Preoperative Diagnostic Workup before Antireflux Surgery: An Evidence and Experience-Based Consensus of the Esophageal Diagnostic Advisory Panel

Blair A Jobe, MD, FACS, Joel E Richter, MD, Toshitaka Hoppo, MD, PhD, Jeffrey H Peters, MD, FACS, Reginald Bell, MD, FACS, William C Dengler, MD, FACS, Kenneth DeVault, MD, Ronnie Fass, MD, C Prakash Gyawali, MD, Peter J Kahrilas, MD, Brian E Lacy, MD, PhD, FACG, John E Pandolfino, MD, Marco G Patti, MD, FACS, Lee L Swanstrom, MD, FACS, Ashwin A Kurian, MD, Marcelo F Vela, MD, Michael Vaezi, MD, Tom R DeMeester, MD, FACS

BACKGROUND: Gastroesophageal reflux disease (GERD) is a very prevalent disorder. Medical therapy improves symptoms in some but not all patients. Antireflux surgery is an excellent option for patients with persistent symptoms such as regurgitation, as well as for those with complete symptomatic resolution on acid-suppressive therapy. However, proper patient selection is critical to achieve excellent outcomes.

STUDY DESIGN: A panel of experts was assembled to review data and personal experience with regard to appropriate preoperative evaluation for antireflux surgery and to construct an evidence and experience-based consensus that has practical application.

RESULTS: The presence of reflux symptoms alone is not sufficient to support a diagnosis of GERD before antireflux surgery. Esophageal objective testing is required to physiologically and anatomically evaluate the presence and severity of GERD in all patients being considered for surgical intervention. It is critical to document the presence of abnormal distal esophageal acid exposure, especially when antireflux surgery is considered, and reflux-related symptoms should be severe enough to outweigh the potential side effects of fundoplication. Each testing modality has a specific role in the diagnosis and workup of GERD, and no single test alone can provide the entire clinical picture. Results of testing are combined to document the presence and extent of the disease and assist in planning the operative approach.

CONCLUSIONS: Currently, upper endoscopy, barium esophagram, pH testing, and manometry are required for preoperative workup for antireflux surgery. Additional studies with long-term follow-up are required to evaluate the diagnostic and therapeutic benefit of new technologies, such as oropharyngeal pH testing, multichannel intraluminal impedance, and hypopharyngeal multichannel intraluminal impedance, in the context of patient selection for antireflux surgery. (J Am Coll Surg 2013;217:586−597. © 2013 by the American College of Surgeons)

Abbreviations and Acronyms

BE	=	Barrett esophagus
GERD	=	gastroesophageal reflux disease
HMII	=	hypopharyngeal multichannel intraluminal impedance
LA	=	Los Angeles
LES	=	lower esophageal sphincter
LPR	=	laryngopharyngeal reflux
MII	=	multichannel intraluminal impedance
PPI	=	proton pump inhibitor
SAP	=	symptom association probability
SI	=	symptom index

Gastroesophageal reflux disease (GERD) is the most common esophageal disorder in Western countries. Epidemiologic studies have demonstrated that as many as 7% of Americans have episodes of heartburn every day, and approximately 42% experience heartburn at least once a month.[1,2] Symptoms of gastroesophageal reflux negatively affect patient quality of life. Research studies have established that some patients with GERD have a worse quality of life than those with angina or congestive heart failure.[3] Gastroesophageal reflux disease is associated with the retrograde flow of gastric and duodenal contents into the esophagus, and potentially reaching proximal organs, such as the larynx and airway, causing a wide variety of symptoms with or without tissue damage.[4,5] Gastroesophageal reflux disease causes typical symptoms, such as heartburn (a retrosternal burning sensation), regurgitation, and dysphagia, and atypical symptoms, such as cough, hoarseness, globus sensation, and throat clearing. Additionally, GERD can contribute to development of pulmonary diseases, such as adult-onset asthma[6] and idiopathic pulmonary fibrosis.[7] It is important to keep in mind that these extraesophageal presentations can have multifactorial, often non-GERD, causes, and causality between reflux and these clinical entities is difficult to prove.

