The Reflux Symptom Score-12: Cross-cultural Adaptation and Validation for European Portuguese Speakers With Laryngopharyngeal Reflux

[#]Isabel Guimarães, [†]Ana P. Batista, [‡]Aldora Quintal, [§]Rita Bom, [¶]Cláudia Romeiro, [¶]Madalena Saraiva, [‖]Maura Cunha, [**]Daniela B. Ferreira, [‡]Paula Correia, [††]Lina Almeida, and [‡‡]Gabriela Torrejano

Abstract: Objectives. To translate and cross-culturally adapt the 12-item reflux symptom score (RSS-12) to European Portuguese (EP) and determine its clinimetric properties for symptomatic individuals with laryngopharyngeal reflux (LPR).

Study design. Multinational cross-sectional cohort study.

Methods. The English RSS-12 was cross-culturally adapted according to the recommendations of the international guidelines. The validation study included the completion of the RSS-12, reflux symptom index, and voice handicap index by symptomatic and asymptomatic subjects with LPR. The RSS-12 was completed a second time by symptomatic subjects. Nine clinimetric properties were analyzed according to the international guidelines for validation of patient-reported outcome measures.

Results. The EP RSS-12 is equivalent to the English version (content, depth, and scoring). A total of 155 adults (84 with LPR symptoms) aged 21–78 years participated in the validation study. Statistical analyses revealed high internal consistency (Cronbach alpha >0.90), high test-retest reliability (intraclass correlation coefficient > 0.70, $P < 0.001$), low measurement error (Standard measure error of 5.21 for RSS and 1.59 for quality of life), good content validity (omission data $< 1\%$ and item-total correlations > 0.652), good construct validity (61.9% of the total item variance with moderate item loadings), strong concurrent validity with reflux symptom index ($r_p = 0.772$, $P < 0.001$) and moderate validity with voice handicap index ($r_p = 0.531$, $P < 0.001$), and significantly known-groups validity ($P < 0.001$). The EP RSS-12 showed cross-cultural validity with French and Persian versions and high predictive validity with a cut-off value > 8 for a sensitivity of 91.7% and a specificity of 91.5%.

Conclusions. The EP RSS-12 retained the features of the English version and is a reliable and valid patient-reported outcome measure for EP individuals with LPR in the study.

Key Words: Laryngopharyngeal reflux–Dysphonia–Outcome–Reflux symptom score-12.

INTRODUCTION

Laryngopharyngeal reflux (LPR) is a multidimensional disorder estimated to affect up to 15% of the outpatients in ear, nose, and throat (ENT) clinics.[1,2] LPR signs and symptoms are mainly nonspecific and are often associated with other ENT disorders, such as chronic pharyngolaryngitis (which is related to tobacco or alcohol dependence) making it difficult to evaluate clinically and follow the course of disease consistently.[1]

The need for a comprehensive assessment of the experience and well-being of the patient with LPR should be a prime consideration when seeking an accurate clinical diagnosis. Over the past few years, one of the measures recommended as part of the multidimensional LPR assessment protocol is the patient-reported outcome measure (PROM). The most recent systematic review found the existence of 16 LPR PROMs but pointed out several limitations at the level of the framework and of the methodological and validation processes.[3] For example, one of the oldest PROMs, the 9-item reflux symptom index (RSI), is based on the LPR symptoms but does not include sore throat, odynophagia, nausea, and empirical data have provided limited confirmation of its reliability and validity.[4,5]

The study group of young otolaryngologists of the international federation of oto-rhino-laryngological Societies has outlined an LPR PROM and made an important and innovative contribution to the field. Their 22-item PROM is called the reflux symptom score (RSS) and includes ENT, digestive, and respiratory LPR symptoms, that allow determination of the frequency and severity of symptoms, and assessment of their impact on quality of life (QoL). The formal validation study has confirmed the RSS-22 reliability and validity, and several cross-cultural adaptations and validations have been developed.[6] Considering that, subjects may undergo multiple assessments in routine

Accepted for publication June 16, 2023.

From the #Speech and Language Pathologist (SLP), Speech Therapy Department, Alcoitão Health School of Sciences; Clinical and Therapeutics Pharmacological Unit, Faculty of Medicine, Instituto de Medicina Molecular, University of Lisbon, Portugal; †PMR Department, Centro Hospitalar e Universitário do Algarve, Portimão, Portugal; ‡ENT Department, Hospital Garcia de Orta, Almada, Portugal; §ENT Department, Hospital do Espírito Santo de Évora, EPE, Évora, Portugal; ¶ENT Department, Hospital do Divino Espírito Santo, Ponta Delgada, EPE, Portugal; ‖PMR Department, Centro Hospitalar e Universitário do Algarve, Faro, Portugal; **ENT Department Centro Hospitalar de Entre Douro e Vouga, Santa Maria da Feira, Portugal; ††ENT Department, Hospital dos Lusíadas, Lisboa, Portugal; and the ‡‡ENT Department, Centro Hospitalar Universitário Lisboa Norte, EPE, Lisboa, Portugal.

