The Laryngoscope

Validity and Reliability of the Reflux Symptom Score

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Objectives/Hypothesis: To develop and validate the Reflux Symptom Score (RSS), a self-administered patient-reported outcome questionnaire for patients with laryngopharyngeal reflux (LPR).

Study Design: Prospective controlled study.

Methods: A total of 113 patients with LPR were enrolled and treated with diet and 3 months of pantoprazole, alginate, and/or magaldrate depending on the LPR characteristics (acid, nonacid, or mixed). Eighty asymptomatic individuals completed the study. Patients and controls completed the RSS twice within a 7-day period to assess test-retest reliability. Internal consistency was measured using Cronbach's α for the RSS items in patients and controls. Validity was assessed by comparing the baseline RSS with the Reflux Symptom Index (RSI) and Voice Handicap Index (VHI). Seventy-seven patients completed the RSS at baseline and after 6 and 12 weeks of treatment to assess responsiveness to change. The RSS cutoff for determining the presence and absence of LPR was examined by receiver operating characteristic analysis.

Results: Test-retest reliability (r_s = 0.921) and internal consistency reliability (α = 0.969) were high. RSS exhibited high external validity indicated by a significant correlation with the RSI (r_s = 0.831). Internal validity was excellent based on the higher RSS in patients compared with controls (P = .001). RSS, RSI, and VHI scores significantly improved from pre- to post-treatment, indicating a high responsiveness to change. RSS >13 can be considered suggestive of LPR-related symptoms. RSS was not influenced by the occurrence of gastroesophageal reflux disease, LPR subtypes, or patient characteristics.

Conclusions: RSS is a self-administered patient-reported outcome questionnaire that demonstrates high reliability and excellent criterion-based validity. RSS can be used in diagnosing and monitoring LPR disease.

Key Words: Laryngopharyngeal, reflux, laryngitis, tool, outcome, symptom.

Level of Evidence: 3b

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INTRODUCTION

Laryngopharyngeal reflux (LPR) is an inflammatory condition of the upper aerodigestive tract tissues related to the direct and indirect effect of gastric or duodenal content reflux, which induces morphological changes in the upper aerodigestive tract.[1] LPR-related symptoms are found in approximately 10% of outpatients visiting ear, nose, and throat (ENT) departments[2] and up to 75% of patients with refractory ENT symptoms.[2,3] The majority of symptoms are nonspecific, including globus sensation, cough, throat clearing, hoarseness, and throat pain.[4,5] In addition, fiberoptic examination usually identifies nonspecific laryngeal and extralaryngeal findings; the most common are posterior commissure hypertrophy, laryngeal and pharyngeal erythema, and retrocricoid hypertrophy.[5–7] The nonspecificity of both symptoms and findings makes the clinical diagnosis uncertain, and follow-up can be difficult.

To improve tracking the changes in LPR symptoms throughout treatment, some patient-reported outcome (PRO) questionnaires have been developed over the past few years, but their properties remain controversial.[8] Thus, a recent systematic review of current LPR PRO questionnaires highlighted that they are characterized by disparate developmental rigor and important methodological deficiencies.[8] Additionally, it has been demonstrated that the majority of the current PRO questionnaires only focused on some

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laryngopharyngeal symptoms and do not take into consideration all prevalent symptoms encountered in LPR disease, leading to inconsistency between studies in the evolution of symptoms throughout treatment.[1]

It has been established that patients with LPR have fewer typical symptoms of gastroesophageal reflux disease (GERD), such as heartburn or regurgitations. However, an association between both conditions exists, and many studies have reported that GERD patients have a higher risk of LPR and vice versa.[9–11] Consequently, LPR patients with typical symptoms of GERD can benefit from gastrointestinal (GI) endoscopy to exclude some complications of GERD, including Barrett's esophagus.[12,13] In the same vein, LPR is suspected to exacerbate some respiratory diseases; thus, symptoms of both GERD and LPR can be manifested as respiratory-related symptoms (e.g., cough, breathing difficulties, and wheezing).[14,15]

To date, there is no clinical PRO questionnaire that takes into account all symptoms attributed to LPR, as well as the GERD and respiratory symptoms that can be associated with LPR. Moreover, the lack of consideration of some common symptoms associated with LPR has recently been suspected as an important factor in the unclear conclusion about the efficacy of proton pump inhibitors (PPIs) in the treatment of LPR.[1] The members of the LPR Study Group of Young Otolaryngologists of the International Federation of Oto-Rhino-Laryngological Societies (YO-IFOS)[16] have developed a self-administered Reflux Symptom Score (RSS) for the evaluation of symptoms of LPR patients. The RSS includes ENT, digestive, and respiratory symptoms and assesses the impact of the disease on quality of life (QoL), all in one PRO questionnaire. The aim of this study is to evaluate the properties of the French version of the RSS, which is the original version of this instrument.

MATERIALS AND METHODS

The local ethics committee approved the study protocol (no. BE076201837630). All patients were invited to participate, and informed consent was obtained from those who enrolled in the study.

Development of the Reflux Symptom Score

The development of the RSS started after the World ENT Congress of IFOS (Paris 2016), in which international experts had decided to develop a new valid and reliable PRO questionnaire for both the diagnosis and follow-up of LPR patients. The RSS can be used for both suspected LPR patients and patients with a confirmed LPR diagnosis based on pH studies.

The content of the RSS (symptoms, structure, and presentation) had been established according to expert opinions (roundtable at the World ENT Congress of IFOS)[17] and a systematic review describing symptoms attributed to LPR in the current literature.[1] In addition, the first author of this study (J.R.L.) involved patients in the development of the RSS by identifying all main symptoms of 20 LPR patients at the time of consultation. To rigorously study the validity and reliability of the original version of the RSS, the current study was conducted according to a checklist of recommendations and key characteristics to obtain valid and reliable PRO measures (Table I).

TABLE I.
Definition of the Measurement Properties of Signs of Instruments Analyzed in the Study.

