Ambulatory esophageal pH monitoring in gastroesophageal reflux disease

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Gastroesophageal reflux disease (GERD) is a common disorder which results from excessive reflux of gastric contents into the esophagus. While numerous clinical tests are available for its diagnosis, prolonged ambulatory esophageal pH monitoring is the only available test which can quantify the amount of acid refluxed into the esophagus over a circadian cycle and correlate patient symptoms with the refluxed acid. The development of compact data recorders and multiple electrodes has helped us study the normal and pathological physiology of GERD as well as identify many atypical presentations of this protean disease. With advancing technology, prolonged ambulatory esophageal pH monitoring is fast becoming the best test not only to diagnose GERD, but also to define its relationship to numerous other gastrointestinal and nongastrointestinal diseases.

Key Words: Antireflux surgery, Chest pain, Esophagus, Gastroesophageal reflux disease, Heartburn, pH testing

Monitoring ambulatoire du pH œsophagien dans le reflux gastro-œsophagien

RÉSUMÉ: Le monitoring ambulatoire du pH œsophagien a fait l'objet d'intenses recherches et est considéré comme une aide diagnostique fiable bien qu'il ne s'agisse pas là d'un étalon-or lorsqu'il est question de reflux gastro-œsophagien. De toute évidence, les patients qui souffrent des symptômes typiques du reflux ou d'œsophagite doivent subir des épreuves diagnostiques plus approfondies. Le

PROLONGED MONITORING OF ESOPHAGEAL pH has been instrumental in helping us better understand the pathophysiology of gastroesophageal reflux disease (GERD). It is the only precise method for quantifying the amount of acid reflux over the circadian cycle and, more importantly, it helps identify patients with atypical presentations of GERD including nausea, vomiting, belching, hiccups, chest pain, hoarseness, recurrent coughing, globus sensation, or pulmonary symptoms such as asthma or recurrent pneumonia. Symptoms can be accurately correlated with acid reflux which adds an extra dimension to the mere quantification of acid exposure. Currently, prolonged pH monitoring is the most sensitive and specific test for GERD and a near 'gold standard' for the diagnosis of this syndrome.

HISTORICAL PERSPECTIVE

The development of a glass pH electrode by Rovelstad and colleagues (1) was soon followed by short term diagnostic tests for GERD such as the acid clearance and standard acid reflux tests.

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monitoring ambulatoire du pH peut justement fournir des renseignements extrêmement utiles dans plusieurs cas compliqués. Cette épreuve est généralement demandée et effectuée par des gastro-entérologues et certains chirurgiens, mais nous croyons que d'autres groupes la trouveront utile, notamment les cardiologues, les pneumologues, les oto-rhino-laryngologistes et les internistes. Pour mieux répondre à cette demande croissante, il faut affiner la technique, particulièrement faciliter l'insertion de la sonde qui sert à mesurer le pH. Les applications cliniques et de recherches futures en ce qui concerne le monitoring prolongé du pH œsophagien est prometteur. Cette technologie pourrait bien devenir pour le diagnostic du reflux gastro-œsophagien ce que l'endoscope a été pour le diagnostic de l'ulcère gastro-duodénal.

Figure 1) Various patterns of gastroesophageal reflux are recorded by 24 h ambulatory esophageal pH monitoring. **Top** Normal or 'physiologic' reflux pattern characterized by rapidly cleared reflux episodes after meals but no acid reflux while asleep. **Middle** 'Upright' reflux pattern, which primarily represents an exaggeration of the physiologic pattern without supine reflux. Although symptoms may be severe, esophagitis is infrequent. **Bottom** 'Combined' reflux pattern with excessive acid reflux both in the upright and supine position. These patients have severe symptoms, esophagitis and complications of gastroesophageal reflux disease. M Meal; S Sleep; P Postprandial period

Miller et al (2,3) were the first to use glass electrodes for measuring esophageal and gastric pH for longer periods (up to 24 h). Soon afterwards, Spencer (4) measured prolonged esophageal acidity in healthy volunteers and patients with hiatal hernia; he found that normal controls had some postprandial gastroesophageal reflux but patients with hiatal hernia had excessive distal esophageal acid exposure when compared with healthy subjects.

