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Diagnostic Accuracy of Patient-Reported Outcome Measures and Finding Instruments in Laryngopharyngeal Reflux Disease

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Abstract

Objective. To investigate the diagnostic accuracy of various combinations of patient-reported outcome measures (PROMs) and upper aerodigestive tract finding instruments dedicated to the clinical diagnosis of laryngopharyngeal reflux disease (LPRD).

Study Design. Prospective, multicenter study.

Setting. University hospital.

Methods. Patients with LPRD at the 24-hour hypopharyngeal-esophageal multichannel intraluminal impedance-pH monitoring were recruited from three European hospitals. Asymptomatic individuals served as the control group. Participants completed the Reflux Symptom Index (RSI), Reflux Symptom Score (RSS), and Reflux Symptom Score-12 (RSS-12) at baseline and 3-month posttreatment. Clinical signs were evaluated with the Reflux Finding Score (RFS), Reflux Sign Assessment (RSA), and Reflux Sign Assessment-10 (RSA-10). Sensitivity (SE), specificity (SP), positive predictive value (PPV), and negative predictive value (NPV) were calculated for each instrument and their combinations.

Results. A total of 542 LPRD patients and 204 healthy controls were included. The RSS was the PROM with the highest SE (95.4%), whereas RSS-12 reported the highest SP (94.7%). RSA had the highest SE (94.0%), and RSA-10 reported the highest SP (76.3%). The highest SE and SP of combination tools were found for RSS+RSA (90.4%) and RSS+RSA-10 (99.4%), respectively. RSS+RSA-10 achieved the highest PPV value (99.7%) and RSS+RSA had the highest NPV (79.3%). Overall, the RSS demonstrated the greatest diagnostic accuracy with an area under the curve (AUC) of 0.985. The combination RSS +RSA reported an AUC of 0.934.

Conclusion. The combination of RSS and RSA provided the most accurate diagnostic performance, maximizing SE, SP, PPV, and NPV. This combination offers enhanced utility for the preliminary diagnosis of LPRD.

Keywords

diagnosis, gastroesophageal, instrument, laryngopharyngeal, otolaryngology, otorhinolaryngology, reflux, threshold, tool, voice

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Introduction

Laryngopharyngeal reflux disease (LPRD) is defined as a disease of the upper aerodigestive tract resulting from the direct and/or indirect effects of gastroduodenal content reflux, inducing morphological and/or neurological changes in the upper aerodigestive tract.[1] The prevalence of LPRD ranges from 10% to 30% of outpatients visiting otolaryngology departments[2] and up to 50% of patients with voice disorders.[3,4] The nonspecific nature of LPRD's laryngeal and extralaryngeal symptoms and signs complicates its diagnosis. Common symptoms—such as hoarseness, throat clearing, globus sensation, cough, and throat pain—overlap with those of many otolaryngological conditions, including allergies, rhinosinusitis, and chronic pharyngolaryngitis.[4-6] Clinical signs observed during fiberoptic laryngoscopy are nonspecific, further contributing to diagnostic challenges.[5,7,8]

The current gold standard for diagnosing LPRD is the 24-hour hypopharyngeal-esophageal multichannel intraluminal impedance-pH (HEMII-pH) monitoring with pharyngeal sensors.[1,9] However, the use of HEMII-pH is limited by its cost, patient inconvenience, and restricted availability in many clinical settings. Consequently, many practitioners suggest diagnosing LPRD through a clinical approach, which can involve an empirical therapeutic trial.[1]

To enhance diagnostic accuracy, several patient-reported outcome measures (PROMs) and upper aerodigestive tract finding instruments have been developed. These instruments document both laryngeal and

