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Importance of esophageal manometry and pH monitoring for the evaluation of otorhinolaryngologic (ENT) manifestations of GERD. A multicenter study

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Abstract

Background/Aims Patients with otorhinolaryngologic (ear, nose, and throat—ENT) symptoms attributed to gastroesophageal reflux disease (GERD) are usually treated with medication based on the findings of nasal endoscopy and laryngoscopy only. This study aims to determine sensitivity and specificity of symptoms, nasal endoscopy, and laryngoscopy for the diagnosis of GERD as compared to pH monitoring.

Methods We studied 79 patients (mean age 53 years, 38 % males) in whom ENT symptoms were assumed to be secondary to GERD. All patients underwent a transnasal laryngoscopy by the ENT team and upper endoscopy and esophageal function tests by the surgical team. GERD was defined by a pathological pH monitoring.

Results Pathologic reflux by pH monitoring was documented in 36 of the 79 patients (46 %), with a mean DeMeester score of 44. In 25 of the 36 patients (69 %), distal and proximal reflux was present. Among patients with negative pH monitoring, one patient was diagnosed with achalasia. ENT symptom sensitivity for globus, hoarseness and throat clearing was respectively 11, 58, and 33 %; specificity was respectively 77, 42, and 58 %. Positive predictive value for nasal endoscopy and laryngoscopy was 46 %. Among patients with positive pH monitoring, 13 (36 %) had a hypotensive lower esophageal sphincter ($p < 0.01$) and 27 (34 %) had abnormal peristalsis ($p < 0.01$).

Conclusions In conclusion, the results of this study showed that (a) ENT symptoms were unreliable for the diagnosis of GERD and (b) laryngoscopy had a low positive predictive value for the diagnosis of GERD. These data confirm the importance of esophageal manometry and pH monitoring in any patient with suspected ENT manifestations of GERD before starting empiric therapy with acid-reducing medications since pathologic reflux by pH monitoring was confirmed in less than half of the patients with suspected GERD.

Keywords Gastroesophageal reflux disease · Globus · Hoarseness · Throat clearing · Laryngoscopy · Esophageal manometry · Esophageal pH monitoring

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Introduction

The clinical spectrum of gastroesophageal reflux disease (GERD) ranges from asymptomatic patients to extra-esophageal symptom such as hoarseness, globus, and throat clearing.[1, 2] Several of these patients are evaluated in otorhinolaryngologic (ear, nose, and throat—ENT) clinics and frequently treated with proton pump inhibitors based solely on the presence of symptoms and on the findings of transnasal flexible laryngoscopy.[3, 4] Similarly, about half of the gastroenterologists prefer an initial approach favoring therapeutic trials instead of objective testing in these patients (proton pump inhibitors—PPI trial).[4] Esophageal (typical) symptoms and upper gastrointestinal endoscopy have been repeatedly shown to be inaccurate for the diagnosis of GERD.[5, 6]

Extra-esophageal symptoms may be even more inaccurate since many diseases, apart from GERD, may cause these symptoms.

We hypothesized that esophageal manometry and dual probe pH monitoring are essential to evaluate esophageal motility (and ruling out achalasia), allow a correct placement of the pH catheter (5 cm above the border of the manometrically determined lower esophageal sphincter), and assess the presence of abnormal reflux and its proximal extent in patients with ENT symptoms though to be secondary to GERD.

This study aims to determine sensitivity and specificity of symptoms and laryngoscopy for the diagnosis of GERD as compared to pH monitoring.

Methods

We performed a retrospective review of data from prospectively maintained databases in two quaternary care centers. In each institution, both the ENT and the esophageal services were involved.

Inclusion Criteria

Between July 2008 and July 2015, we evaluated 79 patients in whom cough, hoarseness, globus, and throat clearing were assumed to be secondary to GERD. Twenty patients were treated at the Escola Paulista de Medicina, Federal University of Sao Paulo, São Paulo, Brazil, and 59 at the University of Chicago Medical Center (USA).

All patients were initially seen at the ENT clinics and referred to a surgical team for antireflux surgery. All patients were under pharmacological treatment for GERD with PPI. The reason for referral was non-response to PPI or unwillingness to maintain long-term medication intake.

Symptom prevalence is summarized in Table 1. Esophageal symptoms (either heartburn or regurgitation) were present in addition to ENT symptoms in 56 patients (71 %).

Upper Gastrointestinal Endoscopy All patients underwent an upper endoscopy after evaluation by the surgical team. Endoscopic findings are shown in Table 2.