Domain	Definition
Conceptual model	
Construct definition	It provides a rationale for and description of the concepts and target population that a measure is intended to assess.
Target population	
Expected subscales	Is the conceptual model based on single construct/scale or multiple subscales. Justification about the existence of multiple subscales.
Content validity	It refers to evidence that the PRO questionnaire is appropriate for its intended use. Items and conceptual domains must be relevant to the targeted population.
Content expert involved	The PRO measure's development must include direct input from experts. There should be a clear description of the process by which included items were derived.
Description of item development and patient devised	The items described in the PRO questionnaire must reflect the most common symptoms encountered in the disease. Have patients devised items?
Reliability	The degree to which scores are free from random (measurement) error.
Internal consistency reliability	Extent to which items within each domain are interrelated.*
Test-retest reliability	Stability of scores over time when no change is expected in the concept of interest.*
Construct validity	It refers to whether the PRO questionnaire measures intended theoretic constructs or traits and directly affects the appropriateness of the measurement-based inferences.
Responsiveness to change	The extent to which the PRO questionnaire detects meaningful changes over time that have occurred after baseline.†
Convergent validity	The degree to which the symptom score correlates with the other PRO questionnaire measuring the same construct or with related clinical indicators.‡
Known-groups validity	The extent to which the PRO questionnaire can discriminate between groups that are known to differ on the variables being measured.†
Interpretability and scoring	The degree to which the meaning of the scores can be easily understood.
Plan for scoring measure	A description of how to score the measure should be provided (sum, algorithm).
Plan for missing data	A prespecified plan for managing missing responses can mitigate the risk of bias resulting from the necessity to exclude cases with missing data.
Scaling described	The process of distributing the full range of respondents' possible scores with respect to the measured attribute.

*Consistent: >0.70 for group-level comparisons and 0.90-0.95 for individual comparisons.
†Large change, >0.80; moderate change, 0.50-0.79; small change, 0.2-0.49.
‡Low correlation, <0.30; moderate correlation, 0.30-0.60; strong correlation, >0.60 (Pearson or Spearman analysis).
PRO = patient-reported outcome.

A multidisciplinary team composed of two laryngologists (C.F., J.R.L.), one general otolaryngologist (F.B.), one head and neck surgeon (S.S.), one gastroenterologist (V.M.), one statistician (K.H.), and one psychologist (B.H.), who were all native French speakers, developed the RSS (Fig. 1). The United States/English version of the RSS is

Reflux Symptom Score

Au cours du dernier mois, j'ai souffert d'un/plusieurs symptôme(s) suivant: évaluation à faire entre 0 et 5.

Sévérité: 0=le problème n'est pas du tout sévère, 5 = le problème est très gênant lorsqu'il survient - **Fréquence**: 0= je n'ai pas eu ce symptôme au cours du dernier mois; 1;2;3;4 = j'ai eu ce symptôme 1-2; 2-3; 3-4; 4-5 fois par semaine au cours du dernier mois. 5= la plainte est présente une à plusieurs fois par jour.

	Fréquence des plaintes	**Sévérité des plaintes**		**Impact sur la qualité de vie**	
Symptômes O.R.L.			Score total		Score total
1. Problèmes avec ma voix	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	……..	0 - 1 - 2 - 3 - 4 - 5	……..
2. Douleur(s) de gorge	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	……..	0 - 1 - 2 - 3 - 4 - 5	……..
3. Douleurs de gorge lorsque j'avale	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	……..	0 - 1 - 2 - 3 - 4 - 5	……..
4. Difficultés à la déglutition de gélules, de liquides, ou d'aliments solides	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	……..	0 - 1 - 2 - 3 - 4 - 5	……..
5. Raclements de gorge	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	……..	0 - 1 - 2 - 3 - 4 - 5	……..
6. Sensation d'avoir quelque chose de coïncé dans la gorge	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	……..	0 - 1 - 2 - 3 - 4 - 5	……..
7. Excès de sécrétions collantes dans la gorge ou sensation d'écoulements à l'arrière du nez	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	……..	0 - 1 - 2 - 3 - 4 - 5	……..
8. Sensation de pressions ou de douleurs d'oreille(s) diurnes ou nocturnes	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	……..	0 - 1 - 2 - 3 - 4 - 5	……..
9. Sensation de brûlures au niveau de la langue	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	……..	0 - 1 - 2 - 3 - 4 - 5	……..
10. Autres: ……..	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	……..	0 - 1 - 2 - 3 - 4 - 5	……..
Symptômes digestifs					
1. Remontées acides et/ou brûlures d'estomac	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	……..	0 - 1 - 2 - 3 - 4 - 5	……..
2. Régurgitations d'aliments, de liquides, ou rots (roter)	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	……..	0 - 1 - 2 - 3 - 4 - 5	……..
3. Douleurs abdominales	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	……..	0 - 1 - 2 - 3 - 4 - 5	……..
4. Diarrhées	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	……..	0 - 1 - 2 - 3 - 4 - 5	……..
5. Constipation	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	……..	0 - 1 - 2 - 3 - 4 - 5	……..
6. Indigestion	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	……..	0 - 1 - 2 - 3 - 4 - 5	……..
7. Distensions abdominales et/ou flatulences	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	……..	0 - 1 - 2 - 3 - 4 - 5	……..
8. Mauvaise haleine	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	……..	0 - 1 - 2 - 3 - 4 - 5	……..
9. Nausées	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	……..	0 - 1 - 2 - 3 - 4 - 5	……..
10. Autres: ……..	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	……..	0 - 1 - 2 - 3 - 4 - 5	……..
Symptômes respiratoires ou thoraciques					
1. Toux après avoir mangé ou en position couchée	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	……..	0 - 1 - 2 - 3 - 4 - 5	……..
2. Toux pendant la journée	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	……..	0 - 1 - 2 - 3 - 4 - 5	……..
3. Douleurs thoraciques	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	……..	0 - 1 - 2 - 3 - 4 - 5	……..
4. Difficultés respiratoires, essouflement, ou sifflements lors de la respiration	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	……..	0 - 1 - 2 - 3 - 4 - 5	……..
5. Autres: ……..	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	……..	0 - 1 - 2 - 3 - 4 - 5	……..