Johnson and DeMeester (5), using a bedside recording apparatus, performed landmark studies in control subjects and patients with various degrees of GERD. Acid reflux was defined as intraesophageal pH less than 4.0. A pH of 4 was chosen because: it is unequivocally distinct from the usual esophageal pH (ranging between 5 and 7); 80% of the proteolytic activity of pepsin which may be the most damaging component of acid reflux is activated at this pH; and patients with symptomatic reflux show a reasonable association between an intraesophageal pH of 4 and the onset and resolution of their symptoms. These workers (5) developed a scoring system based on six variables characterizing the pattern of acid reflux: percentage of recorded time with intraesophageal pH less than 4 in the upright and supine position (as well as during the total observation period), total number of reflux episodes, number of reflux episodes lasting longer than 5 mins and duration of the longest reflux episode. Their studies in healthy subjects introduced the concept of 'physiologic reflux', characterized by rapidly clearing upright episodes occurring primarily postprandially (infrequently associated with esophagitis). Studies in symptomatic patients with varying degrees of endoscopic and histological esophagitis identified three patterns of pathological reflux: upright refluxers, supine refluxers and those with a combination pattern (Figure 1) (6). More importantly, their work called attention to the importance of recumbent reflux episodes, primarily occurring during sleep, as a major risk factor for the development of esophagitis. Subsequent studies (7,8) have shown that supine reflux is damaging,

particularly to the esophageal mucosa, because of the absence of acid clearing mechanisms while asleep (ie, decreased esophageal peristalsis, saliva and absence of gravity).

Great improvements have been made in recording equipment since the early studies of the 1960s and '70s. Small, portable lightweight data recorders are now available which can record pH for 24 h at home or work (9). More importantly, these profuse data can be analyzed by computer programs in a very short time (10). These advancements make 24 h esophageal pH measurements a practical tool for both clinical testing and research investigation into GERD.

TECHNICAL ASPECTS

Equipment: The basic equipment for measuring 24 h pH consists of a pH electrode with a reference electrode and a portable data recorder. The pH and reference electrodes can be thought of as two terminals with opposite charges. The speed of an electrical current between these terminals is rate-dependent on the pH of the solution through which it passes. Using this principle, the esophageal pH can be sampled and stored for up to 24 h by the recorder.

Two types of pH electrodes – glass and monocrystalline antimony – are available. The glass electrode was introduced first and has a built-in reference electrode. An intraluminal reference electrode is superior to an external skin electrode because the electrical potential difference of the skin introduces an error of 0.3 to 0.6 pH units and skin contact may be poor owing to drying out of the gel (9,11). These electrodes are also bulkier and stiffer than antimony electrodes.

Monocrystalline antimony electrodes are most commonly used for clinical esophageal pH studies. These electrodes have a corrosion potential which limits their lifespan to approximately 10 studies (glass electrodes are good for 20 to 30 studies). Antimony electrodes require an external skin reference which usually is attached to the anterior chest wall by electrode jelly. Since these electrodes use an external reference, they are smaller in size than glass elec-

trodes (1.5 to 2.0 versus 2.5 to 3.0 mm, respectively) and are better tolerated by patients over prolonged periods.

A recent study (11) has shown that in all examined characteristics (response time, sensitivity, pH drift and temperature coefficient), antimony electrodes are inferior to glass electrodes. Whereas glass electrodes have a linear response over pH range 1 to 12, this is not the case for antimony electrodes, even over pH range 1 to 7. Nevertheless, most authorities (9,12,13) believe that antimony electrodes can be used with satisfactory results in clinical studies measuring esophageal acid reflux; in such studies the most important measurement is the period of time that acid exposure is below a predetermined threshold – eg, pH 4 – versus magnitude of pH fall. Studies of alkaline reflux in the esophagus or gastric acid studies, however, require the use of glass electrodes.

