

# Incidental Laryngeal Findings in Routine Laryngopharyngeal Reflux Diagnosis

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**ABSTRACT** **Background:** Laryngopharyngeal reflux (LPR) refers to the backflow of acidic stomach content into the larynx, pharynx, and upper aerodigestive tract. The diagnosis of LPR is based on the patient's history and findings of the laryngoscopy associated with LPR. Other possible manifestations consistent with LPR symptoms include laryngeal cancer, vocal fold granulomas, Reinke's space edema, and vocal polyps. In this study, we compared the characteristics of patients with LPR symptoms and incidental laryngeal findings (ILF) in the laryngoscopic evaluation to those without ILF (WILF).

**Objectives:** Determine the characteristics of LPR-symptomatic patients with ILF versus WILF.

**Methods:** In this retrospective study, we examined 160 medical charts from patients referred to the otolaryngology clinic at Galilee Medical Center for LPR evaluation 2016–2018. The reflux symptoms index (RSI), reflux finding score (RFS), and demographics of the patient were collected. All patients with a positive RSI score for LPR (RSI > 9) were included, and the profiles of patients with versus without ILF on laryngoscopy examination were compared.

**Results:** Of the 160 patients, 20 (12.5%) had ILF during laryngoscopy. Most had vocal cord findings such as leukoplakia (20%), polyps (15%), and nodules (20%). Hoarseness, throat clearing, swallowing difficulty, breathing difficulties, and total RSI score were significantly higher in patients with ILF.

**Conclusions:** Evaluation of LPR symptoms may provide otolaryngologists with a tool to identify patients with other findings on fiberoptic laryngoscopy. A laryngoscopic examination should be part of the examination of every patient with LPR to enable diagnosis of incidental findings.

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**KEY WORDS:** fiberoptic laryngoscopy, incidental laryngeal findings (ILF), laryngopharyngeal reflux (LPR), reflux finding score (RFS), reflux symptom index (RSI)

Laryngopharyngeal reflux (LPR) refers to the backflow of acidic stomach content into the larynx, pharynx, and upper aerodigestive tract [1]. It has been estimated that 4–10% of all ear, nose, and throat (ENT) outpatients are referred to due to symptoms possibly associated with LPR [2]. These symptoms are not pathognomonic to LPR and could be seen in other laryngeal disorders [3]. The most common laryngeal findings of LPR are subglottic edema, vocal fold and laryngeal edema, erythema, posterior commissure hypertrophy, and granulation tissue [4].

The 24-hour dual sensor pH probe, which monitors acidity in the larynx and the lower esophageal sphincter, has been the gold standard LPR diagnostic tool for many years. However, this method has many limitations, as it is invasive, uncomfortable, costly, and not readily available in all clinics [5]. Currently, diagnosing LPR based on patient history and physical examination is more common. This includes fiberoptic evaluation for findings associated with LPR. Belafsky et al. [4] proposed two tests to help diagnose LPR. This first is the Reflux Symptom Index (RSI), which is a validated 9-item self-reporting questionnaire aimed at detecting symptoms commonly associated with LPR, including hoarseness, throat clearing, excess throat mucus, difficulty swallowing, coughing after eating, breathing difficulties, annoying cough, lump (globus) sensation, and heartburn. In the Likert-type scale, the possible value for each item ranges from 0 to 5. We considered a RSI score greater than 13 was an indication of LPR [6]. The second test is the Reflux Finding Score (RFS), an 8-item scale designed to assess the severity of fiberoptic laryngoscopy findings related to LPR, including vocal fold and subglottic edema, erythema, ventricular obliteration, diffuse laryngeal edema, granuloma/granulation tissue, thick endolaryngeal

mucus, and posterior commissure hypertrophy. It ranges from 0 to 26, where 0 indicates that there are no abnormal findings and 26 indicates the worst score possible. Patients with an RFS > 7 are considered positive for LPR [4]. Both tests have been verified in several studies [7-9].

Another well-accepted method for LPR diagnosis is the response to empiric treatment, composed of behavioral changes, such as smoking cessation and dietary modifications, combined with drug therapy. Proton pump inhibitor acid suppression is the most widely used medication [1].

LPR has been associated with nasal obstructive symptoms, vocal fold granulomas, laryngospasm, Reinke's space edema, and vocal polyps [1,5,10,11]. Other manifestations such as asthma, sinusitis, otitis media, and laryngeal cancer have also been associated with LPR [12]. Therefore, a laryngoscopy examination as part of an evaluation of LPR could have added value in the early diagnosis of these associated incidental conditions.

