Laryngopharyngeal Reflux: Correlation Between Symptoms and Signs by Means of Clinical Assessment Questionnaires and Fibroendoscopy. Is This Sufficient for Diagnosis?

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Objective: Laryngopharyngeal reflux (LPR) is diagnosed by the presence of laryngeal signs and symptoms. Some studies have noted that signs and symptoms may be nonspecific and may have poor correlation. The goal of this study was to assess correlation of the reflux finding score (RFS) and reflux symptom index (RSI) as a fibroendoscopic assessment protocol.
Patients and method: A sample of 34 consecutive volunteers with no prior history of voice disorders were enrolled.
All completed a self-administered laryngeal symptom questionnaire (amended RSI) and underwent a comprehensive transnasal fiberoptic laryngoscopy to document LPR findings in a reflux finding score (RFS).
Results: We found a statistically significant correlation between RSI and RFS. This correlation is greater when the RFS score reaches 7 or more points.
Conclusions: In view of the cost and system overload implied by the use of pH-metry, empiric pharmacological therapy is warranted on the basis of a diagnosis of LPR based on RFS and RSI.

Key words: Laryngopharyngeal reflux. LPR. Reflux finding score. RFS. Reflux symptom index. RSI.

Reflujo faringolaríngeo: correlación entre los síntomas y los signos mediante cuestionarios de valoración clínica y fibroendoscópica. ¿Es suficiente para realizar el diagnóstico?
Objetivos: Algunos autores señalan que los síntomas y los signos del reflujo faringolaríngeo (RFL) son inespecíficos y no se correlacionan entre ellos. El objetivo de este estudio es determinar la correlación entre el Reflux Finding Score (RFS) como protocolo de valoración fibroendoscópica y el Reflux Symptom Index (RSI).
Pacientes y método: Se estudió una muestra de 34 pacientes sin historia previa de alteraciones laríngeas, a quienes se entregó el cuestionario RSI (modificado) y se practicó una fibroendoscopia flexible para evaluar el RFS.
Resultados: Hay correlación estadísticamente significativa entre el RFS y el RSI, especialmente si el resultado del RFS es ≥7 puntos.
Conclusiones: Debido a los costes y la saturación asistencial que supone el uso de pH-metría, pensamos que el diagnóstico basado en la aplicación del RFS y el RSI justifica el tratamiento farmacológico empírico.

Palabras clave: Reflujo faringolaríngeo. RFL. Reflux Finding Score. RFS. Reflux Symptom Index. RSI.

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In memoriam

To Dr Rafael García-Tapia Urrutia, for his generosity as a teacher and dedication to those of us who were honoured to be his pupils.

Table 1. Questionnaire (Amended) for Assessment of Clinical Conditions Caused by Laryngopharyngeal Reflux Using the Reflux Symptom Index[a]

In the Last Month, Have the Following Symptoms Affected You?	*0 = Not at All*	*1 = Yes*	*2 = Severely*
Snoring (dysphonia) or other voice problems	0	1	2
Constantly swallowing saliva, clearing throat	0	1	2
Excess of catarrh in the throat, postnasal mucosity	0	1	2
Coughing when lying down	0	1	2
Difficulty breathing	0	1	2
Paroxysmal dry cough	0	1	2
Sensation of a foreign body in the throat	0	1	2
Chest pain, heartburn, indigestion, acidity	0	1	2

[a]The scores marked are added with 16 as the maximum total.

INTRODUCTION

In a prospective study carried out in 2000 on 113 patients with voice disorders, Koufman et al[1] estimated that 57 (50%) of those patients had laryngopharyngeal reflux (LPR) documented by pH-metry.

Patients with LPR have varying symptoms when they seek medical advice: loss of voice strength (98.3%), persistent cough (96.6%), the sensation of a foreign object in the throat (94.9%), and change in voice tone (94.9%) are the most frequent chronic-intermittent symptoms (more than 1 symptom may be present).