Prior to a study, the pH electrode is calibrated using neutral buffer and acid buffer (usually pH 1 or 4). The calibration should be repeated after the study to ensure that dramatic pH shifts have not occurred to invalidate the accuracy of the study. A drift of 0.2 to 0.4 pH units is acceptable over a 24 h study.

Glass electrodes cost approximately \$500 while monocrystalline antimony electrodes are less expensive, ranging from \$50 to \$100. Catheters with two and three antimony electrodes are now available for studying gastropharyngeal or gastropulmonary reflux. Similarly, two or more glass electrodes can be combined to study esophageal and duodenogastric reflux simultaneously.

Data recorders are compact, weigh approximately 0.9 kg and are worn on waistbelts. The important consideration is the ability to record accurately for desired time; sampling rates of every 4 s provides reliable estimates of fluctuation in intraesophageal pH (9). Reflux data recorded from the same pH electrode on both standard physiography and ambulatory recorders agree very closely (14,15). An event marker in the recording system allows patients to indicate their symptoms (which can be correlated with their diary and pH changes). At the completion of the

monitoring period, the data are stored and analyzed in a computer which prints a graphic display of intraesophageal pH over time. There are several ambulatory pH systems available in the United States (Sandhill, Colorado and Synectics, Texas) that range in price from US\$10,000 to \$15,000.

Placement of pH electrode: Spencer (4), when performing the first studies in control subjects and reflux patients, placed the pH electrode at the junction of the middle and lower third of the esophagus. Johnson and DeMeester (5) positioned their pH electrode 5 cm above the manometrically determined upper border of the lower esophageal sphincter (LES). This location was chosen as a point clearly within the esophageal body that was close enough to the gastroesophageal junction to detect reflux but sufficiently far to ensure the probe would not slip into the stomach when the esophagus shortened with swallowing. Most subsequent studies, especially those defining normal pH parameters, have continued to position the pH electrode manometrically 5 cm above the LES. Unfortunately, the need for stationary motility for locating the LES is a possible limitation to the widespread use of pH monitoring.

Other proposed methods of pH electrode placement include fluoroscopy, endoscopy or step-up of the pH as the electrode is moved from the stomach into the esophagus. All these measurements have been compared with esophageal manometry and are not accurate enough for placement (16). Recently, the addition of a solid state pressure transducer to the pH electrode has been shown to locate the LES accurately, thereby overcoming the inconvenience of two esophageal intubations and additional time for esophageal manometry (17).

Standardization of diet and activities: The type, quality and pH of ingested foods may affect intraesophageal pH recordings. Patients are frequently asked to avoid acidic foods such as fruit juices, tomato-based products, carbonated beverages, tea, coffee and yoghurt during prolonged pH monitoring. However, a recent study (18) found that

TABLE 1
Twenty-four hour pH values for normal patients

	Median	Range	95th percentile
Percentage total	1.10	0 to 8.6	5.78
Percentage upright	1.45	0 to 12.4	8.15
Percentage supine	0.10	0 to 8.5	3.45
Total episodes	18.0	0 to 101	46.00
Episodes more than 5 mins	0	0 to 7	4.0
Longest episode (min)	3.0	0 to 46	18.45

n=110 (47 males, 67 females, mean age 38 years)

esophageal pH changes from ingested acidic foods are so transitory that the effects on overall 24 h acidity are minimal. This observation is supported by a preliminary report suggesting that an ad libitum diet (compared with pH less than 5 standardized diet) does not affect the discrimination and reproducibility of esophageal pH monitoring (19). Since many reflux symptoms primarily occur postprandially, dietary restriction may unnecessarily modify patient regimen, thereby interfering with an accurate recording of the symptoms and normal reflux patterns. Similarly, smoking, alcohol consumption and exercise should not be restricted during esophageal pH monitoring.

Duration and timing of pH testing: The duration of the pH recording period and its timing in the diurnal cycle are both important considerations. Widely different recommendations have been made including a 3 h postprandial period (18,20), two consecutive 3 h postprandial periods (21), between 10 to 18 h total duration (22) and a 24 h recording period.

