

# Original Article Artigo Original

Gabriela Ricci<sup>1,2</sup> Aline Epiphanio Wolf<sup>2</sup> Aline Pires Barbosa<sup>2</sup> Felipe Moreti<sup>1</sup> Ingrid Gielow<sup>1</sup> Mara Behlau<sup>1</sup>

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## Correspondence address:

Gabriela Ricci R. Machado Bittencourt, 361/1001, Vila Mariana, São Paulo (SP), Brasil, CEP: 04044-905. E-mail: gabrielaricciribeiro@gmail.com

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# Signs and symptoms of laryngopharyngeal reflux and its relation to complaints and vocal quality

Sinais e sintomas de refluxo laringofaríngeo e sua relação com queixas e qualidade vocal

## ABSTRACT

**Purpose:** To verify the association between laryngopharyngeal reflux (LPR) with age, gender, vocal deviation and voice complaints. **Methods**: The study included patients between 18 and 70 years old, referred to the Otorhinolaryngology service for complaints of voice or reflux, of both sexes. Endolaryngeal findings were classified using the Reflux Finding Score (RFS) scale. The presence or absence of vocal and reflux complaints was verified and correlated with the RFS classification. On the same date, they were submitted to sustained vowel voice recording and chained speech. The auditory-perceptual assessment was performed by a speech therapist, classifying the general degree of vocal deviation based on the GRBASI scale. **Results**: Ninety-seven patients were evaluated, with a mean age of 42.6 years, 62.3% female, and mean RFS scores of 6.26 points. Among the patients, 48 subjects had vocal complaints, 34 women with a mean age of 44.9 years and an average RFS score of 6.94 points. The other 49 individuals had no vocal complaints, and of these 27 were women, with a mean age of 41.2 years and a mean RFS score of 5.5 points. The variables "reflux complaint", "vocal complaint" and age were the ones that most correlated with the RFS scale scores. **Conclusion**: There is a relationship among reflux complaints, laryngeal findings and vocal complaint.

#### RESUMO

**Objetivo:** Verificar a associação entre Refluxo laringofaríngeo (RLF) com idade, sexo, desvio vocal e queixas de voz. **Método:** Participaram do estudo pacientes entre 18 e 70 anos, encaminhados ao serviço de otorrinolaringologia por queixas de voz ou refluxo, de ambos os sexos. Os achados endolaríngeos foram classificados utilizando a escala Reflux Finding Score (RFS). A presença ou não de queixas vocais e de refluxo foi verificada e correlacionada com a classificação RFS. Na mesma data, os pacientes foram submetidos à gravação de voz de vogal sustentada e fala encadeada. A avaliação perceptivo-auditiva foi realizada por uma fonoaudióloga, classificando o grau geral do desvio vocal com base na escala GRBASI. **Resultados:** Foram avaliados 97 pacientes, com média de idade de 42,6 anos, sendo 62,3% do sexo feminino e média dos escores da escala RFS igual a 6,26 pontos. Do total de pacientes, 48 indivíduos apresentavam queixas vocais, sendo 34 mulheres com idade média de 44,9 anos e escore RFS médio de 6,94 pontos. Os outros 49 indivíduos não apresentavam queixas vocais, e desses 27 eram mulheres, com idade média de 41,2 anos e média de escore RFS igual a 5,5 pontos. As variáveis "queixa de refluxo", "queixa vocal" e idade foram as que mais se correlacionaram com os escores da escala RFS. **Conclusão**: Há relação entre queixas de refluxo, achados laríngeos e queixa vocal. .

Study conducted at Centro de Estudos da Voz – CEV – São Paulo (SP) and at the Faculdade de Medicina de Ribeirão Preto da Universidade de São Paulo – FMRP-USP – Ribeirão Preto (SP), Brasil as a prerequisite for completing the Especialização em Voz course.

<sup>1</sup> Centro de Estudos da Voz - CEV - São Paulo (SP), Brasil.

<sup>2</sup> Faculdade de Medicina de Ribeirão Preto da Universidade de São Paulo – FMRP-USP – Ribeirão Preto (SP), Brasil

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#### INTRODUCTION

The voice is a unique phenomenon produced by the human being, which represents not only his age, sex and physical type, but also one of the strongest means that identifies his personality characteristics and emotional states<sup>(1)</sup>. Among the factors that may interfere with vocal quality, the occurrence of diseases such as laryngopharyngeal reflux (LPR) stands out, which has been frequent nowadays, as a consequence, among others, of stressful life and poor diet<sup>(2)</sup>.

