



Association of Stress and Laryngopharyngeal Reflux with Vocal Fold Polyps

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Abstract

Aim: Stress and laryngopharyngeal reflux can cause many laryngeal pathologies. In this study, we aimed to investigate the role of stress and laryngopharyngeal reflux (LPR) in the development of vocal fold polyps.

Methods: Forty-five patients who were scheduled for surgery because of vocal fold polyps between October 2021 and May 2022 were included in the study. A control group was formed from 45 patients who applied to the otolaryngology outpatient clinic with the complaint of hoarseness lasting more than 3 weeks and had no vocal cord lesion in their 70-degree rigid endoscopic examination. Participants were asked to complete the reflux symptom index and depression anxiety stress scale (DASS) questionnaires. Reflux finding score (RFS) and grade, roughness, pallor, asthenia, strain, instability (GRBASI) voice analyses were conducted by two otolaryngologists familiar with both scales.

Results: There was no significant difference between the speech characteristics of the patient groups. Reflux symptom index, RFS, and GRBASI scores were significantly higher in the group with vocal fold polyps ($p=0.000$, $p=0.000$, and $p=0.009$, respectively). Stress scores for DASS were significantly higher in the control group ($p=0.025$). There was no significant difference between the two groups in terms of depression and anxiety scores.

Conclusion: Laryngopharyngeal reflux is more prevalent in patients with vocal fold polyps. This may be related to mucosal or submucosal damage from LPR. We also observed that increased stress can cause hoarseness without vocal fold lesions.

Keywords: Voice, vocal cords, laryngopharyngeal reflux, anxiety

Introduction

Hoarseness is defined as an altered voice quality that impairs communication and has a prevalence of approximately 1% among patients (1). The etiology mainly includes laryngitis, functional dysphonia, benign or malignant vocal fold lesions, vocal cord paralysis, aging, and psychogenic factors (2). The duration of the complaint should be carefully questioned in the assessment of hoarseness. For example, hoarseness lasts less than 3 weeks in respiratory tract infections, and psychogenic factors should be considered in cases of sudden loss of voice (3).

Providing high-resolution image quality, rigid transoral laryngoscopy is a favorable way to screen and examine vocal fold mucosal lesions (4). If dysphonia does not resolve within 3 weeks or if a serious underlying cause is suspected, clinicians should perform diagnostic

laryngoscopy at any time and advocate voice therapy for appropriate indications (5). Surgery is preferred in patients with suspected malignancy, benign vocal fold lesions (BVFL) that do not respond to conservative management, or glottic insufficiency. In addition, botulinum toxin injection may be a therapeutic option for patients with spasmodic dysphonia and laryngeal dystonia (6).

Vocal fold polyp (VFP) is a proliferative disease that occurs in the superficial layer of the vocal fold's lamina propria and is a benign lesion. Microsurgery in treatment is a method that improves voice quality and has a low recurrence rate (7). However, the risks associated with surgery and anesthesia lead some patients to opt for voice therapy. Although voice therapy has certain therapeutic effects on VFPs, the success of treatment can be affected by many factors, such as the length of therapy and patient education (8).

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In recent years, studies investigating the relationship between benign vocal cord lesions such as polyps, nodules, Reinke's edema, and laryngopharyngeal reflux (LPR) have become popular. Although there are many studies supporting this association, the epidemiological evidence still remains unclear (9,10). Furthermore, some studies have reported that emotionally maladjusted conditions, including depression and anxiety combined with LPR, could exacerbate the symptoms of BVFL in adults (11,12). In line with this information, we investigated the role of stress and LPR in the development of VFPs.

Methods

Compliance with Ethical Standards

The study was approved by the Institutional Review Board of University of Health Sciences Turkey, Istanbul Training and Research Hospital, (approval no: 2766, date: 05.03.2021). All procedures were performed in accordance with the ethical standards set forth in the World Medical Association Declaration of Helsinki (Scotland 2000). Informed consent forms were obtained from all patients.

