

The Edematous and Erythematous Airway Does Not Denote Pathologic Gastroesophageal Reflux

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Objective To determine if the reflux finding score (RFS), a validated score for airway inflammation, correlates with gastroesophageal reflux measured by multichannel intraluminal impedance (MII) testing, endoscopy, and quality of life scores.

Study design We performed a prospective, cross-sectional cohort study of 77 children with chronic cough undergoing direct laryngoscopy and bronchoscopy, esophagogastroduodenoscopy, and MII testing with pH (pH-MII) between 2006 and 2011. Airway examinations were videotaped and reviewed by 3 blinded otolaryngologists each of whom assigned RFS to the airways. RFS were compared with the results of reflux testing (endoscopy, MII, symptom scores). An intraclass correlation coefficient was calculated for the degree of agreement between otolaryngologists' RFS. Receiver operating characteristic curves were created to determine the sensitivity of the RFS. Spearman correlation was calculated between the RFS and reflux measurements by pH-MII.

Results The mean \pm SD RFS was 12 \pm 4. There was no correlation between pH-MII variables and mean RFS (Irl < 0.15). The concordance correlation coefficient for RFS between otolaryngologists was low (intraclass correlation coefficient = 0.32). Using pH-metry as a gold standard, the positive predictive value for the RFS was 29%. Using MII as the gold standard, the positive predictive value for the RFS was 40%. There was no difference in the mean RFS in patients with (12 \pm 4) and without (12 \pm 3) esophagitis (*P* = .9). There was no correlation between RFS and quality of life scores (Irl < 0.15, *P* > .3).

Conclusions The RFS cannot predict pathologic gastroesophageal reflux and an airway examination should not be used as a basis for prescribing gastroesophageal reflux therapies. (*J Pediatr 2017;183:127-31*).

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s part of the evaluation for patients with cough, hoarseness, croup, and other respiratory symptoms, otolaryngologists frequently perform a direct laryngoscopy and bronchoscopy (DLB) and, when a red, inflamed larynx is seen, otolaryngologists frequently implicate gastroesophageal reflux disease (GERD) as a cause for the laryngeal findings. As a result, otolaryngologists have become one of the main prescribers of proton pump inhibitors for adults and children despite a lack of evidence suggesting causality.¹

Adult studies show an inconsistent relationship between acid reflux and laryngeal findings and these studies are limited by their use of pH-metry, which lacks the sensitivity needed to detect proximal reflux and nonacid reflux events.^{2,3} Overcoming this limitation, multichannel intraluminal impedance (MII) with pH (pH-MII) offers the same strengths as pH-metry but offers the advantage that the catheters can accurately detect both full column reflux and acid and nonacid reflux events. As a result, at many institutions, pH-MII has become the gold standard tool to measure full column reflux, which has the potential to reach the oropharynx and larynx. There is only a single adult study using pH-MII to determine the relationship between laryngeal findings and full column acid and nonacid reflux events.³ In this study of 142 healthy volunteers who underwent both pH-MII and laryngoscopy, there was no correlation between reflux events and the appear-

ance of the airway scored using the reflux findings score (RFS), a validated scoring system of laryngeal findings suggestive of GERD.³ There are no studies in symptomatic adults or any studies in pediatrics.

Determining if there is a significant, positive relationship between the appearance of the larynx and gastroesophageal reflux is critical not only for diagnostic

DLB	Direct laryngoscopy and bronchoscopy
GERD	Gastroesophageal reflux disease
MII	Multichannel intraluminal impedance
pH-MII	Multichannel intraluminal impedance with pH
PedsQL	Pediatric Quality of Life Inventory
PPI	Proton pump inhibitor
RFS	Reflux finding score

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0022-3476/\$ - see front matter. © 2016 Published by Elsevier Inc. http://dx.doi.org10.1016/j.jpeds.2016.11.035 purposes but most importantly, to ensure that only patients with documented extraesophageal reflux disease receive proton pump inhibitor (PPI) therapy. This is particularly critical in patients with respiratory symptoms, as PPI use has been associated with increased risk of respiratory infections, which may actually worsen the symptoms for which they are prescribed.^{4,5}

It is the goal of this study to determine (1) the relationship between reflux events by pH-MII and the RFS⁶; and (2) the interrater reliability of the RFS among otolaryngologists of different experience levels.

