AMERICAN GASTROENTEROLOGICAL ASSOCIATION

American Gastroenterological Association Medical Position Statement: Guidelines on the Use of Esophageal pH Recording

This document presents the official recommendations of the American Gastroenterological Association (AGA) on the use of esophageal pH recording. It was approved by the AGA Patient Care Committee on January 25, 1996, and by the AGA Governing Board on February 3, 1996.

The following guidelines were developed to assist the physician in the appropriate use of esophageal pH recording in patient care. They emanate from a comprehensive review of the medical literature pertaining to the pH recording technique.[1] Esophageal pH recording is widely available and, when done in a technically appropriate manner, provides quantitative data on both esophageal acid exposure and on the temporal correlation between patient symptoms and reflux events. Despite these strengths, the inherent weakness of the technique is its inability to prove causality between symptoms or syndromes and acid reflux events. Alternatively, causality is reasonably assumed in clinical practice by the substantial reduction or elimination of suspected reflux symptoms during a therapeutic trial of a proton pump inhibitor. In view of this viable alternative, the major indications for esophageal pH monitoring are in documenting the failure of either medical or surgical therapy. This position statement should help the clinician apply esophageal pH studies most beneficially within the context of other clinical options.

Guidelines for the Clinical Use of Esophageal pH Recording

- Esophageal pH recording is indicated to document abnormal esophageal acid exposure in an endoscopy-negative patient being considered for surgical antireflux repair (pH study done after withholding antisecretory drug regimen for ≥1 week).
- Esophageal pH recording is indicated to evaluate patients after antireflux surgery who are suspected to have ongoing abnormal reflux (pH study done after withholding antisecretory drug regimen for ≥1 week).
- Esophageal pH recording is indicated to evaluate patients with either normal or equivocal endoscopic findings and reflux symptoms that are refractory to proton pump inhibitor therapy (pH study done after withholding antisecretory drug regimen for ≥1 week

if the study is done to confirm excessive acid exposure or while taking the antisecretory drug regimen if symptom-reflux correlation is to be scored).
- Esophageal pH recording is possibly indicated to detect refractory reflux in patients with chest pain after cardiac evaluation using a symptom reflux association scheme, preferably the symptom association probability calculation (pH study done after a trial of proton pump inhibitor therapy for at least 4 weeks).
- Esophageal pH recording is possibly indicated to evaluate a patient with suspected otolaryngologic manifestations (laryngitis, pharyngitis, chronic cough) of gastroesophageal reflux disease after symptoms have failed to respond to at least 4 weeks of proton pump inhibitor therapy (pH study done while the patient continues taking their antisecretory drug regimen to document the adequacy of therapy).
- Esophageal pH recording is possibly indicated to document concomitant gastroesophageal reflux disease in an adult onset, nonallergic asthmatic suspected of having reflux-induced asthma (pH study done after withholding antisecretory drugs for ≥1 week). Note: a positive test does not prove causality!
- Esophageal pH recording is not indicated to detect or verify reflux esophagitis (this is an endoscopic diagnosis).
- Esophageal pH recording is not indicated to evaluate for "alkaline reflux."

References

1. Kahrilas PJ, Quigley EMM. Clinical esophageal pH recording: a technical review for practice guideline development. Gastroenterology 1996;110:1982–1996.

Clinical Esophageal pH Recording: A Technical Review for Practice Guideline Development

This literature review and the recommendations herein were prepared for the American Gastroenterological Association Patient Care Committee. Following external review, the paper was approved by the Committee on December 21, 1995.

Our present concept of peptic esophagitis dates back to 1935, when Winkelstein suggested that gastric secretions were the cause of mucosal damage observed in peptic esophagitis.[1] The term ''reflux esophagitis'' was later introduced in 1946 by Allison, acknowledging that irritant gastric juices were refluxed from the stomach to the esophagus.[2] Subsequently, it became evident that many patients with reflux symptoms did not have endoscopic or pathological evidence of esophagitis. Another landmark in our understanding of this disease came with the advent of esophageal pH monitoring. Although Spencer first described the technique of using a glass pH electrode to monitor intraesophageal pH continuously,[3] Johnson and DeMeester were the first to study normal volunteers as well as symptomatic patients and to analyze esophageal acid exposure data quantitatively.[4] In so doing, they introduced the concept of physiological reflux; since then, it has become increasingly difficult to define the limits of pathological reflux. This dilemma necessitated the introduction of the descriptor gastroesophageal reflux disease (GERD) to encompass a broader definition of reflux disease: individuals with any symptomatic condition or histopathologic alteration resultant from episodes of gastroesophageal reflux. However, exactly where GERD begins along the continuum extending from physiological reflux at one end to complicated esophagitis at the other is problematic.[5] Although ambulatory esophageal pH testing is potentially useful in resolving this difficulty, the problem of definition persists, leading to considerable confusion regarding the clinical indications for and interpretation of ambulatory esophageal pH studies. Thus, the objects of this review are twofold. First, the technical aspects and limitations of performing clinical ambulatory esophageal pH studies will be discussed. Second, our current understanding of the diagnostic criteria of gastroesophageal reflux syndromes will be summarized, emphasizing the potential role of 24-hour ambulatory esophageal pH monitoring in diagnosis and management. Note, however, that this review pertains to adult patients, and some conclusions and recommendations might differ for pediatric patients.

This critical assessment was accomplished by retrieving and reviewing data published in the medical literature. For each syndrome, relevant key words were used to search the National Library of Medicine database between 1980 and September 1994. The descriptors used for the search were hydrogen ion concentration, esophagus or (exploded) esophageal diseases, and (exploded) monitoring, physiologic. The search identified 433 citations. Papers were included in the discussion if (1) they were designed to address one of the clinically relevant objectives enumerated above, (2) the pH recording methodology used was valid and consistent with current methodological standards, and (3) the reported findings were based on an appropriate experimental design. Additionally, selected studies published during the review process of this manuscript (September 1994 to November 1995) that the authors believed to be of great significance were included in the final draft. Because of variations in study populations and protocols and the lack of a sufficient number of comparable papers, we did not believe that a pooled statistical analysis of results was appropriate in addressing clinical utility.

Technical Aspects of Ambulatory pH Recordings

During the past decade, esophageal pH monitoring has evolved into a relatively standardized method with respect to instrumentation. It is not our intent to review that evolution or to describe the multitude of methodological modifications applied to the pH monitoring technique for data acquisition in an investigative setting. Rather, we will examine the methodological variables of the test as applied in clinical practice along with data showing the impact of these variables on pH recordings obtained. The basic equipment requirements for ambulatory esophageal pH studies are a portable data logger for data storage, a pH electrode, a computer, and software for analysis of pH data.