The primary treatment options for GERD include medical therapy (eg, proton pump inhibitors [PPIs] and/or H2 receptor antagonists) and laparoscopic surgical reconstruction (fundoplication). Most patients with GERD are initially treated with acid-suppressive therapy using PPIs and/or H2 receptor antagonists. A recent systematic review demonstrated that despite adequate acid suppression, 32% of patients in randomized studies and 45% in observational studies were found to have persistent symptoms.[8] Although antisecretory medications reduce or eliminate the symptom of heartburn by increasing the pH of gastric secretions, this therapy does not address the anatomically defective antireflux barrier and episodes of weakly acidic esophageal exposure that continue unabated in some patients. That said, not all patients who fail to respond to medical therapy have GERD and, in some, the ongoing symptoms are due to non-GERD causes or even a functional gastrointestinal disorder. With this in mind, it is very important to study these patients adequately to distinguish those with ongoing symptoms due to GERD vs non-GERD causes. When performed by an experienced surgeon, laparoscopic fundoplication is highly effective in patients with typical GERD symptoms (eg, heartburn and regurgitation) and documented abnormal esophageal acid exposure. However, the long-term outcomes of antireflux surgery have varied depending on the center, from a 61% patient satisfaction rate in a US community setting[9] to up to 94% in experienced centers (>10 years postoperative follow-up).[10,11]

Although GERD is a common entity, the diagnosis of GERD is not easy or straightforward for a number of reasons. First, symptoms are nonspecific.[12] Second, clinical presentation is heterogeneous, depending in part on an individual's perception of their symptoms. Third, there is considerable overlap with other upper gastrointestinal disorders, such as functional dyspepsia and gastroparesis.[13,14] In fact, up to 30% of patients who present with a primary report of GERD symptoms do not have abnormal distal esophageal acid exposure and would not benefit from fundoplication.[15,16] Therefore, objective esophageal testing is critical to document the presence of GERD, especially when surgical treatment is considered. The goal of preoperative esophageal testing is to establish the presence of abnormal distal and proximal esophageal acid exposure and correlate reflux events with symptoms. The testing can include upper endoscopy, barium esophagram, pH testing, esophageal manometry (high-resolution manometry if available), multichannel intraluminal impedance (MII) pH, and, in selective cases, a radiolabeled gastric emptying study. Each testing modality has a specific role in the evaluation of GERD and results are combined to "paint the picture" of disease and assist in planning the operative approach. The Society of American Gastrointestinal and Endoscopic Surgeons recommended that the diagnosis of GERD can be accepted if at least one of the following conditions exists: mucosal break seen on endoscopy in a patient with typical symptoms, Barrett esophagus (BE) confirmed on histology, peptic stricture in the absence of malignancy, or positive pH testing. These recommendations were based on a review of existing literature.[17] In the era of PPIs, the severity of mucosal injury encountered in the workup of GERD has been reduced, and new technologies have been introduced in an attempt to improve the sensitivity

of GERD diagnosis in patients being considered for anti-reflux surgery. The purpose of this consensus conference and the subsequent article was to define the optimal preoperative diagnostic evaluation before primary antireflux surgery and to construct an evidence and experience-based consensus with practical application. The workup and management of reoperative antireflux surgery was not discussed as part of this consensus.

ESOPHAGEAL DIAGNOSTIC ADVISORY PANEL

Experts who manage GERD, including gastroenterologists and surgeons, in both academic and community practices were assembled as the Esophageal Diagnostic Advisory Panel to achieve a practical consensus on the optimal preoperative diagnostic evaluation before antireflux surgery at Digestive Disease Week 2012 in San Diego, CA on May 19, 2012. Given Imaging, who provided funding for honoraria and logistical support to organize the meeting, sponsored the Esophageal Diagnostic Advisory Panel. Members of Given Imaging were present for the meeting, however, they were not involved in constructing the consensus statement or preparing the article. Drs Richter and Jobe framed the topics and questions addressed by the panel.

To provide consensus for practice in the United States with attention to Food and Drug Administration labeling issues and insurance considerations, the members of the Esophageal Diagnostic Advisory Panel were selected from the United States based on criteria developed by the 2 chairs of the meeting (Drs Jobe and Richter) to enhance the discussion and assemble the clinical experience of each member to construct an evidence and experience-based consensus. Chairs led a free discussion on each question and at the end of each discussion an informal vote was held to determine a consensus. The meeting was recorded and the chairs reviewed the transcript. A draft was generated and distributed to each member for review and edits. Once all issues were addressed, a final document with consensus was generated and sent back to the members for final approval.

Is a symptom-based diagnosis of gastroesophageal reflux disease sufficient for antireflux surgery?

Preoperative evaluation starts with meticulous history taking, including clinical symptoms (typical vs atypical); use of antisecretory medication; existing comorbidities; and additional symptoms, such as bloating, nausea, vomiting, and diarrhea, all of which can affect the outcomes of antireflux surgery (Table 1). The first panel discussion centered on the question: are symptoms alone (typical and atypical) or with PPI response sufficient to support

a diagnosis of GERD before antireflux surgery? It was noted that the clinical presentation of GERD is heterogeneous and dependent on an individuals' perception, with or without PPI response. In the DIAMOND study, the sensitivity and specificity for the symptom-based diagnosis of GERD in patients with heartburn and/or regurgitation is 49% and 74%, respectively, and symptomatic response to a 2-week course of PPI did not improve the diagnostic yield.[19,20] In addition, previous work has demonstrated that PPI therapy is associated with a considerable placebo effect, especially in patients with extraesophageal symptoms.[21,22] It is noted that the symptoms of both functional dyspepsia[14] and irritable bowel syndrome[23] can overlap with those of GERD, and a GERD-specific questionnaire might not adequately distinguish these 3 entities. Based on these considerations, the consensus of the Esophageal Diagnostic Advisory Panel was that symptoms by themselves or their responsiveness to PPIs are not sufficient criteria to support a diagnosis of GERD before antireflux surgery.