LPR, designated by Koufman et al in 1996, is one of the most common extraesophageal manifestations of gastroesophageal reflux disease (GERD) <sup>(3,4)</sup>. Appointed as one of the most relevant causes for the development of dysphonia<sup>(3,5)</sup>, LPR is the retrograde flow of gastroduodenal content to the upper aerodigestive tract, encompassing signs, symptoms and tissue injuries<sup>(2,5,6)</sup>. It is related to the incompetence of the lower esophageal sphincter and ineffective whitening due to decreased peristalsis<sup>(7)</sup>. Among the refluxed contents, hydrochloric acid and pepsin are the main ones<sup>(8)</sup>. The larynx is more susceptible to reflux injury than the esophagus, as it lacks the epithelial defenses (anti-reflux barrier) of the esophagus<sup>(3)</sup>.

The symptoms most frequently related to laryngopharyngeal reflux are: sore throat, the sensation of pharyngeal globus, throat clearing, dysphonia, dry cough and laryngospasm attacks<sup>(5,8,9,10,11,12,13,14)</sup>, and a considerable portion of these symptoms is associated with voice<sup>(4,6,15,16,17,18)</sup>. Vocal folds can suffer from the effects caused by acid reflux, since the acid itself, cough and throat clearing can aggravate laryngeal lesions, altering the constitution of the vocal folds and resulting in typical lesions such as granulomas and contact ulcers<sup>(7)</sup>.

It is estimated that LPR is one of the most frequently encountered chronic inflammatory conditions of the larynx and that it occurs in at least 50% of individuals with laryngeal and voice disorders<sup>(13)</sup>.

Among the examinations provided in the diagnostic evaluation, the laryngoscopic examination is included, in which it is possible to see signs suggestive of reflux, such as hyperemia and diffuse laryngeal edema, edema of vocal folds and vestibular folds, edema of the subglottic mucosa, hypertrophy of the interarytenoid region, thick endolaryngeal mucus and granuloma or granulation tissue<sup>(3,14)</sup>. However, these inflammatory signs may be present in other pathologies that affect the laryngopharyngeal tract, resulting in diagnostic difficulty for the LPR<sup>(10,12,14)</sup>.

To contribute to the diagnosis of laryngopharyngeal reflux, the Reflux Finding Score (RFS) was a questionnaire designed to document the physical findings related to reflux and the intensity of symptoms <sup>(19)</sup>. This instrument produces a score that points to the laryngeal inflammatory signs mentioned above through videolaryngoscopic findings, to make the diagnosis less subjective. The score assigns degrees of intensity of these inflammatory signs and determines the presence or absence of lesions suggestive of laryngopharyngeal reflux. The RFS scale has high reproducibility and reliability so that an individual with a total score above 7 points has a 94% probability of presenting laryngopharyngeal reflux. Furthermore, it is also used to monitor the evolution of the disease and the response to treatment<sup>(19)</sup>. This scale demonstrated to contribute to the clinical diagnosis of laryngopharyngeal reflux in 16% to 32% of cases in the groups of randomized clinical trials<sup>(17)</sup>.

Based on the assumption that there is no standard criterion test for clinical diagnosis of LPR and it remains controversial, it was intended to investigate whether there is an association between laryngeal signs and symptoms suggestive of LPR with vocal quality and voice complaints, as well as their relationship with age and sex, using the total RFS score as a meter of reflux endolaryngeal signs.

## **METHODS**

This cross-sectional exploratory study was approved by the Research Ethics Committee of *Hospital das Clínicas* of Ribeirão Preto Medical School under number 2166/201, CAEE: 13066513.0.0000.5440 and all individuals involved signed the Free and Informed Consent Form.

The location for data collection was the *Hospital Estadual* de Ribeirão Preto, which meets the demand of the XIII Departamento Regional de Saúde (DRS) of Ribeirão Preto, where the medical care is performed to the users of the Unified Health System (Sistema Único de Saúde - SUS) of the 26 municipalities that make up its coverage area.