Data Loggers

Modern data loggers for ambulatory esophageal pH studies are lightweight, battery-powered units that

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can be worn on waist belts or shoulder straps. Several models are currently available in the United States with costs ranging from $10,000 to $15,000. Unlike bedside recordings that continuously record pH data, data loggers sample intraesophageal pH at 6–8-second intervals. The main effect of this limited sampling rate is to miss intraesophageal pH decreases to <4 for periods of only a few seconds. However, this has negligible impact on the calculation of overall acid exposure time,[6] and the consensus among authors is that these brief pH decreases are of no clinical relevance.[7,8] An essential feature of a data logger is an event marker that can be activated by the patient during the study to indicate the timing of symptoms, meals, recumbency (sleep), etc. The patient also records these events on a diary card so that specific symptoms and events can subsequently be correlated with the pH tracing. Thus, the raw data obtained from an ambulatory pH study are the number of reflux events, the esophageal acid exposure time associated with each event, and the timing and nature of symptoms.

pH Electrodes

Several types of pH electrodes are available for ambulatory esophageal pH recording: antimony monocrystalline electrodes with a separate skin reference electrode, unipolar glass electrodes with a skin reference, or combined glass electrodes (built-in reference electrode). Desirable electrode characteristics are stability (no drift), short response time, linear response (no hysteresis), sensitivity, small size, being disposable (or easily sterilized), and low cost.[6,7,9] No single electrode is optimal with regard to all of these characteristics. Combined glass electrodes have the longest operational life (40–50 studies with optimal care), most linear response, most rapid response (>90% within 1 second), and least recording drift but are large in diameter (2.5–3.0 mm), are mounted on stiff bulky catheters, and are expensive (approximately $500). On the other hand, antimony monocrystalline electrodes are smaller, more flexible, and less expensive ($50–$100) but have less response fidelity and an operational life of <10 studies. An advantage of antimony electrodes is that, because of their miniaturization, several pH sensors can be incorporated onto a single catheter without changing its diameter or flexibility. Considering all characteristics of glass and antimony electrodes, it can be concluded that either can be used satisfactorily for clinical esophageal pH monitoring,[7,8] even though concurrent recordings obtained by the two types of electrodes have less-than-perfect correlation.[10] Ultimately, ion-sensitive field effect transistor electrodes may become the electrodes of choice because they will probably fulfill all criteria of an ideal electrode.[11,12]

Electrode Placement

A crucial methodological detail of ambulatory pH studies is electrode placement. By convention, the pH electrode is passed through a nostril and positioned 5 cm above the superior margin of the lower esophageal sphincter (LES). The rationale behind the 5-cm spacing is to avoid possible electrode displacement into the stomach, especially during swallow-induced esophageal shortening. Placing the electrode too high above the LES reduces the sensitivity of the test, exemplified by the finding that a recording obtained 10 cm above the sphincter instead of the usual 5 cm altered the clinical diagnosis in 9 of 20 patients so studied.[13] Manometric localization of the LES is the reference method for electrode placement, but it complicates the pH study by requiring an initial manometric study. To circumvent this difficulty, alternate placement techniques have been advocated, including fluoroscopic or endoscopic localization, or referencing the electrode position to the pH step-up that occurs when the electrode is withdrawn from the stomach across the cardia. Fluoroscopic or endoscopic localization techniques have not proven sufficiently accurate and have been abandoned.[14] With regard to the pH step-up, some investigators have found excellent correlation with manometric localization,[14] whereas others find it prone to error, especially in the circumstances of hiatus hernia or free reflux.[15] Regardless, in view of the paramount importance of electrode positioning in obtaining a quality study, it seems prudent to use manometric localization for electrode positioning. The required manometric examination can be simplified using an LES locator, which is a handheld, single-site pressure sensor costing about $2000 that is introduced before the pH electrode exclusively for the purpose of electrode placement.[16]

Scoring Variables

A 24-hour esophageal pH study that samples intraesophageal pH every 6 seconds results in the generation of 14,400 data points in addition to event marker data. Several analysis techniques have been proposed. The original scoring system devised by Johnson and DeMeester examined six variables (percent total time pH was <4, percent upright time pH was <4, percent recumbent time pH was <4, number of reflux episodes, number of reflux episodes with pH < 4 for ≥5 minutes, and the period of the longest single acid exposure episode) and calculated a composite score according to a formula dependent on the deviation of each of these variables from normal values.[17] With the exception of the overall number of reflux episodes, which proves to be poorly reproducible,[18] each of these derived values has merit, at

least in some circumstances. However, there is now a consensus that the percent time with pH < 4 (esophageal acid exposure time) is the most useful discriminator between physiological and pathological reflux. Other variables tend to covary with the esophageal acid exposure time, are less reproducible, and have less discriminatory power.[7,18–20] Nonetheless, most commercially available software packages analyze pH data for all of the six scoring variables identified by Johnson and DeMeester.

Dietary and/or Activity Limitations

Early esophageal pH recordings were performed according to protocols in which the patient's activities were limited and the diet was restricted to avoid acidic foods. Such protocols were aimed at reducing the intrasubject and intersubject variability of the study. However, current practice is exactly the opposite: to minimize restrictions and maximize the diagnostic yield of the test. Because symptom analysis is now a major diagnostic goal, it follows that the ambulatory nature of the study is used to its fullest advantage if patients are allowed to partake in reflux-provoking activities such as exercise, smoking, alcohol consumption, and dietary indulgence.[7] With respect to acidic foods, the event marker data can be used to exclude the meal period from analysis and, furthermore, pH changes resulting from the ingestion of acidic foods are so transient as to have minimal impact on the overall data.[21]

Interpretative Techniques and Normal Values of Esophageal pH Data

Gastroesophageal reflux is a physiological phenomenon that occurs in normal individuals, particularly in the postcibal period. The task for pH monitoring is to identify patients with GERD by the demonstration of a pathological degree of reflux. In this objective, two problems arise: one intrinsic to the methodology and the other intrinsic to the definition of GERD. With respect to methodology, one must recognize that ambulatory esophageal pH monitoring measures only one pathophysiological determinant in what is widely recognized to be a multifactorial condition. Other than acid exposure time, patients with GERD may differ from controls with respect to the acid sensitivity of the esophageal mucosa, mucosal resistance to inflammation, the extent of mucosal acidification, or constituents of the refluxate other than acid. In view of these unquantifiable variables, it is unreasonable to expect perfect discrimination from the single physiological measurement of mucosal acid exposure. The second problem relates to the definition of GERD and is even more enigmatic. In the absence of esophagitis, there is no gold standard for the definition of GERD,

making it impossible to establish the accuracy of any diagnostic test. Thus, in evaluating the normal data on esophageal pH monitoring, there are really two tasks: contrasting normal individuals with esophagogastroduodenoscopy (EGD)-positive (esophagitis) patients and contrasting normal individuals with EGD-negative patients with GERD.