Patients and the Study Design

Forty-five patients who were scheduled for surgery because of VFPs between October 2021 and May 2022 were included in the study. A control group was formed from 45 patients who applied to the otolaryngology outpatient clinic with the complaint of hoarseness lasting

more than 3 weeks and had no vocal cord lesion in their 70-degree rigid endoscopic examination. The diagnosis was confirmed by videolaryngostroboscopy (VLS) in all patients, and the examinations were recorded. The age distribution between the two groups was matched. Attention was also paid to gender matching between both groups, as women with voice disorders were more likely to report stress, anxiety, and depression.

The following groups were excluded from the study: a) causes of benign vocal cord lesions other than VFPs; b) lesions suggestive of malignant vocal fold tumors such as leukoplakia; c) dysphonic patients with a history of psychiatric medication or suspected psychological-based voice pathology; d) patients diagnosed with dysphonia due to systemic diseases; e) patients with neurological pathologies such as vocal cord paralysis or paresis; and e) patients diagnosed or treated for gastroesophageal reflux (Figure 1).

All patients included in the study were asked to complete the reflux symptom index (RSI) and depression anxiety stress scale (DASS) questionnaires. RFS and grade, roughness, pallor, asthenia, strain, instability (GRBASI) voice analyses were conducted by two otolaryngologists familiar with both scales. The two groups were compared with their questionnaire scores and examination findings (Figure 2). The treatment of patients in the group with VFPs was surgically planned. RSI and RFS were used to evaluate LPR, and reflux treatment was added to patients with high RFS and RSI scores.

