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ORIGINAL ARTICLE

A New Technique for Measurement of Pharyngeal pH: Normal Values and Discriminating pH Threshold

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Abstract
Introduction Identifying gastroesophageal reflux disease as the cause of respiratory and laryngeal complaints is difficult and depends largely on the measurements of increased acid exposure in the upper esophagus or ideally the pharynx. The current method of measuring pharyngeal pH environment is inaccurate and problematic due to artifacts. A newly designed pharyngeal pH probe to avoid these artifacts has been introduced. The aim of this study was to use this probe to measure the pharyngeal pH environment in normal subjects and establish pH thresholds to identify abnormality.
Methods Asymptomatic volunteers were studied to define the normal pharyngeal pH environment. All subjects underwent esophagram, esophageal manometry, upper and lower esophageal pH monitoring with a dual-channel pH catheter and pharyngeal pH monitoring with the new probe. Analyses were performed at 0.5 pH intervals between pH 4 and 6.5 to identify the best discriminating pH threshold and calculate a composite pH score to identify an abnormal pH environment.
Results The study population consisted of 55 normal subjects. The pattern of pharyngeal pH environment was significantly different in the upright and supine periods and required different thresholds. The calculated discriminatory pH threshold was 5.5 for upright and 5.0 for supine periods. The 95th percentile values for the composite score were 9.4 for upright and 6.8 for supine.
Conclusion A new pharyngeal pH probe which detects aerosolized and liquid acid overcomes the artifacts that occur in measuring pharyngeal pH with existing catheters. Discriminating pH thresholds were selected and normal values defined to identify patients with an abnormal pharyngeal pH environment.

Keywords Gastroesophageal reflux disease (GERD) · Laryngopharyngeal reflux (LPR) · 24-h pH monitoring · Pharynx · Esophagus

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Introduction

Respiratory and laryngeal symptoms such as hoarseness, throat clearing, chronic cough, asthma, and laryngospasm can occur in patients with typical symptoms of gastroesophageal reflux disease (GERD).[1] They also can occur in the absence of typical GERD symptoms.[2] In this setting, there are no specific clinical or pathological findings to identify reflux as the cause of the laryngopharyngeal symptoms and existing diagnostic tests lack sufficient sensitivity and specificity to confirm the diagnosis.[3]

The current practice to identify gastroesophageal reflux as a cause of laryngopharyngeal symptoms is to detect increased esophageal acid exposure by a pH probe with dual sensors, one placed 5 cm above the upper border of the lower esophageal sphincter (LES) determined by manometry and a second placed in the proximal esophagus near the lower border of upper esophageal sphincter (UES). If abnormal acid exposure is measured at both levels, it is inferred that the laryngopharyngeal symptoms are due to reflux.[4] If abnormal esophageal acid exposure is measured only in the upper probe, the relationship of reflux to laryngopharyngeal symptoms is less certain. Clinical experience with this approach has been mixed with only a minority of patients responding well to treatment.[5,6] This has led some investigators to place the proximal pH sensor in the pharynx in an effort to improve the diagnostic accuracy of reflux induced respiratory and laryngeal symptoms.[7]

Measuring pharyngeal pH has unique problems that make interpretation of the pH record difficult. There is a high frequency of artifacts in the pH recordings due to drying of the pH sensor, the accumulation of mucous or food on the sensor or the interruption of electrical continuity due to the loss of contact of the reference electrode with the mucosa. Complex criteria have been described to differentiate between these artifacts and true changes in pH caused by reflux.[8] These criteria have restricted computer reading of the pH record and required laborious hand analysis.

A new pH sensor has been designed specifically to monitor the pharynx. This sensor detects aerosolized or liquid acid, resists drying, and does not require contact with fluid or tissue for electrical continuity. The probe has a teardrop shape with the sensor oriented downward to avoid becoming covered with food or mucus (Fig. 1). The aim of this study was to measure pharyngeal pH with this newly designed sensor in a large series of normal subjects and to propose discriminating pH threshold to identify patients with abnormal pharyngeal pH environment.