Esophageal acid exposure of normal controls versus patients with esophagitis. As evident from the larger representative examples summarized in Table 1, studies comparing the esophageal acid exposure time of normal individuals with patients with endoscopically proven esophagitis have 77%–100% sensitivity and 85%–100% specificity of esophageal acid exposure values in segregating these populations. Although only data on the percent esophageal pH < 4 are shown in Table 1, other pH parameters show similar results. For the studies included in Table 1, the normal population was defined by the absence of esophagitis either by symptom appraisal or endoscopy. In general, the normal subjects were younger than the patients. Even so, a significant minority (up to 23%) of patients with demonstrated esophagitis provided 24-hour pH data within the range of normal.[22,23] However, this observation is of limited clinical impact given that the endoscopic demonstration of erosive esophagitis will establish the diagnosis of GERD, thereby obviating the need for a 24-hour pH study.

Esophageal acid exposure of normal controls versus EGD-negative patients with GERD. Symptom surveys show that heartburn and acid regurgitation, typical symptoms of reflux, occur in up to 40% of the normal population, most of whom do not seek medical attention. Technically, these individuals could be defined as having GERD because there are no conventions regarding the frequency or severity of reflux-related symptoms required to meet that definition. Recent studies evaluating therapeutic efficacy in GERD have addressed this problem by developing symptom severity indices derived from grading the frequency and severity of major GERD symptoms.[24] However, as evident in Table 2, the criteria of "normal" used in analysis of ambulatory pH data varies considerably among studies, with scant detail regarding the method of symptom assessment. It should come as no surprise that these studies have shown considerable overlap between the control and EGD-negative groups (Table 3)[22,25] and in one instance failed to show any clear separation.[23] Furthermore, many EGD-negative subjects exhibit acid exposure rates that are only modestly above the normal range for the particular study, a gray area in which there is poor reproducibility of pH data.[18] Thus, although acid exposure values show group differences

Table 1. Esophageal Acid Exposure in Patients With Esophagitis

Reference	Controls	Patients with esophagitis			
	Upper limit of normal percent pH < 4[a]	n	Mean age (yr) (range)	Mean percent pH < 4	Sensitivity and specificity
Vitale et al.[22]	7.2	35	51 (20–82)	9.6	77% and 91%
Schlindbeck et al.[19]	7.0	16	47 (18–73)	18.8	89% and 93%
Johnsson et al.[20]	3.4	20	51[b] (28–74)	Not stated	87% and 97%
Mattioli et al.[23]	5.0	11	48 (21–78)	29.8	100% and 100% (grade 2)[c]
		37		27.6	92% and 100% (grade 3)[c]
Masclee et al.[25]	4	44	48	12.6	91% and 85%
Kasapidis et al.[67]	3.9	21	37	31.7	Not provided

[a]See Table 2 for method of determination.
[b]Median.
[c]Savary–Miller grade of esophagitis.

between controls and patients with EGD-negative GERD, the extensive overlap between the groups makes the measurement far less reliable for categorization of individual patients.

Symptom-reflux correlation. Realizing that the significance of reflux events may be in causing atypical symptoms (especially chest pain) regardless of the overall esophageal acid exposure time, several schemes have been devised to analyze ambulatory pH data in conjunction with symptoms indicated by patient activation of the event marker. However, because it is clear that a one-to-one correspondence between reflux and symptoms does not exist, a number of statistical manipulations have been developed to quantify this relationship. The two problems that must be addressed are the required temporal relationship between pain and reflux and the definition of "significant association." There is no convention defining the time interval around a pain episode within which a reflux event is accepted as causative. Investigators have used schemes as liberal as pain ± 10 minutes[26] or as restrictive as confined to the 2-minute interval before the onset of pain.[27] Although the more restrictive defini-

tion seems more reasonable, there are no data proving one method to be superior to another.

The first attempt at defining significant reflux-pain association was the symptom index, defined as the number of reflux-related symptom episodes divided by the total number of symptom episodes, expressed as a percentage.[28] Although logical, this concept fails to consider the total number of reflux episodes. For example, if a patient had only one episode of chest pain during a 24-hour study, but this happened to coincide with an episode of reflux, the symptom index would be 100%, even though 100 other episodes of reflux during the recording period were symptom-free. To circumvent this limitation, the symptom sensitivity index was developed, defined as the percentage of symptom-associated reflux episodes.[29] However, with both the symptom index and the symptom sensitivity index, the cut-off point defining a positive score is arbitrary. A recently proposed means of establishing a cause-and-effect relationship between symptoms and reflux events calculates the symptom-association probability by statistically comparing esophageal pH data temporally related to symptoms with pH data

Table 2. Esophageal Acid Exposure in Control Populations

Reference	n	Mean age (yr) (range)	Reflux symptoms	Statistical methods	Percent pH < 4
Vitale et al.[22]	22	25 (19–77)	"Asymptomatic"	Mean ± 3SD	7.2
Schindlbeck et al.[19]	42	33 (18–76)	"No history, symptoms, or digestive tract disease" "Occasional reflux excluded" questionnaire	Receiver operated characteristics	7.0
Johnsson et al.[20]	20	38 (30–76)[a]	"No previous or present GI symptoms"	95th percentile	3.4
Mattioli et al.[23]	20	43 (25–68)	"Asymptomatic"	Mean ± 2SD	5.0
Smout et al.[107]	32	46 (20–73)	"Symptom-free for GER symptoms"	95th percentile	<45 yr: 5.0 >45 yr: 12.0
Masclee et al.[25]	27	47 (23–73)	"Without gastroesophageal reflux symptoms" "Occasional reflux excluded"	Linear discriminant analysis	4.0
Richter et al.[106]	110	38 (20–84)	>2 episodes of heartburn per month	95th percentile	5.78
Kasapidis et al.[67]	18	38 (21–73)	"Without GER symptoms" questionnaire	Mean ± 2SD	3.9

[a]Median.