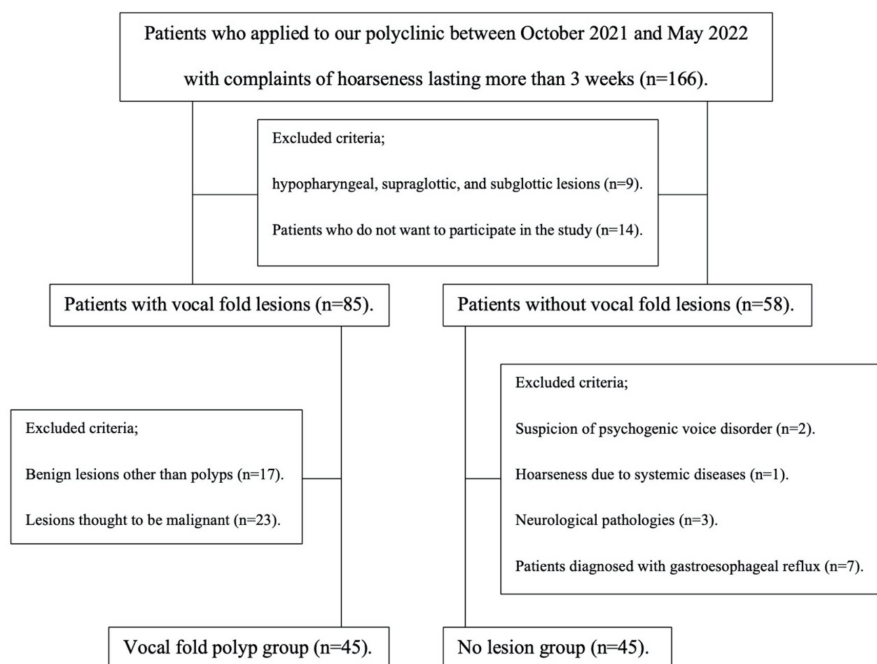


Figure 1. Flowchart of the study

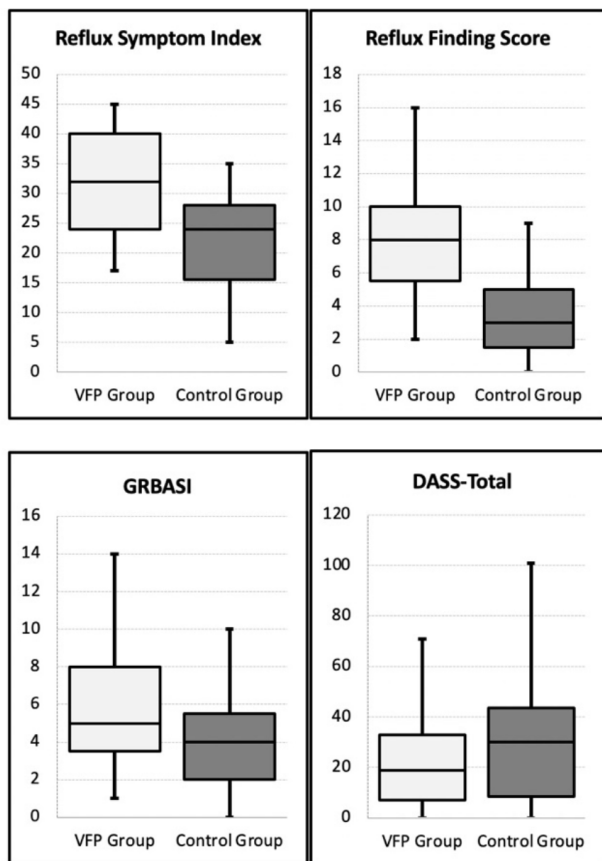


Figure 2. Comparison of the scores of both groups
VFP: Vocal fold polyp, GRBASI: Grade, roughness, pallor, asthenia, strain, instability, DASS: Depression anxiety stress scale

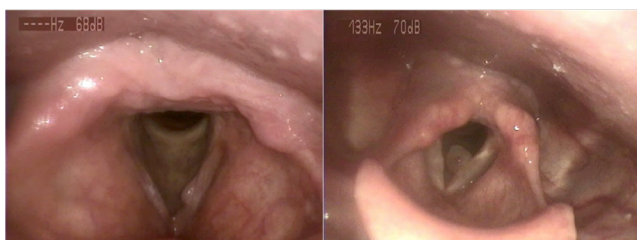


Figure 3. Videolaryngostroboscopic examination of patients with vocal fold polyp

Videolaryngostroboscopy

Videolaryngostroboscopic was examined by two otolaryngologists via a rigid endoscope using the Xion stroboscopy system (Xion EndoSTROB, Berlin, Germany) (Figure 3). The records were based on the visualization of the participants' comfortable loudness and modal phonation of the/ee/vowel sound on VLS. The standard evaluation forms of the reflux finding score (RFS) and voice quality scale GRBASI were scored and filled out during enrollment.

Reflux Finding Score

This scale provides an assessment of the physical manifestations of reflux in videolaryngostroboscopy. Scores were assessed and rated by a single otolaryngologist. Subglottic edema, ventricular obliteration, erythema/hyperemia, vocal fold edema, diffuse laryngeal edema, posterior commissure hypertrophy, granuloma/granulation tissue, and thick endolaryngeal mucus were scored using the standard RFS evaluation form. Based on previous confirmed studies, an RFS of 7 was considered positive (13).

Grade, Roughness, Pallor, Asthenia, Strain, Instability

The GRBASI scale, which evaluates the grade of dysphonia, roughness, shortness of breath, asthenia, strain, and instability, is used by clinicians as a vocal assessment tool (14). In this study, auditory-perceptual voice analyses were conducted by an otolaryngologist blind to diagnoses and a speech therapist familiar with both scales using the sustained vowel and reading tasks of the sentences. Each evaluation on the scale was evaluated over 18 points out of 3 as normal (0 points), mild (1 point), moderate (2 points), and severe (3 points).

Reflux Symptom Index

We used the Turkish version of the RSI developed and validated by Akbulut et al. (15). Reflux symptom index is a nine-item questionnaire created to scale the severity of reflux symptoms. Each item was scaled from 0 to 5, with 0 representing no problem and 5 representing a severe problem. Based on the validated Turkish version, an RSI of 12.5 was considered positive for reflux.