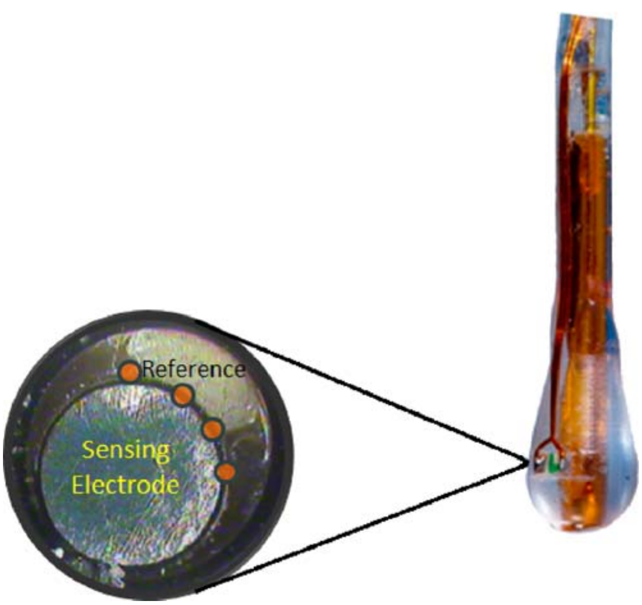


Figure 1 A magnified photograph of the Restech® pharyngeal pH probe showing the downward-oriented teardrop shape of the probe and the special proximity of the reference and sensing electrodes.

Materials and Methods

The goal was to recruit a minimum of 50 normal volunteers between the ages of 18 and 75 years. All volunteer subjects were questioned regarding the presence of GERD symptoms including heartburn, regurgitation, dysphagia, the presence of a known motility disorder or esophageal stricture, current or previous heavy alcohol or tobacco use, nasal obstruction or recent nasal surgery, anticoagulation therapy, and potential pregnancy. Subjects who answered yes to any of these questions were excluded. Out of 250 subjects screened, 78 asymptomatic volunteers were identified for participation in this study. These subjects underwent video esophagram, esophageal manometry, and esophageal pH monitoring with a catheter containing dual-pH sensor, one placed in the distal and the other in the proximal esophagus to exclude occult esophageal reflux disease. Pharyngeal pH monitoring was performed using the new pH probe. For the subjects' convenience, pharyngeal pH monitoring was performed in the same day as esophageal pH monitoring.

Technique of Esophageal pH Monitoring

Esophageal Manometry

Esophageal manometry was performed in the supine position using an eight-channel water-perfused catheter with lateral openings placed 5 cm apart and oriented radially 45° from each other. At the start of the study, all recording channels were placed in the stomach. The catheter was withdrawn in 1-cm increments every 20 s. The position of the catheter was recorded in centimeters from the ala of the nostril. The motility record was assessed using a commercially available software program (Polygram® Net, Medtronic Inc., Minneapolis, MN, USA).

Ambulatory pH Monitoring Using a Catheter with Dual-pH Sensor

A dual-pH probe was positioned in the esophagus with the distal sensor 5 cm above the upper border of the LES determined by manometry and the proximal sensor within 5 cm of the lower border of the UES. The subjects were instructed to remain in the upright or sitting position until retiring to bed in the evening, not to eat or drink between meals, refrain from chewing gum or smoking, and to go about their normal duties at home or at work. Patients were instructed to eat the meals in one sitting, accompanied only by water, milk, coffee, or tea. Carbonated beverages, alcohol, and fruit drinks with an acid pH were not permitted. Subjects were instructed to lie flat at night, if possible, with a single pillow. Medications effecting gastrointestinal function were not allowed during the monitored period. Subjects were asked to keep a diary of events that included the beginning and the end of meals, and the times of retiring in the evening and rising in the morning. Subjects returned the following day and the data were downloaded from the recording units to a personal computer and analyzed using commercially available software (Polygram® Net, Medtronic Inc., Minneapolis, MN, USA). Distal and proximal esophageal acid exposure was expressed using six components of the 24-h record and the calculated pH score for a pH threshold of <4 (Table 1).

