Baptista Morgagnus. First description of a hiatal hernia (Source: National Library of Medicine Images from the History of Medicine)

Fig. 1.1 Heinrich Quincke. First description of esophagitis (Source: National Library of Medicine Images from the History of Medicine)

Fig. 1.3 Philip Rowland Allison. Initiator of the modern antireflux surgery (Reproduced from Bani-Hani and Bani-Hani [90] with permission)

back to experimental tries in 1957 and the first clinical experience in 1960 [16]. Some complications have been reported associated to the use of prosthetic hiatal reinforcement, but the rate of hernia recurrence seems to be lower forcing surgeons at present to face the dilemma of choosing between a risk of recurrence and the fear of complications [16]. Modernly, different devices were created in order to perform an endoscopic fundoplication using intraluminal suturing or plug [17]. Although the esophagus is wrapped, a hiatoplasty is obviously not performed. Not surprisingly, even in much selected patients, all published series show symptomatic improvement but some important complications, 40% of hernia recurrence and amelioration but not reestablishment to normal values of acid exposure measured objectively by pHmonitoring [18].

After experimenting on the diaphragm, surgeons focused on the His angle. Norman Rupert Barrett (Australia, 1903 – England, 1979), the famous surgeon that gives the name Barrett's esophagus [19] pioneered the idea on restoration of the cardioesophageal angle as the critical element in the prevention of reflux [20]. In fact, latter studies showed that a fundoplication performed ex vivo in human stomachs is competent in preventing reflux to the point of gastric explosion, probably by accentuating the His angle [21]. Clinical experience; however, showed that the solely restoration of the His to an acute angle does not show good physiologic and clinical outcomes [22] as in patients submitted to a Lortat-Jacob antireflux repair [23].

Other natural antireflux mechanism that gained attention of surgeons was the length of the abdominal portion of the esophagus. In fact, historically, the length of the abdominal esophagus was a concern due to the necessity to reduce the herniated stomach and the chance of a short esophagus [9]. Latter, the length of the abdominal esophagus proved to be direct linked to GERD control based on clinical, in vitro [24], and experimental [25] studies. Currently, a segment of 2 centimeters is desirable when performing an antirreflux operation. Esophageal alongation may be achieved with extensive dissection of the organ in the mediastinum [26].

Rudolf Nissen (Fig. 1.4), the famous German surgeon (1896–1981) [27] developed in 1955 the most successful and widespread surgical therapy for GERD, the fundoplication [28]. He repeated a lesson learned from the past when he was reminded of an operation done in 1936 when the anastomosis of a cardia resection was protected by the stomach like a Witzel gastrostomy and the patient did not develop esophagitis. This operation suffered modification along time [27] and gained wild acceptance with close to 20,000 fundoplications performed annually in the US [29]. Excellent and good outcomes may be expected in over 90% of the patients [30, 31]. It is noteworthy that the first minimally invasive fundoplication occurred in 1991 [32], 4 years after the first laparoscopic cholecystectomy!

The Nissen fundoplication evoluted with several modifications (Fig. 1.5). First, different authors proposed a partial fundoplication, in which the gastric fundus wraps partially, not circumferentially, the esophagus, creating techniques and eponyms known as Toupet, Dor and Guarner [33]. These partial fundoplications were developed in order to minimize some of the side effects of a fundoplication, namely dysphagia and gas bloating. These techniques proved to be a good option to be added to a myotomy in the treatment of achalasia, since esophageal peristalsis is absent and a total fundoplication may

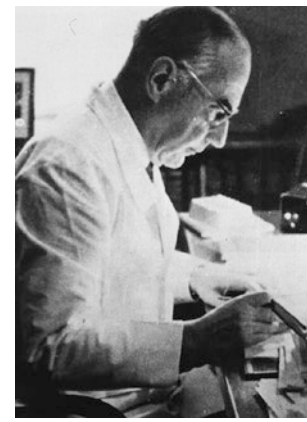

Fig. 1.4 Rudolf Nissen. Creator of the fundoplication (Source: National Library of Medicine Images from the History of Medicine)

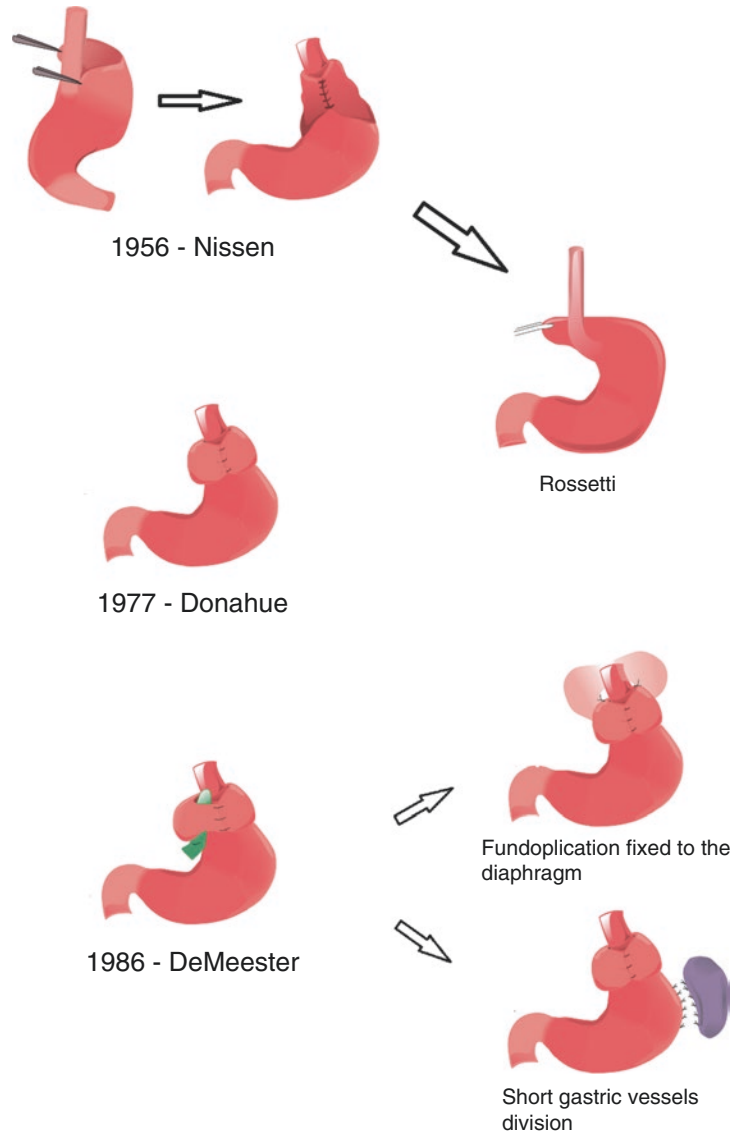

Fig. 1.5 Evolution of Nissen's fundoplication (Reproduced from Herbella et al. [91])

cause dysphagia [34]. Good outcomes in achalasia patients lead some surgeons to tailor the fundoplication to match the strength of esophageal peristalsis as measured by esophageal manometry, so a total fundoplication was recommended for patients with normal peristalsis, and a partial fundoplication for those with impaired peristalsis [35]. Late follow-up; however, showed that better reflux control was obtained with a total fundoplication [36] and that esophageal motility may be restores after total fundoplication and GERD control [37].

Other important modification of Nissen's fundoplication was the loosening of the wrap and the shrinking of the size of the valve, the so called "short-floppy" Nissen. The first technical amendment was developed by Donahue et al. [38] to avoid "gaseous eructations or vomiting (normal reflux) when appropriate". This technique revoked the theory that a fundoplication would work solely as a pneumatic valve that should be applied close-fitting to the esophagogastric junction, since GERD control was achieved even with a loose valve. Latter, DeMeester et al. [39]

showed that a 1 cm wrap was as effective as a 4 cm fundoplication to control GERD. Other modifications of the original technique also took place, such as the use or not of a calibrating intraesophageal bougie to perform the fundoplication; the need for short gastric vessels division and the anchoring of the fundoplication on the hiatus. There is not enough high quality evidence-based data to support the use or not of these topics; however.

Even though Nissen fundoplication proved to be an excellent operation for symptoms control [40] and increment in quality of life [41], with an irrelevant mortality [42] and sustained outcomes in a long-term follow-up [43], some authors looked for alternatives to this operation, some with procedures acting solely at the esophagogastric junction.

Angelchick and Cohen [44], in 1979, tried to reinforce the lower esophageal sphincter (LES) with silicon ring prosthesis around the esophagogastric junction. A great popularity was achieved with over 25,000 implants [45]. Years later, a strange body at this location showed to induce poor outcomes and a large number of complications related to unmanageable dysphagia and prosthesis erosion or migration [46, 47]. Most of the surgeons experienced with this device deemed the procedure not recommendable anymore [46, 47]. Fortunately, the device is not currently in use. Interestingly, other methods for GERD control tried to decrease the esophagogastric junction complacence by injecting foreign substances in the LES. Following previous experiences with foreign body, bad outcomes and significant complications made these methods to be withdrawn from market [48].

GERD has a complex and multifactorial genesis [49]. Parallel to the development of surgical techniques, surgeons also studied esophageal physiology and make significant progress on the understanding of GERD pathophysiology. Barrett was one of the first to acknowledge the fact that duodenal contents may also reflux and damage the esophagus [20]. Lately after, different tests were created to evaluate biliary or non-acid reflux [50]. The most significant was multichannel intraluminal impedance, a test that proved that non-acid reflux is able to produce symptoms [51] and that medical therapy for GERD is able to neutralize the pH of the refluxate but not the backflow of gastroduodenal contents to the esophagus [52]. Physiologic studies also showed that the simple restoration of the basal pressure of the LES to normal values is not enough to control GERD, since GERD may exist in the setting of sphincters with normal pressure [53] due to a defect in the other previously mentioned antireflux mechanisms or due to abnormal transient relaxations of the sphincter, identified since 1980 [54]. Thus, LES basal pressure must not be used alone as a primary endpoint to evaluate new antireflux procedures. It must be remembered as well that a fundoplication is able to restore all natural antireflux mechanisms [49] and decrease transient relaxations of the LES [55].

Lessons Learned from the Past

The adequate reflux control must reestablish the normal anatomy of the distal esophagus / proximal stomach / hiatus. Based on historical experience: (1) a hiatoplasty is essential but should not be used alone; (2) accentuation of the His angle is essential but should not be used alone; (3) acid as well as biliary reflux must be controlled; (4) a fundoplication brings excellent results in the majority of patients if proper technical elements are followed irrespective of esophageal motility; and (5) foreign bodies at the level of the esophagogastric junction may lead to dreadful consequences.

Medical Therapy

Symptoms of reflux disease were known since ancient Rome, with reflux sensations associated with Falernian wine ingestion, but for 100 years diseases of the esophagus were poorly understood, since the organ itself received little attention.

Therapy of acid-related diseases was obscure up until the late nineteenth century, mostly because lack of ability to distinguish between

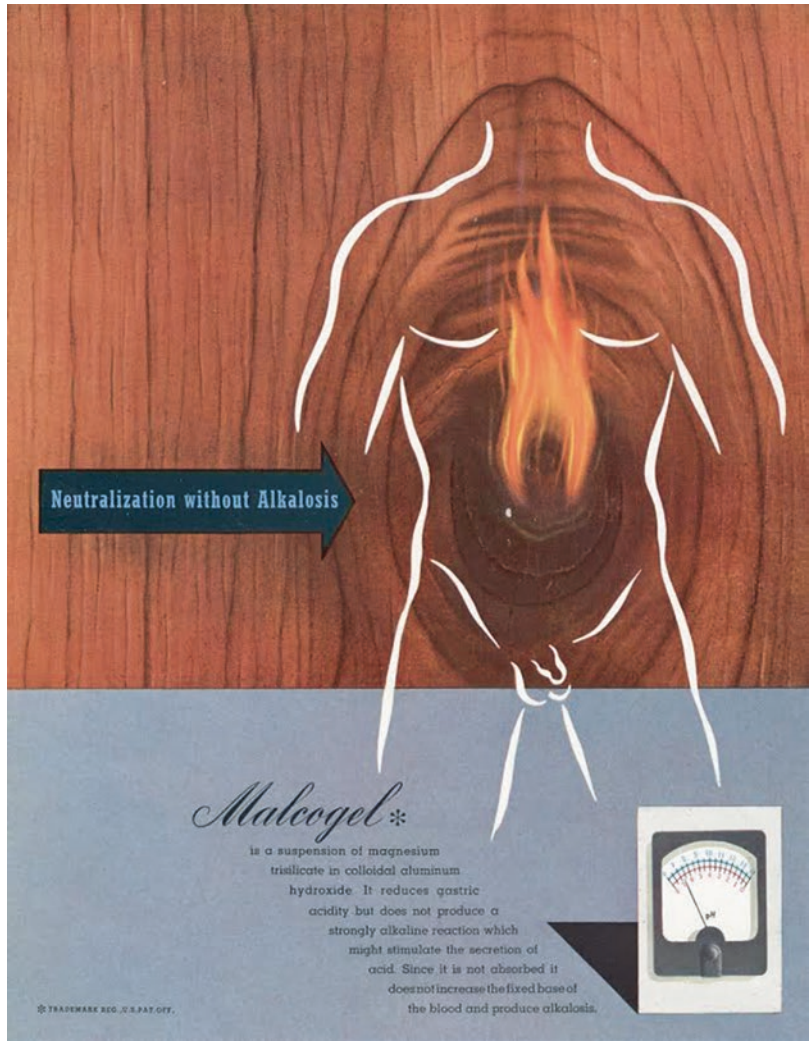

Fig. 1.6 Antacid advertisement from a 1944 magazine (Source: National Library of Medicine Images from the History of Medicine)

the esophagus and the stomach as the source of the problem. Chalk and charcoal were used to relieve dyspepsia [56]. Pathophysiology evolved in last 50 years with the techniques that allowed measurement of acid secretion and recognition of acid and pepsin as pathogenic to the mucosa. This allowed recommendation of lifestyle changes and development of several classes of drugs to improve symptoms and heal esophagitis (Fig. 1.6).

In twentieth century lifestyle changes, as dietary and drug restrictions, elevating the head of the bed, decreasing the volume of foods and weight reduction in obeses were the mainstay of medical therapy [57]. Dietary restrictions were directed to agents decreasing lower esophageal sphincter pressure as caffeinated drinks, fat, chocolate, alcohol, peppermint or fatty foods. Avoidance of smoking, thophyline and prostaglandins was also recommended [58]. Although several lifestyle and dietary modifications have been used in clinical practice, a systematic review of 16 randomized trials that evaluated the impact of these measures on GERD concluded that only weight loss and elevation of the head end of the bed improved GERD symptoms [59, 60].

Neutralization of gastric acid through antacids was another management strategy used since early twentieth century. Antacids (Fig. 1.6) were thought to act not only by neutralizing

acid secreted in stomach, but also by increasing pressure in lower esophageal sphincter through increasing circulating levels of gastrine [61, 62]. Gastric acid neutralisation remained the mainstay of medical therapy for several years and is still recommended in patients with mild reflux disease, to control acid regurgitation and reduce heartburn [63].

The development of histamine-2 receptor antagonists (H_2RAs) in the 1970s by James W. Black revolutionized the treatment of acid-related peptic diseases. To that date, therapies lack solid scientific bases as much of the thinking about antacid preparations was based on in vitro studies or in vivo observations of the extent and duration of antacid effects under fasting conditions [62]. The first H_2RA developed by Black et al. was burimamide, which contained the imidazole ring structure of histamine but was modified to inhibit selectively histamine-stimulated acid secretion. Burimamide blocked acid secretion but not the hypotensive effect of histamine mediated by histamine 1 receptors, which precluded it for clinical use [64, 65].

Cimetidine, which selectively blocks gastric acid secretion, was developed thereafter and the number of operations for duodenal ulcers decreased by 38% in 2 years in the United Kingdom. Cimetidine became the best-selling drug in the world and James Black was awarded the Nobel Prize in 1988 [66–68]. Other H_2 receptor antagonists (H_2RAs), like ranitidine, nizatidine and famotidine were then developed and all were best-selling prescription drugs in the 1980s.

The proton pump, driven by a H^+-K^+ ATPase, was identified in 1976 after report of a potassium-stimulated ATPase in amphibian gastric mucosa different from the known sodium-potassium ATPase [69]. Omeprazole, the first proton pump (PPI) inhibitor without significant toxicity, showed to irreversibly block the pump and potently inhibit acid secretion [70, 71]. As it proved to be effective for Zollinger-Ellison-related ulcers, reflux esophagitis and, in combination with antibiotics, for *H. pylori*-related ulcers, the introdution of this class of drugs in 1980s again revolutionized the management of GERD. Other benzimidazole PPIs subsequently introduced included lansoprazole, pantoprazole, rabeprazole and esomeprazole. All these agents consist of a pyridine and a benzimidazole moiety.

PPIs are still the most potent inhibitors of gastric acid secretion available and have become the therapy of choice for healing esophagitis and providing symptomatic relief. However, as gastric acid can still be secreted during the night, despite twice-daily PPIs [72, 73] some studies in last two decades have evaluated the usefullness of H_2RAs at bedtime to suppress this acid reflux [74–76] with results showing enhanced nocturnal gastric pH control. However, continuous use of H_2RAs is associated with tolerance development, limiting their long-term use and efficacy as add-on therapy [77, 78].

Prokinetic drugs could theoretically improve GERD by increasing LES basal pressure, improving esophageal peristalsis and accelerating acid clearance. Metoclopramide, a dopamine D2 receptor antagonist, has been shown to increase LES basal pressure without significant effect on peristalsis [79].

Domperidone, a peripheral dopamine receptor antagonist that does not cross the blood-brain barrier, was initially shown to be effective in the treatment of functional dyspepsia [80]. In the 1980s, several trials evaluated the effect of prokinetics in GERD treatment, all showing symptomatic improvement.

Cisapride was developed in the late 1980s and launched to the world in early 1990s [81]. Cisapride is a serotonin 5-HT4 agonist with 5-HT3 antagonist activity, therefore with widespread prokinetic effects in gastrointestinal tract. Initial studies showed symptomatic improvement and esophagitis healing, though results were neither consistent nor robust [82–85]. One reason for the relatively weak effects of cisapride in GERD might be the fact it does not address the critical mechanisms of the disorder.

Initial experience with cisapride showed good safety, but reports of various arrhytmias and sudden death culminated with a FDA announcement in 2000 that the manufacturer of cisapride would voluntarily withdraw its product from the U.S. Market [86, 87].

Baclofen, a GABA-B agonist, has been available for many years for the treatment of spastic diseases. The drug was found to inhibit TLESR and to decrease the number of postprandial acid and nonacid reflux events [88]. Given the limited treatment options for GERD patients refractory to PPIs, drug may be a useful approach for the treatment of these patients.

Currently, PPIs are the cornerstone of GERD treatment, with a potent inhibitory effect on gastric acid secretion that results in high rates of esophageal mucosal healing and effective symptomatic control. However, there are still many areas of unmet needs in the treatment of GERD, as refractory GERD, atypical and extraesophageal manifestations of GERD and nighttime heartburn [89].

History of medical treatments for GERD suggests that, predictably, advances will come not from a 'one size fits all' approach but rather from a personalized reflux therapy to patients who do not benefit from the therapeutic options currently available.

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Establishing the Diagnosis of GERD

2

Wai-Kit Lo and Hiroshi Mashimo

Gastroesophageal reflux disease (GERD) is a highly prevalent disorder with worldwide distribution [1]. However, GERD may present with a variety of symptoms, including heartburn, dysphagia, and even chronic cough. In 2006, the Montreal classification was created as a global consensus definition for GERD to encourage diagnostic standardization for clinical management and research [2]. This defined GERD as a condition resulting from reflux of stomach contents and causing troublesome symptoms or complications, occurring at least 2 times per week, with an adverse effect on an individual's well-being. The Montreal classification further defines symptoms as esophageal, including typical symptoms of heartburn and regurgitation, and dysphagia as a manifestation of esophageal injury; and extraesophageal, including cough, laryngitis, and asthma (Fig. 2.1). Generally, esophageal symptoms are more clearly associated with GERD, while extraesophageal symptoms are often multifactorial [2].

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Of course, not all patients with heartburn or regurgitation have GERD, and this heterogeneity of patients with GERD-associated symptoms poses a great dilemma in diagnosis and management. Specific symptom questionnaires, such as the Reflux Disease Questionnaire [3] and the ReQuest symptom scale [4] have sensitivity and specificity for GERD in the range of 65–75%, and thus, serve poorly as diagnostic modalities. What are the available tools to make the diagnosis of GERD, and which are most reliable? In order to better understand the diagnosis and management of GERD, a review of the pathophysiology is informative. Gastroesophageal reflux is a physiologically normal phenomenon. A small amount of gastric refluxate, consisting of gastric acid, bile, pancreatic secretions, and food matter, occurs regularly on a daily basis. However, a number of processes including decreased salivary function, poor esophageal clearance, impaired esophageal tissue resistance, visceral hyperalgesia, decreased resting tone of the lower esophageal sphincter (LES), hiatal hernia, poor gastric emptying, increased acid secretion, obesity, and pregnancy may contribute to pathologic GERD development [5, 6] (Table 2.1). Increased transient LES relaxation (TLESR), initially described as part of the belch reflex, has been implicated as the primary etiology of GERD [6, 7]. These brief and pathologic episodes of LES relaxation, unrelated to physiologic swallowing or esophageal peristalsis, occur most often in the postprandial and nocturnal sleeping periods, and account for

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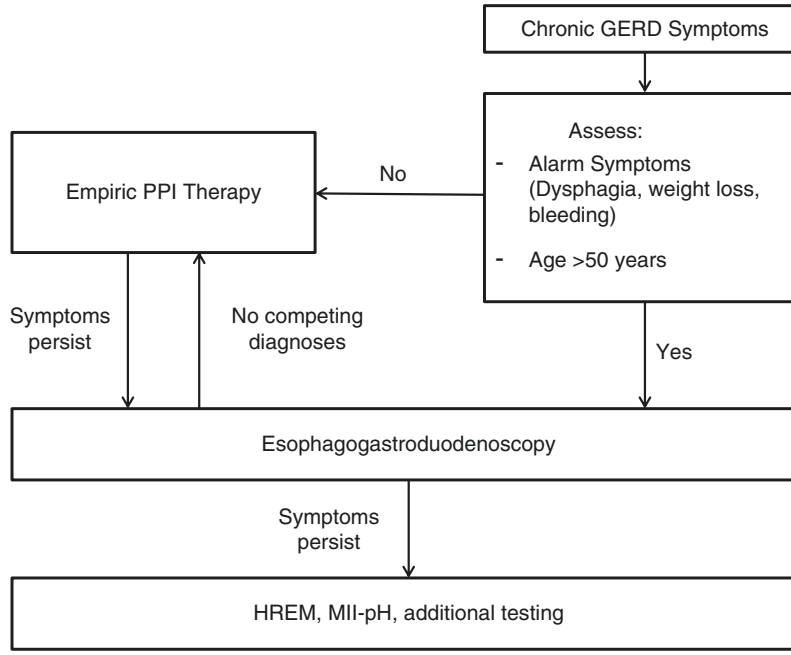

Fig. 2.1 Recommended pathway for GERD evaluation and management (*GERD* gastroesophageal reflux disease, *PPI* proton-pump inhibitor, *HREM* high resolution esophageal manometry, *MII-pH* multichannel intraluminal impedance and pH)

Table 2.1 Processes contributing to GERD pathophysiology

Decreased salivary function
Impaired esophageal clearance
Impaired esophageal tissue resistance
Visceral hyperalgesia
Decreased resting tone of the lower esophageal sphincter (LES)
Transient LES relaxation (TLESR)
Hiatal hernia
Impaired gastric emptying
Increased gastric acid secretion
Obesity
Pregnancy

up to 70% of reflux symptoms in patients with GERD [8]. Diet, alcohol, and smoking may also contribute to TLESR occurrence.

In theory, the pathophysiology of GERD should allow for a myriad of testing opportunities to make the diagnosis. However, no diagnostic gold standard exists, likely due to the heterogeneity of the patient population with GERD-associated symptoms. GERD is largely a clinical diagnosis; nevertheless, a number of tests can be performed to help support a diagnosis of GERD, including trial of medical management, assessment of GERD-related complications, or direct detection of reflux.

Empiric Treatment

The most recent clinical guidelines published by the American College of Gastroenterology supports empiric treatment with proton pump inhibitor (PPI) medication for patients with suggestive clinical symptoms of GERD [9], and without any alarm symptoms. In this setting, resolution of symptoms following PPI use may be diagnostic. Alarm symptoms, such as dysphagia, odynophagia, weight loss, or bleeding, should trigger additional evaluation for GERD-associated complications, as well as any patients with persistent symptoms on empiric therapy.

Esophagogastroduodenoscopy (EGD)

Upper endoscopy, or EGD, is the mainstay of GERD-associated symptom evaluation. In patients with clinical alarm symptoms, older

age, confounding illnesses or multiple competing diagnoses, or poor response to empiric therapy, further evaluation with EGD is indicated [9]. Detection of erosive esophagitis, peptic stricture, Barrett's esophagus, or malignancy can support a diagnosis of GERD and offer targets for direct intervention. Additionally, competing diagnoses such as peptic ulcer disease and non-reflux esophagitis, including infectious and eosinophilic, can be excluded.

Barium Swallow and Esophageal Imaging

Barium swallow has largely been supplanted by EGD for anatomic evaluation of symptoms associated with GERD complications. However, a finding of hiatal hernia, sometimes missed on EGD, and possibly frank reflux of contrast, would present an anatomic risk for GERD separate from TLESR, with implications for peri-operative planning. In rare cases, barium swallow may diagnose an esophageal diverticulum, which may also result in GERD-associated symptoms. A full-column barium swallow may also sufficiently distend the esophagus to reveal an otherwise occult muscular ring, which can be missed on EGD given the difficulty of retaining air for sufficient distention during careful inspection of the lower esophagus. Given these findings, barium swallow has been advocated by some radiology experts for further evaluation of GERD symptoms with concomitant dysphagia. Other types of esophageal imaging include video fluoroscopy/ modified barium swallow (MBS), which is more commonly used to assess aspiration, as well as oropharyngeal dysphagia and suspected extraesophageal manifestations of GERD. MBS may be diagnostic and therapeutic, in helping to identify maneuvers and food consistencies that reduce aspiration risk. Air contrast or double contrast barium swallow allows for the non-invasive assessment of esophageal mucosa, but has largely been replaced by EGD for direct visualization. Similarly, timed barium swallow can be used to assess esophageal transit, but has been supplanted by esophageal manometry testing, discussed in detail below.

Ambulatory pH Testing

Ambulatory pH testing offers direct assessment of reflux episodes and symptom occurrence in patients with GERD-associated symptoms requiring further evaluation. General indications include clarification of GERD diagnosis in patients with persistent symptoms and without mucosal damage on EGD; assessment of treatment adequacy in patients with persistent symptoms on PPI; and pre- and post-antireflux surgery evaluation [9]. To assess for contribution from baseline GERD, testing is performed after holding PPI treatment for at least 7 days. The options for direct pH testing include multichannel intraluminal impedance and pH (MII-pH), BRAVO® pH capsule (Given Imaging, Yoqneam, Israel), and ResTech™ (Respiratory Technology Corporation, San Diego, CA, USA) . MII-pH is a trans-nasal catheter that monitors acid and non-acid reflux over a 24-h period, and includes sensors in the proximal and distal esophagus. BRAVO® is a directly deployed capsule that monitors acid reflux over 48–96 h. In both cases, patients receive a wireless transceiver unit to document body position, meal periods (which are excluded from analysis), and symptom events. ResTech™ is a single-channel pH probe device which can be placed without need for manometry or endoscopy. It detects both liquid and aerosol reflux in the oropharynx, and is particularly useful in the assessment of patients with extraesophageal symptoms and suspected laryngopharyngeal reflux (LPR) [10]. The pros and cons of each technique are outlined in Table 2.2. However, in most cases, pH or combination impedance-pH testing have sensitivity and specificity of 65–75%, which is much lower compared to endoscopic evidence of esophagitis in making the diagnosis of GERD.

Interpreting ambulatory pH test results can be challenging. The DeMeester score was developed as a composite predictor of acid reflux based on ambulatory pH data [11], to aid in the selection of candidates for antireflux surgery, and pH data has previously been shown to be a strong predictor of fundoplication success [12]. As technology has progressed to include impedance data, additional variables of symptom association, patient

Table 2.2 Comparison of ambulatory pH assessment tools

MII- pH
Pros:
Does not require endoscopy prior to placement
Detects both acid and non-acid reflux events
Distal and proximal esophageal sensors
Cons:
Shorter recording time (24 h)
Difficult placement requiring manometry or LES position locator for positioning catheter
Risk of catheter movement
Difficult to ensure proper position
Possible patient discomfort from catheter
BRAVO®
Pros:
Less cumbersome wireless recording for patient
Longer recording time (48–96 h)
Cons:
No direct measurement of non-acid reflux episodes (no impedance data)
Only single channel distal esophageal measurement, no proximal esophageal reflux assessment
Requires upper endoscopy to ascertain positioning and proper deployment
Risk of early capsule dislodgement
ResTech™
Pros:
Ease of placement without endoscopy or manometry
Greater comfort based on thinner catheter
Cons:
Direct assessment of supraesophageal but not intraesophageal reflux

position, non-acid reflux, and proximal location of reflux can be considered in making the diagnosis of GERD for candidate selection. Symptom association probability (SAP) is a statistical calculation expressing the association between clinical symptoms and presence of acid or non-acid reflux [13]. SAP greater than 95% is equivalent to a p-value less than 0.05, the common threshold of statistical association. A recent retrospective study demonstrated that of the impedance variables, only positive SAP was associated with successful postoperative outcome [14]. Reflux in the upright, rather than supine position, may indicate greater severity of reflux, although this interpretation and its implications are still being defined. Non-acid reflux may be detected which can be associated with symptoms; however, the optimal management of this remains under investigation, and prior studies investigating only this variable in MII-pH measurement found no association with surgical outcomes [15, 16]. Finally, proximal location of reflux may indicate LPR, which presents with distinct features compared to GERD and implicates additional dysfunction of the upper esophageal sphincter (UES). LPR appears to respond differently to conventional treatments, often requiring higher doses and longer duration of PPI treatment, and has poor correlation to endoscopic presence of esophagitis [17]. A diagnosis of LPR may be suggested through an endoscopic grading system called the Reflux Finding Score, which accounts for laryngoscopic findings of edema, erythema, and ulceration [18], but such appearances have poor diagnostic specificity and high interobserver variability [19].

High Resolution Esophageal Manometry (HREM)

HREM is a trans-nasal catheter with multiple sensors that measure intra-esophageal pressures. Although esophageal manometry is not a direct measurement of GERD, it can be helpful to rule out motility disorders that produce secondary reflux symptoms [20]. Additionally, it is often performed to exclude motility disorders in the selection of candidates for fundoplication. Finally, HREM can be used to detect the level of the LES in order to guide proper placement of the MII-pH catheter. While information about UES physiology can also be obtained, studies are lacking regarding potential associations with a diagnosis of LPR, possibly owing to the limited recording time of HREM and the generally rare occurrence of proximal reflux episodes.

Other Measurements of Reflux

Salivary pepsin (PepTest™, RD Biomed Limited, Hull, UK) is a simple, non-invasive and inexpensive test found to correlate with GERD, particularly in the post-prandial setting [21], and may also have implications in the diagnosis of LPR

[22]. However, to date, there are limited outcome studies of LPR treatment based on salivary pepsin, despite its increasing use in clinical practice, and it remains to be determined which cutoffs best predict the presence of esophagitis and/or LPR. While sensitivities and specificities for GERD and LPR are moderate, they remain comparable to other diagnostic modalities such as symptom questionnaires, response to PPIs, and reflux monitoring, in part highlighting the lack of a true gold standard test for diagnosis of GERD and LPR.

Gastric Emptying Scintigraphy and SmartPill®

While gastroparesis is a distinct pathologic entity, it may be associated with GERD symptoms. A prior study has shown that 16 (5.8%) of a cohort of 275 patients with GERD symptoms had objective evidence of gastroparesis by scintigraphy [23]. For this reason, a gastric emptying study performed over 4 h may be helpful to assess for gastroparesis and to guide further treatment, particularly in patients with GERD symptoms refractory to acid suppression. Additionally, a diagnosis of gastroparesis should be considered in patients with concomitant risk factors such as diabetes, chronic opiate use, and in the postoperative setting. Finally, newer technologies are being introduced to assess not only gastric emptying, but also gastric acid secretion. SmartPill® (Given Imaging, Yoqneam, Israel) contains a wireless pH sensor in pill form that allows for measurement of transit times and pH throughout the digestive tract, including gastric acid output [24], which has been independently associated with GERD [25]. Although the role of gastric assessment in GERD remains poorly defined, these tools may provide useful data in select patients for diagnosis and further management.

Summary

Patients who have failed medical management may be candidates for endoscopic or surgical therapy. We suggest a combination of the above testing modalities to aid in the selection of patients most likely to respond to antireflux surgery, and to plan the surgical approach (Fig. 2.1). Clinical review is important to detect alarm symptoms. Older patients and those with alarm symptoms should proceed to EGD. Empiric trial of PPI therapy for at least 3–4 weeks may help establish the diagnosis, extending to 8 weeks with suspicion of LPR, and to determine need for further testing. Though there remains no gold standard for GERD diagnosis, likely due to the heterogeneity of patients with reflux symptoms, ambulatory pH testing can help detect patients with objective evidence of reflux that may be candidates for further management, while HREM can exclude patients with competing diagnoses who are poor surgical candidates. The role of supplemental tests such as salivary pepsin and gastric assessment are still being determined, but may be appropriate in select cases.

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Medical Management of GERD: Algorithms and Outcomes

3

Wai-Kit Lo and Hiroshi Mashimo

As previously discussed, gastroesophageal reflux disease (GERD) may arise from a number of pathologic occurrences. Treatment of GERD symptoms therefore aims to address these pathologic pathways. In general, the primary medical treatment of GERD focuses on (1) decreasing the acidity of refluxate; (2) minimizing reflux events; and (3) enhancing esophageal clearance. Additionally, because there is no gold standard test for the diagnosis of GERD, clinical response to empiric trial of proton pump therapy is often sufficient to establish the diagnosis, although ambulatory pH testing (performed on acid suppression to assess treatment efficacy, or off acid suppression to establish baseline presence of GERD) may be helpful in the assessment of select individuals.

In general, empiric antireflux medical therapy should be applied to address traditional heartburn and regurgitation symptoms suggestive of reflux [1]. Patients with competing diagnoses (such as atypical chest pain), older age >50, or alarm symptoms such as bleeding, weight loss, or dysphagia, should undergo esophagogastroduodenoscopy (EGD) first to exclude malignancy and to clarify the diagnosis (Fig. 3.1).

The following recommendations follow clinical guidelines of GERD management as established by the American College of Gastroenterology [1].

Dietary and Lifestyle Modification

A number of dietary and lifestyle modifications have been applied to minimize exposure to acidic foods and reduce anatomic and physiologic causes of reflux (Table 3.1). Of these, only head of bed elevation for nighttime symptoms, weight loss [2], and smoking cessation [3], have been demonstrated to reduce objective pH measures of reflux severity, although mixed data exists when evaluating the impact of weight loss on subjective reflux symptoms [4, 5]. Head of bed elevation physiologically reduces acid reflux with the assistance of gravity. This generally requires raising the head of bed with the frame by 6–8 inches rather than using wedges and electric hospital-type beds that flex the patient at the hip and potentially increase intra-abdominal pressures. Weight loss, on the other hand, reduces intra-abdominal pressure, and may also have a hormonal influence on reflux that is incompletely understood. Tobacco may weaken the lower esophageal sphincter (LES) and increase transient lower esophageal sphincter relaxation

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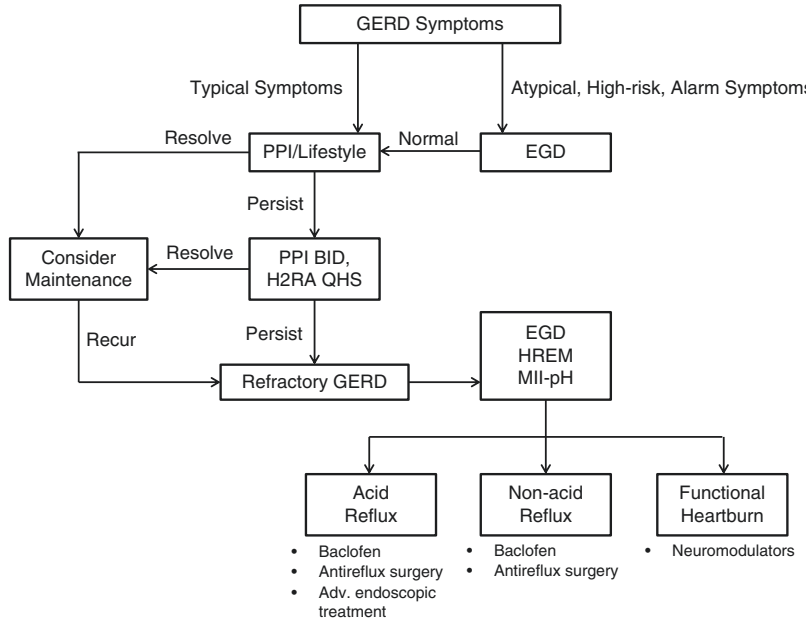

Fig. 3.1 Approach to medical management of GERD symptoms (*GERD* Gastroesophageal reflux disease, *PPI* Proton-pump inhibitor, *EGD* Esophagogastroduodenoscopy, *BID* Twice daily, *H2RA QHS* H2-receptor antagonist every evening, as applied to nighttime breakthrough reflux, *HREM* High resolution esophageal manometry, *MII-pH* Multichannel intraluminal impedance and pH)

Table 3.1 Diet and lifestyle management of reflux disease

Weight loss
Smoking cessation
Elevation of head of bed for nighttime symptoms
Avoiding supine position after meals and within 3–4 h of bedtime
Avoiding heavy meals within 3 h of bedtime, particularly for nighttime symptoms
Avoidance of dietary triggers (fatty food, caffeine, chocolate, spicy food, peppermint, citrus)
Alcohol reduction
Avoid tight-fitting garments
Lozenges or chewing gum to promote salivation
Breathing exercises to train diaphragm

Starred recommendations have been associated with statistically significant improvement in objective reflux measures

(TLESR) episodes that characterize most episodes of pathologic GERD [6]. Because of the relatively low risk of pursuing such measures, general lifestyle modification is a reasonable initial management tool for all patients suspected of GERD. Routine elimination of all potential food triggers is not recommended [1], although avoidance of specific triggers may be reasonable on an individual basis. Additionally, medications with anticholinergic properties, such as calcium channel blockers, nitrates, and antidepressants, may promote GERD, so a careful medication review may be helpful.