For inclusion in the study, the following criteria were used: to be between 18 and 70 years old, of both sexes and to have a medical indication for nasofibrolaryngoscopy due to voice complaints or reflux in the period from March to October 2015. All SUS users who had received prior medical care in any of the municipalities that comprise DRS and who had a medical referral to the hospital otorhinolaryngology outpatient clinic were included, as long as they met the inclusion criteria within the specified period of eight months.

Individuals with laryngeal lesions other than LPR, as well as respiratory alterations, history of neurological disease and smokers were excluded from the study. Among these criteria, smoking was self-reported, neurological diseases were confirmed via electronic medical records and laryngeal lesions and respiratory alterations were classified by an otorhinolaryngologist among allergies, sinusitis and rhinitis.

The total sample, selected for convenience within the given period, was composed of 97 patients with or without selfreported voice complaints (hoarseness, breathiness, dry throat) or laryngopharyngeal reflux (throat clearing, pharyngeal globus, cough, burning, heartburn). Values 0 and 1, respectively, were used to classify the absence and presence of vocal complaints, as well as complaints of laryngopharyngeal reflux.

Endolaryngeal findings were classified through nasofibrolaryngoscopy by an otolaryngologist using the reflux endolaryngeal findings scale (RFS), which ranges from 0 to 26 points, with 26 being the most serious score.

The speech sample for auditory-perceptual analysis consisted of the prolonged vowel emission  $\langle \mathcal{E} \rangle$  and counting numbers from 1 to 10. Such activities were performed in the morning, assuming a minimum nocturnal vocal rest. The registration was done in a portable computer (Toshiba, Windows 7), coupled with a CAD C195 microphone cardioid condenser, placed at 10 cm from the research participant. An external sound capture card model Mobile Pre from the M-Audio brand was used to guarantee the quality of the collected sound. The software used to record the voices was the Sony Sound Forge 8.0.

The samples were analyzed by a speech-language therapist specialized in voice, with 25 years of experience in clinical care in the voice area and who was not aware of the subjects' identity or their clinical condition.

The analysis of the vocal quality was performed through an auditory-perceptual assessment, based on the GRBASI scale (Grade, Roughness, Breathiness, Asthenia, Strain, Instability), a highly reliable instrument that classifies the voices according to the general grade of alteration (G), roughness (R), breathiness (B), asthenia (A), strain (S) and instability (I). For this purpose, the values were assigned to each parameter: 0 (absence), 1 (slight alteration), 2 (moderate alteration) or 3 (intense alteration).

According to this research proposal, the voices were classified as absence (0) or presence (1) of alteration in vocal quality. The presence of alterations in vocal quality (1) was considered when the voice was classified as grade 1, 2 or 3 on the GRBASI scale.

The perceptual-visual evaluation was carried out with a 3.4 mm flexible nasofibroscope (Olympus, model ENF-P4) and an Olympus brand video system. The visualization was made using topical xylocaine gel applied to the optical fiber. The laryngological evaluation was performed during breathing and the vowel /i/ emission.

Data on the anatomofunctional condition of the larynx were recorded considering endolaryngeal findings suggestive of reflux involvement, such as: subglottic edema, ventricular obliteration, erythema/hyperemia, vocal fold edema, diffuse laryngeal edema, interarytenoid region hypertrophy, granuloma/ granulation tissue and thick endolaryngeal mucus. For such classification, the Reflux Finding Score (RFS), proposed and validated by Belafasky et al. in 2001, was used. The scale ranges from 0 (no abnormal findings) to a maximum of 26 (worst possible score). The final items included in the scale comprise subglottic edema, ventricular obliteration, erythema/ hyperemia, vocal fold edema, diffuse laryngeal edema, hypertrophy, granuloma/granulation tissue and excessive endolaryngeal mucus.

An exploratory analysis of the data was carried out, with the basic objective of summarizing the values, organizing and describing the data through tables with descriptive measures. Continuous variables were expressed in terms of basic descriptive statistics (mean, median, standard deviation), whereas categorical variables were expressed in terms of frequency.

Statistical analyzes were performed using the SAS® 9.0 software, through PROC GLM. To verify the statistical association of categorical variables, Fisher's exact test was used. The association between two quantitative variables (Age and Reflux Score) was made using Pearson's Correlation Coefficient.