Although more convenient, the sensitivity of shorter test periods for detecting GERD is controversial. For example, one group (18) showed a high correlation ($r=0.92$, $P<0.001$) between reflux measured in the upright period over 23 h. On the other hand, another group (22) compared three different periods of pH monitoring (24, 12 and 10 h postprandially) in 20 healthy controls and 20 outpatients with symptomatic esophagitis; the sensitivity was 81, 50 and 70% for the 24, 12 and 10 h recording periods, respectively. Also, no significant differences were observed in terms of patient tolerability for the test during any of the three

periods. The authors believe prolonged intra-esophageal pH monitoring should involve at least 18 h of testing to maximize the ability to discriminate abnormal refluxers while also providing sufficient time to study the patient's normal activities and spectrum of complaints.

DATA INTERPRETATION

Normal control values: Establishment of cutoff points for normal limits is a prerequisite for interpretation of any test data. However, the mean age of controls and patients should be similar if these values are to be applicable clinically. A normal database established from younger control subjects may represent one of the more important limitations of current pH methodology.

In a recent review of nine studies (23), the mean age of the controls was 35.8 years compared with 48.9 years for the patients. The widely used normal values given by Johnson and DeMeester (5) come from 15 control subjects whose mean age and sex was not stated. Using their six variables and a composite score, these investigators found that 85% of symptomatic patients could be distinguished from controls. On the other hand, Schleisinger et al (24) used the same pH variables but found that only 41% of symptomatic patients and 71% of patients with erosive esophagitis could be distinguished from controls; in their study the mean age of controls (58 years) was closely matched to the patients (56 years) but the mean ± 1 SD for five of six variables was markedly higher than reported by Johnson and DeMeester (5) which suggests that age differences among control groups may be an important clinical variable.

Recent studies (25,26) have shown the esophageal pH variables from healthy adults are not normally distributed, but rather have an asymmetrical distribution (skewed to the right). Therefore, it is not appropriate to establish an upper limit of normal using mean ± 2 SD. Nonparametric analysis should be applied with normal data presented as either the 95th percentile of the actual individual reflux points or a receiver operating characteristic analysis may be used to define optimal thresholds. The latter analysis correlates true and false positive rates for a series of cutoff points thereby maximizing the sensitivity without compromising the specificity. Using a receiver operating characteristic analysis, Schindlbeck et al (26) achieved a maximum sensitivity of 93.3% and specificity of 92.9% using the percentage time with pH less than 4 in both the upright (10.5%) and recumbent (6%) position as reflux parameters. These threshold values, however, were considerably higher than values previously reported (5,19,22, 24).

Recently, three American academic medical centres compared their normal databases obtained by similar methodology (27). Using stringent statistical methods, the six traditional pH parameters were deemed comparable across study centres. Therefore, the groups were combined giving a total population of 110 healthy subjects (47 men, 63 women, mean age 38 years) (Table 1). This large database permitted a better assessment of the influence of pH electrode, age and gender on physiological acid reflux parameters. The type of pH electrode (glass or antimony) did not significantly affect any pH parameter (27). Age, based on a comparison of 24 older controls (mean age 64 years) and 86 younger controls (mean age 36 years), was also found to not influence reflux parameters (27). Gender, however, had a significant effect on the amount of physiological gastroesophageal reflux in healthy adults, ie, men usually reflux more acid than women, especially when awake (27).

Discriminating pH parameters for separating abnormal and normal subjects: Many variables have been advo-

cated as the best discriminator of abnormal GERD including total percentage time with acid reflux (26,28,29), percentage time with acid reflux while erect (30), percentage time with acid reflux while supine (5), daytime percentage time with acid reflux (31) and the number of reflux episodes longer than 5 mins (24). The majority of studies (26,28,29) favour the total percentage time at pH less than 4 as the single best and most reproducible determinant of GERD with a sensitivity and specificity approaching 88 and 96%, respectively.