Address correspondence and reprint requests to Ana P. Batista, PMR Department, Centro Hospitalar e Universitário do Algarve, Portimão, Portugal. E-mail: ana.batista@chalgarve.min-saude.pt

Journal of Voice, Vol xx, No xx, pp. xxx–xxx
0892-1997

https://doi.org/10.1016/j.jvoice.2023.06.016

diagnostics, a shortened version with 12 items (RSS-12) and two final scores (RSS and QoL) was proposed to reduce the subject burden. Two versions of the RSS-12, in French and English, were developed by the original authors and adapted cross-culturally to Brazilian Portuguese, German, and Persian.[7–10] Empirical data demonstrate the reliability and validity of the RSS-12 based on the samples collected in France and Iran.[7,8] French dataset, which included 154 individuals aged 19–90 years, mainly women, showed high reliability (Cronbach alfa = 0.97), strong reproducibility (r_s = 0.92 for RSS-12 and r_s = 0.95for QoL), high concurrent validity (r_s = 0.83) with the RSI, discriminated between LPR patients and healthy individuals ($P < 0.001$) and had high accuracy in predicting LPR (sensitivity and specificity of 94.5% and 86.2%, respectively).[7] The available data for the Persian version included a cohort of 113 adults, aged 20–59 years, mainly men. Statistical analyses revealed high reliability (Cronbach alfa = 0.85 for RSS and 0.72 for QoL), excellent reproducibility, and low standard error of measurement (SEM) for RSS (intraclass correlation coefficient [ICC] = 0.98 and SEM = 6.51) and QoL (ICC = 0.94 and SEM = 2.56), high concurrent validity with RSI (r_p = 0.87), moderate validity with voice handicap index (VHI) (r_p = 0.57), and discriminant validity between LPR and healthy subjects ($P < 0.001$).[8]

Currently, there is no reliable and valid LPR PROM for European Portuguese (EP), which limits the knowledge of the patient perspective in the clinical decision-making process and disease progression. The current study aimed to cross-culturally adapt the RSS-12 to EP and determine its clinimetric properties in individuals with LPR.

METHODS AND MATERIAL

This multicentre cross-sectional study was carried out in compliance with the Declaration of Helsinki following authorization from eight hospitals' institutional review boards.

Cross-cultural Adaptation

The methodology of cross-cultural RSS-12 adaptation to EP followed a systematic procedure according to PROMs guidelines[11]: (i) Forward translation from English to EP was performed independently by two native Portuguese authors with good knowledge of the English language and a consensus version was produced; (ii) Back translation was performed by an English teacher with good knowledge of EP who was completely unaware of the content of the original questionnaire. A test version was provided by the first two authors and the back translator; (iii) Using the Delphi method, an expert panel consisting of three speech and language pathologists compared the EP translated version with the original, item-by-item, considering the semantic, idiomatic, experiential (whether the situations evoked in the original culture of the tool had the same reference in the target culture), and conceptual equivalences. A preliminary version of the RSS-12 was then produced; (iv) A final cognitive debriefing was conducted with five adults aged 45–63 years, including both women and men. The procedure was performed between January and February 2022.

Validation Process

Participants and Data Collection Procedures

To be eligible for the study, all volunteer participants declared: (i) be over 18 years of age; (ii) to be proficient in written EP; (iii) have no prior medical history of physical or neurological conditions; (iv) to be nonsmokers; (v) keep alcohol consumption below three daily doses (12 g) or 21 doses/week (heavy consumption); (vi) have no active seasonal allergies or asthma.

Specific eligibility criteria for the symptomatic subjects were a past or current medical history of LPR and a positive diagnosis by ENT surgeons via laryngoscopy. For the asymptomatic subjects, the following criteria applied: (i) no past or current medical history of LPR and a total RSI score of less than 13; and (ii) normal voice as assessed by speech and language pathologists. Symptomatic subjects were recruited from an ENT outpatient clinic in eight Portuguese hospitals in different geographical locations. The asymptomatic nearly age- and sex-matched subjects were recruited by the authors through word of mouth. At enrollment, and before completing the questionnaires, each participant provided written informed consent. Data collection occurred between March and December 2022.

Material

In addition to the EP RSS-12 (Appendix 1), a demographic and clinical information questionnaire and the EP versions of the reflux symptom index (RSI)[12] and (VHI-EP)[13] were used.

The demographic and clinical questionnaire included information on age, sex, weight, height, educational level, occupational status, smoking habits, and alcohol consumption.