This statement is supported by the recent recommendations issued by the Esophageal Diagnostic Working Group,[24] stating that symptom type or severity is a poor predictor of baseline GERD status, especially for extraesophageal symptoms, thereby highlighting the necessity to document objective findings of GERD in patients not responding to PPI therapy in whom an antireflux procedure is being contemplated. Although not formally addressed by the panel, some believed that the outcomes of an antireflux procedure should be assessed based not only on patient-reported symptomatic improvement, but also with anatomic (eg, resolution of esophagitis) and physiologic (eg, normalization of distal esophageal acid exposure using pH monitoring) benchmarks.[25] Table 2 highlights the currently available testing modalities, the rationales for performing the tests, the result that would best support the decision to proceed with antireflux surgery, and potential pitfalls associated with each test.

Testing for esophageal structural abnormalities
Upper endoscopy
Esophageal mucosal injury, such as esophagitis or BE, is a very specific but not sensitive indicator for the presence of GERD. Mucosal injury occurs secondary to predisposing factors, including a mechanically defective lower esophageal sphincter (LES), poor esophageal motility, hiatal hernia, and a subsequent increase in esophageal exposure to gastric refluxate with a pH <4.[26] To objectively describe the severity of esophagitis, the Los Angeles (LA) Classification was introduced into practice[27]; however, LA grades A and B esophagitis can be

Table 1. Approach to the Patient Being Evaluated for Antireflux Surgery

Goals in preoperative evaluation prior to ARS
Define symptoms potentially attributable to GERD
Understand comorbid conditions as they relate to surgical risk
Objectify GERD with physiology testing
Identify esophageal anatomic abnormalities
Identify esophageal functional abnormalities
Set expectations with patient
Plan surgical approach
History and expectation setting
Query typical versus atypical symptoms
Exclude non-GERD causes of typical and atypical symptoms
Understand primary and secondary symptoms ("if you could only pick one to eliminate")
Gauge the degree of response to and dependence upon antisecretory therapy
Query for non-GERD associated symptoms such as bloating, emesis, nausea, vomiting, diarrhea
Ask about eating disorder
Counsel patient as to the probability of success

(Reprinted from Watson and Peters,[18] with permission.)
ARS, antireflux surgery; GERD, gastroesophageal reflux disease.

diagnostically nonspecific,[16] and there can be unacceptable inter-observer variability.[28] Based on this observation and much debate within the consensus panel, we reached the ultimate decision that patients with endoscopic findings of LA grade A or mild B esophagitis require pH testing to document the presence of GERD, and those with LA grade C or D do not need it, providing that pill esophagitis and achalasia have been excluded. It was noted that in the era of PPI therapy, endoscopic findings of esophagitis are much less common, and the absence of esophagitis in no way excludes a diagnosis of GERD. Ambulatory pH testing can be used with any classification of esophagitis if there is ambiguity related to the diagnosis or if the clinician wishes to gauge the severity of reflux as a baseline before surgery.

Nonerosive reflux disease is thought to be a distinct phenotype of GERD that can be subcategorized into the following types based on the results of pH testing: patients with an abnormal pH test but no mucosal injury; patients with a normal pH test but with symptoms and reflux events that temporally correlate, suggesting acid hypersensitivity; and patients with a normal pH test and no symptom correlation with reflux events.[29] Patients with an abnormal pH test but no mucosal injury are commonly encountered, and these patients require additional testing to document the presence of pathological GERD. In these patients, it is particularly important that a meticulous surgical history and/or history of other gastrointestinal symptoms (eg, irritable bowel syndrome) be obtained to carefully consider whether the correction of abnormal acid exposure by antireflux surgery will worsen the existing non-GERD gastrointestinal symptoms. A patient with pH-negative nonerosive reflux disease might not be adequately treated with antireflux surgery, and it is important to identify these patients with objective testing. The Esophageal Diagnostic Advisory Panel did not formally discuss these subcategories of nonerosive reflux disease and, in post-hoc discussions, agreed that there might be insufficient data to support clinical decision making based on this taxonomy; however, all participants agreed that the use of antireflux surgery in patients with a negative pH test should be avoided. In patients with suspected GERD and a negative pH test, it is critically important to eliminate any errors in pH testing, such as a misplaced pH probe, and to measure the esophageal acid exposure using the composite pH score.[12] Because the differential between normal and abnormal acid exposure in early-stage disease is extremely small, errors in pH testing are more likely to occur; the composite pH score might provide a more detailed evaluation of the patterns of acid exposure in these patients so that subtle differences are not overlooked. A pH probe should be carefully positioned based on the manometric measurement of the upper border of the LES and a measured delivery catheter containing the pH capsule inserted through the nose. Alternatively, a measured nasogastric tube can be placed through the nose to target the site of attachment and the delivery catheter containing the pH capsule inserted through the mouth and attached under endoscopic control.