Technique of Pharyngeal pH Monitoring

Restech® Pharyngeal pH Sensor Technology

The Restech® pH probe (Respiratory Technology Corp., San Diego, CA, USA) contains a newly developed pH sensor based on proven antimony technology. The antimony sensor changes voltage potential relative to the pH of its surrounding environment. The sensor design includes both antimony and reference electrodes bound tightly together into a miniaturized package less than 1 mm in diameter. The sensor is mounted at the tip of the probe rather than placed on the side of the shaft, as in traditional pH probe designs. The combination of miniaturization and geometric positioning of the reference electrodes allows for the sensor to operate in the environment of the pharynx without drying out. Condensation from exhaled breath continually saturates the sensor with moisture. Miniaturization of the electrode also allows the measurement of hydrogen ion concentration in both liquid and aerosolized droplets. The tip of the probe contains a light-emitting diode (LED) that aids the clinician in catheter placement. The pH is measured at a frequency of two times per second and transmitted wirelessly to a data recorder.

Table 1 Assessment of 24-h Esophageal Acid Exposure

Percent total time pH<4
Percent upright time pH<4
Percent supine time pH<4
Number of reflux episodes
Number of reflux episodes ≥5 min
Longest reflux episode (minutes)
Composite score[a]

[a] The 24-h composite pH score is the sum of the scores for each of the six components calculated by the formula: [(patient value − mean)/mean)SD] + 1

Figure 2 A photograph showing the Restech® pharyngeal pH probe properly positioned in a subject with a 5-mm flashing LED light that can be used as a guide to place the probe 5–10 mm below the uvula.

Restech® Pharyngeal pH Probe Preparation and Placement

The Restech® pH sensor was calibrated in solutions of pH 7 and pH 4 prior to use. The nasal passage was topically anesthetized using Q-tips soaked with 2% lidocaine. The sensor was inserted until the flashing LED was seen in the back of the subject's throat and then positioned so that the flashing light was 5–10 mm below the uvula. The length of the LED light is 5 mm and serves as a useful guide for placement (Fig. 2). The catheter was secured to the patient's face, as close to the nares as possible using a Tegaderm™ and then passed over the ear and secured to the neck with a second Tegaderm™. The transmitter at the end of the catheter was either taped to the skin or attached to the subjects' clothing using a clip-on case. A data recorder was attached to the patients' belt. Patients were asked not to shower during the recording period and to keep a diary indicating the time of the meal periods and the time spent in the supine and upright positions. The meal periods were excluded in the analyses of pharyngeal pH recordings. The esophageal and pharyngeal pH data were collected by two different recording devices. The timers of both data recorders were synchronized prior to the start of the monitoring period to assure simultaneous monitoring of esophageal and pharyngeal pH. The Restech® data recorder was downloaded to a proprietary software program and correlated with the patient's diary. Data from the esophageal pH probe with dual sensor were also exported to the same software. This program allowed simultaneous comparison of the pH records to determine the temporal relationships between the pH changes in the distal esophagus, proximal esophagus, and pharynx.

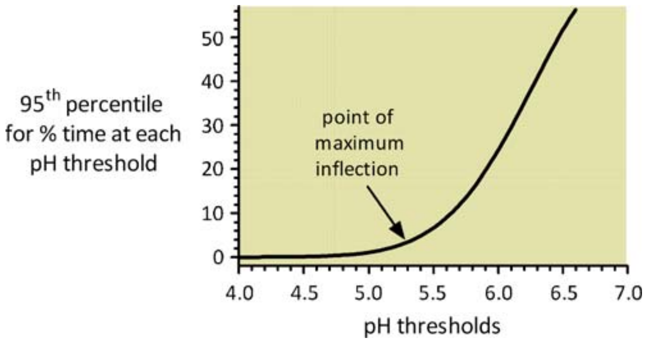


Figure 3 An example of the mathematical graphic model used to determine the discriminating pH threshold. The 95th percentile values for percent time the pH is below various pH thresholds is plotted to construct a curve. The point of maximum inflection is calculated using the equation for the plotted curve. The equation for this illustrated curve is: $y = 4.1852x^3 - 50.952x^2 + 202.45x - 261.19$.