Antacids and Surface Agents

Over-the-counter antacids are often used by patients or primary care practitioners to treat mild reflux symptoms occurring less than once per week. These medications often include calcium carbonate, aluminum hydroxide, and other chemicals that neutralize gastric pH temporarily for symptom relief. These effects are usually not durable. Additionally, surface agents such as sucralfate and sodium alginate (Gaviscon®) can adhere to peptic mucosa and protect against further injury. The latter, generally compounded with varying particulate antacids, floats on top of the gastric pool and is touted to protect the

cardia, which is susceptible to an "acid pocket" effect. However, the limited clinical efficacy of sucralfate in GERD symptom management has reduced its applicability in non-pregnant patients [1]. Additionally, there is poor agreement on the clinical role of these agents, as sodium alginate was not discussed as a treatment option in the most recent clinical guidelines, although it has demonstrated some efficacy as an adjunctive treatment for GERD in a recent clinical trial [7].

Acid Suppression

Acid suppression medications form the bulk of GERD management. Histamine-2 receptor antagonists (H2RA) decrease acid secretion through inhibition of the histamine-2 receptor on the gastric parietal cell. Proton-pump inhibitors (PPI) irreversibly bind and inhibit the hydrogen-potassium ATPase proton pump, creating more potent inhibition of gastric acid secretion. A recent Cochrane systematic review demonstrated that H2RA are less effective than PPI in the treatment of clinical symptoms of non-erosive reflux disease [8]. Another downside is the potential development of tachyphylaxis with H2RA use [9]. Due to common hepatic clearance pathways, H2RA, and cimetidine in particular, are more susceptible than PPI to interaction with frequently prescribed medications such as beta blockers, warfarin, anti-epileptic drugs, calcium channel blockers, and tricyclic antidepressants, among others. Finally, the superiority of PPI in erosive esophagitis treatment [10] relegates H2RA to acute treatment of mild GERD with non-erosive disease, or for maintenance therapy. H2RA also has been studied as an adjunctive medication to PPI in controlling nocturnal acid breakthroughs, and can be applied at bedtime for this purpose [11].

Given the above findings, empiric treatment of GERD should begin with an 8-week course of PPI [1], which addresses reflux symptoms as well as any possible contribution from erosive esophagitis. PPI should be administered 30-60 minutes before the first meal of the day. In patients with incomplete response, a second dose may be added 30-60 minutes before the last meal of the day, or a different PPI can be tried. In patients with minimal response, further evaluation by a gastroenterologist should be considered, which may include upper endoscopy or motility testing.

Notably, a significant number of patients with non-erosive reflux and almost all patients with erosive esophagitis will experience symptom relapse [1]. Patients that redevelop symptoms after completion of the initial 8-week course require additional clinical evaluation, and possibly longer term maintenance therapy. For maintenance, the lowest effective dose of PPI should be used or changed to H2RA in the absence of erosive disease. This will hopefully reduce the potential side effects of long-term PPI use, which have been documented with greater frequency over the past few years (Table 3.2). However, it should be noted that while patients with reflux esophagitis maintained on standard PPI dose have relapse rates well under 20% over the first year, patients changed to H2RA have increased relapse rates of 50–70% [12], so one must carefully weigh the risks and benefits of long term PPI therapy.

The effect of PPI use on Barrett's esophagus (BE) is less clear. BE arises as a consequence of recurrent esophageal injury and repair in the setting of GERD, with an associated increased risk of esophageal adenocarcinoma. Although neosquamous epithelium may develop following antisecretory therapy, complete elimination of Barrett's mucosa was not achieved [13]. Nevertheless, a recent systematic review and

Table 3.2 Side effects and complications of long-term PPI use

Clostridium difficile
Small intestinal bacterial overgrowth
Pneumonia (on PPI initiation)
Vitamin B12 and magnesium malabsorption
Hip fracture and calcium malabsorption
Drug-induced acute interstitial nephritis and chronic kidney disease
Heart attack
Dementia

Causal relationship cannot be proven in many cases given the retrospective nature of these studies

meta-analysis suggested a decrease in risk of adenocarcinoma and/or high grade dysplasia with PPI use [14]. Thus, PPI treatment of BE is recommended, although the mechanism of chemoprevention remains unclear.

Adjunctive Treatments to Address GERD Symptoms Refractory to Acid Suppression

Evidence of clinical non-response to medical treatment should trigger an assessment of medication adherence. Prior research has demonstrated that suboptimal PPI timing, perhaps from inadequate physician education, is highly prevalent among patients with refractory symptoms [15]. Additional testing should be offered if maximal dosing of acid suppression and proper timing of administration can be confirmed. The goal of such testing is to detect residual reflux, or identify alternative diagnoses, to provide targets for additional treatment. Such alternative diagnoses may include residual acid reflux, non-acid reflux, gastroparesis, and functional heartburn. An approach has been described by Scarpellini et al. for the evaluation and management of patients with refractory GERD symptoms [16] using additional motility testing to clarify the diagnosis.

Adjunctive treatments have no role in the initial management of reflux symptoms, but can be used in a targeted approach following manometry and impedance-pH testing while on PPI therapy, in the setting of persistent symptoms [16]. For example, baclofen, a nonselective gamma-aminobutyric acid (GABA) type B receptor agonist, can be applied in cases demonstrating evidence of residual acid or non-acid reflux. Baclofen has been shown to reduce postprandial TLESRs and acid reflux episodes in healthy volunteers [17] and in patients with reflux esophagitis [18], as well as both acid and nonacid postprandial reflux episodes on impedance and pH testing [19]. However, the side-effect profile of dizziness and nausea often restricts its clinical utility. Bethanechol, a cholinergic M2 agonist, increases very low basal LES pressures [20] and may be of therapeutic benefit in patients with GERD and hypotensive LES following vagotomy and antrectomy [21]. It may also enhance gastric emptying, but is seldom used given its frequent association with side effects including mood changes, drowsiness, and muscle spasms.

Neuromodulating medications, such as tricyclic antidepressants and selective serotonin reuptake inhibitors, can be applied in patients with refractory symptoms and a negative impedance-pH study, for treatment of functional heartburn or dyspepsia. Prokinetic agents, such as metoclopramide, have a more controversial role, with minimal effect on GERD symptoms and significant potential for side effects (including tardive dyskinesia, which is irreversible even with discontinuation of metoclopramide), and are not presently recommended in the absence of contributing disorders such as gastroparesis [16, 22]. Advanced endoscopic [23] or surgical approaches may also be considered with confirmation of acid or non-acid reflux on impedance-pH testing, and without evidence of esophageal dysmotility on manometry, as detailed further in a subsequent chapter.

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Principles of Successful Surgical Antireflux Procedures

4

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Introduction

Laparoscopic Nissen fundoplication is a very successful therapy for gastroesophageal reflux disease (GERD) with 90–96% of good and excellent results [1–4]. However, referrals for surgical treatment are yet limited due to unfounded claims that the benefits of surgery for GERD must be weighed against the following complications: (a) mortality; (b) high risk of side effects; (c) need for continuous use of acid-reducing medications after surgery; (d) need for revision surgery; and (e) unclear benefit of surgery on the risk of cancer [5].

Laparoscopic Nissen fundoplication is a very successful therapy for GERD with 90–96% of good and excellent results [1–4]. However, a procedure that once experienced a raise in the annual rate of operations after the dissemination of minimally invasive approach [6], currently undergoes a significant decline in the number of annual operations [7].

Laparoscopic Nissen fundoplication is a very successful therapy for GERD with 90–96% of good and excellent results [1–4]. However, although a good therapy is available, GERD is increasing as a cause of morbidity and mortality in the general population [8, 9].

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Laparoscopic Nissen fundoplication is a very successful therapy for GERD with 90–96% of good and excellent results reported [1–4]. However, these results are not always reproducible [10].

This chapter focuses on how to obtain 90–96% of good and excellent results based on the principles for a successful surgical antireflux procedure.

Proper Workup

Similar to other surgical procedures, patients to undergo an antireflux operation must be clinical evaluated. A fundoplication for GERD is an elective procedure and high risk patients or those with uncontrolled co-morbidities should not be offered this kind of therapy.

An extensive esophageal work up is also mandatory before an antireflux operation [11, 12]. The certainty of the correct diagnosis and the esophageal function status brings better outcomes. In summary, 3 questions must be answered positively before a fundoplication is indicated.

Question #1: Does the Patient Have GERD?

Although it may seem at first look a question easy to answer – such as in an individual with esophageal symptoms, endoscopic erosive esophagitis and a positive pHmonitoring – the answer may

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not always be straightforward – in an individual with extra-esophageal symptoms and normal endoscopy, e.g.

Symptoms are not very accurate to diagnosis GERD. Heartburn may have specificity for the diagnosis of GERD of only 40% [12]. Extra-esophageal presentations are even worse since they can have multifactorial, often non-GERD, causes and causality between reflux and these clinical entities are sometimes difficult to prove.

Similarly, low degrees of erosive esophagitis and the presence of reflux at the barium esophagram have a low specificity for the diagnosis of GERD [12]. Even pHmonitoring in combination with impedance or not has a non-neglectable rate of false-negative tests.

The diagnosis of GERD must be based on a sum of clinical parameters, not from a single piece of information, since the accuracy of a sole particular diagnostic test (laryngoscopy, endoscopy, and pH- or pH-impedance monitoring) is suboptimal [13].

Question #2: Are the Symptoms Attributable to GERD?

Even though the diagnosis of GERD may be certain, symptoms may have other cause and be coincidentally present. This is especially true for extra-esophageal symptoms. Asthma, as an example, may be caused by GERD in 40–60% of the cases but be associated to other factors in the remaining percentage [13].

The association of the symptom and GERD may be assessed by a temporal correlation between symptoms and episodes of reflux at the pHmonitoring (or impedance-pH) and the clinical response to pharmacological therapy for GERD.

Question #3: Is Surgery the Appropriate Therapy?

Indications for operative therapy for GERD falls within 2 categories: (1) failure of the medical therapy, that may be broadly interpreted as non-response to medication to desire to discontinue medication or intolerance to the drugs; and (2) complications unrelated to the pH of the refluxate, such as aspiration or Barrett's esophagus, since pharmacologic therapy for GERD is currently aimed at acid blockage [14].

Obviously, those patients with a higher chance of failure of the surgical therapy should not be offered a surgical treatment.

Proper Patient Selection

Some predictors of worse outcomes after a fundoplication have been identified (Table 4.1). A group of predictors include patients whose diagnosis of GERD may not be confidently confirmed, such as normal pHmonitoring, absence of hiatal hernia, extra-esophageal symptoms, lack of response to acid suppression therapy and psychiatric disorders. Other group is related to technical difficult, such as obesity. Female gender was found to have worse outcomes compared to males [14–17]. Older age and esophageal dysmotility – excluding achalasia – do not influence outcomes [18, 19].

Since diverse symptoms respond differently to antireflux surgery, patients´ expectations must be evaluated before the operation. In a very simplistic way, patients must be alerted that the operation is excellent to esophageal symptoms (heartburn and regurgitation); moderate to extra-esophageal symptoms; and bad for gastric symptoms (bloating, epigastric pain, etc.) and the more predictors of worse outcomes are present, less likely the operation will be successful.

Proper Technique

A proper technique is essential to ensure good outcomes (Fig. 4.1).

Table 4.1 Predictive factors for bad outcomes after a laparoscopic Nissen fundoplication

Normal pHmonitoring
Extra-esophageal symptoms
Lack of response to acid suppression therapy
Psychiatric disorders
Obesity
Female gender
Absence of hiatal hernia
Low socioeconomic status

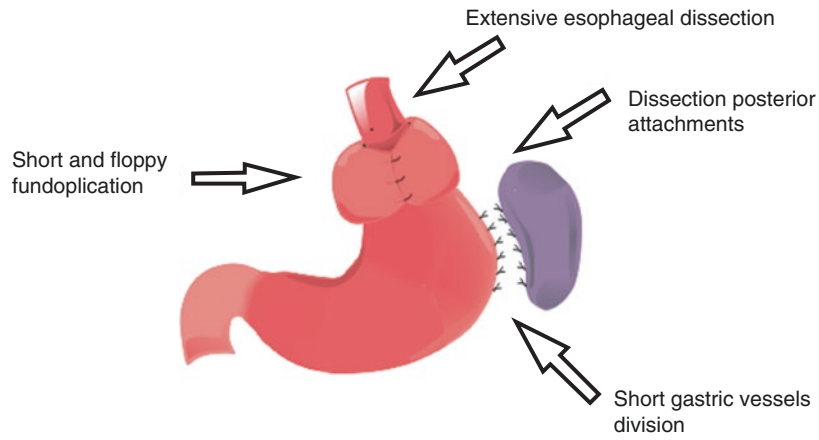

Fig. 4.1 Technical tips for a successful laparoscopic Nissen fundoplication

Access Route

While a thoracic approach was popular in the beginning of the antireflux surgery, it evolved to be used only in cases of large hiatal hernias due to the fear that gastric reduction would be more difficult to accomplish through the abdomen; to current abandonment in favor of the abdominal route.

Laparoscopic approach to antireflux surgery started in 1991. Although some initial studies showed an increase in the rate of complications and worse outcomes compared to open operation [20], nowadays, it is common sense that the laparoscopic route is superior.

Esophageal Dissection

Although a minimal esophageal/hiatal dissection has been proposed in order to preserve natural antireflux mechanisms [21], most surgeons believe that an extensive esophageal dissection is mandatory in order to obtain 2–4 cm of esophagus without tension below the diaphragm. This manoeuver helps avoiding hernia recurrence and improve GERD control, since a long segment of abdominal esophagus is an efficient antireflux mechanism [22]. It must be in mind that each centimeter of esophagus dissected in the posterior mediastinum leads to a 0.3 centimeters gain in abdominal esophagus length [23].

Vagal trunks and branches must be carefully identified and preserved during dissection of the esophagus [14].

Hiatal Closure

Hiatal closure is a mandatory step during an antireflux operation: (1) it avoids herniation of the wrap through the hiatus and (2) the diaphragm has a synergistic action with the lower esophageal sphincter protecting against sudden increases in intra-abdominal pressure such as during coughing [24]. One of the main causes of failure after antireflux operation is gastric (wrap) herniation through the hiatus that may be attributed to breakdown of the hiatal closure or a faulty repair.

The use of prosthetic material (mesh) for hiatal reinforcement (hiatoplasty) is a controversial topic (Fig. 4.2). It brings the question of the balance between the risk of recurrence and the risk of mesh-related complications (especially esophageal and gastric erosion) [25]. While some surgeons are more liberal in the use of mesh [26], other are more selective [25]. Recent publication of the results of the late follow-up of a large multicenter trial, shows a high index of recurrence even with mesh [27].

Fundoplication

A total fundoplication (Nissen) is the procedure of choice for most cases due to lower reflux recurrence and similar postoperative dysphagia, even in individuals with hypotensive peristalsis [28]. A partial fundoplication (Dor, Toupet) are reserved for cases with impaired peristalsis as in achalasia or scleroderma [29, 30].

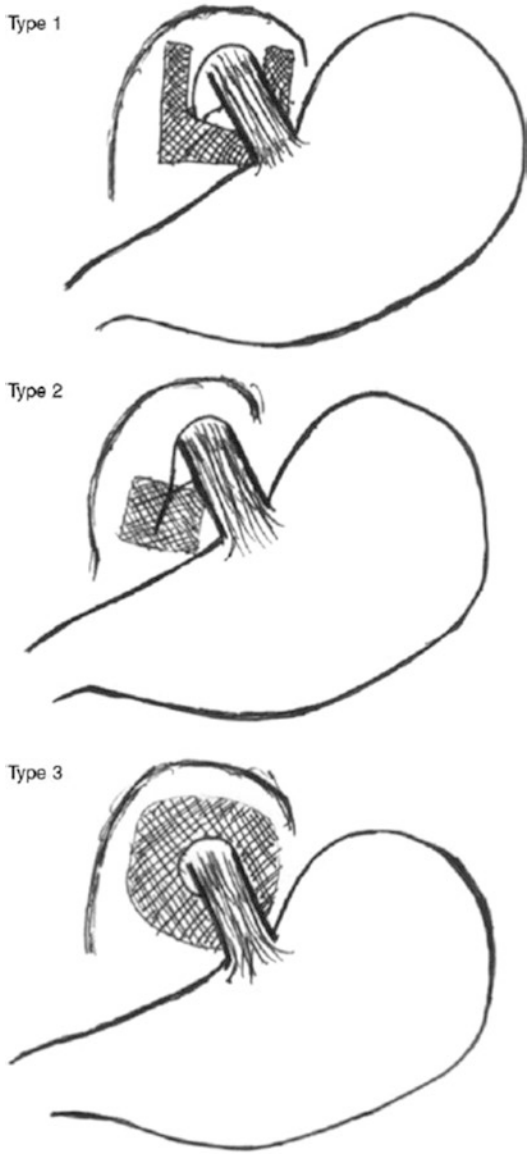

Fig. 4.2 Methods of mesh placement (Reproduced from Herbella et al. [25], with permission from Wolters Kluwer Health, Inc.)

Some well-established points are fundamental in achieving a good fundoplication [31].

An ideal fundoplication must be tension-free. An extensive dissection of the posterior attachments of the gastric fundus and an ample retroesophageal window are essential for this purpose. Short gastric vessels division may also help attain a floppy fundoplication. Randomized controlled trials did not show advantages when short gastric vessels are divided [32, 33]; however, in this trials a significant number of patients randomized to not divided the vessels were converted to vessel division due to intraoperative judgement of tension in the fundus after wrapping the esophagus. Moreover, some degree of tension is found in more than 50% of the cases when the short gastric vessels are not sectioned [34] justifying routine division of the vessels. An intraluminal bougie is advocate by some to calibrate the fundoplication [35]. Although one trial showed a higher incidence of dysphagia when a bougie is not used [33] (although esophageal perforation occurred due to the bougie), different series do not show advantages [36].

Another key step in this operation is the choice of the right place to create and position the wrap. Thus, gastro esophageal junction should be well identified, with the removal of the fat pad that is frequently located there, to make sure that the gastric fundus is brought around the esophagus not the stomach. Also, the gastric fundus not the gastric body should be used to create the fundoplication. Failure to this principles may lead to a faulty fundoplication.

Finally, the wrap must be short (1.5–2 cm) and floppy. Tight and long fundoplications are not associated to better reflux control but increases the risk for postoperative dysphagia and gas symptoms [37].

Proper Follow-Up

GERD does not seem to be a progressive disease where the presentation deteriorates from the nonerosive spectrum to erosive to Barrett's esophagus to esophageal adenocarcinoma [38]. Thus, a periodic and perennial follow-up is not theoretically necessary, unless a Barrett's esophagus is present. A short follow-up; however, is essential to guarantee good outcomes based on expectations fulfillment and understanding of a normal postoperative period.

Patients must be alerted that transitory dysphagia is normal up to 3 months after a laparoscopic Nissen fundoplication, due to edema and an esophageal ileus [39]. Also, the improvement for extra-esophageal symptoms may not

be immediate. New onset symptoms may occur, such as gas symptoms, but in general quality of life is not impaired and patients' satisfaction with the operation is sustained [5].

The need for continued usage of medication after antireflux surgery is used as an argument against the operation [40]. Most of the patients on medications after a Nissen fundoplication; however, do not have an objective indication for continued antacid therapy since the majority of patients with postoperative symptoms are either not tested for reflux or have a normal pH-monitoring; the medication is often prescribed for the treatment of symptoms not attributable to GERD, such as nasal and abdominal symptoms; primary-care physicians or gastroenterologists do not to discontinue the medications after the operation; or patients restart their medications by themselves [5].

Conclusion

We believe that Nissen fundoplication, after more than 50 years of age, can be considered a very successful creation. It treats a high proportion of cases; brings excellent results in more than 80% of the patients; improves patients' quality of life and seems to prevent the progression of Barrett's esophagus to adenocarcinoma [5]. Unfortunately, patients are still not offered surgical therapy based on some untrue concepts that still misguide indications for surgery and bad results when basic principles are not followed.

In conclusion, laparoscopic Nissen fundoplication is a very successful therapy for GERD with 90–96% of good and excellent results [1–4]; however, these results only come with a proper preoperative workup, patient selection, surgical technique and follow-up (Fig. 4.3).

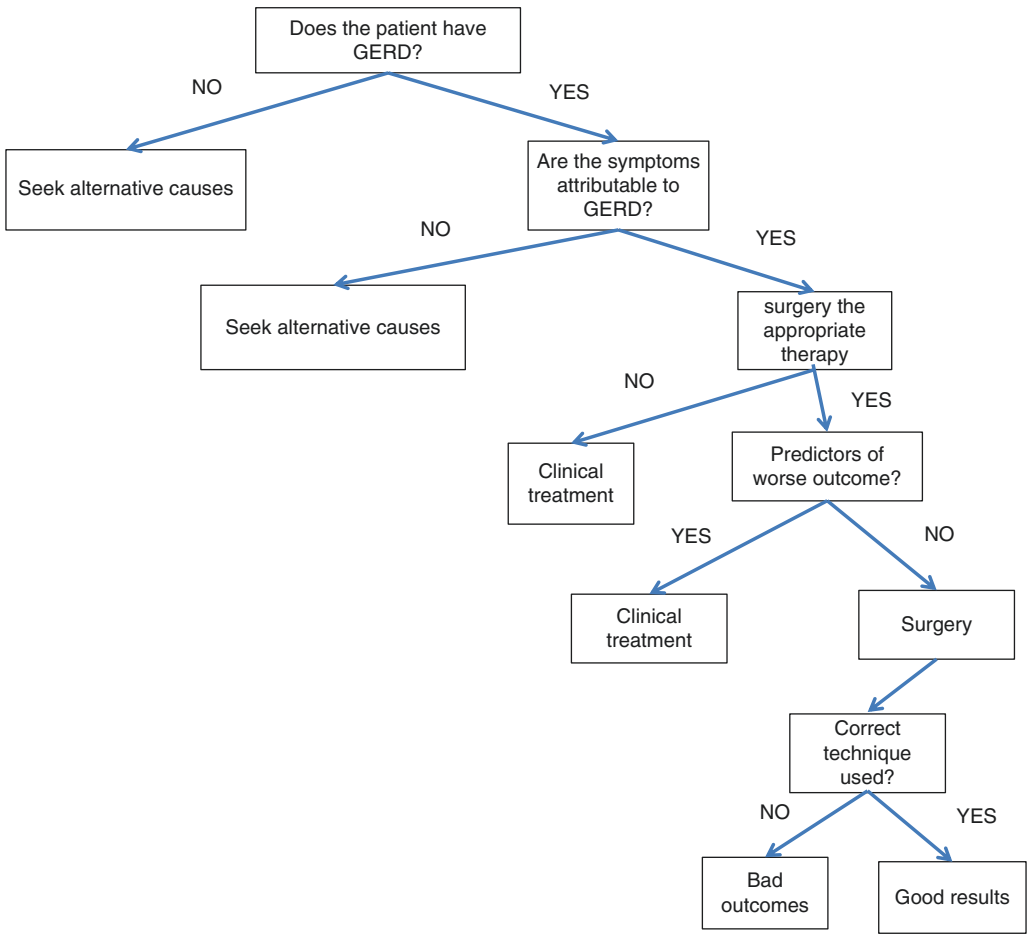

Fig. 4.3 Road to a successful laparoscopic Nissen fundoplication

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5 Diagnosis and Treatment of the Extraesophageal Manifestations of Gastroesophageal Reflux Disease

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Introduction

Extraesophageal manifestations of gastroesophageal reflux disease (GERD) include cough, laryngopharyngeal reflux (LPR), and asthma. Both GERD and its extraesophageal manifestations are prevalent in clinical practice. In population-based studies, 19.8% of North Americans complain of typical symptoms of GERD (heartburn and regurgitation) at least weekly [1, 2]. Also in the late 1990s, GERD accounted for $9.3–$12.1 billion in direct annual healthcare costs in the United States, higher than any other digestive disease. As a result, acid-suppressive agents were the leading pharmaceutical expenditure in the United States. The prevalence of GERD in the primary care setting becomes even more evident when one considers that, in the United States, 4.6 million office encounters annually are primarily for GERD, while 9.1 million encounters include GERD in the top three diagnoses for the encounter. GERD is also the most frequently first-listed gastrointestinal diagnosis in ambulatory care visits [1, 2].

Extraesophageal manifestations of reflux have been estimated to cost $5438 per patient in direct medical expenses in the first year after presentation and $13,700 for 5 years. Estimates of the economic burden of extraesophageal reflux have shown that expenditures for extraesophageal manifestations of reflux could surpass $50 billion, 86% of which could be attributable to pharmaceutical costs [2]. Additionally, the National Health Care Survey carried out by the Center for Disease Control and Prevention has demonstrated that the chief complaint for primary care patient visits was cough in 6.1%, throat symptoms in 4%, and asthma in 2.8% [3]. Within these visits for cough, asthma and throat symptoms are contained the hidden prevalence of extraesophageal manifestations of GERD which to date have not been adequately addressed from a medical or surgical perspective due to their obscurity.

Distinguishing whether cough, LPR, and asthma are caused by GERD remains challenging for both the primary care physician and the specialist. This distinction is important because treatment of GERD with the intent of improving or curing extraesophageal manifestation can be ineffective. This review summarizes the current literature on extraesophageal manifestations of reflux to assist in clinical decision-making.

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Clinical Presentation

Extraesophageal manifestations of GERD include cough, laryngopharyngeal reflux (LPR), and asthma. Chronic cough due to reflux is caused by gastric refluxate irritating the larynx and activating the afferent limb of the cough reflex. This is typically caused by direct irritation of the tracheobronchial tree after aspiration of gastric contents into the airway, or by stimulating an esophageal-bronchial neural cough reflex. Most studies define chronic a cough lasting more than 8 weeks [4].

LPR results from reflux of gastric contents beyond the upper esophageal sphincter and onto the tissues of the laryngopharynx, triggering chronic laryngitis or laryngopharyngitis. As in chronic laryngopharyngitis caused by other insults, patients often complain of chronic throat clearing, globus sensation, cough, throat pain, and/or vocal changes, especially hoarseness [5].

Asthma due to reflux might be induced by reflux of gastric contents into the tracheobronchial tree, causing direct irritation and bronchoconstriction. Alternatively, it might be caused by reflux of gastric contents into the esophagus, activating a neural reflex arc through the vagus nerve that leads to bronchoconstriction. As with asthma due to other causes, patients typically complain of wheezing and/or shortness of breath [6].

Patients presenting with extraesophageal manifestations of GERD often present without typical GERD symptoms (heartburn and regurgitation), which challenges the clinician's ability to identify the cause of the patient's complaint and risks misdiagnosis.

Diagnosis

Cough

There is no gold standard for diagnosing cough due to reflux [7]. However, investigators have used different methods to link chronic cough to reflux. Empiric therapy with antisecretory drugs over 8–16 weeks has been the traditional method used to distinguish cough due to reflux [8, 9]. Recurrence of cough upon discontinuation of therapy has also been used for diagnosis [10]. These diagnostic modalities have some drawbacks. First, antisecretory therapy may allow pharyngolaryngeal tissues to heal and resist activation of the cough reflex despite ongoing reflux. Second, the placebo effect in all related trials is large and variable. In fact, in RCTs that included a placebo arm, outcomes improved 1–34% in the placebo groups, and these improvements often met statistical significance [11, 12]. Other diagnostic have included: pathological reflux discovered with esophageal pH-monitoring or combined multichannel intraluminal impedance and pH (MII-pH) monitoring, esophageal dysmotility on esophageal manometry, or erosive esophagitis on esophagoscopy in patients with chronic cough [8, 13, 14]. However, the finding of abnormal esophageal acid exposure in a patient with chronic cough does not necessarily indicate that the cough is due to reflux. Therefore, to study the association and draw inferences on causality between chronic cough and reflux, investigators have evaluated combining esophageal (or pharyngoesophageal) pH-monitoring and MII-pH monitoring - a technique that can detect non-acid reflux – with a method of statistical analysis known as symptom association probability (SAP). SAP analysis consists in conducting a Fisher's exact test of association between reflux events (measured by the intraluminal pH or MII-pH monitor) and cough (which is usually self-reported). If a cough event is recorded within 2 min of a reflux event, then the two are considered associated and the Fisher's exact test for association between cough and reflux may confirm their association. SAP has been shown to be more sensitive to detect cough due to reflux than other indexes, such as the symptom index and symptom sensitivity index [14, 15]. Positive SAP on esophageal pH monitoring showed in one study to be the only statistically significant predictor of response to antisecretory therapy, with a sensitivity, specificity, positive predictive value,

and negative predictive value of 0.47, 0.82, 0.28 and 0.72, respectively [16]. Using MII-pH monitoring, another study showed that those with chronic cough without typical GERD symptoms and normal pH monitoring were SAP positive 44% of the time, 75% of which from non-acidic or weakly acidic reflux [7].

Attempts to prove a statistical association between cough episodes and esophageal reflux episodes in order to distinguish cough due to reflux has been complicated by the way cough is recorded. Patients record their symptoms using a symptom button on a monitoring device and/or in a symptom diary, so recording delays might be substantial. In fact, when patient reporting and concurrent recording of cough bursts on esophageal manometry are examined concurrently, Sifrim et al. demonstrated that only 39% of cough bursts recorded by manometry were reported by patients, and with an average delay of 28 s [7]. These delays and lost data might increase the false-negative rate of SAP testing.

Laryngopharyngeal Reflux

The diagnosis of LPR is equally challenging. Patients who present with symptoms of laryngitis, in whom other common causes, such as smoking, alcohol, industrial exposures, or chronic cough, have been ruled out, are usually started on an empiric trial of PPIs. If symptoms fail to resolve after 8–12 weeks, one might consider the possibility of LPR caused by non- or weakly acidic reflux, or other organic or functional disorders.

As for cough, there is no gold standard for diagnosing LPR. Diagnostic test include the response to antisecretory therapy, which is limited by a 40% placebo effect. Nevertheless, introducing the Reflux Symptom Index and the Reflux Finding Score (which incorporate symptoms of LPR and GERD) into clinical diagnosis has improved the diagnostic yield by 16–32% in the placebo arms of randomized controlled trials [17–19]. Esophageal and oropharyngeal pH monitoring have also been used as a diagnostic tool. However, their use is problematic because of the unclear role of non-acid or weakly acidic refluxate on pharyngolaryngeal tissues [20–22]. In addition to these methods, symptoms suggesting LPR, the finding of laryngitis on laryngoscopy, and the presence of esophagitis on endoscopy or in esophageal mucosal biopsies have been used to diagnose LPR [21, 23]. This methodology is potentially too restrictive, as patients without esophagitis may still have laryngitis caused by reflux as the tissues of the larynx may not be as resilient as the esophagus to exposure to gastric contents. By using these reference standards, many patients with LPR would be classified as not having LPR and the negative impacts on the specificity and the positive predictive value of the diagnostic tests might be significant.

Asthma

The diagnosis of asthma due to reflux is complicated by the nonspecific nature of the presenting complaints and the lack of a standard diagnostic test. Two methods have been used to link asthma to reflux: the presence of symptoms of asthma in those with GERD on esophageal pH monitoring [24], and the response of symptoms of asthma and/or pulmonary function tests to antisecretory therapy [25]. These reference standards might have excluded those with non- or weakly acid reflux as not having asthma due to reflux.

Treatment

Cough

Four randomized controlled trials have found no significant difference between proton-pump-inhibitors (PPI) and placebo groups in relieving cough due to reflux [11, 12, 26, 27] (Table 5.1). However, we point out that a large numbers of patients who might not have had cough due to

Table 5.1 Randomized trials on medical management of extraesophageal manifestations of GERD

Source	Sample size	Intervention	Primary outcomes	Main findings	P-value
Cough					
Shaheen 2011	40	Esomeprazole 40 mg bid for 12 weeks versus placebo	Change in Cough Specific Quality of Life Questionnaire score (CSQLQ)	Mean improvement in CSQLQ of 9.8 and 5.9 in treatment versus placebo group.	0.3
				Mean improvement in Fisman Cough Severity score of 1.0 vs. 0.8	0.7
				Mean improvement in Fisman Cough Frequency score of 3.2 vs. 2.3	0.3
Faruqi 2011	49	Esomeprazole 20 mg bid for 8 weeks	Change in integral response score for cough, change in Leicester Cough Questionnaire, change in Hull Airway Reflux Questionnaire, Reflux Finding Score (RFS), citric acid cough challenge	Change in cough frequency was 1.6 vs. 1.5	0.92
				Change in cough severity was 1.2 vs. 1.7	0.8
				Change in the Leicester Cough Questionnaire was 2.6 vs. 0.7	0.25
				Change in the RFS was 0.72 vs. 2.4	0.94
				Change in the Hull Airway Reflux Questionnaire was 7.3 vs. 7.1	0.61
				Change in log of inhaled citric acid concentration to produce 2 coughs was −0.15 vs. −0.04	0.66
				Change in log of inhaled citric acid concentration to produce 5 coughs was 0.02 vs. −0.09	0.57
Baldi 2006	35	Lansoprazole 30 mg qd and placebo dose in PM (control) versus lansoprazole 30 mg bid for 12 weeks.	Changes in cough scoring system and Visual Analog Scale (VAS)	Median change in VAS was 1.0 in both the treatment and control groups.	> 0.05
				Median change in cough scoring system was 1.0 vs. 0.5	> 0.05
				59% vs. 61% of patients had complete resolution of their symptoms.	> 0.05
Kiljander 2000	21	Omeprazole 40 mg qd for 8 weeks	Changes in cough symptom score	Cough symptom score −1.5 vs. +0.7	< 0.05
LPR					
Lam 2010	82	Rabeprazole 20 mg bid for 12 weeks	Change in Reflux Score Index (RSI) and RFS	At week 12, RSI −2.8 vs. +0.93	0.002
				At week 12, RFS −2.21 vs. −2.75	0.017
				At week 18, RSI −0.9 vs. + 0.58	0.12
				At week 18, RFS −3.2 vs. −3	0.68
McGlashan 2009	45	10 mL liquid dose of sodium alginate 1000 mg and potassium bicarbonate 200 mg after meals and at bedtime	Change in RSI and RFS from baseline at 2 month and 6 month follow up	At 2 months, RSI −12.7 vs. −7.8	0.005
				At 6 months, RSI −12.7 vs. −6.3	0.008
				At 2 months, RFS −2.2 vs. −0.6	0.08
				At 6 months, RFS −3.2 vs. −0.7	0.005

Table 5.1 (continued)

Source	Sample size	Intervention	Primary outcomes	Main findings	P-value
Reichel 2008	58	Esomeprazole 20 mg bid for 3 months	Change in RSI and RFS at 6 weeks and 3 months follow up, and subjective report of being symptom-free at 3 months.	At 6 weeks, RSI −9.87 vs. −6.93	NS
				At 3 months, RSI −14.27 vs. −7.79	< 0.05
				At 6 weeks, RFS −3.47 vs. −2.46	NS
				At 3 months, RFS −4.6 vs. −2.32	< 0.05
				At 3 months, 78.6% vs. 42.3% patients reported being symptom-free.	0.006
Wo 2006	35	Pantoprazole 40 mg daily for 12 weeks	Change in RFS, and subjective "adequate relief" of laryngeal symptoms.	Median RFS −1.0 vs. −3.0	NS
				Adequate relief of laryngeal symptoms was reported by 40% vs. 42% of patients	0.89
Vaezi 2006	145	Esomeprazole 40 mg bid for 16 weeks	Resolution of primary symptom, change in chronic posterior laryngitis index, and change in LPR-HRQL score.	Resolution of primary symptom was reported in 14.7% vs. 16% of patients	0.799
				CPLI −1.6 vs. −2.0	0.446
				LPR-HRQL score −11.6 vs. −7.8	0.424
Steward 2004	37	Rapeprazole 20 mg bid for 8 weeks	Change in reflux symptom score, subjective report of "significant global improvement", change in laryngeal grading of video-recorded strobe-laryngoscopy signs scoring system	Mean reflux symptom score −9.7vs. -6.6	0.44
				Significant global improvement was reported in 53.3% vs. 50% of patients.	1
				Laryngoscopic grade +0.6 vs. +0.5	0.69
Ehrer 2003	14	Pantoprazole 40 mg bid for 3 months (Placebo-controlled case-crossover trial)	Change in symptom score, change in laryngoscopic signs score	No statistically significant difference in mean symptom scores between groups (values unreported).	NS
				Mean laryngoscopic signs score −8.0 vs. −5.6 in the placebo-first group.	NS
Noordzij 2001	30	Omeprazole 40 mg bid for 8 weeks	Change in symptom score, change in laryngoscopic scores for vocal fold edema, arytenoid erythema, arytenoid edema, interarytenoid irregularity, and mucus accumulation.	Laryngeal symptom score −1078.6 vs. 1944.9	0.098
				No significant difference was found in the change in laryngoscopic sign scores.	NS
El-Serag 2001	20	Lansoprazole 30 mg bid for 3 months	Resolution of all presenting laryngeal symptoms, complete or partial resolution of all presenting laryngoscopic signs	Resolution of all presenting laryngeal symptoms was reported in 55% vs. 11% of patients	0.04
				Complete or partial resolution of laryngeal signs was found in 58% vs. 30% of patients	0.123

(continued)

Table 5.1 (continued)

Source	Sample size	Intervention	Primary outcomes	Main findings	P-value
Asthma					
Kiljander 2010	828	Three randomization groups: esomeprazole 40 mg daily and placebo daily, esomeprazole 40 mg bid, or placebo bid for 26 weeks	Changes in lung function tests, change in asthma quality of life questionnaire score, and experiencing a severe asthma exacerbation	Mean morning PEF improved +3.5 L and +5.5 L more in patients receiving esomeprazole daily and bid, respectively, compared to placebo.	NS
				Mean FEV1 improved 0.07 L more in patients receiving esomeprazole bid compared to placebo.	<0.0042
				Esomeprazole once daily was not statistically significantly better than placebo.	NS
				Mean AQLQ score increased 0.2 in patients receiving esomeprazole 40 mg daily, 0.3 in patients receiving esomeprazole bid, and 0.1 in patients receiving placebo.	< 0.001
				Severe asthma exacerbations experienced by 10%, 7.5%, and 10% of patients on esomeprazole once daily, bid, and placebo, respectively.	NS
Peterson 2009	30	Three randomization groups: rabeprazole 20 mg daily and placebo daily, rabeprazole 20 mg bid, or placebo bid	Subjective determination by subjects of improved exercise symptoms, changes in pulmonary function test, spirometry, SF-36 score, and mini-AQLQ score	Subjectively improved exercise tolerance was reported by 70% vs. 25% in patients on rabeprazole	0.03
				No statistically significant difference in change in FEV1, FVC, or FEV1/FVC between the rabeprazole groups and placebo.	NS
				There were no statistically significant difference in change in SF-36 or mini-AQLQ scores.	NS
Mastronarde 2009	393	Esomeprazole 40 mg bid	Rate of episodes of poor asthma control, change in PFTs, asthma symptoms, or asthma control	No. of episodes of poor asthma control per person-year was 2.5 vs. 2.3	0.66
				Change in FEV1 was 0 L vs. −0.02 L	0.36
				Change in FVC was 0 vs. −0.03	0.3
				Change in PEF was 9.2 L/min vs. 3.2 L/min	0.24
				Change in PC20 was 0.3 mg/mL vs. 1.5 mg/mL	0.04
				Change in JACQ, ASUI, mini-AQLQ, and SF-36 scores were not statistically significantly different between the treatment and placebo groups.	0.11–0.56

Table 5.1 (continued)

Source	Sample size	Intervention	Primary outcomes	Main findings	P-value
Sharma 2007	198	Omeprazole 20 mg bid and domperidone 10 mg tid for 16 weeks	Changes in asthma symptom score, rescue albuterol use, daytime and nighttime PEF, post-bronchodilator FEV1, and FVC	Daytime asthma symptom score decreased −0.48 vs. −0.22.	0.0001
				Nighttime asthma score decreased −0.51 vs. −0.14	0.0001
				Rescue albuterol puffs/week decreased −0.76 vs. −0.1	<0.0001
				Morning PEF increased +22.78 L/min vs. −0.76 L/min	<0.004
				Evening PEF increased +27.76 L/min vs. −1.43 L/min	0.002
				FEV1 increased +0.21 L vs. +0.07 L	0.0013
				FVC increased +0.18 L vs. −0.03 L	0.0023
Kiljander 2006	624	Esomeprazole 40 mg bid for 16 weeks	Change in morning and evening PEF	Morning PEF increased +22.3 L/min vs. +16 L/min in the last 28d of the study.	0.061
				Morning PEF increased +5.6 L/min more in the treatment group than in the placebo group after treatment was completed.	0.042
				In patients with GERD and nocturnal respiratory symptoms, morning PEF increased +8.7 L/min more in the treatment than the placebo group.	0.03
				Evening PEF increased +5.9 L/min more in the treatment group than in the placebo group.	0.053
				In patients with GERD and nocturnal respiratory symptoms evening PEF increased +11.2 L/min more in the treatment group than in placebo group.	0.02
Littner 2005	173	Lansoprazole 30 mg bid for 24 weeks	24-week average of asthma symptom score calculated from patient diaries, albuterol use, changes in PEF, post-bronchodilator FVC and FEV1, AQLQ score, and asthma exacerbations.	Asthma symptom scores decreased −0.36 vs. −0.21 in the placebo group.	NS
				Morning PEF increased +5 L/min vs. +10 L/min	NS
				Evening PEF increased +4 L/min vs. +12 L/min in the placebo group.	< 0.05
				Post-bronchodilator FEV1 changed 0 L in both groups.	NS
				Post-bronchodilator FVC changed 0 L vs. −0.1 L in the placebo group.	NS
				AQLQ score +0.9 vs. +0.7	< 0.05
				Albuterol use decreased 1 puff/day vs. −0.9 puffs per day	NS
				Asthma exacerbations were experienced by 8.1% vs. 20.4% of patients	0.017
				Moderate or severe asthma exacerbations were experienced by 4% vs. 13.9% of patients	0.016

(continued)

Table 5.1 (continued)

Source	Sample size	Intervention	Primary outcomes	Main findings	P-value
Sontag 2003	Total: 62 Control: 24 Medical: 22 Surgical: 16	Three randomization groups: lifestyle modifications and prn medications only (control), lifestyle modifications and ranitidine 150 mg tid, and lifestyle modifications and Nissen fundoplication, followed for 2 years	Change in asthma symptom score, requirement for pulmonary medications, and overall clinical response	Mean asthma symptom score improved significantly in 75% of surgical patients, 20% of control patients, and 0% of medical treatment patients.	0.008 (surgery vs. control and med. Groups combined)
				Need for rescue pulmonary medications decreased in 9.1% of patients in the medical group but increased in 18.2% of control patients. Pulmonary medication requirement decreased in 50% of patients in the surgical group. Zero patients in the control group changed their need for pulmonary medications.	NS
				Overall improvement occurred in 9.1% of medical, 75% of surgical, and 4.2% of control patients.	< 0.001 (surgery versus control and medical groups)
Jiang 2003	30	Two randomization arms: asthma treatment only versus asthma treatment plus omeprazole 20 mg qd, and domperidone 10 mg tid, for 6 weeks	Change in PFTs and histamine-induced bronchial sensitivity.	FVC increased +0.8 L vs. −0.2 L	< 0.05
				FEV1 increased +0.6 L vs. +0.1 L	< 0.05
				PEF increased +1.3 L/s vs. + 0.4 L/s	< 0.05
				Bronchial sensitivity improved +0.51 g/L vs. −0.03 g/L	< 0.05

reflux might have been enrolled in these trials, biasing the trials toward type II error. In addition, inclusion and exclusion criteria and outcomes varied between studies, making comparisons and meta-analysis difficult and inconclusive.