The RSS-12 questionnaire consists of 12 questions asking about seven ear, nose, and throat symptoms, three digestive symptoms, and two respiratory symptoms. Responses are rated on a 5-point Likert-type scale for frequency, severity, and impact on quality of life (QoL). For each item, the frequency and severity scores are multiplied to obtain an RSS ranging from 0 to 25. The final RSS score is calculated by summing the scores of the 12 items, with a total possible value ranging from 0 to 300. The QoL score is obtained by summing the responses to the 12 items, with a possible total score ranging between 0 and 60. Higher scores indicate higher levels of symptom frequency, severity (RSS score), and impact (QoL score).[7]

The RSI is a 9-item PROM with a response scale of 0 (no problem) to five (severe problem), and a maximum total score of 45. According to the original authors, a cut-off value greater than 13 is indicative of LPR problems.[4] The RSI has been validated for EP individuals with LPR.[12]

The VHI is a well-known generic voice PROM with 30 items that has been cross-culturally adapted to EP and validated for speakers with dysphonia. Its equivalence to seven European versions and the original American VHI has been established.[13,14]

Data Analysis

Descriptive statistics were calculated for all participants. Nine clinimetric properties were analyzed following the recommendations for validation of cross-cultural PROMs of the consensus-based standards for the selection of health measurement instruments (COSMIN).[15] For internal consistency, Cronbach alpha was used, and a coefficient value greater than 0.70 was considered appropriate. A 1-week test-retest was performed with 40 (47.6%) randomly selected symptomatic subjects using the intraclass correlation coefficient (ICC) and its 95% confidence intervals (CI). Recommended values greater than 0.70 for clinical purposes were considered. SEM = √sum of squares total/(n-1) x √1-ICC) was determined for RSS and QoL scores. Content validity adequacy was assessed using item rate (missing data accepted if < 5%) and item-total Pearson correlations (r_p). An r_p greater than 0.40 was recommended as more representative of scale content. Exploratory factor analysis (EFA) and principal component analysis with varimax rotation were conducted for the RSS score to determine the structural validity of the scale according to the following criteria: Kaiser-Meyer-Olkin measure of sampling adequacy at 1–0.9 very good or 0.8–0.9 good and Bartlett's Test of Sphericity criterion of $P < 0.001$. Only those factors whose eigenvalues were greater than one were retained. Item loading was considered large if it was equal to or greater than 0.80, moderate between 0.79 and 0.50, and small if was < 0.50. To determine the concurrent validity of RSS-12, RSI, and VHI, Pearson product-moment correlations were computed ($r_p \geq 0.70$ strong; between 0.70 and 0.40 moderate, and < 0.40 weak). To examine validity for known-groups validity, the independent-sample *t*-test was used to compare RSS-12 scores between symptomatic and asymptomatic individuals. Cross-cultural validity was analyzed by comparing the RSS-12 dataset of the present study with the French dataset (with similar target groups) and with published data for the Persian version.[7,8] A receiver-operating characteristic curve (ROC) for sensitivity and specificity was calculated to determine the best cut-off points for predicting LPR risk using the RSS score. The areas under the ROC curves (AUCs) and their 95% CI were also calculated. The AUC criteria were 1–0.90 (perfect sensitivity and specificity), 0.89–0.80 (good), 0.79–0.70 (moderate), 0.69–0.60 (poor), and < 0.59 (useless, no better than chance). The RSS value at which overall sensitivity and specificity were greatest was chosen as the cut-off value.

Data from all participants were processed and analyzed using Statistical Package for Social Sciences software (version 23, Inc., Chicago, IL). A *P*-value of less than 0.05 was defined as the level of significance.

RESULTS

Cross-cultural Adaptation

The expert panel approved the translation (100%) and some semantic and grammatical comments were made to reach the standard EP and to avoid doubts about the fulfillment of RSS-12. Original expressions and words such as "within last month", "excess mucus", "voice problem", "swallowing", "troublesome", "severe", "disorders" literally translated as "durante o último mês", "muco excessivo", "problema vocal", "deglutir", "incomodativo", "severo" and "distúrbios", were adapted to the common EP expressions "no último mês", "excesso de muco", "problema de voz", "engolir", "desconfortável", "grave" and "perturbações". In the pretest, the five adults indicated that all sentences were easy to understand, and no other changes were suggested.

Validation Process

Participants

A total of 155 volunteers (84 with LPR symptoms) participated in the study (Table 1). They were predominantly females (80%) with full-time employment (85.8%). Although symptomatic subjects had a slightly higher mean age and body mass index (BMI) than asymptomatic subjects, there was no significant effect on age ($t = 1.321$, $df = 153$, $P = 0.191$) and BMI ($t = 1.171$, $df = 153$, $P = 0.244$). In terms of educational level, the symptomatic subjects mainly had completed secondary education, while the asymptomatic subjects had a university degree. Most symptomatic subjects suffered from voice disorder.

Cronbach's alpha coefficients for RSS and QoL ranged from 0.908 to 0.921 for all data, between 0.860 and 0.880 for symptomatic subjects, and from 0.629 to 0.620 for asymptomatic subjects.