Estimez vous que ce questionnaire évalue bien vos plaintes actuelles liées au reflux ? OUI - NON **Score total**: …….. **Score total de qualité de vie**: ……..

Fig. 1. Reflux Symptom Score (French version). The questionnaire is subdivided into three parts according to the complaints: ear, nose and throat (part 1, 9 items), digestive (part 2, 9 items), and respiratory (part 3, 4 items) symptoms. The frequency and severity of each symptom are rated with a 5-point scale. Regarding the frequency, 0 = patient did not have the complaint over the past month; 1, 2, 3, 4 = patient had the complaint one to two, two to three, three to four, four to five times weekly over the past month; 5 = patient had the complaint daily over the past month. Regarding the severity, 0 = the complaint is absent and 5 = the complaint is very troublesome when it occurs. For each item, the severity score is multiplied by the frequency score to obtain a symptom score ranging from 0 to 25. The sum of these symptom scores is calculated to obtain the RSS final 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). The RSS also assesses the symptom impact on QoL. The total QoL score is calculated by the sum of each item score. At the end of the questionnaire, the patient is invited to judge whether the questionnaire assessed all of their complaints (yes/no). QoL = quality of life; RSS = Reflux Symptom Score.

available in Figure 2. The questionnaire is subdivided into three parts according to the symptoms: ear, nose, and throat (part 1, 9 items); digestive (part 2, 9 items); and respiratory (part 3, 4 items). The frequency and severity of each symptom are rated on a 5-point scale, with each point of the frequency measure being precisely defined (Fig. 1). For each item, the severity score is multiplied by the frequency score to obtain a symptom score ranging from 0 to 25. The sum of these symptom scores is calculated to obtain the RSS final score. The RSS also assesses the symptom effect on QoL. The QoL score is calculated by the sum of each item score. At the end of the questionnaire, the patient is invited to judge whether the questionnaire assessed all of the encountered complaints (yes/no).

Subjects and Setting

One hundred and thirteen adult patients with LPR-related symptoms and findings were enrolled from January 2017 to December 2018 from the Department of Otolaryngology–Head and Neck Surgery of CHU Saint-Pierre (Brussels, Belgium) and the Polyclinique of Poitiers (CHU de Poitiers, Poitiers, France). The LPR diagnosis was made with 24-hour multichannel intraluminal impedance-pH monitoring (MII-pH).

As recommended,[12] GI endoscopy was performed in patients with GERD symptoms. Because some studies have reported a reduction of GERD symptom perception in older people with LPR, GI endoscopy was also performed in patients age ≥60 years.[18] Patients were excluded if they presented with one of the following conditions: smoking; alcohol dependence; pregnancy; neurological or psychiatric illness; upper respiratory tract infection within the last month; current use of antireflux treatment (e.g., PPI, antihistamine, alginate, magaldrate); previous history of neck surgery or trauma; benign vocal fold lesions; malignancy; history of ear, nose, and throat radiotherapy; and active seasonal allergies or asthma.

The therapeutic algorithm was based on recent recommendations of our LPR Study Group.[4] According to the MII-pH data and the reflux profile (acid, nonacid, mixed), patients were treated with a personalized treatment scheme including diet, behavioral changes, and use of PPIs (pantoprazole, 20 mg twice daily) ± alginate (Gaviscon Advance; Reckitt Benckiser, Slough, UK) ± magaldrate (Riopan; Takeda, Zaventem, Belgium). Each

Reflux Symptom Score

Within the last month, I suffered from one/several followed symptoms

Severity: 0= problem is not severe, 5 = problem very troublesome when it occurs

Frequency: 0= I don't have this complaint over the past month, 1;2;3;4 = I had 1-2;2-3;3-4;4-5 weekly over the past month; 5= complaint occurs daily

	Disorder Frequency	Disorder Severity	Total score	Quality of Life impact	Total score
Ear Nose and Throat Disorders					
1. Hoarseness or a voice problem	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
2. Throat pain	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
3. Pain during swallowing time	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
4. Difficulty swallowing (pills, liquids or solid foods)	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
5. Clearing your throat	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
6. Sensation of something sticking in the throat	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
7. Excess mucous in the throat or post nasal drip sensation	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
8. Ear pressure/pain (daytime or nigh-time)	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
9. Tongue burning	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
10. Other:	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
Abdominal Disorders					
1. Heartburn, stomach acid coming up	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
2. Regurgitations of liquids, solid foods or burps	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
3. Abdominal pain	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
4. Diarrheas	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
5. Constipation	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
6. Indigestion	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
7. Abdominal distension and/or flatus	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
8. Halitosis	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
9. Nausea	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
10. Other:	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
Chest/respiratory Disorders					
1. Cough after eating or lying down	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
2. Cough (daytime)	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
3. Breathing difficulties,breathlessness, or wheezing	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
4. Chest pain	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
5. Other:	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....

Do you think that this questionnaire well assesses your current complaints ? YES - NO **RSS total score:**..... **Quality of Life score:**.....

Fig. 2. Reflux Symptom Score, United States/English version. This version has not yet been validated.

patient received a validated grid with diet recommendations and behavior changes, which took into account the patient's personalized habits.[19] The therapeutic effectiveness was assessed for each patient by the RSS after 6 and 12 weeks of treatment.

The control group comprised 80 asymptomatic persons age 18 to 59 years without any evidence of LPR. They had no MII-pH. Asymptomatic persons were recruited at the University of Mons and at CHU Saint-Pierre (Brussels). They completed a questionnaire to investigate the presence of the exclusion conditions described above and were excluded if one or more exclusion criteria were met.