The surgical treatment of cough due to reflux is hampered by many of the same problems discussed for medical therapy and the difficulty of performing blinded, placebo-controlled trials. Observational studies varied in patient selection and the definition of outcomes measured [28–36]. With these limitations, most studies reported success rates of 65–74% [30, 32, 37, 38]. Patients who are more likely to report resolution of symptoms are those with concomitant typical GERD symptoms or positive esophageal pH monitoring [39]. The use of MII-pH monitoring in patients on bid PPI therapy has been limited but has shown that in patients with a positive non-acid symptom index for cough, antireflux surgery can achieve complete resolution of cough [40].

Laryngopharyngeal Reflux

Nine randomized trials have evaluated the efficacy of antisecretory therapy, primarily twice-daily PPIs, on LPR. These studies were relatively small, ranging in sample size from 14 to 145 subjects, and enrolled patients based on a varied combination of symptoms and laryngoscopic findings (Table 5.1). Six trials found no difference between treatment and placebo groups [17, 19, 41–44], whereas three trials reported statistically significant results [18, 45, 46]. Again, the difference in results might be explained by the placebo effect and the varied patient inclusion criteria.

No randomized controlled trials have compared medical and surgical intervention for LPR and only few small observational studies have been published [31, 47]. It is important to note that, as with other extraesophageal manifestation of GERD, patients who are more likely to report

resolution of symptoms (up to 72% of cases) are those with concomitant typical GERD symptoms and positive esophageal pH monitoring [47, 48].

Asthma

Nine randomized trials evaluated the effect of medical treatment of GERD on asthma due to reflux. Six randomized trials enrolled patients based on some combination of asthma and GERD [49–54]. Most studies reported changes in self-reported asthma symptoms and/or asthma-related quality of life indexes [49–53, 55, 56], and some reported differences in rescue bronchodilator use [49, 50, 52, 53] or in unscheduled healthcare visits for asthma [50, 56] (Table 5.1).

Among the three randomized trials that enrolled patients with both asthma and GERD, all reported greater improvement in the treatment than the placebo (or no treatment) groups. However, the differences in outcomes varied. Kiljander et al. found significant improvement in morning PEF, FEV_1, and the Asthma Quality of Life Questionnaire in subjects treated with esomeprazole 40 mg QD or BID compared to placebo. However they found no difference in changes in evening PEF, time to asthma exacerbation, number of severe asthma exacerbations, use of rescue inhalers, or asthma-free days [49]. Sharma et al. found greater improvement in mean daytime asthma symptom scores, mean nighttime asthma symptom scores, rescue inhaler use, morning PEF, evening PEF, FEV_1, and FVC in subjects treated with omeprazole 20 mg BID and domperidone 10 mg TID for 16 weeks compared to placebo [50]. Littner et al. found no significant differences in changes in diary-recorded asthma symptoms, rescue inhaler use, morning or evening PEF, FEV_1, FVC, or the Standardized Asthma Quality of Life Questionnaire score. However, they found significantly fewer patients in the treatment group experienced an asthma exacerbation or a moderate-severe asthma exacerbation [52].

The differences in outcomes between these trials may be explained by patient selection, both in terms of the severity of asthma and the severity of reflux in the study subjects. None of these trials utilized MII-pH monitoring to assess for non-acid esophageal reflux, and only one study enrolled patients with clinically silent GERD discovered on esophageal pH monitoring.

Only one trial randomized patients with both asthma and GERD (on pH monitoring and esophagitis on endoscopy) to medical or surgical treatment. After 2 years of follow-up, mean asthma symptom scores decreased more in the surgical group than in the medical group. Furthermore, 75% of surgical patients improved, markedly improved, or were cured of asthma when compared to 9% of the medical group. However changes in mean PEF, mean PEF percentage variation, PFTs, or asthma medication requirements were not significantly different [53].

Current Guidelines

Cough

The American College of Chest Physicians (ACCP) guidelines define chronic a cough lasting 8 weeks or longer. In patients who do not smoke and do not take an ACE inhibitor, ACCP recommends to evaluate for upper airway cough syndrome (UACS, also known as post-nasal drip syndrome), asthma, non-asthmatic eosinophilic bronchitis (NAEB), and GERD – the most common causes of chronic cough. Patients with chronic cough and typical symptoms of GERD, or patients whose chronic cough persists after ruling out or treating UACS, asthma, and NAEB should undergo medical treatment for GERD – dietary and lifestyle modifications with acid suppression therapy, and prokinetic therapy if there is no response to the initial therapy. Response should be assessed 1–3 months after initiation of therapy. Patients with typical symptoms of GERD whose cough does not resolve with antisecretory therapy should undergo esophageal pH monitoring while on therapy to determine if antisecretory therapy has failed. Maximal medical therapy includes an antireflux diet (<45 g of fat per day, elimination of coffee, tea, soda, chocolate, mints, citrus, and alcohol), eliminating smoking, and limiting activities that increase intraabdominal pressure, maximal PPI therapy, and prokinetic therapy. Antireflux surgery is recommended in patients who have positive esophageal pH monitoring, in whom cough has not

improved after a minimum of 3 months of maximal medical therapy, and in whom reflux is present while on maximal medical therapy. The ACCP guidelines do not address the diagnostic role of MII-pH monitoring or association tests, and they state that esophageal pH monitoring is the most sensitive and specific test for cough due to reflux [4, 57, 58]. However, more recent data support using combined MII-pH monitoring with SAP analysis while continuing medical therapy when patients fail to respond to antisecretory therapy, instead of using pH monitoring alone. Furthermore, more recent data might support using in selected patients concomitant esophageal manometry to objectively record cough episodes instead of less reliable patient recordings. Finally, patients who have been ruled out or treated for the three other most common causes of chronic cough and in whom MII-pH monitoring shows acid or non-acid reflux while on maximal antisecretory therapy, might be considered for evaluation for antireflux surgery (Table 5.2).

Table 5.2 Level of recommendation for systematic review of recent literature compared to current practice guidelines for management of extraesophageal manifestations of GERD

		Recommendation	
Intervention	Current evidence review and guidelines	Level	Class
Cough			
Treating chronic cough with medical antisecretory therapy.		**A**	**IIb**
Evidence review	Randomized controlled trials on treating suspected cough due to reflux with PPIs have had mixed results. Shaheen 2011 (patients with chronic cough and without typical GERD symptoms) and Faruqi 2011 (patients with chronic cough and with or without typical GERD symptoms) showed no improvement in cough-related quality of life, cough severity, cough frequency, induced cough threshold compared to placebo. However, Kiljander 2000 (patients with chronic cough and abnormal esophageal pH monitoring) showed greater improvement in cough symptoms with omeprazole compared to placebo.		
Practice guidelines	Patients with persistent chronic cough, who do not smoke and are not taking an ACE inhibitor, after ruling out upper airway cough syndrome, asthma, and non-asthmatic eosinophilic bronchitis, should undergo medical treatment for GERD. (ACCP)		
Treating patients with chronic cough and typical symptoms of GERD with medical antisecretory therapy.		**B**	**IIb**
Evidence review	Two randomized controlled trials enrolled patients with chronic cough and a diagnosis of GERD. Baldi 2006 compared daily to twice-daily lansoprazole, and found that bid therapy was not significantly better than daily therapy. Kiljander 2000 showed greater improvement in cough symptoms with omeprazole compared to placebo. While patients with typical symptoms of GERD should be treated, whether or not treating their GERD has a positive impact on their chronic cough is not clear.		
Practice guidelines	Patients with chronic cough and typical symptoms of GERD should undergo medical treatment for GERD (ACCP).		
Using esophageal monitoring to diagnose cough due to reflux.		**B**	**IIa**

Table 5.2 (continued)

		Recommendation	
Intervention	Current evidence review and guidelines	Level	Class
Evidence review	Studies evaluated the utility of esophageal monitoring – pH and MII-pH monitoring, on and off antisecretory therapy, with subjective and objective reporting of cough in diagnosing cough due to reflux. A prospective case-control study found that weakly acidic gas reflux was unique to patients with cough due to reflux compared to patients with GERD and healthy controls. (Kawamura 2011) Retrospective studies found esophageal pH monitoring with SAP analysis with self-reported cough off antisecretory therapy (Hersh 2010) had 26% of patients with cough due to reflux with a positive SI for non-acid reflux during esophageal MII-pH monitoring, and with self-reported cough on antisecretory therapy (Tutuian 2006). A prospective cohort study on esophageal MII-pH monitoring off antisecretory therapy with SAP analysis and cough recorded with concurrent manometry found 77% of patients with cough due to reflux were SAP positive, while 44% of patients without cough due to reflux were SAP positive. This study also reported that only 39% of cough bursts were not recorded by patients, and those that were recorded were delayed by 28 s. (Sifrim 2005) These studies were all small ($n \leq 61$) and some had significant methodological flaws.		
Practice guidelines	Patients with typical symptoms of GERD whose cough does not resolve with antisecretory therapy should undergo esophageal pH monitoring while on antisecretory therapy to determine whether medical therapy has failed (ACCP).		
Antireflux surgery for the treatment of cough due to reflux.		**B**	**IIb**
Evidence review	No randomized controlled trial has compared medical to surgical treatment of cough due to reflux in any patient population. Two prospective cohort studies have observed patients who underwent antireflux surgery after a negative workup for other causes of chronic cough. Allen 2004 reported on 79 patients who had a negative workup for UACS and asthma and complained primarily of respiratory symptoms before undergoing laparoscopic Nissen fundoplication. At 5-years follow-up patients subjectively reported 36% were cured of cough, 35% were improved, 24% were unchanged, and in 5% cough was worse. Brouwer in 2003 reported on 28 patients who underwent laparoscopic Nissen fundoplication for predominantly respiratory symptoms. Mean cough score decreased from 4.7 to 0.4 at mean 650 days follow-up. 19 patients had cough or "aspiration-type symptoms": 53% reported resolution of their symptoms (symptom score of 0/5), 32% had marked improvement (symptom score of 1/5), 11% reported some improvement, and 5% were unchanged.		
Practice guidelines	Antireflux surgery is recommended in patients who have positive esophageal pH monitoring in whom cough has not improved after a minimum of 3 months of maximal medical therapy and lifestyle modifications and esophageal monitoring studies show continued reflux while on maximal medical therapy (ACCP).		

(continued)

Table 5.2 (continued)

		Recommendation	
Intervention	Current evidence review and guidelines	Level	Class
LPR			
Use of the Reflux Symptom Index to diagnose LPR		**B**	**IIb**
Evidence review	One prospective study has evaluated the Reflux Symptom Index (Belafsky 2002). The authors reported mean RSI of patients with LPR was 19.9, and of healthy controls was 11.6. They considered RSI > 13 abnormal and indicative of LPR.		
Practice guidelines	Patients with suspected LPR should be evaluated with the Reflux Symptom Index and Reflux Finding Score. If > 13 and > 7, then patients should undergo an empiric trial of antisecretory therapy (Ford 2005).		
Use of the Reflux Finding Score to diagnose LPR		**B**	**IIb**
Evidence review	Belafsky 2001: mean RFS of patients with LPR was 11.5. Interrater reliability was 0.9.		
Practice guidelines	Patients with suspected LPR should be evaluated with the Reflux Symptom Index and Reflux Finding Score. If > 13 and > 7, then patients should undergo an empiric trial of antisecretory therapy (Ford 2005).		
Use of the Laryngoscopic Reflux Index score to diagnose LPR		**C**	**IIb**
Evidence review	Jonaitis 2006: LRI significantly higher in patients with LPR versus healthy controls. LRI > 5 significantly more common in cases than controls, but test characteristics unreported.		
Practice guidelines	Not addressed.		
Use of laryngoscopy to diagnose LPR		**B**	**IIa**
Evidence review	Three prospective studies have examined the use of laryngoscopy to diagnose LPR. In one case-control study (Vavricka 2007), only posterior pharyngeal wall cobblestoning was more common in cases than controls (66% vs 55%). Agreement between blinded observers on laryngeal findings ranged from good to poor. Another prospective study found that only interarytenoid mucosal inflammation and inflammation of the true vocal cords were significant predictors of response to antisecretory therapy (Park 2005). Another prospective study compared transnasal flexible fiberoptic laryngoscopy to transoral rigid laryngoscopy, finding fiberoptic laryngoscopy superior in detecting laryngeal findings.		
Practice guidelines	Laryngoscopic findings are highly suggestive of LPR: posterior laryngitis, contact granuloma, and pseudosulcus (Ford 2005).		
Esophageal pH or MII-pH monitoring to diagnose LPR		**B**	**IIb**
Evidence review	Two prospective studies have examined esophageal or pharyngoesophageal pH monitoring to diagnose LPR. One found increased laryngopharyngeal bolus exposure time and increased distal AET were only two significant predictors of response to PPI therapy (Wang 2012), while the other found that 52% of patients with laryngeal symptoms and 38% of patients with typical GERD symptoms had laryngopharyngeal acid reflux episodes during monitoring (Yorulamz 2003).		
Practice guidelines	In patients whose symptoms do not resolve after 6 months, or improve after 3 months, pharyngoesophageal MII-pH monitoring should be utilized to demonstrate reflux (Ford 2005).		

Table 5.2 (continued)

		Recommendation	
Intervention	Current evidence review and guidelines	Level	Class
Empiric PPI trial to diagnose LPR		**B**	**IIb**
Evidence review	One prospective trial examined the sensitivity and specificity of an empiric trial of twice daily PPIs to diagnose LPR, reporting positive and negative predictive values of 86% and 25%, respectively (Masaany 2011).		
Practice guidelines	If patients have RSI > 13 and RFS > 7, initiate 3–6 months of anti-reflux diet, lifestyle modifications, and twice daily PPI therapy.		
Treatment of LPR with PPIs		**A**	**IIb**
Evidence review	Eight randomized trials have compared twice daily PPI therapy with placebo. Some followed changes in the RSI and RFS. Six of these trials reported no differences between the placebo and treatment groups while 2 did report significant differences. Reichel 2008 showed RSI and RFS both improved at 3 months in patients treated with esomeprazole 20 mg bid, while El-Serag 2001 reported a greater percentage of patients in the treatment group reporting complete resolution of their symptoms than in the placebo group (55% vs 11%), but no difference in change in laryngeal signs of inflammation between the two groups (Lam 2010, Reichel 2008, Wo 2006, Vaezi 2006, Steward 2004, Ehrer 2003, Noordzij 2001, El-Serag 2001).		
Practice guidelines	Recommends treating patients with 3–6 months of twice daily PPI therapy.		
Treatment of LPR with sodium alginate and potassium bicarbonate.		**B**	**IIa**
Evidence review	One randomized non-placebo controlled trial has evaluated the effect of treating LPR with sodium alginate and potassium bicarbonate found RSI and RFS improved significantly from baseline to 2 months (RSI only) and baseline to 6 months (RSI and RFS) (McGlashan 2009).		
Practice guidelines	Not addressed.		
Antireflux surgery for LPR		**C**	**IIb**
Evidence review	No randomized trials have compared medical to surgical therapy for LPR. Swoger 2006 reported a prospective cohort of 25 patients who were unresponsive to PPI therapy. 10 chose to have surgery. At 1 year follow up, 1 patient in the surgery group and 1 patient in the medical groups reported resolved symptoms.		
Practice guidelines	In patients whose pharyngoesophageal MII-pH monitoring demonstrates reflux, referral should be made for surgery.		
Asthma			
Use of esophageal acidification to diagnose asthma due to reflux		**C**	**IIb**
Evidence review	One prospective case-control study used an increase of 100 μg in PD_{20} FEV_1 of a methacholine inhalation test after esophageal acidification to diagnose asthma due to reflux. Positive and negative predictive values were reported as 86% and 82%, respectively. (Dal Negro 2009)		
Practice guidelines	Not addressed		

(continued)

Table 5.2 (continued)

		Recommendation	
Intervention	Current evidence review and guidelines	Level	Class
Use of esophageal pH monitoring to diagnose asthma due to reflux		**B**	**IIb**
Evidence review	One randomized case-crossover trial (Kiljander 2001) studied esophageal pH monitoring to diagnose asthma due to reflux. The authors found that mean distal esophageal acid exposure time (11% vs 8%) and supine distal esophageal acid exposure time (12% vs 8%) were statistically significantly higher in patients whose asthma responded to therapy with omeprazole than in patients whose asthma did not respond to omeprazole.		
Practice guidelines	The Expert Panel recommends that patients with poorly controlled asthma despite maximal medical therapy should be evaluated for GERD with esophageal pH monitoring. (NIH-EPR3)		
Use of antisecretory therapy in patients with typical GERD symptoms and asthma		**A**	**I**
Evidence review	Three placebo-controlled randomized trials and 1 uncontrolled randomized trial have evaluated the effect of twice daily PPI therapy on asthma symptoms and pulmonary function tests in patients with GERD. Three (Kiljander 2010, Sharma 2007, Jiang 2003) found improvement in PFTs, while 1 (Littler 2005) did not.		
Practice guidelines	The Expert Panel recommended that patients with asthma and GERD symptoms should be treated for GERD. (NIH-EPR3).		
Use of antisecretory therapy in patients without typical GERD symptoms but with positive pH monitoring and asthma.		**B**	**IIb**
Evidence review	One randomized trial evaluated the effect of twice-daily PPI therapy on asthma symptoms in patients without typical GERD symptoms. Mastronarde 2009 found no difference in episodes of poor asthma control, PFTs, or asthma symptoms in patients without typical GERD symptoms, including patients with silent GERD discovered on esophageal pH monitoring.		
Practice guidelines	Not addressed.		
Antireflux surgery for asthma due to reflux.		**B**	**IIb**
Evidence review	One randomized controlled trial compared antireflux surgery to H2 blocker therapy for asthma due to reflux (Sontag 2003). It found that at 2 years asthma symptom scores decreased significantly more in the surgical group than in the H2 blocker and placebo groups combined. 75% of surgical patients had improvement, marked improvement, or cure of asthma after 2 years follow up. However pulmonary function tests and asthma medication requirements were not significantly different between the groups. Rakita 2006 found mean asthma symptom scores decreased from 4.7 to 1.7 after antireflux surgery (laparoscopic Nissen fundoplication) in patients who presented with a mean asthma symptom score of at least 4.		
Practice guidelines	Surgical treatment has been reported to reduce the symptoms of asthma and medication requirements (NIH-EPR3)		

Laryngopharyngeal Reflux

The American Academy of Otolaryngology published guidelines on hoarseness in 2009 [59]. Ford published a review of the available evidence in 2005. He recommended evaluating patients with suspected LPR with both the Reflux Symptom Index and the Reflux Finding Score. If greater than 13 and 7, respectively, he recommended proceeding to treatment with 3–6 months of an antireflux diet, lifestyle modifications (quitting smoking and alcohol intake), and twice daily PPI therapy. He recommended titrating medications off in patients whose symptoms resolved after 3 or 6 months. If symptoms improved but did not resolve after 6 months, or if symptoms did not improve at all after 3 months, Ford recommended evaluation with MII-pH monitoring to demonstrate reflux, and esophageal manometry and endoscopy to guide possible operative planning [5]. More recent data support supports prescribing 8–12 weeks of twice-daily PPIs and reevaluation in patients in whom LPR is suspected and in whom other common causes of chronic laryngitis have been ruled out. Similarly, evaluation for antireflux surgery should include extensive counseling about the uncertainty of outcomes, and patients with objective evidence of GERD should be offered surgery with the understanding that resolution of extraesophageal symptoms is less reliable than those of typical symptoms.

Asthma

The National Heart, Lung, and Blood Institute of the National Institutes of Health released its Expert Panel Report 3 in 2007, with guidelines for the diagnosis and management of asthma [6]. These guidelines recommend that clinicians should evaluate patients with asthma for GERD when asthma is poorly controlled on maximal medical therapy. The panel recommended that patients with concomitant GERD symptoms should be treated for GERD, while patients with poorly controlled asthma despite maximal medical therapy should undergo evaluation for GERD even in the absence of typical GERD symptoms. The panel noted that antireflux surgery has been reported to reduce asthma symptoms and medication requirements, but did not explicitly endorse antireflux surgery as a means of controlling asthma due to reflux. The guidelines do not specifically address how to diagnose asthma due to reflux.

Recent evidence provides further support for the role of GERD in patients with uncontrolled asthma. Given the morbidity and mortality associated with uncontrolled asthma it is reasonable to initiate antisecretory therapy on an empiric basis in patients with uncontrolled asthma without definitive proof of pathologic reflux. In patients who do not respond to maximal antisecretory therapy and appropriate asthma therapy it might be reasonable to resort to MII-pH monitoring while on antisecretory therapy. It may be reasonable to refer patients for antireflux surgery, however as in the case of LPR, antireflux surgery is largely an unproven therapy for asthma due to reflux. Patients should be extensively counseled about the unknown likelihood of benefit before referral for surgery, and should only be offered an operation if their asthma is accompanied by objective evidence of GERD, an event that can increase the likelihood of a successful operation.

Conclusions

Extraesophageal manifestations of reflux are estimated to cost $50 billion in healthcare expenditures annually and are responsible for 12.9% of all primary care provider encounters, yet they remain difficult to diagnose and treat. Extraesophageal manifestations of reflux may be most effectively diagnosed with a stepwise approach incorporating empiric treatment with antisecretory therapy, combined MII-pH monitoring, and surgical intervention in highly selected cases.

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Acute Complications of Antireflux Surgery

6

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Introduction

Laparoscopic antireflux surgery (LARS) is considered the gold standard for the surgical management of severe gastroesophageal reflux disease [1]. While underutilized for fear of occasional long-term side effects, it remains a safe operation with a very low complication rate in appropriately selected patients. A recent analysis of the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database determined an overall, 30-day morbidity and mortality rate of 3.8% and 0.19%, respectively, with rates even lower in patients younger than 70 years [2]. LARS is reported as equally safe in the morbidly obese with no difference in the overall complication or mortality rate in patients with a BMI $\geq$ 35 kg/m^2 [3], although its efficacy is matter of debate and beyond the scope of this chapter.

The prevention of acute and chronic complications begins with adequate patient selection, as detailed in earlier chapters of this book [1, 4]. The importance of a thorough diagnostic workup cannot be understated. Before considering LARS, all patients should undergo evaluation of symptoms, upper endoscopy, 24-h pH testing, esophageal manometry, and barium esophagram. This workup aids to ensure appropriate patient selection and surgical planning to minimize unwanted postoperative side effects [5]. Furthermore, surgeon training and experience contribute to improved outcomes, decreased complication rates, and shorter hospital stay [6].

This chapter will serve as a review of the acute complications that can occur in the perioperative period of antireflux operations, focusing primarily on laparoscopic fundoplication. A properly conducted LARS can be summarized as a sequence of key steps as detailed in Table 6.1. Complications will be reviewed in the chronologic, stepwise manner in which they can be encountered during both the intraoperative and immediate postoperative period. While this chapter reviews the pitfalls of primary antireflux procedures, the reader should be aware of the fact that any reoperative LARS is always associated with increased risks of any of the events described below and the operating surgeon should be especially cautious in those instances.

Acute Intraoperative Complications

General Operative Considerations

There are several general considerations that apply to the safety of all laparoscopic procedures, including general anesthetic concerns, adequate

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Table 6.1 Key intraoperative steps for laparoscopic antireflux surgery

General operative considerations
Mobilization
Incision of gastrohepatic ligament
Incision of phrenoesophageal membrane
Dissection of right crus away from gastroesophageal junction[a]
Division of short gastric vessels and exposure of left crus
Creation of retroesophageal window
Mediastinal dissection
Cruroplasty
Fundoplication

[a]Variation: dissection can be started along the left side in the setting of a large hiatal hernia or based on surgeon preference.

use of energy devices, and tissue handling; however, a detailed discussion of these are beyond the scope of this chapter. Specific to LARS, the availability of an advanced minimally invasive surgery suite and trained personnel are key to success. The operating team must be well versed in the procedure and utilization of all equipment such as advanced energy devices, suture material, esophageal bougies, and endoscopes. Communication between team members is particularly important, especially during esophageal bougie insertion.

During patient positioning, care should be taken to protect and pad all pressure points. If the patient is placed in lithotomy, stirrups should be appropriately positioned to avoid iatrogenic injury to the sciatic or common peroneal nerve. Additionally, the knees must be flexed and the legs in-line with the abdominal wall to prevent interference with the trocars or instruments (so-called "relaxed" dorsal lithotomy). Alternatively, the patient can be positioned supine with either a footboard or on a split leg table with the legs parted. The patient should be secured to the table and stability confirmed prior to initiation of surgical prepping and draping. Pneumatic compression devices should be applied to minimize the risk of deep venous thrombosis. Finally, standard techniques should be employed during trocar placement to ensure safe entry and avoid iatrogenic vascular or intestinal injury.

Mobilization

Retractor Injury

The left lateral section of the liver is retracted ventrally in order to expose the gastrohepatic ligament and gastroesophageal (GE) junction (Fig. 6.1). Aggressive retraction can cause an iatrogenic liver injury, such as a liver laceration or a "sub-Glisson" capsular hematoma formation. Additionally, excessive and prolonged compression of the liver can contribute to hepatic arterial ischemia with the potential for delayed liver abscess formation and sepsis. Gentle utilization of a self-retaining retractor may minimize movement and chances of an iatrogenic livery injury. Attention to the amount of time the liver remains retracted is important, and re-positioning may be required in prolonged cases.

Injury to an Aberrant Left Hepatic Artery

Variation of the "standard" hepatic arterial anatomy is the norm, and surgeons must be aware of clinically relevant deviations. Specifically important during antireflux procedures, approximately 8–18% of patients may have either an "accessory" or "replaced" left hepatic artery contained within the gastrohepatic ligament (Fig. 6.1) [7, 8]. This aberrant artery typically originates from the left gastric artery, but may arise directly from the celiac trunk or aorta [9]. During LARS, it is frequently encountered during division of the gastrohepatic ligament for initial right crural exposure. Care must be taken to seek out and identify any aberrant left hepatic artery in order to avoid inadvertent transection. As a general rule, any aberrant left hepatic arterial branches should be identified and preserved, unless causing critical obstruction for safe dissection and mobilization. If vessel ligation is required, appropriate hemostatic maneuvers must be utilized to avoid perioperative hemorrhage. Additionally, in patients with underlying liver disease (i.e. cirrhosis, hepatic compromise), ligation of an aberrant left hepatic artery may lead to significant hepatic ischemia and therefore preservation should be attempted. In otherwise healthy patients, ligation of an accessory artery may lead to temporary

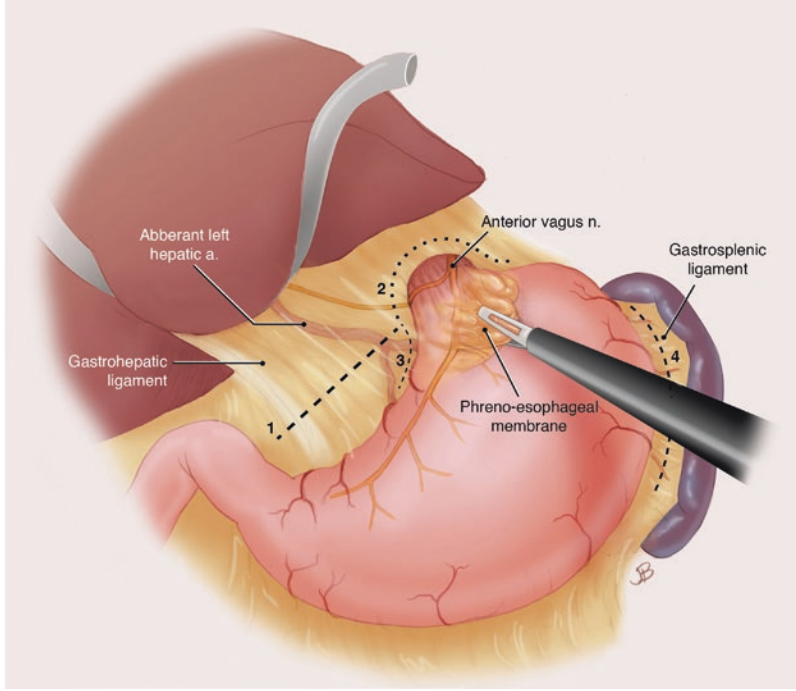

Fig. 6.1 Intraoperative view of the esophageal hiatus prior to dissection and mobilization. (*1*) Note the presence of an aberrant left hepatic artery coursing through the gastrohepatic ligament, which can be injured while incising the pars flaccida. (*2*) With division of the phrenoesophageal membrane, the anterior vagus nerve is at risk for injury. (*3*) Subsequently, during separation of the right crus from the esophago-gastric junction, the posterior vagus nerve, aorta, and pleura may be encountered. (*4*) Additionally, mobilization of the fundus of the stomach requires takedown of the gastrosplenic ligament where injury to the short gastric vessels or spleen/splenic capsule may occur

elevation of liver transaminases [8]; however, if ligation of a fully "replaced" left hepatic artery is necessary, the risk of a delayed ischemia liver abscess must be considered.

Vagal Nerve Injury

As dissection continues along the right crus with division of the phrenoesophageal membrane, the vagal nerves are at risk for injury (Fig. 6.2). The incidence of iatrogenic vagal nerve injury during fundoplication is reported to be as high as 20% [10]. The left vagus lies anteriorly on the esophagus and may run through the gastroesophageal "fat pad". The right vagus is encountered along the posterior esophagus and may be injured when creating the retroesophageal/retrogastric window. Both nerves should be carefully identified and preserved to prevent postoperative pyloric dysfunction, delayed gastric emptying, and post-vagotomy diarrhea. Post-fundoplication diarrhea is common (18–33%) and may be due to vagal injury or accelerated gastric emptying from the fundoplication itself [11]. It is worth noting however, that while the nerves should always be respected, Pellegrini et al. have proposed vagotomy as an alternative method for esophageal lengthening, without significant adverse effects [12].

Short Gastric Vessel Bleeding/ Splenic Injury

Routine division of the short gastric vessels during LARS is controversial. Studies have failed to demonstrate a significant decrease in long-term postoperative dysphagia and gas-bloat syndrome after ligation of short gastric vessels [13, 14]. However, many surgeons prefer to ligate these vessels to allow for more extensive mobilization of the gastric fundus, as well as improved exposure to the posterior gastric space, to aid in

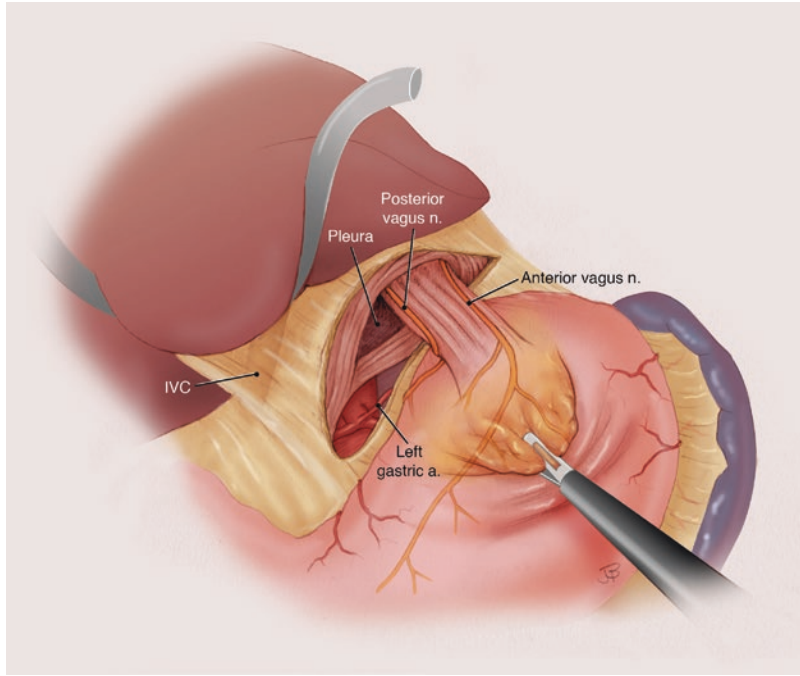

Fig. 6.2 View of the esophageal hiatus after dissection of the gastrohepatic ligament and right crus. Potential pitfalls include injury to the vagus nerves, celiac trunk, aorta, vena cava, and pleura which all lie in close proximity to the dissection field. *IVC* inferior vena cava

fundoplication creation. Dissection begins along the mid-portion of the greater curvature of the stomach at the level of the inferior pole of the spleen and extends superiorly. Some of the short gastric vessels may directly supply the upper pole of the spleen and division can lead to infarction of the tip of the spleen. This is usually without consequence and no further intervention is required. If the short gastric vessels are poorly visualized, tearing or incomplete ligation can lead to excessive bleeding. Careful tissue handling between the operating and assistant surgeon is necessary to expose the short gastric vessels. Before attempting ligation, the surgeon must be sure the vessel is completely encompassed in the tissue-sealing device. Additionally, minimal tension should be placed on this tissue when sealing to avoid tearing with incomplete hemostasis. Besides the formal, well-known short gastric vessels, there often are posterior gastric vessels that run dorsally (the so-called "pancreatogastric vessels"). The surgeon should make a conscious effort to identify these vessels, as they can be a source of troubling bleeding, and if not divided may limit the mobility of the gastric fundus (Fig. 6.3). If significant short gastric vessel bleeding occurs, conversion to an open operation may be required to achieve hemostasis, as this situation is, at times, difficult to manage laparoscopically. Additionally, traction on the capsule of spleen can cause a splenic laceration or subcapsular hematoma. The overall incidence of splenic injury appears to be less than 3% [15]. Careful tissue handling around the spleen is paramount to safe LARS.