Reproducibility proved to be high (ICC coefficients > 0.70) with low SEM (Table 2).

Content validity was verified considering that in the pooled RSS-12 data set, item missing data was less than 1% and item-total correlations were higher than 0.40 for RSS (r_p between 0.652 and 0.898) and QoL (r_p between 0.587 and 0.689).

Structural validity was determined considering that the data met the criteria for analysis with a good Kaiser-Meyer-Olkin (0.808), highly significant Bartlett's Test of Sphericity ($\chi = 483.436$, $df = 66$, $P < 0.001$), and moderate item loadings (0.522–0.735) so that EFA for RSS could be performed. The resulting factorial model yielded three factors with an eigenvalue greater than one, as indicated by the scree slope plot, which explained 61.9% of the total item variance (Table 3).

Table 4 shows that all instruments except QoL with RSI had significantly positive correlations for asymptomatic subjects. For symptomatic subjects, RSS showed a strong positive correlation with RSI and a moderate one with VHI whereas QOL showed a moderate positive correlation with RSI and VHI. In the asymptomatic subjects, RSS showed a weak positive correlation with RSI and VHI and QoL with VHI.

TABLE 1.
Subjects' Demographic and Clinical Data

N (%)	Symptomatic 84 (54.2%)	Asymptomatic 71 (45.8%)
Age (years; m ± sd; [range])	52.0 ± 12.7 (21–78)	49.4 ± 11.8 (23–74)
Sex (female| male; N [%])	67 (79.8) | 17 (20.2)	53 (74.6) | 18 (25.4)
Level of education N (%)		
Primary (≤ 4 years)	16 (19)	0
Secondary (5–12 years)	39 (46.4)	13 (18.3)
Post-secondary (Professional diploma)	3 (3.6)	3 (4.2)
Tertiary (Higher education)	26 (31)	55 (77.5)
Occupational status N (%)		
Full time employment	67 (79.8)	66 (93.0)
Body Mass Index (BMI) m ± sd	26.0 ± 4.6	25.2 ± 3.7
N (%)		
Underweight (BMI < 18.5)	0	0
Normal weight (BMI 18.5–24.9)	43 (51.2)	38 (53.5)
Overweight weight (BMI 25.0–29.9)	24 (28.6)	27 (38.0)
Obesity (BMI > 30.0)	17 (20.2)	6 (8.5)
Voice N(%)		
Normal	12 (14.3)	71 (100)
Disorder	72 (85.7)	0

TABLE 2.
Test-Retest for RSS and QoL Scores for Symptomatic Subjects

	ICC	95% CI	*P*-value	SEM
RSS ENT symptoms	0.881	0.819–0.929	< 0.001	
RSS digestive symptoms	0.870	0.796–0.924	< 0.001	
RSS respiratory symptoms	0.886	0.815–0.935	< 0.001	
RSS total score	**0.907**	**0.860–0.944**	**< 0.001**	**5.21**
QoL ENT symptoms	0.885	0.826–0.931	< 0.001	
QoL digestive symptoms	0.845	0.758–0.909	< 0.001	
QoL respiratory symptoms	0.837	0.735–0.906	< 0.001	
Quality of life (QoL) total score	**0.923**	**0.883–0.953**	**< 0.001**	**1.59**

RSS, reflux symptom score; CI, confidence intervals; ENT, ear, nose, and throat; ICC, intraclass correlation coefficient; SEM, standard error of measurement.

Symptomatic subjects achieved significantly higher RSS mean (t = 10.731, df = 87.848, $P < 0.001$) and QoL (t = 11.130, df = 90.960, $P < 0.001$) compared to asymptomatic subjects (Table 5). When the symptomatic subjects were dichotomized by gender, no effect was found for the RSS score (t = 1.917, df = 82, $P = 0.059$), but a significant effect was found for the QoL score (t = −2.472, df = 28.527, $P = 0.020$) with females having higher mean scores than males (Table 5).

Table 6 presents the RSS-12 results for the existent datasets. A comparison of the symptomatic subjects' scores showed that the mean total scores of the French and EP datasets were similar with nominal differences of 2.6 and 0.4 for RSS and QoL respectively, whereas the Persian dataset had higher nominal differences with the scores of the EP dataset (RSS = 40.5 and QoL = 6.7). Similarities were also found in the comparisons of asymptomatic subjects in the three data sets for QoL mean scores but not for RSS overall mean scores with nominal differences ranging from 0.5 to 3.0.

The ROC curve had perfect discriminatory properties with an AUC of 0.949 (95% CI 0.913–0.984) for RSS and an AUC of 0.908 (95% CI 0.859–0.956) for the QoL. An RSS cut-off value > 8 was obtained with high sensitivity (91.7%) and specificity (91.5%) (Figure 1).