In this study, we evaluated whether patients with incidental laryngeal findings (ILF) RSI and specific symptoms associated with LPR differed from patients without incidental laryngeal findings (WILF). The characteristics of patients with LPR symptoms and incidental findings in the laryngoscopy evaluation were compared with those suffering from LPR without ILF.

## PATIENTS AND METHODS

The study was conducted according to the STROBE reporting guidelines. Before conducting this study, the approval of the institutional review board of the Galilee Medical Center was obtained. This retrospective study of patients referred with a working diagnosis of LPR by otolaryngologists or primary care physicians to the Galilee Medical Center ENT clinic between 2016 and 2018. Patients with known laryngeal disease or lesions were excluded from the study. Demographic data from the patients was collected, including sex, age, medical history, and smoking status. All patients completed an RSI questionnaire. In this study, a validated Hebrew translation of

the RSI questionnaire was used [13]. Only patients with an RSI score > 9 were included in the study.

Subsequently, the patients underwent a laryngoscopy examination by physicians from the ENT department. The laryngoscopy videos were then evaluated by three board-certified fellowship-trained otolaryngologists, each with more than 10 years of experience (examiners). All examiners assigned an RFS score to each video and noted any other findings in the laryngoscopy video. The RFS score for each patient was the mean value of the scores assigned by the three examiners.

## DATA ANALYSIS

Statistical analyses were performed using IBM Statistical Package for the Social Sciences statistics software, version 25 (SPSS, IBM Corp, Armonk, NY, USA). Mean ranges and standard deviations for the continuous variables and frequencies were calculated. Welch's *t*-test (unequal variance *t*-test) was applied to find significant differences between groups in quantitative variables (RSI and RFS).

For the ILF group, different items of the RSI were compared using the Friedman test for multiple comparisons and the Wilcoxon sign test for each pair. The Bonferroni correction test was used to confirm the results. A *P*-value < 0.05 was considered significant for each test.

## RESULTS

The study was comprised of 160 patients who presented symptoms of LPR and RSI > 9, 20 in the ILF group and 140 in the WILF group. The demographic data of the patients are summarized in Table 1. The medical history and co-morbidities are presented in Figure 1. In the ILF and WILF groups, 29% and 18% of the patients, respectively, were smokers. No other significant differences were found between the groups. Gastroesophageal reflux disease was the predominant disease in both groups, followed by hypertension and other unrelated ENT diseases. A range of ILFs were found among the ILF patients, as shown in Table 2.

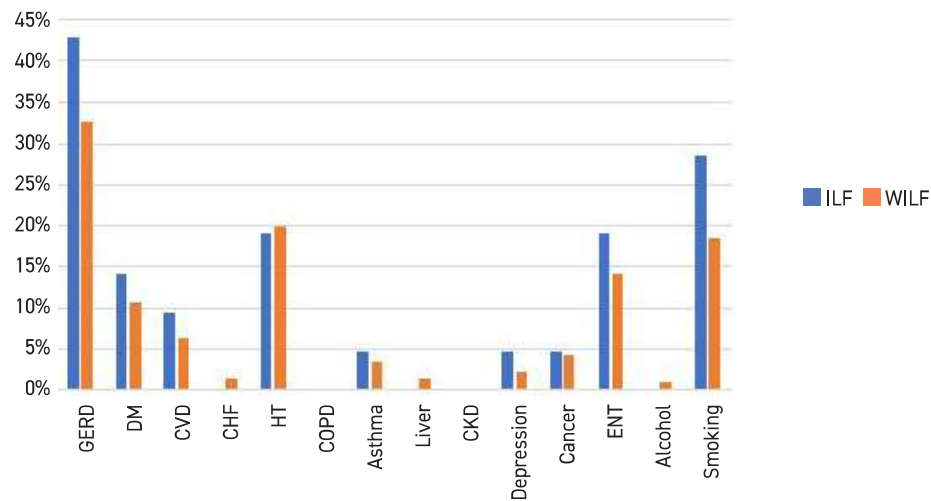
**Table 1.** Characteristics of the incidental laryngeal findings and without incidental laryngeal findings groups

	Incidental laryngeal findings (N=20)	Without incidental laryngeal findings (N=140)
Age, in years, mean (range)	43 (18–89)	48 (25–65)
Sex, Female (%)	13 (65)	83 (59.3)
RSI	26.81	20.38
RFS	4.91	4.89

RFS = reflux finding score, RSI = reflux symptoms index

Figure 1. Patient medical history and habits

CHF = chronic heart failure, CKD = chronic kidney disease, CVD = cardiovascular disease, DM = diabetes mellitus, ENT = ear, nose, throat, GERD = Gastroesophageal reflux disease, HT = hypertension, ILF = incidental laryngeal findings, WILF = without incidental laryngeal findings