Methods

Between 2008 and 2014, we prospectively recruited 77 consecutive patients (who were not currently receiving acid suppression therapy) undergoing direct laryngoscopy, endoscopy, and pH-MII testing at Boston Children's Hospital for the evaluation of chronic cough. The study was approved by Boston Children's Hospital institutional review board and all parents signed consent forms to participate. Parents of recruited patients completed the Pediatric Quality of Life Inventory (PedsQL) and the PedsQL Gastrointestinal Symptoms Module.^{7,8} At the time of endoscopy, DLBs were videotaped and deidentified. Each patient underwent, immediately after the DLB, an esophagogastroduodenoscopy with biopsies and pH-MII placement. Three otolaryngologists (1 junior, 1 midlevel, and 1 senior) independently reviewed the airway videos and assigned each airway a total RFS including all of its 8 subscores. Subscores include subglottic edema (0 = absent, 2 = present), ventricular obliteration (0 = none, 2 = partial, 4 = complete),erythema (0 =none, 2 =arytenoid only, 4 =diffuse), vocal fold edema (0 = none, 1 = mild, 2 = moderate, 3 = severe, 4 = polypoid), diffuse laryngeal edema (0 = none, 1 = mild, 2 = moderate, 3 = severe, 4 = obstructing), posterior commissure hypertrophy (0 =none, 1 =mild, 2 =moderate, 3 =severe, 4 =obstructing), granuloma presences (0 =absent, 2 =present), and thick mucus presence (0 = absent, 2 = present). The total RFS and the subscores were compared with the pH-MII reflux measurements including the total number of reflux episodes, the number of acid and nonacid reflux events, the percentage of the study time during which the pH<4, the percentage of time reflux was in the proximal and distal esophagus (sum of the bolus clearance times at each site divided by the total study duration), and the percentage of reflux episodes that were full column. The pH portion of the study was considered abnormal if the pH was <4 for >6% of the study duration, and the MII portion was considered abnormal if the total number of reflux episodes were >73.9,10 For each pH-MII tracing, pH-MII tracings were analyzed by 1 expert reviewer after running automated analysis software.

Total RFS was calculated as the mean of the 3 otolaryngologists, rounded to ensure the optimal cut point would be an integer. A sensitivity analysis was conducted using the mean RFS of the 3 otolaryngologists. Agreement among otolaryngologists was assessed by the concordance correlation coefficient with 95% CI. The correlation of RFS with number of reflux episodes is shown in a scatterplot of normalized RFS by normalized reflux episodes, where the data have been transformed to a standard normal distribution.

An empirical receiver operating characteristic curve was used to characterize the relation of total RFS with abnormal pHmetry from the pH portions of the study and with abnormal numbers of reflux events by the MII portion of the study. An optimal cut point for each curve was determined by Youden's Index and used to determine the positive predictive value.

The association of RFS items with reflux measurements was assessed with the Spearman rank correlation coefficient. Means are presented as means \pm SD. All data analysis was performed with SAS v 9.4 (SAS Institute, Cary, North Carolina).

Results

The mean age (\pm SD) of patients was 6.5 \pm 3.7 years. The mean RFS of the 77 patients was 12 \pm 3. Eighteen percent of patients had an abnormal MII study, and 28% had an abnormal pH portion of the study. The mean number of total, acid, and nonacid reflux episodes per 24-hour period was 48 \pm 27, 25 \pm 15, and 23 \pm 23 episodes, respectively. The mean percentage time pH <4 per 24 hour study was 4.8 \pm 5.6. None of the patients had evidence of erosive esophagitis endoscopically, but 21% had histological evidence of reflux esophagitis, and 5% had evidence of eosinophilic esophagitis. The distribution of the most severe findings for each of the RFS characteristics is shown in **Figure 1**.

The concordance correlation coefficient was low at 0.32 (95% CI 0.22, 0.42) indicating poor agreement among otolaryngologists regarding the RFS. There was no correlation between any reflux measurement (total number of reflux episodes, number of acid or nonacid reflux episodes, percentage of time reflux was in the distal or proximal esophagus) and the mean RFS ($|\mathbf{r}| < 0.14, P > .21$). Sixty-six patients completed symptom and quality of life questionnaires; there was no significant correlation between the mean RFS and the PedsQL or the PedsQL Gastrointestinal Symptoms Module ($|\mathbf{r}| < 0.27, P > .06$). There was no difference the mean RFS in patients with (12 ± 4) and without (12 ± 3) esophagitis (P = .9).

There was no relationship between abnormal pH and MII testing and RFS at every experience level as shown in the **Table**. There is a lack of relationship between the RFS at every experience level and the total reflux burden as shown in **Figure 2**.

The receiver operating characteristic curves for the RFS based on an abnormal pH probe or MII are shown in **Figure 3**. Using pH-metry as the gold standard, the sensitivity, specificity, positive predictive value and negative predictive value, and accuracy of the RFS with a cut point of >7 was 95%, 9%, 29%, 83%, and 33%, respectively. Using MII as the gold standard, the sensitivity, specificity, positive predictive value and negative predictive value, and accuracy of the RFS with a cut point of >16 was 14%, 95%, 44%, 83%, and 81%, respectively. Importantly, the positive predictive values of RFS in predicting pathologic reflux by pH-MII are extremely low supporting the idea that the laryngeal appearance cannot diagnose pathologic reflux. Download English Version:

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