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extralaryngeal symptoms and signs, with their related severity, to improve diagnostic accuracy and patient management in clinical settings.[1,10,11] The most employed PROMs include the Reflux Symptom Index (RSI),[12] the Reflux Symptom Score (RSS),[13] and the Reflux Symptom Score-12 (RSS-12).[14] Upper aerodigestive tract finding instruments such as the Reflux Finding Score (RFS),[15] Reflux Sign Assessment (RSA),[16] and Reflux Sign Assessment-10 (RSA-10)[17] have demonstrated moderate-to-high validity and reliability in detecting morphological changes associated with LPRD. These clinical instruments play a crucial role in screening patients before initiating objective diagnostic testing or empirical treatments.[1,4] Given the array of available diagnostic tools, combining PROMs with upper aerodigestive tract finding instruments offers the potential to enhance diagnostic accuracy by providing a more holistic view of patient conditions.

This study aimed to evaluate the diagnostic accuracy of various combinations of PROMs and upper aerodigestive tract finding instruments in diagnosing LPRD.

Methods

Patients with LPRD-related symptoms and signs were consecutively enrolled from January 2017 to April 2024 from the Otolaryngology–Head and Neck Surgery Department of three European hospitals: CHU Saint-Pierre (Brussels, Belgium), EpiCURA (Mons, Belgium), and the Elsan Polyclinique of Poitiers (Poitiers, France). LPRD diagnosis was confirmed through 24-hour HEMII-pH monitoring, in accordance with the Dubai guidelines, which consisted of the identification of more than one pharyngeal reflux episode for confirmation.[1] Gastrointestinal (GI) endoscopy was performed on patients with symptoms of gastroesophageal reflux disease (GERD) or those with a history of complications.[12,14] Individuals aged 60 years or older were systematically offered endoscopy due to the reduced perception of GERD symptoms in this population.[12,14] The control cohort included asymptomatic adults recruited from University of Mons personnel (Mons, Belgium) and otolaryngology clinic attendees who demonstrated no clinical evidence of LPRD, GERD, or upper aerodigestive tract symptoms. Exclusion criteria for both LPRD patients and the control group included the following: excessive smoking (more than 5 cigarettes/day), alcohol dependence (>2 glasses of alcohol/day), pregnancy, neurological or psychiatric illness, upper respiratory tract infections within the last month, current use of antireflux treatments (eg, proton pump inhibitors, antihistamines, alginates, and magaldrates) or inhaled corticosteroids, previous neck surgery or trauma, vocal fold lesions (benign or malignant), history of ear, nose, and throat radiotherapy, and active seasonal allergies or asthma.

The study protocol was approved by the local ethics committee (CHU Saint-Pierre Committee, protocol no. BE076201837630). Informed consent was obtained from those who chose to enroll.

HEMII-pH Monitoring

HEMII-pH monitoring was conducted using a Versaflex Z® catheter (Digitrapper pH-Z Testing System, Medtronic), introduced transnasally in the morning before breakfast. The catheter consisted of eight impedance segments and two pH electrodes, tailored to the patient's esophageal length. Six impedance segments were positioned along the esophagus zones (Z1-Z6), positioned at 19, 17, 11, 9, 7, and 5 cm above the lower esophageal sphincter (LES). The remaining two sensors were positioned 1 and 2 cm above the cricopharyngeal sphincter, within the hypopharyngeal cavity. The two pH electrodes were placed 2 cm above the LES and 1 to 2 cm below the cricopharyngeal sphincter. This configuration allowed for real-time monitoring of intraluminal impedance changes at each point, while the esophageal pH levels were recorded by the attachment of the pH electrodes to an external electronic recorder. After 24 hours, HEMII-pH tracings were downloaded (Digitrapper; Medtronic) and analyzed using a standardized method.[1,9] A distal reflux event was defined when reflux reached the two impedance sensors closest to the LES, while a proximal reflux event (pharyngeal reflux) occurred when reflux reached the two hypopharyngeal sensors. In accordance with a recent study defining normative data of HEMII-pH in LPRD, LPRD was diagnosed as the occurrence of more than one proximal reflux episode.[1,9] GERD was diagnosed based on Lyon consensus criteria, in which patients reported either a Los Angeles grade C or D esophagitis, long-segment Barrett's esophagus, peptic esophageal strictures, or a distal acid pH ($pH < 4.0$) exposure time exceeding 6% of the 24-hour monitoring period.[18] Patients were advised to maintain their usual daily diet and activities throughout the 24-hour test. Acid reflux episodes involved gaseous or liquid reflux with a $pH < 4.0$, weakly acidic reflux with a pH between 4.0 and 7.0, and nonacid reflux episodes had $pH > 7.0$.[1]