Table 3. Esophageal Acid Exposure in EGD-Negative Patients With GERD

Reference	Upper limit of normal percent pH < 4[a]	Patients with GERD[b]		Sensitivity and specificity
		n	Mean percent pH < 4	
Vitale et al.[22]	7.2	11	5.8	64% and 91%
Schindlbeck et al.[19]	7.0	29	10.2	Not provided
Mattioli et al.[23]	5.0	6	1.9	0% and 100% (grade 0)[c]
		32	13.6	71% and 100% (grade 1)[c]
Masclee et al.[25]	4	23	6.4	61% and 85%
Kasapidis et al.[67]	3.9	21	11.6	Not provided

[a]See Table 2 for method of determination.
[b]Age of patients with GERD and patients with esophagitis not distinguished.
[c]Savary–Miller grade of esophagitis.

recorded during symptom-free episodes.[30] In an insightful and critical editorial, Orr emphasized the appropriateness of this statistical approach, which uses contingency table analysis and Fisher's Exact Test to analyze the four potential associations of pain and reflux: reflux and pain, reflux and no pain, pain and no reflux, and no reflux and no pain.[31] Prior analyses focused solely on the frequency of occurrence of reflux and pain, ignoring the fact that equal consideration must be given to the frequency of periods of chest pain without reflux or neither reflux nor pain if one is to show a statistically meaningful cause-and-effect relationship. The importance of the analysis scheme used is shown in a recent report that computed all three symptom indices in the same set of 96 patients with chest pain and showed very little correlation between the symptom index and the symtom association probability ($r = 0.25$) but better (though still imperfect) correlation between the symptom sensitivity index and the symptom association probability ($r = 0.65$).[32] However, despite the evolution in sophistication, none of the proposed schemes of reflux-symptom association have been prospectively validated against an independent criterion of diagnostic accuracy such as symptomatic response to antireflux therapy. Furthermore, additional factors have been shown to influence pain perception. The probability of reflux events being symptomatic is influenced by their temporospatial characteristics; episodes of prolonged acid exposure and those acidifying a greater length of esophageal mucosa (i.e., a greater volume of refluxate) are more likely to elicit symptoms.[33] Also, the interaction between visceral stimuli such as exemplified by balloon distention and acid exposure influence pain perception.[34,35]

Concurrent Medications

The interpretation of an ambulatory pH study must take into account therapeutic agents that might affect the results. If the study was performed to assess the efficacy of treatment on esophageal acid exposure, the patient's pharmacological regimen and the duration of that therapy should be carefully recorded both on the entry data sheet and in the report of results. If the study was intended to define the extent of esophageal acid exposure without therapy, a washout period of 3 days is prudent for most drugs (H$_2$-receptor antagonists, prokinetic agents, smooth muscle relaxants, etc.) but should be prolonged to a week for proton pump inhibitors.[7]

Role of Esophageal pH Recording in Clinical Practice

Ambulatory esophageal pH recording can potentially aid in the diagnosis and management of esophageal syndromes involving gastroesophageal reflux, extraesophageal manifestations of GERD, or chest pain. In each of these clinical scenarios we will attempt to (1) identify the pH recording abnormality associated with the condition, (2) assess the potential for identifying patients on the basis of pH recordings, and (3) determine the effect of detecting pH recording abnormalities on clinical management decisions of either GERD or extraesophageal GERD.

Esophageal Manifestations of GERD

Ambulatory esophageal pH recording abnormalities. As evidenced by the extensive data in Table 1, measurements of esophageal acid exposure can discriminate reasonably well between normal controls and patients with endoscopic evidence of esophagitis. Furthermore, the discriminant ability increases with increasing degrees of esophagitis.[36] However, because neither controls nor patients with esophagitis are generally viewed to be a diagnostic dilemma, the more relevant question pertains to ambulatory esophageal pH findings in individuals between these extremes: individuals with reflux symptoms but without esophagitis. In this setting, the data are fewer and less consistent, as evident in Table 3.

One group of investigators found a continuum of progressively increasing acid exposure with increasing degrees of symptomatology,[37] whereas another showed essentially no correlation between symptom severity and the ambulatory pH score.[38] These observations argue for the importance of additional factors such as mucosal sensitivity in the pathogenesis of GERD symptoms.[7]

A controversial issue regarding the interpretation of ambulatory pH studies is their role in the detection of refluxed duodenal contents that have been shown to be injurious to the esophageal mucosa in animal models.[39] Investigators have suggested that an intraluminal esophageal pH value of >7 (alkaline reflux) is an indirect indicator of refluxed duodenal contents[40] and, using this marker, have correlated the occurrence of alkaline reflux with the occurrence of complications in Barrett's epithelium.[41] It should be noted, however, that these patients also had substantially higher values of esophageal acid exposure and acid reflux was mixed with photometrically detected bile,[42] making it difficult to establish causality by any particular component of the refluxate. Furthermore, two subsequent investigations questioned whether or not alkaline reflux was a valid marker of refluxed duodenal contents.[39,43] The more recent of these investigations attributed esophageal alkalinization to swallowed saliva (pH 7.0–7.2) and, perhaps, esophageal submucosal gland secretion rather than refluxed duodenal contents.[39] Furthermore, the frequency of alkaline reflux events paralleled the circadian rhythm of salivary secretion. Thus, although the issue of the role of bile reflux in the pathogenesis of complications of reflux disease is unresolved, it is clear that ambulatory esophageal pH monitoring has no role in the detection of refluxed duodenal contents.

Potential of using ambulatory pH studies for identifying patients with GERD. Although widely accepted as the most prevalent esophageal disorder, there is remarkably little agreement on what constitutes typical reflux disease. Unless a complication of reflux such as esophagitis is present, one must use symptomatology to define the disease, and people differ substantially in their sensitivity to acid reflux. Both the broad spectrum of GERD symptoms and the discordance between symptoms and ambulatory pH monitoring findings are shown by the data in Table 4 from 304 patients referred for evaluation of symptoms possibly related to the esophagus. Note that minimal difference exists in the frequency of symptoms reported by patients with normal reflux values compared with those with abnormal reflux values.[44] Only when heartburn and acid regurgitation were dominant complaints was there reasonable correlation between symptoms and findings from 24-hour ambulatory esophageal pH testing. In the setting of a patient

Table 4. Symptom Prevalence in Patients with Normal and Abnormal Esophageal Acid Exposure

Symptoms reported by patients with suspected esophageal disorders	Normal esophageal acid exposure values (%) (n = 138)	Abnormal esophageal acid exposure values (%) (n = 166)
Odynophagia	11 (8)	17 (10)
Pharyngeal pain	21 (15)	32 (19)
Nausea	44 (32)	63 (38)
Belching	55 (40)	81 (49)
Epigastric pain	73 (53)	90 (54)
Retrosternal pain	84 (61)	95 (57)
Acid regurgitation	66 (48)	100 (60)
Retrosternal burning	68 (49)	100 (61)
Heartburn	66 (48)	112 (68)

Klauser AG, Schindlebeck NE, Müller-Lissner SA. Symptoms in gastrooesophageal reflux disease. Lancet 1990;335:205–208. © by The Lancet Ltd. 1990.

with multiple dyspeptic symptoms, there was poor correlation. Another analysis of dyspeptic symptoms similarly concluded that only when heartburn and acid regurgitation were dominant symptoms did their occurrence correlate with endoscopic evidence of esophagitis.[45] In yet another analysis, 50 patients were evaluated for acid sensitivity as determined by a Bernstein test and by ambulatory pH monitoring. A poor correlation was noted between the two.[46] Finally, a recent study compared the diagnostic utility of ambulatory pH recording with a 2-week trial of 40 mg omeprazole every day and found 66% concordance but 34% discordance; 17% of patients had a positive pH study but no response to omeprazole, and 17% responded to omeprazole but had a negative pH study.[47] Thus, one has to conclude that ambulatory pH studies quantify esophageal acid exposure but that this has an imperfect correlation with reflux-related symptoms, esophageal sensitivity, or response to acid suppressive therapy.