MII Impedance-pH Monitoring

The MII-pH consisted of eight impedance segments and two pH electrodes (Versaflex Z, Digitrapper pH-Z Testing System; Medtronic, Europe). The catheter model used was introduced transnasally and was based on the esophageal length of the patient.

Six impedance segments were placed along the esophagus zones (Z1 to Z6) and centered at 19, 17, 11, 9, 7, and 5 cm above the lower esophageal sphincter (LES). The last two impedance segments were placed 1 and 2 cm above the upper esophageal sphincter in the hypopharyngeal cavity. The configuration of this catheter enabled the recording of changes in intraluminal impedance at each point. The two pH electrodes were placed 2 cm above the LES and 1 to 2 cm below the upper esophageal sphincter. The probe was attached to an external electronic data recorder to monitor the esophageal pH. To study the association between symptoms and reflux episodes, patients recorded the time of meals and the occurrence of key symptoms (e.g., cough, heartburn, globus, sore throat, regurgitation). The data were downloaded after 24 hours (Digitrapper; Medtronic, Europe), and a senior gastroenterologist (V.M., Brussels) or a senior otolaryngologist (F.B., Poitiers) analyzed the MII tracings with a standardized method.[20] A distal reflux event was defined as an episode reaching the two impedance sensors closest to the LES. A proximal reflux event was defined as an episode that reached two impedance sensors in the hypopharynx. An acidic event consisted of a gaseous or liquid reflux with a pH ≤4.0, whereas a nonacidic event was a gaseous or liquid reflux with a pH >4.0. According to a recent study that defined normative data of MII-pH in LPR, the LPR diagnosis was based on the occurrence of ≥1 proximal episodes.[21] GERD was defined as a length of time >4.0% of the 24-hour recording spent below pH 4.0 or a DeMeester score >14.72. An acid reflux episode consisted of an episode with pH >4.0; a non–acid reflux episode consisted of an episode with pH ≤4.0. Because there are no guidelines in the definition of acid, nonacid, and mixed LPR disease, LPR was defined as acid when the ratio of the number of acid reflux episodes to the number of nonacid reflux episodes was >2. LPR was defined as nonacid when the ratio of the number of acid reflux episodes to the number of nonacid reflux episodes was <0.5. Mixed reflux consisted of a ratio ranged from 0.51 to 2.0.

Statistical Analysis

One hundred and thirteen LPR patients and 80 asymptomatic subjects completed the RSS twice over a 7-day period (RSS d0, which corresponds to the time of first consultation; and RSS

TABLE II.
The Epidemiological and Clinical Characteristics of the Included Patients.

Characteristic	Value
Age, yr	
Mean ± SD	48.23 ± 16.72
Range	19–90
Sex, n (%)	
M	38 (34)
F	73 (66)
GI endoscopy, n = 80, n (%)	
Normal	18 (22.5)
Esophagitis (Los Angeles grading system*)	30 (37.5)
A	25
B	1
C	1
D	3
Hiatal hernia	24 (30.0)
LES insufficiency	41 (51.3)
Gastritis	29 (36.3)
Duodenitis	5 (6.3)
Helicobacter pylori infection	5 (6.3)
LPR profiles, n (%)	
Acid reflux	49 (44.5)
Nonacid reflux	26 (23.6)
Mixed reflux	35 (31.9)
GERD	44 (40)
Symptom presentation (% prevalence)/main symptoms	
ENT symptoms	
1. Voice disorder	55.1/6
2. Throat pain	68.5/19
3. Pain during swallowing	46.1/1
4. Dysphagia	40.4/3
5. Throat clearing	76.4/3
6. Globus sensation	73.0/21
7. Excess throat mucus	69.7/15
8. Ear pressure/pain	49.4/2
9. Tongue burning	29.2/0
Digestive symptoms	
1. Heartburn	76.4/14
2. Regurgitations or burps	65.2/5
3. Abdominal pain	48.3/0
4. Diarrhea	40.4/0
5. Constipation	42.7/0
6. Indigestion	28.1/0
7. Abdominal distension/flatus	57.3/0
8. Halitosis	62.9/3
9. Nausea	48.3/0
Respiratory symptoms	
1. Cough after eating/lying down	50.6/0
2. Cough	59.6/15
3. Breathing difficulties	42.7/2
4. Chest pain	51.7/1

*The Los Angeles grade of reflux esophagitis was used for the grading of esophagitis (A to D). The ratio of the number of proximal acid episodes to the number of proximal nonacid episodes was used for the definition of reflux profile (acid LPR, ratio >2; nonacid LPR, ratio <0.4; mixed LPR, ratio = 0.4–2.0).

ENT = ear, nose, and throat; F = female; GERD = gastroesophageal reflux disease; GI = gastrointestinal; LES = lower esophageal sphincter; LPR = laryngopharyngeal reflux; M = male; SD = standard deviation.

TABLE III.
Test-Retest Reliability for Each Item Score and Total Score.

RSS Items	r_s	*P* Value
ENT symptoms		
1. Voice disorder	0.885	<.001
2. Throat pain	0.844	<.001
3. Pain during swallowing	0.874	<.001
4. Dysphagia	0.905	<.001
5. Throat clearing	0.878	<.001
6. Globus sensation	0.828	<.001
7. Excess throat mucus	0.919	<.001
8. Ear pressure/pain	0.901	<.001
9. Tongue burning	0.839	<.001
ENT total score	0.920	<0.001
Digestive symptoms		
1. Heartburn	0.885	<.001
2. Regurgitations or burps	0.844	<.001
3. Abdominal pain	0.874	<.001
4. Diarrhea	0.905	<.001
5. Constipation	0.878	<.001
6. Indigestion	0.828	<.001
7. Abdominal distension/flatus	0.919	<.001
8. Halitosis	0.901	<.001
9. Nausea	0.839	<.001
Digestive total score	0.748	<.001
Respiratory symptoms		
1. Cough after eating/lying down	0.868	<.001
2. Cough	0.886	<.001
3. Breathing difficulties	0.825	<.001
4. Chest pain	0.808	<.001
Respiratory total score	0.884	<.001
Total score	0.921	<.001
QoL score		
ENT QoL	0.937	<.001
Digestive QoL	0.903	<.001
Respiratory QoL	0.905	<.001
Total score	0.950	<.001

ENT = ear, nose, and throat; QoL = quality of life; r_s = Spearman rank correlation coefficient; RSS = Reflux Symptom Score.

d7, which corresponds to 1 week after the first consultation). Seventy-seven patients completed the RSS throughout treatment. The LPR patients completed items of the French versions of the Reflux Symptom Index (RSI)[22] and Voice Handicap Index (VHI)[23] at baseline and 3 months posttreatment.