Clinical Evaluations

Participants completed the French versions of the RSS,[13] RSS-12,[14] and RSI.[19] Briefly, RSI is a nine-item PROM designed to assess the severity of otolaryngologic symptoms associated with LPRD. Symptoms are rated on a scale from 0 to 5, with a total score ranging from 0 to 45. A $RSI > 13$ suggests LPRD.[12]

RSS is a 22-item PROM including the most prevalent otolaryngological ($N = 9$), digestive ($N = 9$), and respiratory ($N = 4$) symptoms, which are rated on a five-point scale for frequency and severity. The frequency and severity scores are multiplied for each symptom. The sum of these symptom scores is calculated to obtain the RSS total score, ranging from 0 to 550 (with the possibility for the physician and the patient to add three symptoms not identified in the RSS, leading to a maximal possible score of 625). A cutoff value above 13 suggests LPRD.[13]

RSS-12 is a shortened version of RSS, including the 12 most prevalent symptoms of LPRD.[14] The calculation is

similar to RSS with a score ranging from 0 to 300. A total score above 11 suggests LPRD.[14]

The RFS,[15] RSA,[16] and RSA-10[17] assessments of patients were carried out in a blind manner by two experienced laryngologists (the senior authors of the paper and a retired laryngologist) regarding the symptoms (RSS). The senior investigator performed RSA evaluation of control subjects in an unblinded manner, given the absence of laryngopharyngeal symptoms. Note that RSA-10 was developed by combining some items of RSA.[17] RFS rates the severity of eight laryngeal signs. Each item is scored individually, with a total score ranging from 0 to 27. RFS > 7 is suggestive of LPRD.[15]

RSA documents and evaluates the severity of 17 LPRD signs located in the oral cavity, larynx, and pharynx. The total score is the sum of each item score. The maximal total score is 72. A RSA > 14 is suggestive of LPRD.[16] RSA-10 is a streamlined version of the RSA, reducing the number of items to 10 by merging related items. It focuses on the most prevalent LPRD signs while still incorporating atypical signs.[17] The score ranges from 0 to 40. A total score higher than 13 suggests a higher likelihood of LPRD.[17]

Statistical Analyses

Statistical analysis was conducted using the Statistical Package for the Social Sciences for Windows (SPSS version 29.0; IBM Corp.). Clinical scores were compared between LPRD and controls with Mann-Whitney *U* test. Sensitivity (SE), specificity (SP), positive predictive value (PPV), and negative predictive value (NPV) were calculated from each PROM and upper aerodigestive tract finding instrument, considering their validated thresholds, for several combinations of PROM + upper aerodigestive tract finding instrument. Receiver operating characteristic (ROC) curve, area under the curve (AUC), and its related 95% confidence interval were assessed for individual PROM, upper aerodigestive tract finding instruments, and combinations. A significance level of $P < .05$ was used.

Results

A total of 542 adult patients with positive HEMII-pH results completed the evaluations. The cohort comprised 231 males (43%) and 311 females (57%). The mean age was 51.4 ± 15.5 years, and the mean body mass index (BMI) was 25.1 ± 5.2. The epidemiological and clinical features of the patients are summarized in **Table 1**. Among the 348 patients who underwent GI endoscopy, the most frequently reported findings were LES insufficiency (38%), esophagitis (34%), gastritis (29%), and hiatal hernia (27%). Additionally, Barrett's esophagus was identified in eight patients, while 52 patients (15%) exhibited no abnormalities on endoscopy. Following the Lyon criteria, 172 patients (32%) were diagnosed with both LPRD and GERD. Details of the HEMII-pH characteristics are summarized in **Table 1**. Hypopharyngeal reflux events primarily occurred in the upright position and were predominantly weakly acid events.