Barrett esophagus represents an advanced form of GERD defined as a columnar-lined segment of esophagus visible on endoscopy in conjunction with pathologic findings of intestinal metaplasia with the presence of goblet cells. There is a distinction between short-segment BE (<3 cm) and long-segment BE (≥3 cm), and the validated Prague classification has been used to objectively describe the endoscopic appearance of BE. However, this classification system can be associated with inter-observer variability, especially involving short-segment lesions with <1-cm length of BE.[30] In addition, this study demonstrated that approximately 50% of patients who had endoscopic findings of short-segment BE were confirmed histologically.[31] Based on these findings, we believed that short-segment BE still requires additional documentation to validate the presence of GERD, although histologically confirmed short-segment BE is diagnostic of GERD. The consensus was that patients with long-segment BE (≥3 cm) do not require pH testing; however, those with short-segment BE (<3 cm), including intestinal metaplasia of the cardia, require pH testing to document the presence of GERD before antireflux surgery.

Table 2. Overview of Esophageal Testing Modalities to Be Considered in Patients Being Evaluated for Antireflux Surgery

Testing modality	Required in every patient considered for ARS	Principal reasons the test is performed	Result that supports GERD diagnosis and might suggest success with ARS	Potential pitfall
Symptom stratification	Yes	Symptom type is predictor of surgical outcomes	HB, regurgitation	Symptoms unrelated to GERD
PPI test	No	Response supports diagnosis and is a predictor of surgical outcomes	PPI dependence to control primary symptom	Intolerance of PPI; placebo effect; symptomatic nonacid reflux
Barium esophagram	Yes	Evaluate global anatomy for structural problem	Hiatal hernia (any size) and reflux to level of clavicles	Normal examination; poor-quality examination
Upper endoscopy	Yes	Evaluate mucosa for BE and esophagitis	Esophagitis	Normal examination
Esophageal manometry	Yes	Rule out achalasia and plan surgical approach	Defective LES, intact effective peristalsis	Error in interpretation
Off-PPI pH testing	Yes (unless LA C, LA D, or long-segment BE on endoscopy)	Document pathologic acid reflux and correlate reflux events with symptoms, especially in patients with nonerosive GERD	Positive pH test and/or positive symptom correlation for HB, chest pain, or regurgitation	Atrophic gastritis; lactic acid production in achalasia; wrong position of pH probe; positive test in patients with eating disorder
Gastric emptying study	No	Evaluate for delayed gastric emptying in patients with bloating and/or nausea in the face of a normal LES pressure and length	Normal gastric emptying study	Gastric outlet obstruction "masquerading" as delayed gastric emptying
HMII-pH and MII-pH	No (the addition of impedance to standard pH testing might be advantageous, especially in patients on PPI or those with laryngeal symptoms)	Understand the contribution of symptomatic nonacid reflux in the face of PPI therapy	Symptom correlation with nonacid reflux events combined with a positive pH test	HMII distal pH probe misplaced leading to inaccurate pH test

ARS, antireflux surgery; BE, Barrett esophagus; HB, heartburn; HMII, hypopharyngeal multichannel intraluminal impedance; LA, Los Angeles; LES, lower esophageal sphincter; LPR, laryngopharyngeal reflux; PPI, proton pump inhibitor; MII, multichannel intraluminal impedance.