Gastric Injury

Extensive gastric retraction during crural dissection or short gastric ligation can lead to a serosal injury and/or full-thickness perforation. It is best to grasp the epiphrenic fat pad or use a babcock clamp to retract the fundus. Injury is more likely in patients with a shortened esophagus or a large hiatal hernia with intrathoracic adhesions. In the setting of a large paraesophageal hernia, gastric injury can occur from an unwise attempt to

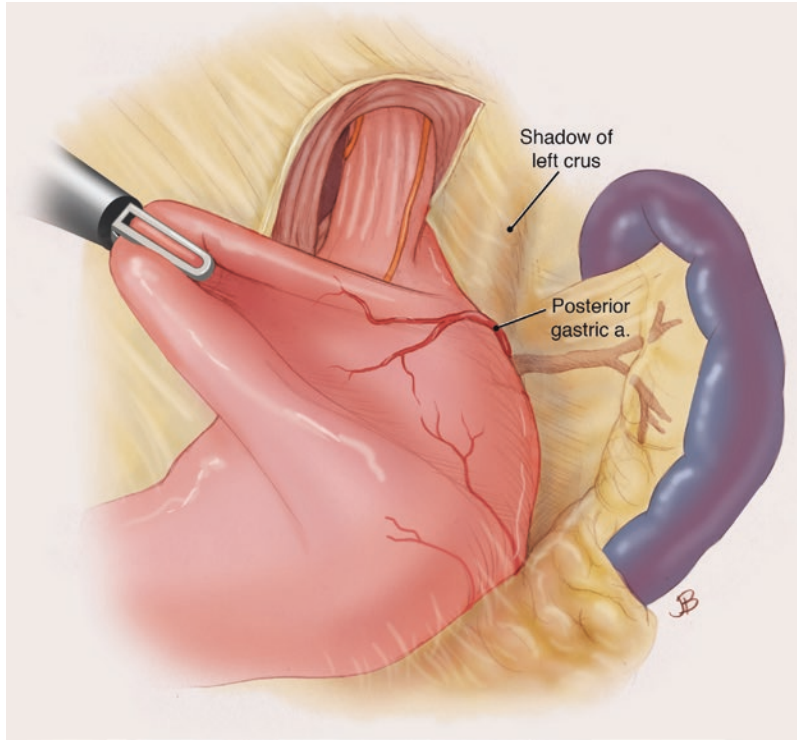

Fig. 6.3 Division of the short gastric and posterior gastric vessels allows for complete mobilization of the gastric fundus and improved exposure to the posterior gastric space. Division of the short gastric vessels begins along the mid-portion of the greater curvature and extends superiorly. Careful tissue handling is necessary to prevent tearing or incomplete ligation, which can lead to excessive bleeding

reduce the hernia contents instead of focusing on dissection and retraction of the hernia sac itself. Limiting traction to the hernia sac will prevent undue retraction on the stomach and will ultimately result in reduction of all herniated organs. Additionally, if using an energy device to ligate the short gastric vessels, it is best to stay at least 2–3 mm away from the gastric wall to prevent thermal injury and delayed perforation. Intraoperative gastric perforation or serosal injury can almost always be repaired primarily.

Esophageal Perforation

Esophageal perforation is a rare but serious complication of antireflux surgery. The incidence of esophageal injury appears to be less than 1%; however, it may increase in the setting of reoperative procedures or surgical team inexperience [15–17]. Typically, esophageal injury occurs by one of two mechanisms. The first mechanism of injury occurs by iatrogenic esophageal myotomy with mucosal perforation. This tends to occur when normal tissue planes are obscured by either inflammatory or scar tissue (usually in reoperative procedures), or when bleeding and inappropriate technique obscure the anatomic landmarks. This can occur with manipulation of the esophagus or stomach at the earlier stages of dissection of the right/left crus or when developing the retroesophageal window. As such, we recommend constant gentle tension be applied by grasping the gastroesophageal fat pad and careful precise bloodless dissection. Additionally, utilizing a penrose drain around the distal esophagus to assist with retraction during retroesophageal dissection and cruroplasty can help minimize the risk of injury. The second mechanism of esophageal injury is iatrogenic perforation by placement of the esophageal bougie dilators/sizers. This will be discussed below. If a perforation is encountered

intraoperatively, it can be repaired primarily with a one- or two-layered closure depending on surgeon preference and the integrity of the esophageal tissue. Key to a successful repair is the identification/exposure of the proximal and distal limits of the mucosal injury that needs to be approximated in its entirety without tension.

Pneumothorax (Capnothorax)

The right and left pleura are in close proximity to the esophagus during mediastinal dissection (Fig. 6.2), and if dissection extends too far lateral from the esophagus, the pleura can be entered, causing a CO_2 pneumothorax and/or subcutaneous emphysema. The incidence of pneumothorax appears to be less than 3% during primary procedures and slightly higher with reoperative surgery [16]. When injury to the pleura occurs, and there is no underlying lung injury or severe preexisting pulmonary disease, typically a chest tube is not needed. The capnothorax can be managed with supplemental oxygen alone, as CO_2 should reabsorb spontaneously within a few hours postoperatively. Constant communication with the anesthesia staff is important to alert them to the situation, so they can appropriately adjust ventilation. If the patient has trouble tolerating the capnothorax, a drainage catheter can be placed into the pleural space and brought out through one of the trocars to evacuate the CO_2. The tube can be removed at the end of the procedure, negating the need for formal tube thoracostomy placement.

Cruroplasty

Esophageal Perforation from Bougie

To avoid an overly tight crural closure (and to appropriately size a complete fundoplication), a 50–60F bougie – based on surgeon's preference – is routinely used across the GE junction prior to cruroplasty. This should be advanced slowly, with clear communication between the anesthesiologist and surgeon. It is our practice to have the anesthesia staff verbalize every 5 cm of advancement of the bougie, in order for the entire team to clearly understand how far the esophageal dilator has been introduced. If any resistance is met, force should not be used, and instead the bougie should be exchanged for a smaller size. The bougie should be clearly visualized as it is passed across the GE junction. During placement, any instrument previously retracting the stomach is disengaged. Placing traction on the stomach at this time can cause angulation of the GE junction and increase the chances of esophageal or gastric perforation. Similarly, if a nasogastric tube is to be placed at the start of the procedure, it is best done under direct visualization, especially if a hiatal hernia is present. Repair of an esophageal injury from a bougie insertion depends upon the location and extent of the injury, ranging from layered primary closure to esophageal resection and replacement.

Aortic Injury

Aortic injury is a rare complication of LARS, but can be fatal if encountered [18]. The aorta lies directly posterior to the esophagus and the crura and is at risk for injury during mediastinal dissection and cruroplasty (Fig. 6.2). Is it imperative that the surgeon has a clear understanding of these anatomical relationships to avoid life-threatening bleeding. Particularly when placing the most posterior crural stitch, the aorta should be visualized and protected. The use of electrosurgery should be minimized in this area. In the event of bleeding, the surgeon should have a low threshold for converting to a laparotomy for hemorrhage control.

Fundoplication

Construction of the fundoplication is often an area of frustration for the laparoscopic surgeon. In order to craft a functional wrap, full clearance of the retroesophageal/retrogastric space is necessary. Additionally, we believe takedown of the short gastric and posterior gastric vessels is essential. These maneuvers allow for easier posterior passage of the gastric fundus when creating either a partial or complete fundoplication. Also, as discussed previously, appropriate tissue handling is key to avoid inadvertent serosal injuries to the stomach when passing the fundus posteriorly. Some authors propose using a temporary

placed suture in the posterior fundus to aid in gentle and simple passage of the fundus [19]. Similarly, when anchoring the wrap to the esophagus, it is important to avoid full thickness bites that penetrate the esophageal mucosa as it may result in micro-abscesses post-operatively [20].

Incorrectly Created Wrap

When creating a 360° fundoplication, it is important to maintain the stomach in the correct orientation and to anchor the wrap appropriately on the esophagus. The standard tenets of a complete fundoplication include creation of a short (<2 cm), loose (allows passage of a large esophageal dilator), and floppy (full mobilization of the fundus) wrap [20]. Twisting the fundus can place tension on the wrap and contribute to postoperative dysphagia. This typically occurs when the fundus is not fully mobilized by division of the short gastric and posterior gastric vessels, as previously discussed. Additionally, a fully dissected retroesophageal/retrogastric window is necessary to improve visualization, aid in gentle tissue handling, and allow the fundus to pass without tension posteriorly to the esophagus. After passage of the fundus, a "shoe shine" maneuver should be performed to ensure the correct orientation. This maneuver includes stretching and pulling the two portions of the fundus that will be affixed anteriorly to confirm they are in continuity and not twisted. Additionally, a "drop test" should be performed to ensure the wrap is not under tension [20]. This involves releasing the posterior-placed fundus to make sure it remains in position. Lastly, some authors recommend overlapping the right and left wings of the fundoplication with minimal force to ensure a tension-less wrap [20]. Once tension is minimized, the wrap should be created in a ball valve configuration, to minimize post-operative dysphagia. The wrap should be anchored just proximal to the GE junction and created over a bougie to appropriately size the fundoplication. The integrity, position, "tightness," and configuration of the wrap can be (and should be) confirmed with intraoperative endoscopy. We view intraoperative endoscopy as an important step to confirm ease of passage through the GE junction, and to provide intraluminal confirmation of an adequately constructed, appropriately positioned wrap. Endoscopic testing may allow for adjustments in as many as 24% of fundoplications [21]. If the fundoplication is not constructed appropriately, postoperative dysphagia may follow. Additionally, dilation or distention of the wrapped fundus may occur causing an "hourglass" configuration.

Acute Postoperative Complications

The majority of acute complications in LARS transpire at the time of the operation; however, acute postoperative complications can occur. Besides the usual post-operative complications such as wound infection, deep venous thrombosis, pulmonary complications, urinary tract infections, surgeons must be vigilant to identify complications specific to LARS as early as possible.

Pneumothorax (Capnothorax)

A clinically significant pneumothorax is extremely rare after LARS. If pleural injury was recognized during the surgery, the patient may continue to have evidence of subcutaneous emphysema in the post anesthesia recovery unit. As long as the patient is asymptomatic, all team members should be informed that this is normal and self-limited. A chest radiograph is only needed if the patient has symptomatic shortness of breath or dyspnea. As described previously, a CO2 pneumothorax will reabsorb spontaneously and a chest tube is generally not needed. The patient can be supported with supplemental oxygen therapy alone. In the setting of a pulmonary parenchymal injury, ongoing "air leak" may necessitate the placement of a tube thoracostomy.

Early Failure (i.e. Slipped Nissen or Hiatal Herniation)

Early post-operative dysphagia occurs in 10–50% of patients [11]. This is usually due to postsurgical edema and is typically self-limited. Marked dysphagia combined with chest or epigastric pain can be a sign of crural disruption, fundoplication

slippage, and/or acute hiatal herniation [22]. This can be seen in the setting of a large hiatal hernia, especially if the GE junction is not fully mobilized into the abdominal cavity. Additionally, early post-operative vomiting or retching can increase intra-abdominal pressure and disrupt the wrap or cruroplasty. The reported incidence of anatomic failure ranges from 7% to 30% [22, 23]. The risk of early failure is reduced with surgeon experience and proper technique, including: adequate esophageal dissection, lengthening of the abdominal esophagus if needed, and secure cruroplasty [23]. Similarly, anti-emetics should be given post-operatively to minimize nausea and retching

Delayed Bleeding

Although rare, patients may present with delayed bleeding, especially if bleeding was encountered intra-operatively. As discussed previously, the surgeon should have an appreciation for the anatomic relationship between the dissection field and potential areas of vascular injury. Post-operative tachycardia and anemia can be signs of ongoing bleeding and should be investigated.

Esophageal or Gastric Perforation/ Leak

If an esophageal or gastric injury was not identified intraoperatively, it will usually manifest within the first 48 h following the operation. This potentially devastating complication must be identified as quickly as possible to minimize its sequelae, such as sepsis. Any signs of systemic inflammation must be carefully evaluated. Esophageal leak within the mediastinum or chest cavity can cause mediastinitis, infected pleural effusions, or empyema. An esophageal or gastric leak into the abdomen will cause typical peritoneal symptoms, with associated abscess formation or abdominal sepsis. In the post-LARS patient who develops fevers, tachycardia, and/or leukocytosis, the surgeon should a have a low threshold to order a contrast study to confirm the presence and site of a leak. If a perforation is detected, the patient should almost always return to the operating room for repair.

Special Considerations

Magnetic sphincter augmentation is a recent addition to the surgeon's armamentarium for the treatment of gastroesophageal reflux. This involves placing an expandable ring of titanium beads around the lower esophageal sphincter to increase its resting pressure. Unlike the technique for fundoplication, crural dissection is limited to a small tunnel in front of the right crus minimizing the risk of injury around the hiatus. Similarly, there is no need for gastric mobilization so the short gastric vessels are left in tact, avoiding potential splenic injury or bleeding. In a review of the first 1000 patients who underwent magnetic sphincter augmentation, there were no intra-operative complications [24]. One patient (0.1%) developed acute respiratory arrest immediately post-operatively, but this was thought to be unrelated to the device itself.

Conclusions

In summary, LARS is a safe option for the surgical management of gastroesophageal reflux disease. Appropriate patient selection, surgical planning, and surgeon experience are critical to successful outcomes and the prevention of complications. Complications can be compartmentalized into specific "steps" within the procedure allowing for appropriate recognition and prevention.

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7 Management of Complications: After Paraesophageal Hernia Repair

Nisha Dhanabalsamy, Melissa M. Carton, and Carlos Galvani

Introduction

For over four decades the management of paraesophageal hernias (PEH) has experienced a great deal of controversy. Surgeons have gone from watchful waiting to advocating elective repair even for asymptomatic patients due to the high mortality rates reported from mere observation, sometimes in spite of high operative risk [1, 2]. Nonetheless, more recent literature has shown that the mortality rates for emergency PEH repair may not be as high as previously believed [3]. In fact, a study by Stylopoulos et al. demonstrated that the elective repair of completely asymptomatic patients may not be justified considering that the development of emergency symptoms was 1.16%/year [4]. Thus, symptomatic patients with an acceptable operative risk are recommended for repair.

The use of this approach has rapidly spread; numerous series have demonstrated the safety profile of the surgery [5–8]. Despite the encouraging low morbidity and mortality rates, most studies have noted that PEH repair is a technically demanding operation with a significant learning curve [9–11]. Furthermore, patient factors such as age >70, obesity, comorbidities, and the complexity of the disease process play a significant role in the incidence of postoperative complications [9, 12]. In a decade-long series of 662 patients, Luketich et al. demonstrated a morbidity of 19% and a mortality of 1.7% [13] suggesting that even in experienced hands complications still happen. Nevertheless, the discussion and management of complications after paraesophageal hernia repair in the literature is amazingly sparse. This is potentially due to the fact that laparoscopic antireflux surgery for reflux disease and paraesophageal hernia repair share a number of complications (Table 7.1). Nonetheless, Trus et al. reported that complications after paraesophageal hernia repair were significantly greater than those observed with laparoscopic Nissen fundoplication for reflux disease [14]. In addition, identifying frail patients at high risk for postoperative morbidity and mortality is becoming increasingly important to determine operative risk and prevent complications [15].

From the technical standpoint, every effort must be made to avoid complications, for this purpose extensive minimally invasive and foregut surgery experience is mandatory.

In this review we describe the most significant side effects and complications that may appear after laparoscopic paraesophageal hernia repair, their prevention, recognition and management according the current literature.

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Table 7.1 Specific acute complications of laparoscopic PEH repair

Esophageal perforation	1.5–6.5%
Gastric perforation	1.5–4.5%
Splenic injury	Rare
Pneumothorax	2–7.4%
Immediate failure	2–4.5%
Acute post-op volvulus	3–8%
Delayed esophageal leak	3–4.5%
Death (attributable)	0.5–3%

Preventing Complications

Pre-surgical Care

Preoperative Preparation

The preoperative physical status of the patient dictates anesthetic management of patients with paraesophageal hernia. Patients suffering from this disease often can experience chronic aspiration leading to a poor preoperative respiratory status. Consideration of co-morbid conditions is equally important, as the diagnosis is frequently made in older debilitated patients and preoperative evaluation is essential for assessing the operative risk in the individual patient. It is essential for the anesthesia team to have a detailed understanding of the surgical procedure in terms of approach, the extent of the operation, and associated complications. Special emphasis should be placed on the assessment of cardiopulmonary function, because intraabdominal CO2 insufflation may be poorly tolerated in patients with severe cardiopulmonary compromise. Preoperative cardiac and pulmonary morbidity will determine the extent of preoperative cardiac testing as well as the need for pulmonary function testing (PFT) especially in those patients with restrictive lung disease secondary to recurrent aspiration pneumonia.

Patients with PEH are at an increased risk for aspiration during induction of anesthesia. For that reason they are advised to ingest only clear liquids 2 or 3 days before surgery, to decrease the risk of aspiration. In older patients with several comorbid conditions, a Foley catheter is placed and usually removed after the case. Premedication with a prophylactic anti-aspiration is highly recommended. The patient is placed in the supine position before the induction of general endotracheal anesthesia. In order to minimize the aspiration risk during the induction of anesthesia, the airway can be secured either after a rapid sequence induction with cricoid pressure, or awake with the aid of a fiberoptic bronchoscope. With the identification of risk factors, patients undergoing esophageal surgery could be stratified. Standard intraoperative monitoring will suffice for American Society of Anesthesiologists (ASA) physical status class I and II patients. More invasive monitoring may be required in patients with underlying cardiopulmonary pathology [16]. Adequate attention should be paid to the hemodynamic changes resulting from the combined effects of pneumoperitoneum and placing the patient in a reverse Trendelenburg position. Venous stasis in the lower extremities during the head-up position may be aggravated in the lithotomy position. Consequently, prophylactic measures to minimize the risk for deep venous thrombosis and pulmonary embolism must be considered such as the use pneumatic compression stocking for mechanical deep venous thrombosis (DVT) prophylaxis, and consideration should be given to chemical prophylaxis as well (e.g. low molecular weight heparin).

Postoperative Side Effects

It has been documented that the majority of patients experience transient gastrointestinal symptoms after antireflux surgery [17]. Nonetheless, the symptomatology subsides in the majority of patients within 3 months of the initial operation.

Subcutaneous Emphysema

Due to the extensive mediastinal dissection, subcutaneous emphysema is frequently observed. Subcutaneous crepitus may be palpated in the face, neck, shoulders, and upper chest. Often times this issue is discovered after the completion of the case when the surgical drapes are taken down. This issue is infrequently of clinical significance and resolves without therapy [18]. However, if discovered

early during the case the recommendation is to lower the CO2 insufflation pressure.

Postoperative Shoulder Pain

Another relatively common postoperative complaint from patients is left shoulder pain. This is the result of irritation of the left diaphragm and is self-limited.

Post-operative Nausea and Vomiting

Nausea and vomiting after laparoscopic foregut surgery is considered a major setback, since it is not only a reason for patient distress but can also predispose the patient to anatomical failure. It has been reported that up to 60% of patients suffer from postoperative nausea and as many as 5% experience vomiting soon after a fundoplication [19]. A number of pre and intraoperative anesthesia considerations should be taken into account to enhance postoperative patient recovery such as different ventilation strategies, minimizing intraoperative fluids, multimodal analgesia, limiting use of long acting opioids as well as routine antiemetic strategies like prophylactic treatment with intravenous antiemetics are always recommended. Patients with intractable postoperative vomiting should be carefully assessed before they are discharged in order to assure the integrity of their recent repair [20]. Gastric distension should be recognized early as it can be potentially dangerous in the immediate postoperative phase, and can be treated successfully by the placement of a nasogastric tube.

Flatulence and Gas Bloating Syndrome

An increased incidence of flatulence occurs in approximately in half of patients undergoing hiatal hernia repair [21]. In addition, patients often complain of bloating and reduced ability to belch. The occurrence of gas bloating syndrome is associated with competent wrap, aerophagia and in some patients it is possibly associated with delayed gastric emptying due to unrecognized vagal nerve injury. Nevertheless, in the majority of patients these symptoms are transient, but if persistent it will decrease patient satisfaction and could result in failure of the procedure [22]. Patients with these adverse events should initially be treated conservatively with dietary counseling (avoid gas producing foods) and the use of anti-gas medications (simethicone) as needed.

Diarrhea

New onset of diarrhea is a common side effect after hiatal hernia repair, identified in almost 20% of patients [23]. The cause of the diarrhea is unknown; however, it is important to document the presence of gastrointestinal symptoms before surgery since is expected that these patients will experience the same symptoms after surgery. The suggested mechanisms include (1) rapid gastric emptying, and (2) vagal nerve injury with subsequent bacterial overgrowth. The diarrhea tends to be low volume and postprandial. Antimotility agents including codeine, antibiotics for small bowel overgrowth, and cholestyramine may ease the diarrhea, but the management is empirical.

Postoperative Dysphagia

A significant number of patients experience dysphagia mainly for solids after paraesophageal hernia repair. This is primarily due to the modified anatomy and postoperative inflammatory changes. This dysphagia is transient in more than 90% of patients and resolves within the first 6–8 weeks of the surgery. In the early postoperative period patients usually receive dietary counseling and are recommended a special diet with slow progression from liquids to solid food paying special attention to adequate caloric intake. One should be vigilant about patients that experience severe dysphagia for liquids in the early postoperative period. Further workup may be warranted to rule out any anatomic failure. Patients that present with persistent dysphagia beyond 3 months of surgery need further investigation in order to determine the etiology of the dysphagia. This will be discussed later in this chapter.

Intraoperative and Early Postoperative Complications (< than 30 Days Postop)

Some of the medical complications after paraesophageal hernia repair are common to a number of surgical procedures such as atelectasis,

pneumonia, deep vein thrombosis, wound infections, and cardiac complications (i.e. atrial fibrillation, myocardial infarction).

For the purpose of this chapter we will focus our attention to mainly surgical intraoperative and early postoperative complications specific to paraesophageal hernia repair.

A number of intraoperative complications have been described with the laparoscopic repair of paraesophageal hernias. Understandably, the distorted anatomy, intraoperative difficulty and the complexity of the surgical technique can predispose patients to well defined complications during the different steps of the procedure. The recognition and appropriate management of these complications is key for optimal results.

Pneumothorax

Pleural injury or tear is not an uncommon complication due to the close relationship between the hernia sac and the mediastinal pleura. Factors predisposing patients to this complication are periesophagitis, the presence of large hernias and obesity. Although intraoperative pneumothorax may develop after the opening of the mediastinal pleura its consequences for the patient are negligible since CO2 is quickly reabsorbed and the lung is rarely involved. Rates of pneumothorax during laparoscopic antireflux surgery in most series range from 0% to 1.5% but may be as high as 10% especially in repairing paraesophageal hernias [24]. It is extremely important for the operating surgeon to communicate with the anesthesiologist if pleural injury ensues. Adequate monitoring of end-tidal carbon dioxide levels (EtCO2) and airway pressures will facilitate early diagnosis. Positive end-expiratory pressure (PEEP) application is an effective way of managing pneumothorax secondary to the passage of gas into the pleural space. In our experience, intraoperative closure of the pleural defect with locking clips as well as decreasing the intraabdominal pressure have helped stop CO2 diffusion into the pleural cavity (Fig. 7.1). Because the CO2 is highly diffusible, sealing the pleural injury has not resulted in tension pneumothorax.

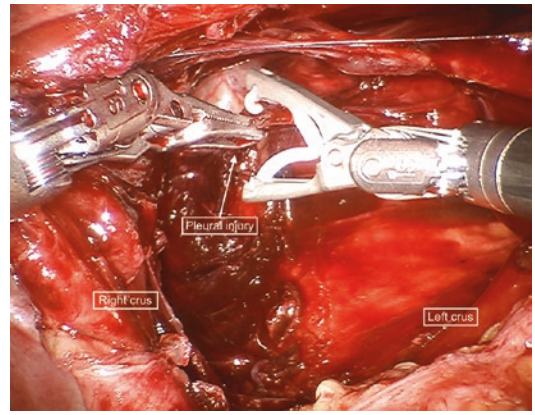

Fig. 7.1 Intraoperative closure of the pleural defect with locking clips

Bleeding

Substantial bleeding during paraesophageal hernia repair is uncommon mainly due to new developments in energy devices and increased surgeon's experience. The most commonly reported causes for bleeding come from ineffective division of the short gastric vessels, splenic injury, or liver laceration. Less frequently, bleeding results from injury to the left gastric artery, aorta or inferior vena cava.

The so-called "left crus approach" entails early division of the short gastric vessels, which provides the advantage to identify the left crus of the diaphragm and avoid the vascular structures from the gastroepiplioc omentum. Excessive traction from the fundus to reduce the herniated stomach and inappropriate use of energy devices are amongst the primary causes of bleeding that can result in splenic capsular tear or short gastric vessels disruption. This maneuver is especially more difficult if the uppermost short gastric vessels are exceedingly short. In this case one alternative is to use to the assistant surgeon to retract the body and fundus of the stomach medially to further separate the stomach from the spleen to create a plane posteriorly for safe transection. Of course this dissection is more tedious in obese patients. If bleeding were to occur, individualization of the bleeding vessel and control with an atraumatic grasper are the first steps to stop the hemorrhage. Direct application of ultrasonic or bipolar energy generally is effective; however, if

the stump of the vessel is too short suture ligation can be considered.

The incidence of splenectomy has decreased considerably with the implementation of laparoscopic surgery (0.06%) compared to open surgery (around 5%) [22, 25]. This is likely due to more precise and delicate maneuvers along with the enhanced energy devices (ultrasonic shears, bipolar), and visualization of the operative field. In addition, the adjunctive use of topical hemostatic agents can control intraoperative bleeding. Today there is a broad range of products such as, Bovine gelatin and pooled human thrombin (FLOSEAL, Baxter Corporation, Deerfield, Il), Pooled human plasma (EVICE), Oxidized regenerated cellulose (SURGICEL) (ETHICON Johnson & Johnson, Inc., Somerville, NJ) etc. However, is not advised to use these agents as the first line of response.

Vagus Nerve Injury

The anterior and posterior vagus nerves should be identified and preserved during the esophageal mobilization and dissection of the hernia sac. If while attempting to resect the hernia there is concern regarding the location of the nerves then it is prudent to preserve a portion of the sac. The exact incidence of accidental vagus nerve injury during antireflux surgery is not well known, but is thought to be approximately 2%. The risk is clearly higher with paraesophageal hernias. This can result in significantly delayed gastric emptying and is associated with diarrhea bloating and early satiety. These patients should undergo a gastric emptying study to confirm their gastroparesis. If post-surgical gastroparesis is diagnosed, and symptoms relapse despite adequate medical treatment a pyloroplasty may be indicated [26].

Visceral Injury

Injury to the esophagus and stomach are undoubtedly the most serious complications during paraesophageal hernia repair with potentially life-threatening consequences. However, the information provided in the literature is rather scarce. The incidence of these dreaded complications range from 0% to 4% [24]. Commonly, such injuries occur by very defined mechanisms, namely excessive traction of the stomach or the hernia sac, inadequate dissection of the esophagus or placement of the esophageal bougie. Understanding of these mechanisms as well as the morbid anatomy is fundamental to prevent these serious complications. It is essential for the operating surgeon to recognize the intrinsic challenges of paraesophageal hernias and the increased complications associated with their repair are knowingly higher than those seen in laparoscopic fundoplication for reflux disease [14]. In addition, the surgeons' level of experience is an important factor to contemplate [27]. The majority of perforations are recognized and repaired intraoperatively with no major consequences for the patient [28]. Still, the greatest threat to the patient are unrecognized perforations that could lead to mortality.

Most gastric injuries are minor serosal tears usually caused by forceful traction from the fundus to reduce the herniated stomach. Intrathoracic gastric tissues tend to be congested and friable and therefore can lead to increased incidence of perforations if inadequately handled. Gastric perforation can also happen while performing the posterior mobilization of the gastric fundus. Perforation of the stomach should be identified before constructing the fundoplication. Seromuscular injuries should be reinforced with Lembert sutures. Full thickness perforations can be repaired with interrupted absorbable/non-absorbable, full thickness stitches or linear stapler.

Esophageal injury is a known complication of laparoscopic antireflux surgery. Authors have reported a higher incidence of this complication with paraesophageal hernia repair [14]. Strategies to prevent esophageal perforations are essential and can be summarized as: (1) optimization of exposure, (2) recognition of the anatomical landmarks, (3) avoidance of excessive traction of the stomach/hernia sac, (4) avoidance of excessive use of energy, (5) experienced anesthesiologist passing the bougie, (6) correction of the gastroesophageal junction angulation, (7) avoidance of esophageal dissection with intraesophageal bougies or nasogastric tubes, and (8) identifying and repairing the perforation

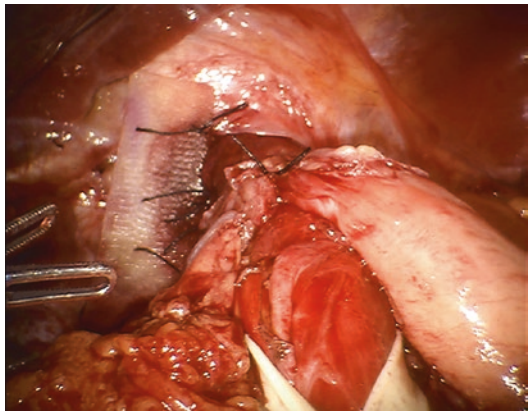

Fig. 7.2 Insertion of the bougie into the stomach after the first stitch of the fundoplication has been placed

intraoperatively (leak test with upper endoscopy and air insufflation; or with methylene blue). Other procedural steps that carry an added risk of esophageal or gastric injury are: the resection of the hernia sac, generally due to either excessive traction or thermal injury and the creation of the fundoplication with the bougie in place. For that reason, we bring the bougie into the stomach after the first stitch of the fundoplication has been placed (Fig. 7.2).

A recognized injury to the esophagus should be immediately repaired. This could be undertaken laparoscopically since the exposure of the area is better. However, the decision to convert to open should be made based upon the location of the perforation and the surgeon's intracorporeal suturing skills. The perforation should be repaired with a single layer full thickness interrupted absorbable sutures. The fundoplication can be used to buttress the repair. A postoperative swallow study should be obtained before starting the diet.

Delayed/Unrecognized Perforation

Esophageal perforation remains a major diagnostic and therapeutic challenge. Despite all the strategies to prevent a perforation, it has been reported to be as high as 1.5–6.5% after paraesophageal hernia repair [29]. The clinical presentation is variable; whereas some patients may present with obvious mediastinitis/peritonitis and sepsis that can lead to multi-organ failure, others present with subtle signs and symptoms that can lead to treatment delays. For that reason, it is important to have a high index of suspicion since a delay in diagnosis greater than 24 h post-perforation doubles the risk of mortality [30]. If stable, the patients should be evaluated with a water-soluble contrast study as well as a CT scan to evaluate for fluid collections. After the confirmation of the diagnosis, stabilization of the patient (NPO, IV fluids, broad spectrum antibiotics) the surgeon must decide whether to opt for operative or conservative management. Historically, esophageal perforation has been considered a surgical emergency. Nonetheless, changes in surgical practice have occurred in recent years, expanding the management options. The stability of the patient is an important factor at the time of deciding for treatment. In stable patients with minimal extra luminal contamination, conservative treatment is an acceptable alternative [31]. On the other hand; patients with extensive mediastinal/peritoneal contamination require emergency surgery. At the time of the exploration primary repair can be attempted. Often times, primary repair cannot be accomplished because of the delayed presentation of the perforation and the widespread contamination [32]. If primary repair is not feasible, either percutaneous or surgical drainage should be attempted in conjunction with endoscopic clips and stenting [33]. Coated stents have demonstrated to be useful for the treatment of leaks. Stents are left in place for an average of 6–8 weeks. PEG tube or jejunostomy feeding can be implemented while progressing to oral feeding with the stent in place. We perform our own stent placement in the operating room under endoscopic guidance (Fig. 7.3).

Pulmonary Embolism

Pulmonary embolism after PEH repair is a potential life-threatening complication that ranges from 1.72% to 3.33% according to various studies despite standard prophylactic measures (mechanical and chemical). Surgeons must be aware of this complication since symptoms of pulmonary embolism such

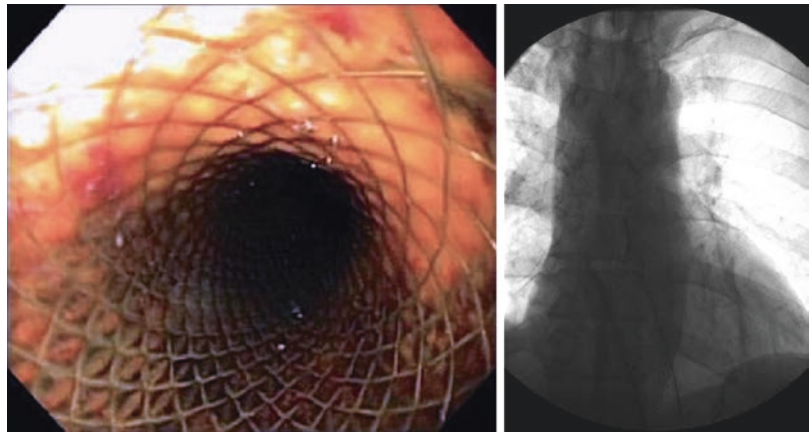

Fig. 7.3 Stent placement in the operating room under endoscopic/fluoroscopic guidance

as tachycardia, hypoxia and pain with deep inspiration may be undistinguishable from a leak from a delayed or unrecognized perforation. Preferably confirmation of the diagnosis should be obtained before implementation of therapeutic anticoagulation due to the increased risk of abdominal or mediastinal bleeding in the early postoperative period. Yet, the overall risk of death after pulmonary embolism of about 6% outweighs the risk of early postoperative bleeding while using intravenous anticoagulation [34].

Acute Wrap Migration

Sudden increases in intra-abdominal pressure are thought to predispose the patient to early wrap herniation, generally defined as occurring within 48 h of operation [22]. Patients with abrupt post anesthesia awakening, early postoperative nausea and/or vomiting are at an increased risk of disrupting the crural repair causing intrathoracic herniation of the fundoplication [35]. This situation can also be provoked if adequate esophageal length was not obtained during the index procedure. Although its incidence is difficult to define, it is recognized in about 1–5% of cases [30]. The adequate management of this complication is based on early recognition and treatment (Fig. 7.4). These patients may experience sudden pain, acute obstruction, volvulus and/or gastric ischemia. For those reasons, the patient should be taken back to surgery as early as possible. During the surgery, the wrap should be reduced back into the abdomen after taking down the crural repair if necessary.

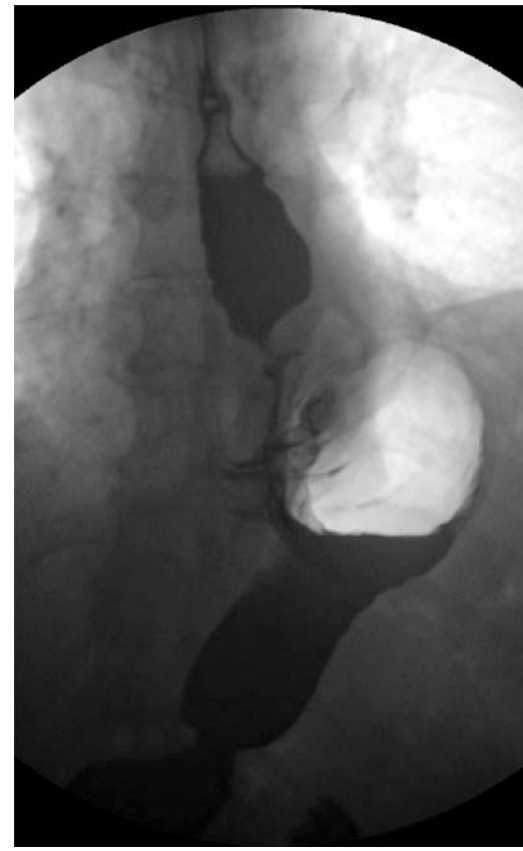

Fig. 7.4 Postoperative UGI showing acute wrap migration

Postoperative Dysphagia

About 30–60% of patients diagnosed with paraesophageal hernia suffer from preoperative dysphagia [30]. A significant number of patients experience early dysphagia mainly for solids after paraesophageal hernia repair [36]. Generally, transient dysphagia is a consequence of the inflammation and edema generated by the extensive peri-esophageal dissection and manipulation of tissues during the repair. Patients should be reassured and counseled extensively regarding their nutrition/hydration in order to prevent not only postoperative vomiting but readmission to the hospital. It has been suggested that most patients will lose 10–15 pounds after hiatal hernia repair [37]. One should be vigilant about patients that experience severe dysphagia for liquids in the early postoperative period, since clinically significant early postoperative dysphagia has been reported in 6–25% of patients [38]. The use of steroids can sometimes relieve the distal obstruction and enhance patient recovery. However, if severe dysphagia persists further investigation is warranted. Patients with suspected outflow obstruction should undergo a barium swallow or a timed barium swallow and/or detailed upper endoscopy in order to rule out anatomic failures that can have a significant impact on esophageal emptying. There are recognized patterns of technical failure such as excessively tight crural closure, fundoplication that is too tight or twisted, slipped fundoplication, and distal migration of the wrap. If the wrap is intact, the majority of patients respond well to early through-the-scope balloon dilation [39]. This is our customary practice using up to 20-mm balloons (Fig. 7.5). Patients with anatomic failure will likely require re-operation (reoperation rate 1.8–10.8%) [24], since those are thought to predict poor response after dilation. Before reoperation for dysphagia, repeat esophageal manometry is essential. The likelihood of successful re-operation will increase with the appropriate indication. Yet, patients should be advised that reoperative surgery for dysphagia carries a lower success rate than surgery for recurrent reflux [40, 41].

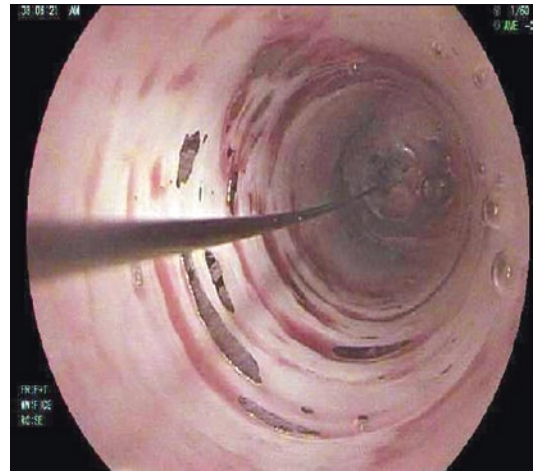

Fig. 7.5 Through-the-scope balloon dilation

Late Postoperative Complications (> than 30 Days Postop)

Recurrent Hiatal Hernia

The reported recurrence rate after laparoscopic paraesophageal hernia repair is as high as 59% in the patients with primary repair, and 54% in the mesh group [9]. The evidence has demonstrated that the incidence of anatomic recurrence tends to be higher when a routine esophagram is performed during follow-up. Common causes for failure include wrap disruption, migration or herniation. Factors that contribute to the recurrence of the paraesophageal hernias are: inadequate mobilization of the esophagus, and closure of the hiatus, short esophagus and diaphragmatic stressors (such as vomiting, coughing, obesity, etc). Despite the high incidence of anatomical failure, the majority of patients still remain asymptomatic. Nonetheless, in patients who have objective evidence of hernia recurrence and recurrent, persistent or new symptoms, revisional surgery may be indicated. The proper patient selection is the key for successful management of recurrent hiatal hernias, since morbidity and mortality is

higher than the primary repair. Patients should undergo an extensive workup including barium swallow, esophageal manometry, upper endoscopy, pH study and gastric emptying study if necessary [42]. It is suggested that a strong correlation between symptoms, workup and patterns of failure has been associated with higher success rate after a reoperation [43].