However, even though we link the terms "reflux" and "gastroesophageal dysfunction," we find ourselves facing a disorder that is clinically and physiopathologically different from gastroesophageal reflux (GER). Thus LPR is different from GER due to the absence of the typical "retrosternal heartburn" or pyrosis that patients with GER have, aside from there being no oesophagitis on the endoscopic exam (this must be present in GER). On the other hand patients with LPR have orthostatic position reflux episodes (during the day) whereas GER symptoms can usually be seen more in the decubitus position (at night).[3] Regarding physiopathology, there are prolonged periods of exposure to acid with GER, but not so with LPR, and in those patients with GER there is a deficit in the acid clearance time basically due to a change in the lower oesophageal sphincter (LES), while the main LPR defect is a dysfunction in the upper oesophageal sphincter (UES) with shorter acid reflux episodes, but more intense (ie, with a lower pH).[4] The differences in LPR and GER physiopathological mechanisms and patterns of course explain the different symptoms in each case but it is important to point out that, even though most LPR patients do not have GER, some do have both occurring simultaneously.[5] In view of this, when a patient is suspected of having LPR we must explain that the absence of gastrointestinal symptoms does not rule out what we suspect is the diagnosis.

Even though many patients with LPR mention intermittent dysphonia as the symptom that most frequently pushes them into seeing an otorhinolaryngologist, we must not forget that LPR is linked to the development of organic problems of the larynx (laryngospasms, subglottic stenosis, recurring leukoplasia, laryngeal nodes and polyps, granulomas, cancer of the larynx, etc), of the pharynx (dysphagia, Zenker's diverticulum, etc), of the lungs (bronchiectasias, aspiration pneumonia, exacerbation of asthma, or chronic obstructive pulmonary disease, etc) and others such as cot death, sinusitis, otitis media, or obstructive sleep apnoea syndrome (OSA).[6] It is, therefore, a disease that does not just occur frequently but may also have important consequences if it not correctly diagnosed and treated.

The methodology used to diagnose LPR includes different methods[7]: laryngeal examination (fibrolaryngoscopy), 24-hour out-patient pH-metry (with pharyngeal and oesophageal sensors), oesophageal manometry, laryngeal sensitivity test with intraluminal impedance monitoring and oesophagoscopy, or oesophagography.

Of all these, out-patient pH-metry is the most sensitive and diagnostic-specific method.[8] It is considered the gold standard if we compare it with the rest of the diagnostic tests available. But is the systematic use of pH-metry justified to confirm LPR in those patient cases in which we have a pretty good suspicion of the diagnosis? The prevalence of the disease, the invasive test method, the costs and development of organizational strategies that 24-hour out-patient pH-metry implies if we use it as an LPR diagnostic tool for every patient suspected of having it make it impossible to use; therefore it is reserved for special cases, such as when the patient is not responding to medical treatment or has associated complications (stenosis, Barrett's oesophagus, etc). It may also be used as a complementary examination before deciding to proceed with surgery.[9]

In fact, the patient's history, guided by the reflux symptom index (RSI) (Table 1) and the fibroendoscopy done to look for LPR symptoms through the reflux finding score (RFS) (Table 2)[9] are validated methods[9,10] for diagnosing LPR, with 75.6% and 80.7% sensitivities for RSI and RFS,[11] for a definitive diagnosis of LPR (compared with the standard) and an 18.8% specificity for RSI, and 37.5% for RFS. Is it possible for us to diagnose LPR when we have symptoms that point to it along with a simple flexible fibrolaryngoscopy? Statistically, some authors[10] state that there is a 95% probability of someone having LPR if his or her RFS score reaches ≥7 (out of a maximum of 26) and an RSI score ≥13 (on a scale of 0 to 5 for each item, the maximum is 45 points); however, the RSI and RFS specificities are low when both tools are used independently.

The aim of this article is not to confirm the validity of the RSI and RFS as methods for diagnosing LPR since there is already medical literature on the subject which supports this,[10,12,13] but instead we propose revising our LPR diagnostic method using RFS and RSI in a sample of patients possibly having LPR and then analyze the correlation between the

symptoms (RSI) and signs (LPR) in order to see if the two methods simultaneously may be valid for diagnosing LPR.