Esophageal Function Tests Esophageal manometry was performed in all patients after evaluation by the surgical team. Medications that interfere with esophageal and gastric motility were discontinued 3 days before the study. Acid-reducing medications were discontinued 3 (H2-blocking agents) to 10 days (proton pump inhibitors) prior to the study. Lower esophageal sphincter (LES) resting pressure, esophageal body peristalsis, and upper esophageal sphincter resting pressure were recorded. The data were analyzed by computer, using a dedicated software program. Manometric findings are shown in Table 3.

Esophageal pH monitoring was performed in all patients after evaluation by the surgical team. During the study, the patients consumed an unrestricted diet. Ambulatory pH monitoring was performed by placing a dual pH probe catheter with sensors positioned 5 and 20 cm above the upper border of the manometric determined LES. The data were incorporated into a composite score (DeMeester score), and a score greater than 14.7 was set as abnormal. Proximal reflux was defined by proximal acid exposure greater than 1 %.[7]

Laryngoscopy Transnasal laryngoscopy was performed in all patients by the ENT team. Endoscopic findings are shown in Table 2.

Main Outcome Measures Correlation among abnormal reflux on pH monitoring, symptoms and laryngoscopy findings.

Statistics Bayesian diagnostic testing (sensitivity, specificity, positive predictive value, negative predictive value) was applied. Student's t test was used for mean comparison and Fisher test for proportion comparison. Confidence intervals (CI) are given for 95 % reliability. Statistical significance was defined as $p < 0.05$.

Ethics There are no conflicts of interest. There is no funding. The authors are responsible for the manuscript and no professional writers were hired. The study was approved by the IRB of each Institution. Informed consent was waived due to the retrospective format of the study.

Results

Pathologic reflux by pH monitoring was documented in 36 of the 79 patients (46 %), with a mean DeMeester score of 44 (normal less than 14.7). In 25 of the 36 patients (69 %), distal and proximal reflux was documented.

Symptoms The prevalence of esophageal and ENT symptoms was similar between GERD+ and GERD− patients (Table 1). Overall symptom sensitivity for globus, hoarseness, and throat clearing was respectively 11, 58, and 33 %, and specificity was respectively 77, 42, and 58 %.

Upper Gastrointestinal Endoscopy The prevalence of hiatal hernia and esophagitis was similar between GERD+ and GERD− patients (Table 2). Additional findings were two cases of Barrett's esophagus and two cases of Zenker's diverticulum, all in GERD+ patients.

Table 1 Prevalence of symptoms for the whole population ($n = 79$) and according to the presence ($n = 36$) or absence ($n = 43$) of gastroesophageal reflux disease

	All patients	GERD negative	GERD positive	*p* value	Sensitivity	Specificity	PPV	NPV
	79 (100)	43 (54.4)	36 (45.6)					
Age (years) (19–88)	52.8 ± 17.6	50 ± 17.7	55.9 ± 17.3	0.1518				
Gender (male), *n* (%)	30 (37.9)	14 (32.6)	16 (44.4)	0.2783				
Body mass index (kg/m2)	28.6 ± 7	27.9 ± 7.5	29.3 ± 6.4	0.4298				
Symptoms								
Globus, *n* (%)	14 (17.7)	10 (23.3)	4 (11.1)	0.1591	11.1	76.7	28.6	50.8
Hoarseness, *n* (%)	46 (58.2)	25 (58.1)	21 (58.3)	0.9861	58.3	41.9	45.6	27.3
Throat clearing, *n* (%)	30 (38)	18 (41.9)	12 (33.3)	0.4367	33.3	58.1	40	51
Sore throats, *n* (%)	25 (31.6)	15 (34.9)	10 (27.8)	0.4988	27.8	65.1	40	51.8
Upper dysphagia, *n* (%)	50 (65.8)	27 (62.8)	23 (63.9)	0.9196	63.9	37.2	66	55..2
Cough, *n* (%)	52 (65.8)	27 (62.8)	25 (69.4)	0.5346	69.4	37.2	48.1	59.3
Heartburn, *n* (%)	43 (54.4)	21 (48.8)	22 (61.1)	0.2753	61.1	51.2	51.2	61.1
Regurgitation, *n* (%)	40 (50.6)	19 (44.2)	21 (58.3)	0.2103	58.3	55.8	25.5	61.5
Heartburn and regurgitation, n (%)	27 (34.2)	12 (27.9)	15 (41.6)	0.1990	41.7	72.1	55.6	59.6

GERD gastroesophageal reflux disease, *PPV* positive predictive value, *NPV* negative predictive value

Laryngoscopy The majority of patients (86 %) had at least one laryngoscopic finding compatible with GERD but the prevalence of these findings was not different in GERD+ and GERD− patients (Table 2). Laryngoscopy as a diagnostic test for GERD had sensitivity of 86 % (CI 70–95 %), specificity of 9 % (CI 3–22 %), accuracy of 44 % (CI 33–55 %), positive predictive value of 44 % (CI 32–57 %), negative predictive value of 44 % (CI 13–78 %), positive likelihood ratio 0.95 (CI 0.8–1.1), and a negative likelihood ratio 1.49 (CI 0.4–5.1).