Options for revision include redo hiatal hernia repair with fundoplication (partial or total) with mesh, collis gastroplasty, and conversion to Roux-en-Y (RNY) anatomy, but sometimes the final decision is made based on intraoperative findings. Another important point to highlight is that only surgeons with vast experience in foregut surgery should undertake re-operative surgery since higher perioperative complications (21.4% intraoperative and 15.6% postoperative complications), longer operative times, longer hospital stay, and a 0.9% mortality have recently been reported in a systematic review [44].

Mesh Erosion

The use of mesh for paraesophageal hernia repair is still a matter of debate. This is mainly due to reports stating that the use of mesh does not necessarily improve long-term outcomes [42, 45]. On the other hand, there is a body of literature suggesting that non-absorbable mesh might produce more durable results than absorbable mesh [46–48]. Nevertheless, concern has been raised regarding the increased risk of mesh related-complications like erosions, ulcerations and esophageal stenosis or the higher risk of complications if redo hiatal surgery is undertaken after mesh has been used [49]. Moreover, these complications have been reported with all types of mesh, both synthetic and biologic [38]. The reported incidence of esophageal erosion is 0.2% and that of extensive fibrosis is 0.5% in a systematic review [50]. Yet, the true rate is unknown since mesh-related complications are likely more common than reported. Esophageal erosion due to mesh is a major problem and can frequently lead to intraluminal migration. Common signs of complications after mesh buttressing of the hiatus include dysphagia, chest pain, weight loss, and epigastric pain. Reoperation is the only possible treatment, frequently requiring mesh excision, redo-hiatal hernia repair, gastric repair, esophageal resection and/or gastrectomy [50]. Some patients may benefit by endoscopic removal of the mesh.

At this point, the current literature emphasizes that this issue is far from being resolved. Numerous unanswered questions remain such as type of mesh, mesh configuration, and methods of mesh fixation. Until then, surgeons should use caution when reinforcing the crural repair with mesh.

Summary

Numerous reports have suggested that only surgeons with substantial experience in foregut and minimally invasive surgery should attempt laparoscopic repair of paraesophageal hernias. The nature of paraesophageal hernias poses a distinctive challenge for the surgeon due to its morbid anatomy and the many procedural steps described to obtain optimal results. In addition, patient factors such as age >70, obesity, comorbidities, play a significant role in the incidence of postoperative complications and must be taken into account preoperatively. It is also recognized that complications after paraesophageal hernia repair are significantly greater than those observed with laparoscopic Nissen fundoplication for reflux disease.

The main purpose of this chapter was to summarize well-known complications after paraesophageal hernia repair. Figure 7.6 outlines well-known immediate complications and an algorithm for recognition and management. The adequate management of these complications requires a low threshold of suspicion and early diagnosis.

The evaluation of patients with recurrent, persistent or new symptoms after antireflux surgery, the identification of the cause of failure, and the selection of patients who need revisional surgery remains a challenge.

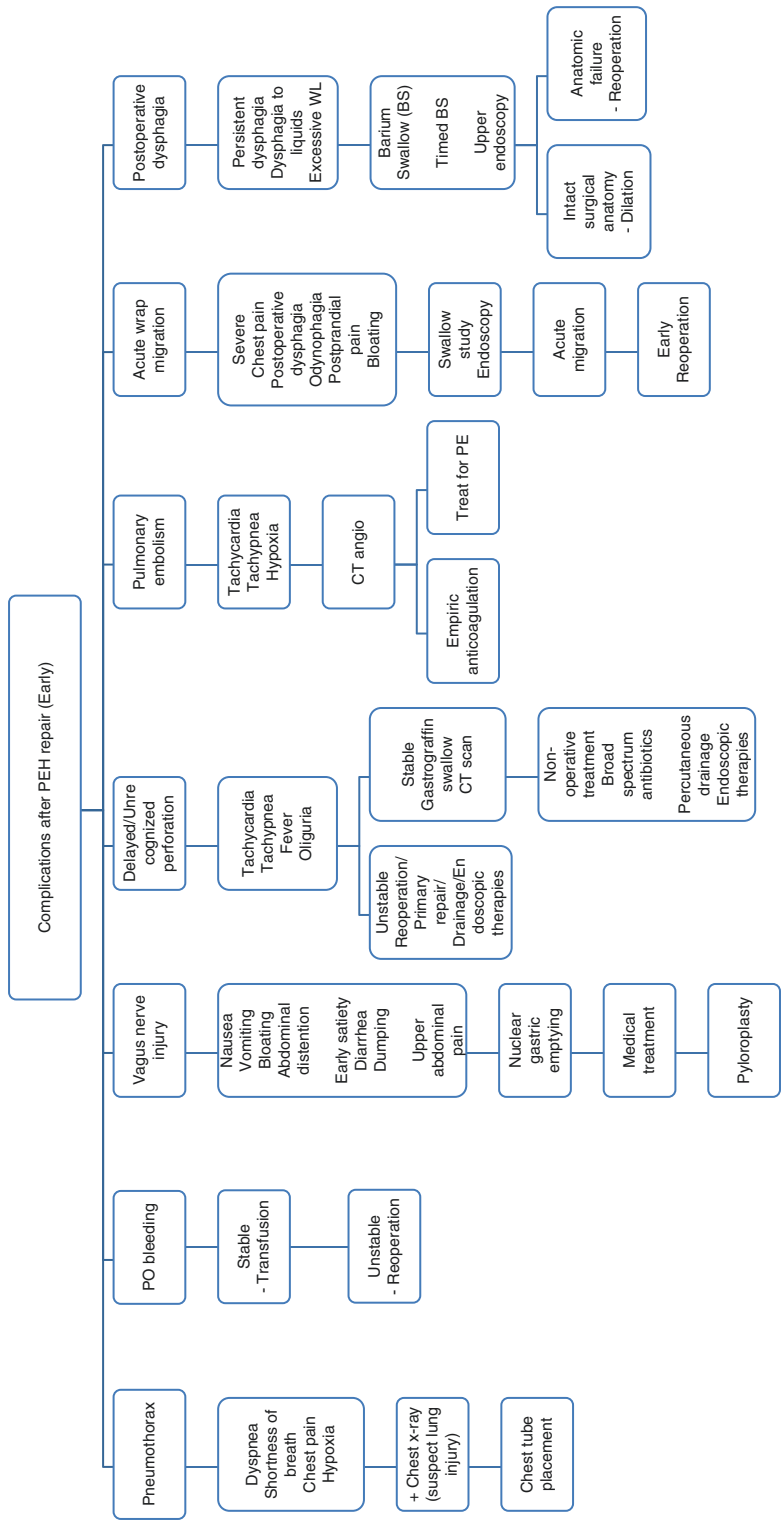

Fig. 7.6 Complications and Algorithm for recognition and management

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8 Persistent Symptoms After Antireflux Surgery and Their Management

Lawrence F. Borges and Walter W. Chan

Introduction

Persistent or recurrent upper gastrointestinal symptoms following anti-reflux surgery can present in different ways and with varying severity. These symptoms can include dysphagia, typical reflux symptoms such as acid burning in the chest and regurgitation, and an uncomfortable sensation of gas bloating in the upper abdomen. Given the common occurrence of these symptoms, it is helpful to follow a structured approach when trying to determine the cause and treatment strategy. Often, symptoms are self-limited and can be managed expectantly. However, particularly in the case of persistent symptoms, deliberate evaluation with certain radiographic, endoscopic, and manometric tools is essential to ascertain the underlying cause and determine the most appropriate therapy.

This chapter is organized into three sections, each addressing one of three common complaints reported after antireflux surgery (1): dysphagia (2), reflux/heartburn, and (3) gas-bloat symptoms. Each section describes the prevalence and known risk factors of the particular symptom after anti-reflux surgery, presents a stepwise diagnostic approach to consider, and suggests treatment modalities, which may range from simple lifestyle adjustments, to medical therapy, to surgical or endoscopic revision. Whenever possible, the practice recommendations made in this chapter are based on available evidence in the literature. In areas where there is a paucity of literature to guide practice, the proposed algorithms are based on expert opinion and consensus.

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Dysphagia

Prevalence

The most common early post-operative symptom reported by patients who have undergone fundoplication is dysphagia, or a feeling of difficulty when swallowing. Studies have shown that between 10% and 25% of patients report dysphagia after anti-reflux surgery [1, 2]. Fortunately, early post-operative dysphagia is often transient and not associated with persistent long-term symptoms [3]. For the majority of patients, this early dysphagia resolves within the first few weeks after surgery, and may be due to post-surgical edema and inflammation. As the patient's body recovers and acclimates to the new anatomy, the sensation also often dissipates.

If the feeling of dysphagia persists beyond 2–3 months or causes significant difficulty in maintaining adequate nutrition, however, additional evaluation is recommended. Patients with

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persistent dysphagia may have a fundoplication that is too tight. Other potential causes include operative injury, an alteration in the post-surgical anatomy such as a wrap migration, or a previously unrecognized or new-onset motility disorder, such as achalasia.

Risk Factors

One of the most important risk factors to consider for the development of persistent post-operative dysphagia is whether any swallowing symptoms were present prior to the operation. Pre-operative dysphagia has been reported to confer up to a 4-fold increased risk of post-operative symptoms [4], even among patients with normal esophageal manometry or other swallowing evaluations prior to surgery.

Interestingly, an abnormal pre-operative manometry without subjective dysphagia has not been shown to reliably predict post-operative dysphagia. Nevertheless, pre-operative esophageal manometry is still recommended in all patients being considered for fundoplication surgery [5]. Many surgeons preferentially perform only partial fundoplications such as Toupet for patients with abnormal motility demonstrated on pre-operative manometry in order to create a more "physiologic" lower esophageal sphincter pressure. The benefits of this practice remains debated, as many early studies have demonstrated that tailoring surgical approach according to esophageal dysmotility is not necessary [6–8], although a recent meta-analysis that included 13 randomized controlled trials suggested that Toupet fundoplication may result in less dysphagia than Nissen [9]. These previous analyses were limited by inconsistent definitions of esophageal dysmotility, and the Chicago classification using high-resolution esophageal manoemetry was not employed in these trials. Laparoscopic anterior fundoplication has also been associated with lower rates of dysphagia than laparoscopic posterior (Nissen) fundoplication in some studies, although at the expense of poorer control of reflux symptoms [10].

Upper endoscopy is also an integral part of pre-operative assessment to identify anatomic abnormalities, such as esophageal stricture. While the presence of stricture may influence the operative approach, the finding of an asymptomatic esophageal stricture on endoscopy does not itself appear to predict post-operative dysphagia [4]. Esophageal strictures in this patient population are typically a result of damage from persistent acid reflux and inflammation. The prevention of further acid reflux by the fundoplication may thus prevent worsening of the stricture, and this may explain why stricture alone, in the absence of pre-operative dysphagia, is not enough to predict dysphagia after the operation.

Diagnostic Approach

The first step in the work-up of persistent dysphagia after fundoplication is to obtain an esophagram, during which swallowing of both liquid barium contrast and a barium tablet are performed. Care should be taken to ensure that the patient swallows the whole barium tablet without chewing it, as passage of the intact tablet helps gauge whether solids of similar size are able to pass the LES. Failure of the barium tablet to pass normally in a patient with normal pre-operative esophageal manometry may suggest a new-onset esophageal dysmotility, over-tightness of the surgical wrap, or, if symptoms are late-onset, adhesions.

In most patients with persistent dysphagia, a trial of endoscopic balloon dilation may be considered as an initial intervention. However, the barium esophagram may sometimes show evidence of a new or previously unrecognized motility disorder. This should prompt further investigation by esophageal manometry to evaluate the patterns of dysmotility. Though uncommon, secondary achalasia as a result of surgery can also be seen. This may be an indication to forego endoscopic dilation in favor of moving directly to surgical revision.

The barium esophagram can also be helpful in revealing altered post-surgical anatomy, such as wrap migration or herniation of the stomach

through the diaphragm. This is discussed in more detail in the reflux symptom section below.

In patients with a normal esophagram, upper endoscopy should be performed to evaluate for signs of mucosal abnormalities, such as inflammation or erosions, and mild strictures/rings not visualized on radiographic study. Biopsies of the esophageal mucosa may be performed, especially if there are signs of conditions such as eosinophilic esophagitis or infections. During endoscopy, any resistance or difficulty in traversing the gastroesophageal junction by the endoscope should be noted. The appearance of the fundoplication wrap should also be carefully examined on both direct and retroflexion views.

An intact fundoplication has a distinct appearance best appreciated by examining the stomach with the endoscope in retroflexion (Fig. 8.1a, b). After a full fundoplication (Nissen), a retroflexed view should provide an assessment of the length of the entire valve body created by the fundoplication (measured from the valve lip to the apex of the fundus), a visual assessment of how tightly the valve adheres to the endoscope throughout the phases of respiration, and confirmation of the intra-abdominal location of the valve by demonstrating that the valve body lies distal to the indentation made by the crural diaphragm. In addition, the confluence of the rugal folds of the stomach and the tubular esophagus should be visualized at least 1 centimeter distal to the narrowing caused by the fundoplication. This confirms that the repair was done around the distal esophagus, as the entirety of the gastric mucosa is visualized [11].

If barium esophagram and upper endoscopy both fail to identify specific causes for postoperative dysphagia, and the patient does not respond to empiric endoscopic dilations, an esophageal manometry should be performed to assess for signs of esophageal dysmotility that may not be identified on barium esophagram. Repeat objective reflux assessment with ambulatory pH or combined pH-impedance monitoring should also be considered, as persistent reflux may sometimes manifest with swallowing symptoms.

Management

For patients with dysphagia and delayed passage of the barium tablet, a trial of endoscopic

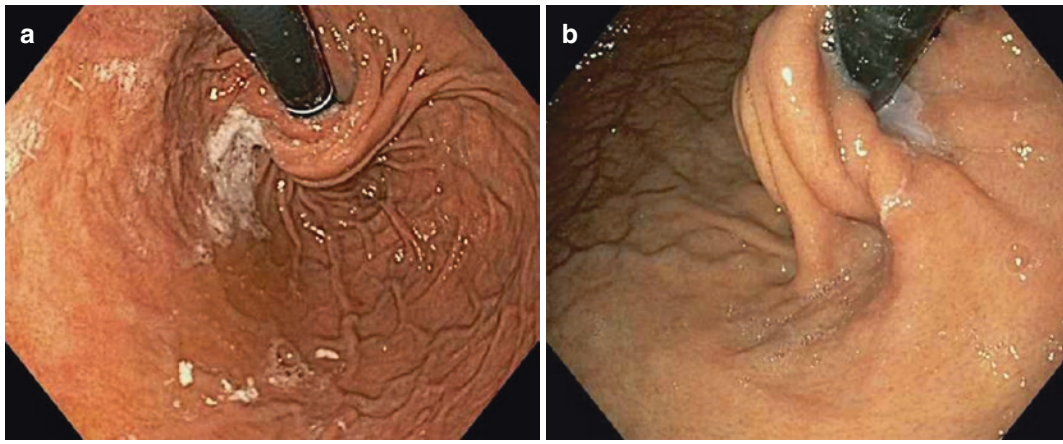

Fig. 8.1 (**a**) Normal endoscopic appearance of an intact Nissen fundoplication on retroflexion view. The entire valve body is located below the crural diphragm, confirming its intra-abdominal location. It conceals the traversing endoscope throughout all phases of respiration, suggesting that the fundoplication is intact. (**b**) Normal endoscopic appearance of an intact Nissen fundoplication on retroflexion view. The valve body nicely conceals the traversing endoscope throughout all phases of respiration, suggesting an intact fundoplication. In addition, the confluence of the rugal folds of the stomach and the tubular esophagus (z-line) can be seen distal to the narrowing, confirming that the fundoplication was performed around the distal esophagus

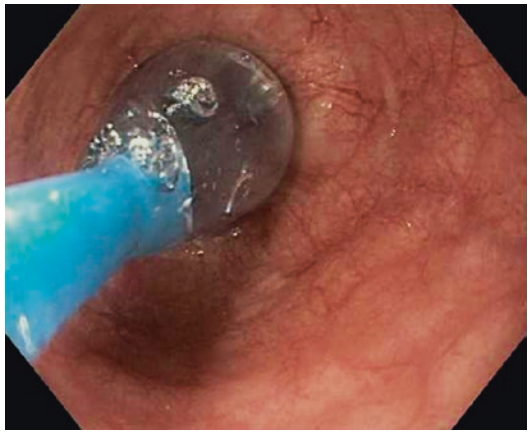

Fig. 8.2 Endoscopic view of balloon dilation performed at the level of the gastroesophageal junction in a post-Nissen fundoplication patient presenting with dysphagia

dilation at the level of the gastroesophageal junction is recommended (Fig. 8.2). About 6–12% of patients will require endoscopic dilation following fundoplication [12, 13]. Of those patients, most will achieve relief of dysphagia with a single dilation. The need for repeat dilations has been reported in less than 5% of patients [13]. Patients who do not improve even after repeat dilation and are unable to tolerate their dysphagia symptoms may require revision surgery. Fortunately, this occurs only in a small minority of patients, reported in less than 3% in one series of over 1500 patients [14].

There is currently no clear consensus on the optimal technique for endoscopic dilation in post-fundoplication patients. Over-the-wire advancement of a bougie dilator and balloon dilation have both been reported [3, 15], but no studies have compared the relative efficacy of each technique. For this reason, the choice of dilation technique is most commonly based on individual provider preference and experience. In our center, we generally prefer performing dilations using multi-size balloons, given the ability to attempt dilations at several different sizes with a single passage, and to directly visualize the balloon inflation and dilation.

Reflux

Prevalence

Fundoplication surgery generally provides excellent short-term relief from the classic symptoms of reflux, including typical heartburn or acid burning in the chest, epigastric discomfort, and regurgitation. However, many patients may experience a return of these symptoms to some degree over the long term. Existing literature suggests that about 10–40% of patients will report at least mild reflux symptoms at 5-year follow-up [2, 16], Continued use of acid suppression medications after surgery is also common. One review of over 2400 patients in the United States VA healthcare system found that more than 40% were prescribed PPI therapy at least once 6 months or more after anti-reflux surgery, and more than 30% were prescribed an H2 blocker [12].

However, it is not always clear whether continued acid reflux is truly the cause of persistent or recurrent symptoms after surgery. Studies have found that only 38% of patients reporting subjective symptoms have objective evidence of reflux found on endoscopy or barium swallow [1], and this number falls to 23% when routine pH testing is performed [17]. Both functional and psychiatric co-morbidities may be the underlying cause when objective reflux testing does not explain the persistent symptoms [18].

Risk Factors

Predicting which patients will suffer a recurrence of their reflux symptoms after surgery is difficult and studies looking for risk factors have produced mixed results. A 2009 systematic review in the American Journal of Gastroenterology looked at 63 observational studies (53 cohort, 10 case-control) and did not find consistent evidence for any individual risk factors for symptom occurrence after fundoplication. This included age, sex, BMI, and pre-operative response to acid suppression. Interestingly, studies looking at stress

and psychological co-morbidities generally supported an association with poor symptomatic outcome after fundoplication, but the authors warn that many of these studies had significant methodological limitations [19]. Some other factors on pre-operative testing previously associated with poor symptomatic outcome include lack of objective signs of reflux on pre-operative assessment, negative symptom-association, and spastic or hypermotility patterns on esophageal manometry [20].

Contrary to popular belief, the rate of persistent reflux symptoms reported after surgery is no different in patients receiving laparoscopic full (Nissen) fundoplication versus a partial (Toupet) fundoplication. This was shown in a 2015 meta-analysis that looked at 13 randomized controlled trials involving over 1500 patients [9].

In contrast, laparoscopic posterior (Nissen) fundoplication has been shown to provide superior control of reflux symptoms when compared to laparoscopic anterior fundoplication [10]. However, as previously mentioned, posterior fundoplication also produces a higher rate of post-operative dysphagia.

Diagnostic Approach

In all patients who report subjective reflux symptoms after fundoplication, it is important to first determine whether the surgical anatomy remains intact. Barium esophagram provides a quick, non-invasive way of assessing the post-operative anatomy in these cases. A normal, intact fundoplication characteristically appears as smoothly narrowed distal esophagus surrounded by a large fundal filling defect that correlates with the wrap itself (Fig. 8.3) [21]. In addition, in patients with persistent gastroesophageal reflux, the esophagram may sometimes demonstrate refluxing of contrast up the esophagus above the level of the LES. However, the lack of reflux events visualized on esophagram does not exclude persistent reflux as a cause of symptoms.

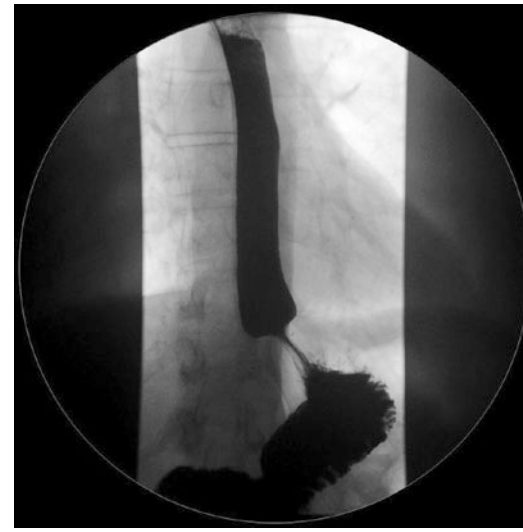

Fig. 8.3 Barium esophagram demonstrating an intact fundoplication, characterized by a large fundal filling defect surrounding a smoothly narrowed distal esophagus below the diaphragm

Free reflux seen on barium esophagram may indicate an incompetent repair, breakdown or alteration of the fundoplication wrap. In addition, an abnormal appearance or loss of the fundal defect may indicate wrap disruption, and the appearance of a new or recurrent hiatal hernia sac may suggest slippage of the proximal stomach or wrap itself above the diaphragm [21]. Images from an abnormal barium esophagram following gastric slippage through a fundoplication leading to hiatal hernia can be seen in Fig. 8.4.

In cases where a barium swallow is suggestive of gastric herniation or disruption of the repair, upper endoscopy should be done to further assess the abnormality. As seen in Fig. 8.5a, b, extension of the rugal folds of the stomach above the narrowing of the repair can indicate formation of a hiatal hernia. It is important to have a radiologist, surgeon and/or gastroenterologist experienced in evaluating post-surgical gastric anatomy take part in this work-up, as their impression may factor heavily into any decision regarding revision surgery.

For patients with reflux-type symptoms after fundoplication with a normal post-surgical

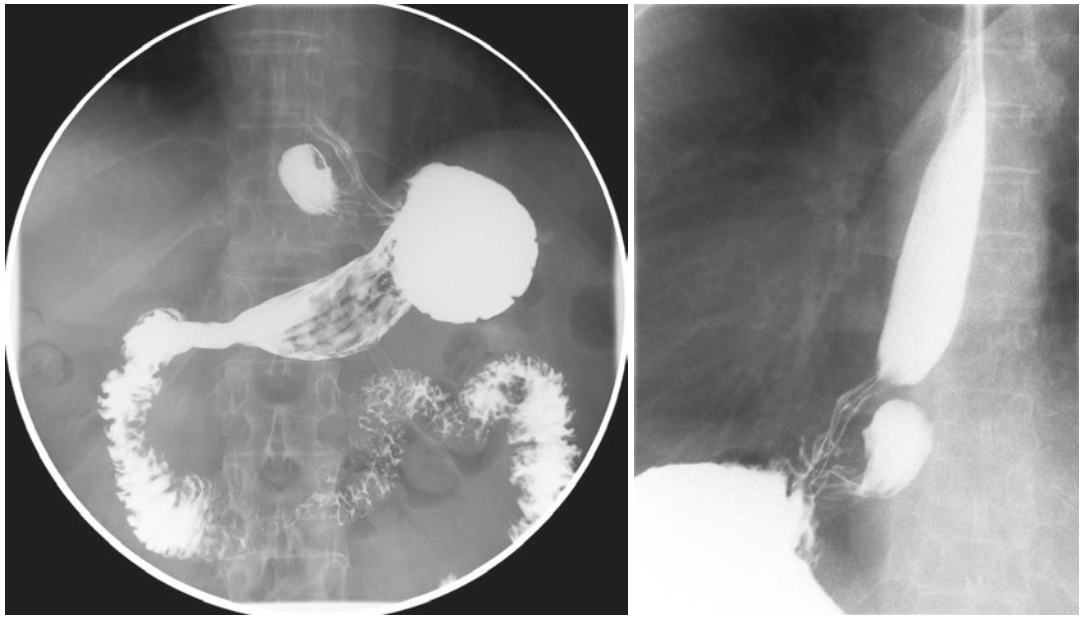

Fig. 8.4 Right lateral and postero-anteral views from a barium esophagram showing slippage of the gastric cardia above the level of fundoplication wrap, leading to formation of a small hiatal hernia (Image courtesy of Dr. Kunal Jajoo, Brigham and Women's Hospital, Boston, MA)

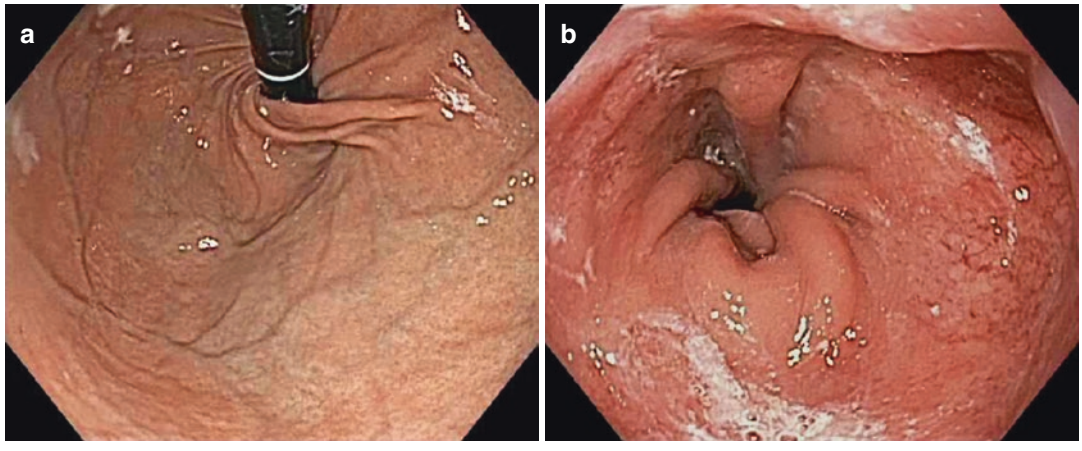

Fig. 8.5 (**a**) Retroflexed view on upper endoscopy of a recurrent hiatal hernia following Nissen fundoplication. Note that the separation between stomach and tubular esophagus is not visible, and the rugal folds extend above the narrowing created by the surgical repair (Image courtesy of Dr. Kunal Jajoo, Brigham and Women's Hospital, Boston, MA). (**b**) Direct endoscopic view of the gastroesophageal junction in a patient with recurrent hiatal hernia following Nissen fundoplication. Note that the rugal folds of the stomach are visible above the level of narrowing created by the repair (Image courtesy of Dr. Kunal Jajoo, Brigham and Women's Hospital, Boston, MA)

anatomy seen on barium swallow and endoscopy without obvious signs of reflux, repeat objective reflux testing (ambulatory pH or combined pH-impedance study) can be used to assess whether their symptoms are actually attributable to abnormal reflux. Positive reflux testing in this setting may indicate that the wrap is not sufficient in providing an adequate barrier to reflux between the stomach and esophagus, despite appropriate positioning. This may be due to looseness of the wrap or other factors resulting in a high transdiaphragmatic pressure gradient, such as obesity, delayed gastric emptying, or pulmonary diseases. Esophageal manometry should also be performed to help assess the pressure at the gastroesophageal junction and identify esophageal dysmotility, such as frequent ineffective swallows or absent contractility that may predispose to increased or worsened reflux.

Management

The first-line approach to patients with persistent or recurrent reflux symptoms post-fundoplication is empiric medical therapy, similar to that for the general population, utilizing proton pump inhibitors (PPI) and H2-receptor blockers. As of yet, there have not been any specific studies or data to guide either PPI or H2 blocker dosing in this setting. For this reason, we recommend an initial trial of a daily PPI at low dose for 8 weeks as a first step, either in the morning or in the evening, regardless of the patient's pre-operative acid suppression requirement. Importantly, PPIs must be taken 15–30 min prior to eating to allow maximal efficacy. This allows sufficient time for medication absorption, where it works at the cellular level to block the gastric acid production that is stimulated by eating.

If symptoms do not improve on low-dose PPI, escalation of dosage can be attempted or an alternative PPI may be used. In our practice, we typically begin with up-titrating the PPI dose, although there is evidence to show that either approach can be effective [22].

Patients who continue to experience no or inadequate symptom improvement after high-dose PPI trials are considered PPI non-responders. Objective reflux testing should be performed in this population, as their lack of response may suggest an alternate cause for their symptoms. In this population, we prefer performing the combined pH-impedance testing while on acid suppression to help quantify any persistent reflux, the nature of reflux episodes (acidic vs. weakly acidic vs. alkaline), and symptom-association. If available, a dual channel pH catheter, with a pH channel at both the distal esophagus and the stomach, may provide further information regarding the adequacy of acid suppression by the PPI.

For patients with refractory reflux-type discomfort after fundoplication and who test positive for weakly acidic or non-acidic reflux on pH-impedance testing, a trial of oral GABA-B receptor agonist (e.g. baclofen) may be tried. Baclofen has been shown to reduce reflux episodes by decreasing the rate of transient LES relaxation, increasing basal LES pressure, and accelerating gastric emptying [23, 24]. However, baclofen is often associated with CNS side effects such as drowsiness that may limit its use. Surgical revision, including tightening of the fundoplication or repair of anatomic defects such as hiatal hernia, is often indicated in patients with persistent reflux confirmed on objective testing. In obese patients, conversion to bariatric surgery, specifically Roux-en-Y gastric bypass, may allow for better control of gastroesophageal reflux through weight loss and a decrease in transdiaphragmatic pressure gradient.

Patients with refractory reflux-type discomfort after fundoplication and normal pH-impedance testing may suffer from a functional disorder or visceral hypersensitivity. For non-fundoplication patients with functional chest pain, there is evidence to suggest that antidepressant use – specifically imipramine, sertraline, or venlafaxine - may reduce symptom severity [25]. This practice is also supported by evidence that the use of TCA and SSRI medications can be helpful in neuropathic disorders and in irritable bowel syndrome [26, 27]. As such, a trial of these medications is reasonable in patients reporting persistent reflux symptoms after

fundoplication suspected to be related to a functional cause or visceral hypersensitivity.

Gas-Bloat Syndrome

Prevalence

Gas-bloat syndrome encompass a wide range of symptoms including bloating, abdominal distension, nausea, upper abdominal discomfort, early satiety, and the inability to belch and/or vomit. The reported prevalence of gas-bloat syndrome varies widely from 1% to 80%, depending on the specific symptoms identified and the type of fundoplication surgery performed [19]. The exact cause of this syndrome is not clear. One proposed mechanism is a decreased ability of the post-surgical gastric anatomy to comfortably distend after eating. There may also be a decreased ability of the wrapped stomach to vent gas by belching, which can be exacerbated by aerophagia, a habit commonly seen in patients with reflux. Intra-operative injury to the vagus nerve has also been suggested in some cases as this may impair normal gastric emptying and interfere with normal gastric relaxation.

Risk Factors

The type of fundoplication performed can influence the likelihood of a patient experiencing post-operative gas-bloat symptoms. For instance, patients who undergo laparoscopic Nissen fundoplication are more likely to report bloating, postprandial fullness, flatulence and an inability to belch. Patients who are status post a Toupet fundoplication, on the other hand, typically report fewer gas-bloat symptoms [9].

The likelihood of developing gas-bloat symptoms in patients who undergo full Nissen fundoplication is even greater for those who report pre-operative aerophagia [28]. Swallowed air becomes trapped in the stomach and is unable to escape through eructation in these patients due to the barrier creased by the wrap. Partial wraps such as Toupet can mitigate this problem to some extent due to the lower-pressured barrier. Regardless of the type of surgery planned, patients with severe pre-operative aerophagia and those with bloating, nausea, gas, and abnormal gastric motility at baseline should receive appropriate counseling regarding their increased risk of persistent symptoms and gas-bloat syndrome after surgery.

Diagnostic Approach

Given their high prevalence, mild gas-bloat symptoms are often treated empirically without further investigation. The treatment approaches used are discussed below. For more significant or unexpected symptoms, however, a solid-phase barium study is an appropriate initial investigation. In addition to assessing the post-surgical anatomy, this allows for evaluation of gastric and small bowel motility through estimating promptness of contrast passage. A 4-h gastric emptying scintigraphy may also be performed for standardized evaluation of gastric motility among patients with suggestive symptoms, as inadvertent vagal injury during surgery may sometimes result in decreased antral motility and impaired pyloric relaxation, leading to delayed gastric emptying. Upper endoscopy can be considered to evaluate for any signs of mucosal abnormality that may contribute to these symptoms, such as peptic ulcer disease or significant gastritis. Other causes for gas and bloating in the general population, such as *Helicobacter pylori* infection or small intestinal bacterial overgrowth should also be considered, as the inability to belch in post-fundoplication patients may further exacerbate the bloating symptoms associated with these conditions. Breath testing, stool antigen, serum antibody, or gastric mucosal biopsies are testing options for *H. pylori*, while hydrogen breath testing is the most commonly used strategy for bacterial overgrowth.

Management

Various therapies can be used to treat gas-bloat symptoms and most are aimed at reducing the amount of air and gas introduced into the

stomach. Patients with aerophagia are usually counseled to eat more slowly in an effort to minimize swallowed air. In addition, there is anecdotal evidence that speech therapy can be helpful in these patients [29]. All patients should also be given lifestyle counseling that includes avoidance of gas-producing foods and carbonated beverages, and cessation of smoking.

Simethicone is an oral anti-foaming agent that decreases the surface tension of small air bubbles. It, therefore, allows larger gas bubbles to form, thereby facilitating easier excretion of gas through flatulence. There is no strong clinical evidence to support its efficacy reducing gas-bloat symptoms in post-fundoplication patients. However, it is widely considered safe and well tolerated.

Pro-motility agents are also sometimes tried to increase gastric emptying, thereby shortening the time that trapped gas remains in the stomach and causes discomfort. Interestingly, however, while delayed gastric motility can be seen as an exacerbating factor in patients with reflux disease, antireflux surgery has also been observed to improve gastric emptying time in these patients [30]. There is no strong evidence to suggest that pharmacologic pro-motility agents improve upon this effect further. Given the potential significant side effects associated with pro-motility agents, such as neurological symptoms that may be irreversible, caution should be exercised with the use of these medications, which should be reserved for those with evidence of significant decrease in gastric motility on standardized, objective testing together with suggestive symptoms.

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9 Technical Surgical Failures: Presentation, Etiology, and Evaluation

Chase Knickerbocker, Devendra Joshi, and Kfir Ben-David

Introduction

Esophagectomies have come a long way since first being described more than 100 years ago. However, they remain a very challenging procedure that can come with significant morbidity and mortality. The most recent major advance in this field is the advent of minimally invasive esophagectomies. While there are many different methods for performing the surgery and minimally invasive techniques seem to have further reduced some of the associated morbidity and mortality, however, most of the pitfalls remain the same. This chapter is dedicated to the surgical failures that may present during and following a minimally invasive esophagectomy (MIE) including presentation and evaluation.

Gastrointestinal

Leak

The first, and arguably most frustrating, technical failure that will be discussed is a leak. This involves the extravasation of ingested food or gastrointestinal (GI) fluids out of the GI tract directly into the cervical neck area or mediastinum. Although, a leak may occur at any point along the tract where it was manipulated and freed from the surrounding structures. There are several common etiologies for leaks following surgery including true anastomotic leaks, leaks from an enterotomy, and gastric conduit necrosis. Leaks in general are particularly devastating as they have historically resulted in up to 35% mortality [1]. Although, with advances in leak surveillance and treatment including endoscopic stenting procedures and the ability to start and continue jejunal feeds or total parenteral nutrition (TPN) there has been a decline in the associated mortality to 3% [2].

Presentation of a leak ranges from repairable intraoperative identification to devastating postoperative sepsis. Excluding those that are found with routine intraoperative and postoperative surveillance, the majority of patients will present with fever (57%), leukocytosis (52%), pleural effusion (70%), and septicemia (70%). Less common signs include pneumothorax (35%), wound infection (13%), coughing bile (4%), and dysphagia (4%) [3]. These patients can become very ill fairly quickly and often require prolonged intensive care unit (ICU) stays and re-exploration procedures [4].

The causes for leaks following surgery are plentiful. The anastomosis between the esophagus and the stomach comes in several varieties including end to end and side to side approaches [5]. Both of which may be made using stapling

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devices or hand-sewn techniques and are susceptible to technical failures [6]. There is also extensive manipulation of the esophagus as it is freed from the surrounding structures, which places it in danger of an injury that may go unrecognized. Twenty-one percent of patients who experienced a hypotensive episode during surgery ended up with leaks versus 3% in patients who did not have such an episode [7]. Another potential source of leak is gastric tip or gastric conduit necrosis.

Evaluation of a leak depends on the stage and clinical status of the patient. As mentioned before, the earliest presentation is while the patient is still undergoing surgery when the anastomosis is tested with insufflation. The escape of air denotes a leak and at this time corrective measures can be undertaken to ensure it is closed prior to completing the surgery. Hence, intraoperative endoscopic evaluation is routinely done in some centers to evaluate for leaks [8]. Postoperative endoscopy is championed by some clinicians as a safe and reliable way to evaluate for leaks 1 week after surgery, with repeat endoscopy of patients with necrotic findings [9]. It is argued that the procedure is safe and is 100% sensitive for detecting leaks and can be performed on all patients, including those who remain intubated [10]. It is also routine at some centers for the anastomosis to be evaluated radiographically between 5 and 7 days following surgery with a contrast swallow where a leak will present as contrast extravasation during the study [8]. Although some would argue that the rates of false positive (4.7%) and false negative (5.4%) studies is too high for routine use [11]. Also, drains left in close proximity to the anastomosis and surgical field will give advanced warning of a leak by draining GI contents. This becomes especially apparent if a patient is given a swallow trial with a colorful liquid and the drainage begins to change color and/or increases.