PATIENTS AND METHOD

A sample of 34 patients was studied (17 men and 17 women), aged 21 to 85 (mean [standard deviation], 58.32 [4.7] years). The study included patients who randomly sought out-patient care from an otorhinolaryngologist for any of the following symptoms (reason for seeing the doctor): "unspecified throat problems," "throat itchiness," "scratchy cough," "sudden onset of coughing with loss of breath," "hoarseness," "dry throat," "a feeling of a foreign object in the throat," and/or "voice changes." The following cases were excluded: smokers, asthmatics, or chronic obstructive pulmonary disease sufferers; those patients who had received previous treatment with antacids or proton pump inhibitors; those with organic laryngeal disease (such as polyps, nodes, etc); those patients who received radiotherapy or surgery in the head and neck area; and psychiatric patients.

The enrolling of patients in the study, anamnesis and the RSI questionnaire, as well as the fibrolaryngoscopy (RFS) (Table 2) were all done by the same researcher, in every case.

It was decided to use the amended RSI questionnaire (Table 1), with only 3 options for evaluating the severity of the symptoms (0=nothing; 1=yes; 2=severe) instead of the original 5,[14] in order to avoid too much bias since it is a very subjective questionnaire, especially if our aim is for patients to describe their symptoms on a 5 point scale. In fact, in a study prior to this work, we observed that most patients had serious difficulties describing a specific symptom on a qualitative ordinal scale with 5 possible options. The difference between grade 3 and 4 of the original questionnaire, for example, is so slight that it is not significantly different and the patients would just give random answers.

The material used for the laryngeal examination was a transnasal fiberoptic laryngoscope with a work channel (Karl-Storz®) and a Sass-Wolf® halogen light source.

The statistical analysis was done with the SPSS software (v. 11.5 for Windows), defining the bilateral *P* value of <.05 as significant. The Shapiro-Wilks normality test showed that the RFS and RSI ordinal qualitative variables are not normally distributed; this did not happen with the discrete quantitative variable of "age" or the continuous quantitative variable of "weight." However, the normality test was not taken into account since the variables analyzed (RFS and RSI) are ordinal and therefore should be analyzed using a non-parametric statistical analysis. For comparison of means, Mann-Whitney's non-parametric *U* test was used in which the dependent variables were the pathological value (RFS ≥7) and the RFS non-pathological value (<7). In the correlation study, Spearman's non-parametric coefficient (*r*) was used as well as Kendall's Tau-b correlation coefficient, which is conceptually similar to Pearson's parametric coefficient. Since we are dealing with ordinal variables (RFS and RSI) the use of statistical inference (non-parametric) was more appropriate.

Table 2. Laryngopharyngeal Reflux Finding Score[a]

Pseudosulcus	0 = absent; 2 = present
Ventricular obliteration	0 = no; 2 = partial; 4 = total
Erythema/hyperaemia	0 = no; 2 = arytenoids; 4 = diffuse
Oedema of the vocal cards	0 = no; 1 = medium; 2 = moderate; 3 = severe; 4 = polypoid
Diffuse laryngeal oedema	0 = no; 1 = medium; 2 = moderate; 3 = severe; 4 = obstructive
Hypertrophy of the posterior commissure	0 = no; 1 = medium; 2 = moderate; 3 = severe; 4 = obstructive
Granuloma/granulation	0 = absent; 2 = present
Dense endolaryngeal mucus	0 = absent; 2 = present

[a]The reflux finding score (RFS) documents the presence of 8 characteristic signs of laryngopharyngeal reflux by fibroscopic examination; the maximum score possible is 26.

RESULTS

In the descriptive study (Figure 1), it is worth mentioning that the values from the RFS (6.4 [4.7]; 95% CI, 4.5-8.2) are relatively low if we take into account that we are 95% sure of diagnosing a patient with LPR who had a score ≥7.[1] The sample distribution regarding the RFS value description was as follows: a "pathological" RFS (RFS ≥7) for 12 (35.3%) patients and a "normal" RFS (RFS <7) for 22 (64.7%) patients. Regarding the RSI outcome, a mean of 6.52 (4.7), (95% CI, 4.5-8.3) resulted. The median (P_{50}) corresponded to RFS and RSI values of 6 and 7, respectively.