Extraesophageal Manifestations of GERD

Ambulatory esophageal pH recording abnormalities. Gastroesophageal reflux can cause asthma or laryngitis. Because each of these entities has other potential etiologies, it would be of great clinical value to detect reflux-related cases with a diagnostic test. With respect to laryngitis, studies performed placing a pH electrode 5 cm above the LES have detected no abnormalities in patients with dysphonia[48] or biopsy-proven posterior laryngitis.[49] Alternatively, a second electrode can be placed in the vicinity of the upper esophageal sphincter to detect potentially regurgitated refluxate. In groups of patients with GERD with and without ear, nose, and throat symptoms (dysphonia, cough, globus sensation, frequent

throat clearing, or sore throat), the groups with laryngitis were found to have a similar degree of distal acid exposure but increased proximal acid exposure (particularly at night) than control patients with GERD.[50,51] Other studies have suggested a relationship between gastroesophageal reflux and chronic cough[52,53] or hoarseness[54–56] either on the basis of the distal acid exposure times (chronic cough) or on the detection of regurgitant events. With respect to asthma, a recent endoscopic study found that 39% of 186 consecutive asthmatics had esophagitis.[57] Ambulatory esophageal pH monitoring in a similar group of 104 unselected asthmatics found that asthmatics taking bronchodilators or not taking bronchodilators had 20-fold and 11-fold frequency of prolonged reflux episodes, respectively, compared with normals.[58] Another study of 44 consecutive asthmatics found abnormal esophageal acid exposure in 34%. Thus, current data suggest that GERD is prevalent in asthmatics by endoscopic or pH-monitoring criteria.

Potential of using ambulatory pH studies for identifying patients with extraesophageal reflux. Asthma, laryngitis, and GERD are all common disorders and may well coexist in an individual without a causal relationship. With regard to laryngitis, despite data suggesting differences in the proximal esophageal pH profile of subjects with GERD with laryngitis, no attempt has been made to prospectively identify patients with reflux laryngitis on the basis pH recordings.[50] With respect to asthma, one study sought to correlate the pattern of morning bronchospasm with nocturnal reflux.[59] Forty-four asthmatics with or without reduced morning peak expiratory flow rate were evaluated, and no between-group difference in nocturnal pH profile was detected. Another attempt at prospectively identifying patients with GERD-related asthma used proximal and distal esophageal pH monitoring in 23 consecutive patients with pulmonary symptoms.[60] Patients were subdivided according to whether or not discrete wheezing episodes were associated with proximal esophageal pH decreases during the ambulatory pH study; there was no significant difference in the distal pH profile of these patients compared with the other 12. The 11 patients with proximal pH decreases suspected of having aspiration-related asthma were offered fundoplication as therapy. Of the 5 patients who consented to surgery, 4 had a complete resolution of respiratory symptoms at an unspecified time postoperatively. Of the 6 patients who refused surgical treatment, symptoms remained unchanged in 5 and slightly improved in 1 after an unspecified period of treatment with H_2 blockers or omeprazole. Thus, one has to conclude that distal pH monitoring has no proven benefit in establishing causality between GERD and

asthma but that proximal pH monitoring is potentially useful. Presently, however, there are insufficient data to state this with any certainty.

Potential Impact of Ambulatory pH Studies on Management of GERD

In most cases, patients with GERD can be managed empirically without resorting to any diagnostic tests. There are, however, some circumstances in which supportive evidence from a diagnostic test can be of value to the clinician. Thus, a diagnostic test might be called upon to answer one of several key management questions for a given patient who is either known to have or is suspected of having GERD. (1) Are a patient's atypical symptoms related to gastroesophageal reflux? (2) Does the patient have a complication of GERD (esophagitis, peptic stricture, or Barrett's epithelium) or are they likely to sustain one? (3) Is the patient likely to benefit from medical therapy for GERD and, if so, which therapy? (4) Is the patient likely to benefit from antireflux surgery? (5) Why has GERD therapy (medical or surgical) failed in this patient: incorrect diagnosis or failed therapy?

When confronted with any of these diagnostic or therapeutic dilemmas, the clinician has several options, including an upper endoscopy, a barium swallow and meal, esophageal manometry, an ambulatory esophageal pH study, or a therapeutic trial of medical therapy. Thus, the relative merit of ambulatory esophageal pH recordings must be examined with respect to each of these questions.

Are a patient's atypical symptoms related to GERD? In the patient with typical symptoms of GERD (heartburn and acid regurgitation), there is little reason to pursue any diagnostic test beyond a history and physical examination before embarking on a therapeutic plan. In the case of atypical symptoms, the most relevant clinical question is whether or not those symptoms will be effectively treated by antireflux therapy. Although use of the symptom-association scoring system of ambulatory esophageal pH studies is potentially useful in making this determination, currently available data have not shown any superiority of this approach over an empirical therapeutic trial. No data support using the acid exposure time derived from an ambulatory esophageal pH study as the criterion for determining the relationship between GERD and atypical symptoms.

The major extraesophageal manifestations of GERD to consider are laryngitis and asthma. Key observations relevant to laryngitis are that groups of patients with symptoms or findings of posterior laryngitis have greater median values of proximal esophageal acid exposure[50] and that these patients have been shown to respond to

GERD therapy (lifestyle modifications, H_2 blockers, omeprazole, or antireflux surgery) in uncontrolled trials.[61,62] Similarly, chronic cough was resolved in 12 of 12 patients with lifestyle modifications, H_2 blockers, and metoclopromide therapy.[63] In neither case was ambulatory pH monitoring used to identify the responders; instead, the investigators relied on either direct inspection of the larynx or the systematic elimination of other diagnostic possibilities in patient selection. In the case of reflux-induced asthma, evidence suggests that as many as 50% of carefully selected adult onset, nonallergic asthmatics can be cured of their asthma by antireflux surgery.[64] Similarly, 27% of asthmatics with asthma and reflux disease diagnosed by either endoscopy or ambulatory esophageal pH monitoring showed improvement in pulmonary function test performance after 6 weeks of therapy with 20 mg omeprazole twice daily.[65] In that study, no therapy was attempted in the 15 asthmatics with heartburn not meeting the study criteria of GERD, and all of the omeprazole responders had endoscopic evidence of esophagitis, obviating the need for pH monitoring. To summarize, there are presently no prospective data showing that ambulatory esophageal pH monitoring can identify either patients with laryngitis or asthmatics likely to respond to antireflux therapy.