DISCUSSION

The EP RSS-12 proved to be congruent with the English version in terms of general and referential meaning as well as content, scale structure (number of items and subscales and covered symptoms), and format (scaling and scoring procedures). This is an advantage for future international

TABLE 3.
EFA Analysis-Rotation Matrix for RSS-12

	Factors		
RSS-12 items	1	2	3
1. Hoarseness or a voice problem	0.667		
2. Throat pain or pain during swallowing	0.712		
3. Difficulty swallowing (pills, liquids, or solid foods)	0.698		
4. Throat clearing (not cough)	0.689		
5. Sensation of something being stuck in the throat	0.677		
6. Excess mucous in the throat and/or postnasal drip sensation		0.673	
7. Bad breath			0.758
8. Heartburn, stomach acid coming up, regurgitation, burping, or nausea			0.619
9. Abdominal pain or diarrhea			0.753
10. Indigestion, abdominal distension, and/or flatus			0.743
11. Coughing (not just throat clearing)		0.822	
12. Breathing difficulties, breathlessness, or wheezing		0.659	
Explained variance (%)	39.66	13.07	9.15

RSS-12, reflux symptom score.

TABLE 4.
Concurrent Validity for RSS and QoL

	All data (n = 155)		Symptomatic (n = 84)		Asymptomatic (n = 71)	
	RSS	QoL	RSS	QoL	RSS	QoL
RSI	0. 837 $P < 0.001$	0.727 $P < 0.001$	0.772 $P < 0.001$	0.613 $P < 0.001$	0.228 $P = 0.012$	0.032 $P = 0.732$
VHI	0.726 $P < 0.001$	0.695 $P < 0.001$	r = 0.531 $P < 0.001$	0.473 $P < 0.001$	0.359 $P < 0.001$	0.462 $P < 0.001$

RSS, reflux symptom score; RSI, reflux symptom index; VHI, voice handicap index; QoL, quality of life.

TABLE 5.
RSS-12 Data Set

		RSS score		QoL score	
		Mean ± SD	95% CI	Mean ± SD	95% CI
Group symptomatic	84	74.6 ± 59.8	61.6–87.6	19.3 ± 14.3	16.2–22.4
Asymptomatic	71	3.5 ± 9.4	1.3–5.7	1.5 ± 2.9	0.9–2.2
Symptomatic subjects					
Females	67	80.8 ± 61.8	65.7–95.9	21.0 ± 14.3	17.5–24.5
Males	17	50.1 ± 44.7	27.1–73.1	12.5 ± 12.1	6.3–18.8

RSS, reflux symptom score; CI, confidence intervals; QoL, quality of life.

TABLE 6.
Cross-cultural Validity for Symptomatic Subjects

	French		Persian		European Portuguese	
	Symptomatic	Asymptomatic	Symptomatic	Asymptomatic	Symptomatic	Asymptomatic
Sample (n)	73	80	63	50	84	71
Age (years, mean ± sd) [min-max]	47.5 ± 16.8 (19–90)	*NR (18–59)	39.3 ± 9.8 (20–59)	37.2 ± 10.3 (20–58)	52.0 ± 12.7 (21–78)	49.4 ± 11.8 (23–74)
Females (%)	59	NR	36.5	38	79.8	74.6
RSS score	77.2 ± 50.3	6.5 ± 11.1	115.1 ± 51.5	2.8 ± 2.8	74.6 ± 59.8	3.5 ± 9.4
QoL score	19.7 ± 11.4	2.0 ± 3.2	26.0 ± 10.1	1.5 ± 1.9	19.3 ± 14.3	1.5 ± 2.9

* Not reported (NR).

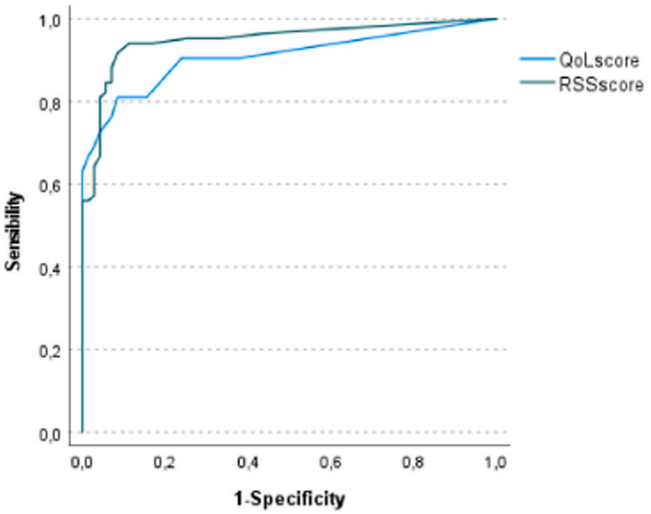

FIGURE 1. Reflux symptom score-12 (RSS-12) score receiver-operating characteristic (ROC) curve.

cross-cultural comparisons that will contribute to the understanding of how to improve the quality of health care for EP subjects with LPR.