The mean comparison by Mann-Whitney's non-parametric *U* test showed that there were statistically significant differences (*P*<.001) among those patients who has a RFS score ≥7 and those who had a RFS score <7 regarding the RSI. This means that those patients with LPR clinical signs have more symptoms and therefore higher RSI scores. In fact the RFS and RSI correlation is statistically significant (τ_b=0.3; *P*=.007) (Figure 2) and a maximum correlation is reached (τ_b=1; *P*<.001) if we separately analyze those patients who had a RFS score ≥7.

Regarding the analysis of those differences that may arise regarding patient gender, age or weight, there were no statistically significant results. It is worth mentioning, however, that there is trend (*P*>.05) toward higher RSI questionnaire scores in older patients.

DISCUSSION

It is difficult to estimate LPR prevalence in the general population.[15] Looking at the laryngeal and pharyngeal symptoms of those patients with LPR some authors point out that 50%[1] and even 64% of those patients who visit an otorhinolaryngologist for "voice problems" have underlying LPR.

If after a transnasal fiberoptic laryngoscopy we think that the symptoms pointing to a possible LPR are significant

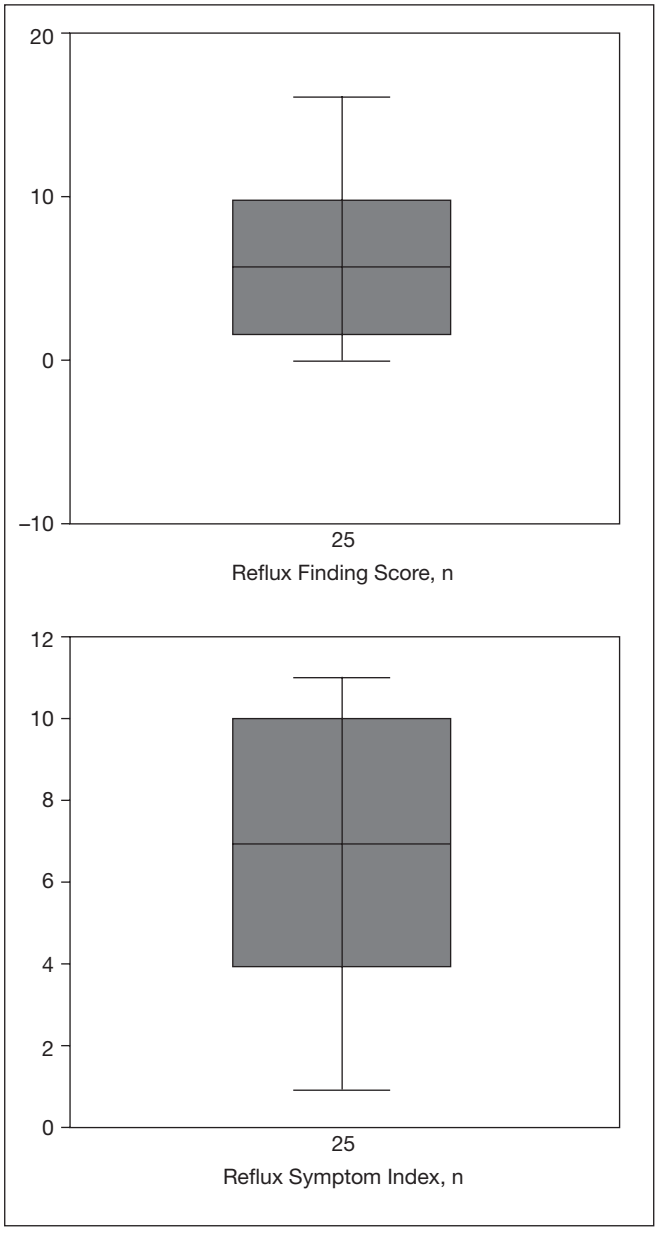

Figure 1. Box graph describing the distribution of the scores obtained with the reflux symptom score and the reflux symptom index in our sample.