Barium esophagram

Barium esophagram provides anatomic and functional information on esophageal length, presence and size of hiatal hernia, diverticulum, esophageal stricture, as well as the presence of gastroesophageal reflux events with provocation. The esophagram is ideally a video-recorded examination to evaluate the dynamic changes of the esophagus in terms of esophageal peristalsis, bolus transport, and reducibility of hiatal hernia. One potential objective of the preoperative esophagram is to differentiate between a type III paraesophageal (mixed) hernia and type I sliding hernia, as upper endoscopy can be inaccurate in this context.[32] The consensus of the Esophageal Diagnostic Advisory Panel was that all patients who are considered for antireflux surgery require barium esophagram. A type III paraesophageal (mixed) hernia is associated with progression of symptoms (heartburn, dysphagia, chest pain, regurgitation) in up to 45% of patient without surgical intervention,[33] and also significant, sometimes catastrophic, complications, such as torsion, gangrene, perforation, and massive hemorrhage.[34] Based on this, a paraesophageal hernia should be electively repaired regardless of whether patients have documented GERD; contrast esophagram, upper endoscopy, and manometry should be performed as for GERD because an antireflux procedure is most often performed as an integral component of this procedure (pH is not required in these patients). It should be noted that the optimal preoperative evaluation of paraesophageal hernia was not discussed as part of this consensus panel.

It is noted that barium esophagram is not dependable in GERD patients with a large hiatal hernia or peptic stricture in the preoperative determination of short esophagus that will require Collis gastroplasty. This is supported by previous studies demonstrating that preoperative esophagram and manometry are not reliable predictors of the short esophagus (sensitivity 66% and 43%, respectively),[35] and the endoscopic findings of either a stricture or BE are the most sensitive indicators that a lengthening procedure might be necessary.[35,36] This examination raises awareness of the possibility of short esophagus, thereby enabling more detailed preoperative counseling and planning. Because the quality of a given esophagram is highly variable among radiologists and institutions, a standardized protocol that highlights the important aspects of anatomy and function (presence and type of hernia, reducibility of hernia in the upright position, signs of obstruction, presence and level of gastroesophageal reflux, motility status, diverticulum, and provocative maneuvers) is suggested.

Testing for esophageal physiology abnormalities
Esophageal manometry

Esophageal manometry is the most reliable method to assess the function of the LES and the esophageal body. Patients with GERD might have manometric findings of a defective LES (approximately 60%)[26,37] or impaired esophageal motility that is associated with the severity of esophagitis (25% of patients with mild esophagitis had impaired esophageal motility vs 48% of those with severe esophagitis).[38] The primary purposes of performing esophageal manometry before antireflux surgery are to exclude achalasia, which might be misdiagnosed as GERD; assess peristaltic coordination and contractile force of the esophageal body based on which antireflux surgery can be tailored (total vs partial fundoplication); and measure the precise location of the gastroesophageal junction for accurate pH probe or impedance catheter placement. The clinical application of 32-channel high-resolution manometry has made esophageal manometry easier, faster, and more accurate. High-resolution manometry provides real-time monitoring of contractile activity over the entire esophageal length and, when coupled with impedance, measures effectiveness of bolus clearance with each swallow. However, there have been no controlled data to support the therapeutic benefit of tailoring the degree of fundoplication based on preoperative esophageal motility status.[39,40] Based on these findings, the consensus of the Esophageal Diagnostic Advisory Panel was that esophageal manometry should be performed in all patients being considered for antireflux surgery to exclude achalasia, and esophageal manometry can be useful to guide the type of antireflux surgery, as patients with frequent failed peristalsis and/or weak peristalsis with peristaltic defects might have less dysphagia with partial fundoplication. The Esophageal Diagnostic Advisory Panel did not discuss the type of partial fundoplication that should be used in the context of peristaltic failure.

Esophageal pH testing with/without impedance

Ambulatory pH testing is the gold standard to determine if there is pathological GERD. This can be done via a transnasal catheter for 24 hours or the wireless pH system, which collects 48 hours of pH data.[41,42] It has been reported that 48-hour pH testing can increase detection accuracy and sensitivity for abnormal esophageal acid exposure by as much as 22%.[43] Previous studies demonstrate that an abnormal 24-hour pH test in a PPI-dependent patient with typical symptoms predicts successful outcomes with antireflux surgery,[44] and those with typical symptoms without an abnormal pH test are less likely to have successful outcomes.[45] Recently,
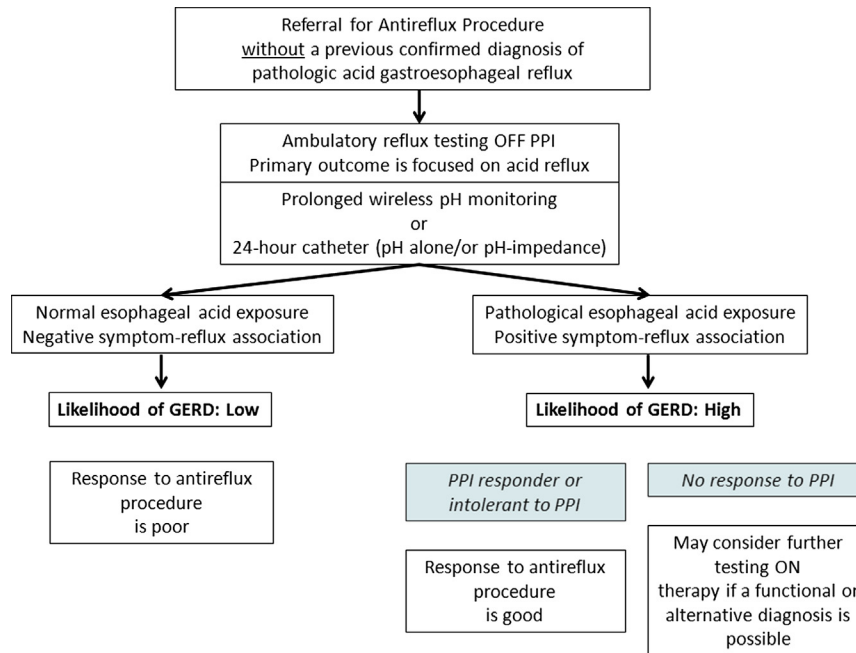
Figure 1. The approach to patients with gastroesphogeal reflux disease symptoms not responding to medical therapy, constructed by the Esophageal Diagnostic Working Group.