The reliability of the EP version of the RSS-12 was demonstrated by its excellent internal consistency, high reproducibility, and low SEM results. The internal consistency results were in line with those of the two previous studies, although the values of the alpha coefficient for the overall data in the present study (alpha ranging from 0.921 to 0.908) were higher than those reported for the French and Persian versions (alpha between 0.73 and 0.85 respectively).[7,8] In contrast to the present study, the French and Persian data did not report Cronbach's alpha in relation to symptomatic and asymptomatic subjects.[7,8] With the exception of the French version of the RSS-12 study, the present and Persian studies used the statistical reproducibility analysis (ICC test and SEM) recommended by COSMIN. The results indicate high stability and reproducibility over time (test-retest ICC results > 0.70) in the present and Persian studies. The magnitude of SEM was slightly lower in the present study (RSS = 5.21 and QoL = 1.59) and showed higher accuracy than the Persian results (RSS = 6.51 and QoL = 2.56).[8]

The data presented here provide evidence that EP RSS-12 is a valid PROM. Its content proved valuable for the 155 individuals tested in the present study, as the number of missing data (1%) was below the cut-off criterion (< 5%) indicating the absence of literacy difficulties that limit independent reading, as recommended for PROMs. These results corroborate the findings of the formal validation study in Persian.[8] In the present study the item-total correlations were above the recommended criteria which is evidence of the items' representation of the scale content.

The present results showed that is possible to distinguish between independent symptomatic and asymptomatic subjects which is an indication of the validity of RSS-12 known-groups and is in line with the results of the French and Persian studies. The present study also demonstrated that the RSS can discriminate between symptomatic females' and males' impact (QoL score) but not for symptoms (RSS score). Data from the other versions are not available for comparison.[7,8]

Construct validity was confirmed by EFA with 61.5% of the total item variance by moderate item loading. No information regarding this issue was found in earlier RSS-12 studies.[7,8]

In the present study, a significant and strong correlation (concurrent validity) was found between RSS-12 and RSI ($r_p = 0.808$) indicating that these two PROMs can assess a similar construct, which is consistent with the results of the French and Persian versions ($r_s = 0.845$; $r_p = 0.87$ respectively). A moderate relationship between RSS and VHI was expected, as this has been mentioned in previously published data suggesting that both PROMs represent independent but complementary information.[7,8]

In accordance with the COSMIN recommendation, an attempt was made to compare the present results with those obtained in France and Iran. Generally, similar LPR symptoms and QoL impact were found, confirming that the EP RSS-12 has cross-cultural validity. Specifically, cross-cultural invariance was found in symptomatic subjects between the two European countries, with similar RSS scores (EP = 74.6 and French = 77.2) and QoL scores (EP = 19.3 and French = 19.7), but not in Iran, where scores were higher (RSS = 115.1 and QoL = 26.0). One possible reason for the existing similarities between the European symptomatic subjects is the sample features (EP versus French: 84 and 73 subjects, mainly females, mean ages between 52 and 47.5 years, and similar BMI mean). On the other hand, the discrepancies with the Iran data may also be related to the sample differences (eg, 113 subjects, mainly men, and a mean age of 39 years old). Despite the finding that women predominate in Western ENT clinics[3,9,14] future studies in larger male cohorts would be relevant to better understand the gender-related differences in the diagnosis of the LPR.

As for the asymptomatic subjects, in the present study, the RSS mean values were slightly higher than in the Persian data and lower than in the French data.[7,8] Nevertheless, the results on QoL are similar in all three data sets. An in-depth analysis of this issue was beyond the scope of this study, but it is possible that it is due to the exclusion criteria used. In the present study, the asymptomatic subjects were nonsmokers without voice disorders, which is not the case in the other two studies.[7,8]

The accuracy of the RSS score was verified suggesting that it can be used as a screening tool to predict LPR in EP

adults. The observed high sensitivity and specificity (91.7% and 91.5% respectively) suggest that the RSS score identifies a high proportion of true positive LPR cases and has a low risk of false positive screening. The present results are similar to the sensitivity reported for the French RSS (94.5%) and lower than that for specificity (86.2%) indicating a lower risk of false-positives results compared with the French data. The cut-off value predicted in the present study (> 8) is lower than that reported in the French version (cut-off > 11).[7] Data from the Persian version are not available for comparison.[8]