In these analyzes, a significance level of 5% was considered and the adjustments were obtained using the SAS software (version 9.2). The graphics were built in R (The R Project for Statistical Computing), version 3.1.

## RESULTS

97 individuals were evaluated, with a mean age of 42.6 years (SD = 13.9), a median of 41, ranging between 18 and 67 years, with 62.3% being female. Of the 48 volunteers who presented vocal complaints, 34 were women and 14 men, with an average age of 44.9 (SD = 13.3) years. Of the 49 volunteers without vocal complaints, 27 were women and 22 men, with an average age of 41.2 (SD = 12.3) years.

The variables gender, vocal complaint, reflux complaint and vocal quality were analyzed to verify if there was an association among them, using Fisher's exact test (5% significance level). An association was found only between sex and reflux complaints (p = 0.02), in which it was observed that women have more reflux complaints than men (Table 1).

 Table 1. Association between gender and reflux complaint using the

 Fischer's Exact Test

| 0 and an | Reflux compla | <b></b> |         |  |
|----------|---------------|---------|---------|--|
| Gender   | No            | Yes     | - Total |  |
| Male     | 16            | 20      | 36      |  |
| Female   | 13            | 48      | 61      |  |
| Total    | 29            | 68      | 97      |  |
| P value  | 0.0219        |         |         |  |

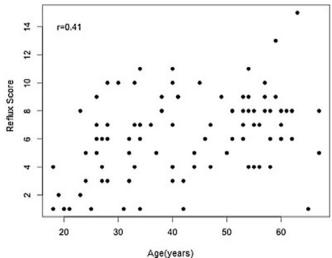
When comparing the variables studied with the scores of the RFS scale, there is evidence of a relationship between this score and the variables "vocal complaint" (p = 0.02) and "reflux complaint" (p < 0.0001) (Table 2).

 Table 2. Comparison between the studied variables and the RFS scale score using the linear regression model

| Effect                    | Average RFS<br>Score |        | Comparison |      | P-value |
|---------------------------|----------------------|--------|------------|------|---------|
|                           | No                   | Yes    | Lotination | 2    |         |
| Vocal<br>complaint (0-1)  | 5.59                 | 6.94   | -1.34      | 0.58 | 0.0231  |
| Reflux<br>complaint (0-1) | 3.93                 | 7.25   | -3.31      | 0.55 | <0.0001 |
| Vocal<br>quality (0-1)    | 6.08                 | 6.47   | -0.38      | 0.59 | 0.5170  |
|                           | Male                 | Female |            |      |         |
| Gender (1-2)              | 6.08                 | 6.36   | -0.27      | 0.61 | 0.6553  |

When correlating age with the RFS scale scores, a coefficient r = 0.41 was obtained, which indicates a highly positive relationship

(p < 0.01) with a tendency that, the older the age, the greater the endolaryngeal findings of reflux, as shown in Figure 1.





#### DISCUSSION

The present study (i) verified the association between laryngeal signs and symptoms suggestive of LPR with vocal quality and voice complaints in patients seen at a secondary level hospital in the city of Ribeirão Preto - SP and (ii) statistically analyzed these characteristics, looking for possible relationships among them.

Age indicated evidence of a statistical relationship with the presence of signs indicative of LPR through the RFS scale since individuals with older age were more likely to have LPR findings when compared to younger subjects. The incidence of reflux probably increases as one gets older<sup>(20,21,22)</sup>. This finding is in line with findings in the literature, in which it was observed that 69% of the subjects who presented signs of LPR had a mean age between 53 and 55 years<sup>(3)</sup>.

In another study, it was found that the likelihood of reflux signs being found is higher in older people; as also, older female individuals present a risk factor for the appearance of extra-esophageal alterations, such as LPR<sup>(13)</sup>. With aging, there may be a breakdown of the natural anti-reflux barrier. Transient relaxation of the lower esophageal sphincter (LES) is the most common pathophysiological mechanism of reflux episodes<sup>(22)</sup>. According to Mendelsohn<sup>(21)</sup>, although an aging esophagus is unlikely to produce an increase in transient LES relaxations, elderly patients are much more likely to take one or more medications that can promote these inappropriate relaxations, such as calcium channel blockers, benzodiazepines, anticholinergics and antidepressants. The other pathophysiological mechanism that explains the increase in the incidence of reflux in the elderly is a decreased clearance of esophageal  $acid^{(22)}$ . It is observed that acid reflux remains in the esophagus for longer in the elderly due to the weak esophageal propulsion towards the stomach.