Esophageal Manometry GERD+ patients had a higher prevalence of hypotensive LES, and GERD− had a higher prevalence of normal manometry (Table 3).

Discussion

The results of this study showed that (a) ENT symptoms were unreliable for diagnosing GERD, and (b) laryngoscopy had a low accuracy for the diagnosis of GERD.

ENT Manifestations of GERD

A myriad of ENT symptoms may be attributed to GERD. These symptoms, however, may be caused by diseases other than GERD. As such, extra-esophageal complaints have been repeatedly shown to be inaccurate for the diagnosis of GERD[8, 9] and this finding was once more confirmed by our study. Moreover, up to 75 % of the patients may not have concomitant esophageal symptoms.[2]

Table 2 Upper gastrointestinal endoscopy and laryngoscopic findings

	All patients ($n = 79$)	GERD negative ($n = 43$)	GERD positive ($n = 36$)	*p* value
Upper endoscopy				
Hiatal hernia, *n* (%)	28 (35.4)	13 (30.2)	15 (41.6)	0.2899
Esophagitis, *n* (%)	18 (22.8)	7 (16.3)	11 (30.6)	0.1318
Zenker's diverticulum, *n* (%)	2 (2.5)	0	2 (5.6)	0.1174
Barrett's esophagus, *n* (%)	2 (2.5)	0	2 (5.6)	0.1174
Laryngoscopy				
GERD-related laryngopharyngitis, *n* (%)	70 (88.6)	39 (90.7)	31 (86.1)	0.5228
Chronic sinusitis, *n* (%)	9 (11.4)	3 (7)	6 (16.7)	0.1770
Other vocal cord findings (ulceration, red lesions, spasm, polyps), *n* (%)	9 (11.4)	4 (9.3)	5 (13.9)	0.5228

GERD gastroesophageal reflux disease

Table 3 Manometric findings

	All patients ($n = 79$)	GERD negative ($n = 43$)	GERD positive ($n = 36$)	p value
Lower esophageal sphincter				
Hypotensive, *n* (%)	16 (20 %)	3 (7 %)	13 (36 %)	0.0013*
Hypertensive LES, *n* (%)	2 (2 %)	1 (2 %)	1 (3 %)	0.8986
Peristalsis				
Hypertensive esophageal peristalsis, *n* (%)	4 (5 %)	2 (5 %)	2 (6 %)	0.8551
Ineffective esophageal motility, *n* (%)	17 (21 %)	8 (19 %)	9 (25 %)	0.4908
Achalasia, *n* (%)	1 (1 %)	1 (2 %)	0	0.3571
Upper esophageal sphincter				
Hypotensive UES, *n* (%)	4 (5 %)	1 (2 %)	3 (8 %)	0.2251
Hypertensive UES, *n* (%)	4 (5 %)	2 (5 %)	2 (6 %)	0.8551
Normal manometry				
Normal, *n* (%)	37	28 (65 %)	9 (25 %)	0.0003*

GERD gastroesophageal reflux disease

*Statistical significance

Although GERD may induce extra-esophageal symptoms due to reflux of gastroduodenal contents to target organs or neuronal reflex due to vagal stimulation, ENT symptoms occur as a result of the upward extent of reflux (also known as laryngopharyngeal reflux).[1, 2] Thus, the direct detection or indirect evidence of proximal reflux would be an important clue to the correct diagnosis. However, many studies have shown low diagnostic accuracy for symptoms, upper endoscopy, pH monitoring, temporal symptoms correlation, and therapeutic trial with PPI, believing that GERD-induced ENT manifestations should be rather considered a diagnosis of exclusion[2]

ENT Testing as Predictor for GERD

Transnasal flexible laryngoscopy is the preferred diagnostic test of otorhinolaryngologists to establish a diagnosis of GERD.[3, 4, 10] Different classifications and scores are used to diagnose GERD, including several endoscopic findings such as subglottic, laryngeal, or vocal fold edema; ventricular obliteration; laryngeal erythema/hyperemia; posterior commissure hypertrophy; and granuloma and thick endo-laryngeal mucus.[10, 11] In our study, endoscopic findings commonly related to GERD (laryngeal edema, erythema, hypertrophy, and granuloma) plus other findings suspected to be related to GERD (laryngeal spasm, ulceration, polyps) were present in 74 out of 79 patients (94 %) confirming that the diagnosis of GERD and consequent referral by otorhinolaryngologists were mostly based on laryngoscopy.