Depression Anxiety Stress Scale-42

We used the DASS-42 item validated by Hekimoglu et al. (16), which measures depression, anxiety, and stress moods in the last week. For each of the 3 subscales, 14 responses were evaluated between 0 (did not apply) and 3 (applied most of the time) points. Responses were evaluated to form each subscale and the total DASS-42 score.

Statistical Analysis

The IBM SPSS 28.0 package program (SPSS Inc.; Chicago, IL, USA) was used for the analysis. In the descriptive statistics of the data, the mean, standard deviation, and median values were used. The distribution of variables was measured using the Kolmogorov-Smirnov test and the Mann-Whitney U test in the analysis of quantitative independent data. The chi-square test was used in the analysis of qualitative independent data, and the Fischer test was used when the chi-square test conditions were not met. Spearman correlation analysis was used in the correlation analysis. Statistical significance was granted at a p level ≤ 0.05 .

Results

The mean age of the patients included in our study was 41.5 years (range from 17 to 73). The mean age of the VFP group was 43.0±11.9 years, and that of the control group was 39.1±14.3. Given the likely influence of gender on the findings, there were equivalent numbers of women in both groups that permit a fair and valid comparison. Of the 90 patients, 45 were smokers. The demographic status and speech characteristics of the patients are given in Table 1. As stated in this table, no significant difference was found between the VFP and control groups in terms of age, gender, smoking, talkativeness, and speaking loudly.

The reflux symptom index, RFS, and GRBASI score were found to be significantly higher in the group with VFPs (p=0.000, p=0.000, and p=0.009, respectively) (Table 2). When the VFPs and control groups were evaluated in terms of DASS scores, the stress scores were significantly higher in the control group (p=0.025). There was no significant difference between the groups in terms of depression, anxiety, and total DASS scores (Table 2). A significant (p<0.05) correlation was observed between the reflux symptom index, RFS, GRBASI score, and DASS scores (Table 3).

Table 1. The demographic status and speech characteristics of the patients

		VFP group (n=45)		No lesion group (n=45)		p-value
		Mean ± SD / n%	Median	Mean ± SD / n%	Median	
Age		43.0±11.9	44.0	39.1±14.3	37.0	0.111 ^m
Gender	Female	21±46.7%		32±71.1%		0.018 ^{x2}
	Male	24±53.3%		13±28.9%		
Smoking	No	25±55.6%		20±44.4%		0.292 ^{x2}
	Yes	20±44.4%		25±55.6%		
Talkativeness	Average talker	1±2.2%		3±6.7%		0.421 ^{x2}
	Talkative	30±66.7%		32±71.1%		
	Extremely talkative	14±31.1%		10±22.2%		
Speaking loudly	Rarely	20±44.4%		21±46.7%		0.495 ^{x2}
	Sometimes	20±44.4%		22±48.9%		
	Often	5±11.1%		2±4.4%		

^m: Mann-Whitney U test, ^{x2}: Chi-square test (Fisher's exact test), VFP: Vocal fold polyps, SD: Standard deviation

Table 2. Comparison of the scores of both groups

		VFP group (n=45)		No lesion group (n=45)		p-value
		Mean ± SD / n%	Median	Mean ± SD / n%	Median	
Reflux symptom index		31.9±8.7	32.0	22.0±9.0	24.0	0.000 ^m
Reflux finding score		7.7±3.1	8.0	3.2±2.6	3.0	0.000 ^m
GRBASI		5.7±3.1	5.0	4.0±2.6	4.0	0.009 ^m
DAS scales						
Depression		4.0±5.7	2.0	4.4±7.0	1.0	0.511 ^m
Depression	Normal	42±93.3%		38±84.4%		0.180 ^{x2}
	Mild	1±2.2%		2±4.4%		
	Moderate	0±0.0%		3±6.7%		
	Severe	1±2.2%		1±2.2%		
	Extremely severe	1±2.2%		1±2.2%		
Anxiety		8.7±6.3	9.0	9.3±7.6	8.0	0.945 ^m
Anxiety	Normal	20±44.4%		21±46.7%		0.832 ^{x2}
	Mild	5±11.1%		5±11.1%		
	Moderate	14±31.1%		9±20.0%		
	Severe	2±4.4%		5±11.1%		
	Extremely severe	4±8.9%		5±11.1%		