Gastric Tube Necrosis

Gastric conduit necrosis is a complication that involves the necrosis of part or all of the gastric tube that connects with the esophagus. The necrosis is most commonly noted at the tip that connects with the esophagus as it is the farthest removed from the preserved right gastroepiploic blood supply [12]. The presentation of gastric tip necrosis is extremely variable ranging from asymptomatic patients where it is only identified with endoscopy to persistent coffee ground nasogastric tube material, fevers, leukocytosis, an otherwise unexplained acidosis, and eventually sepsis.

Gastric tube necrosis seems to have several etiologies including improper alignment of the gastric conduit where the anastomosis is made under tension or a twist is present, creation of a tube that is too narrow, strangulation within the hiatus, failure to preserve the gastroepiploic vessels, and an anastomosis created in an area with poor blood supply [13–15].

The evaluation of gastric tip necrosis is done via an endoscopic approach where the necrotic mucosa can be directly visualized and assessed for leaks. Studies show that not all cases of identified gastric tip necrosis will lead to leaks, however they may warrant closer observation and follow up endoscopic procedures to monitor for progression [9, 16, 17]. Prompt diagnosis is important so proper treatment can be initiated.

Stricture

There are several other GI related complications that arise from surgical failures that, while maybe not as devastating as a leak or necrosis, can significantly impact a patient's life. Strictures plague up to 27% of patients [18]. Presentation of strictures range from subclinical, found only on endoscopic or radiographic evaluation, to symptomatic patients presenting with dysphagia. Strictures are related to the type of anastomosis performed with 40% of end-to-end (ETE) anastomosis having strictures, whereas 18% of end-to-side (ETS) anastomoses developed strictures [19]. It was once thought that end to side or side to side anastomoses were more prone to complications, however it is now generally accepted that they are safe and effective [20, 21]. Hand sewn anastomoses also appear to be correlated with a higher rate

of stricture, 20.3%, than stapled anastomoses, 6.3% [22]. It is worth noting that late stricturing, greater than 1 year after surgery, are very often, if not always related to recurrent cancer [18].

Gastric Dysmotility

Dysphagia is also a risk of MIE that can be found with or without the aforementioned stricture. There also seems to be no difference in rates of dysphagia between thoracic and cervical anastomoses [23]. Radiographic, manometry, and visual evaluations show several possible etiologies including poor coordination of the deglutitive response, decreased pharyngeal pressure, decrease in total laryngeal elevation, increased pharyngeal transit time, and hypertensive peristalsis [24–26]. It is possible that all patients have some degree of impairment of their swallowing mechanism following cervical anastomosis [27].

Delayed gastric emptying (DGE) is also a common issue found after surgeries that alter the structure and innervation of the stomach. In the case of esophagectomies between 10 and 50% of patients are affected [28]. It is thought that damage to the vagus nerve and alteration of the stomach's ability to achieve pressures greater than the pylorus often contributes to this entity. Patients typically present with regurgitation, reflux, aspiration, early satiety, chest pressure, and halitosis. Evaluation can be done with gastric emptying studies. The technical failure associated with DGE is the inability to strike a balance between a gastric conduit that is wide enough to prevent gastric necrosis yet narrow enough to allow stomach pressures to overcome the pylorus [29–31].

Dumping syndrome (DS) is the complete opposite problem where hypertonic stomach contents are evacuated from the stomach into the intestines too quickly. This results in a patient who presents with a combination of diarrhea, bloating, abdominal pain, and assorted hypovolemic symptoms. The etiology of DS is similar to that of DGE in that denervation and alteration of the stomach architecture can cause food to progress too rapidly. One technical aspect of surgery known to result in DS is intraoperative or postoperative pyloroplasty which is employed at some centers to assist with symptoms of DGE. There is no consensus on performing pyloroplasty routinely during surgery as there is no significant increase in post-op DGE in patients who did not have an operative pyloroplasty along with their esophagectomy [32].

Reflux

Reflux following esophagectomy is relatively common and clinically apparent in as many as 70% of surgical patients [33]. Patients suffering from reflux run the whole range from subclinical esophagitis, found only on endoscopy, to reflux that causes severe impairment in daily activities. This reflux is thought to be related to the loss of the lower esophageal sphincter, poor gastric emptying, disruption of the diaphragm, and diminished length of the esophagus. It has been shown on several occasions that the degree of esophagitis is not well correlated with symptoms; however, the degree of reflux is correlated with the severity of esophagitis noted on biopsy [34–36]. Evaluating reflux is challenging since not all patients with reflux will have symptoms but endoscopy with biopsy is the gold standard for surveillance and determining the extent of damage and epithelial cellular change. Esophageal pH monitoring and impedance along with a contrast radiograph are also options for evaluating patients for reflux [36].

Pulmonary

In addition to the many failures that can befall the GI system, the respiratory system is also at risk. Historically, respiratory complications are credited as the greatest cause for postoperative morbidity affecting 28.5% of patients [37]. Due to its proximity to the surgical field, the trachea and lungs make easy targets for errors. Additionally, selective lung inflation during thoracoscopic surgical maneuvers and previously mentioned compromised swallowing place the lungs at risk for injury and infection.

Aspiration

Aspiration is a very common finding after esophagectomy and comes in two varieties, vocal and silent. Vocal aspiration is easier to diagnose as it presents with the usual clinical signs of aspiration including a cough [8]. Many, if not all patients have some degree of impaired swallowing that may lead to aspiration for at least a short time following an esophagectomy [38, 39]. From a surgical perspective, this is related to modifiable factors including extended operative time and vocal cord paralysis [40]. Evaluation of aspiration is done routinely with fluoroscopy as contrast can be seen entering the trachea and circumventing the epiglottis, bedside swallow evaluation by a speech pathologist, or direct visualization with an endoscope [39]. This is an important topic as it appears aspiration and the degree of severity is directly related to the development of pneumonia [41].

Pneumonia

Pneumonia following esophagectomy is devastating with a 20% mortality rate and is considered to be the most lethal complication [37]. It is also highly correlated with short and long term mortality, reducing the 5 year overall survival rate by 26.7% [42]. Pneumonia presents in the typical fashion with cough, leukocytosis, fever, and is often evaluated with radiographs, blood and sputum cultures, and clinical correlation. The etiology of this complication is not fully understood however there are related technical issues that can be avoided. First and foremost it is important to remember that not all technical failures occur within the operating room. Thorough investigation with swallow evaluations, radiographic or bedside and endoscopy prior to resuming a diet can reduce the likelihood of pneumonia to 9% [43]. It has also been theorized that thoracic dissection in the prone position versus the left lateral decubitus position may reduce pneumonia due to partial inflation of the lung, but there has been no compelling or statistically significant evidence to date and the practice has not been widely adopted [44]. Finally, higher rates of blood loss and longer operating times also seem to be related to adverse pulmonary outcomes including pneumonia [38, 45].

Chylothorax

Chylothorax is an uncommon but potentially lethal complication of esophagectomy, affecting between 1.9 and 3.8% of patients [3, 46]. Presentation involves dyspnea, with decreased breath sounds on the ipsilateral side, high chest tube output, hypovolemia, malnutrition, and even immunosuppression that may progress very rapidly to a sepsis picture [47]. With respect to the technical surgical failures as the cause, it is generally assumed that damage to either the thoracic duct or smaller lymphatic vessels that are divided and not properly sealed are at fault. It is important to note that there is evidence that no difference exists between transthoracic and transhiatal approaches [48]. Some researchers have been advocating the use of prophylactic thoracic duct ligation during the initial surgery as a way to prevent chylothorax formation and have reported a significant reduction [49]. The evaluation of a chylothorax involves monitoring chest tube output, greater than 400 milliliters per day is generally considered high output, although greater than 1 liter of output is not unheard of [3]. The fluid will typically be milky to brownish/greenish in color and laboratory tests will show higher than peripheral blood numbers of lymphocytes, a high concentration of triglycerides (> 1.24 mmol/L) and chylomicrons [50, 51].

Nervous System

Recurrent Laryngeal Nerve

Damage to the recurrent laryngeal nerve (RLN) is a major factor in post esophagectomy morbidity and mortality with rates reported as high as 50% in patients receiving cervical anastomoses [52]. Injuries are mostly unilateral (83%) with a propensity for the side of the cervical incision

(83%) [21]. What makes this injury particularly dangerous is the association with aspiration pneumonia. Patients typically present with hoarseness or aphonia [21]. Recurrent laryngeal nerve damage is due to trauma to the nerve during surgery, including transection, stretching, or thermal injury. In minimally invasive esophagectomies with cervical anastomosis one surgical technique that has been shown to decrease the propensity for RLN injury is a thoracoscopic approach with dissection close to the esophagus when above the azygous vein [30]. Patients with suspected RLN injury are evaluated with direct visualization using a laryngoscope.

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Symptoms After Antireflux Surgery: Not Everything Is Caused By Surgery

10

Meredith C. Duke and Timothy M. Farrell

Appropriate Patient Selection

Gastroesophageal reflux disease (GERD) has been defined as "a condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications" [1]. Esophageal symptoms include heartburn, regurgitation and sometimes dysphagia. Extra-esophageal symptoms, such as chest pain, wheezing, cough or hoarseness, may also be attributed to GERD when other etiologies are not suspected. Studies have shown that esophageal symptoms associate with anatomic and physiologic testing abnormalities, and respond predictably to antireflux surgery at high levels [2]. However, extra-esophageal symptoms are less well-correlated during testing and are variably improved by antireflux surgery [2–6].

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	Resolution of heartburn	Resolution of extraesophageal symptoms
Group 1 – Severe heartburn/Minimal extraesophageal symptoms	87%	–
Group 2 – Severe heartburn/Severe extraesophageal symptoms	76%	42%
Group 3 – Minimal heartburn/Severe extraesophageal symptoms	–	48%

Response rates of esophageal and extraesophageal symptoms of gastro-esophageal reflux to antireflux surgery [3]

During preoperative evaluation, the surgeon should mandate anatomic and physiologic testing to prove the presence of GERD, and should carefully counsel patients about the likelihood of responsiveness for all symptoms present. A low correlation between extra-esophageal symptoms and reflux episodes on pH-impedance testing has been shown to predict poor responsiveness of these symptoms after antireflux surgery [7].

Objective evidence of GERD is needed before a surgeon offers antireflux surgery. This may include significant mucosal manifestations in the setting of esophageal symptoms (ulcerative esophagitis, Barrett's esophagus, peptic stricture) or abnormalities in pH or impedance testing [8].

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In addition, many experts advocate for routine esophageal manometry testing to rule out unrecognized esophageal motility disorders, since approximately 30% of patients with GERD will have ineffective esophageal motility due to low-amplitude waves or simultaneous contractions [9]. Awareness of the manometric profile allows tailoring of the degree of fundoplication for the purpose of reducing postoperative dysphagia, although this has been a highly debated topic since the inception of laparoscopic antireflux surgery 25 years ago. Currently, a 360° floppy Nissen fundoplication is the recommended treatment for patients with GERD, with reservation of a partial fundoplication for patients with achalasia and scleroderma. This practice has been supported by many studies [10–13]. A recent meta-analysis showed that Nissen fundoplication was associated with significantly more dysphagia compared to Toupet fundoplication, affecting 80/637 (12.56%) and 30/620 (4.84%) respectively [14]. There is significant heterogeneity in how dysphagia is quantified; authors may rely on visual analogue scale or questionnaire, and fail to stratify data for solids and liquids [15]. Gastric emptying studies have been examined to potentially identify patients at risk for significant nausea, bloating and gassiness after antireflux surgery, but there are no data to support correlation between results and postoperative outcomes. Gastric emptying studies may be helpful in patients with new or persistent symptoms following fundoplication, as it provides indirect evidence for vagal nerve injury during the index operation [2, 16, 17].

Common Postoperative Symptoms

Approximately 80% of patients experience new symptoms after antireflux surgery [18, 19]. Often these symptoms include "gas-bloat syndrome" and dysphagia. These are generally attributed to the inflammation that exists after an operative intervention and the presence of an intact fundoplication.

Gas-bloat syndrome is associated with the reduced ability to belch after fundoplication. It affects up to 85% of patients after surgery, and usually includes early postoperative bloating, flatulence and abdominal distention that improves over the weeks to months after operation [20]. Gas-bloat syndrome may also be associated with early satiety, nausea, and abdominal pain. These symptoms may become especially prominent in patients with a habit of aerophagia or with delayed gastric emptying, whether pre-existing or related to unintended vagotomy [21]. Temporary avoidance of carbonated beverages and the use of simethicone or prokinetic drugs will usually temper the gas-bloat symptoms. In rare cases, a venting gastrostomy, endoscopic dilation, conversion to a partial fundoplication or a pyloroplasty may be necessary [22].

Dysphagia is expected in all patients for the first 2–3 months after operation, presumably due to postoperative edema which affects bolus transit. Patients with preexisting esophageal dysmotility may have more significant postoperative dysphagia, but by 3 months, there is no statistical difference [9, 23]. Dietary modifications and time are usually all that is needed. In 3–12%, persistent dysphagia may require endoscopic dilation. In some cases, such as a too-tight or slipped fundoplication or motility disorder, surgical revision is necessary [24].

Postoperative diarrhea is a frequent occurrence after fundoplication, affecting 18–33% of patients [25, 26] It usually develops within 6 weeks of operation and is typically mild and of low volume and frequency, occurring after meals. Mechanisms may include accelerated gastric emptying after fundoplication with dumping syndrome, or vagal injury with subsequent small bowel overgrowth [25]. Management is empirical [18].

Flatulence has been reported in 12%–88% of patients after antireflux surgery [26, 27]. This is a downstream effect of gas-bloat syndrome during the recovery phase when patients have limited ability to belch. It can be treated with Simethicone and speech therapy.

Most of the expected symptoms after fundoplication are transient, and therefore they do not mandate an extensive evaluation. In one study of postoperative symptoms, 94% were resolved by 1 year, with most abating within the first 3 months [19].

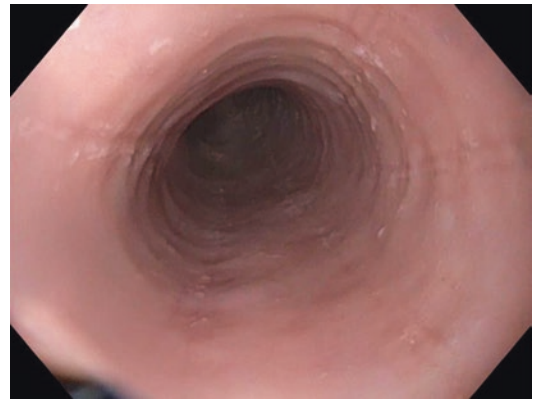
Unexpected Postoperative Symptoms

In some situations, persistent or recurrent esophageal symptoms may occur after antireflux surgery and raise suspicion for a failing fundoplication. In fact, acid suppressive medications are resumed in up to 62% of patients after antireflux surgery [28, 29], with most studies reporting <20% [2]. However, studies of patients who resume medications show only 24–37% actually have pH-metric evidence of recurrent GERD [30–33]. Therefore, while it may be reasonable to use PPIs empirically at first, it is not appropriate to escalate medication utilization or consider antireflux surgery without objective evidence of associated pathologic reflux [18].

Esophageal and extra-esophageal symptoms after antireflux surgery may also be attributable to esophageal hypersensitivity, eosinophilic esophagitis, and non-specific spastic esophageal motor disorders.

Esophageal hypersensitivity refers to heightened esophageal symptom perception. Patients may suffer more dramatic symptoms of GERD, and can also sense non-GERD related mechanical or chemical stimuli, such as distension of the esophagus from refluxed or swallowed air, as GERD. These patients may have high correlation indices but normal acid exposure on pH monitoring. GERD may contribute to the etiology, and GERD therapy may improve esophageal sensitivity. However, esophageal hypersensitivity may also exist without GERD, and can sometimes raise suspicion for failed antireflux surgery. Beyond traditional antireflux therapies, inhibitors of transient lower esophageal sphincter relaxation, such as baclofen, and neuromodulators, such as low-dose antidepressants, may suppress symptoms [34].

A small percentage of patients who carry the diagnosis of refractory GERD actually have eosinophilic esophagitis (EoE) [35], which is a chronic allergic condition of the esophagus. The diagnosis requires a high index of suspicion, and is confirmed by proximal and distal esophageal biopsies which demonstrate eosinophilia. The diagnosis requires esophageal biopsies demonstrating at least 15 eosinophils per high-powered field in the setting of appropriate antireflux therapy [36]. In a post-fundoplication patient, anatomic and physiologic studies will support an intact fundoplication. Once diagnosed, treatment involves avoidance of food allergens, steroidal anti-inflammatory medications and dilation(s) of the esophagus [37].



This endoscopic image shows esophageal rings, mild narrowing, white plaques/exudates, edema/loss of vascularity, and linear furrows (Courtesy of E Dellon, UNC 2016 [38])

Incomplete preoperative evaluation may result in esophageal symptoms after surgery. For example, unrecognized motility disorders, such as achalasia, can contribute to GERD-like symptoms due to esophageal stasis [39]. Postoperative symptoms may incorrectly be attributed to a failure of antireflux surgery when the true issue is an unrecognized motility disturbance. Morais et al. identified 41 patients with persistent postoperative dysphagia, defined as dysphagia greater than 6 months following initial operation. They were evaluated with endoscopy, barium swallow, and esophageal manometry, and compared to 19 controls, also greater than 6 months out from Nissen fundoplication, without dysphagia. Half of the symptomatic group had normal manometry, but the other half had evidence of esophageal dysmotility [40]. Preoperative testing was not performed, highlighting the need for thorough preoperative evaluation.

Esophageal motility	Normal	Aperistalsis	NCE	DES	IEM
Controls [19]	19	–	–	–	–
Patients with dysphagia [41]	20	4	3	4	10

Esophageal peristalsis of controls and patients with persistent postoperative dysphagia
DES diffuse esophageal spasm, *IEM* ineffective esophageal motility, *NCE* nutcracker esophagus [40]

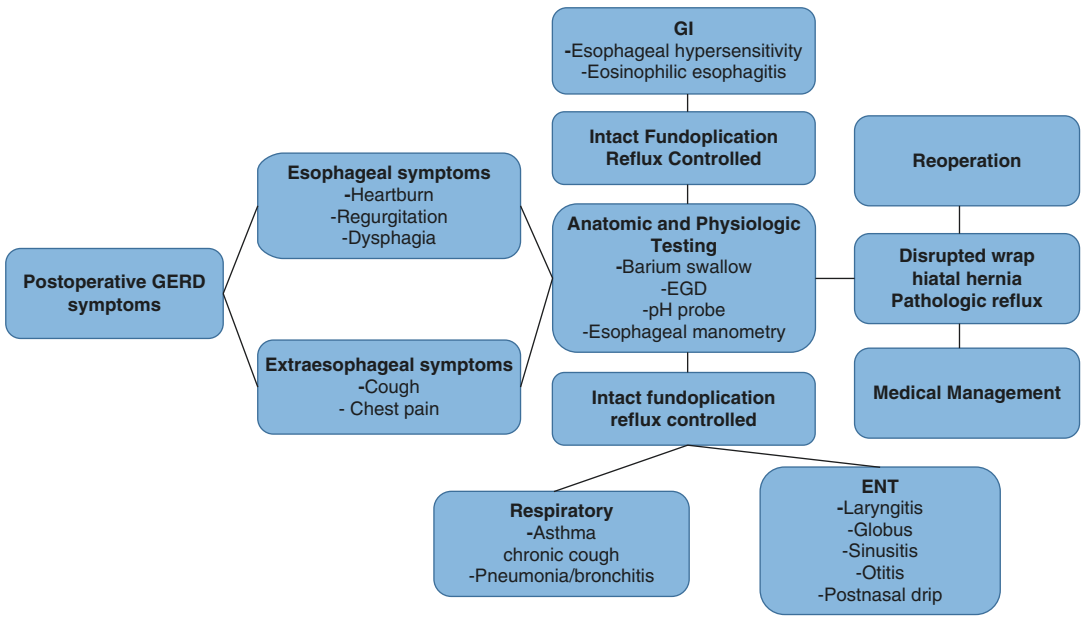
It is imperative to complete a full diagnostic evaluation including upper endoscopy, barium swallow, pH testing and esophageal manometry when evaluating post-fundoplication symptoms. Nuclear medicine gastric emptying study should be considered, as well.

Persistent extra-esophageal symptoms may also be prominent in the postoperative phase. This may be reflective of a non-GERD etiology. Response rates for laryngeal, pulmonary, and chest pain symptoms have been reported as 78%, 58% and 48%, respectively, highlighting that improvement in these symptoms cannot be guaranteed after antireflux surgery [41]. Thorough pulmonary and upper respiratory evaluation should be considered in symptoms that persist or develop.

GERD has emerged as a comorbidity of chronic obstructive pulmonary disease (COPD) with prevalence ranges from 17% to 78%, and there is significant overlap in symptoms of these two common diseases. GERD has been identified as a significant predictor of acute exacerbations of COPD [42].

Some patients and surgeons may have concern that downstream functional gastrointestinal conditions, such as irritable bowel syndrome (IBS), will be "unmasked" by antireflux surgery. There is certainly a significant amount of overlap between symptoms associated with GERD and IBS. While there needs to be a discussion that certain symptoms may become more prominent, available data support that fundoplication is associated with reduction of IBS symptoms below the Rome II criteria in 80.6% of patients with a preoperative IBS diagnosis [43]. The emersion of IBS symptoms has not been extensively studied, although patients have been identified that were evaluated preoperatively with normal Rome II criteria that transitioned to positive IBS criteria postoperatively.

There may also be a psychological contribution to gastrointestinal symptoms [2]. While major depression does influence physiologic



Algorithm for postoperative evaluation of esophageal and extraesophageal symptoms of GERD

outcomes after fundoplication, it appears to impact postoperative quality of life. Quality-of-life scores in depressed patients improve to a lesser degree, and severe postoperative dysphagia and bloating are more common, compared with controls [44]. Partial fundoplication may have better outcomes in patients with major depression than complete fundoplication due to a lower incidence of postoperative dysphagia and gas-bloat symptoms. Cognitive therapy also improves these symptoms in patients with a preoperative diagnosis of anxiety [45].

Summary

GERD prevalence is increasing. Antireflux surgery is an effective therapy for well-selected patients, with well documented response rates for esophageal and extraesophageal symptoms. Patients and primary care providers will often attribute abdominal and other symptoms to the presence of a fundoplication, or become concerned there is a disruption. Therefore, surgeons should be prepared to be involved in the assessment of a wide range of symptoms and able to identify expected side effects, and distinguish fundoplication failure from other causes of esophageal and extraesophageal symptoms.

There are symptoms that are common after antireflux surgery. Transient dysphagia, bloating and gassiness are usually self-limited. Uncommonly, these symptoms will be severe or last beyond the usual recovery time, and mechanical causes should be assessed and addressed by endoscopy or surgery as appropriate.

Recurrent esophageal GERD symptoms or escalating medication requirement should prompt evaluation for fundoplication failure, with a full anatomic and physiologic evaluation. If this is not apparent, gastroenterologic evaluation for esophageal hypersensitivity, eosinophilic esophagitis or an undocumented esophageal motility disorder is appropriate. In cases where extra-esophageal symptoms predominate, other referrals should also be considered.

Not every preoperative symptom will be cured by surgery, and not every postoperative symptom is caused by surgery. Anatomic and physiologic testing should drive decisions regarding treatment.

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11 The Medical and Endoscopic Management of Failed Surgical Anti-reflux Procedures

Aparna Repaka and Hiroshi Mashimo

Background

The current gold standard and most widely-applied surgical intervention in GERD is minimally invasive gastroesophageal fundoplication or laparoscopic Nissen fundoplication (LNF). Variations include partial (270°) vs total fundoplication (360°). Other variations of antireflux surgery include conventional or open Nissen fundoplication, anterior (Dor 120°) fundoplication, Toupet fundoplication, and Robot-assisted LNF [1]. Overall, surgery is a safe and effective modality for treatment of GERD with 80–90% of patients having relief of symptoms [2–5]. However, outcomes of anti-reflux surgery are variable and reported failure ranges from 2% to 30% depending on how "failure" is defined, e.g., required reoperation or resumed medical therapy. Similar variability of failure is reported for Nissen fundoplication performed for paraesophageal hernias in the surgical literature. Failure rates also depend on experience of the surgeon, with only a 50–60% success rate in less experienced centers [6, 7]. Up to 62% of patients who have had anti-reflux surgery report requiring proton pump inhibitor therapy in the long term [8]. In addition, up to 7.5% patients experience other symptoms such as dysphagia and bloating [9]. These patients are often managed medically and endoscopically with 1.6–9.6% needing re-operation [10, 11]. Newer surgical and endoscopic approaches to treatment of GERD are being introduced into the market. One such technique, Magnetic Sphincter Augmentation (MSA, LINX® Reflux Management System, Torax, St. Paul, MN), which involves laparoscopic placement of magnetic beads around the GE junction, was approved by the FDA in 2012. Retrospective studies show 97.8% improvement in GERD symptoms with MSA, similar to LNF [12], but a common side effect necessitating device removal is dysphagia. The device removal rate is 1–3%, with the outcomes for this technique improving with surgeon experience as was noted upon introduction of LNF [13, 14]. Thus with introduction of newer antireflux procedures, increasing rates of anti-reflux surgery, and ever-rising GERD prevalence paralleling the prevalence of obesity, it is expected that there will be an increasing number of patients with failed anti-reflux surgery needing medical, endoscopic or surgical management. In this chapter, we discuss medical and endoscopic management for patients with failed anti-reflux surgery, but not requiring surgical correction such as of slipped wraps and paraesophageal hernias.

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Anti-reflux Surgical Failures

Surgery for reflux is associated with variable success. Recurrent or persistent heartburn is the most common reason for failure of anti-reflux surgery. Other symptoms that could be considered as "failure" of surgery include dysphagia, gas bloat syndrome and early satiety. Anatomic problems that result in failure of anti-reflux surgery include a fundoplication that is too tight, disrupted fundoplication, or slipped/herniated fundoplication. The latter, with or without disrupted fundoplication, was the most common reason for redo fundoplication [15]. In addition, paraesophageal hernias can be seen in the post-operative period.

Recurrent GERD Symptoms About 62% of patients need antireflux medications at a median of 10 years of follow-up evaluation after fundoplication [8]. Recurrence of GERD symptoms may be typical, atypical, or even extra esophageal in nature. Persistence of symptoms or recurrence of heartburn after surgery can often be attributed to one of three possibilities: inappropriate patient selection, misdiagnosis of underlying condition, and technical failure of fundoplication. Atypical GERD symptoms, poor response to PPI therapy prior to surgery, and BMI of >30 to 35 are associated with poor response to anti-reflux surgery [16]. Incomplete workup prior to anti-reflux surgery may result in missed diagnosis of underlying motility disorders such as achalasia, functional heartburn, or eosinophilic esophagitis, which may mimic reflux symptoms. Technical failure can be related to a poor initial wrap, which would present with incomplete response to surgery, or subsequent disruption of the fundoplication, which may manifest as sudden recurrence of GERD symptoms.

Dysphagia Difficulty swallowing particularly solid foods within the first 6 weeks of surgery is common, and should be managed conservatively unless patients have concomitant red flags such as weight loss, dehydration, bleeding, or persistent vomiting. Dysphagia during this period is typically attributed to transient edema or hematoma in the operative field. Beyond the immediate recovery period, the short term (2 years) and long term (5 years) rates of dysphagia are about 7.5% and 5.1% respectively [9]. Dysphagia could be associated with too tight of a wrap, which is due to a suboptimal surgical procedure, or a normal wrap, which indicates a hiatus that is too tight, or undiagnosed conditions such as esophageal motility disorders or eosinophilic esophagitis [17]. Moreover, paraesophageal hernia may lead to dysphagia as well. Predictors of post-operative dysphagia include pre-operative hiatus hernia, high pre-operative dysphagia scores, delayed esophageal emptying on barium swallow, and high residual GEJ pressure post-operatively [18, 19]. Dysphagia is even more common after MSA, with up to 83% of patients experiencing immediate post-operative symptoms [20]. The majority of dysphagia resolves by 3 months, with dysphagia rates of 6% in the long term [21].

Dyspepsia/Early Satiety Dyspepsia type symptoms after fundoplication could be due to gas bloat syndrome or gastroparesis. Gas bloat syndrome results from air trapping and inability to belch after fundoplication. This is associated with abdominal discomfort and bloating. At 5 years after surgery, prevalence of gas bloat syndrome is about 7.5% [9]. Gastroparesis may present with nausea, bloating, abdominal discomfort, early satiety, regurgitation of foods many hours after meals, and even worsened GERD symptoms. This condition can be preexisting, related to medications (including pain medications), or related to vagus nerve injury during surgery. Gastroparesis is commonly seen post operatively, but generally resolves by 3 months. Prevalence of gastroparesis after 3 months is about 9% [9]. Small Intestinal Bacterial Overgrowth (SIBO) could also be a potential contributor to bloating in patients who have had a fundoplication.

Evaluation

History A thorough history should be obtained from the patient to confirm the nature of their symptoms, as well as the heartburn frequency and intensity, associated symptoms of dysphagia,

abdominal pain, and use of PPI therapy. Description of patient symptoms is essential in discerning potential causes, and may influence the order of evaluation. For example, odynophagia (pain on swallowing) should not be confused with dysphagia (difficulty with swallowing) and would be suggestive of a compromise in mucosal integrity of the oropharynx and esophagus such as by ulcer, infection and inflammation. Since patient perception or reporting of symptoms as heartburn may not be accurate for acid reflux, it is important to correlate symptoms with objective evidence obtained through physiological testing for acid reflux.

Barium Esophagram Barium esophagram may help with identification of a sliding or paraesophageal hernia, or incorrect configuration of the wrap. Barium swallow may also reveal frank esophageal reflux or a Zenker's diverticulum as cause of oropharyngeal dysphagia, which can be readily missed by upper endoscopy. There are different types of barium studies, each directed for optimizing detection of different pathophysiological entities. For example, an air-contrast barium study best reveals mucosal abnormalities (e.g., erosive esophagitis from GERD, or appearance of feline esophagus suggestive of eosinophilic esophagitis), but has been largely supplanted by upper endoscopies that allow for mucosal biopsies. Full-column barium study can distend the esophageal wall to reveal a muscular ring which is often missed on endoscopy owing to difficulty adequately distending the esophagus with air despite careful and deliberate inspection. A timed barium esophagram can assess esophageal emptying, but has also been largely replaced by manometry, which reveals the underlying contraction patterns. A video swallow study is generally performed by speech pathologist, and can assess dysmotility in the oropharynx and presence of aspiration. This can also identify certain maneuvers and food consistencies to reduce the risk of aspiration.

Endoscopy Careful endoscopic exam will be able to evaluate for evidence of reflux esophagitis, and exclude the presence of malignancy. Moreover, mucosa can be evaluated for changes suggestive of eosinophilic esophagitis (e.g., linear furrows, mucosal rings, exudates), and if present, at least five biopsies spanning the length of the entire esophagus should be taken to improve sensitivity of detection. Presently, pathological diagnosis of eosinophilic esophagitis is made by finding >15 eosinophils per high power field.

Endoscopy is key to identifying normal and abnormal postoperative anatomy after Nissen fundoplication. The esophagus should be assessed with adequate insufflation. Presence of esophagitis especially in the lower esophagus suggests recurrence or persistence of gastroesophageal reflux. Biopsies should be taken to rule out infections and malignancies, and brushing obtained for cytology if candidiasis is suspected. A sniff test may be performed, if patient is able to cooperate, to better visualize the diaphragmatic pinch and to evaluate for the presence of a sliding hiatus hernia. Resistance to passage of the endoscope may suggest a wrap that is too tight. Retroflexed view in the stomach should be performed with adequate insufflation to ensure proper position and configuration (Fig. 11.1) and assure no evidence of herniation. The squamocolumnar junction (z-line) or top of gastric folds should be noted just above or within the wrap. Presence of squamocolumnar junction >1 cm proximal to the wrap usually indicates improper surgical technique or a slipped wrap. The fundus should also be evaluated for a paraesophageal hernia, which may sometimes be very subtle, yet cause persistent dysphagia. The appearance of the wrap should be noted (intact, loose, disrupted, or tight). With an intact wrap, the folds of the fundoplication are short (1–2 cm), of even width, parallel to the diaphragm at the level of the lower esophageal sphincter and snugly wrapped around the endoscope upon retroflexion (Fig. 11.2). Several authors described endoscopic appearance of various anti-reflux surgeries [22–24]. Not much consensus exists with regards to endoscopic appraisal of post antireflux surgery anatomy. In order to standardize this post-surgical anatomy, Jobe et al., characterized the normal "valve" appearance after various anti-reflux operations including Nissen, and suggested medical terminology that could be

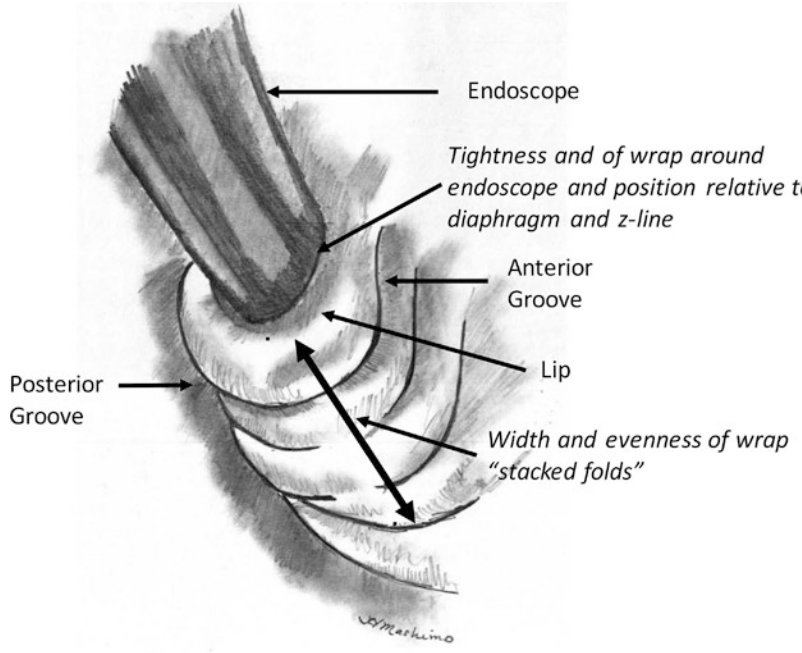

Fig. 11.1 Retroflexion view in stomach of normal fundoplication appearance. With sufficient insufflation careful assessment should be made of features of wrap folds' position (below the z-line and diaphragm), length (1–2 cm), straightness (now skewed), and orientation (parallel to diaphragm)

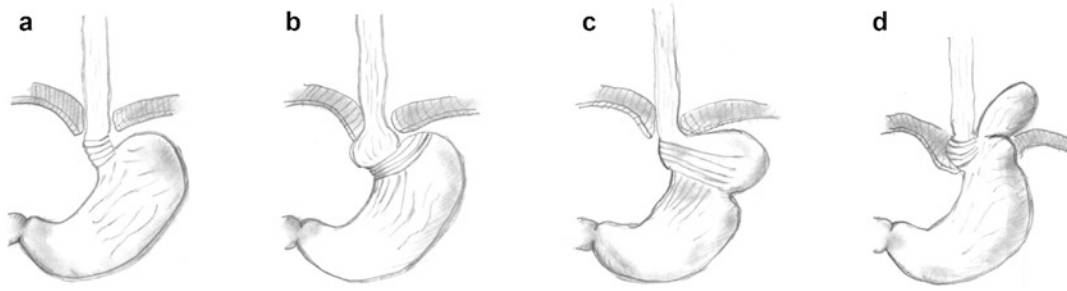

Fig. 11.2 Various types of failures of fundoplication anatomic failures. (**a**) Normal post-fundoplication appearance. (**b**) Wrap too low with gastric folds and z-line above the wrap. (**c**) Wrap twisted or too long. (**d**) Wrap herniated, with stomach above the wrap and in the chest

used to describe universally the appearance of the fundoplication. They devised a classification scheme with ten criteria to judge the competence of the surgically created valve. These criteria include lip thickness (width of the most distal aspect of the valve), body length (distance from the apex of the fundus to the valve lip), anterior groove (depth of the anterior impression made by the repair), posterior groove(depth of the posterior impression made by the repair), lesser curvature width, tightness of the valve lip around the endoscope, valve adherence to the endoscope during respiration, location of the valve distal to the crural impression, position of the fundoplication 3 cm proximal to anatomic GEJ, and valve type characterized as a nipple or a flat valve. The criteria and the ratings are listed in Table 11.1 [22].

Table 11.1 Valve characteristics and rating

Valve criteria	Rating
Lip thickness	Thin or broad
Body length	Length in centimeters
Anterior groove	Absent, shallow, or deep
Posterior groove	Absent, shallow, or deep
Lesser curvature	Narrow or wide
Adherence to endoscope	Loose, moderate, or tight
Adherence to the endoscope in all phases of respiration	Adherence through all phases
Valve type	Flap or nipple
Intraabdominal location	Yes or no
Proper repair position	Yes or no

Adapted from Jobe et al. [25]

Ambulatory pH/Impedance Monitoring Ambulatory pH testing is the gold standard for confirming acid reflux in patients with persistent or recurrent reflux symptoms. This can be performed with either a 24 h transnasal catheter placement or a 48-h BRAVO wireless esophageal pH probe monitoring. This test is performed off antacids and withholding antisecretory medications for at least 7 days. A drop of pH below 4 for more than 4% over a 24-h period or a DeMeester score greater than 14.7 would be indicative of pathological acid reflux at most centers. Abnormal reflux appears to be present in only 26–39% of patients who have recurrent heartburn after fundoplication [26–28]. Hence it is important to confirm presence of acid reflux or positive Symptom Association Probability in patients with recurrent symptoms with ambulatory pH testing, prior to restarting PPI therapy, particularly since patients may have poor or different conception of what is "heartburn.". Combined impedance/pH testing (MII-pH) has gained popularity in most motility centers, and may help identify patients with volume or alkaline reflux, which is not possible with the BRAVO single sensor (see Chapter on Diagnosis of Gastroesophageal Reflux Disorder). In patients who demonstrate no improvement in reflux time or composite reflux score compared to pre-operative pH testing would suggest failure of the surgery. Care should be exercised in interpreting these results, as the combined impedance/pH testing may show a high rate of non-specific abnormalities in patients after Nissen fundoplication [28].