However, in the present study, although the age factor was related to the presence of endo-laryngeal signs of reflux, such influence should be balanced, since the mean age was 42.6 years, with few individuals over 60 years.

The influence of LPR on the pathogenesis of laryngeal alterations is widely studied<sup>(11,13,14,15,23)</sup>, however, its implications for vocal production are not well established. Of the most frequent vocal symptoms in patients with LPR, hoarseness is one of the main<sup>(14,23)</sup>, just as LPR can be present in up to 50% of patients with voice problems<sup>(11,15)</sup>, as well as being involved in up to 75% of patients with refractory otorhinolaryngological symptoms<sup>(24)</sup>. In the present study, it was found that the vocal complaint was statistically related to the RFL score, and the higher the score, the greater the vocal complaints.

In the literature, the association between the presence of vocal alteration and signs suggestive of LPR is controversial. In this study, it was not associated, as well as in other studies that mention a possible relationship, but do not prove a causal relationship between LPR and vocal pathology<sup>(2,5,14,17,18,12,22)</sup>.

It was also found that the more complaints of reflux the patient had, the higher the score on the RFS scale, which corroborates to infer that this scale is a method that can be used to measure laryngeal signs of reflux.

It is worth mentioning that some individuals in the present study did not have reflux complaints or vocal complaints, but did have signs of LPR in the otorhinolaryngological exam. The opposite also occurred, that is, there was a record of individuals who reported having vocal alterations and LPR symptoms, but did not show signs on the exam. This fact confirms the complexity mentioned in the literature to arrive at a clinical diagnosis of LPR<sup>(4,12,16)</sup>.

Most clinicians readily recognize the ease of diagnosing severe cases of reflux when tissue signs are dramatic. However, many patients have subtle profiles, thus hindering interpretation<sup>(4)</sup>. LPR symptoms can be found in about 10% of patients referring to otorhinolaryngology services<sup>(16)</sup>. The most frequent complaints found in individuals with LPR are: sore throat, the sensation of pharyngeal globus, throat clearing, dysphonia, dry cough and attacks of laryngospasm<sup>(8,9,11,12,14,15,16)</sup>.

However, despite the relatively high prevalence of this clinical condition, the diagnosis of LPR remains controversial, since currently there are no standard criterion tests<sup>(17,18)</sup>. This clinical dilemma will continue until a specific and reliable definition of reflux signs can be established, since LPR is a multifactorial syndrome, with wide clinical representation and requires a multidisciplinary approach<sup>(6)</sup>.

Vocal quality assessments can help to better understand voice disorders and can be used as indicators of treatment effectiveness in patients with symptoms related to laryngopharyngeal reflux<sup>(5,24,25)</sup>.

This study has some limitations, important to be mentioned. It was carried out in a single hospital, which limits the generalization of the results. We could still consider the possibility of testing intra-rater reliability, both in the auditory-perceptual analysis and in the visual (endoscopic) analysis with duplication of part of the audio and video sample, as well as the analysis considering the degree of intensity of the vocal alteration.

Thus, the data point to the need for new research to investigate such interrelations, which can assist in the construction of knowledge and contribute to the multidisciplinary treatment of this population.

## CONCLUSION

Gastroesophageal reflux, when manifesting beyond the esophagus, may produce signs and symptoms, which can produce laryngeal and vocal alterations.

The presence of video laryngoscopic signs suggestive of LPR through the RFS scale was not associated with sex or with the presence of voice alterations, but was related to LPR complaints, vocal complaints and older age.

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#### Authors' contributions

*GR* was responsible for the research design, collection, tabulation, data analysis and preparation of the text of the article; *AEW* was responsible for the research design, data analysis and revision of the text of the article; *APB* was responsible for the collection, tabulation, data analysis and revision of the text of the article; *FM* was responsible for the research design, data analysis and revision of the text of the article; IG was responsible for the research design, data analysis and revision of the text of the article; MB was responsible for the proposal and design of the research, data analysis and final revision of the text of the article.