Does the patient have a complication of GERD (esophagitis, peptic stricture, or Barrett's epithelium) or are they likely to sustain one? The complications of GERD (esophagitis, peptic stricture, or Barrett's epithelium) are evident by endoscopic and histological evaluation, making these the gold standards for their detection. Once so detected, there is no need for further testing before embarking on an appropriate therapeutic plan. A more difficult issue is predicting which patients are at risk for developing a complication of GERD. No prospective, longitudinal study has addressed this issue. The best available data pertain to esophageal acid exposure after complications are detected, and several investigations have shown this to have a significant correlation with the severity of esophagitis.[25,36,66–69] The correlation is, however, imperfect with a calculated correlation coefficient of 0.59,[25] suggesting that acid exposure time, determined by an ambulatory pH study, accounts for only 35% of the variance in esophagitis severity among individuals. Thus, this measurement cannot predict the development of complications. A potential use of this correlation, however, is to gauge the severity of reflux disease in an individual with a healed mucosa as a result of pharmacological therapy.

Will the patient benefit from medical therapy for GERD and, if so, which therapy? Medical therapies for GERD can be stratified by their effectiveness in treating progressively severe disease. Ranked from least to most potent, these therapies are lifestyle modifications, antacids, H_2 antagonist or cisapride, and proton pump inhibitors. Theoretically, a clinical test would be useful if it helped the clinician select among these therapeutic options a priori or predicted the need for long-term as opposed to short-term therapy. At the mild end of the disease spectrum, a medical history satisfies these criteria in that the clinician knows to treat patients with relatively rare or mild symptoms with lifestyle modifications and antacids. Similarly, the patients with endoscopically evident grade 2 or worse esophagitis will predictably be better treated with a proton pump inhibitor than with less potent therapy[70,71] and will predictably be prone to recurrence of mucosal disease without maintenance therapy.[72,73] With respect to ambulatory pH monitoring, there are no data showing its utility in the a priori stratification of medical treatment requirements in patients with GERD. One group of investigators addressed this issue by obtaining ambulatory pH studies on 106 patients with GERD before treatment and then attempting to correlate the eventual treatment needs of individual patients with findings from their pretreatment pH study. No correlation could be found.[74] Thus, the only evaluative procedures with proven utility for predicting the effectiveness of any therapy for GERD are a symptom profile as elicited by a medical history (in the case of mild disease) or endoscopic examination (in the case of severe disease). For the patients between these extremes, no diagnostic test is superior to an empirical trial of pharmacological agents in devising an individualized therapeutic plan.

Will the patient benefit from antireflux surgery? Antireflux surgery, most commonly a Nissen fundoplication in the United States, has been shown to be an effective means of controlling chronic reflux disease and has compared favorably with medical therapy in large controlled trials.[75,76] In the more recent of these trials, patients were selected for the study on the basis of having complications of reflux (esophagitis, stricture, or Barrett's epithelium), and the surgery group had superior outcomes to patients randomized to medical therapy (ranitidine, metoclopromide, sucralfate). Unfortunately, with the acceptance of laparoscopic Nissen fundoplication as an effective antireflux procedure[77–80] and proton pump inhibitors as effective long-term treatment for severe reflux disease,[24,73,81] both treatment arms of the Veterans Administration study are now obsolete. Thus, the clinician is presently left with making the choice between excellent medical therapy and seemingly excellent surgical therapy without the benefit of a controlled trial comparing the two.

Several surgical series used ambulatory esophageal pH

monitoring as a means of patient selection, although it is not clear how those data were used. In a recent analysis of the influence of preoperative tests on surgical therapy, Waring et al. found ambulatory esophageal pH monitoring to have an impact only in patients without endoscopically demonstrable esophagitis.[82] In the Hinder series, all 198 patients underwent 24-hour monitoring, despite the fact that 104 patients had endoscopically shown ulceration, stricture, or Barrett's epithelium. Presumably, the definition of disease in the remaining 94 patients was based on the manometric detection of a defective sphincter and/or an abnormal acid exposure time. The overall success rate in this series after 6–32 months of follow-up was 97%, so, in a limited way, the ambulatory pH study was a valid predictor of surgical success. However, data are not given as to how many patients were excluded from surgery on the basis of findings from an ambulatory pH study or how findings from the ambulatory pH study correlated with surgical outcome. Thus, although there are data supporting the view that an abnormal ambulatory pH study is a useful selection criterion for patients undergoing antireflux surgery, there are no data on the more difficult question of whether or not the test identifies patients for whom surgery is the optimal therapy.

Why has GERD therapy (medical or surgical) failed in this patient: incorrect diagnosis or failed therapy? No therapy for reflux disease enjoys a 100% success rate. This, coupled with ambiguities in the diagnosis of GERD, speak of the need for an objective means of assessing treatment failures. In terms of empirical therapy, even the most enthusiastic clinician reaches a limit of dose escalation at which point the question is asked, why is this treatment not working? Is it ineffective, or do I have the wrong diagnosis? Faced with this scenario, endoscopy is potentially useful, because the finding of persistent esophagitis confirms that the treatment has been unsuccessful. In the instance of a normal endoscopic examination, however, ambulatory pH monitoring is potentially useful to verify the presence of inadequately treated GERD. Notably, this study should be performed while the patient continues with the apparently ineffective regimen.

The premise of using ambulatory pH studies to assess clinical outcome is that symptomatic improvement in the ambulatory esophageal pH profile parallels symptomatic improvement, a premise that is not completely supported by existing data. Lieberman examined the pretreatment and posttreatment ambulatory pH studies of 20 patients involved in a controlled trial of medical treatment (H_2 blockers and metoclopramide) of reflux esophagitis.[83] Eleven patients improved clinically, and 8 of these im-

proved endoscopically. However, improvement in the 24-hour pH result was noted in only 5 patients (3 responders and 2 nonresponders), leading the investigators to conclude that successful symptom relief could occur despite persistence of an abnormal pH study. A similar conclusion was reached in an analysis by preoperative and postoperative ambulatory pH studies. Martin et al. studied a group of patients undergoing a Collis–Nissen gastroplasty and found that of 23 patients who agreed to the postoperative evaluation, 7 had persistently abnormal esophageal acid exposure even though 6 of these were asymptomatic and free of esophagitis.[84] The investigators conclude that pH monitoring has utility only for analyzing a poor clinical result. On the other hand, an earlier study assessing the efficacy of Nissen fundoplication in 27 patients found perfect correlation between the 3 patients with persistently abnormal pH scores and persistent symptoms.[85] However, in that study, an additional 7 patients had reflux symptoms with a normal pH profile postoperatively, and no data were given as to whether or not these patients subsequently responded to antireflux therapy. Finally, a recent report used ambulatory pH monitoring to show an instance of omeprazole failure and subsequent successful treatment with nizatidine in a patient with reflux.[86] Taken together, these data suggest that ambulatory pH monitoring can be useful in documenting antireflux treatment failures, but its precise sensitivity and specificity in this application are unclear.