Table 1. Demographics and Clinical Features of Patients

Characteristics	Patients (N = 542)
Age (range, y)	51.4 ± 15.5
Body mass index (m; SD)	25.1 ± 5.2
Gender (N, %)	
Male	231 (43)
Female	311 (57)
Gastrointestinal endoscopy (N, %)	N = 348
Normal	52 (15)
Esophagitis	
LA grade A	96 (27)
LA grade B	9 (3)
LA grade C	6 (2)
LA grade D	8 (2)
Hiatal hernia	95 (27)
LES insufficiency	133 (38)
Gastritis	100 (29)
Helicobacter pylori infection	20 (6)
HEMII-pH feature (*m* ± SD)	
Pharyngeal events	35.7 ± 45.2
Pharyngeal acid reflux episodes	11.0 ± 15.6
Pharyngeal weakly acid reflux episodes	35.8 ± 58.7
Pharyngeal nonacid reflux episodes	8.5 ± 13.1
Position events	
Pharyngeal reflux episodes upright	31.4 ± 42.3
Pharyngeal reflux episodes supine	5.1 ± 11.3
Pharyngeal reflux episodes (total)	35.7 ± 45.2
GERD	
Number of patients (%)	172 (32)
Percentage of time with distal pH < 4 (%)	12.9 ± 21.8

Abbreviations: GERD, gastroesophageal reflux disease; HEMII-pH, hypopharyngeal-esophageal multichannel intraluminal impedance-pH testing; LA, Los Angeles; LES, lower esophageal sphincter; *m*, mean; N, number; SD, standard deviation.

The control group included 204 individuals (79 females) with a mean age of 43.6 ± 20 years, and a mean BMI of 23.1 ± 5.9, which were comparable to those of the LPRD cohort.

Clinical Findings

Patients with LPRD reported significantly higher mean PROM scores compared to asymptomatic controls (**Table 2**). Precisely, LPRD patients reported a mean RSI score of 17 ± 9.9, a mean RSS of 115.6 ± 80.5, and a mean RSS-12 of 73.4 ± 49.2. A similar trend was observed in upper aerodigestive tract finding instruments, where LPRD patients had mean scores of 6.3 ± 2.6 for the RFS, 27.4 ± 8.0 for the RSA, and 21.0 ± 5.9 for the RSA-10. The control group's mean scores were 4.8 ± 4.4 for RFS, 13.2 ± 6.8 for RSA, and 10.3 ± 5.3 for RSA-10. All differences between LPRD patients and controls were statistically significant (**Table 2**).

Epidemiological Data

Epidemiologic data (SE, SP, PPV, and NPV) for individual scores and combinations of scores are presented in **Table 3**. Among the PROMs, the RSS > 13 demonstrated the highest SE (95.4%) and AUC (0.985). In upper aerodigestive tract finding instruments, RSA > 14 reported the highest SE (94.0%), NPV (78.7%), and AUC (0.910).

The combination analysis reported that RSS > 13 + RSA > 14 was associated with the highest SE (90.4%), NPV (79.3%), and AUC (0.934) (**Table 3**). The highest SP (99.4%) and PPV (99.7%) were found for the RSS > 13 + RSA-10 > 13 combinations. In contrast, the combination of RSI + RFS exhibited the lowest SE (22.7%) and PPV (76.9%). RSI > 13 and RSA > 14 reported the lowest AUC (0.826).

The ROC curves of PROMs and upper aerodigestive tract finding instruments are summarized in **Figure 1**.