Reliability. Internal consistency was measured using Cronbach's α for all items on RSS d0 for both patients and controls (N = 193). Test-retest reliability between RSS d0 and RSS d7 was assessed for each item and for the total score in the entire cohort using the Spearman rank correlation coefficient. Regarding reliability analysis and correlation analysis, $r \geq 0.80$ was considered ideal and $r \geq 0.70$ was considered adequate.[8]

Validity. External validity was measured by correlations between RSS d0, RSI d0, and VHI d0 using the Spearman rank correlation coefficient. Internal validity was assessed through a statistical comparison between the RSS d0 item score and the total score of both patients and asymptomatic individuals using the Mann-Whitney *U* test.

Responsiveness. Responsiveness to change of the RSS was assessed by a comparison of baseline, 6 weeks posttreatment, and 12 weeks posttreatment RSS. Changes in the RSS, RSI, and VHI from pre- to posttreatment were evaluated using the Wilcoxon signed-rank test.

Statistical analyses were performed using SPSS version 22.0 (IBM Corp., Armonk, NY). Multiple linear regression was used to identify potentially significant relationships between patient characteristics, relevant GI findings, reflux types (GERD, acid, nonacid, mixed), and clinical presentation. The RSS cutoff for determining the presence and absence of LPR was examined by receiver operating characteristic analysis. A level of significance of $P < .05$ was used.

RESULTS

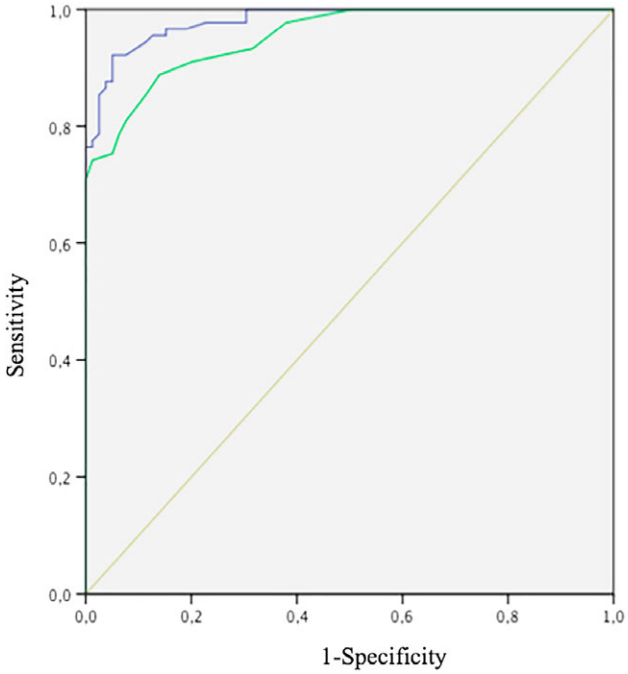
The epidemiological and clinical characteristics of the included patients are described in Table II. Globus sensation, throat pain, chronic cough, and sticky mucus or postnasal drip were the main reasons for consultation. Ninety-eight percent of patients considered that their symptoms were all described in the RSS (n = 111/113). Missing items were from three patients who had been contacted to complete the missing items. There were 49 acid reflux, 35 mixed reflux, and 29 nonacid reflux. Forty-four (40%) patients had both LPR and GERD. Among the 80 patients who had GI endoscopy, the most commonly reported findings were LES insufficiency (51.3%), esophagitis (37.5%), gastritis (35.3%), and hiatal hernia (30.0%). Three patients had Barrett's esophagus (3.8%). GI endoscopy was normal in 22.5% of the tested patients. The length of time needed to complete the RSS was ≤2 minutes.

Association Between GI, Patient, Reflux, and Symptom Characteristics

The multiple linear regression analysis did not find a significant association between patient characteristics (age, body mass index, sex), relevant GI endoscopy (esophagitis and gastritis), GERD, types of reflux (acid, nonacid, mixed), and symptom presentation (RSS total and subcategory scores). RSS QoL score was significantly correlated with RSS total score ($P < .001$).

Reliability. Cronbach's α for the items of the RSS for all individuals (N = 193) was 0.969, which indicates high internal consistency. The test-retest reliability between RSS d0 and RSS d7 was high for the total score ($r_s = 0.921$; $P < .001$) and all item scores (Table III).

Validity. According to Spearman analysis, the RSS total score of the LPR patients was correlated with RSI ($r_s = 0.831$; $P < .001$) and VHI ($r_s = 0.492$; $P = 0.001$) scores, indicating high external validity. The mean RSS of asymptomatic individuals was 9.68 (95% confidence interval: 5.85-13.52). According to our receiver operating characteristic analysis, an RSS cutoff value >13 is suggestive of LPR and exhibits high sensitivity and specificity. Our analysis showed that the RSS has a higher discrimination than does the RSI (Fig. 3). This normative value was significantly less than that of LPR patients at baseline ($P < .001$, Mann-Whitney *U* test). Moreover, all item scores of RSS were significantly higher in



RSS score	Sensitivity	Specificity
2.00	100	48.1
3.50	100	51.9
5.00	99.1	58.2
6.50	99.1	60.8
7.50	99.1	63.3
8.50	98.2	69.6
9.50	96.4	69.6
10.50	95.5	75.9
11.50	95.5	77.2
13.00	94.5	81.0
14.50	93.6	82.3
15.50	92.7	82.3
16.50	92.7	83.5
18.00	92.7	84.8
19.50	91.8	84.8
20.50	91.8	86.1
22.00	91.8	87.3
24.00	90.9	88.6
25.50	90.0	88.6
28.00	.882	92.4

Fig. 3. Receiver operating characteristic curve of the RSS and RSI. A cutoff >13 is suggestive of LPR with a sensitivity of 94.5 and a specificity of 81.0. RSS is significantly more discriminating than RSI for the LPR diagnosis ($P < .05$). LPR = laryngopharyngeal reflux; RSI = Reflux Symptom Index; RSS = Reflux Symptom Score. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

TABLE IV.
RSS at Baseline (d0) of Patients With LPR and Asymptomatic Individuals.