Determination of pH Thresholds and Normal Pharyngeal Acid Exposure

Pharyngeal pH recordings performed with the Restech® probe prior to the study showed that changes in the pharyngeal pH environment can be caused by the reflux of gastric juice, i.e., true reflux events, alteration in salivary flow during sleep and awake periods, and small fluctuations due to noise in the recording system. The best discriminating threshold should detect the majority of true reflux events while minimizing the influence of saliva and the noise of the system.

The best discriminatory pharyngeal pH threshold was determined using a mathematical graphic methodology in which the 95th percentile value for the percent time the pH was below 4, 4.5, 5, 5.5, 6, and 6.5 was calculated and plotted to construct a curve. The slope in the curve reflects the noise in the system (Fig. 3). The horizontal portion of the curve represents the thresholds that are less affected by the noise of the system but fail to recognize many true reflux events. The vertical portion of the curve represents thresholds that are more affected by the noise of the system but detect higher number of true reflux episodes. The equation that defined the curve was used to calculate the point of its maximal inflection. This is the point at which the ability to detect true reflux events is maximized while the noise of the system is minimized as illustrated in Fig. 3.

Determination of the Pharyngeal Composite pH Score

A composite pH score was calculated for the pH threshold identified by applying the same method used to calculate the composite pH score for esophageal pH monitoring. This required calculating for each subject the scores for each component by the formula:

$$\frac{\text{subject value} - \text{mean of 55 normal subjects}}{\text{SD}} + 1$$

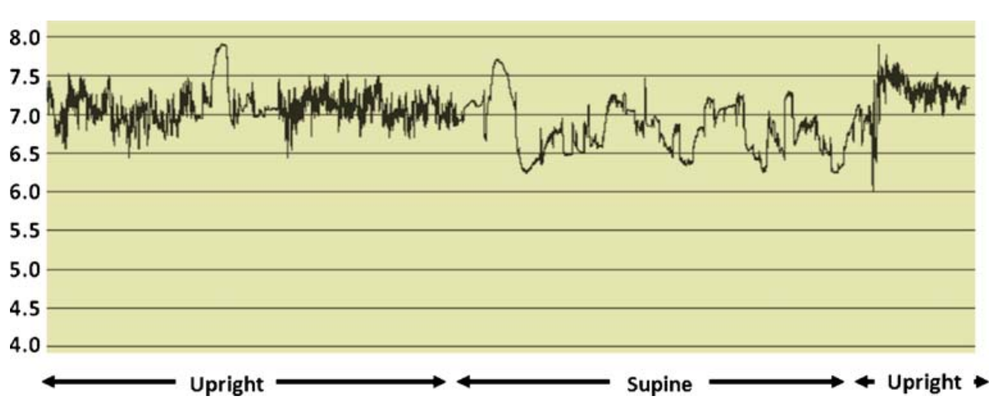
The sum of the three component scores (percent time below threshold, number of reflux episodes, and duration of the longest episode) equals the pharyngeal composite pH score.

Results

Among the 78 volunteers, 12 had abnormal distal esophageal acid exposure (DeMeester Score>14.7); five had a hiatal hernia larger than 2 cm on video esophagogram, and six had technical difficulties with either their esophageal (n=3) or pharyngeal (n=3) pH recorders rendering their tracings unusable. These 23 subjects were excluded. In the remaining 55 normal subjects, pharyngeal pH monitoring was performed with the new pharyngeal pH sensor without encountering artifacts or technical problems.

The study population consisted of these 55 normal subjects. There were 28 males and 27 females with a median age of 28 years (range 19–72). A representative pharyngeal pH tracing is shown in Fig. 4. The pattern of the pharyngeal pH environment was visibly different between the upright and supine periods. Further, the mean pharyngeal pH was significantly higher in the upright than supine period (Fig. 5). Consequently, separate analyses were done for the upright and supine periods.

Figure 4 A representative 24-h pharyngeal pH tracing from a normal subject. The upright and supine periods can be identified easily by the pattern of the pH recording.