Scoring systems that incorporate several of these individual parameters have been proposed to increase the discrimination between physiological and pathological reflux. The scoring system of Johnson and DeMeester (32) incorporates six weighted pH variables, depending on their deviation from normal values, into a composite score. The calculations are somewhat complex but can rapidly be done by computer to give a 90.3% sensitivity and a 90% specificity. A simpler frequency duration index derived by multiplying the mean number of reflux episodes per hour by the mean cumulative duration of reflux episodes per hour has been popularized by European investigators (33). This score appears to provide good discrimination between normal subjects and symptomatic patients during the day, but it is less discriminating at night. However, the authors have found that the number of reflux episodes per hour is the least reproducible of pH parameters (29). This shortcoming results from the somewhat subjective definition of the end of a reflux episode and because minor oscillations of pH above the threshold value can produce a great variation in number of reflux episodes with little change in actual acid exposure time. The authors suggest that acid contact time (expressed as percentage acid exposure) in the upright position, in the supine position and during the total study be the primary criterion for identifying abnormal reflux. In the current authors' experience, an abnormal value among any combination of these three pH parameters has a 93% sensitivity and 93% specificity (29).

Figure 2) Sample of a 1 h esophageal pH tracing in a man with recurrent chest pain. Diagnosis was confirmed only after 24 h esophageal pH monitoring. Overall acid exposure during study was only minimally increased (ie, 7%); however, seven of eight chest pain episodes (four shown on this tracing) correlated well with acid reflux. Chest pain resolved with antireflux regimen including bid dose of H₂ blocker

Reproducibility and variability of pH

parameters: The reproducibility of 24 h pH monitoring is confounded by the potential for large daily variability in acid exposure resulting from diet, activity, position and idiosyncrasies in the pH probe (eg, position, mucus, drift). The authors have studied 53 subjects on two occasions at least 10 days apart using the three variables of acid exposure time (total, upright, supine) as the criteria of abnormal reflux. The differentiation of abnormal from normal agreed overall in 89% of cases (29). Among subsets, the reproducibility was 93% for the normals and esophagitis patients and 84% for the subjects with atypical chest symptoms. There was considerable variability, however, in total daily acid exposure occurring in any one individual. The overall inter-study variability was 3.2-fold with the absolute percentage time of reflux varying from 69% lower to 224% higher compared with the initial study. Nevertheless, subjects usually did not cross the cutoff point separating normal and abnormal reflux parameters.

Other studies confirm the reproducibility of pH monitoring despite the considerable variability in acid exposure times (29,34-37). Three different studies (34-36) in 50 patients found agreement in 75% of the tests reported

on two occasions. Donald et al (37) noted a twofold variation in the total duration of reflux in six patients studied for 24 h; this group advised caution when interpreting values near the upper limit of normal. The large daily variability in acid exposure also makes 24 h pH monitoring a poor indicator of therapeutic efficacy in the individual patient unless medical or surgical therapy can reduce previously high acid exposure times well into the normal range (29).

CORRELATION OF SYMPTOMS AND pH EVENTS

Documentation of abnormal GERD does not prove that the patient's symptoms are acid-related. Furthermore, some patients can have 'physiological' amounts of acid reflux but a close relationship between symptoms and pH less than 4. Therefore, the ability to provide direct correlation between symptoms and pH activity may be the most important feature of ambulatory esophageal pH monitoring systems, especially in patients with atypical presentations of GERD (Figure 2). The authors have developed a 'symptom index' – defined as the quotient of the number of symptoms specifically associated with acid reflux divided by the total number of symptoms during the

TABLE 2
Algorithm for diagnosis of gastroesophageal reflux disease; symptoms are alarming, atypical and unresponsive

Patients with typical symptoms of heartburn and regurgitation can be treated without further diagnostic studies. Alarming symptoms (dysphagia, bleeding, weight loss), atypical symptoms (chest pain, ENT or pulmonary complaints) or "classic" symptoms unresponsive to H₂ blockers require further evaluation. Depending upon availability, endoscopy or x-rays will be first diagnostic study. If esophagitis is found, no further testing is necessary to pursue more aggressive medical or surgical therapy. If these studies are negative, esophageal pH monitoring should be done even if it requires referral to a major medical centre

recording interval, expressed as a percentage (38).