	Clinical RSS			QoL RSS		
RSS Items	LPR	Controls	*P* Value	LPR	Controls	*P* Value
ENT symptoms						
1. Voice disorder	4.48 ± 6.51	0.08 ± 0.31	.001	1.14 ± 1.54	0.09 ± 0.32	.001
2. Throat pain	6.02 ± 7.47	0.61 ± 1.49	.001	1.83 ± 1.75	0.21 ± 0.52	.001
3. Pain during swallowing	3.36 ± 5.39	0.36 ± 1.23	.001	1.20 ± 1.60	0.11 ± 0.39	.001
4. Dysphagia	3.31 ± 5.59	0.74 ± 3.41	.001	1.15 ± 1.65	0.07 ± 0.47	.001
5. Throat clearing	10.22 ± 9.48	0.60 ± 1.54	.001	2.30 ± 1.93	0.19 ± 0.62	.001
6. Globus sensation	9.91 ± 9.71	0.25 ± 0.56	.001	2.44 ± 1.99	0.14 ± 0.34	.001
7. Excess throat mucus	10.96 ± 10.41	0.60 ± 2.90	.001	2.47 ± 2.10	0.24 ± 0.75	.001
8. Ear pressure/pain	4.02 ± 6.23	0.43 ± 1.91	.001	1.34 ± 1.68	0.10 ± 0.34	.001
9. Tongue burning	2.31 ± 5.77	0.03 ± 0.16	.001	0.64 ± 1.27	0.02 ± 0.16	.001
ENT total score	51.33 ± 40.34	3.69 ± 8.22	.001	13.51 ± 9.68	1.28 ± 2.46	.001
Digestive symptoms						
1. Heartburn	9.21 ± 9.23	0.79 ± 2.05	.001	2.45 ± 2.02	0.41 ± 0.92	.001
2. Regurgitations or burps	5.78 ± 7.83	0.38 ± 1.20	.001	1.79 ± 1.90	0.16 ± 0.64	.001
3. Abdominal pain	4.25 ± 6.75	0.79 ± 2.81	.001	1.44 ± 1.89	0.25 ± 0.75	.001
4. Diarrhea	3.27 ± 6.63	0.24 ± 1.37	.001	1.00 ± 1.63	0.19 ± 0.73	.001
5. Constipation	3.72 ± 7.14	0.18 ± 0.69	.001	1.15 ± 1.77	0.16 ± 0.64	.001
6. Indigestion	2.07 ± 4.89	0.18 ± 0.69	.001	0.71 ± 1.36	0.14 ± 0.63	.001
7. Abdominal distension/flatus	6.17 ± 8.20	0.55 ± 2.67	.001	1.70 ± 1.79	0.12 ± 0.51	.001
8. Halitosis	6.30 ± 8.71	0.79 ± 3.08	.001	1.83 ± 1.97	0.23 ± 0.80	.001
9. Nausea	3.47 ± 6.23	0.69 ± 3.07	.001	1.25 ± 1.65	0.27 ± 0.91	.001
Digestive total score	43.61 ± 35.25	4.56 ± 12.08	.001	12.75 ± 9.06	1.66 ± 3.33	.001
Respiratory symptoms						
1. Cough after eating/lying down	4.64 ± 7.57	0.09 ± 0.51	.001	1.36 ± 1.75	0.02 ± 0.16	.001
2. Cough	4.83 ± 7.43	0.28 ± 1.15	.001	1.40 ± 1.62	0.15 ± 0.61	.001
3. Breathing difficulties	3.08 ± 5.90	0.23 ± 1.21	.001	1.05 ± 1.57	0.11 ± 0.50	.001
4. Chest pain	4.85 ± 7.72	0.84 ± 2.68	.001	1.47 ± 1.78	0.27 ± 0.69	.001
Respiratory total score	20.58 ± 26.29	1.43 ± 3.95	.001	5.63 ± 5.18	1.43 ± 3.95	.001
RSS–total score	112.49 ± 78.41	9.68 ± 17.51	.001	31.89 ± 19.34	3.41 ± 5.23	.001

Data are presented as mean ± SD.
The statistical comparison between groups was performed using the Mann-Whitney *U* test.
ENT = ear, nose, and throat; LPR = laryngopharyngeal reflux; QoL = quality of life; RSS = Reflux Symptom Score; SD = standard deviation.

LPR patients than in asymptomatic individuals (Table IV), suggesting high internal validity.

Responsiveness. The RSS, RSI, and VHI total scores significantly improved from baseline to 3 months posttreatment (Table V). The RSS responsiveness to change was especially higher from baseline to 6 weeks posttreatment. According to our multiple linear regression analysis, the improvement of patients with acid, nonacid, and mixed LPR did not significantly differ. About QoL, the symptoms that had the most negative impact on QoL are excess throat mucus, heartburn, globus sensation, throat clearing, throat pain, and halitosis (Table IV). The QoL score of some of these symptoms (throat clearing, throat pain, excess throat mucus, and heartburn) significantly improved from baseline to 3-month posttreatment ($P < .05$).

DISCUSSION

The purpose of this study was to report the properties of the original version of the RSS, a PRO questionnaire developed for the assessment of LPR-related symptoms at the time of diagnosis and throughout the therapeutic course.