Study Limitations

The present results have several limitations that should be explored in the future. First, a major limitation of the current study is the method of LPR diagnosis used. Portuguese procedures for LPR diagnosis in the hospital include the clinical history, laryngoscopy examination, and self-reporting of symptoms. Unfortunately, the most accurate gold standard complementary diagnostic test (intraluminal multichannel impedance and pH monitoring) is expensive and hardly available in Portuguese hospitals. The fact that invasive examinations were not performed on healthy subjects in the present study had an ethical basis. Second, it is important to note that subjects with conditions such as tobacco use, and alcohol dependence were not included in the present study. This was chosen to avoid bias from similar LPR signs and symptoms, which was consistent with the French and Persian RSS-12 validation studies; however, future research may strengthen the EP RSS-12 validation by including a broader range of people with different conditions. Third, the size ratio between groups (symptomatic and asymptomatic subjects) is partly due to the exclusion criteria used in the present study. A total of 87 subjects were not included in the study, of which 38 were symptomatic smokers and 49 were asymptomatic smokers without voice disorder and RSI > 13. Future research may strengthen these results by including more asymptomatic subjects. Fourth, another limitation is its cross-sectional design as it was not possible to collect information on EP RSS-12 sensitivity to change. Despite the limitations described above, this study has contributed to the adaptation and validation of a PROM in EP subjects with LPR and has provided useful information that would not otherwise have been obtained.

CONCLUSIONS

The EP RSS-12 retained the features of the English version, and it is a reliable and valid PROM for EP subjects with LPR in the study.

CRediT authorship contribution statement

(1) A. Conception, B. Organization, C. Execution.

(2) Statistical Analysis: A. Design, B. Execution, C. Review, and Critiques.

(3) Manuscript: A. Writing of the First Draft, B. Review and Critique.

Isabel Guimarães: 1A, 1B, 1C, 2A, 2B, 3A.
Aldora Quintal.: 1B, 1C, 3B.
Rita Bom: 1B, 1C, 3B.
Cláudia Romeiro: 1B, 1C, 3B.
Madalena Saraiva: 1B, 1C, 3B.
Maura Cunha: 1B, 1C, 3B.
Daniela Brás Ferreira: 1B, 1C, 3B.
Paula Correia: 1B, 1C, 3B.
Lina Almeida: 1B,1C, 3B.
Gabriela Torrejano: 1B, 1C, 3B.
Ana Paula Batista: 1A, 1B, 1C, 2C, 3B.

Declaration of Competing Interest

None.

Acknowledgments

We would like to thank all participants who accepted to participate in this study.

Appendix A. The Reflux Symptom Score| Escala de sintomas de refluxo (RSS-12)

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

No último mês tive um/vários dos seguintes sintomas.

Frequency|Frequência: 0 = I don't have this complaint over the past month| 0 =Não tive esta queixa durante o último mês.
1,2,3,4 =I had| 1, 2, 3, 4 =Tive.
1–2; 2–3; 3–4; 4–5 weekly over the past month| 1–2; 2–3; 3–4; 4–5 vezes por semana, durante o último mês.
5 = complains occur daily| 5 =As queixas ocorrem diariamente.
Severity and Quality of Life (QoL) impact| Gravidade e Impacto na Qualidade de Vida:
0 =problem is not severe| 0 = O problema não é grave;.
5 =problem very troublesome when it occurs| 5 =O problema é muito desconfortável quando ocorre.

Ear, nose and throat disorders Perturbações ORL (ouvidos, nariz e garganta)	Frequency Frequência						Severity Gravidade						Total	QoL impact Impacto na qualidade de vida (IQV)						Total
1. Hoarseness or a voice problem| Rouquidão ou um problema de voz	0	1	2	3	4	5	0	1	2	3	4	5		0	1	2	3	4	5	
2. Throat pain or pain during swallowing| Dor de garganta ou dor ao engolir	0	1	2	3	4	5	0	1	2	3	4	5		0	1	2	3	4	5	
3. Difficulty swallowing (pills, liquids or solid foods)| Dificuldade em engolir (comprimidos, líquidos ou sólidos)	0	1	2	3	4	5	0	1	2	3	4	5		0	1	2	3	4	5	
4. Throat clearing (not cough) | Pigarreio (não é tosse)	0	1	2	3	4	5	0	1	2	3	4	5		0	1	2	3	4	5	
5. Sensation of something being stuck in the throat| Sensaç ão de ter algo preso na garganta	0	1	2	3	4	5	0	1	2	3	4	5		0	1	2	3	4	5	
6. Excess mucous in the throat and/or post nasal drip sensation| Excesso de muco na garganta e/ou sensação de corrimento nasal posterior	0	1	2	3	4	5	0	1	2	3	4	5		0	1	2	3	4	5	
7. Bad breath| Mau hálito	0	1	2	3	4	5	0	1	2	3	4	5		0	1	2	3	4	5	
8. Heartburn, stomach acid coming up, regurgitation, burping, or nausea| Azia, subida de acidez do estomago, regurgitaço, arrotos ou náusea	0	1	2	3	4	5	0	1	2	3	4	5		0	1	2	3	4	5	
9. Abdominal pain or diarrhea| Dor abdominal ou diarreia	0	1	2	3	4	5	0	1	2	3	4	5		0	1	2	3	4	5	
10. Indigestation, abdominal distension and/or flatus| Indigestão, distensão abdominal e/ou flatulência	0	1	2	3	4	5	0	1	2	3	4	5		0	1	2	3	4	5	
11. Coughing (not just throat clearing) | Tosse (não apenas pigarreio)	0	1	2	3	4	5	0	1	2	3	4	5		0	1	2	3	4	5	
12. Breathing difficulties, breathlessness, or wheezing| Dificuldades respiratórias, falta de ar ou pieira	0	1	2	3	4	5	0	1	2	3	4	5		0	1	2	3	4	5	
							RSS total =							QoL| IQV total =						