An obvious limitation of the symptom index is the requirement that patients have their symptoms during the study interval. By investigating patients with frequent symptoms (at least weekly) and encouraging them to participate in activities known to bring on their complaints, only 10 to 15% of patients have no symptoms during the monitoring period. In addition, it is difficult to define clearly the lower limits of a positive symptom index. The authors' initial study suggested that a correlation between 75 and 100% was highly suggestive of a causal relationship, while correlations between 25 and 75% were indeterminate (38).

Recently, the authors (39) have applied the symptom index for heartburn and chest pain to three groups of symptomatic patients: patients with normal 24 h pH measurements and normal endoscopy; abnormal 24 h pH measurements and no endoscopic esophagitis; and abnormal 24 h pH parameters and endoscopic esophagitis. The symptom index for heartburn was significantly higher for the groups with abnormal acid exposure compared with the group with no esophagitis and normal acid profile. Receiver operating characteristic analysis found that a symptom index of more than 50% suggested that acid reflux was responsible for heartburn symptoms with a sen-

sitivity of 93% and specificity of 71%. In contrast, there was no difference among the three groups for the chest pain symptom index and a best symptom index for chest pain could not be found; a chest pain symptom index of more than 50% had poor sensitivity (56%) but good specificity (68%), while a symptom index of more than 25% increased the sensitivity to 68% but decreased specificity to 50%.

COMPARISON OF PROLONGED pH MONITORING AND OTHER TESTS FOR GASTROESOPHAGEAL REFLUX DISEASE

The physician has a large number of tests available to help in diagnosing GERD. These tests evaluate different variables in a disease spectrum – potential for reflux (low LES pressure, hiatal hernia), esophageal mucosal damage (esophagram, endoscopy, mucosal biopsy), esophageal acid sensitivity (Bernstein test, prolonged pH monitoring) and the actual presence of reflux (esophagram, standard acid reflux test, esophageal scintigraphy, prolonged pH monitoring). Unfortunately, no single test has been accepted as the gold standard for GERD nor may any single test answer all questions in a difficult case. In addition, availability of the tests, requirements for special equipment and training, expense and patient discomfort are important factors in

determining the priority in which these tests are obtained.

When the purpose of the test is screening for GERD, the high sensitivity (88 to 95%) of prolonged pH monitoring makes it the best test currently available (23). The data support this contention with typical reflux symptoms and suggest it is the best study to identify the possible contributions of GERD in patients with atypical reflux presentations. Patient discomfort and cost (US\$250 to \$400 including physician fees) are comparable with upper gastrointestinal endoscopy. However, general widespread application of prolonged 24 h pH monitoring has been limited by equipment availability (currently used primarily by gastroenterologists and surgeons in large medical centres or private groups) and need for pH probe placement by manometric measurements of the LES. For these practical reasons, endoscopic examination of the esophagus or a barium esophagram usually is the first diagnostic study ordered in patients with GERD. Endoscopy with mucosal biopsies has 100% sensitivity and specificity for identifying esophagitis but only 50 to 70% sensitivity for the presence of GERD. Similarly, the barium esophagram, particularly double contrast studies, has a sensitivity and specificity approaching 90% for erosive or ulcerative esophagitis (40) and has excellent diagnostic accuracy for identifying strictures, rings or carcinomas; this test, however, is insensitive for mild degrees of inflammation and the fluoroscopic presence of free reflux only has a GERD sensitivity of 40%. Esophageal manometry has a unique role in the assessment of esophageal motility and should be performed prior to all antireflux operations. The presence of a low LES pressure (less than 10 mmHg) has poor sensitivity (12 to 73%) for GERD (29). The suggested algorithm for using prolonged esophageal pH monitoring in the diagnosis of GERD is summarized in Table 2.