Discussion

Diagnosing LPRD without objective testing remains a challenging process in clinical settings. The limitations and the unavailability of HEMII-pH monitoring lead many practitioners to use PROMs and upper aerodigestive tract finding instruments, throughout an empirical therapeutic trial, to manage LPRD patients. To date, a myriad of PROMs and upper aerodigestive tract finding instruments dedicated to LPRD have been developed,[10,11] but their accuracies were poorly investigated in prospective controlled studies.

In this study, the accuracies of six individual or combined questionnaires—RSI, RSS, RSS-12, RFS, RSA, and RSA-10—were investigated, consisting of fifteen diagnostic methods evaluated in patients with an LPRD diagnosis at the 24-hour HEMII-pH. The primary results of the study suggest that the association between

Table 2. Differences in Clinical Tools Between Patients and Controls[a]

Clinical instruments	Patients (n = 542)	Controls (n = 204)	*P*-value
Reflux Symptom Index (RSI)	17 ± 9.9	2.1 ± 3.8	.001
Reflux Symptom Score (RSS)	115.6 ± 80.5	4.2 ± 7.6	.001
Reflux Symptom Score-12 (RSS-12)	73.4 ± 49.2	2.6 ± 5.1	.001
Reflux Finding Score (RFS)	6.3 ± 2.6	4.8 ± 4.4	.029
Reflux Sign Assessment (RSA)	27.4 ± 8	13.2 ± 6.8	.001
Reflux Sign Assessment-10 (RSA-10)	21 ± 5.9	10.3 ± 5.3	.001

[a]The data in this table are mean values and standard deviations. Mann-Whitney U test was used to compare patients and controls.

Table 3. Sensitivity, Specificity, Predictive Values, and Area Under the Curve of Combinations[a]

Clinical instruments	SE	SP	PPV	NPV	AUC	95% CI
Patient-reported outcome questionnaires						
RSS > 13	95.4	94.1	97.6	88.8	0.985	0.961-0.999
RSI > 13	59.7	94.4	98.7	25.0	0.936	0.918-0.954
RSS-12 > 11	93.3	94.7	97.8	84.8	0.983	0.967-0.999
Clinical instruments						
RSA > 14	94.0	62.5	87.5	78.7	0.910	0.886-0.934
RSA-10 > 13	90.4	76.3	91.6	73.5	0.909	0.888-0.930
RFS > 7	31.3	66.2	38.5	58.8	0.617	0.560-0.674
Clinical instrument associations						
RSS > 13 and RSA > 14	90.4	98.7	99.5	79.3	0.934	0.898-0.970
RSS > 13 and RSA-10 > 13	87.2	99.4	99.7	73.8	0.932	0.895-0.961
RSS > 13 and RFS > 7	30.4	94.3	77.8	67.3	0.849	0.730-0.946
RSS-12 > 11 and RSA > 14	88.6	98.1	99.2	76.2	0.930	0.889-0.971
RSS-12 > 11 and RSA-10 > 13	85.2	98.8	99.5	70.9	0.928	0.902-0.954
RSS-12 > 11 and RFS > 7	28.3	94.4	76.5	67.0	0.855	0.741-0.950
RSI > 13 and RSA > 14	55.9	98.6	99.6	28.1	0.826	0.632-0.990
RSI > 13 and RSA-10 > 13	54.7	98.6	99.6	27.0	0.832	0.650-0.985
RSI > 13 and RFS > 7	22.7	95.8	76.9	66.7	0.856	0.774-0.937

Abbreviations: AUC, area under the curve; NPV, negative predictive value; PPV, positive predictive value; RFS, Reflux Finding Score; RSA, Reflux Sign Assessment; RSA-10, Reflux Sign Assessment-10; RSI, Reflux Symptom Index; RSS, Reflux Symptom Score; RSS-12, Reflux Symptom Score-12; SE, sensitivity; SP, specificity.

[a]Area under the curve values were evaluated through the ROC analysis for individual and combined (mean AUC) instruments.