References

1. Koufman JA, Amin MR, Panetti M. Prevalence of reflux in 113 consecutive patients with laryngeal and voice disorders. *Otolaryngol Head Neck Surg.* 2000;123:385–388. https://doi.org/10.1067/mhn.2000.109935.
2. Fourie K, Richardson M, Van der Linde J, et al. The reported incidence and nature of voice disorders in the private healthcare context of Gauteng. *J Voice.* 2017;31:774.e23–774.e28. https://doi.org/10.1016/j.jvoice.2017.02.013.e23–774.e28.
3. Lechien JR, Saussez S, Schindler A, et al. Symptoms and signs outcomes of laryngopharyngeal reflux treatment: a critical systematic review and meta-analysis. *Laryngoscope.* 2019;129:1174–1187. https://doi.org/10.1002/lary.27591.https://doi.org/ 10.1002/lary.27591.
4. Belafsky P, Postma G, Koufman J. Validity and Reliability of the reflux symptom index. *J Voice.* 2002;16(2):274–277. https://doi.org/10.1016/s0892-1997(02)00097-8.
5. Lechien JR, Akst LM, Hamdan AL, et al. Evaluation and management of laryngopharyngeal reflux disease: state-of-the-art review. *Otolaryngol Head Neck Surg.* 2019;160(5):762–782. https://doi.org/10.1177/0194599819827488.
6. Lechien JR, Schindler A, Hamdan AL, et al. The development of new clinical instruments in laryngopharyngeal reflux disease: the international project of Young Otolaryngologists of the International Federation of Oto-rhino-laryngological Societies. *Eur Ann Otorhinolaryngol Head Neck Dis.* 2018;135:S85–S91. https://doi.org/10.1016/j.anorl.2018.05.013.
7. Lechien JR, Bobin F, Rodriguez A, et al. Development and validation of the short version of the reflux symptom score: reflux symptom score-12. *Otolaryngol-Head Neck Surg.* 2021;164(1):166–174. https://doi.org/10.1177/0194599820941003.
8. Kohansal A, Koddami SM, Ansari NN, et al. Validity and reliability of the Persian version of reflux symptom score-12. *J Voice.* 2022. https://doi.org/10.1016/j.jvoice.2022.07.022.S0892-1997(22)00224-7.
9. Ceccon FP, Aires MM, Lechien JR, et al. Translation and cultural adaptation of the short version of the reflux symptom score: reflux symptom score-12 into Brazilian Portuguese Brazilian. *J Otorhinolaryngol.* 2022;89(2):264–270. https://doi.org/10.1016/j.bjorl.2022.05.005~.
10. Bruhn J, Brockmann-Bauser M, Swing T, et al. Transkulturelle deutschsprachige Ubersetzung des Fragebogens reflux symptom score-12. *HNO.* 2022;70:886–890. https://doi.org/10.1007/s00106-022-01233-2.
11. Beaton DE, Bombardier C, Guillemin F, et al. Guidelines for the process of cross-cultural adaptation of self-report measures. *Spine LWW.* 2000;25:3186–3191. https://doi.org/10.1097/00007632-200012150-00014.
12. Costa I, Sousa M, Costa D, et al. Pharyngolaryngeal reflux disease—can symptoms predict endoscopic findings? *Revista Portuguesa de Otorinolaringologia e Cirurgia de cabeça e pescoço.* 2020;54:241–247. https://doi.org/10.34631/sporl.914.
13. Guimarães I, Abberton E. An investigation of the voice handicap index with speakers of Portuguese: preliminary data. *J Voice.* 2004;18(1):71–82.https://doi.org/:10.1016/j.jvoice.2003.07.002.
14. Verdonck-de Leeuw IM, Kuik DJ, De Bodt M, et al. Validation of the voice handicap index by assessing equivalence of european translations. *Folia Phoniatrica Logopaedica.* 2008;60:173–178.https://doi.org/:10.1159/000127836.
15. Mokkink LB, Terwee CB, Patrick DL, et al. The COSMIN study reached international consensus on taxonomy, terminology, and definitions of measurement properties for health-related patient-reported outcomes. *J Clin Epidemiol.* 2010;63:737–745. https://doi.org/10.1016/j.jclinepi.2010.02.006.