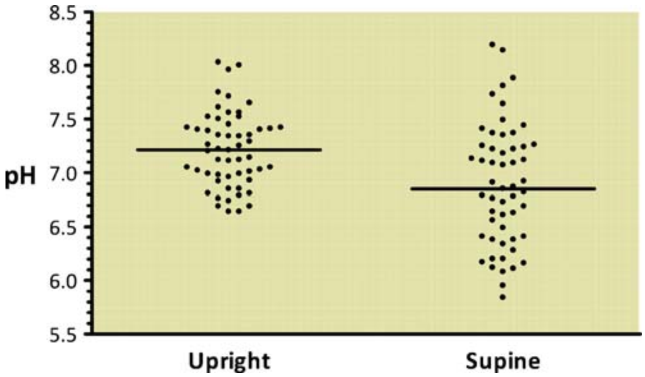


Figure 5 The mean values for the pharyngeal pH environment in each subject are plotted for the upright and supine periods. The mean pharyngeal pH was higher in the upright period (7.2 vs. 6.8, $p<0.0001$, Wilcoxon matched-pairs test).

The mean, median, interquartile range, and 95th percentile values for the components of pharyngeal pH monitoring at different pH thresholds are shown in Tables 2 and 3. The 95th percentile values for percent time the pH was below the various pH thresholds for the upright and supine periods are plotted in Fig. 6. The point of maximal inflection of the curves was at the pH of 4.8 for the supine period and 5.6 for the upright period. These were selected as discriminating pH thresholds and were rounded off to 5.0 for the supine period and 5.5 for the upright period.

Since pharyngeal pH exposure for the upright and supine periods were calculated separately, only three of the six components (percent time, number of episodes, and duration of longest episode) were used to calculate the composite score. The 95th percentile values for pharyngeal pH exposure at the discriminating pH thresholds in the

Table 2 Normal Values for 24-h Pharyngeal pH Monitoring in the Upright Position at Different pH Thresholds (n=55)

	Mean	Median	IQR		95th percentile
			25th percentile	75th percentile	
Ph<4.0					
% Time	0.0	0.0	0.0	0.0	0.0
No. of episodes	0.0	0.0	0.0	0.0	0.0
Longest episode	0.0	0.0	0.0	0.0	0.0
No. of episodes ≥5 min	0.0	0.0	0.0	0.0	0.0
pH<4.5					
% Time	0.0	0.0	0.0	0.0	0.0
No. of episodes	0.0	0.0	0.0	0.0	0.0
Longest episode	0.0	0.0	0.0	0.0	0.0
No. of episodes ≥5 min	0.0	0.00	0.0	0.0	0.0
pH<5.0					
% Time	0.004	0.0	0.0	0.0	0.021
No. of episodes	0.073	0.0	0.0	0.0	1.00
Longest episode	0.021	0.0	0.0	0.0	0.118
No. of episodes ≥5 min	0.0	0.0	0.0	0.0	0.0
pH<5.5					
% Time	0.015	0.0	0.0	0.001	0.133
No. of episodes	0.255	0.0	0.0	0.0	1.20
Longest episode	0.068	0.0	0.0	0.0	0.71
No. of episodes≥5 minutes	0.0	0.0	0.0	0.0	0.0
pH<6.0					
% Time	0.846	0.170	0.0	0.65	6.29
No. of episodes	5.33	1.0	0.0	5.0	40.2
Longest episode	1.98	0.010	0.0	1.29	12.83
No. of episodes ≥5 min	0.218	0.0	0.0	0.0	2.0
pH<6.5					
% Time	6.55	1.32	0.074	8.42	32.9
No. of episodes	34.18	10.0	2.0	43.0	154.4
Longest episode	27.12	2.85	0.18	14.2	144.1
No. of episodes ≥5 min	1.66	0.0	0.0	2.0	10.0

Table 3 Normal Values for 24-h Pharyngeal pH Monitoring in the Supine Position at Different pH Thresholds (n=55)