The RSI items with the worst manifestation among patients with ILF were throat clearing (mean 4.19) and sensation of a lump in the throat (mean 4), which were assigned significantly higher scores than cough after eating or after lying down (mean 2.62,  $P$ -value < 0.01), troublesome cough (mean 2.24,  $P$ -value < 0.01), and heartburn (mean 2.48,  $P$ -value < 0.01). Statistically significant differences between cohorts in RSI scores were observed for hoarseness (mean 2.67,  $P$ -value < 0.05), throat clearing (mean 4.19,  $P$ -value < 0.01), difficulty swallowing (mean 2.7,  $P$ -value < 0.01), and breathing difficulties (mean 3.29,  $P$ -value < 0.05) [Figures 2A and 2B]. The total RSI score was also significantly different between cohorts (mean 26.81,  $P$ -value < 0.01). The mean RFS score was 4.91 and 4.89 for ILF and WILF patients, respectively.

Table 2. Laryngeal findings in the incidental laryngeal findings group

Findings	Number of patients (%)
VC leukoplakia	4 (20)
VC nodule	4 (20)
VC polyp	3 (15)
Epiglottitis/Reinke's edema	2 (10)
VC cyst	2 (10)
VC paresis	2 (10)
Laryngeal papillomatotic findings	2 (10)
Omega-shaped epiglottis	1 (5)
Oral thrush	1 (5)

VC = vocal cords

DISCUSSION

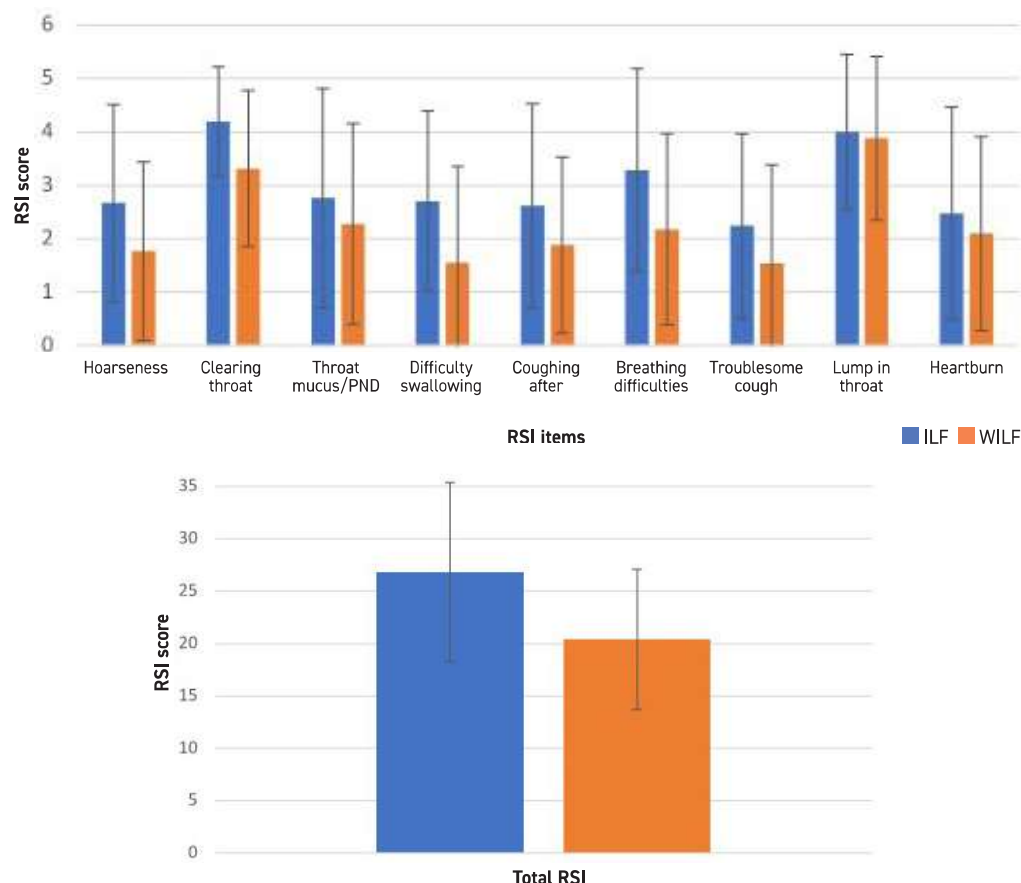
LPR symptoms are common complaints in the primary care setting, and patients are often referred to an ENT specialist. The symptoms are not pathognomonic to LPR and could be associated with other laryngeal disorders. In many cases, a laryngoscopy examination is not performed; rather, an empiric LPR treatment protocol is initiated, ignoring other related conditions, possibly leading to a missed diagnosis [14]. In a systematic review that included 42 studies that investigated the role of LPR in the development of benign vocal cord lesions, it was suggested that a mucosal injury caused by LPR could contribute to the development of benign vocal cord lesions such as nodules, polyps, or Reinke's edema [15].