Interestingly, studies correlating laryngoscopy and pH monitoring in adults are rare. Oeslchlager et al.[12] reported a sensitivity and specificity for the diagnosis of proximal GERD of 65 and 34 %, respectively, for laryngoscopy as compared to pH monitoring. Our results showed a higher sensitivity and a much lower specificity; however, in our study, we compared laryngoscopy to the presence of pathologic distal reflux. Other series calculated merely the specificity of laryngoscopy for the diagnosis of distal reflux since only patients with positive findings were included, with numbers ranging from 12 to 48 %.[13, 14] Regardless, the accuracy of laryngoscopy has been shown to be very low.

Esophageal Function Tests for ENT Manifestations of GERD

LES basal pressure is not a good marker for GERD[15]; even though our data revealed a higher proportion of hypotensive LES in the GERD + group. Esophageal peristalsis; however, was not different between groups, and ineffective motility was found in less than a quarter of patients, similar to other studies.[14] Achalasia was incidentally diagnosed in one patient. Additional unsuspected diseases (such as Zenker diverticulum) were diagnosed by the upper endoscopy, suggesting that a complete work-up is necessary in these patients. Some authors believe the upper esophageal sphincter is often hypertensive in patient with proximal GERD, as a physiologic barrier to aspiration.[16] Others claim that the lack of this barrier defined by a hypotensive UES is part of the manometric profile of these patients.[17] In our study, the UES profile was similar in patients with and without abnormal GERD.

Ambulatory pH monitoring is still the most reliable diagnostic method for establishing a diagnosis of GERD, with well-established reference values. While this is true for distal reflux, it is still unclear for proximal reflux. Pathologic distal reflux is not a guarantee that GERD is the cause of extra-esophageal symptoms while a

consensus was never achieved for the placement of the proximal probe, and for reference values.[18] The fact that proximal amount of reflux may not be different between healthy volunteers and patients with extra-esophageal GERD symptoms[9, 19] brings more confusion to the topic. Certainly, individual sensibility and responses to visceral stimulation may play a significant role although this is impractical and difficult to measure. Temporal correlation between reflux and symptoms is an indirect method to evaluate such individuality. However, apart from cough and perhaps throat cleaning, most ENT symptoms are related to the chronic effect of GERD and not to acute episodes of reflux.

PPI trial, compared to a full work-up and diagnosis-oriented treatment, has been shown to be inaccurate costly, associated to side effects and inferior outcomes[6, 20] so that PPIs should be used only in ENT patients with proven distal and proximal reflux.

Study Limitations

This study includes a small number of patients. This is related to the lack of referral of patients with extra-esophageal symptoms to esophageal teams even though two highly specialized centers were included in the study. This same pattern of referral brings a significant bias to our results, since patients with a negative laryngoscopy are rarely believed to have GERD. Moreover, most patients had symptoms refractory to the low doses of proton pump inhibitors usually prescribed by otorhinolaryngologists[3] as another selection bias. This may account for the high proportion of patients GERD – in the series.

Oropharyngeal pH monitoring (DX-pH probe) was not used since its value is yet to be proven.[21]

Conclusions

The correct identification of GERD as a cause of ENT symptoms needs a high degree of suspicion, and an extensive work-up that includes EGD, esophageal manometry, and pH monitoring in addition to laryngoscopy.

In conclusion, these data confirm the importance of a complete work-up in any patient with suspected extra-esophageal manifestations of GERD before starting empiric therapy with acid reducing medications since symptoms and transnasal laryngoscopy are not accurate to diagnosis GERD as compared to pH monitoring that confirmed GERD in less than half of the patients with suspected GERD.

Author's Contribution FAMH: acquisition of data, analysis and interpretation of data, drafting the article, final approval of the version to be published

CA: acquisition of data, analysis and interpretation of data, final approval of the version to be published

YV: acquisition of data, analysis and interpretation of data, final approval of the version to be published

MGP: conception and design, review for intellectual content, final approval of the version to be published

BRP: review for intellectual content, final approval of the version to be published

Compliance with Ethical Standards The study was approved by the IRB of each Institution. Informed consent was waived due to the retrospective format of the study.

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