	Mean	Median	IQR		95th percentile
			25th percentile	75th percentile	
pH<4.0					
% Time	0.68	0.0	0.0	0.0	1.26
No. of episodes	0.16	0.0	0.0	0.0	1.00
Longest episode	1.16	0.0	0.0	0.0	5.93
No. of episodes ≥5 min	0.09	0.0	0.0	0.0	0.2
pH<4.5					
% Time	0.92	0.0	0.0	0.0	1.54
No. of episodes	0.22	0.0	0.0	0.0	1.20
Longest episode	1.88	0.0	0.0	0.0	7.11
No. of episodes ≥5 min	0.11	0.0	0.0	0.0	0.2
pH<5.0					
% Time	1.33	0.0	0.0	0.0	5.15
No. of episodes	0.55	0.0	0.0	0.0	4.0
Longest episode	2.91	0.0	0.0	0.0	18.97
No. of episodes ≥5 min	0.18	0.0	0.0	0.0	0.2
pH<5.5					
% Time	3.98	0.0	0.0	5.07	23.9
No. of episodes	3.38	0.0	0.0	3.0	16.2
Longest episode	9.79	2.71	0.0	6.11	52.7
No. of episodes ≥5 min	0.76	0.0	0.0	1.0	4.4
pH<6.0					
% Time	13.94	3.51	0.0	22.8	55.1
No. of episodes	10.95	4.00	0.0	17.0	45.0
Longest episode	27.8	5.8	0.0	33.8	152.3
No. of episodes ≥5 min	2.51	1.0	0.0	4.0	10.2
pH<6.5					
% Time	31.1	23.0	1.9	60.7	77.9
No. of episodes	24.95	16.0	2.00	34.0	114.0
Longest episode	74.5	34.9	2.27	98.6	334.2
No. of episodes ≥5 min	3.84	4.0	0.0	7.0	10.0

upright and supine positions and their RYAN composite score values are shown in Table 4.

Discussion

Acid-related laryngeal ulcerations and granulomas were first described in 1968.[4] Since that time, acid reflux has been implicated as the cause of several laryngeal and pharyngeal symptoms including hoarseness, globus sensation, chronic cough, otalgia, and laryngospasm.[9] Acid reflux has also been implicated as the cause of laryngeal stenosis and carcinoma.[2] Of interest, only a minority of these patients have typical reflux symptoms such as heartburn and regurgitation.[1] Further, even when abnormal distal esophageal acid exposure is confirmed by 24-h pH monitoring, the effectiveness of antireflux surgery in eliminating laryngopharyngeal reflux (LPR) symptoms is not predictable.[10] These results have led to the monitoring of the esophagus using a catheter with dual-pH sensors, one located in the distal and the other in the proximal esophagus, to better identify acid reflux as the etiology of LPR symptoms.[7]

Clinical experience has shown that even when monitored with catheters containing dual-pH sensors the ability to predict relief of LPR symptoms by acid suppression therapy or antireflux surgery is inconsistent. Studies by Wo and colleagues[11] and Cool and colleagues[12] claim that there is no convincing evidence that proximal esophageal pH monitoring predicts response to acid-suppressive therapy in patients with LPR symptoms. Further, Wo and colleagues have reported that only 25% of patients with increased proximal esophageal acid exposure were relieved of their LPR symptoms following antireflux surgery.[5] In

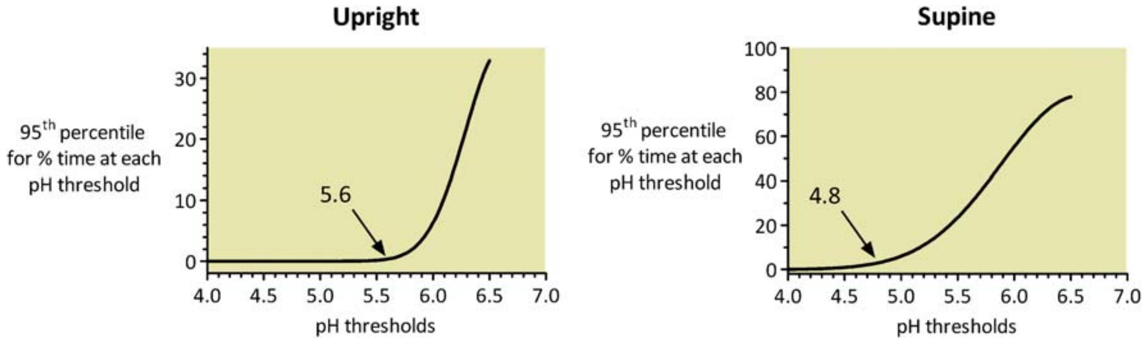


Figure 6 The mathematical graphic model plotting the 95th percentile values for percent time below different pH threshold values is shown for the upright and supine periods. The equations that define these curves were used to calculate the point of maximum inflection (*arrows*) to identify the best discriminating thresholds.