CLINICAL APPLICATIONS

GERD can be diagnosed accurately by history alone in patients with major complaints of heartburn and regurgita-

TABLE 3
Indications for ambulatory prolonged pH monitoring

Typical symptoms of gastroesophageal reflux disease (GERD) not responding to medical therapy
Atypical symptoms of GERD
Noncardiac chest pain
ENT or pulmonary symptoms
Other atypical presentations (eg, belching, hiccups, epigastric pain)
Preoperative and postoperative assessment of antireflux surgery

tion with a sensitivity of 78% and a specificity of 60% (41). Prolonged pH monitoring adds little to the diagnosis of this group of patients. On the other hand, esophageal pH monitoring may be the most helpful diagnostic test in patients with atypical presentations of gastroesophageal reflux or typical reflux symptoms not responding to medical therapy. In the latter group, the authors observed that over half of these patients did not have abnormal acid exposure to account for their symptoms while the remaining patients required greater acid suppression to control symptoms and esophagitis. Table 3 summarizes indications for ambulatory prolonged esophageal pH monitoring.

Noncardiac chest pain: Prolonged esophageal pH monitoring may be very useful in the evaluation of patients with noncardiac chest pain resembling angina. Gastroesophageal reflux has been found in 10 to 50% of these patients (42-46) and currently is believed to be two to three times more common than esophageal motility disorders as a cause of chest pain. Most patients usually have symptoms of heartburn or regurgitation, but 10% complain only of angina-like chest pain (46). The authors' group has (46) recently used prolonged pH monitoring to study 100 consecutive patients with noncardiac chest pain referred by cardiologists. Forty-eight patients (52%) had abnormal reflux parameters. Seventeen patients did not have chest pain during pH monitoring but 11 had abnormal reflux parameters. Of the remaining 83 patients with chest pain during pH monitoring, 37 patients (46%) had abnormal acid exposure times and 50 (50%) had symptoms coinciding with documented reflux episodes. Overall,

gastroesophageal reflux definitely contributed to chest pain in 50% of patients and may have contributed to pain in an additional 11%.

GERD and heart disease increase in prevalence as the population grows older. Therefore, reflux-induced chest pain can also occur in patients with coronary artery disease and may be exacerbated by common anti-anginal medications (nitrates, beta-blockers or calcium channel blockers) which can decrease LES pressure. Since these pain syndromes can be identical, objective data are essential for determining the source of pain. Prolonged ambulatory esophageal pH monitoring combined with simultaneous multilead cardiac monitoring (Holter) permits the concurrent recording of esophageal and cardiac events. In 18 patients with angiographically documented obstructive coronary artery disease, seven patients (39%) had abnormal acid reflux parameters and eight of 16 (50%) experienced chest pain episodes coinciding with acid reflux during prolonged monitoring. Four patients also had evidence of ischemia, two with associated acid-induced chest pain and one with abnormal reflux parameters. Therapy based on these findings resulted in coronary artery disease bypass grafting in two patients, increased nitrates in one and H₂ antagonist therapy in seven; in the last group, five of seven patients with reflux-associated chest pain improved while receiving famotidine 40 mg twice daily (47).

Pulmonary disorders: The link between GERD and respiratory disease recently has gained increased recognition (48,49). Asthma (50,51), chronic cough (52), bronchitis (53), pneumonitis (54), apnea (55,56), atelectasis (54)

and pulmonary fibrosis (57) can occur in adults and children in association with acid reflux disease. The proposed mechanisms of reflux-induced pulmonary disease include microaspiration and intraesophageal acid stimulating a vagal reflex (48,50). Asthma is the most extensively studied pulmonary complication associated with GERD – 30 to 85% of selected groups of asthmatics may have abnormal acid reflux (51,58, 59). When compared with control subjects, asthmatic patients have significantly greater esophageal acid exposure time, more frequent reflux episodes and longer clearance time in both the upright and supine positions during prolonged pH monitoring (59). In addition, first-line asthma drugs (theophylline or beta-adrenergic agonists) may exacerbate reflux by decreasing LES pressure, although a recent report questions this relationship (59).