Esophageal Manometry This is an important modality for investigation of dysphagia or recurrent symptoms in patients with normal endoscopy. Scleroderma can lead to severe reflux and pulmonary changes suggestive of chronic aspiration, and 20% of patients with achalasia also report heartburn indistinguishable from GERD. As such, prior pre-operative manometry should be reviewed. Post-operatively, manometry can give insight into wrap dysfunction: for example, high pressure zone above the respiratory inversion point indicating slipped wrap into the thorax, low basal pressures with a lax wrap, and high basal pressures with an overly tight wrap, or perhaps most informatively, a high residual pressure upon swallow (normal <8 mmHg). In addition, the length of the wrap can be determined with manometry: a high pressure zone that is too long (>3 cm) may result in dysphagia, while one that is too short (<1 cm) may be associated with persistent GERD symptoms. Finally, manometry can rule out abnormal esophageal motility patterns such as achalasia, scleroderma, diffuse esophageal spasms, hypercontractile ("Nutcracker") esophagus and other underlying motility disorders that may not have been appreciated in prior studies, or has subsequently evolved. Impedance manometry used currently in most centers allows assessment of bolus transit time and percent clearance of swallows, which is particularly helpful in assessing dysphagia and documenting dysfunction, which may not be apparent in setting of borderline or seemingly non-specific motility changes after fundoplication.

Management

Early Post-operative Dysphagia Postoperatively, a full liquid diet is recommended for 7 days followed by a soft diet and prn anti-emetics for nausea

and prevention of retching. Within the first 3 months, full liquid diet is restarted or continued if patients experience dysphagia. Rarely, naso-gastric tube feeding may be required. Between 1 and 3 months, endoscopic dilation with balloon or bougie may be performed for relief of dysphagia, guided generally by manometric findings of high residual pressures on manometry and delayed transit on impedance studies, but there are no specific studies to compare efficacy compared to pneumatic dilation which would stretch beyond the diameters of mucosal pathology.

Late Post-operative Dysphagia Barium esophagram, endoscopy and manometry are useful in discerning the etiology of dysphagia. In those patients with normal barium esophagram and mild to moderate dysphagia, endoscopic dilation may be attempted. In those with severe dysphagia, without response to dilation, or evidence of anatomical abnormalities such as too tight of a wrap, slipped Nissen, paraesophageal herniation or ineffective peristalsis on manometry, re-operation may be indicated. This should be guided and substantiated workup including manometry, ambulatory pH, and endoscopy. Dysphagia after MSA is particularly common, and should be initially managed conservatively in absence of the red flags, as described above. Endoscopic dilation may help with symptom relief for persistent dysphagia after MSA placement, attributed to possible fibrosis. Refractory dysphagia will necessitate device removal laparoscopically, or readjusting the magnet ring. However, there is one case report of endoscopic removal of the device after erosion through the mucosa into the lumen [29].

Bloating, Nausea and Epigastric Pain Nausea is common in the post-operative period and is also managed conservatively with anti-nausea medications. Prolonged nausea beyond the immediate post-operative period may be due to gastroparesis. This can be confirmed with a gastric emptying study by traditional scintigraphy, SmartPill® test (GivenImaging), Gastric Emptying Breath Test (Advanced Breath Diagnostics, Brentwood, TN) or observation of retained food in the stomach during endoscopy despite patient reliably fasting overnight. Management is directed towards symptom control with small frequent meals, avoidance of fibrous and fatty meals, anti-emetics and prokinetics such as metoclopramide, promethazine, and ondansetron. Erythromycin has been used as promotilide in acute settings, but nausea and tachyphylaxis often limits its prolonged use. Naso-enteric feeding is rarely needed. A small proportion of patients may need surgical management with pyloroplasty or a subtotal gastrectomy with Roux-en-Y gastrojejunostomy. Gastric emptying study would also rule out dumping syndrome, which has been described in various post-fundoplication case reports, although the true prevalence after the surgery remains unknown.

Gas-Bloat Syndrome Bloating after anti-reflux syndrome can be due to inability of the gastroesophageal junction to relax in response to gastric distention caused by either post-surgical changes or vagus nerve injury, gastroparesis, or aerophagia, which typically predates the surgery [30]. Symptoms typically improve over the first year after surgery. This can be managed with dietary interventions such as reduction in consumption of gas-producing foods or possibly initiating a popularized "Fermentable Oligo- Di- Monosaccharides and Polyol" (FODMAP) elimination diet, eating slowly to avoid aerophagia, gas-reducing agents such as simethicone, treatment of underlying conditions such as gastroparesis with prokinetic agents or SIBO with antibiotics, and assessment for bite malocclusion or replacement of ill-fitting dentures as potential causes of increased bloating. Patients who fail to respond to the above conservative measures or have debilitating symptoms may require surgical revision of their fundoplication.

Refractory or Recurrent Heartburn Presence of gastroesophageal reflux should be confirmed by 24-h pH study with a positive symptom association probability in patients that experience recurrent heartburn or have atypical or extraesophageal manifestations of GERD. Medical management, endoscopic management and

surgical revision are all options for patients with refractory or recurrent heartburn after anti-reflux surgery. Patient preference, presence or absence of underlying anatomical abnormalities and availability of surgical and endoscopic expertise will typically determine the course.

Pharmacological Management The decision to choose pharmacological therapy over surgical or endoscopic options is for the most part based on patient's preference, their particular anatomy and physiology, as well as available local expertise. Medications are aimed largely to reduce symptoms or reduce caustic elements of the refluxate, but would not necessarily reduce reflux events for example in the setting of a slipped wrap, or reduce dysphagia associated with a paraesophageal hernia, for which surgical correction should be advised in most cases. However, pharmacologic therapy might be more cost effective than repeat surgery depending on patient age, or the main option in non-surgical candidates owing to comorbidities. Patients who have responded to proton pump inhibitor(PPI) therapy prior to surgery and now have a failed anti-reflux surgery with recurrence of GERD symptoms typically respond to resumed PPI therapy. In addition to PPI therapy, other classes of medications such as H2 receptor antagonists and antacids can be used in patients with milder and sporadic symptoms. Baclofen, a GABAB receptor antagonist, which reduces the number of transient lower esophageal sphincter relaxations (TLESR) can be helpful in a subset of patients with GERD, but often its use is limited by central nervous side effects such drowsiness, weakness, dizziness, confusion and insomnia, or systemic effects such as constipation and urinary retention. Also, the role of baclofen in patients who have had prior anti-reflux surgery is unclear. In some patients, ambulatory pH study and impedance testing may exclude acid or reveal non-acid reflux contributing to the GERD symptoms, and Symptom Association Probability may be helpful in identifying the cause of symptoms, even in the setting of overall normal pH scores (see Chap. 2). Patients with predominant alkaline reflux may be responsive to surface agents such as sucralfate or sodium alginate, as discussed in the Chap. 3. In the setting of normal impedance-pH testing and workup and presentation suggestive of functional heartburn and reflux hypersensitivity, neuromodulators such as low-dose tricyclic antidepressants, trazodone, serotonin-norepinephrine reuptake inhibitors, and selective serotonin reuptake inhibitors may be considered.

Endoscopic Management There have been several procedures that were developed for reinforcement of the lower esophageal sphincter for management of GERD based on an endoscopic platform. Several devices and techniques have been developed in the past few decades with the majority no longer available because of lack of efficacy or unfortunate serious adverse events, such as with injectable bulking agents, or from lack of financial survival of the company. The viable technology in use at this time include:

1. Radiofrequency treatment of Lower esophageal sphincter(Stretta)
2. Trans-Oral Incisionless Fundoplication (TIF) using the EsophyX® device and MUSE™ system.

Radiofrequency Treatment of Lower Esophageal Sphincter(Stretta) The Stretta procedure delivers RF energy to the deep muscle layer of the gastroesophageal junction and cardia, with subsequent wall thickening, increase in basal LES pressure, reduced LES compliance, decrease TLESRs, reduced refluxate volume, and improved GERD symptoms. This procedure has the longest track record of use, with over 20,000 procedures performed world-wide, four randomized control trials, and lowest complication rate of any non-medical treatment for GERD. The procedure is generally performed in an endoscopy unit without the need for general anesthesia or operating room. The Stretta procedure significantly reduced GERD HRQL, use of PPI drugs, esophageal acid exposure, LES pressure, and grade of esophagitis compared with sham control [31]. Up to 75% of patients who were on double dose PPI therapy were able to eliminate daily PPI therapy, with only occasional use of OTC

medications after Stretta treatment [32]. At 10 year follow up, 72% of patients had normalization of GERD-HRQL scores, with 64% of patients achieving a 50% or more reduction in the medication use, of whom 41% were able to eliminate the use of PPIs completely [33]. Stretta appears to be a viable option for patients with GERD who choose an alternative to PPI therapy but not willing to undergo surgery. A prospective study of 217 patients with medically refractory GERD that underwent Stretta procedure included 15 patients with failed Nissen fundoplication who successfully had a Stretta procedure for relief of GERD symptoms. While there are no large studies specifically evaluating Stretta after failed fundoplication, this supports the feasibility and safety of Stretta in patients who have had failed anti-reflux surgery.

Transoral Incisionless Fundoplication (TIF) Using the EsophyX® Device and the MUSE™ System

The EsophyX (EndoGastric Solutions, Inc., Redmond, WA, United States) is introduced transorally under direct vision with an endoscope and allows for endoluminal fundoplication with creation of a 2–3 cm, 210–300° fundoplication at the level of the GE junction [34]. Two multicenter RCT's have demonstrated symptom control and improvement in quality of life with transoral fundoplication. In The Randomized EsophyX vs. Sham, Placebo-Controlled Transoral Fundoplication (RESPECT) trial, elimination of troublesome regurgitation was achieved in 67% of TIF/placebo patients vs. 45% sham/PPI patients at 6-month follow-up ($P < 0.023$) [35]. In the TIF EsophyX vs Medical PPI Open Label (TEMPO) trial, troublesome regurgitation was eliminated in 97% and 93% of TIF patients at 6 and 12-month follow-up respectively [36]. The failure rate of this technique across studies is about 8.1% [37].

The Muse™ system (Medigus, Omer, Israel) employs a disposable endoscopic device with ultrasound and surgical endostapler to mimic a partial anterior fundoplication (270° loop). An uncontrolled 6-month follow-up study of 66 treated patients showed at least 50% improved GERD-Health Related Quality of Life (HRQL) scores off PPI in 73%, and 64.6% were no longer using daily PPI medication. The mean percent of total time with esophageal pH < 4.0 decreased from 20/9% at baseline to 7.3% at 6 months post-procedure ($p < .001$) [38]. A long-term multicenter follow-up study of 36 patients showed that 69% of patients remained off daily PPI at 4 years post-procedure, and HRQL scores (off PPI) were also significantly decreased. The daily dosage of GERD medications, measured as omeprazole equivalents (mean ± SD, mg), decreased from 66.1 ± 33.2 at baseline to 10.8 ± 15.9 at 6 months and 12.8 ± 19.4 at 4 years post- procedure ($P < 0.01$). Thus while the majority of patients were using PPI at 4 years follow-up, they had improved symptom scores and most were on reduced dose of PPI [39]. Similarly, another small study of 13 patients followed for 5 years showed reduced HRQL scores and 9/13 had stopped all GERD medications [40]. When MUSE was compared to LNF, at 6 months mean follow up, proton-pump inhibitor use was insignificantly higher in the TIF group ($P > 0.05$). Mean GERD-HRQL scores dropped in 87% and in 64% of patients ($P > 0.05$) from 29.3 to 4.1 and from 24.8 to 8.9 ($P = 0.016$) in LNF and TIF groups, respectively [41].

Both TIF procedures are performed in the operating room under general anesthesia and both procedures have been associated with serious adverse events included esophageal injury/perforation and bleeding, with a systematic review of the published TIF literature in 2013 reporting a 3.2% major complication rate. This is most likely attributable to early part of the learning curve of these methods as no such serious adverse effects were reported in the RESPECT and TEMPO trials. There are no reports thus far, of the Muse™ system being utilized for revision of failed anti-reflux surgery. Small studies have shown feasibility of revision of failed Nissen fundoplication with the EsophyX transoral fundoplication. Eight out of 10 patients who underwent such a revision procedure

reported resolution of their primary symptoms and demonstrated improvement in pH studies post operatively as well as significant improvement in GERD-HRQL scores from 28.6 (10.6) preoperatively to 6.7 (6.1) post-TIF (p = 0.016) [42]. This data suggests improvement of GERD without the risks of repeat surgery and laparoscopic dissection in patients who need revision of their wrap after a Nissen fundoplication. However, the long term efficacy of this procedure, in comparison to repeat surgery needs to be evaluated. Furthermore, we need cost effectiveness data for endoscopic anti-reflux therapy, especially in comparison to repeat surgery and long term PPI therapy prior to widespread application of endoscopic therapies for revision of failed anti-reflux surgery.

Conclusion

Minimally invasive laparoscopic fundoplication, or laparoscopic Nissen is the gold standard for surgical management of GERD with 80–90% of patients obtaining relief of symptoms. There is wide variability in the definition of "failure" of antireflux surgery, from resumption of medications to requirement of surgery, with failure rates widely ranging from 2% to 30%. Given the ever-rising prevalence of GERD, and increasing number of surgical interventions for GERD, there will be expectedly increasing number of patients with failed anti-reflux surgery. The currently available options for non-surgical management of failed anti-reflux surgery, based on objective evidence of recurrent reflux, are re-instatement of pharmacological therapy or endoscopic treatments for symptom relief. Specifically regarding patients who have failed antireflux surgery, there are no prospective controlled studies to compare the medical vs. endoscopic treatment options, and despite great promise as alternatives to re-surgery, further studies of endoscopic treatment options regarding long-term efficacy, cost effectiveness, and identification of ideal patient subsets are needed prior to their routine use after a failed anti-reflux surgery.

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Reoperation for Failed Antireflux Surgery

12

Luigi Bonavina

Antireflux surgery aims to improve function and provide relief of symptoms and complications of gastroesophageal reflux disease (GERD) while permitting physiological swallowing and avoiding side-effects such as bloating and inability to vomit. Although the definition of surgical success and failure vary considerably, the reported success rate up to 25 years of follow-up with the open Nissen fundoplication has been 70–80% [1], and it is likely that similar long-term results could be expected with the laparoscopic approach.

Revisional antireflux is necessary in 3–6% of patients [2, 3]. Failed antireflux surgery may be related to inappropriate patient selection and choice of the operative procedure, as well as technical errors occurring during the course of the operation. In most circumstances, these causes of failure can be prevented by strict adherence to established criteria and avoidance of extemporary technical modifications dictated by surgeon's fantasy rather than scientific evidence [4–6].

Laparoscopic fundoplication, first reported in 1991, has been rapidly adopted and established as the procedure of choice for GERD. It is a safe, effective, and durable antireflux procedure when performed in specialized centers. A multicenter European trial comparing medical therapy with fundoplication performed in selected centers by expert surgeons showed that 92% of medical patients and 85% of surgical patients remained in remission at 5 years of follow-up [7]. However, despite a remarkably low morbidity and mortality rates, the operation is underused due to the perception of long-term side effects and fear of failure, which impacts referral patterns [8]. Also, wide variability in clinical outcomes related to inter-individual surgical expertise and/or technical modifications, have restricted the adoption of this procedure mainly to patients with long-lasting severe disease and large hiatal hernias [9].

A downward trend in the utilization of surgical fundoplication has been noted in the United States over the past decade [10, 11], and the decline in surgical volume has been attributed, among other factors, to the perceived risk of fundoplication failure. The apparent decline of the current gold standard, the Nissen fundoplication, has induced many surgeons to offer a partial fundoplication such as the 270° Toupet technique as the primary antireflux procedure. More recently, the Linx procedure has emerged as a feasible alternative to fundoplications [12, 13].

The results of remedial operations for persistent or recurrent symptoms following antireflux surgery are generally less satisfactory than the results obtained following the primary procedure,

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especially after multiple failed surgical attempts [14–16]. This may be related to the difficulties in recognizing the pattern of failure and the inherent technical difficulties due to adhesions and gross anatomical distortion from the previous operation. However, when the cause of failure has been properly identified and addressed by appropriate surgical technique, the majority of patients can benefit from a reoperation [17–20].

Preventing Failures of Primary Antireflux Surgery

There are four categories of errors that have the potential to cause immediate, early, or late failure of the antireflux repair. Recognition of such errors may reduce the complication rate and the need for reoperation.

Errors in patient selection When patients are properly selected and procedures are properly performed, most surgical failures can be prevented. The critical issue is to make sure that preoperative symptoms are clearly related to gastroesophageal reflux and not to achalasia, gallstones, myocardial ischemia, etc. The accuracy of endoscopy is quite limited in this setting and, therefore, especially in the absence of typical symptoms, the preoperative work-up should be extensive and routinely include esophageal manometry and ambulatory esophageal pH monitoring.

Errors in choice of operative procedure In addition to avoiding antireflux surgery in patients with extra-esophageal disorders unrelated to reflux, the pattern of esophageal motility should be carefully investigated and a potentially obstructive Nissen fundoplication be avoided when the patient complains of dysphagia and/or there is evidence of an esophageal body motility disorder or a high outflow resistance at the gastroesophageal junction. Female sex is associated with poorer outcome [21]. In such circumstances, a Toupet fundoplication is expected to cause less obstruction and is better tolerated by the patient.

Errors in surgical technique These include failure to adequately mobilize the distal esophagus and fundus, to recognize a true shortened esophagus, to properly repair the hiatus, and to properly construct the fundoplication. Esophageal shortening may result in the incorrect identification of the gastroesophageal junction. This usually causes placement of the fundoplication around the proximal stomach rather than at the gastroesophageal junction. This type of error is often referred to as the "slipped Nissen", but in most circumstances represents a misplaced rather than a slipped wrap. Intraoperative endoscopy can help to identify the true gastroesophageal junction. From the surgical perspective, the fat pad around the angle of His is a useful landmark. In addition, placement of the fundic wrap between the posterior vagus nerve and the esophagus can ensure that the fundoplication is not placed too low around the stomach [4]. Intraoperative confirmation of a true short esophagus should alert the surgeon to perform a Collis lengthening procedure instead of a standard fundoplication. Disruption of the fundoplication is another common reason of technical failure of the primary repair, and may be due to excessive radial tension especially when the short gastric vessels have not been divided and only the anterior fundic wall has been used. In fact, the laparoscopic Nissen-Rossetti fundoplication has been associated to a higher failure rate, especially during the learning curve phase [22]. Herniation of the wrap in the mediastinum with an intact fundoplication occurs as a result of excessive longitudinal tension or inadequate closure of the hiatus. Other causes of failed antireflux surgery include a too long and/or tight fundoplication, and a twisted fundoplication that can cause severe postoperative dysphagia which is usually refractory to dilatation.

Errors in postoperative management Immediate failures are commonly the result of uncontrolled postoperative nausea and vomiting causing abrupt rises in intra-abdominal pressure and

subsequent mediastinal migration of the wrap. Early failures can occur also as a result of sentinel events such as heavy lifting, abdominal straining or trauma. Control of early retching and vomiting is critical after antireflux surgery. It has been found that about one-third of patients with early retching developed mediastinal herniation of the wrap requiring revisional surgery [23]. Avoiding use of nasogastric tubes and opioids, and routine application of a pharmacologic protocol including desamethazone and metoclopramide can reduce the incidence of this complication.

Assessment of Failed Antireflux Surgery and Indications for Remedial Procedure

A detailed evaluation of recurrent or persistent symptoms, and correlation with the pre-surgical status and current anatomic and pathophysiological abnormalities, is critical before considering a reoperation. The most common postoperative complaints are dysphagia, heartburn, and abdominal discomfort related to meals. It is important to remind that all these symptoms may be compatible with a normal postoperative course, especially during the first 3 months after surgery. Most symptomatic failures, such as the slipped Nissen with "hour-glass" stomach, are usually observed in the first 2 years after the initial procedure and half of them will undergo reoperation within 5 years [24]. Late mediastinal migration of the wrap is frequently observed in patients operated for large type III hiatal hernia, but it may not require correction if the hernia is small and asymptomatic [25].

Anatomical assessment is based on endoscopy, barium swallow study, and CT scan to evaluate the presence of strictures, paraesophageal hernia, and status of the previous fundoplication [26] (Fig. 12.1). Functional assessment includes esophageal manometry and ambulatory esophageal pH-impedance monitoring to evaluate the presence of a motility disorder or persistent gastroesophageal reflux. High resolution manometry allows to pick up abnormalities that are not discernable with conventional perfused manometry, such as the double hump configuration of the high-pressure zone that indicates spatial separation and implies sphincter failure [27, 28].

Indications to reoperation should be based on the patient's physiological state, the severity of symptoms, and the response to conservative therapy. In most patients with refractory reflux or dysphagia combined with mechanical outflow resistance, a reoperation is mandatory due to the risk of respiratory complications and even pulmonary fibrosis secondary to aspiration [29].

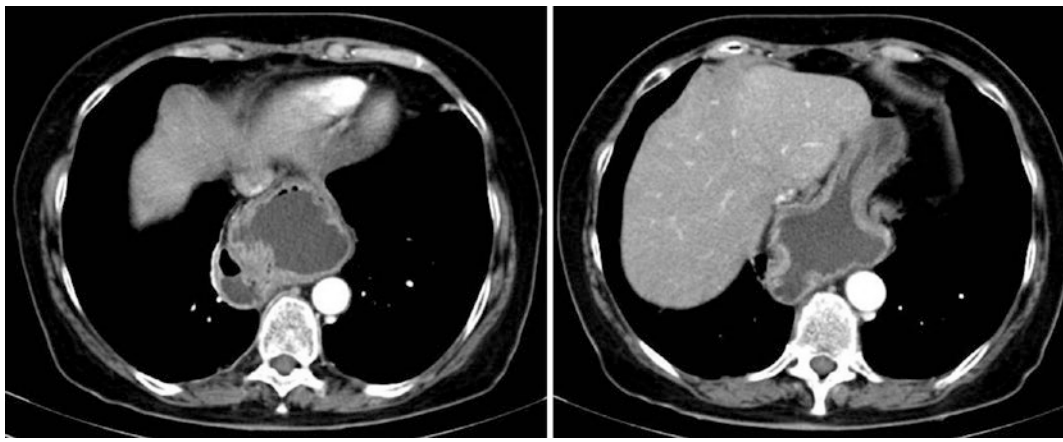

Fig. 12.1 Computed tomographic scan in a patient with chest herniation of a Nissen fundoplication

Choice of the Remedial Operation

The choice of the surgical procedure should be tailored to the individual patient by considering a number of factors: reasons for failure of the first operation, esophageal length, peristaltic reserve, presence of Barrett's esophagus, and concomitant gastric pathology. In most patients, laparoscopic fundoplication revision is feasible, although dealing with adhesions of a previous laparotomy may require extra time and increase the morbidity of the procedure. Esophageal resection should only be considered in patients with multiple previous repairs, extensive fibrosis with stricture refractory to endoscopic dilatation, and evidence of dysplasia on Barrett's esophagus [30].

Patients with a slipped/misplaced Nissen require an esophageal lengthening procedure combined with re-fundoplication if the esophagus is found to be truly short. Complete takedown of the old repair is a mandatory step before considering any surgical option. A stapled wedge resection of the gastric fundus [31] provides a safe esophageal elongation and is easier to perform and to teach compared to the Steichen "buttonhole" technique, requiring both a circular and linear stapler, and to the transthoracic gastroplasty [32]. It has been proposed that in borderline case vagotomy may represent a safe alternative to the Collis gastroplasty in patients with excessive longitudinal tension [33]. In patients with chest herniation of the wrap attention should be directed to assess the tissue quality of the crura and to consider the opportunity of mesh reinforcement [25] and/or crural relaxing incisions [34].

Impairment of esophageal motility may indicate the opportunity to perform a partial 270° Toupet rather than a 360° Nissen fundoplication. This is the case when more than 30% of the esophageal waves are synchronous or the mean amplitude is less than 30 mmHg, or when the criteria for the diagnosis of ineffective esophageal motility are met at high-resolution manometry based on the Chicago classification. An esophageal myotomy combined with a Dor fundoplication is usually performed in patients with previously misdiagnosed achalasia [35, 36].

In some patients, a re-fundoplication cannot be performed because the fundus is inadequate for any type of repair. An alternative surgical strategy, which is especially useful after multiple previously failed surgical attempts, consists of vagotomy, antrectomy, and Roux-en-Y reconstruction to effectively reduce both acid and alkaline components of the refluxate [15, 37]. Laparoscopic gastric bypass is another option that can be considered in obese patients with recurrent reflux symptoms after failed antireflux surgery [38, 39].

Pyloroplasty, or even a total gastrectomy in extreme cases, may be indicated in the occasional patients who present with severe gastroparesis, especially after inadvertent vagotomy at the time of the index operation [40].

Techniques of Laparoscopic Revisional Surgery

Historically, reoperations for failed antireflux procedures were performed through an open trans-abdominal or trans-thoracic technique [41–44]. As experience with advanced minimally invasive surgery has increased, more redo operations are performed laparoscopically, and it appears that the thoracic approach has now been actually abandoned.

The principles of reoperative laparoscopic surgery are similar to those of the open approach. All redo procedures should be considered complex and should be scheduled as the first case of the day. On table endoscopy is routinely planned after induction of anesthesia, and the scope is left in the esophagus for intraoperative evaluation. Five access ports are used. Initial port placement is generally performed using the Hasson trocar inserted away from any previous incisions. Adhesiolysis between the stomach and the liver and around the hiatus may be long and tedious. Extreme care should be taken to avoid perforations of the stomach and esophagus and injury to the vagal trunks. Full mobilization of the fundoplication and the lower mediastinum is performed by removing the crural sutures and by taking down the short gastric vessels. A linear stapler

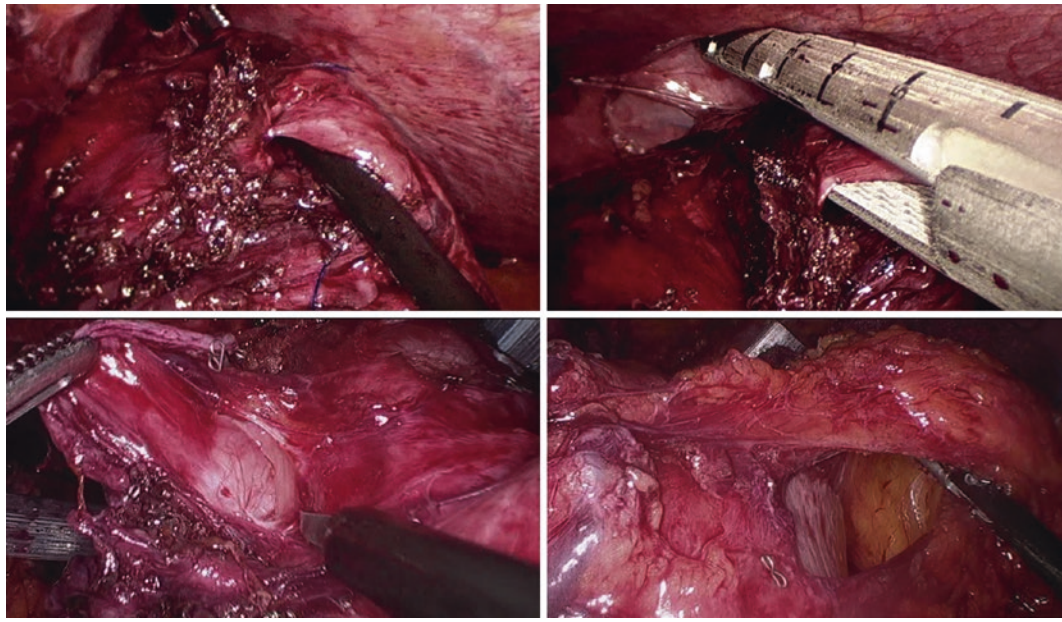

Fig. 12.2 Take-down of a misplaced Nissen fundoplication. *Up*: division of the two valves using a linear stapler; *Down*: complete separation of the two valves from the gastric body

can help dividing the two halves of the wrap (Fig. 12.2). The fat pad should be routinely excised to identify the true gastroesophageal junction, and a 3 cm tension-free intra-abdominal esophageal segment should be obtained. Care should be taken to minimize tension on the crura repair by clearing the entire surface of the right crus and decrease the insufflation pressure to less than 10 mmHg to facilitate approximation of the muscle bundles. The hiatus can be repaired with interrupted non-absorbable stitches, and placement of a composite or synthetic absorbable mesh should be considered (Fig. 12.3).

If a short esophagus is suspected, a modified Collis wedge gastroplasty procedure can be performed. Once the gastric fundus has been completely freed from posterior and lateral adhesions, a bougie is inserted in the esophagus under direct laparoscopic visualization and placed across the gastroesophageal junction along the lesser curve. The fundus is retracted inferiorly to the patient's left side, and sequential fires of a linear stapler are directed toward the bougie to a point 3 cm below the gastroesophageal junction. The gastroplasty is then completed by resecting the wedge of fundus with the stapler applied parallel to the bougie toward the angle of His. The operation ends with a Nissen or Toupet procedure around the neo-esophagus (Fig. 12.4).

Outcome of Laparoscopic Redo Fundoplication Procedures

A systematic review and meta-analysis of laparoscopic revisional antireflux surgery, including 19 case series and one case-control study, reported on 922 patients operated between 1990 and 2010 [45]. The mean surgical duration was 166 minutes and the conversion rate to open revision 7%. The most prevalent indication to reoperation was reflux (61%) followed by dysphagia (31%), gas-bloat syndrome (4%), regurgitation or vomit (3%), and chest pain (2%). The most common anatomic problem found at reoperation was mediastinal migration of the wrap. Nissen fundoplication was performed in 70% of patients. The overall complication rate was 14% (0–44%). A satisfactory to excellent result was reported in 84% of patients, while 5% of patients required further surgery.

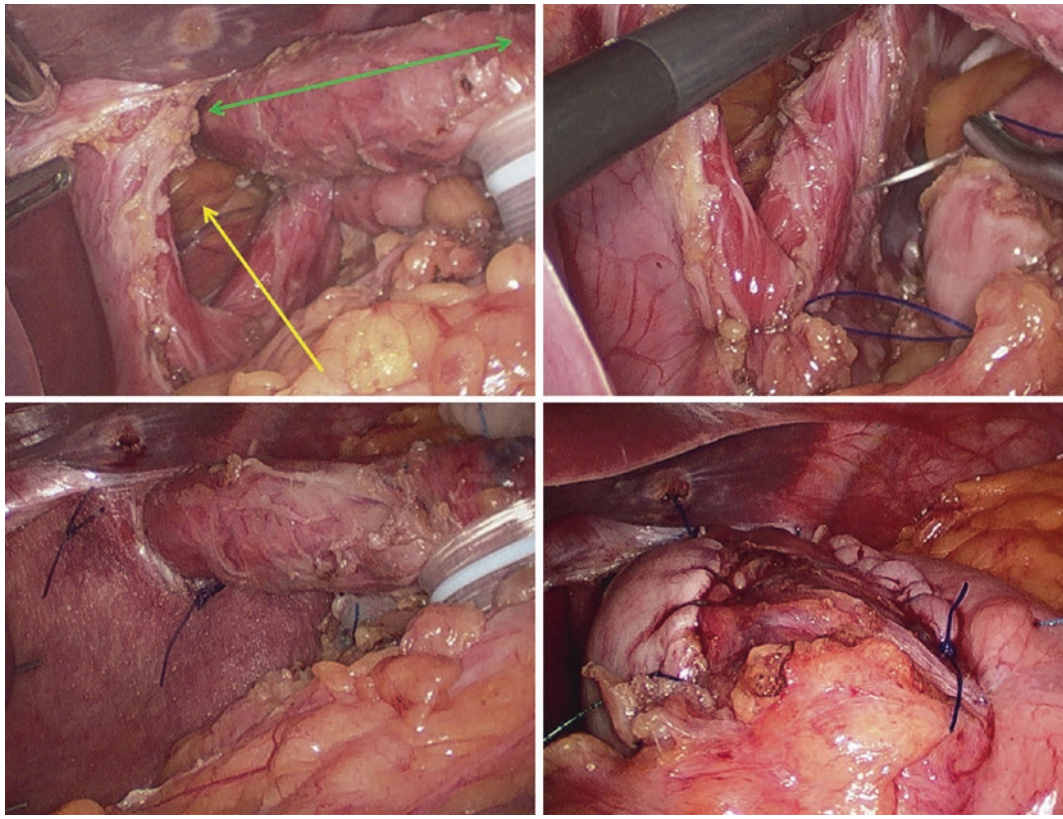

Fig. 12.3 Reinforced crural repair and Toupet fundoplication. *Up*: evaluation of hiatus area (*yellow arrow*) and esophageal length (*green arrow*) followed by hiatoplasty with interrupted non-absorbable stitches recruiting the left crus; *Down*, *left*: a synthetic absorbable mesh is placed over the crura repair; *right*: 270° Toupet fundoplication

Redo Surgery After the Linx Procedure

Long-term results of the Linx procedure in patients with uncomplicated gastroesophageal reflux disease have shown relief of reflux symptoms, discontinuation of daily therapy with proton pump inhibitors, and objective reduction of esophageal acid exposure. In addition, patients maintain the ability to belch and vomit [46, 47]. A recent case-control study found similar control of reflux symptoms after Nissen fundoplication or Linx implant at 1 year follow up. However, the Nissen group showed a higher rate of patients with inability to belch and vomit, along with more severe gas-bloat symptoms [48]. Concerns regarding the safety of the Linx procedure, especially the fear of erosions, stem from past adverse experience with the Angelchick device and, more recently, with the gastric banding device. However, a recent analysis of the safety profile of the first 1000 worldwide implants in 82 hospitals showed 1.3% hospital readmission rate, 5.6% need of postoperative endoscopic dilations, and 3.4% reoperation rate [49].

Reoperation for removal of the Linx device consists of a one-stage laparoscopic procedure with intraoperative endoscopic assistance. Pneumoperitoneum is established with a Veress needle and the abdomen is entered through the prior port-sites. The scar tissue at the gastroesophageal junction corresponding to the site of the Linx implant is identified. A monopolar electrocautery hook is used to cut the scar tissue and to expose a pair of anterior titanium beads. The

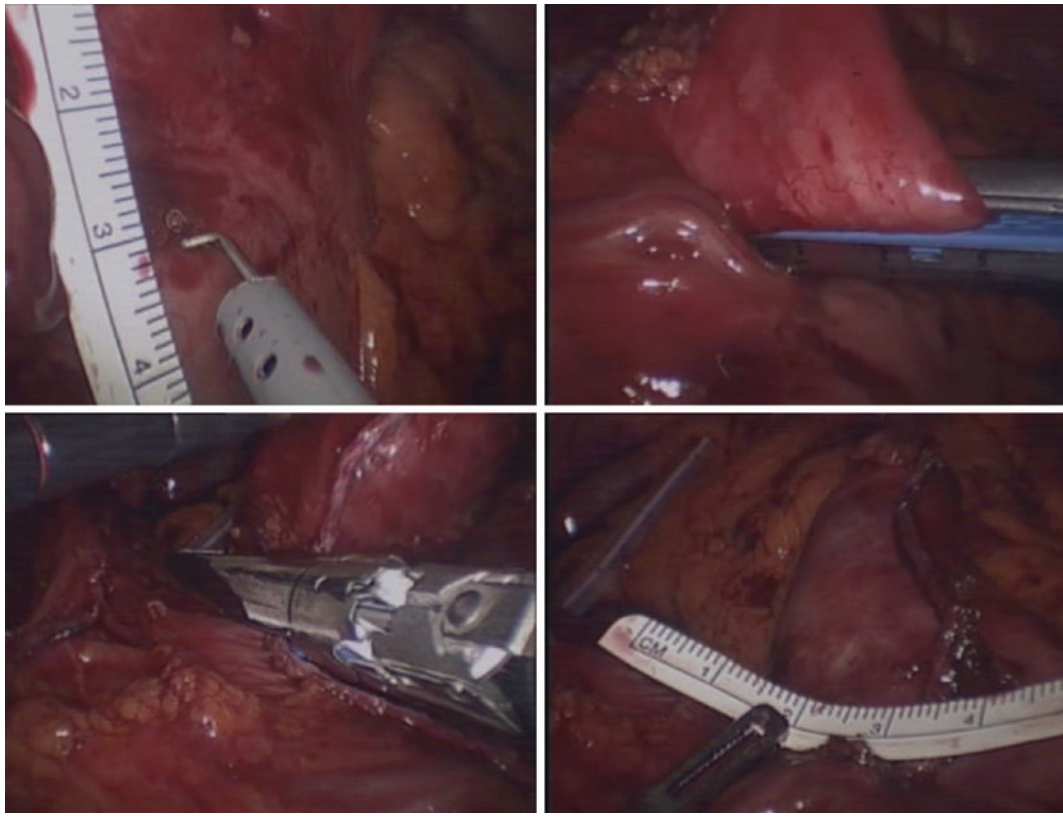

Fig. 12.4 Staple wedge Collis gastroplasty. *Up*: a point 3 cm below the gastroesophageal junction is marked with cautery and a linear stapler is applied across the upper fundus toward the lesser curve; *Down*: the gastroplasty is completed by applying the stapler parallel to the lesser curve toward the angle of His

independent titanium wire connecting the beads is cut with ultrasonic scissors, and one bead is grasped with an Endoclinch and retracted upward (Fig. 12.5). This allows step by step cutting of the thin fibrous capsule overlying each bead and pulling out of the device, entirely or in two pieces. The total bead count in the explanted device is confirmed and the device removed through a 10 mm port. Intraoperative endoscopic assistance helps to check the integrity of the esophageal mucosa during and after removal, and/or to assist during retrieval of the beads migrated into the esophageal lumen. A concurrent antireflux repair (partial or total fundoplication) is then performed.

A recent study focused on reoperations for Linx removal and reported the long-term results of one-stage laparoscopic removal and fundoplication [50]. In this series, out of 164 patients implanted with a Linx device, 11 (6.7%) were explanted at a later date. The main presenting symptom requiring device removal was recurrence of heartburn or regurgitation in 46%, dysphagia in 37%, and chest pain in 18%. In two patients (1.2%) full-thickness erosion of the esophageal wall with partial endoluminal penetration of the device occurred. The median implant duration was 20 months, with 82% of the patients being explanted between 12 and 24 months after the implant. Device removal was most commonly combined with partial fundoplication. There were no conversions to laparotomy and the postoperative course was uneventful in all patients. At 12–58 months after surgery, the GERD-HRQL score was within normal limits in all patients.

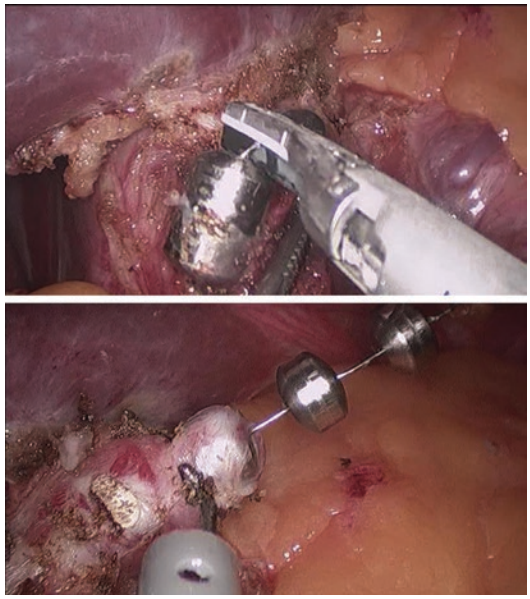

Fig. 12.5 Removal of the sphincter augmentation magnetic device (Linx). *Top*: the titanium wire connecting two beads is cut using ultrasonic scissors; *Bottom*: one bead is grasped and retracted upward, allowing step by step cutting of the thin fibrous sheath encapsuling the device

Conclusions

A comprehensive symptomatic, anatomical, and functional assessment is mandatory in patients who present after failure of an antireflux repair. Surgeon's judgment and expertise, and the choice of the appropriate surgical approach and technique, are essential for the outcome of these patients.