Table 2. Continued

		VFP group (n=45)		No lesion group (n=45)		p
		Mean ± SD / n%	Median	Mean ± SD / n%	Median	
Stress		8.9±7.6	8.0	15.1±11.8	16.0	0.025 ^m
Stress	Normal	34±75.6%		20±44.4%		0.003 ^{x2}
	Mild	4±8.9%		8±17.8%		
	Moderate	6±13.3%		7±15.6%		
	Severe	1±2.2%		7±15.6%		
	Extremely severe	0±0.0%		3±6.7%		
DASS-total		21.4±16.3	19.0	28.8±23.0	30.0	0.159 ^m

^m: Mann-Whitney U test, ^{x2}: Chi-square test (Fisher's exact test), VFP: Vocal fold polyps, SD: Standard deviation

Table 3. Correlation of RSI, RFS, GRBASI with DASS

	Reflux symptom index		Reflux finding score		GRBASI	
	r	p	r	p	r	p
DAS scales						
Depression	0.318	0.002	0.236	0.025	0.299	0.004
Anxiety	0.493	0.000	0.284	0.007	0.379	0.000
Stress	0.296	0.005	0.190	0.073	0.273	0.009
DASS-total	0.413	0.000	0.247	0.019	0.374	0.000

Spearman Correlation Coefficient, DASS: Depression, anxiety, stress scales, RSI: Reflux symptom index, RFI: Reflux finding score, GRBASI: Grade, roughness, pallor, asthenia, strain, instability

Discussion

Hoarseness can be caused by many diseases, from simple upper respiratory tract infections to malignancies. Hoarseness that lasts longer than 3 weeks should be evaluated by an otolaryngologist because it may be a sign of cancer. The most common benign lesions were polyps, nodules, and Reinke's edema. In an incidence study by Jung et al. (17), it was revealed that the incidence and prevalence increased over the years and that BVFL was more common in women. We did not observe any difference in terms of age or gender between the groups included in our study.

Our intensive observation of LPR findings in patients who presented with hoarseness and in whom we could not detect any pathology during endoscopic laryngeal examination led us to this study. LPR can cause many symptoms due to caustic mucosal damage to gastric contents in the larynx and pharynx (13). Some of these symptoms are hoarseness, throat clearing, post-nasal drip, difficulty breathing, troublesome cough, heartburn, chest pain, or stomach acid coming up (18). 24-hour ambulatory pH monitoring is accepted as the gold standard for diagnosis. In their 2023 meta-analysis study, Ren et al. (19) concluded that LPR diagnosed by pharyngeal pH monitoring is associated with the formation of BVFLs. However, many clinical studies have shown that

the diagnosis of LPR can be confirmed by RSI and RFS assessments (13,18,20,21). We also used RSI and RFS for LPR. The most common LPR findings in patients with vocal cord polyps were posterior commissure hypertrophy and hyperemia/edema in the arytenoid mucosa.

In the literature review of Lechien et al. (22), it was reported that the frequency of LPR was high in the patient group with BVFL and that caustic mucosal vocal fold injury caused by LPR may cause nodule, polyp, or Reinke's edema formation. Similarly, Chung et al. (23) showed that LPR may play a role in the etiology of Reinke's edema and vocal cord polyps. In addition, vocal abuse, smoking, alcohol intake, or LPR may be other etiological factors in the development of BVFL. Apart from these studies revealing the relationship between LPR and BVFL, there are also studies emphasizing that the diagnosis of reflux may be overdiagnosed and other causes of hoarseness should be considered when empirical proton pump inhibitor therapy is unsuccessful (24-26). We believe that LPR is a disease that can lead to overdiagnosis. It should not be forgotten that starting treatment by diagnosing only anamnesis, especially without endoscopic evaluation, may lead to delays in the diagnosis of laryngeal diseases. Carroll (26) stated that VLS should be applied to all patients with dysphonic complaints and that manometry or pH testing should be recommended if no pathological