To adopt a rigorous approach in accordance with previous recommendations for the development of reliable PRO measures in LPR,[1,9] the conception of the RSS has involved the participation of international experts, practitioners, scientists, and patients; the last group was invited to judge the comprehensiveness of the questionnaire. According to 98% of our patients, the RSS completely assessed their complaints that could have been associated with LPR. The RSS has the advantage of including some common symptoms associated with LPR, such as odynophagia,[24] throat pain,[25] tongue burning,[26] nausea,[1] and halitosis,[27] which had been ignored in previous PRO questionnaires.[1] As demonstrated in the present study, the inclusion of these symptoms makes sense in regard to their prevalence in LPR patients and their related impact on QoL. Some of them are associated with negative impact on QoL, especially excess throat mucus, heartburn, globus sensation, throat clearing, throat pain,

TABLE V.
RSS, RSS QoL, RSI, and VHI Scores for the LPR Patients Throughout Treatment.

RSS Items	Baseline (d0)	6 Weeks	*P* Value (d0–6 Weeks)	12 Weeks	*P* Value (d0–12 Weeks)
ENT symptoms					
1. Voice disorder	4.48 ± 6.51	2.65 ± 3.54	0.156	2.32 ± 3.59	0.021
2. Throat pain	6.02 ± 7.47	5.81 ± 8.24	0.303	3.25 ± 5.51	0.010
3. Pain during swallowing	3.36 ± 5.39	2.10 ± 4.92	0.324	2.44 ± 5.14	0.508
4. Dysphagia	3.31 ± 5.59	2.55 ± 4.52	0.176	1.79 ± 3.49	0.148
5. Throat clearing	10.22 ± 9.48	7.52 ± 7.90	0.001	7.31 ± 8.77	0.001
6. Globus sensation	9.91 ± 9.71	7.13 ± 8.34	0.009	7.88 ± 9.67	0.110
7. Excess throat mucus	10.96 ± 10.41	7.74 ± 9.21	0.010	7.46 ± 8.95	0.011
8. Ear pressure/pain	4.02 ± 6.23	2.19 ± 4.81	0.026	1.90 ± 3.65	0.038
9. Tongue burning	2.31 ± 5.77	2.65 ± 5.97	0.900	2.27 ± 5.51	0.875
ENT total score	51.33 ± 40.34	40.32 ± 34.51	0.001	37.71 ± 32.59	0.001
Digestive symptoms					
1. Heartburn	9.21 ± 9.23	3.68 ± 5.66	0.002	4.85 ± 7.22	0.047
2. Regurgitations or burps	5.78 ± 7.83	2.00 ± 4.65	0.004	2.42 ± 4.45	0.072
3. Abdominal pain	4.25 ± 6.75	3.35 ± 5.20	0.585	3.33 ± 6.87	0.676
4. Diarrhea	3.27 ± 6.63	1.23 ± 2.28	0.126	2.08 ± 5.85	0.032
5. Constipation	3.72 ± 7.14	2.29 ± 4.07	0.793	1.94 ± 4.76	0.346
6. Indigestion	2.07 ± 4.89	0.94 ± 1.59	0.220	0.94 ± 3.69	0.030
7. Abdominal distension/flatus	6.17 ± 8.20	5.52 ± 7.46	0.141	5.52 ± 8.15	0.096
8. Halitosis	6.30 ± 8.71	3.35 ± 5.33	0.080	4.92 ± 7.67	0.184
9. Nausea	3.47 ± 6.23	2.10 ± 5.52	0.443	1.83 ± 4.51	0.017
Digestive total score	43.61 ± 35.25	24.45 ± 22.02	0.002	27.83 ± 28.38	0.008
Respiratory symptoms					
1. Cough after eating/lying down	4.64 ± 7.57	3.06 ± 5.93	0.011	2.52 ± 5.30	0.031
2. Cough	4.83 ± 7.43	3.23 ± 5.91	0.028	3.35 ± 6.78	0.508
3. Breathing difficulties	3.08 ± 5.90	2.52 ± 4.34	0.238	2.87 ± 6.23	0.700
4. Chest pain	4.85 ± 7.72	4.26 ± 6.85	0.346	2.92 ± 5.78	0.201
Respiratory total score	20.58 ± 26.29	13.06 ± 15.34	0.112	11.65 ± 18.32	0.112
RSS total score	112.49 ± 78.41	77.84 ± 54.85	0.001	77.19 ± 63.36	0.002
QoL total score	31.89 ± 19.34	26.65 ± 15.37	0.003	23.65 ± 13.60	0.001
ENT QoL	13.51 ± 9.68	12.29 ± 8.08	0.008	10.87 ± 6.96	0.001
Digestive QoL	12.75 ± 9.06	9.61 ± 7.26	0.044	8.94 ± 6.78	0.003
Respiratory QoL	5.63 ± 5.18	4.74 ± 4.61	0.001	3.85 ± 4.75	0.107
RSS	17.06 ± 9.76	—	—	11.71 ± 11.99	0.001
VHI	13.27 ± 17.33	—	—	9.21 ± 13.88	0.002

ENT = ear, nose, and throat; LPR = laryngopharyngeal reflux; QoL = quality of life; RSI = Reflux Symptom Index; RSS = Reflux Symptom Score; VHI = Voice Handicap Index.

and halitosis, the last two symptoms being not described in the majority of PRO questionnaires. According to the digestive complaints, our analysis has shown that, in comparison with asymptomatic individuals, LPR patients suffered more from digestive symptoms (e.g., indigestion, diarrhea, and nausea, the last of which improved throughout treatment). In addition, 44.0%, 37.5%, and 36.3% of patients had GERD, esophagitis, and gastritis, respectively; the presence of these conditions was not associated with significant differences in the RSS digestive subscore between groups. These observations demonstrate the benefit of concurrently assessing ENT and digestive symptoms in LPR patients. The same reasoning should also be applied to respiratory symptoms associated with LPR, but we found significant pre- to posttreatment improvement of cough after eating or lying down. The exclusion of patients with asthma or those who take inhaled corticosteroids could have contributed to this lack of change throughout treatment.