the Esophageal Diagnostic Working Group published their recommendations on the appropriate use of wireless pH testing,[24] stating that documentation of pathologic acid gastroesophageal reflux off acid suppression is an important measurement in the management of GERD in patients not responding to PPI therapy and those being considered for antireflux surgery (Fig. 1). Similarly, the consensus of the Esophageal Diagnostic Advisory Panel was that pH testing at least 7 days off acid suppression should be performed in all patients with nonerosive GERD, those with LA Classification grade A or mild B esophagitis, and in patients with short-segment BE (<3 cm).

Esophageal pH testing can be combined with MII-pH. Because MII-PH can detect any type of reflux event (acid, pH <4; weak acid, pH 4 to 6; and nonacid, pH >6; nonacid) regardless of pH, it is a promising tool to evaluate GERD, especially in patients who are refractory or unresponsive to PPI therapy.[46,47] Three studies involving healthy subjects have established normative values for ambulatory 24-hour MII-pH for a specific catheter configuration.[48-50] Using these data as a reference point, subsequent studies have demonstrated that both the numbers of reflux events and GERD symptoms improved after antireflux surgery in patient groups with symptomatic acid and nonacid reflux on PPI therapy.[51,52] There are 3 studies (1 in abstract form) that have established the normative MII-pH values in patients on acid

suppression.[53,54] However, a recent study involving 237 patients with GERD did not show any benefit of 24-hour MII-pH on acid suppression to predict the outcomes of antireflux surgery; the implication of this study is that the role of antireflux surgery in patients with abnormal nonacid reflux on acid suppression remains unclear.[55] The consensus of the panel was that there is insufficient data to justify the decision to proceed with antireflux surgery in patients with a positive MII-pH on acid suppression who are refractory to PPI therapy or in patients who had a negative pH test but an abnormal number of reflux events as measured by MII-pH. The Esophageal Diagnostic Advisory Panel recognized the need for additional studies to clarify the role of MII-pH monitoring findings to select patients for antireflux surgery. They agreed that if a pH study was performed on acid suppression that resulted in a positive pH test, regardless of whether it is combined with impedance, that positive study could be used to select a patient for antireflux surgery; however, the same abnormal values off acid suppression should be used to determine if there is pathologic GERD.

Symptom association and pH testing

It is important to determine if there is any correlation between patients' symptoms and reflux events. A symptom is usually considered to be associated with a reflux event if it occurs within a 2-minute interval after

the reflux event. The Symptom Index (SI)[56] and the Symptom Association Probability (SAP)[57] are commonly used to evaluate the temporal association between clinical symptoms and reflux events. The SI provides an assessment of the overall strength of the relationship, and any SI $\geq$50% is considered positive.[58] The SAP determines whether this relationship could have occurred by chance, and an SAP >95% is statistically significant.[57] However, the SI and SAP, which are calculated by the analysis software without manual reading of the tracings, were validated only for acid-related (not nonacid by MII-PH) heartburn, regurgitation, and chest pain, and are highly dependent on the numbers of symptoms provided by patients during the testing period. Patients who have a positive SI and/or SAP in the evaluation of typical symptoms likely have GERD as the cause of their symptoms; however, the primary issue of whether there is hypersensitivity to acid exposure or a component of functional heartburn is not addressed by this scoring system. Although there is some evidence to support the effectiveness of antireflux surgery in patients with esophageal hypersensitivity,[59] this is a clinical scenario that requires individualization and careful preoperative counseling. The Esophageal Diagnostic Advisory Panel believed that the decision to proceed with antireflux surgery should not be made based solely on a positive SI and/or SAP. It is noted that the reflux-related symptoms should be severe enough to outweigh the potential side effects of antireflux surgery, and this should be reflected in long-term post-procedure quality of life improvement.[60,61]