Summary

Revisional surgery after failed antireflux repairs is technically demanding and requires careful preoperative and intraoperative assessment to identify the cause of the failure and to tailor the procedure to the individual patient. Appropriate training, expertise, and strict adherence to established surgical principles is necessary to overcome the challenge of redo antireflux surgery. Today, more redo operations are attempted laparoscopically with reported low conversion rates, minimal morbidity, and good success rate. Due to the continuously rising epidemic of gastroesophageal reflux disease, reoperative hiatus surgery remains a challenge whose complexity and volume is likely at least to remain stable in the future.

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Short Esophagus

13

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Introduction

The gastroesophageal junction (GEJ) is an anatomically complex area. Usually, a portion of distal esophagus and the gastroesophageal junction are in the abdomen below the diaphragm. A hiatal hernia is present when the GEJ, the fundus of the stomach, or both migrate into the chest through the hiatus. In this case, GEJ becomes mostly incompetent which facilitates the development of gastroesophageal reflux disease (GERD). In patients with severe chronic GERD or with large hiatal hernias, shortening of the esophagus can occur.

When surgery to treat GERD is indicated, all antireflux operations must adhere to four basic principles:

1. The fundoplication must be created with the gastric fundus.
2. The fundoplication must be created around the esophagus.
3. The fundoplication should be situated below the diaphragm.
4. The fundoplication cannot be under axial tension.

To fulfill all these criteria, it is imperative to have at least 2–3 cm of intraabdominal esophagus.

History

Dietlen and Knierim first described in 1910 a short esophagus (SE) in a pregnant woman whose stomach was found to be intrathoracic on a chest X-ray [1]. However, some authors have attributed this description to Akerlund [2] or Findlay [3]. A shortened esophagus shown on esophagram was first reported by Fineman and Conner [4, 5] in 1924, whereas Woodburn Morison [6] provided the earliest endoscopic description in 1930.

Definition and Prevalence

Short esophagus has been defined as the esophagus that cannot reach the abdominal cavity despite performing an extensive mediastinal dissection. Some other surgeons prefer a more accurate

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definition considering that the abdominal esophagus should measure around 2.5–3 cm in order not to have a SE [7]. Based on barium swallow (BS) findings, some other authors defined SE as the GEJ being >5 cm above the hiatus [8].

Reported prevalence varies from 0% [9–11] to 60% [12]. Moreover, Maziak et al. reported up to 80% prevalence in patients with massive incarcerated paraesophageal hernias [13].

Yet, the existence of this entity is still a matter of debate.

Etiology and Pathophysiology

Initially, SE was considered a congenital anomaly. There were several theories proposed such as congenital hypoplasia of the esophagus, lack of normal growth stimulant due to the abnormal position of the stomach in the chest [14], and deficient fixation of the distal esophagus to the hiatus [5, 15].

The most current and accepted theory extensively associates SE with the presence of long-standing gastroesophageal reflux disease (GERD). This phenomenon can cause inflammation throughout the layers of the esophageal wall extending from the mucosa up to the longitudinal muscle. As inflammation progresses fibrosis occurs leading to retraction of the collagen in the fibrous scar. This contraction can occur circumferentially causing strictures or longitudinally producing shortening of the esophagus [16]. As such, SE appears as a consequence of GERD, instead of GERD as a consequence of SE as it was believed before.

Some other special circumstances such as long segment Barrett's esophagus, sarcoidosis, caustic ingestion, scleroderma, type III paraesophageal hernias, and Chron's disease, were associated to SE esophagus as well [16, 17]. Likewise, patients who had previous failed antireflux operations are at risk of having SE.

Diagnosis

Multiple preoperative tests have been suggested in order to diagnose SE beforehand. However, it seems that true diagnosis can only be made during the intraoperative assessment of the anatomy.

Are There Any Strong Predictors?

Some predictors might be useful at the time of identifying patients with SE. Swanstrom et al. described them as follows: history of long-standing GERD, prior esophageal and/or antireflux surgery, barium swallow (BS) demonstrating hiatal hernia >5 cm, non-reducing hiatal hernia and/or type III paraesophageal hernia (GEJ and stomach body above the diaphragm), esophagogastroduodenoscopy (EGD) with peptic stricture and/or Barrett's esophagus, and esophageal manometry (EM) showing aperistalsis and/or GEJ to crura distance >5 cm. An esophageal length index (ELI) <19.5 was also considered a strong predictor of SE. The ELI is calculated as the ratio between the esophageal endoscopic length (EEL) (cm) to patient height (meters) on EGD [7].

How Accurate Can Preoperative Test Be??

Gastal et al. reported their experienced on 236 patients undergoing either thoracic or abdominal antireflux procedures; 65 patients (27%) were suspected to have SE preoperatively. Of those 65, only 37 (56%) required an esophageal lengthening procedure. This means that based on intraoperative assessment, the number of SE decreased from 27% to 16% [17].

Mittal et al. published their experienced on 39 patients with SE diagnosed preoperatively. SE was identified during intraoperative assessment only in 10 of them (25.6%) [18].

What Tests Should Be Mandatory?

Recognition of this pathology is crucial to achieve satisfactory outcomes after any antireflux operation. Certainly, identifying this pathology during the preoperative evaluation would allow the surgeon to be prepared to perform a more complex procedure to increase the esophageal length.

Regardless of the success rate of each test in recognizing SE preoperatively, all patients should undergo the following testing when evaluating them for GERD:

- Clinical assessment
- Barium swallow
- Esophagogastroduodenoscopy
- Esophageal function tests (EFT's) including esophageal manometry (EM) and pH monitoring (either 24 h pH monitoring or Bravo).

Clinical Assessment

GERD symptoms are usually classified in typical and atypical. Typical symptoms are heartburn, regurgitation and dysphagia. Atypical symptoms are cough, wheezing, belching, chest pain, nausea, hoarseness. Although it is well known that symptoms are poor indicators of the presence/absence of reflux [19], they might orient the physician to set up a baseline for further comparison during follow up.

Barium Swallow

This test provides key information about the anatomy. Presence, type, size, and reducibility of hiatal hernia can be assessed. Based on this, it seems that BS could offer all the data the surgeon needs to approach these type of cases. Unfortunately, that is not true for all the cases. In fact, Jobe et al. reviewed their experience on 15 patients who required lengthening procedures such as Collis gastroplasty, finding that BS had only 50% positive predictive value for preoperative diagnosis of SE [20].

This test acquires particular relevance in cases of previous failed antireflux surgery. Horgan et al. published their data on 48 patients who were referred for evaluation for failed antireflux surgery. They found that BS was abnormal in 90% of these patients [21]. This means BS could objectivize the failure of the previous repair in the majority of cases.

Mittal et al. analyzed preoperative BS in 31 patients; approximately half of those patients had a hiatal hernia ≥5 cm. Of these, 37% required gastroplasty. The remaining half had a hiatal hernia smaller than 5 cm. Of them, 20% required a lengthening procedure. They concluded that BS has 66% sensitivity and a positive predictive value of 37% [18].

Swanstrom et al. also published their series on laparoscopic fundoplications (n = 213) and giant paraesophageal hernia repairs (n = 25). Preoperatively, 34 (14%) patients were diagnosed with SE defined by the GEJ being > 5 cm above the hiatus. Interestingly, SE was confirmed intraoperatively in only 20% of those 34 patients [8].

Esophagogastroduodenoscopy

Esophagogastroduodenoscopy (EGD) provides information about the presence/absence of any mucosal injury such as esophagitis, Barrett's esophagus, strictures, ulcers or tumors. It is worth of mention that the absence of esophagitis on EGD does not exclude the diagnosis of GERD [22].

Mittal et al. analyzed EGD results in 39 patients with SE diagnosed preoperatively. They compared need for performing Collis gastroplasty in patients with Barrett's esophagus and/or strictures (31%) vs. patients without these findings (15%). Sensitivity for EGD was 80% while positive predictive value was 31%. They concluded that endoscopy was the best preoperative test for identifying patients who require gastroplasty [18].

Yano et al. studied the value of measuring the esophagus while performing the preoperative EGD. Endoscopic esophageal length (EEL) was defined as the distance measured from the incisors to the GEJ. Esophageal length index (ELI) was calculated as the ratio of EEL (cm) to patient height (meters). They observed that using ELI of 19.5 to stratify patients at risk for SE the false-negative rate was 19%, the positive predictive value was 81% and the negative predictive value was 83%; sensitivity was 56%. They concluded that ELI was a good indicator to identify patients who would not need a lengthening procedure [23].

Esophageal Function Tests

Esophageal Manometry

EM supplies information about motility of the esophagus and status of the lower esophageal sphincter (LES). Preoperatively, this test is crucial to exclude diagnosis such as achalasia avoiding a mistaken approach. EM also allows to accurately placing the pH probe by indicating the LES location, minimizing the risks of false-positives or false-negative results during pH monitoring [24].

In addition, EM would provide information about esophageal length. Mittal et al. performed EM in 32 patients with SE diagnosed preoperatively; 12 patients had significantly short esophageal length according to EM findings. In 9 (75%) patients the esophagus could be sufficiently mobilized, whereas 3 (25%) required a gastroplasty. Twenty patients had normal esophageal length; however, 4 (20%) of them also required gastroplasty. This grants EM a sensitivity of 43% and a positive predictive value of 25% [18]. High resolution manometry (HRM) have been introduced lately offering more accurate determinations [25].

pH Monitoring

This is the only test that can provide precise information about the presence/absence of GERD. This test will not offer any information about the existence or not of SE. However, it will serve as a reference for future follow up.

Intraoperative Assessment

While defining a SE during surgery, establishing the relationship between the GEJ and the hiatus is key. A SE is associated mostly with the presence of a large paraesophageal hernia. So, it is important to perform an adequate mediastinal esophageal mobilization (type I dissection: circumferential dissection extending 3–4 cm from the distal mediastinal esophagus [8], reduce the stomach into the abdomen, totally remove the hernia sac and also divide the short gastric vessels. Intra-abdominal esophageal length should be measured after after completing all the steps mentioned above, and in more than 90% of cases the dissection performed will be enough. Careful attention should be paid in order to avoid pulling from the stomach inferiorly. This maneuver could result confusing since it might elongate the proximal stomach resembling it to the esophagus, creating tension on the fundoplication. If there is any doubt about the location of the GEJ, intraoperative endoscopy should be used to transilluminate the esophageal wall and confirm its location [16]. Any objects exerting traction on the GEJ should be removed, including the nasogastric tube or bougie, because these can create superior displacement of the structures leading to mistakes. If at least 2.5 cm of intra-abdominal esophagus is not present (10% of patients), an extended (type II dissection: extensive mediastinal mobilization of the esophagus until the tracheal bifurcation (Fig. 13.1) [26] or inferior pulmonary veins [27]) should be performed [16]. Care should be taken to avoid

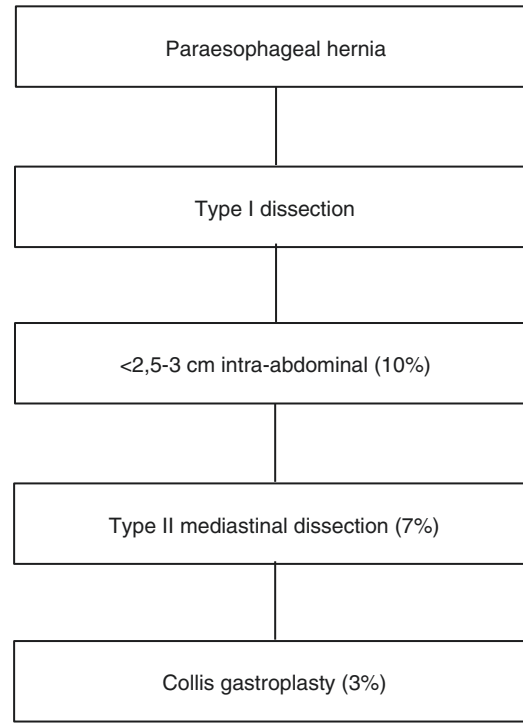

Fig. 13.1 Intraoperative assessment and decision making algorithm

injuring the right and left vagus nerves. In most cases, when a type II dissection is needed, the SE has some transmural inflammation and the vagus nerve can get trapped into the healing inflammatory tissue. A gastric emptying procedure should be considered when suspicion of having injured this nerve is present. Adequate intra-abdominal esophageal length after extended mediastinal dissection can be obtained in about 7% of patients (laparoscopic grasper's jaws can be used to measure), as shown in 106 patients, presented by Bochkarev and colleagues [11]. Mattioli et al. [28] described 180 patients undergoing surgery for the treatment of GERD. At the first measurement (after isolation of the GEJ), the median distance between the GEJ and the apex of the hiatus was equal to or shorter than 1.5 cm in 68 (37.7%) patients; at the second measurement (after full mediastinal isolation), this distance was still shorter than 1.5 cm in 34 (18.8%) patients and between 1.5 and 2.5 cm in 24 (13.4%) patients. An esophageal lengthening procedure was performed in 26 (14.4%) patients. This modification in prevalence, shows that the existence of SE is controversial and that most likely, the intraoperative diagnosis depends on the surgeon's expertise and the extension of mediastinal dissection. Independently of the prevalence rate, if the intra-abdominal esophagus is still less than 2.5 cm after a type II mediastinal dissection, then the diagnosis of SE is confirmed and a Collis-type gastroplasty is needed (Fig. 13.2).

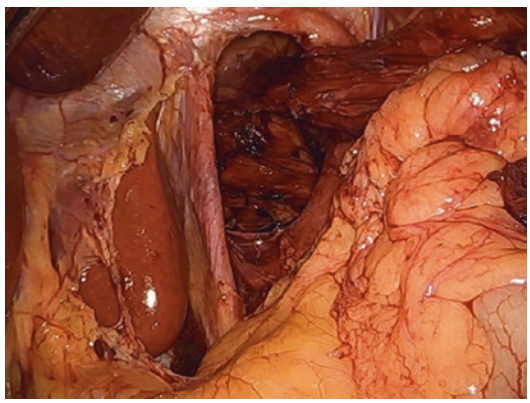

Fig. 13.2 View after mediastinal dissection was completed

Treatment Options

The first totally laparoscopic approach to a modified Collis technique was described by Johnson and colleagues [29] in 1998. With a 48-French bougie in place along the lesser curvature, a transgastric window was created in the fundus using a circular stapler. A linear stapler was then used along the bougie dividing the fundus from the fundal window to the angle of His, constructing the neo-esophagus. A floppy Nissen fundoplication was then created. Because of concerns for tissue ischemia in most cases the gastric fundus needed to be resected. This technique also needed a mini-laparotomy to introduce the circular stapler. The introduction of articulated linear staplers modified this technique and finally Terry [30] first described the stapled-wedge gastroplasty or wedge fundectomy in 2004. This technique allows performing the entire surgery through the abdomen with laparoscopic access using articulating staplers, which surgeons normally use in general surgery. After reducing the herniated stomach and removing the entire hernia sac with the epiphrenic fat pad, a 50 French bougie is placed under laparoscopic visualization and passed into the distal stomach against the lesser curvature. The ideal distance from the GEJ should be determined to ensure that at least 3 cm of esophagus or neo-esophagus lies below the hiatus. This point can be marked with a suture placed at the left edge of the bougie, to serve as a guide, marking the distal extent of the neo-esophagus. The surgeon's left-hand grasper retracts the proximal fundus (Fig. 13.3) and the assistant grasps lower on the greater curvature, which should have already been completely mobilized. These points of retraction are used to stretch the fundus laterally to the patient's left. An endoscopic articulating stapler is then completely articulated to the left. A 45/60 mm length stapler with 3.5 mm height staples (several fires) is passed across the fundus between the two grasping instruments at approximately 90° to the greater curvature towards the bougie and the guiding suture. Once the horizontal fires are completed, the stapler is straightened and a second staple line is begun towards the angle of His, parallel to the left edge of the bougie. Before firing,

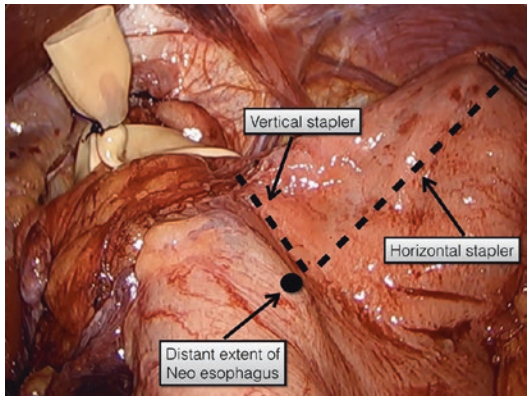

Fig. 13.3 *Dotted line* showing wedge fundectomy

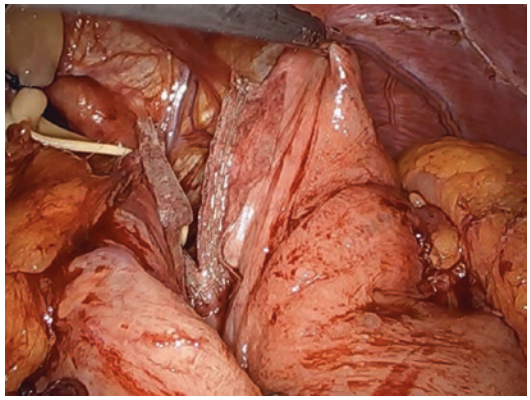

Fig. 13.4 View of the neo-esophagus after the wedge fundectomy

the posterior aspect of the stomach should be examined for redundant tissue. As long as the bougie is in position and the stapler is tight against it, the neo-esophagus will be of adequate diameter. Once this staple line has reached the angle of His, the resected portion of the proximal fundus is removed through the 12 mm trocar, without the need of a mini-laparotomy (Fig. 13.4) [31].

Novel techniques are available nowadays to assess tissue vitality. For example, fluorescence imaging with indocyanine green (ICG) provides a real time assessment of tissue perfusion. Adequate tissue perfusion after wedge fundus resection can be objectivized using ICG (Fig. 13.5).

Another technique for creating a Collis gastroplasty is through the thorax. It was described by Swanstrom and subsequently modified by Filipi

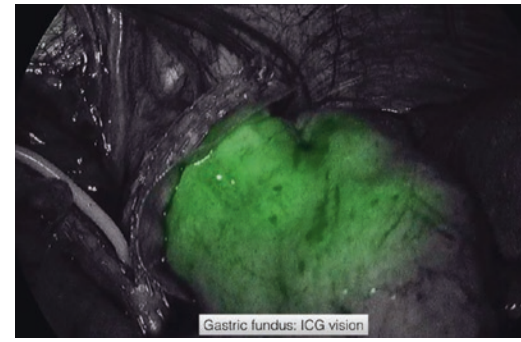

Fig. 13.5 ICG view

and combines laparoscopic and thoracoscopic approach [8, 32]. This technique does not include the wedge resection of the fundus. It has also the potential advantage of creating a shorter stapler line that may be less prone to leak. The intra-abdominal part of the surgery is identical to the first technique described. The left chest is prepped and draped. The thoracoscopy is done under dual-lung ventilation so the lung can be collapsed. A scope is then introduced into the chest to evaluate the presence/absence of adhesions and to judge the path towards the mediastinal parietal pleura just above the hiatus. Then an endoscopic stapler is introduced through the thoracic port. This stapler is passed along the anterior thoracic wall, identifying the location of its tip laparoscopically. Once the stapler is in the abdomen, it is placed adjacent to the bougie and a single stapler fire creates a 3 cm segment of neo-esophagus. The pleural defect is left open and the thoracic trocar is left in place to prevent deflation of the pneumoperitoneum. Generally, a chest tube is not required. This procedure has gained less acceptance than the wedge Collis gastroplasty because it requires thoracic surgery skills, as well as potentially resulting in increased pain from a chest incision and a higher risk of postoperative pneumothorax [33].

Results

Horgan et al. reported their experience on 31 patients who underwent surgical treatment for failed antireflux surgery. Failures were classified

according to the anatomic findings as follows: Type IA The GEJ and the wrap are above the diaphragm, Type IB The GEJ is above the diaphragm, Type II paraesophageal hernia, Type III Malformation of the wrap. They reported Type IA as the most frequent anatomic anomaly found in their series (56%). They attributed these failures to defective closure of the crura, inadequate fixation of the wrap, and/or insufficient esophageal length. According to them, SE esophagus was present in only one of those patients (3%). In the remaining patients, they were able to dissect the esophagus up into the mediastinum, attaining enough esophageal length to perform a fundoplication without tension [21].

Nason et al. published their outcomes on patients undergoing giant paraesophageal hernia repair (GPEH) with fundoplication alone (n = 341) versus fundoplication with Collis gastroplasty (n = 454) (Table 13.1). Collis gastroplasty was performed using either the EEA technique [34] or the wedge technique [35]; They concluded that adding a Collis gastroplasty to the laparoscopic repair of GPEH when needed was not detrimental to the overall outcome or quality of life [36].

Zehetner et al. reported their series of 85 patients undergoing laparoscopic Collis-Nissen gastroplasty using the wedge-fundectomy technique. At 12 months follow up, 93% of patients were free of heartburn or regurgitation. Dysphagia resolved in 71% of patients. A small recurrent hiatal hernia was seen on barium swallow in 2 patients (2.4%). They stated that the addition of a wedge-fundectomy Collis gastroplasty was a safe and effective strategy to manage a shortened esophagus [31].

Table 13.1 Comparison between Collis gastroplasty + fundoplication and fundoplication alone

Nason et al. [36]	Collis gastroplasty + fundoplication	Fundoplication alone	p
# patients	454	341	
Leak rate (%)[a]	2.7	0.6	<0.05
Resolution of symptoms	Similar en both groups		
Radiographic recurrence (%)	16.6	19.7	NS
Reoperation (%)	2.7	5	NS

[a]There were more postoperative leaks in the EEA-Collis group (3.1%) than in the wedge-Collis group (1.6%), but that was not statistically significant ($p = 0.523$)

Short Esophagus: Is It a Real Entity?

Some authors strictly deny the existence of this entity. Instead, they attribute this diagnosis to insufficient mediastinal dissection. For instance, Madan et al. publish their results on 628 fundoplications; 13 (2%) patients had a benign stricture due to advanced reflux disease. According to them, once extensive mediastinal dissection was achieved, no SE was seen. There were 16 (2.5%) recurrences. After revising every case, they concluded that none of the failures were related to SE. They rather attributed them to construction of a loose wrap, disruptions of the three stitches involved in the wrap, or improper crura closure [10].

Moreover, Bochkarev et al. operated 106 patients with GERD and suspected SE on BS. None of these patients required any esophageal lengthening procedure. After proper mobilization of the esophagus, they were able to perform a regular Nissen fundoplication in every case.

All patients had abnormal preoperative pH study results. Postoperatively the median percentage time with pH < 4 dropped from 22.76% to 1.43% ($p < 0.001$) and the DeMeester score from 67.76 to 5.03 ($p < 0.001$). All 106 patients have referred improvement of symptoms ($p < 0.001$) [11].

Concerns About Acid Secretion of Parietal Cells Left Within the Neo-esophagus

On one hand, lengthening procedures allow the surgeon to accomplish all the anatomic requirements to perform a correct fundoplication. On the other hand, there is concern about parietal cells from the neo-esophagus secreting acid into the esophagus. From the last point of view, one can

argue that the Collis gastroplasty would just change the mechanism of the presence of acid in the esophagus. The acid would be produced in situ instead of coming from the stomach. Here there are some published data concerning this subject.

In 1998 Jobe et al. studied 15 patients who had undergone Collis gastroplasty with fundoplication. They found that 50% of patients had abnormal pH studies with acid secretion from functional parietal cells in the Collis segment, and 36% had persistent esophagitis on EGD. Interestingly, despite of the objective evidence of GERD only 14% of patients complained of heartburn. At 14 months follow up, there were no recurrences on BS. They concluded that patients treated with Collis gastroplasty require close objective follow-up and maintenance acid-suppression therapy [20].

Lin et al. also studied outcomes in 68 patients after Collis gastroplasty. Symptoms were significantly improved. They were able to perform objective physiologic testing in 37% of patients. On BS, 16% of patients had recurrent hernia and 80% had either esophagitis or abnormal esophageal pH. They concluded that distal esophageal injury can persist after Collis gastroplasty and questioned the liberal application of esophageal lengthening in antireflux surgery [37].

Conversely, Chen et al., studied 33 patients undergoing Nissen fundoplication and 51 patients in whom Collis-Nissen gastroplasty was performed. The found that the prevalence of esophagitis in the Collis-Nissen group was significantly less than in the Nissen alone group. They affirmed that Collis-Nissen was associated with much better reflux control than the Nissen alone [38].

Zehetner et al. identified esophagitis in 11% of patients on EGD. They attributed the lesser rate of esophagitis compared to other series, to the placement of the fundoplication as high as possible on the gastroplasty close to the native GEJ [31].

However, it should be noticed that conclusions from the last two reports were based on EGD results, but pH monitoring was not done to objectively evaluate the presence or absence of acid in the esophagus.

Conclusions

Identification of SE is key to avoid failures after antireflux surgery. It seems that true diagnosis can only be made during intraoperative assessment. Lengthening procedures can be safely performed by laparoscopy. Special attention should be taken during follow up, since acid can still be present in the esophagus after Collis gastroplasty causing mucosal damage.

Still, for some authors the existence of this entity is a matter of debate.

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14 Esophagectomy for Failed Anti-reflux Therapy: Indications, Techniques, and Outcomes

Daniela Treitl, Robert Grossman, and Kfir Ben-David

Indications for Esophagectomy

Weekly reflux symptoms occur in approximately 20–30% of the United States population [1, 2]. The standard surgical management of reflux is laparoscopic fundoplication, with 43% of patients continuing anti-reflux medication use after surgery, and 3–18% of patients requiring reoperation, most commonly for reflux and dysphagia [3–5]. In addition to intractable recurrent symptoms, other complications after anti-reflux surgery include severe dysphagia and strictures. Thus, long term outcomes are not ideal in either medically or surgically treated patients with gastroesophageal reflux disease (GERD).

Causes for failure of initial anti-reflux operations include poor surgical technique, failure to recognize a shortened esophagus, esophagitis, and underlying motor disorders [6]. In most patients, reoperation without resection is attempted, with adjustments in technique including a lengthening procedure if warranted [6]. Achalasia, surgically treated with myotomy may lead to dysphasia and peptic strictures due to severe reflux, but it may still be amenable to revisional myotomy even in the face of severe disease [6, 7]. In the case of multiple failed reoperations, alternative treatments such as esophagectomy or gastric bypass may be warranted [8].

Esophagectomy is most commonly performed for malignant disease. However, due to the technical difficulty and associated morbidity and mortality, esophagectomy is usually a last resort in the case of benign disease, in elective, and even emergent cases [10]. Resection of the esophagus tends to be difficult for a variety of reasons, but is primarily due to the lack of a serosal layer, the inaccessibility of the organ, and the potential for rapid and dangerous infections due to the esophagus being enclosed in a bony cage [9]. Still, despite these potential complications, after multiple failed attempts at anti-reflux surgery, esophagectomy may be the only viable option [11, 12].

Progression to esophagectomy for benign disease is associated with acquired esophageal disease most commonly achalasia and GERD [13]. The indications for esophagectomy in benign disease typically stem from complications of GERD. Most commonly used as a last resort, indications include multiple failed anti-reflux operations, strictures not amenable to dilation, severe dysphasia, perforation and motility disorders such as achalasia.

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Patient Preparation

When preparing a patient for a repeat operation after a prior gastroesophageal surgery, the determination for the type of surgery should be made on a case by case basis keeping in mind patient history and physical exam in addition to preoperative studies. Preoperative studies following failed anti-reflux operations should include barium esophagram, esophagogastroduodenoscopy, esophageal manometry, 24-h pH testing, and gastric emptying studies.

Techniques

Open Techniques

A variety of techniques have been described for open esophagectomy for achalasia, many of which have formed the basis of the laparoscopic approach. These techniques include the two- and three-field transthoracic as well as the transhiatal approaches [14–20]. These techniques do not vary significantly from those described for esophageal resection in the setting of neoplasms. The three most commonly used surgeries include the Ivor Lewis or two-hole esophagectomy, the McKeown or three-hole esophagectomy, and the transhiatal esophagectomy.

The Ivor Lewis, or two-hole esophagectomy, is perhaps the most commonly used approach to esophageal resection throughout the world. First described by the Welsh surgeon Ivor Lewis, the technique involved a laparotomy and immediate thoracotomy for resection and reconstruction of the esophagus [21]. The technique also allows a variety of conduit choices to be made, either gastric, colon, or small intestine. Generally, this procedure begins in the abdomen with an upper midline laparotomy. After mobilization and construction of the conduit, normally stomach, the abdominal incision is closed and the patient is placed in left lateral decubitus position where an anterolateral thoracotomy is performed. After mobilization of the esophagus and resection, the conduit is pulled into the chest whereby a hand-sewn or stapled anastomosis is created. Drains are commonly used within the chest cavity.

The McKeown, or three-field esophagectomy, is an alternative option for resection. This technique involves thoracic and abdominal incisions followed by a cervical incision to allow for mobilization of the upper esophagus and cervical anastomosis [22]. The key steps for a McKeown esophagectomy involve performing a thoracotomy first with mobilization of the esophagus, subsequent abdominal exploration and conduit formation, and finally a cervical incision for anastomosis [22].

Initially performed by the German anatomist Denk in 1913 and subsequently performed successfully for the first time by the British surgeon Turner, the transhiatal "blunt" esophagectomy was reintroduced in 1978 to the American surgical community [23, 24]. In this technique, an abdominal incision and a cervical incision are made; after construction of the conduit, the operator's hand is inserted across the diaphragmatic hiatus and the esophagus is bluntly dissected in a distal-to-proximal fashion [23]. In a similar fashion the proximal esophagus is bluntly dissected off its attachments to the mediastinum, taking care to avoid injury to the recurrent laryngeal nerves; once the dissection is completed from both proximal and distal ends, the esophagus is delivered from the chest through either the abdominal or the cervical incision. An anastomosis is fashioned using either a hand-sewn or a stapled technique through the cervical incision and drains are placed [23].

Another technique used for some groups in the management of esophageal cancer is esophagectomy via transhiatal resection. If the operating physician is significantly experienced in performing transhiatal esophagectomy, the procedure may also be safely used for end-stage achalasia. However due to the significant vascular collaterals that can occur as well as the challenge of the mediastinal dissection, some authors favor a transthoracic approach, either Ivor Lewis or McKeown [17, 25, 26]. In our practice, we favor a minimally invasive approach.

Minimally Invasive Techniques

Upper gastrointestinal procedures are particularly amenable to a laparoscopic approach. The surgical principles involved in the open procedures have been translated into minimally invasive variations, with thoracoscopic and laparoscopic adaptations of the open procedures being first described in the early 1990s [27–30]. The Ivor Lewis esophagectomy has been adopted into a thoracoscopic and laparoscopic technique with dissection and anastomosis performed laparoscopically with transthoracic side to side stapled anastomosis or transthoracic or transoral circular anastomosis [31]. The minimally invasive McKeown operation uses thoracoscopy and abdominal laparoscopy for dissection and mobilization, with side-to-side or circular stapled cervical anastomosis [32]. The laparoscopic transhiatal esophagectomy has also been performed by some groups [33].

Thus far, there has been a small amount of literature on the use of robot assisted minimally invasive esophagectomies, with 16 articles analyzed in a recent review of the technique. The robot has been used in both transhiatal and transthoracic approaches, but most of the included literature are case series, with the predominating indication for esophagectomy being esophageal carcinoma [34].

Conduit Options

Several options have been created in response to the need for reconstruction of the esophagus, including stomach, colon, and small intestine. The stomach was the most commonly used conduit in esophageal resections for end-stage achalasia [24, 25, 35, 36]. A cervical anastomosis is the preferred method of reconstruction in the majority of studies [24, 25, 35].

The benefits of a gastric conduit include the robustness of stomach due to its excellent blood supply, the fact that only a single anastomosis needs to be created, and that esophageal surgeons who use this approach for cancer are very familiar with its transposition for benign disease [36]. The drawbacks of the procedure include a greater risk for aspiration of gastric fluid, as well as stricture of the cervical anastomosis secondary to chronic gastric reflux or ischemia [15, 37].

Segments of colon have also been advocated as a replacement conduit for esophageal resection [15, 36]. The use of a colon interposition graft is suggested to avoid the risks of anastomotic stricture, regurgitation, and dumping syndrome which may be seen with gastric conduit use [15, 36]. Peters and colleagues, suggest that a colon interposition may be of benefit in patients in whom extended survival is expected, where the conduit may last for 10 or more years [15]. Due to the length of the colon, several areas may be chosen for interposition grafting. Right, transverse, and left colon may all be used as grafts [36, 38]. A more favorable and commonly used approach is the mobilization of the distal transverse and left colon, with blood supply maintained through the left colic artery [36, 38, 39]. As described by Curet-Scott and colleagues, an isoperistaltic segment of colon is anastomosed to the posterior stomach along the greater curvature in an end-to-side fashion, with subsequent end-to-end anastomosis of colon to esophagus. Depending on the length of the colon segment used, an intra-thoracic or cervical anastomosis may be created [39]. Complete resection of the esophagus may not be necessary; a study by Hsu and colleagues demonstrated promising results for short-segment interposition of colon to replace the nonfunctional lower esophageal sphincter [17, 36].

Outcomes

Although primarily performed for oncological resection, esophagectomy has been indicated for cases of benign disease such as failed anti-reflux operations and end stage achalasia. The techniques involved are two and three field esophagectomies and transhiatal esophagectomies, with minimally invasive approaches being adopted in the recent years. Despite advances in minimally

invasive surgical techniques, esophagectomy after a prior upper gastrointestinal surgery has increased technical complexity, higher rates of morbidity and mortality and is therefore used as a last resort. Hence, the use of minimally invasive techniques, esophagectomy remains a challenging operation irrespective of the technique used.

The Ivor Lewis esophagectomy procedure is not without complications, and one study by Griffin and colleagues demonstrated a morbidity of up to 45% within their patient population. These complications included pulmonary (17%), cardiovascular or thromboembolic (7%), mediastinal leaks (4%), isolated anastomotic leaks (2%), extensive leaks from ischemic gastric conduits (1%) or gastrostomy dehiscence (1%), hemorrhage (3%), and chyle leaks (1%). Within their series, 30-day mortality for Ivor Lewis esophagectomy was found to be 2% [40].

Complications of the three-field esophagectomy are similar to those seen in the two-field procedure, but there is a notable addition. Depending on the extent of dissection, complications may be expected to occur in up to 64% of patients [41]. Due to the extent of the proximal thoracic and cervical dissections, injury may occur to the recurrent laryngeal nerves with much higher frequency than one would see with a two-field procedure [42]. This risk may be particularly pronounced when dissecting a megaesophagus for resection.

Outcomes of esophagectomies for benign disease are confounded by the majority of the patients undergoing prior gastroesophageal surgery and unlike oncologic operations, symptoms are typically present for several years prior to surgery [43]. Due to the "blind" nature of the thoracic dissection in a transhiatal esophagectomy, a very real and significant risk for hemorrhage from mediastinal vessels exists [24]. This is particularly true for the patient with end-stage achalasia, where esophageal vessels tend to be enlarged [26]. Other complications are similar to those seen in Ivor Lewis and McKeown esophagectomy [24].

Esophagectomy tends to be more technically difficult in patients with end-stage achalasia due to the enlargement of the esophagus and relevant anatomy. As described by Howard and colleagues, three reasons for this are: alteration in anatomy, with deviation of the esophagus into the right chest; hypertrophy of the muscles of the esophagus with resultant richer blood supply; and additional difficulty in mobilization of the cervical esophagus due to proximal esophageal dilation [26]. For end stage achalasia, anastomotic leak was the most frequently encountered postoperative complication (10%) followed by hoarseness (5%) and wound infection (3%) [35, 36].

Additionally, most of these patients have had previous surgeries to relieve their symptoms of dysphagia, resulting in scar tissue and adhesion formation, particularly to the lungs and adjacent aorta, which may make transhiatal mobilization in particular more difficult [26, 35]. The majority of these patients have excellent or good long-term results, including a restored ability to swallow without dietary restriction in upwards of 80% of patients [25, 36]. However, several studies have found that up to 50% of patients may have recurrent dysphagia after use of a gastric conduit, often requiring post-operative dilation [44–46].

Re-operative surgery after failed anti-reflux surgery has poorer patient satisfaction outcomes and increased risk of failure especially in the presence of abnormal motility [47, 48]. In a retrospective study evaluating a single institution's experience with esophagectomy after fundoplication, higher morbidities were seen in patients with prior anti-reflux surgery, with increased risk associated with increased number of prior anti-reflux surgery. Patients had significantly higher postoperative complications in (62.5%), higher anastomotic leak rates (21.5%) regardless of operation type and significantly higher risk of reoperation [49].

The largest study to date is from another single institution that retrospectively reviewed patients with benign disease who underwent esophagectomy with and without previous gastroesophageal surgery. Reasons for esophagectomy were mostly related to GERD and hiatal hernia, and included high grade dysplasia, obstructive strictures not amenable to dilation, recurrent reflux and hiatal hernia after multiple

operations [47]. Having a prior operation was significantly related to increased blood loss and need for reoperation, with 14% of patients undergoing reoperation in the prior surgery group, and were more likely to require anastomotic dilatations. Complications were not significantly different, including anastomotic leaks and vocal cord palsy. Fewer patients in the prior operation group underwent transhiatal resection than in the group with no prior operations (84% vs 98%). In addition conduit location differed between the two groups, with less patients with prior gastroesophageal surgery having a gastric conduit and more requiring a colonic conduit [47]. Other series echo using a colonic conduit in patients with prior anti-reflux operations [48, 50]. Despite most cases being redo operations, some larger centers still prefer a gastric conduit to replace esophagectomies for benign disease, though colonic and jejunal conduits can also be performed in patients with inadequate stomachs [43]. In terms of quality of life, self-assessment tools have been used with a variety of outcomes ranging from good to poor, with no significant factors affecting quality of life [50, 51].

Conclusions

Although challenging as a repeat operation, esophagectomy can be performed after failed anti-reflux procedures. Complication rates of esophagectomy occur more frequently after prior gastroesophageal surgery. Different strategies for avoiding complications after prior gastroesophageal surgery could include ischemic preconditioning or choice of conduit other than stomach.

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