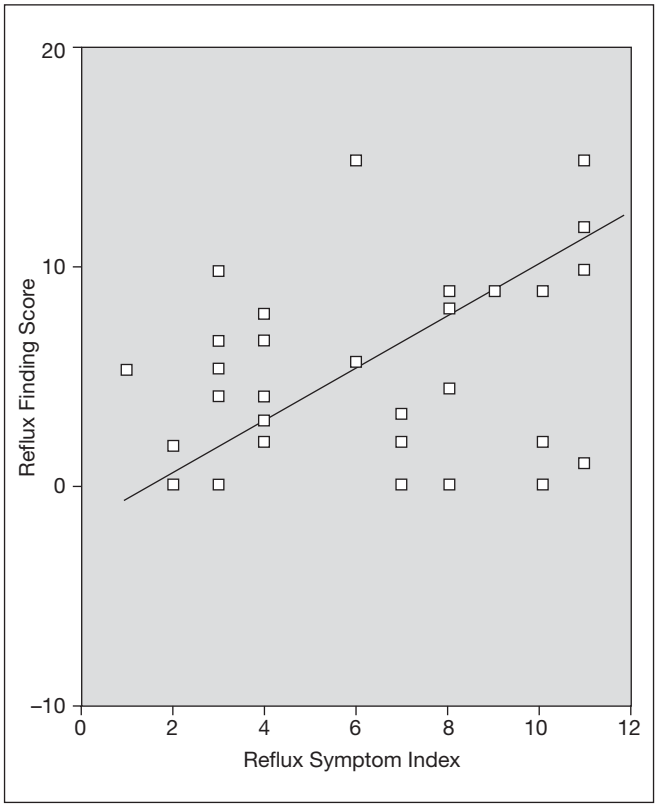

Figure 2. Simple dispersion diagram. Correlation between the reflux symptom score and the reflux symptom index ($P<.05$).

enough (meaning an RFS score of ≥7)[2] to give a practically definitive diagnosis (the pH-metry would be the defining test), we found that only 35% of patients who came to our clinic with "a scratchy throat," "feeling of a foreign object," "dysphonia," "cough and hoarseness," among others, are candidates for being diagnosed with LPR.

Independently of the prevalence of patients with "probable" LPR that we see during visits, we feel that confirming our suspicion by systematically using pH-metry or any other diagnostic tool is neither practical nor beneficial for the patient. We believe this, first of all, because, as we have shown, there is a statistically significant correlation between LPR symptoms (RSI) and signs (RFS) and, above all, this correlation is highest in pathological cases with a 95% probability,[2] meaning an RFS of 7 or more. Even though some authors[16] underestimate LPR's symptom-sign correlation we believe that that association strengthens a presumptive diagnosis. In second place, and in tune with what we have previously shown, the high effectiveness rate of the proton pump inhibitors (PPI) and the fact that they are tolerated[17] well make it possible to treat patients empirically with daily administration of PPI (the highest dose before breakfast, 40 mg for omeprazol, pantoprazol, and lansoprazol, and 30 mg for esomeprazol) for 4 months,[18] with a patient check-up after that period. There is no doubt that those patients who have significant improvements in symptoms after the four-month treatment period in themselves confirm we what initially suspected was the diagnosis. Aside from all that, we think that LPR symptoms are too unspecific to allow for the RSI questionnaire to establish a "diagnosis cut-off point," which is why we think that the RSI is better for evaluating PPI treatment follow-up. The response to PPI treatment is basically symptomatic (which means better RSI scores) since the lesions or laryngeal signs (RFS) may take longer to return to normal.[17]

CONCLUSIONS

In our protocol, when there is a patient with a possible LPR, we do a transnasal fiberoptic laryngoscopy. If the RFS score is 7 or higher we provide a presumptive LPR diagnosis

and finish up the study with the RSI questionnaire. Then we indicate maximum dose PPI treatment (taken in the morning, before breakfast) during 4 consecutive months.

A new evaluation is done once treatment is finished. If the RSI or RFS result is lower than the first, we consider the diagnosis of LPR to be likely and continue with the treatment (at half the PPI dose) for another 4 months, and then check-ups are done after that, twice a year.

If the RSI result has not changed or has increased in relation to the first one (or if the RFS has worsened), the patient is sent for a pH-metry that will confirm the LPR diagnosis.

Therefore, according to our criteria, RFS and RSI mutually complement each other, even though RFS is more useful for a suspected diagnosis and RSI for follow-ups and to see how the treatment is going.

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