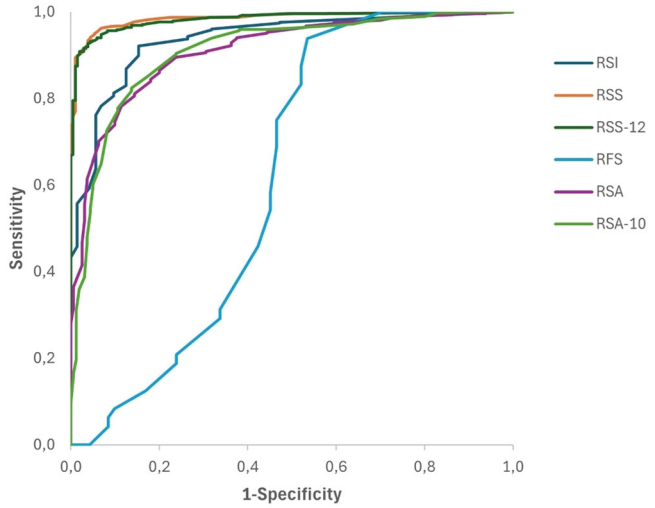

Figure 1. Receiver operating characteristic (ROC) curves of different methods. The Reflux Symptom Score (RSS) is significantly more discriminant than all other individual scores for the diagnosis of laryngopharyngeal reflux disease. RFS, Reflux Finding Score; RSA, Reflux Sign Assessment; RSA-10, Reflux Sign Assessment-10; RSI, Reflux Symptom Index; RSS-12, Reflux Symptom Score-12.

RSS and RSA reports the highest SE, NPV, and discrimination for clinically diagnosing LPRD. The superiority of RSS over RSI was corroborated by Zhang et al who observed, in a cohort of 77 patients with LPRD at the HEMII-pH, that the RSS has a higher consistency and better screening value for LPRD compared to RSI.[20] More recently, this team evaluated the diagnostic value of symptom questionnaires, sign questionnaires, and combinations of RSS, RSI, RSA, and RFS in 52 LPRD patients and 25 controls.[21] Considering individual PROMs, the authors observed that RSS had a better SE (98% vs 69%) and screening value (AUC: 0.750 vs 0.746) compared to RSI, while the association between RSS and RFS reported the highest concordance with the 24-hour HEMII-pH results.[21] The better concordance of RSS over RSI was similarly demonstrated in another recent study using multiple time point pepsin saliva measurements to investigate the association between subjective and objective assessments.[22] The better screening value of RSS over RSI[20,21] or RSS-12 can be explained by the consideration of the most prevalent otolaryngological, digestive, and respiratory symptoms in the development of the 22 items of RSS.[13] The inclusion of otolaryngological, digestive, and respiratory symptoms in the full version of the RSS allows for the consideration of several clinical patterns of LPRD, as some patients may predominantly present digestive symptoms associated with autonomic nerve dysfunction,[23] or both LPRD and GERD,[24] whereas others report an exacerbation of respiratory symptoms, such as cough, in their LPRD clinical presentation.[25] The attempt to reduce the length of RSS in the RSS-12 can be associated with a reduction of the screening value of the questionnaire.

In terms of upper aerodigestive tract finding instruments, RSA and RSA-10 reported substantially better SE, NPV, and AUC than RFS, which corroborates the findings of the validation study of RSA.[16] The potential superiority of RSA over RFS was similarly suggested by Rezaei Fard et al who compared RFS and RSA in a prospective controlled study.[26] However, Zhang et al did not report the superiority of RSA over RFS in their latest studies,[21] which could be attributed to the authors' greater experience with RFS compared to RSA. Indeed, the assessment of upper aerodigestive tract finding instruments is influenced by the experience of the practitioners and the training in using the instrument.[27,28] Because our team is trained in rating RSA and RSA-10, our experience can support the higher value of RSA and RSA-10 over RFS. The consideration of pharyngeal and oral signs in RSA and RSA-10 is an additional hypothesis in supporting the better epidemiological values of these scores over the RFS. Similarly to RSS, the items of RSA were based on a preliminary investigation of the most prevalent laryngeal and extralaryngeal signs associated with LPRD,[16] whereas RFS only includes laryngeal findings. In practice, many patients have pharyngeal, oral, or nasal signs associated with LPRD,[29,30] which strengthens the consideration of an upper aerodigestive tract finding instrument considering laryngeal, pharyngeal, and oral signs. The RSA-10 can be an alternative to RSA regarding its higher SP and PPV compared to RSA. Moreover, studies validating RSA and RSA-10 reported similar internal consistency reliability (RSA-10 $\alpha = .822$ vs RSA $\alpha = .821$), making difficult the determination of the superiority of one over the other, when considered as a single clinical instrument or combined instrument with RSS (**Table 3**).