Laryngopharyngeal disorders: Chronic hoarseness, cough, cervical dysphagia and globus are laryngopharyngeal symptoms that occur in association with GERD (60-63). Structural abnormalities such as vocal cord ulcers and granulomas (64,65), posterior pharyngitis and laryngitis (66), subglottic stenosis (67), and laryngeal and glottic carcinoma (60,61,68,69) have been attributed to GERD. Evidence that laryngeal ulcers and granulomas in dogs can be produced by applying gastric acid to the vocal cords in minute amounts (65) and treatment of reflux leads to improvement in pharyngeal symptoms strongly suggesting that gastroesophageal reflux may have a major role in production of these disease entities.

Prolonged esophageal pH monitoring, especially with the dual probe, can help elucidate the relationship between laryngopharyngeal disorders and GERD. The current authors (60) have studied 33 patients with chronic hoarseness and laryngeal lesions suggestive of acid irritation with a dual probe system; the majority of patients (67%) with hoarseness had abnormal upright or supine acid reflux into the distal esophagus but only one patient had a single episode of detected gastropharyngeal reflux. Likewise, 56% of patients with laryngeal carcinoma had abnor-

mal upright and supine distal acid reflux; two episodes of gastropharyngeal reflux were detected. In contrast, studies by Katz et al (70) documented simultaneous hypopharyngeal and distal esophageal acid reflux in seven of nine patients with chronic refractory dysphonia. Jacob et al (71) also found that proximal esophageal reflux, particularly at night, characterized a large group of patients with persistent laryngeal symptoms, independent of laryngoscopic findings of reflux laryngitis compared with GERD patients without ENT complaints. Further studies by several investigators (60,70,71) have provided some other interesting insights: up to two-thirds of patients presenting with laryngopharyngeal symptoms associated with GERD do not demonstrate typical symptoms of heartburn; endoscopic or radiographic evidence of esophagitis is uncommon in these patients; and repeat studies may be needed to document GERD because false-negative rates may be as high as 15%.

Pre- and postoperative evaluation of patients undergoing anti-reflux surgery: Physiological evaluation of the esophagus is essential prior to anti-

reflux surgery (72). Prolonged ambulatory pH studies can confirm that patient symptoms are due to GERD. Even if ulcerative esophagitis is present, the absence of abnormal reflux parameters, particularly in older patients, should suggest an alternative diagnosis such as pill-induced esophagitis (73). Esophageal manometry ensures the presence of adequate peristaltic forces to propel a bolus through the surgically recreated high pressure zone at the gastroesophageal junction. Because symptoms overlap, inadequate objective documentation may result in poor postoperative results due to the incorrect initial diagnosis of GERD or an unrecognized primary esophageal motor disorder such as achalasia (72,74).

Prolonged esophageal pH monitoring also is useful postoperatively to evaluate persistent or recurrent reflux symptoms. This study will usually show abnormal pH parameters prior to the redevelopment of endoscopic esophagitis (72). Following antireflux surgery, some patients will have postoperative symptoms in the absence of acid reflux. If a preoperative pH study is not available, the unanswerable question about acid reflux causing the preoperative

symptoms is raised, leading to frustration on the part of the patient and the physician.

CONCLUSIONS

Ambulatory esophageal pH monitoring has been extensively investigated and is regarded as a reliable diagnostic aid, although it is not a perfect gold standard for GERD. Clearly, patients with typical reflux symptoms or endoscopic esophagitis need no other confirmation of their diagnosis. Ambulatory pH monitoring, however, can provide extremely useful information in many other difficult cases. This test currently is ordered and performed usually by gastroenterologists and some surgeons, but other groups – including cardiologists, pulmonologists, otolaryngologists, and internists – may find this technology helpful. To meet these expanding applications, test refinements are necessary (particularly easier placement of the pH probe). The future clinical and research applications of prolonged esophageal pH monitoring are bright. This technology has the potential to do for the diagnosis of GERD what endoscopy has done for the diagnosis of peptic ulcer disease.

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