Gastric emptying

Delayed gastric emptying causes bloating, abdominal distension, and nausea; however, these symptoms are not specific for gastroparesis, and functional dyspepsia has the similar, nonspecific upper gastrointestinal symptoms as gastroparesis. A 4-hour solid-phase gastric emptying study has been recommended[62]; however, it cannot distinguish patients with functional dyspepsia from those with nondiabetic gastroparesis, given that 30% of patients with functional dyspepsia have delayed gastric emptying.[63] Approximately 20% of patients with GERD have some degree of delayed gastric emptying by scintigraphic assessment. Fundoplication improves gastric emptying in patients with GERD by reducing the capacity of the fundus reservoir and/or the radius of the proximal stomach, generating a higher intraluminal pressure and promoting the passage of food bolus.[64-66] However, persistent delayed gastric emptying can lead to unsatisfactory outcomes of antireflux surgery and worsen the gas-bloat symptoms that can occur after this operation. Currently, there are no established

preoperative gastric emptying study cut-off values that predict worsening of postoperative gas bloat, although delayed gastric emptying is currently defined as tracer retention >90% at 1 hour, 60% at 2 hours, and 10% at 4 hours.[67] A large prospective trial involving 372 patients with GERD who had undergone fundoplication, demonstrated that 31% of patients were found to have delayed gastric emptying preoperatively; however, there was no relationship between preoperative gastric emptying status and outcomes of fundoplication.[68] The gastric emptying study is not a routine part of the preoperative workup before anti-reflux surgery. The consensus of Esophageal Diagnostic Advisory Panel was that a gastric emptying study should be obtained selectively in the preoperative evaluation of patients with significant nausea, vomiting, and bloating or those with retained food in the stomach after an overnight fast on endoscopy. The study should be performed for 4 hours, not 2 hours.

Objective testing for laryngopharyngeal reflux

Laryngopharyngeal reflux (LPR) has been recognized as a common entity, affecting approximately 20% of the American population.[69,70] However, these symptoms can also be associated with coexisting causative factors other than GERD, such as tobacco/alcohol abuse, allergies, postnasal drip, and chronic sinusitis, which irritate the hypopharynx. A 3-month trial of empiric PPI therapy has been recommended as an initial step in the diagnosis and treatment of LPR[71]; however, recent meta-analyses demonstrated no therapeutic benefit of PPIs in this setting.[72,73] The outcomes of antireflux surgery when performed for LPR symptoms are less favorable compared with those achieved in patients with typical GERD symptoms, because of the potentially multifactorial nature of LPR symptoms (ie, non-GERD causes) and absence of a testing modality with sufficient sensitivity to directly measure LPR events, establishing GERD as the underlying cause. Recently, 2 promising tools including oropharyngeal pH testing (Restech; Respiratory Technology Corporation) and hypopharyngeal multichannel intraluminal impedance (HMII-pH) (Sandhill Scientific Inc.) have been introduced and investigated.

The oropharyngeal pH catheter is a device used to measure oropharyngeal acid reflux and attempts to establish the temporal relationship between extraesophageal reflux symptoms and LPR acid events. The device has an ion flow sensor that enables accurate measurement of the pH in both liquid and aerosolized droplets in the oropharynx. Several studies to evaluate the diagnostic benefit of oropharyngeal pH testing have been reported in patients with LPR symptoms.[74-76] However, there are

Table 3. Experience-Based Consensus Statements Developed by the Esophageal Diagnostic Advisory Panel

Testing approach	Consensus statement based on provider experience
Symptom stratification and PPI test	Symptoms with or without a PPI response are not sufficient to support a diagnosis of GERD when considering antireflux surgery.
Upper endoscopy—esophagitis	Endoscopic findings of Los Angeles grade A or mild B esophagitis require pH testing to document the presence of GERD, and those with Los Angeles grade C or D do not, provided pill esophagitis and achalasia have been excluded.
Upper endoscopy—Barrett esophagus	Patients with long-segment BE (≥3 cm) do not require pH testing; however, those with short-segment BE (<3 cm), including intestinal metaplasia of the cardia, require pH testing to document the presence of GERD before antireflux surgery.
Barium esophagram	Patients who are considered for antireflux surgery require esophagram.
Esophageal manometry	Manometry should be performed in all patients being considered for antireflux surgery to exclude achalasia. Manometry can be useful to tailor antireflux surgery as patients with frequent failed peristalsis and/or weak peristalsis with peristaltic defects can have less dysphagia with partial fundoplication.
pH testing	pH testing 7 days off acid suppression should be performed in all "nonerosive" GERD patients and those with Los Angeles grade A or mild B esophagitis.
pH testing with or without MII	A positive pH test on acid suppression, regardless of whether it is combined with impedance can be used to select a patient for antireflux surgery. In this context, the same cut-offs as with testing off acid suppression should be used to define pathologic GERD.
Symptom association scoring	The decision to proceed with antireflux surgery should not be based solely on a positive SI and/or SAP. It is important that the reflux-related symptoms be severe enough to outweigh the side effects of antireflux surgery.
Gastric emptying	A gastric emptying study should be obtained selectively in patients with significant nausea and bloating or those with retained food in the stomach after an overnight fast. When done, the test should be performed for 4 hours, not 2 hours.
Dual pH probe and HMII	A dual pH probe and/or HMII, not standard pH testing, can be performed in patients with LPR symptoms, However, the minimum justification for antireflux surgery in patients who undergo HMII is abnormal acid exposure in the distal esophagus with the pH monitor located 5 cm proximal to the upper border of the LES.