Another important point regarding RSS content validity is the consideration of both severity and frequency of symptoms with a well-defined rating system. A well-defined rating system for frequency is important because the rating of symptoms with a classic visual analog scale remains subjective and may depend on many sociocultural factors.[1] According to a recent analysis of LPR symptoms and outcomes, the subjectivity in symptom rating as well as the lack of consideration of many common symptoms in some PRO questionnaires could partly explain the inconsistencies

between studies about the superiority of PPI over placebo in LPR disease.[1,4,25] The development of the RSS incorporated these two important points to obtain a reliable clinical PRO questionnaire.

Because LPR-related symptoms are associated with QoL impairments,[7,28] we wanted to include in the RSS a QoL assessment related to the underlying symptoms. Our analysis confirmed the impact of reflux on patient QoL and identified some symptoms that were associated with significant QoL impairment, such as throat pain, heartburn, throat clearing, globus sensation, and excess throat mucus.

The RSS was well accepted among the LPR patients, with high compliance and few missing items. The concurrent internal consistency reliability and test-retest reliability of the RSS were 0.97 and 0.92, respectively, indicating excellent reliability of RSS. These results are competitive with those described for the current validated PRO questionnaires (see Supporting Information, Appendix 1, in the online version of this article).[28–35] The internal consistency of different versions of the RSI,[29,33–35] LPR–Health-Related Quality of Life (LPR-HRQoL),[28] and Pharyngeal Reflux Symptom Questionnaire (PRSQ)[31] ranged from 0.72 to 0.99. Our results of test-retest reliability were slightly higher than those reported for the RSI, LPR-HRQoL, and Supraesophageal Reflux Questionnaire (SERQ), suggesting high reproducibility.[28,29,32]

The convergent validity was evaluated through correlation analyses with the RSI and VHI. The results reported a significant correlation between the RSS and RSI (0.831) and the RSS and VHI (0.492) at baseline. Although the correlation analysis was significant, the lower correlation coefficient between the RSS and VHI can be because the VHI focused on voice disorders and laryngeal complaints, whereas the RSS and RSI include a myriad of symptoms that are not directly associated with voice disorders. This explanation makes particular sense with the RSS, which includes many digestive symptoms that have no impact on voice.

The association between RSS improvement and improvement of the RSI and VHI in the LPR patients after 12 weeks of treatment indicated that the instrument displays high construct validity. To date, only two other LPR PRO questionnaires have reported similar findings: the RSI and LPR-HRQoL.[28,29] In these two studies, the authors reported a significant improvement after 3 to 6 months of PPI therapy in suspected LPR patients[28] and in patients with positive pH monitoring.[29] In the present study, we found that the most important and significant improvements in symptoms occurred from baseline to 6 weeks of treatment. This observation is in accordance with a previous study showing that symptoms mainly decreased during the first 6 weeks of treatment.[36] Interestingly, our statistical analysis did not report significant differences between the improvement in acid, nonacid, and mixed LPR, although nonacid LPR has long been suggested as reflux that is resistant to medical treatment.[37,38] The good improvement of acid, nonacid, and mixed refluxes can be attributed to our personalized therapeutic approach consisting of the associated use of PPIs, alginate, and/or magaldrate according to the MII-pH monitoring characteristics. According to our definition of nonacid LPR, the majority of patients with nonacid reflux had a few acidic reflux episodes. PPIs are active on the pH of acidic droplets through an increase the pH and a decrease of the pepsin activity on the mucosa, but they cannot act on the activity of nonconjugated bile salts and trypsin, which is optimal at pH >6. For this reason, the association of these drugs makes sense because the raft floating over gastric contents of alginates reduces the number of reflux episodes and acts on nonconjugated bile salts and trypsin. The efficacy of this association should, however, be investigated in patients with exclusive nonacid reflux because alginates need some acidity to be effective, and the association of PPIs with alginates in patients with exclusive nonacidic reflux episodes could lead to inconclusive results.

Future studies should specify whether this approach improves the therapeutic efficacy in comparison with the use of PPIs as a single therapy.

The main weakness of the RSS is the length of time needed to complete the PRO questionnaire (≤2 minutes). This is related to the wish of our group to include all symptoms that have been associated with LPR.[1] In practice, at the first consultation, patients completed the RSS in the waiting room at the end of the consultation or during the handwritten prescription of treatment, and the survey was retrieved by the physician a few minutes later. The completion of the RSS was easier during follow-up consultations because patients received the survey in the waiting room before the consultation. The development of smartphone applications as well as the elaboration of a shorter version of the RSS could stem this problem, but we need future investigations on large cohorts to establish which symptoms are the most relevant for the clinical evaluation of LPR patients. Another weakness is the lack of MII-pH study for healthy individuals. However, it was difficult to propose MII-pH to healthy individuals because of the cost and the inconvenience of the examination.

The French version of the RSS is the initial version of RSS. From this version, the Spanish, Persian, Turkish, Korean, and Italian versions of the RSS are in process of development and validation and could confirm the good properties highlighted in the present study.

CONCLUSION

The French version of the RSS is an easily administered, highly reproducible, reliable, and valid PRO questionnaire that includes severity, frequency, and QoL assessments. This instrument could be used to further enhance the LPR diagnosis and the assessment of the therapeutic response in both suspected and confirmed LPR patients. An RSS score >13 could be considered abnormal and suggestive of LPR. However, this cutoff value should be tested in other populations characterized by different diet habits, body mass indices, and genetic patterns. The use of the RSS by other investigators is encouraged to confirm our results and to explore the usefulness of the RSS in daily practice. Currently, Spanish, Korean, Italian, Persian, and Turkish versions of the RSS are in the process of validation. The validation of a United States/English version is required to ensure a large diffusion of the RSS around the world.

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