Chest Pain

Acid reflux is often invoked as a cause of chest pain, and several investigations have examined the utility of ambulatory esophageal pH monitoring in the assessment of patients with noncardiac chest pain. However, the descriptor "noncardiac" is unfortunate, given the possibility of microvascular angina[87] and the ever-increasing awareness of the complex reflex relationships between the heart and the esophagus. Experimental studies have shown provocation of coronary artery spasm by the intraesophageal instillation of acid,[88,89] and it has also been suggested that gastroesophageal reflux could be precipitated by episodes of angina.[90,91] Therefore, one cannot confidently dismiss a cardiac cause of pain because of normal coronary arteriography. Given these limitations and the fact that, despite numerous investigations, the origin of pain ultimately remains unproved in many of these patients,[90] it seems more reasonable to describe this symptom for what it is, chest pain, without any qualifying characteristic.

Esophageal pH recording abnormalities associated with chest pain. In analyzing studies aimed at establishing the relationship between acid reflux and chest

Table 5. Esophageal Chest Pain Studies: Patient Characteristics

Reference	n	Referral[c]/chest pain characteristics	Gastroesophageal reflux symptoms[a] (%)	Esophagitis by EGD[b] (%)
DeMeester et al.[92]	50	Esophageal center/ anginal	>60	18
Janssens et al.[93]	60	Esophageal center/anginal daily in 33%	23	25
Peters et al.[94]	24	Esophageal center/anginal daily in 79%	100	0
Soffer et al.[95]	20	Motility center/anginal, daily in 50%	45	0
Hewson et al.[96]	71	Esophageal center/not stated	Not stated	0
Klauser et al.[97]	289	Esophageal center/''various'' chest symptoms	41	47
Ghillebert et al.[34]	50	Esophageal center/anginal, daily in 24%	42	Not stated
Limburg et al.[98]	22	Cardiology clinics/36% anginal	41	5
Garcia-Pulido et al.[26]	32	Cardiology clinic/100% anginal daily	56	Not stated
Hewson et al.[99]	45	Esophageal center/substernal daily in 82%	89	0
Bortolotti et al.[100]	18	Motility center/anginal	Not stated	17
Breumelhof et al.[101]	44	Motility center/consecutive unselected anginal 55% daily	23	20
Hewson et al.[102]	100	Esophageal center/not stated	89	3
Nevens et al.[35]	37	Coronary care unit/typical angina	Not stated	Not stated
Singh et al.[103]	34	Esophageal center/atypical pain >3/wk, all with coronary artery disease	>50	Not stated
Lam et al.[104]	41	Coronary care unit/severe myocardial infarction type	56	22
Paterson et al.[105]	25	Motility center/atypical more than every other day	Not stated	Not stated

[a]Percentage of patients included with typical gastroesophageal reflux symptoms.
[b]Percentage of patients included with endoscopic esophagitis.
[c]Type of center from which study originated.

pain, several important points emerge. Some studies originate from centers with a special interest in esophageal diseases, others from cardiology referrals or patients in cardiac care units, and still others from community hospitals. Thus, the patient populations among studies are quite heterogeneous (Table 5).[27,34,35,92–105] The nature and severity of chest pain required for inclusion among studies also varies, although most do specify that they tended to involve patients with daily pain. Most studies embark on pH monitoring after patients had first undergone an unrevealing cardiology evaluation, usually an exercise tolerance test and, quite commonly, coronary arteriography. However, the characterization of esophageal symptoms and the extent of gastrointestinal investigations done before or in association with pH monitoring varies greatly. This is a crucial detail because the likelihood of having an abnormal esophageal pH recording is strongly influenced by the frequency and severity of gastroesophageal reflux symptoms and, even more so, by the presence of esophagitis. The inclusion of numerous patients with esophageal symptoms or esophagitis guarantees that there will be ambulatory pH abnormalities indicative of reflux disease in the chest pain populations studied. Unfortunately, because the distinction between patients with and without esophageal symptoms is rarely made during data analysis in these studies, only rarely can the extent to which ambulatory pH monitoring provides information not obtainable from the patient's history or an endoscopic examination be determined. In one analysis that did examine the incremental benefit of esophageal

testing, Klauser et al. obtained the most diagnostic information from clinical history and found minimal information gain from additional tests, including 24-hour pH monitoring.[97]

Potential of using ambulatory pH studies for identifying patients with reflux-induced chest pain. In attempting to define a relationship between reflux and chest pain, ambulatory pH studies have been used to detect excessive esophageal acid exposure or to correlate pain events with reflux events using a variety of statistical manipulations as evident in Table 6.[27,34,35,92–105] As shown in Table 6, an average of 40% of the patients in these chest pain studies either had evidence of abnormal acid exposure or some correlation between reflux events and episodes of chest pain during pH monitoring. The impact of the symptom-association analysis scheme used is evident in the study by Breumelhof et al. in which two different schemes were compared and, depending on which was used, either 18% or 48% of patients had a positive symptom association.[101] Ultimately, the necessary step to validate a scheme of symptom-reflux association is to show that findings from the pH study separates patients who are likely to respond to antireflux therapy from those who will not. Although this is an area of current investigation, no existing, well-designed study provides us with these data.