contrast, Patti and colleagues reported that cough resolved after antireflux surgery in 83% of patients in whom a correlation between cough and reflux was found during proximal esophageal pH monitoring.[6]

These results have prompted investigators to monitor the pharynx.[7] There are several problems with this approach. Technical artifacts are common due to drying of the sensor or disruption of the electrical circuit between the reference and sensing electrodes. Food and mucous can also accumulate on the sensor interfering with the ability to detect acid in the pharynx.[13,14] The Restech® pharyngeal pH probe and sensor utilized in this study has been designed to avoid these limitations, and we did not observe artifacts or technical problems with its use.

A pH of 4 is used as a threshold in distal esophageal pH monitoring[15] based on studies showing that heartburn is associated with esophageal exposure to a pH less than 4.[16] No such typical symptom exists to define a pH threshold in pharyngeal pH monitoring. In addition, there is a pH gradient in the esophagus when reflux occurs due to neutralization of the refluxed gastric juice by swallowed saliva.[17] Consequently, a pH threshold higher than 4 is likely needed to identify abnormal pharyngeal exposure to gastric juice.

In this study, we characterized the pH environment of the pharynx in normal subjects and have shown that the mean pharyngeal pH is lower during the supine period than during the upright period (6.8 vs.7.2, $p<0.0001$). This is because salivary flow is reduced during the night resulting in a lower pharyngeal pH. Consequently, we propose that the upright and supine periods should be analyzed separately using different pH thresholds. When using the chosen discriminating pH threshold, we found that a drop in pharyngeal pH was more frequent and prolonged in the supine compared to the upright position. This is likely also due to the decreased production of saliva during the sleep.

We used a mathematical graphic model to identify the best discriminating pH thresholds to detect the changes in the pharyngeal pH environment during the upright and supine period. This methodology allowed us to select pH thresholds for the two periods in which detection of true reflux episodes was maximized while the noise of the system was minimized. The percent time pH was below these selected thresholds, the number of episodes in which the pH dropped below these thresholds, and the duration of the longest episode were measured and integrated into a pharyngeal pH (RYAN) score for the upright and supine periods. The calculated threshold for the upright period was pH 5.5 and for the supine period 5.0. The normal RYAN composite score for these periods was 9.4 and 6.8, respectively.

Selecting discriminating pH thresholds and defining normal values are necessary first steps toward establishing the utility of this newly designed probe. The mathematical graphic methodology used in this study is a reasonable approach for selecting a discriminating pH threshold for the pharyngeal environment. The selected discriminating thresholds and normal values reported in this study need to be validated by collecting a registry of patients with LPR symptoms who have an abnormal pretreatment pharyngeal pH environment and show relief of symptoms and normalization of pharyngeal pH environment with acid suppression therapy or antireflux surgery.

Finally, an abnormal pharyngeal pH environment can be caused by decreased salivary production, change in bacterial flora of the pharynx, and reflux of gastric juice into the pharynx.[18,19] Only the latter is likely to be associated with LPR symptoms. The pharyngeal pH records in symptom-

Table 4 The 95th Percentile Values (Normal) for the Components and Composite Score of Pharyngeal pH Exposure at the Discriminating pH Thresholds

	Upright pH<5.5	Supine pH<5.0
% Time	0.13 min (8 s)	5.15 min (309 s)
No. of episodes	1	4
Longest episode (min)	0.71	18.97
RYAN[a] Score	9.41	6.79

[a] Composite pH score for pharyngeal acid exposure

atic patients need to be interpreted keeping these other etiologies in mind.

Conclusion

A new pharyngeal pH probe which detects aerosolized and liquid acid overcomes the artifacts that occur in measuring pharyngeal pH with existing catheters. New discriminating pH thresholds were selected to identify patients with abnormal pharyngeal pH environment. The discriminating thresholds and normal values reported in this study need to be validated by patients with LPR symptoms who respond to acid suppression therapy or antireflux surgery.

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