BE, Barrett esophagus; HMII, hypopharyngeal multichannel intraluminal impedance; HRM, high-resolution manometry; LES, lower esophageal sphincter; LPR, laryngopharyngeal reflux; PPI, proton pump inhibitor; MII, multichannel intraluminal impedance; SAP, symptom association probability; SI, symptom index.

currently no data available to support the decision to proceed with antireflux surgery based on the results of oropharyngeal pH testing.

The HMII-pH is a specialized impedance catheter that has been introduced as a tool to directly measure reflux events in the hypopharynx and proximal esophagus.[53,54] The potential benefit of HMII-pH in detecting LPR events has been reported in the management of certain pulmonary and laryngeal conditions, such as end-stage lung disease, adult-onset asthma, and chronic cough.[53,77,78] However, there is a paucity of data supporting that the addition of HMII-pH has improved patient selection and outcomes of antireflux surgery. Well-designed, prospective studies with long-term follow-up are required.

The Esophageal Diagnostic Advisory Panel did not support making the decision to perform antireflux surgery based on the results of either of these tests alone. The Esophageal Diagnostic Advisory Panel agreed that a dual pH probe and/or MII-pH can be performed in patients with LPR symptoms, however, the minimum justification for antireflux surgery in patients who undergo these studies is positive acid exposure in the distal esophagus at a location 5 cm proximal to the upper border of the LES as measured with manometry or upper endoscopy. The consensus of Esophageal Diagnostic Advisory Panel was that these tests are promising, but objective evidence of GERD as measured by standard esophageal physiology testing is still required before antireflux surgery.

CONCLUSIONS

Gastroesophageal reflux disease is a highly prevalent disorder. Medical therapy improves symptoms in some, but not all patients. Antireflux surgery is a valid option for not only those with persistent symptoms, especially patients with volume regurgitation, but also those with complete symptomatic resolution on acid suppressive therapy. However, proper patient selection is critical to obtain the best possible outcomes. For that reason, a panel of experts was assembled to review data and personal experience with regard to the appropriate preoperative evaluation for antireflux surgery. The consensus of

Esophageal Diagnostic Advisory Panel is summarized in Table 3. Symptoms alone with or without PPI response are not sufficient to support a diagnosis of GERD before antireflux surgery. Rather, objective esophageal testing is required to physiologically and anatomically evaluate the presence and severity of GERD in all patients who are considered for antireflux surgery. It is crucial to document the presence of abnormal distal esophageal acid exposure when antireflux surgery is considered, and reflux-related symptoms should be severe enough to outweigh the potential side effects of fundoplication. Each testing modality has a specific role in the diagnosis and workup of GERD and no single test alone can provide the entire clinical picture. The combined results of objective testing establish the presence of disease and assist with planning the operative approach. Currently, upper endoscopy, barium esophagram, pH testing, and manometry are required for the preoperative evaluation for antireflux surgery. Additional randomized studies with long-term follow-up are required to evaluate the diagnostic and therapeutic benefit of new technologies, such as oropharyngeal pH testing and HMII-PH.

Author Contributions

Study conception and design: Jobe, Richter

Acquisition of data: Jobe, Richter, Hoppo

Analysis and interpretation of data: Peters, Bell, Dengler, DeVault, Fass, Gyawali, Kahrilas, Lacy, Pandolfino, Patti, Swanstrom, Kurian, Vela, Vaezi, DeMeester

Drafting of manuscript: Jobe, Hoppo, Richter

Critical revision: Jobe, Richter, Hoppo, Peters, Bell, Dengler, DeVault, Fass, Gyawali, Kahrilas, Lacy, Pandolfino, Patti, Swanstrom, Kurian, Vela, Vaezi, DeMeester

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