Impact of ambulatory pH studies on management decisions in chest pain. What does ambulatory esophageal pH monitoring contribute to the management of patients with chest pain? Its superiority over

Table 6. Esophageal Chest Pain Studies: Ambulatory pH Study Findings

Reference	Abnormal percent pH <4[a]	Symptom association[b] (%)	Symptom association definition[c]
DeMeester et al.[92]	46	46	Any association; window not defined
Janssens et al.[93]	22	22	Any association; window not defined
Peters et al.[94]	Not stated	42	Any association; window = reflux ± 2 min
Soffer et al.[95]	Not stated	45	Any association; window = reflux ± 5 min
Hewson et al.[96]	51	48	>50% association; window = pain ± 5 min
Klauser et al.[97]	56	Not stated	Not applicable
Ghillebert et al.[34]	24	38	Association <5% chance; window = reflux ± 2 min
Limburg et al.[98]	Not stated	9	Any association; window = reflux ± 2 min
Garcia-Pulido et al.[26]	Not stated	53	Any association; window = pain ± 10 min
Hewson et al.[99]	44	42	Any association; window = reflux ± 2 min
Bortolotti et al.[100]	28	11	Any association; window not defined
Breumelhof et al.[101]	20	18	>75% association; window = pain onset ± 2 min
		48	>75% association; window = −2 min to end of pain
Hewson et al.[102]	48	50	Any association; window = reflux ± 5 min
Nevens et al.[35]	41	14	Association <5% chance; window = reflux ± 2 min
Singh et al.[103]	41	59	Any association; window = reflux to reflux + 5 min
Lam et al.[104]	63	43	>75% association; window = pain ± 2 min
Paterson et al.[105]	Not stated	44	Any association; window = reflux ± 5 min

[a]Percentage of patients with an abnormal value of esophageal acid exposure (total percent time pH < 4).
[b]Percentage of patients with a positive symptom association according to each study's definition.
[c]Percentage of symptoms needing to be related to reflux events to constitute a positive association and the time interval (window) surrounding a reflux event or pain episode within which the two were considered to be related events.

clinical evaluation has not been directly assessed, and we do not have information on the number of patients with chest pain who will be discovered to have significant reflux not evident from clinical history. Because chest pain is a commonly encountered symptom of reflux disease, patients who additionally have typical GERD symptoms would rightly be given a trial of medical therapy without any esophageal investigation other than an endoscopy. The benefit of endoscopy is that if esophagitis is detected, the clinician can approach therapy with great certainty, an attribute that can be claimed for no other diagnostic test in this circumstance. Thus, the most difficult clinical challenge becomes the patient with chest pain who does not have esophagitis and does not respond to antisecretory therapy. Perhaps, in this scenario, ambulatory esophageal pH monitoring will be useful in evaluating treatment failures much the same as in the case of GERD outlined above; patients would be studied on therapy with the question in mind of whether treatment failure is attributable to an incorrect diagnosis (reflux-induced chest pain) or inadequate therapy. To date, however, such studies have not been performed.

Conclusions And Clinical Recommendations

Ambulatory esophageal pH monitoring has emerged as a widely available method for quantifying esophageal acid exposure, and this measurement has been invaluable as a research tool in the investigation of the pathogenesis and treatment of GERD. The test is performed with compact portable data loggers, miniature pH electrodes, and computerized data analysis. There is an emerging consensus that the pH electrode should be positioned 5 cm above the manometrically defined upper limit of the LES, that analysis for the total percent time of pH < 4 provides the optimal discriminant value, that symptom association is essential when evaluating atypical or sporadic symptoms, and that patients should have unrestricted diets and activities for the duration of the monitoring period. Enthusiasm for 24-hour pH monitoring must, however, be tempered with an analysis of its clinical utility in the management of patients with GERD or chest pain.

GERD

Our analysis of the management of the patient with GERD suggested that clinical decision making could be reduced to five broad management questions faced by the clinician. The utility of ambulatory esophageal pH monitoring was analyzed according to its potential impact in addressing each of these clinical questions.

Are a patient's atypical symptoms related to GERD? Although there is no doubt that ambulatory esophageal pH monitoring can define abnormal esophageal acid exposure, this measurement does not equate to GERD. The definition of GERD depends on reflux-related symptoms or mucosal inflammation. Reflux symptoms are multifactorial in origin, dependent on esophageal mucosal re-

sistance and acid sensitivity as well as esophageal acid exposure. The optimal way to determine whether symptoms are related to GERD is to eliminate gastroesophageal reflux and observe whether or not the symptoms abate. Fortunately, this can usually be accomplished by empirical trials of behavioral modification and/or medication with proton pump inhibitors used for severe or refractory symptoms. Ambulatory esophageal pH monitoring should be reserved for the evaluation of treatment failures.

Does the patient have a complication of GERD (esophagitis, peptic stricture, or Barrett's epithelium) or are they likely to sustain one? Endoscopy (with biopsy if indicated) is the only examination capable of ascertaining the presence or absence of all of these complications. There are no data suggesting that ambulatory pH studies allow the clinician to predict the development of these complications.

Will the patient benefit from medical therapy for GERD and, if so, which therapy? The only evaluative procedures with proven utility for predicting the effectiveness of any therapy for GERD are a symptom profile as elicited by a medical history (in the case of mild disease) or endoscopic examination (in the case of severe disease). For patients between these extremes, there are no data showing any diagnostic test superior to an empirical trial of pharmacological agents in devising an individualized therapeutic plan.

Will the patient benefit from antireflux surgery? Published surgical series (characterized by a high success rate) have used ambulatory esophageal pH monitoring as a method for patient selection. Thus, in the absence of inflammatory changes in the esophagus, an abnormal ambulatory pH study is a useful selection criterion for undergoing antireflux surgery. However, there are no data indicating that surgical treatment is the optimal treatment for any particular finding derived from an ambulatory pH study.

Why has GERD therapy (medical or surgical) failed in this patient: incorrect diagnosis or failed therapy? This is probably the main indication for ambulatory esophageal pH monitoring. By documenting the persistence of excessive acid reflux events, ambulatory pH monitoring can be useful in documenting antireflux treatment failures. However, its precise sensitivity and specificity in this application are unclear.

In summary, patients with GERD are usually well managed using a careful medical history, endoscopy, and empirical trials of antireflux medications. Extended esophageal pH monitoring is unnecessary in most patients but can be of considerable value in managing patients with typical or atypical symptoms who are refractory to standard therapy for GERD. Furthermore, the test can be useful in documenting abnormal reflux in an individual without esophagitis being evaluated for antireflux surgery.

Chest Pain

Numerous published series have shown that reflux is common among patients with chest pain who have already passed the scrutiny of a cardiology evaluation. About 40% of patients in published series have abnormal pH studies whether they be interpreted in terms of overall esophageal acid exposure time or symptom-reflux association. However, about 50% of the patients in these trials have typical GERD symptoms, and it is unclear whether or not ambulatory esophageal pH monitoring detects additional cases of reflux-related chest pain that would not already be suspected on the basis of a history and endoscopic examination. Ultimately, the potential value of any diagnostic test in this population is in guiding therapy and, at present, there are no data showing any advantage to an ambulatory esophageal pH study as opposed to an empirical trial of antireflux therapy in the management of patients with suspected reflux-induced chest pain. Ambulatory esophageal pH monitoring is, however, potentially useful in evaluating patients without typical symptoms of reflux disease or in the management of patients with suspected reflux-induced chest pain whose pain has not improved or resolved with antireflux therapy. However, these uses remain untested in any large, prospective, controlled clinical trial.

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