The present study comprised 160 patients presenting with LPR symptoms with RSI > 9. None of these patients was known to have any other laryngeal disease, and they were referred for LPR evaluation. Twenty patients (12.5%) were found to have ILF on laryngoscopic examination. Most of the patients had vocal cord findings such as leukoplakia, polyps, and nodules, which required surgery. Rafii and colleagues [16] investigated the underlying laryngeal lesions in 21 patients referred by primary care physicians and otolaryngologists due to dysphonia and a working diagnosis of LPR that did not respond to LPR treatment. In our study, three raters evaluated videolaryngoscopy exams. Six patients (28%) were found to have benign laryngeal lesions and three patients (14%) presented with a neoplastic lesion,

**Figure 2.** RSI score in ILF versus WILF patients

**[A]** RSI items **[B]** Total RSI

ILF = incidental laryngeal findings, PND = post-nasal drip, WILF = without incidental laryngeal findings, RFS = reflux finding score, RSI = reflux symptoms index



compared to 14 patients (8%) who had benign lesions and four patients (2.5%) who had neoplastic lesions. This percentage difference could be explained because Rafii et al. included only dysphonic patients with a working diagnosis of LPR who did not respond to LPR treatment, while in the current study, all patients with a working diagnosis of LPR and who had not been treated with anti-acids during the 3 months before presentation were enrolled. Consequently, the results of the present study, which included 160 patients, could represent the percentage of underlying lesions in the overall group of patients suspected of having LPR and not only in the unresponsive and severe ones, as demonstrated by Rafii's group of 21 patients.

A comparison of RSI of patients with ILF versus WILF identified significantly higher scores for hoarseness, throat clearing, difficulty swallowing, breathing difficulties, and higher total RSI scores among patients with ILF. These findings are consistent with the results of two previous stud-

ies. In the first study, hoarseness, throat clearing, and globus sensation were observed in patients initially diagnosed with LPR and were found to have incidental laryngeal lesions [16]. Another study showed that patients with vocal cords lesions were most likely to present with hoarseness [17].

When comparing patients with vocal cord nodules, polyps, and Reinke's edema with a control group, Chung et al. [17] found that patients with Reinke's edema had a higher RSI score than control individuals. These findings are inconsistent with the present study, as the main lesions we found were vocal cord nodules, polyps, and leukoplakia. The primary risk factor for Reinke's edema is tobacco use [18]. In the current study, 29% of the patients in the ILF group were smokers. Had the percentage of smokers been higher, there could have been a higher prevalence of Reinke's edema lesions. Hoarseness was expected to be the leading symptom reported by patients with ILF, as most of the lesions were related to the vocal



cords. However, the most common concurrent symptoms were throat clearing (71%), excess mucus (62%), globus (38%), and cough (33%) [16].

RSI subscale analysis found clearing throat and sensation of a lump in the throat to be the most severe symptoms. This finding may have been due to the limitations of eligibility for patients with RSI > 9, which may have increased the prevalence of patients who presented with other symptoms caused by LPR. In general, LPR is not the sole cause of vocal cord lesions, such as nodules and polyps, which can result from trauma and mechanical stress [19]. Such patients are less likely to have LPR symptoms.

No significant differences were found in the RFS score between the two groups. Both groups scored on average RFS < 7, which means that they are not considered to have LPR, which contrasts with the finding that all patients exceeded the RSI threshold for the diagnosis of LPR. Although the correlation between RSI and RFS was not examined in the present study, other studies demonstrated significantly high correlations between the two scores [7-9]. However, a study based on data similar to those we collected found poor inter-rater reliability in determining total RFS and concluded that further studies are needed to determine whether LPR can be diagnosed using RFS [20].

#### STUDY LIMITATIONS

In this prospective study, some data were unavailable. Furthermore, the raters examined the recorded videos without any time limitation, unlike in a real-life situation in a clinic.

#### CONCLUSIONS

We characterized an LPR symptoms profile in patients with ILF. Some LPR symptoms were predominant in the ILF group compared to patients without incidental findings. To the best of our knowledge, this cohort study is the first conducted on incidental findings and different RSI items. Further studies are needed in larger groups of patients to support these results. However, based on the results of this study, primary care physicians and otolaryngologists should routinely refer patients suspected of having LPR for a fiberoptic laryngoscopy, as incidental findings are frequent.

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