condition beyond the classical LPR findings is observed. We also evaluated all our hoarseness patients with VLS. In this study, we found high RSI and RFS scores in patients with vocal cord polyps and recommended proton pump inhibitor therapy to patients without polyps but with high RSI and RFS scores.

Grade, roughness, pallor, asthenia, strain, instability is one of the most traditional approaches for describing vocal quality and is used for the auditory-perceptual evaluation of voice (27). In our study, auditory-perceptual voice analyses were conducted by two experienced otolaryngologists. Regardless of the etiology, GRBASI is widely used in all voice disorders. Nemr et al. (14) evaluated the GRBASI scale as an objective test focusing on the glottic level compared with other voice analysis scales. We compared patients with VFPs and patients without lesions using the GRBASI scale and found that patients with VFP had lower voice quality.

VHI-30 is a tool for measuring patients' perceptions of voice disorders. It is self-administered and can be scored quickly during the assessment. Evaluation is made using three subscales: Functional, physical, and emotional. Each index is evaluated over 30 questions, between 0 and 4 points, and a maximum of 120 points. Since the early 2000s, VHI has provided a concise tool for the initial and follow-up assessment of patients with any voice disorder (28). Townes et al. (29) demonstrated that VHI was significantly associated with the presence of BVFL in pediatric patients and could be useful in predicting the etiology of dysphonia. In our opinion, unlike this study, VHI cannot be expected to be specific to any voice disorder.

The relationship between depression, anxiety, stress, and voice disorders has been evaluated in many studies in the literature, and a significant relationship has been found in patients with and without BVFL (30,31). In a study by Dietrich et al. (30), it was observed that patients with hoarseness had similar profiles in depression, anxiety, and stress assessments with or without vocal cord lesions. Considering the high LPR scores in our lesion-free control group and the publications indicating that depression, anxiety, and stress are associated with LPR, we added the DASS questionnaire to our study (32,33). Stress scores were significantly higher in the group without lesions. However, there was no significant difference between the groups in the depression and anxiety scores. Considering this information, psychiatric evaluation may be considered in addition to reflux treatments in selected hoarseness patient groups.

Study Limitations

The present study has several limitations. First, further studies with larger case numbers are required. Second, as previously discussed, 24-hour pH monitoring is the gold

standard for diagnosing reflux. However, RSI and RFS were used in our study. Third, the evaluation of patients with acoustic analysis and long-term results may increase the importance of the study. Despite these limitations, our study is the first to combine RSI and DASS questionnaires with RFS and GRBASI analyses to investigate the relationship between LPR and VFPs.

Conclusion

Laryngopharyngeal reflux is more prevalent in patients with VFPs. This may be related to mucosal or submucosal damage from LPR. Although we prioritize surgery in our clinical approach to VFPs, the combined treatment of antireflux and voice therapy may be an alternative for small VFPs. We also observed that increased stress can cause hoarseness without vocal fold lesions. Psychotherapy can be added to patient education as a treatment for these patients.

Ethics

Ethics Committee Approval: The study was approved by the Institutional Review Board of University of Health Sciences Turkey, Istanbul Training and Research Hospital, (approval no: 2766, date: 05.03.2021).

Informed Consent: Informed consent forms were obtained from all patients.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: O.O., E.C., Concept: O.O., T.K., O.Y., Design: O.O., T.K., O.Y., Data Collection or Processing: O.O., E.C., Analysis or Interpretation: O.O., T.K., O.Y., Literature Search: O.O., E.C., Writing: O.O., O.Y.

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