The present study is the largest cohort study investigating the accuracy of individual and combined clinical LPRD PROMs and instruments, which is its primary strength. The consideration of patients with a positive diagnosis at the 24-hour HEMII-pH is an additional strength. While two experienced authors rated the RSA, RFS, and RSA-10 on LPRD patients, the evaluation of laryngeal, pharyngeal, and oral signs associated with LPRD remains subjective, which can substantially influence the results of the study. Note that both evaluators reported moderate-to-high interrater reliability ($r = 0.663$), according to the RSA study.[16] The lack of HEMII-pH testing in controls is the primary limitation of the study. The 24-hour HEMII-pH testing was not carried out in healthy individuals due to both the inflated cost and the discomfort associated with the procedure. Furthermore, this study did not include a symptomatic control group with atypical LPRD symptoms but confirmed negative pH testing. Future studies should incorporate such a control group to better distinguish the diagnostic accuracy of PROMs and upper aerodigestive tract finding instruments in differentiating LPRD patients from patients with overlapping

symptoms unrelated to reflux. Moreover, future studies should incorporate power analysis and sample size calculations to ensure adequate control group representation, which was not performed in the present study. Another limitation was the lack of consideration for distinct types of LPRD (acidic, nonacidic, or weakly acidic) in assessing epidemiological parameters. To the best of our knowledge, the existence of several clinical patterns of LPRD, according to these parameters, was rarely investigated, but it has been suggested that alkaline LPRD should present different symptoms than weakly acid or acid LPRD, which could influence the results of our study. Similarly, age and gender are additional factors influencing the clinical presentation of LPRD and, consequently, the clinical assessments.[31,32] The inclusion of GERD-positive patients (32% of the cohort) may confound the analysis by making it more challenging to distinguish LPRD-specific diagnostic accuracy. Finally, the patients and healthy individuals with otolaryngological conditions (eg, rhinitis, allergy, and chronic rhinosinusitis) were carefully excluded from both the study and control groups, consistent with most studies validating PROMs and clinical instruments for LPRD, as the non-SP of symptoms and signs can bias the LPRD clinical evaluations. These exclusion criteria allow the reproducibility of the results of this study on patients without confounding conditions; however, in clinical practice, many patients consulting otolaryngology clinics present with several conditions associated with upper aerodigestive tract symptoms and findings. In that way, future studies could investigate the accuracy of reflux PROMs and find instruments in a more heterogeneous population to ensure their use in a large number of clinical situations.

Conclusion

The clinical diagnosis of LPRD remains the most widely used approach for LPRD diagnosis. Combining both symptom and sign questionnaires enhances the effectiveness of LPRD screening with the combination of RSS and RSA maximizing screening and discrimination of LPRD symptoms and findings between patients and controls. This combination offers greater utility in establishing a preliminary diagnosis of LPRD, particularly in settings without access to HEMII-pH testing.

Author Contributions

Catherine Muscato, data interpretation, revising the manuscript for important intellectual content; final approval of the version to be published, final approval, and accountability for the work; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; **Jerome R. Lechien**, data interpretation, revising the manuscript for important intellectual content; final approval of the version to be published, final approval, and accountability for the work; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Disclosures

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